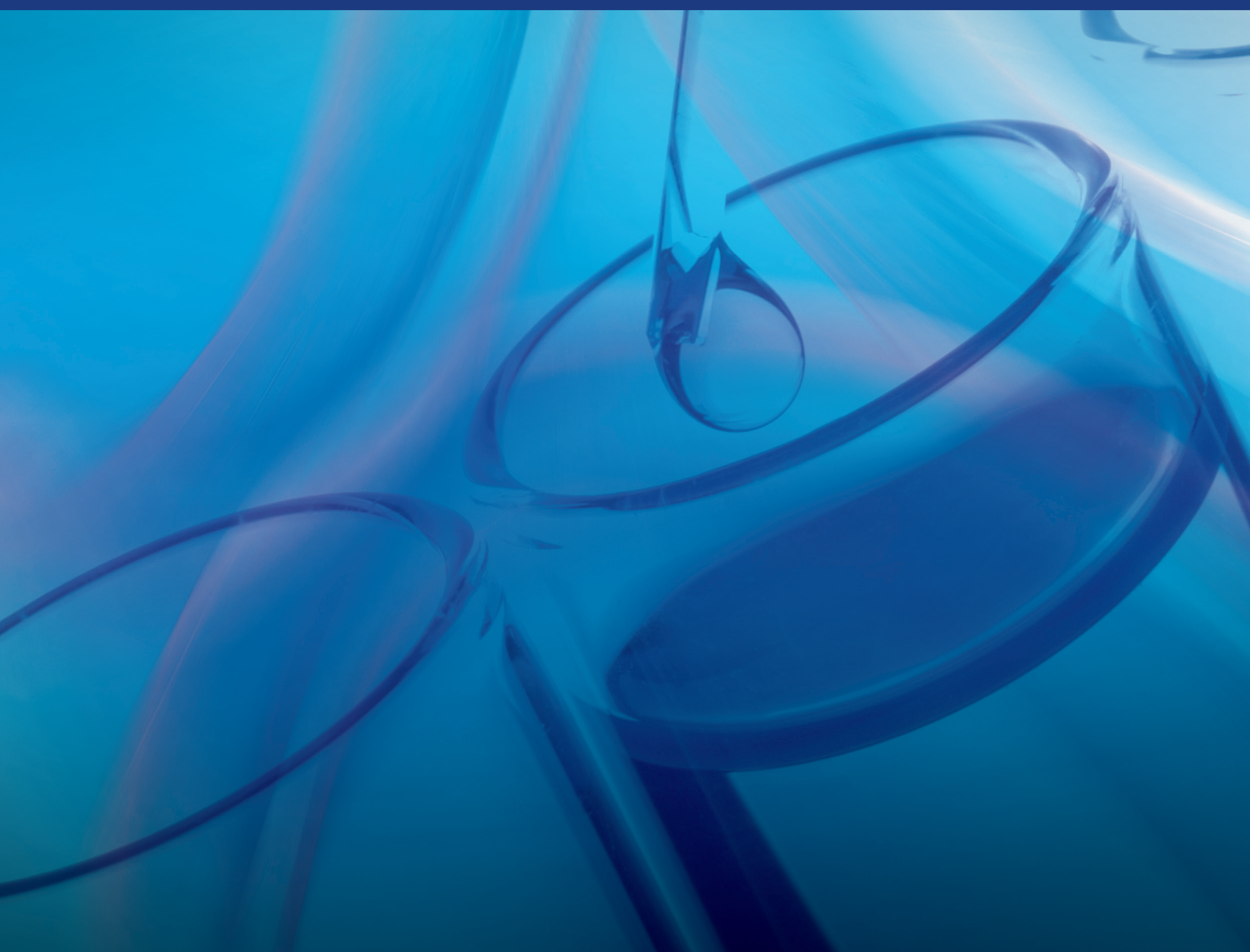
Advances in Urology

Urethral Stricture Disease: Challenges and Ongoing Controversies

Guest Editors: Miroslav L. Djordjevic, Francisco E. Martins, Vladimir Kojovic, and Dmitry Kurbatov



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Editorial Board

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Editorial

Urethral Stricture Disease: Challenges and Ongoing Controversies

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Management of urethral stricture disease presents constant challenge for all reconstructive urologists. Urethral stricture disease is generally defined as stenoses that are typically long, involving broad areas of varying spongiofibrosis, and result from inflammation and/or infection, rather than trauma. Although the management of urethral strictures may be complex and challenging, very often they are treated by health care personnel without the necessary and proper training and knowledge of the current, modern, validated techniques and procedures. Notable changes in surgical approach have been adopted worldwide, resulting in significant improvement of successful outcomes and simultaneously decreasing the complication rate. Nowadays, most urethral strictures can be reconstructed in a one-stage procedure, leaving some complex cases for a less convenient, but safer, two-stage repair strategy. The exciting and enjoyable "nature" of reconstructive surgery, in general, and urethral reconstruction, in particular, is the unexpected and unpredictable nature of the stricture and, consequently, the need for the creative combination of different techniques and strategies, often involving tissue transfer procedures, either as grafts or as flaps, for achieving a successful outcome. This special issue contains a number of articles with description of different aspects, presentations, and treatments of urethral stricture disease with the aim to make further improvement of understanding and managing this severe surgical condition.

Multi-institutional review article from Portugal, India, and USA presents modality of challenging treatment of long-segment and panurethral stricture disease. Francisco E. Martins and colleagues evaluated etiology, pathogenesis, and diagnostic work-up and, finally, presented different surgical options for treatment, together with outcomes and complications. They concluded that one-stage repair with buccal mucosa grafts presents an excellent option in the treatment of long urethral stricture. However, for obliterative disease, two-stage urethroplasty offers a viable alternative.

J. Gelman and E. S. Wisenbaugh presented a review article about management of patients who suffer pelvic fracture urethral injuries which usually develop into obliterative strictures with distraction defect. They comprehensively evaluated initial management, preoperative planning, and techniques for posterior urethral stricture disease. The authors emphasize the importance of adequate vascularization of urethra for successful repair. They believe that possible future modification of operative technique could be a bulbar artery sparing surgery during posterior urethral reconstruction. Results from referral centers confirm that when open repair fails, excision and primary anastomosis still remains the procedure of choice and offers a very high success rate. In another article entitled "The Use of Flaps and Grafts in the Treatment of Urethral Stricture Disease," the same authors described the use of versatile flaps and grafts in the various clinical presentations of anterior urethral stricture disease. Selecting the appropriate technique for each patient is highly individualized and dependent on stricture characteristics. However, the proper selection of tissue transfer technique is paramount to success. The authors provided a logical, easily comprehensible approach to the appropriate selection of grafts and flaps in urethral reconstruction, followed by practical clinical guidelines.

Another article, trying to give answers when to choose dorsal, ventral, or lateral onlay approach for buccal mucosa graft urethral reconstruction, is presented by K. Venkatesan and colleagues. The authors concluded that comparative studies are limited and choice of techniques is typically determined on location and length of stricture and surgeon preference.

The article titled "Bipolar Transurethral Incision of Bladder Neck Stenoses with Mitomycin C Injection," written by T. D. Lyon and colleagues from Pittsburgh, presented efficacy of bipolar transurethral incision with mitomycin C injection on thirteen patients who had refractory bladder neck stenosis. Overall success was achieved in 77% (10/13) of patients. Bipolar transurethral incision with mitomycin C injection was comparable in efficacy to previously reported techniques and did not result in any serious adverse events.

Urethral stricture disease is an underrecognized and poorly reported complication after radiation therapy, and that can cause severe morbidity for cancer survivors. Radiated urethral tissue in particular poses a great challenge for the reconstructive urologist. I. Khourdaji and colleagues provided a comprehensive discussion of etiology, incidence, and available treatment options for urethral stricture disease following pelvic radiation in the article titled "Treatment of Urethral Strictures from Irradiation and Other Nonsurgical Forms of Pelvic Cancer Treatment."

H. Okafor and D. Nikolavsky examined the impact of short-stay urethroplasty on health-related quality of life and patient's perception of timing of discharge. Over a 2-year period, a validated health-related quality-of-life questionnaire, EuroQol (EQ-5D), and additional question assessing timing of discharge were administered to all patients after urethroplasty. Postoperatively, patients were offered to be sent home immediately or to stay overnight. In this research article, the authors concluded that the majority of patients discharged soon after their procedure felt that discharge timing was appropriate and their health-related quality of life was only minimally affected.

A clinical study, published by W. Al Taweel and R. Seyam, has a goal to determine the long-term stricture-free rate after visual internal urethrotomy following initial and follow-up urethrotomies. During a period of eight years, 301 patients underwent visual internal urethrotomy. The overall stricture-free rate at the 36-month follow-up was 8.3% with a median time to recurrence of 10 months. The authors confirmed that visual internal urethrotomy for adult male urethral stricture has poor long-term results without significant difference in the stricture-free rate between single and multiple procedures.

In a multicentric clinical study that has been conducted in Italy and two centers from Belgium, M. Beysens and colleagues evaluated alterations in sexual function and genital sensitivity after anastomotic repair and free graft urethroplasty for bulbar urethral strictures. The patients who underwent anastomotic repair or free graft urethroplasty were prospectively evaluated before urethroplasty and 6 weeks and 6 months after urethroplasty. Evaluation included standardized questionnaires as IPSS, IIIEF-5, and Ejaculation/Orgasm Score and questions on genital sensitivity. The authors concluded that anastomotic repair is associated with a transient decline in erectile and ejaculatory function, and that was not observed with free graft urethroplasty. Bulbar anastomotic repair and free graft urethroplasty are likely to alter genital sensitivity. However, it should be noted that the authors are highly experienced and expert urologists, and results from any surgery performed at center of excellence may not be generalizable.

Finally, the management of urethral stricture disease is continually evolving. Although numerous strategies are available, there is still no single optimum solution suitable for all conditions. The clinical selection of stricture recurrence prevention techniques should be carefully tailored to every individual patient. Last but not least, reconstructive urologist must be familiar with a variety of these techniques, to ensure the use of the best one, as dictated by situation.

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Review Article

Sexual (Dys)function after Urethroplasty

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There is a paucity of published literature on the andrological consequences of urethral repair. Until recently authors have focused mainly on technical aspects and objective results. Reported outcomes of urethral reconstruction surgery have traditionally focused only on urodynamic parameters such as flow rates. Patient reported outcome measures have largely been neglected and there is a scarcity of well conducted systematic studies on the subject. For these reasons whether the different components of sexual life are more or less affected by different types of urethral reconstruction remains largely unknown. In an attempt to clarify the available scientific evidence, the authors make a critical review of available literature, systematizing it by sexual domain and study type. Brief pathophysiological correlations are discussed.

1. Introduction

Urethral stenosis, although relatively uncommon in the universe of urologic diseases, is by no means a rare condition. It accounts for about 52% of urethral and 1.8% of urologic pathology, respectively, and presents an estimated prevalence of 0.6% [1, 2]. Relatively young, active individuals are mostly affected. Its association with an unequivocal negative impact on the quality of life, whether resulting from the disease itself and its complications or whether consequence of the treatment(s) employed, is well established.

At present, there is no doubt that reconstructive surgery in the form of different types of urethroplasty represents the "gold standard" in the treatment of these patients. Urethroplasty is associated with reproductively high success rates, when properly employed. There is enough data in the literature regarding the results obtained with several techniques, anastomotic or substitution. When objective variables such as flow rates are considered, several authors describe success rates that exceed in many cases 80% whether for anterior urethra, bulbar [3–5] or penile [6–8], or whether for posterior urethra [9–11].

These data reflect however only one aspect of results, as patients carry out a substantially different perception of success than physicians, not only taking into account flow rates and radiological or endoscopic data. It is well known that there is a significant mismatch between what is considered a urethral reconstruction failure/success between treatment physicians and patients [12–14]. Aspects such as aesthetics or those related to sexual function are obviously important from the perspective of patients and often overlooked in the literature. If we do a simple exercise as, for example, an electronic search using the most widespread scientific literature database, PubMed, this disparity becomes obvious. If researches using terms like "urethroplasty and results" provide thousands of references, terms such as "urethral stenosis" or "urethroplasty" and "erectile dysfunction" or "impotence" result in only a few dozen scientific papers. Moreover, many books that specifically address urethral reconstruction almost exclusively focus on anatomical or technical aspects and there is a virtual absence of information about the andrological aspects of urethroplasty.

Although in recent years there has been a growing interest in relation to urethral stricture's andrologic implications, the relationship between urethroplasty and erectile dysfunction, for example, remains controversial up to the present day. The existence of few specific studies, heterogeneous study populations, differing methodologies, and diversity of procedures analyzed makes it very difficult to provide definitive answers.

Pathophysiology of Sexual Dysfunction. Surgical approaches involving the external genitalia have an unmistakable noxious potential in several domains of sexual function, aesthetic and dysmorphic changes.

Consequences in aesthetics and change of body image, mostly related to the distal urethroplasties, have obvious potential impact in terms of self-esteem and possibly sexual behavior. Although of subjective nature, these aspects are particularly noticeable in multioperated hypospadias patients, a group of patients of increasing importance in percentage terms that pose a particularly difficult approach.

Concerning erectile and ejaculatory dysfunction, potentially injured structures in the course of urethroplasty include several arterial structures, nerve branches (autonomic and/or somatic), and eventually myogenic components.

There is a recognized potential for injury of branches of the Common Penile Artery, essential in the hemodynamics of erection in posterior urethroplasties, and of more distal vessels, of smaller and questionable practical importance, in anterior urethroplasties.

Equally important are neurogenic autonomic lesions due to the proximity of the neurovascular bundles to the membranous urethra, potentially damaged in instrumentation of the posterior urethra [15, 16]. Somatic neurogenic components, either sensory or motor, involving the dorsal penile or perineal nerve and its branches, are also at risk, particularly during anterior urethroplasties [17–19].

Of potential functional importance, though debatable and still practically in the field of scientific curiosity, are the neuronal connections identified between autonomic and somatic pelvic, perineal, and even genital nerve terminals, making the latter capable of nitrergic activity. Authors like Yucel and Baskin [20] and Alsaid et al. [21] using immunohistochemistry-based studies in fetuses unequivocally demonstrate connections between the neurovascular bundles from the pelvic plexus, nitrergic, and components of the somatic nervous system (branches of the pudendal nerve such as the dorsal nerve of the penis and perineal nerve), giving them the capacity to release erectogenic mediators.

Finally, section and aggressive mobilization or denervation of the bulbospongiosus muscle to expose the bulbar urethra may result in more or less subtle changes in ejaculation dynamics, since the rhythmic contractions of the muscle during the expulsion phase are fundamental in seminal fluid expulsion [22–24].

2. Materials and Methods

A systematic review of several databases including PubMed, Cochrane Library, Embase, and Google Scholar was conducted. Systematic searches of these databases used terms as “urethroplasty,” “urethral reconstruction,” “urethral anastomosis,” “urethral stricture,” “urethral stenosis,” and “urethral obstruction,” and terms such as “erectile dysfunction,” “impotence,” “sexual dysfunction,” “ejaculatory dysfunction,” and “orgasmic dysfunction.” The search strategy used both keywords and MeSH terms and was limited to human studies.

The purpose of this study was to review the existing literature about the impact of urethroplasty in all domains of sexual function and to analyze it.

3. Results and Discussion

3.1. Body Image/Self-Esteem. Literature is absolutely lacking in terms of evaluation of the aesthetic consequences of urethroplasties performed in adulthood for urethral strictures. We can only infer conclusions based on findings from literature in the context of hypospadiology, a study population with necessarily different and very particular characteristics.

Despite all the limitations pointed out, there are a few studies that looked specifically at the cosmetic aspect of the reconstruction of the penile urethra in this context that allow us at least some critical reflections.

Authors as Bubanj et al. [25] used a postal questionnaire including questions about genitosexual functioning and sexual behavior in a comparative study of 37 patients submitted to urethroplasty for hypospadias repair 2–15 years earlier (mean age 27.8 ± 6.2 years/average number of surgeries 3.81 ± 3.37) and a group of 39 normal men (mean age 25.5 ± 5.3 years). No significant differences were found between the groups with regard to inhibition of search for sexual contacts or sexual relationship patterns. Participants in both groups were mostly satisfied with their body image (83,78% of patients with hypospadias versus 89.74% in the control arm). However, there were significant differences between the groups regarding the frequency of sexual activity and number of sexual partners. Only 51.35% of men with hypospadias regarded their sex life as fully satisfying against 76.92% of the control group.

Even et al. [26] analyzed a group of 15 young adult hypospadias patients (mean age 21.2 years) operated in childhood, employing instruments such as EuroQol 5, IIEF-15, and a nonvalidated questionnaire. One-third of patients thought that overall quality of life was distorted, although 80% were mostly satisfied with their sexual quality of life. The most important complaints were relative to the penile appearance.

Although subject to wide variation in individual perception, these aspects must of course be considered in addressing these patients and integrated with the other facets of the pathology/treatment strategy.

3.2. Erectile Dysfunction

3.2.1. Anterior Urethra: Prospective Studies. There are few prospective studies with correct methodology, making use of fully validated questionnaires such as the IIEF (International Index of Erectile Function) or the BMSFI (Brief Male Sexual Function Inventory) specifically dealing with anterior urethroplasties. Table 1 [27–31] lists these studies and the results obtained. It is evident that all these studies show statistical limitations. The small sample size by itself can obscure statistically significant differences simply as a consequence of underpowered studies. In fact, none of the studies makes explicit reference to calculations in order to define a minimum sample size that would be required to show 5 to 10% difference in outcomes for example. Although with relatively small samples and relatively short follow-up, the overwhelming majority of studies did not find statistically significant degradation of erectile function after urethroplasty compared to baseline.

Table 1: Anterior urethra, erectile dysfunction: prospective studies.

Authors, year	n	Questionnaire	Follow-up (months)	Age (median)	Results
Sharma et al., 2011 [27]	34	BMSFI	3	34,6	Preop BMSFI: 10,21; postop: 10,34 $P = 0{,}554$, NSD
Anger et al., 2007 [28]	25	IIEF	6,2	39	Preop IIEF: 62,6; postop: 59,6 $P = 0{,}29$, NSD
Dogra et al., 2011 [29]	78	IIEF-5	15,5	38,1	38% of postop ED "96% recovery by 6 months," NSD
Raber et al., 2005 [30]	30	IIEF	51	42	Preop IIEF5: 24 ± 8,7; postop, 24,8 ± 4,96 $P = 0{,}77$, NSD
Erickson et al., 2010 [31]	52	IIEF	7,2	40,6	Preop IIEF5: 18,7; postop:12,6 $P < 0{,}0001$: SSD "90% of postop ED recovered by 6 months"

IIEF: International Index of Erectile Function; BMSFI: Brief Male Sexual Function Inventory; NSD: no statistical difference; SSD: statistically significant difference.

The only discordant study is from Erickson et al. [31]. These authors analyze prospectively 52 men with penile or bulbar urethral stenosis subjected to several types of urethroplasties (penile urethra: ventral onlay or inlay, 2-stage; bulbar urethra: end-to-end anastomotic or augmented anastomotic repair). Patients were evaluated serially every 3 to 6 months by the IIEF. *De novo* erectile dysfunction (ED) was defined as an IIEF decrease of at least 5 points and recovery as a score less than 2 points from baseline. Although ED was observed in 38% of patients, 90% of these were found to recover function in accordance with established criteria, with an average recovery time of 190 days.

3.2.2. Anterior Urethra: Retrospective Studies. Table 2 [32–38] summarizes the available retrospective studies that used structured, validated, or nonvalidated questionnaires. Being retrospective, these studies already have inherent limitations in terms of methodology. Additional obvious limitations in terms of sample size in most of them and the frequent use of nonvalidated questionnaires add additional limitations in terms of produced scientific evidence. Moreover, unfortunately these are recurrent limitations in the reconstructive urethral surgery scientific literature.

Other studies [39–41] are available, although with debatable statistical quality, making it difficult to draw any valid conclusions. Data reported are mainly descriptive and the presence of preoperative ED was not uniformly reported. Often the presence of postoperative ED was asserted only by means of a simple question [39–41]. These series have focused above all on technical aspects and success rates, and ED was only briefly referred to. ED rates ranged from 0 [40] to 7% [41].

Concerning the studies included in Table 2, it is apparent that there is some disparity regarding the employed methodology and the way results are presented. Authors like Singh et al. [32] and Erickson et al. [33] present a methodology perfectly intelligible and easy to read. These authors evaluated a cohort of patients submitted to different types of anterior urethroplasties using the same questionnaire. In both cases no statistically significant differences were found concerning the 3 specific questions related to erectile function of the BMFSI. For its part, Coursey et al. [34], perhaps in one of the first published papers specifically on the subject, report a 30.9% rate of degradation of erections after a mean follow-up of 36 months. It is interesting however that the authors used as a control group patients undergoing circumcision in which they found reduction in erectile performance in 27.3%, with no significant differences between the two groups. On the other hand, Morey and Kizer [36] Welk and Kodama [37] and Ekerhult et al. [38] are mainly series in which two techniques or technical variants (end-to-end, extended anastomotic, or onlay graft urethroplasty) are analyzed. There was no difference in the ED occurrence among the techniques. In all groups, reported ED rates were small.

3.2.3. Other Prospective Studies: Anterior and Posterior Urethra. There are 3 additional prospective studies, presented in Table 3, involving mixed cohorts of patients undergoing anterior and posterior urethroplasties [42–44]. All used the IIEF-5 as assessment method. With follow-ups in the range of 6 to 27 months, no significant differences were found between pre- and postoperative scores by any of the authors.

3.2.4. Posterior Urethra. Lesions of the posterior urethra, associated with the overwhelming majority of cases to traumatic injuries of the pelvic ring, are unequivocally linked to erectile dysfunction, either by direct damage to neurovascular structures or by indirect action of edema, inflammation, and fibrosis. Presence of urethral trauma in pelvic fractures is a widely documented risk factor of erectile dysfunction. 42% of patients with pelvic fracture and urethral lesions had ED compared with only 5% of patients with fractures and without urethral injury [45]. The literature accounts for ED percentages ranging from 18% or less to 72% [46], although the relative roles of the traumatic event and potential iatrogeny induced by reconstructive surgery remain unclear. Aspects such as lack of consensus on the definition of ED, heterogeneous series regarding the severity of the trauma, and obvious discrepancies in the evaluation methods explain the variability of results. The potential of spontaneous

Table 2: Anterior urethra, erectile dysfunction: retrospective studies.

Authors, year	n	Questionnaire	Follow-up (months)	Age (median)	Results
Singh et al., 2010 [32]	150	BMSFI	>3	40	Mean preop BMSFI EF: 9,1; postop: 8,8 $P = 0{,}39$, NSD
Erickson et al., 2007 [33]	52	BMSFI	22,3	41,7	Mean preop BMSFI EF: 9,2; postop: 8,8 $P = 0{,}11$, NSD
Coursey et al., 2001 [34]	174	NVQ	36	43,8	69,1% no difference in erectile function 30,9% worsened erectile function
Nelson et al., 2005 [35]	11	IIEF	56,4	30,6	0% ED
Morey and Kizer, 2006 [36]	22	NVQ	26,1	39,95	No difference between end-to-end and extended anastomotic techniques or other types of penile surgery
Welk and Kodama, 2012 [37]	44	NVQ	40	27,6	No difference between nontransecting APA and dorsal graft
Ekerhult et al., 2013 [38]	169	NVQ	12–132	16–75	No difference between anastomotic repair and onlay

IIEF: International Index of Erectile Function; ED: erectile dysfunction; BMSFI: Brief Male Sexual Function Inventory; NSD: no statistical difference; NVQ: nonvalidated questionnaire.

Table 3: Anterior and posterior urethra, erectile dysfunction: other prospective studies.

Authors, year	n	Study type	Questionnaire	Follow-up (months)	Age (median)	Results
Lumen et al., 2011 [42]	20	P	IIEF-5	6	48	Mean preop IIEF5: 15; postop: 11,62 $P = 0{,}11$,NSD
Xie et al., 2009 [43]	125	P	IIEF-5 SLQQ	27,3	?	Mean preop IIEF5: 16,57; postop: 17,22 "significant decrease in EEIF-5 at 3 months but not at 6 months"
Johnson and Latini, 2011 [44]	37	P	IIEF-5	9	45	Mean preop IIEF5: 15; postop: 10 $P = 0{,}39$,NSD

IIEF: International Index of Erectile Function; SLQQ: Sexual Life Quality Questionnaire; ED: erectile dysfunction; BMSFI: Brief Male Sexual Function Inventory; NSD: no statistical difference; P: prospective.

recovery up to about 24 months after the traumatic event is also widely documented, probably related to neuropraxia recovery and development of accessory vessels after vascular trauma. For this reason, the timing of the evaluation in relation to trauma and surgery plays an important role in result variability, since studies that report ED with evaluation 3–15 months after trauma present rates of ED significantly elevated (60–72%), when compared with series in which this evaluation was made at least 2 years after the traumatic event (18–32%) [46].

Table 4 is intended to summarize the existing literature on the subject [9, 10, 47–57]. It is quite apparent that the overwhelming majority of the series did not make use of validated questionnaires in the evaluation of patients and the evaluation methodology in relation to erectile function is, at most, only briefly mentioned. If trauma plays an obvious role in the etiology of ED, it is much harder to distinguish the specific role played by reconstructive surgery. Many of the studies only report global rates of ED after reconstruction and, as such, potentially encompass the effects of trauma and surgical iatrogenesis, more or less ameliorated by the aforementioned spontaneous recovery. Studies that specifically evaluate erectile function before and after urethroplasty are thereby especially enlightening.

Koraitim [10] analyzed a series of 155 patients who suffered posterior urethral trauma, although, without using any validated tool and not specifying the definition of ED used, the author refers to the fact that, of previously potent patients before trauma, 40% became impotent. Of the 66 patients without ED before urethroplasty only 2 were impotent as a result of surgery, in both cases after surgeries of great technical complexity, exceeding 9 hours. On the other hand, 29 of 44 previously impotent patients recovered erectile function after urethroplasty.

Analyzing 76 patients with a follow-up ranging from 14 to 74 months, Yin et al. [50] report an ED rate of 42% after trauma. Of the 58% of potent patients, 95% remained potent after urethroplasty and 5% developed *de novo* ED. 59% of impotent patients after trauma recovered erectile function after surgery.

Table 4: Posterior urethra, erectile dysfunction.

Authors, year	n	Study type	Questionnaire	Follow-up (years)	Age (median)	Results
Anger et al., 2009 [47]	26	R	IIEF	4,4	40,2	54% ED 31% severe ED
Corriere, 2001 [48]	60	R	?	27,3	35	33% "complete" ED
Shenfeld et al., 2003 [49]	25	D	—	<3	28,6	72% preoperative ED
Koraitim, 2005 [10]	155	R	—	1–22	21	34% "definitive" ED 2% after surgery
Mundy, 1996 [9]	82	R	?	>5	?	7% "permanent" ED
Yin et al., 2011 [50]	76	R	—	42,5	34,5	95% remained potent 5% *de novo* ED 59% recovered potency
Lumen et al., 2009 [51]	61	R	—	5,58	34	32,8% ED previous to surgery 2 cases spontaneous recovery
Onen et al., 2005 [52]	49	R	NVQ	12	20	18,4% ED at last follow-up
Mouraviev et al., 2005 [53]	96	R	—	8,8	?	34% after realignment 42% after delayed repair
Tunç et al., 2000 [54]	58	R	—	3,9	24,2	16,2% *de novo* ED
Aboutaieb et al., 2000 [55]	35	R	—	?	25	18,3% ED early repair 5,3% ED delayed repair
Morey and Mcaninch, 1997 [56]	82	R	—	>1	?	54% ED previous to repair 38% ED after repair
Corriere et al., 1994 [57]	50	R	—	>1	?	48% ED previous to repair 32% ED after repair

IIEF: International Index of Erectile Function; NVQ: nonvalidated questionnaire; ED: erectile dysfunction; P: prospective; R: retrospective; D: descriptive.

Tunç et al. [54] described a series of 77 patients with posterior urethra injury treated with deferred urethroplasty after suprapubic diversion. 25.8% of the evaluated patients developed ED after trauma. Erectile function was evaluated prior to surgery through clinical history in 58 patients. Of the previously potent patients, *de novo* ED occurred in 16.2%. The authors make reference to an impotent patient that recovered erectile function after surgery.

Morey and Mcaninch [56] and Corriere Jr. et al. [57] on the other hand report important rates of recovery of erectile function in impotent patients after posterior urethroplasty. A decrease in impotency rates of 54 to 38% and from 48 to 32%, respectively, was observed. No *de novo* ED was reported in both studies after urethroplasty.

Finally, we can make use of a subanalysis of six studies specifically dealing with posterior urethroplasties, analyzing erectile function before and after urethroplasty, encompassed in a broader meta-analysis, discussed later [58]. After elimination of one of the studies in order to improve heterogeneity and thus improve the statistical quality, The analysis reveals advantage for postsurgical status (24,01% versus 43,27%; OR 2,51; 95% CI: 1,82–3,45; $P < 0{,}001$).

With the limitations already mentioned, posterior urethroplasty does not seem to play a significant deleterious effect *per se* on erectile function. The overwhelming majority of these patients have ED prior to surgery and surgical reconstruction might even be beneficial in a subgroup of these patients. Aspects such as removal of fibrosis and scar tissue, essential from a technical point of view to achieve a successful urethroplasty, could lead to decompression of nerve structures and allow recovery of function. Restoration of micturition and the simple removal of a suprapubic catheter, allowing improvement of psychological aspects and self-image, may also play a role in this regard.

3.2.5. Meta-Analysis. Two fairly recent meta-analysis sought to systematize the available studies and shed some light on the subject (Table 5) [58–60].

Feng et al. [58] examined 790 studies of which only 23 met the predefined inclusion criteria (randomized controlled trial (RCT) and cohort studies), corresponding to 1729 patients undergoing anterior and posterior urethroplasties. Five of these studies globally analyzed erectile function before and after urethroplasty and found no significant differences between pre- and postoperative scores [OR 0.85; 95% CI (0,52–1,4); $P = 0{,}53$]. The authors conducted several subanalyses. According to the location of the stenosis, a single study compared the incidence of ED before and after penile urethroplasty specifically and found no statistically significant differences (23.53% versus 35.29%, $P = 0{,}45$). Only two studies compared penile with bulbar substitution urethroplasties and also found no significant differences in erectile scores (23.81% versus 16.67% OR 1.62; 95% CI:

Table 5: Meta-analyses, erectile dysfunction.

Meta-analyses	Studies	n	Urethroplasty	Results
Feng et al. [58]	23	1729	Anterior and posterior urethroplasty	No significant difference before or after urethroplasty [OR 0,85; 95% CI (0,52–1,40); P = 0,53] ED incidence after posterior urethroplasty lower than before [24,01% versus 43,27%; OR 2,51; 95% CI (1,82–3,45); $P < 0{,}01$] No significant difference before or after penile urethroplasty [23,53% versus 35,29%; CI (0,13–2,52); $P = 0{,}45$] No significant difference between penile and bulbar urethroplasty [23,81% versus 16,67% OR 1,62; 95% CI: 0,51–5,81, $P = 0{,}41$] ED incidence after graft urethroplasty significantly lower than anastomotic urethroplasty [(OR 0,32; 95% CI: 0,11–0,93; $P = 0{,}04$)]
Blaschko et al. [60]	36	2323	Anterior urethroplasty	1% incidence of *de novo* ED after urethroplasty ED transient and resolved between 6 and 12 months in 86% of cases No statistical significant association between *de novo* ED and stricture location, mean stricture length, number of previous instrumentations/repairs, or type of repair

0.51 to 5.81, $P = 0{,}41$). These same two studies allowed comparison of buccal mucosa substitution urethroplasties with anastomotic end-to-end urethroplasties revealing lower ED rates for substitution versus anastomotic (OR 0.32; 95% CI: 0.11 to 0.93; $P = 0{,}04$). Finally only one study analyzed ED occurrence before and after bulbar end-to-end urethroplasty; no statistically significant differences were found (24.14% versus 27.59%; $P = 0{,}76$). Regarding posterior urethra, the meta-analysis analyzes aspects such presence versus absence of surgical history, immediate repair versus deferred repair, and primary alignment versus immediate repair; all have discarded statistically significant differences.

In turn Blaschko et al. [60] analyzed studies related to the last 15 years in English language, covering only anterior urethroplasties carried out in adulthood, specifically looking for the occurrence of ED as a consequence of urethroplasty. Of the 736 identified articles, 36 met the inclusion criteria, including 2323 patients who were subject to statistical analysis. *De novo* ED incidence varied between 0 and 38%, and generally it was a very rare occurrence, 1% (CI 1–3). The incidence of *de novo* ED did not increase when patients were directly asked about erectile function [OR 0.83 (CI 0.06 to 10.90)] and there was no association with the location or mean stricture length, type of repair, or number of previous failed instrumentation, urethrotomies or urethroplasties. In the overwhelming majority of cases *de novo* ED resolved spontaneously 6–12 months after surgery; 7 of the 21 studies that have registered the occurrence of *de novo* ED also reported occurrence of ED resolution in 86% (50/58) of cases. There was substantial heterogeneity in the studies (I-squared = 93%, $P < 0{,}001$), attributable in part to the variation in how ED was reported.

In summary, the limitations already mentioned obviously make it impossible to provide complete definitive answers regarding the relationship between urethroplasty and erectile dysfunction. Although it is unwise to assume that there is no relationship (in particular when dealing with any individual patient), globally, the evidence accumulated to date, encompassing progressive methodological and statistical quality, seems to point only to a small deleterious role for either anterior or posterior urethroplasty.

3.3. Ejaculatory Dysfunction. Table 6 summarizes the studies that address the impact of various types of urethroplasty in ejaculatory function [3, 27, 32, 33, 61–63]. Although most of the studies are retrospective and merely assessed the presence of anterograde ejaculation, most used validated instruments, ejaculatory domains of MSHQ or BMFSI.

Most authors comparing pre- and postoperative scores report significant improvement in ejaculatory function [27, 32, 33]. This result is perfectly understandable, given the considerable improvement in urethral caliber achieved, resulting in better expulsive capacity of the seminal fluid. Authors like Erikson et al. [61] although not finding overall statistically significant differences between pre- and postoperative scores refer to statistically significant improvements in men with ejaculatory dysfunction preoperatively.

Authors as Barbagli et al. [3] identified ejaculatory dysfunction after anastomotic urethroplasty in the form of decreased ejaculatory flow or need for urethral milking surpassing 20%, so that some caution is needed when analyzing these results.

In order to minimize this potential problem, several authors have proposed some minimally invasive procedures

Table 6: Ejaculation.

Authors, year	n	Study type	Questionnaire	Follow-up (months)	Urethroplasty	Age (median)	Results
Singh et al., 2010 [32]	150	R	BMSFI	>3	AU	40	Mean preop BMSFI Ej: 4,7; postop: 6,3 $P < 0{,}001$, improved
Sharma et al., 2011 [27]	34	P	BMSFI	3	AU	34,6	Mean preop BMSFI Ej: 4,68; postop: 6,71 $P = 0{,}00$, improved
Erickson et al., 2007 [33]	52	R	BMSFI	4	AU	41,7	Mean preop BMSFI Ej: 5,3; postop: 6,2 $P < 0{,}04$, improved
Barbagli et al., 2008 [3]	60	R	N. Valid.	68	AU*	39	23% ejaculatory dysfunction
Erickson et al., 2010 [61]	43	P	MSHQ	6,8	AU	40,4	Mean preop MSHQ Ej: 25,54; postop: 26,94 $P = 0{,}17$, NSD overall 70% no change 19% improved 11% decreased
El-Assmy et al., 2015 [62]	58	R	MSHQ	61,3	PU	31,6	8,6 ejaculatory dysfunction
Anger et al., 2008 [63]	32	R	N. Valid.	58,8	PU	38,6	100% antegrade ejaculation 15,6% decreased volume

BMSFI: Brief Male Sexual Function Inventory; MSHQ: Male Sexual Health Questionnaire; AU: anterior urethroplasty; *100% end-to-end anastomosis; NSD: no statistical difference.

Table 7: Orgasm.

Authors, year	n	Study type	Questionnaire	Follow-up (months)	Urethroplasty	Age (median)	Results
Anger et al., 2007 [28]	25	P	IIEF	>3	AU	39	Mean preop IIEF (orgasmic domain): 8,6; postop: 8,3 $P = 0{,}28$, NSD
Nelson et al., 2005 [35]	11	R	IIEF	56,4	Hypospadias	30,6	No change "All patients experienced orgasm"

IIEF: International Index of Erectile Function; AU: anterior urethroplasty; NSD: no statistical difference.

in an attempt to maximally preserve structures involved in ejaculatory mechanics. Authors like Barbagli and Kulkarni [23, 24] present approaches referred to as "muscle and nerve sparing urethroplasty" or "one sided urethroplasty," which aim to minimize the potential iatrogeny over the bulbospongiosus muscle or its innervation. Advantages from these technical refinements remain thus far in the field of theoretical or anatomophysiological hypothesis. Results obtained were not disclosed and as such these approaches lack appropriate validation in this specific context.

3.4. Orgasmic Dysfunction. Two studies evaluated this component of sexuality in the context of urethroplasty (Table 7) [28, 35]. In both cases the orgasmic domain was analyzed together with the other domains of IIEF. Both works refer to case series with less than 20 patients on various circumstances, urethroplasty for hypospadias and bulbar urethroplasty. None of the authors found any negative influence of urethroplasty on orgasmic function.

Although a virtual absence of literature on the subject makes it difficult to draw any critical analysis on the subject, a lack of influence of urethral surgery on orgasm is not surprising, since orgasm is essentially considered a neurophysiological phenomenon [64].

3.5. Fertility. There are some specific articles that address fertility in the context of urethroplasty (Table 8) [52, 63, 65]. These studies essentially describe the seminal parameters of patients having undergone posterior urethroplasty. There is no reference to cases of azoospermia. Of course it is impossible to implicate the surgical procedure with these findings, although the relationship does not seem obvious. Anyway, due to the high prevalence of male factor infertility in the general population, it is impossible to draw any conclusion.

4. Conclusions

Although there are a lot of series describing the results achieved with various types of urethroplasties, the andrological aspects of this pathology and its treatment(s) are

Table 8: Fertility.

Authors, year	n	Study type	Follow-up (months)	Urethroplasty	Age (median)	Results
Anger et al., 2008 [63]	13	D	>3	PU	38,6	46% normal (WHO) 53% oligospermia 8% asthenozoospermia 30% oligozoospermia
Iwamoto et al., 1992 [65]	14	D	56,4	PU	?	50% normal (WHO) 21% oligozoospermia 35% asthenozoospermia
Onen et al., 2005 [52]	19	D	144	PU	20	26,3% abnormal semen parameters (WHO)

D: descriptive; R: retrospective; PU: posterior urethroplasty.

clearly insufficiently studied. The available literature is confusing, dispersed, not systematized, and often containing methodological deficits. Although we have been assisting in recent efforts in an attempt to obtain more and better data, there are still obvious gaps that prevent valid conclusions on the subject. Large scale, prospective investigations using standardized validated questionnaires are needed to reliably elucidate the real impact of urethroplasty on the different domains of sexual function.

Conflict of Interests

The author declares that there is no conflict of interests regarding the publication of this paper.

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Research Article

Anterior Urethral Stricture Disease Negatively Impacts the Quality of Life of Family Members

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Purpose. To quantify the quality of life (QoL) distress experienced by immediate family members of patients with urethral stricture via a questionnaire given prior to definitive urethroplasty. The emotional, social, and physical effects of urethral stricture disease on the QoL of family members have not been previously described. *Materials and Methods*. A questionnaire was administered prospectively to an immediate family member of 51 patients undergoing anterior urethroplasty by a single surgeon (SBB). The survey was comprised of twelve questions that addressed the emotional, social, and physical consequences experienced as a result of their loved one. *Results*. Of the 51 surveyed family members, most were female (92.2%), lived in the same household (86.3%), and slept in the same room as the patient (70.6%). Respondents experienced sleep disturbances (56.9%) and diminished social lives (43.1%). 82.4% felt stressed by the patient's surgical treatment, and 83.9% (26/31) felt that their intimacy was negatively impacted. *Conclusions*. Urethral stricture disease has a significant impact on the family members of those affected. These effects may last decades and include sleep disturbance, decreased social interactions, emotional stress, and impaired sexual intimacy. Treatment of urethral stricture disease should attempt to mitigate the impact of the disease on family members as well as the patient.

1. Introduction

It is well known that urethral stricture disease can lead to poor quality of life (QoL) for patients [1–4]. Strictures cause obstructive voiding symptoms, often requiring numerous urethral dilations, direct visual internal urethrotomies (DVIUs), or urethroplasties to achieve definitive resolution. Many patients experience chronic infections and urethral pain, although a minority of patients may develop more severe complications of acute urinary retention, detrusor myogenic failure, urethrocutaneous fistulae, renal failure, or sepsis [3–5]. It has been reported that up to 44% of patients experience sexual dysfunction, particularly in cases of urethral stricture secondary to failed hypospadias repair or lichen sclerosis [6, 7].

Despite the volume of literature discussing the QoL of urethral stricture patients, the effects of this disease on the emotional, social, and physical health of family members have not been previously described. Here, we attempt to quantify the QoL distress experienced by the immediate family members of patients being treated for urethral stricture disease.

2. Methods

A unique questionnaire was created to assess the QoL of family members of urethral stricture disease patients (Appendix). This questionnaire was completed by an immediate family member of 51 patients undergoing anterior urethroplasty by a single surgeon from 2013 to 2014 after obtaining Institutional

Review Board (IRB) approval. Surveys were administered to the person who accompanied the patient to the hospital on the operative day, which in most cases was the patient's spouse or an immediate family member. The questionnaire was designed to assess the emotional, social, and physical consequences experienced by a close family member as a direct result of their loved one and was administered preoperatively. When designing the questionnaire, relevant urethral stricture disease quality of life issues were determined by qualitative interviews with patients and family members, input from reconstructive urologists, and literature review of typical urethral stricture disease symptomatology. The specific questions were formulated to capture issues that were caused exclusively by the patient's urinary dysfunction. Questions covered the age, sex, living and sleeping arrangements of the loved ones, and how the patient's stricture disease affects the loved one's sleeping habits, social life, ability to complete typical daily tasks, stress level, and, if applicable, sexual intimacy with the patient. Descriptive statistics of categorical variables focused on frequencies and proportions. Medians and ranges were reported for continuously coded variables.

3. Results

All patients underwent an anterior urethroplasty, with a mean age of 39.8 years (18–64) and mean stricture length of 5.1 cm (2–14 cm). Stricture development was secondary to hypospadias (2), trauma (7), radiation (1), and idiopathic etiologies (41). The mean number of DVIU/dilations or urethroplasties prior to definitive urethroplasty was 3.9 (0–22) and 0.5 (0–2), respectively. The mean years of voiding dysfunction from urethral stricture was 17 years (0.5–55 yrs). Mean International Prostate Symptom Score (IPSS) was 21 (14–31).

Of the 51 family members, the mean age was 48.9 years (range = 25–83), 92.2% were female (47/51) and 7.8% male (4/51). 86.3% lived in the same household and 70.6% slept in the same room as the patient (44/51, 36/51). 56.9% endorsed sleep disturbances and, of those, 24.1% felt that their sleep was severely disturbed (29/51, 7/29). 43.1% felt that their social life was limited, and of those, 18.2% described this social limitation as "substantial" (22/51, 4/22). However, only 15.7% felt limited by an inability to take care of daily tasks (8/51). 86.3% felt pity for the patient and 82.4% felt stressed by the patient's surgical treatment (44/51, 42/51). 60.8% of respondents were sexually active with the patient, and among these, 83.9% felt that their intimacy was negatively impacted (31/51, 26/31). Of the 83.9% endorsing negative effects on their intimacy, 50% felt that their intimacy was impacted a great deal (13/26).

4. Discussion

It has been shown time and time again that urethral stricture disease is detrimental to patient QoL [1–4]. Patients frequently experience voiding symptoms such as weak urinary stream, incomplete emptying, splayed urinary stream, and dysuria, as well as resting lower urinary tract pain and sexual dysfunction [6]. Patients may need to void multiple times throughout the night due to the nature of the disease, which could certainly disturb family members in the same bed, or even in the same home. Most family members (56.9%) felt that their sleep habits were negatively affected due to their partner's symptoms, 24.1% of which endorsed severe sleep disturbances. 86.3% felt pity for the patient and 82.4% felt stressed by the patient's surgical treatment.

Whybrow et al. described the elaborate plans and routines developed by stricture patients to hide their disease from others and help cope with the obstructive voiding symptoms caused by their urethral stricture disease. Some of these patients even described an inability to attend normal social functions due to the severity of their symptoms [8]. These social intricacies do not only affect the patient, they also take a toll upon the family members, loved ones, and caretakers who interact with the patient regularly. In our study, 43.1% felt that their social life was limited, and of those, 18.2% described this social limitation as "substantial."

Data regarding sexual dysfunction within the stricture population is limited, and reported rates have been highly variable. Nuss et al. reported sexual dysfunction within 11% of all stricture disease patients and up to 24% of patients with prior hypospadias or lichen sclerosis [6]. In contrast, Erickson et al. published rates of preoperative erectile dysfunction in 44% of patients, with 25% complaining of ejaculatory dysfunction [7]. In our study, a strong majority of family members in a sexual relationship with the patient reported diminished sexual intimacy (83.9%). Of the respondents endorsing negative effects on their intimacy, 50% felt that their intimacy was impacted a great deal. This rate is higher than the rates of patient sexual dysfunction reported within the literature, suggesting that sexual dysfunction may be even more prevalent when the patients' intimate partner's opinions are considered. Despite having erections adequate for sexual activity, intimacy between partners is a multifactorial entity. Stricture patients often have Foley catheters or suprapubic catheters that may physically impair sexual contact. In addition, the presence of these tubes and any accompanying urine odor may diminish libido. Although difficult to measure objectively, embarrassment and/or decreased self-confidence due to the patient's urologic condition may also impact sexual intimacy. Thus, stricture disease symptomatology and its subsequent psychological effects have the potential to impact sexual function in a plethora of ways [9].

To our knowledge, no prior studies have investigated the effect of stricture disease on family member QoL. However, there are studies investigating the effect of urinary incontinence on caregiver quality of life. Flaherty et al. first reported that caregiver burden was greater when patients suffered from urinary incontinence and then Gotoh et al. used a validated questionnaire to demonstrate this increased psychological burden [10, 11]. It has also been shown that the QoL of family members is an important consideration when managing all diseases, as family member stress and psychological burden may further diminish patient QoL, as well as overall care and recovery [12]. In addition, diminishing QoL of family members could serve as a surrogate marker of disease severity.

Sells et al. reported that partner morbidity correlates with disease severity when considering a patient population with lower urinary tract symptoms caused by benign prostatic hyperplasia [13]. These studies suggest that the treatment plan should include strategies to mitigate the distress felt by family members, such as family/spousal conferences and therapy referrals. Realistic expectations must be established early in the course of disease, and healthy coping mechanisms for the patient and family members should be encouraged.

Our study is not without limitations. A single surgeon (SBB) performed all urethroplasties and all surveys were administered at a single institution, both of which may limit generalizability. Additionally, individual QoL is inherently multifactorial, and the specific issues investigated by our questionnaire are influenced by a number of factors other than the patient's stricture disease. A validated questionnaire would increase the strength of our conclusions. Jackson et al. created a validated patient-reported outcome measure to quantify the effects of urethral stricture surgery, but a validated questionnaire to assess QoL effects on family members and caretakers does not yet exist [14, 15]. Further directions of study include administration of this survey to more patients and at other institutions, as well as at multiple time points along the urethral stricture disease algorithm, including following successful urethroplasty, in order to evaluate how disease progression and treatment affect the QoL of patients and family members.

5. Conclusions

Urethral stricture disease has a significant impact on family members and caregivers, particularly spouses and partners. The effects on family members may last decades and include sleep disturbance, decreased social interactions, emotional stress, and impaired sexual intimacy. The elements of an effective treatment strategy, including the timing of definitive urethroplasty, are multifactorial and highly patient-specific. While the QoL of the patient is an extremely important consideration, the QoL of immediate family members must not be ignored. Thus, treatment of urethral stricture disease should include family conferences focusing on expectations, basic stricture education, treatment options, and access to counseling services. Further studies may help to elucidate the ideal management strategy to optimize both patient and family quality of life.

Appendix

Stricture Disease: Family Member Survey

(1) Do you live in the same home as the patient?

- ☐ No
- ☐ Yes
- ☐ choose not to answer

(2) Do you sleep in the same room as the patient?

- ☐ No
- ☐ Yes
- ☐ choose not to answer

(3) How are you related to the patient?

- ☐ Spouse
- ☐ Partner
- ☐ friend
- ☐ family member/Other: —
- ☐ choose not to answer

(4) Your age? —

(5) Male or Female (circle one)

(6) Do you experience any sleeping disturbances because of the patient's urinary problem?

- ☐ Not at all
- ☐ Somewhat
- ☐ A great deal
- ☐ choose not to answer

(7) Is your social life limited because of the patient's urinary problem

- ☐ Not at all
- ☐ Somewhat
- ☐ A great deal
- ☐ choose not to answer

(8) Is your ability to take care of tasks inside and outside the home affected by the patient's urinary problem?

- ☐ Not at all
- ☐ Somewhat
- ☐ A great deal
- ☐ choose not to answer

(9) Does the patient's urinary problem make you feel pity or sad for them?

- ☐ Not at all
- ☐ Somewhat
- ☐ A great deal
- ☐ choose not to answer

(10) Is the surgical treatment of the patient's condition stressful for you?

- ☐ Not at all
- ☐ Somewhat
- ☐ A great deal
- ☐ choose not to answer

(11) Are you sexually intimate with the patient? If yes, then answer question (12). If no, STOP.

- ☐ No

□ Yes
□ choose not to answer
□ Not Applicable

(12) Is your sexual intimacy affected by the patient's urinary condition?

□ Not at all
□ Somewhat
□ A great deal
□ choose not to answer.

Abbreviations

QoL: Quality of life
DVIU: Direct visual internal urethrotomy.

Ethical Approval

All research conducted was compliant with ethical standards. IRB # 201304085.

Conflict of Interests

The authors declare that they have no conflict of interests or competing interests.

Authors' Contribution

Jonathan R. Weese was responsible for data collection, data analysis, paper editing, and paper writing. Valary T. Raup was responsible for project development, data collection, data analysis, and paper writing. Jairam R. Eswara was responsible for project development, data analysis, and paper writing/editing. Stephen D. Marshall was responsible for data analysis and paper writing/editing. Andrew J. Chang was responsible for project development, data collection, and data analysis. Joel Vetter was responsible for data analysis. Steven B. Brandes was responsible for project development, data analysis, and paper writing/editing. Jonathan R. Weese and Valary T. Raup contributed equally to this publication.

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Review Article

Management of Long-Segment and Panurethral Stricture Disease

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Long-segment urethral stricture or panurethral stricture disease, involving the different anatomic segments of anterior urethra, is a relatively less common lesion of the anterior urethra compared to bulbar stricture. However, it is a particularly difficult surgical challenge for the reconstructive urologist. The etiology varies according to age and geographic location, lichen sclerosus being the most prevalent in some regions of the globe. Other common and significant causes are previous endoscopic urethral manipulations (urethral catheterization, cystourethroscopy, and transurethral resection), previous urethral surgery, trauma, inflammation, and idiopathic. The iatrogenic causes are the most predominant in the Western or industrialized countries, and lichen sclerosus is the most common in India. Several surgical procedures and their modifications, including those performed in one or more stages and with the use of adjunct tissue transfer maneuvers, have been developed and used worldwide, with varying long-term success. A one-stage, minimally invasive technique approached through a single perineal incision has gained widespread popularity for its effectiveness and reproducibility. Nonetheless, for a successful result, the reconstructive urologist should be experienced and familiar with the different treatment modalities currently available and select the best procedure for the individual patient.

1. Introduction

Management of long-segment urethral stricture remains a challenge in reconstructive urology. The surgical treatment of urethral strictures varies according to etiology, location, length, and density of the lesion and fibrosis involving surrounding tissues [1–3]. Treatment of strictures involving the bulbar urethra is relatively well defined and, in most cases, is amenable to excision and end-to-end anastomosis or a short patch onlay substitution urethroplasty [4]. However, long-segment urethral stricture or panurethral stricture disease is less common and the literature on the subject is not abundant.

In the treatment of this condition, several issues must be factored in, such as cause of the stricture, previous urethral surgeries, the quality of the urethral plate, availability of different autologous tissues to be used as flaps or grafts, experience, expertise, and preference of the treating urologist, including his familiarity with tissue transfer techniques [5]. Lichen sclerosus (LS), also known as balanitis xerotica obliterans (BXO), raises specific problems related to treatment, prognosis, and prolonged follow-up [6–10]. The complexity of this condition may require a different dynamic treatment paradigm. However, although a multistage reconstruction may be used by some surgeons in certain situations due to hostile urethral tissues, in the majority of cases, LS is amenable to a single-stage reconstruction with highly favorable results. Additionally, reconstruction of long-segment urethral strictures is not only about restoring voiding function but also preserving sexual function in all its aspects, such as erection, ejaculation, and orgasm as well as guaranteeing good penile cosmesis.

Current surgical options employed are associated with reasonable success rates and may include a single- or a multiple-stage reconstruction, with the use of a flap, a graft, or a combination of both, and lastly, in extreme circumstances a perineal urethrostomy may offer the best solution for the patient who does not wish to go the extra (long) mile.

2. Materials and Methods

A review of the international literature was conducted using MEDLINE/PubMed database and Google Search, using keywords as "complex urethral stricture," "long segment urethral stricture," "panurethral," "lichen sclerosus," "oral mucosa," and "urethroplasty." We included in the review only articles published in the English language from 1990 to 2015.

3. Epidemiology, Etiology, and Pathogenesis

Generally speaking, male urethral stricture is a common disease worldwide and has been so for centuries. The first known description of urethral dilatation is credited to Shusruta more than 600 years BC [11]. In the 19th century, expert opinion estimated an incidence of 15–20% in the adult male population [12]. In the 21st century in the UK NHS more than 16,000 men required hospital admission annually due to urethral stricture and more than 12,000 of these admissions ended up necessitating surgical treatment with more than £10,000 million [12]. The estimated prevalence in the UK averages 10/100,000 young males doubling this figure by the age of 55 years and rising to over 100/100,000 in males over 65 years. In the USA male urethral stricture accounted for about 5,000 inpatient visits and 1.5 million office visits annually between 1992 and 2000. The incidence was estimated to be approximately 0.6% in susceptible populations [13]. The estimated costs to the medical system for male urethral disease in the USA surpassed US$ 190 million in 2000 [13]. However, there are no direct measures to assess the true incidence of urethral stricture disease worldwide, much less so for panurethral stricture disease in particular. A recent study, including 268 patients, reported panurethral or multifocal anterior urethral stricture in a total of 36 patients (13.4%). However, in a more recent retrospective analysis of all strictures that had been treated surgically at a single institution, the vast majority of strictures were anterior (92.2%) with panurethral strictures totalling 4.9% [14].

Urethral stricture disease can have a profound impact on quality of life, including sexual life, as a result of a number of complications associated with urinary obstruction, such as infection, bladder calculi, urethral diverticulum, fistulation, sepsis, and ultimately chronic renal failure.

The etiology of long-segment or panurethral strictures may vary in industrialized and developing countries. Today, in industrialized countries, most urethral strictures in general have iatrogenic or idiopathic origin [2, 3]. Iatrogenic causes include urethral catheterization, cystourethroscopy, transurethral resection, and previous urethral surgeries. Other causes include idiopathic, trauma, infection/inflammation, and lichen sclerosus. In the developing world, the most common cause of panurethral stricture is genital lichen sclerosus (LS) [6]. Although less frequent, gonorrhea still remains an important cause of long-segment strictures in the developing world.

The pathogenesis of long-segment or panurethral stricture disease has not been widely studied. Historically, and although it is an important cause in some regions of the developing world, infection was blamed as the main cause of urethral stricture [15]. However, it must follow a similar pathogenic process as other types of urethral stricture, that is, injury to the epithelium of the urethra and underlying corpus spongiosum, ultimately leading to fibrosis during the healing process. Excepting a traumatic cause when the urethral lumen is obliterated, corpus spongiosum deep to the urethral epithelium is replaced by dense fibrous tissue and the normal urethral pseudostratified columnar epithelium being replaced by squamous metaplasia [16–18]. Metaplastic change can also occur proximal to a stricture, due to chronic distension under pressure of voiding [12]. Small tears occurring repeatedly in the metaplastic tissue result in focal urinary extravasation, which in turn leads to a fibrotic reaction within the spongiosum. Initially, this fibrosis can be asymptomatic, but, over time, the scar or fibrotic plaque produced can enhance the narrowing of the urethral lumen, resulting in symptomatic urinary obstruction.

The pathology of a urethral stricture is characterized by changes in the extracellular matrix of the spongiosal tissue and replacement of the normal connective tissue by dense fibrosis associated with a decrease in the ratio of type III to type I collagen and a significant decrease in the smooth muscle and nitric oxide content in the strictured urethral tissue [19, 20].

The pathology of lichen sclerosus in inducing urethral stricture is different. LS is a chronic, progressive, inflammatory process which in the male can involve foreskin, glans, and anterior urethra. The etiology is for the most part unclear, although it has been associated with an autoimmune reaction and a genetic pattern. However, an infectious cause has been suggested [21]. This is an atrophic rather than a proliferative process that usually originates in the foreskin or glans as diffuse or patchy plaques of white discoloration giving the glans a characteristically mottled appearance (Figure 1). It can progress further to include the meatus, fossa navicularis, penile urethra, and eventually the bulbar urethra, resulting in a long-segment or panurethral stricture disease [7, 8]. It remains unclear whether LS-induced urethral strictures develop as a consequence of extension of glandular disease into the penile urethra or whether they result from chronically obstructed voiding or instrumentation, or both [22]. Long-segment urethral strictures, as any anterior urethral stricture, typically occur following trauma or infection, but mostly from iatrogenic causes, especially urethral catheterization, dilatation, and endoscopic manipulation, or may be idiopathic. Nonetheless, LS has been reported as the most frequent cause of this type of stricture, especially in India [6, 8, 9].

(a) (b)

Figure 1: Lichen sclerosus of the glans and prepuce (a) and hypospadias cripple (b). Both patients with panurethral stricture.

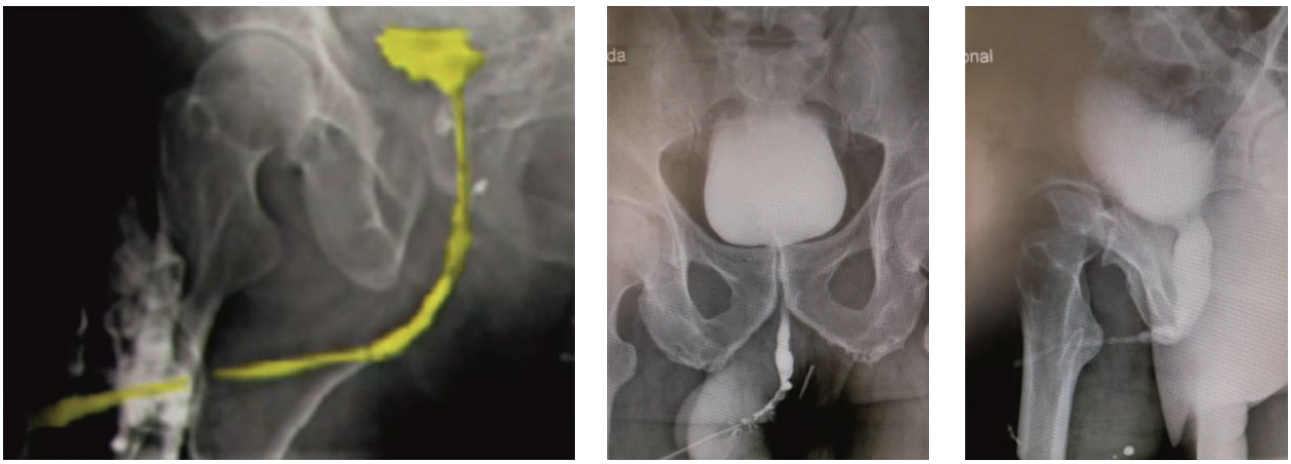


Figure 2: Retrograde and voiding urethrogram of panurethral stricture disease.

4. Diagnostic Evaluation

A critical initial pitfall in the diagnostic evaluation is not to fully understand and properly diagnose the stricture as being panurethral. Symptomatic stricture disease typically presents with progressive obstructive voiding complaints, such as a weak stream, frequency, incomplete emptying, terminal dribbling and straining, or complications of an obstructive voiding syndrome, such as recurrent tract infections, epididymitis, haematuria, and bladder stones. Symptomatic evaluation should be best formalized using a validated questionnaire, such as the AUA symptom index [24, 25].

Physical examination may be vague and uneventful in some cases. Nonetheless, the penis should always be carefully examined for scars related to previous surgery, penile malformations, signs of LS, or associated penile cancer. Careful attention should also be drawn to palpation of the spongiosum and genital area in general. The mouth should also be carefully inspected, particularly if an oral mucosa graft is planned.

Uroflowmetry, ultrasonography, and cystourethroscopy may be important adjuncts in the diagnosis of panurethral stricture disease, but the most critical is retrograde urethrography (RUG) and voiding cystourethrography (VCUG). The latter tests determine the location, length, and severity of the stricture in great detail (Figure 2). Endoscopy can give an idea of the elasticity and appearance of the urethra, especially following previous urethroplasty(ies). Ultrasonography can be used to determine the length and degree of fibrosis and eventually influence the operative approach [26]. Although ultrasonography seems to provide important additional information during preoperative evaluation, it has not gained the expected widespread popularity. This may be due to its relatively limited usefulness in the more proximal bulbar urethra, where the distance between the ultrasound probe and the target area surpasses its resolution accuracy.

It is of paramount importance that these imaging modalities ensure that all diseased portions of the urethra are included in the repair. Often, the narrowing of the lumen can be fairly uniform, with spots of more severe reduction in caliber. Thus, a panurethral stricture can be erroneously interpreted as just a short stricture and the other less severe areas underestimated as being of "normal" caliber. To avoid this diagnostic error, some authors have suggested that if the urethral lumen does not expand to ≥ 8 mm in diameter on imaging, then it is probably stenosed. Sometimes, it may be necessary to proceed to a full examination under anesthesia with endoscopy and bougienage and retrograde urethral imaging [27].

5. Surgical Reconstruction

In rare instances, where symptoms are not particularly troublesome, surgical treatment may not be necessary. In the majority of patients, both urethral dilatation and direct vision internal urethrotomy are inappropriate and, therefore, have no place in the treatment of panurethral stricture disease. At the other extreme end of the spectrum of this disease, typically patients who have undergone multiple failed surgical attempts, particularly when associated with significant comorbidity, might prefer a definitive perineal urethrostomy or even opt a simple suprapubic cystostomy catheter.

Panurethral stricture disease is definitely a complex subset of urethral stricture disease. Defining "panurethral" has been a matter of debate. This has implications in the interpretation of the literature as there is no homogeneity in the study populations. In a recent multi-institution study including 466 patients, long-segment or panurethral stricture was defined as any single stricture or multifocal diseased areas of the penile and bulbar (anterior) urethra measuring ≥ 8 cm in length [23]. Several surgical reconstructive procedures have been described to address this full-length anterior urethral strictures (Table 1). When planning the surgical treatment of panurethral stricture disease, some surgeons have concerns of whether to select a one- or two-stage operation and, if a one-stage operation is chosen, whether adequate transfer tissue for reconstruction is available. Panurethral stricture disease associated with LS has been successfully treated with a single-stage repair and OM onlay grafting. Indeed, the authors' experience has clearly shown that it should be preferred over a multistage approach, which in their opinion has no role in the surgical treatment of genitourethral LS [6, 23]. The main arguments are the high failure rate; the fact that genitourethral LS is a penile skin disease and, lastly, that staged operations will allow ingrowth of the disease into the urethra. In less common instances, where there is significant urethral narrowing with an unsalvageable plate, after multiple failed previous repairs, or if the stricture disease is associated with infection, abscess or calculi, a two-stage marsupializing procedure, like the Johanson procedure, may be preferable. In the majority of cases, substitution urethroplasty is the rule. Substitution urethroplasty can be performed using a flap, a graft, or sometimes a combination of both.

Table 1: Options for surgical reconstruction of long-segment and panurethral strictures.

Flaps
Circular fasciocutaneous penile flap (McAninch flap)
Q-flap and variants (Quartey and Jordan)
Biaxial epilated scrotal flap (Gil-Vernet)
Grafts
Oral mucosa (cheek, tongue, and lower lip)—Kulkarni technique
Postauricular skin (Wolf)
Penile and preputial skin
Bladder mucosa
Colonic mucosa
Combination of flaps and grafts
Staged procedures
Johanson technique and variants
Schreiter's mesh graft technique
Tunica albuginea (Monseur) urethroplasty
Perineal urethrostomy

5.1. Flaps. Several flaps have been described and used in panurethral stricture reconstruction. In 1993, McAninch described the *circular fasciocutaneous penile flap* for the reconstruction of extensive urethral stricture [28]. Circular fasciocutaneous penile flap originates on the distal penis and uses Buck's fascia as the major vascular supply. He reported his results with the use of this flap for 1-stage reconstruction of complex anterior urethral strictures involving long penile and also bulbar urethral strictures in 66 men [29]. The stricture length measured up to 24 cm (average 9.08 cm). The flap was used as an onlay procedure and tubularized flap for urethral substitution. In some cases, additional adjunctive tissue transfer and proximal graft placement were required. Initial success rate was 79%, rising up to 95% after an additional procedure. Recurrent strictures occurred usually at the proximal and distal anastomotic sites. The penile circular fasciocutaneous flap reliably provided 12–15 cm of length for reconstruction in most patients, although approximately 90% had been previously circumcised. The less favorable results were seen in patients after flap tubularization for urethral replacement. The McAninch technique is worldwide considered as a reliable surgical option for panurethral strictures and numerous publications are available in the literature about its use. A major advantage of the McAninch flap is its versatility, as it can be utilized in all areas of the urethra, from the membranous area to the external meatus [29, 30]. Because of compartment syndrome noted in 2 different cases due to prolonged exaggerated lithotomy position that usually occurs if the patient remains in this position more than 5 hours, the authors begin the operation with flap harvesting with the patient in the supine position, thereby reducing exposure to the lithotomy position by 2-3 hours.

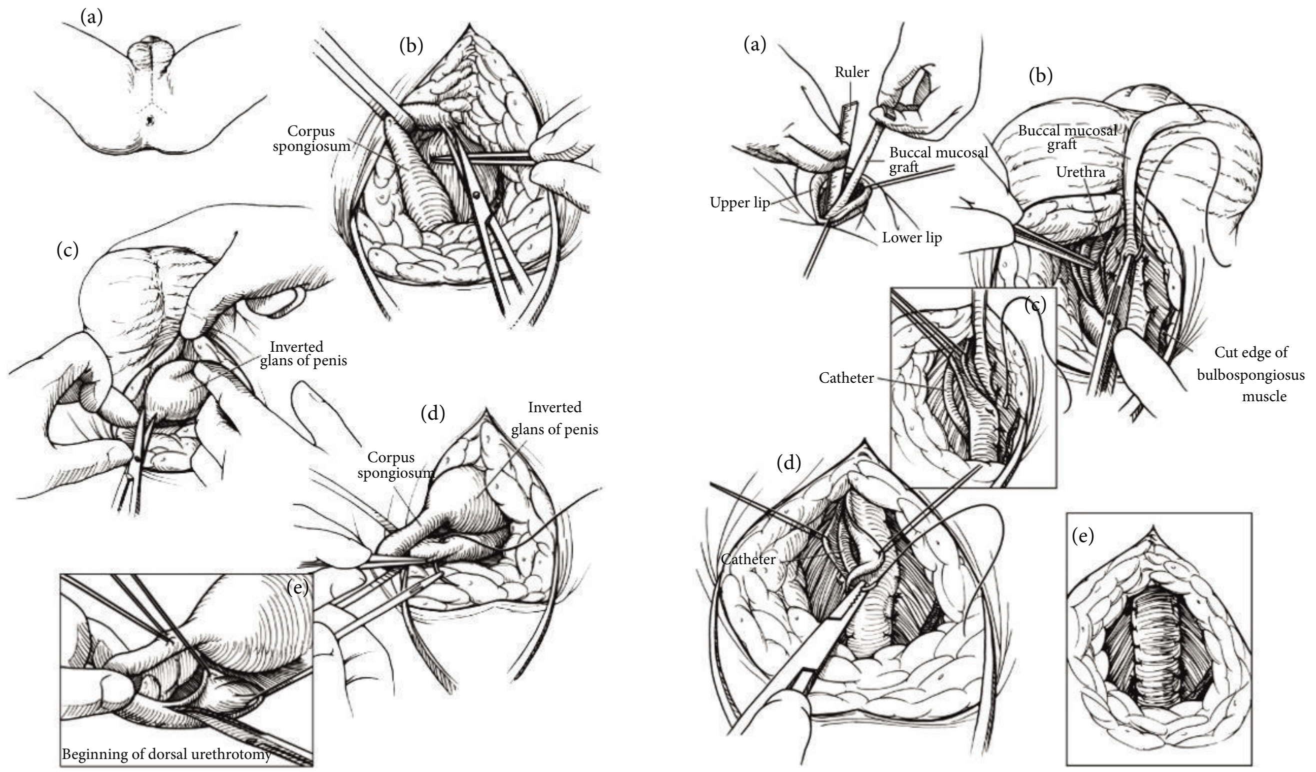
The *Q-flap* is a modification of the McAninch circular penile fasciocutaneous skin flap. It is so called because it incorporates an additional midline ventral longitudinal penile extension, thus resembling the letter Q. Similar "hockey-stick" flap configurations have also been described by Quartey [31]. Morey et al. reported their experience with the Q-flap in 15 patients with a mean stricture length of 15.5 cm (range 12–21) who underwent single-stage urethral reconstruction. All patients had a prepuce and the flap was harvested with the patient initially supine to avoid compartment syndrome [32]. The flap is outlined with the penis on stretch and the penis degloved, meticulously preserving the blood supply on the tunica dartos pedicle. The Q-flap is sewn into place after ventral urethrotomy as an onlay flap with running 4-0 absorbable suture, similar to the McAninch flap procedure. The fossa navicularis is typically reconstructed through a glans-wings or a glans-preserving technique. Once the pendulous portion of the onlay flap is sewn in, the patient is repositioned into the lithotomy position and the flap is transferred to the perineum through a scrotal tunnel wide enough to accommodate loose passage of the flap. The potential major advantage of these flap procedures is to allow a single-stage reconstruction of long-segment and complex strictures and to avoid the need for additional, morbid, time-consuming tissue transfer techniques.

These two procedures are extremely labor-intensive and are among the most difficult and tedious in reconstructive urology. A common complication with the above two flaps, particularly with unexperienced surgeons, is necrosis of penile skin proximal to the flap [29, 30]. In some instances, this penile skin necrosis may lead to wound infection and ultimately to disruption of the flap and necrosis.

In 1997, Gil-Vernet et al. described another type of flap for urethroplasty, the *biaxial epilated scrotal flap* [33]. They used this flap, which measured up to 20 × 2.5 cm, to reconstruct the entire anterior urethra from the bulbomembranous urethra to the external meatus. This flap consists of scrotal skin, dartos, external spermatic fascia, cremasteric fibers and fascia, internal spermatic fascia, and scrotal septum. Tunica vaginalis is not included. Vascular anastomoses between cremasteric (deep) and scrotal (superficial) blood supply plexuses are included in the flap and hence biaxial flap. The authors used this technique in 37 men including 10 with panurethral stricture disease. Two of these 10 patients failed due to graft shrinkage, necessitating perineal urethrostomy. There were also problems with incorrect scrotal skin epilation leading to sclerosis, vascular lesions, and penile ventral curvature. Nonetheless, the authors considered this flap technique ideal for urethral reconstruction from the penoscrotal angle to the prostatic apex. Because of anatomical proximity, good tissue availability, and potentially good tolerance to contact with urine due to abundance of sebaceous glands, this is always the authors' first option for bulbomembranous urethroplasty. They also believe that scrotal skin flap is less likely to develop lichen sclerosus as compared to penile skin. Despite all the potential advantages mentioned by the authors, epilation, deepithelialization, and flap mobilization may not be so straightforward. Epilation is an extremely time-consuming process. Although flaps with their own blood supply would be more appropriate in severely fibrotic urethral beds, such as after previously failed urethroplasties, several problems with postvoid dribbling of urine, ejaculatory dysfunction, and flap outpouching or pseudodiverticulum formation are truly troublesome and impact on quality of life [30]. It should be kept in mind that, in general, the use of skin flaps for urethral reconstruction is more technically demanding than substitution urethroplasty. In a study by McAninch and Morey, for patients with an average stricture length of 9 cm, the initial overall success rate of the fasciocutaneous flap reconstruction was 79%. Recurrent stricture rate was noted in 13% of onlay grafts and in 58% of tubularized repairs [29].

5.2. Grafts. The use of grafts in urethral reconstruction has become a more popularized surgical option worldwide. Theoretically, grafts in general are inherently less reliable because they need to be vascularized. However, they are quick and relatively easier to harvest and deploy. There are several studies of both flaps and grafts showing similar restricture rates [34]. Therefore, in the authors' opinion, a graft should be the procedure of choice due to its simplicity and speed by which it can be harvested and deployed, since the restricture rate is similar. There may be specific indications favoring a flap rather than a graft: revision surgery following multiple failed attempts, any cause of local devascularization such as irradiation or severe peripheral vascular insufficiency, and local infection, all of which hamper the ability of a graft to take. In summary, a graft repair is preferred due to the reasons mentioned above. Both grafts and flaps contract, although full-thickness flaps tend to contract less than split-thickness flaps and grafts, and patch grafts do better than tubed grafts, which may imply a two-stage procedure if a circumferential reconstruction of the urethra is necessary.

The widespread popularity of *oral mucosa* in urethral reconstruction has similarly allowed the introduction of new techniques in long-segment and panurethral stricture repair. In 2000, Kulkarni et al. first described the use of long oral mucosa grafts to repair the entire anterior urethra through a simple perineal incision in a single stage, thus preserving the penile components, their anatomy, function, and cosmesis [35] (Figure 3). In 2009, the same authors described a modification of their original technique, suggesting a minimally invasive procedure with dissection of the urethra from the corpora cavernosa along one side only, thus preserving the entire neurovascular supply to the urethra [36] (Figure 4). Buccal mucosa graft urethroplasty has been used for long anterior urethral strictures by several authors following the initial report by Kulkarni et al. in 2000 [37–40]. All these authors have reported favorable results at short- and medium-term follow-up with acceptable complication rates. In 2004, Gupta et al. described a technique of dorsal graft placement by ventral sagittal urethrotomy and minimal-access perineal approach and used this technique in patients with anterior urethral stricture, including 2 with panurethral stricture disease [40]. In the Kulkarni technique, the whole anterior urethra is repaired by a single perineal incision, single technique, and single substitute material (Figure 4). In a retrospective study including 117 patients with panurethral stricture disease treated from June 1998 to December 2010, the overall success rate was 83.7%. Mean stricture length was 14 cm and median follow-up was 59 months. Most recurrent



(a) A midline perineal incision bifurcated posteriorly which is used for its excellent access to the proximal bulbar urethra
(b) Full mobilization of the anterior urethra through the perineum as for a total urethrectomy. A Gelpi retractor which is used
(c) The glans penis which is inverted and delivered to the perineal wound for dissection of the distalmost segment of the urethra
(d) Placement of stay sutures in preparation for dorsal external urethrotomy
(e) Dorsal external urethrotomy which is begun in the proximal bulbar urethra

(a) Harvesting of buccal mucosa graft involving lower lip and both inner cheeks
(b) The urethra which is fully mobilized and rotated 180° for external urethrotomy along its dorsal surface. A single strip of BM which is spread and sutured to the tunica albuginea of the corpora cavernosa. Quilting sutures which are applied along the graft
(c) The right urethral margin which is sutured to the ipsilateral side of the patch
(d) Suturing of the left side of the urethra-graft anastomosis
(e) Suturing which is completed and the grafted area which is covered by urethral plate

Figure 3: Schematic representation of the Kulkarni operation.

strictures occurred at the proximal anastomotic site and none of these was a full-length recurrence [6]. The major advantage of this technique is that it is minimally invasive and performed in one stage. It also avoids the psychological trauma of 2 (or more) operations and the need of living for 6 months with bifid scrotum after staged procedures. Additionally, because it is a one-side dissection the risk of injury to the neurovascular bundles to the penis and urethra is minimal. This procedure is carried out through the perineum, avoiding a penile scar, and does not lead to a hypospadiac meatus.

More recently, some authors have described the use of *lingual mucosa* in urethroplasty [41–45]. The graft characteristics of lingual mucosa are similar to those of buccal mucosa (cheek and lip) [41, 42]. Lingual mucosal graft was used as the sole graft in 18 men with long anterior urethral strictures by Das et al. [41]. Most cases were etiologically associated with LS or infection. Overall success rate was 83.3%. However, separate results regarding panurethral strictures were not given. A particular advantage of lingual mucosa is that it can be harvested in continuity across the midline with the opposite side of the tongue, allowing a graft of sufficient length for panurethral strictures.

Prepuce and penile skin in the form of flaps or grafts are recognized alternatives for this type of reconstruction and are mentioned in the Table 1. In experienced hands, oral mucosal grafts measuring 10×1.5 cm can routinely be harvested from each inner cheek. If necessary, lingual grafts can be harvested in addition. A great number of our patients who have LS have scarred prepuce and glans and already had circumcision. In LS, no form of genital skin can or should be used. Preputial/distal penile skin graft was described for dorsal onlay anterior urethroplasty. In most studies, panurethral stricture patients were a minority [46, 47]. Most failures occurred if the skin graft was placed onto the penile urethra. Although previous circumcision did not preclude the use of penile skin, buccal mucosa was recommended as the best choice if the shaft skin was not abundant [46].

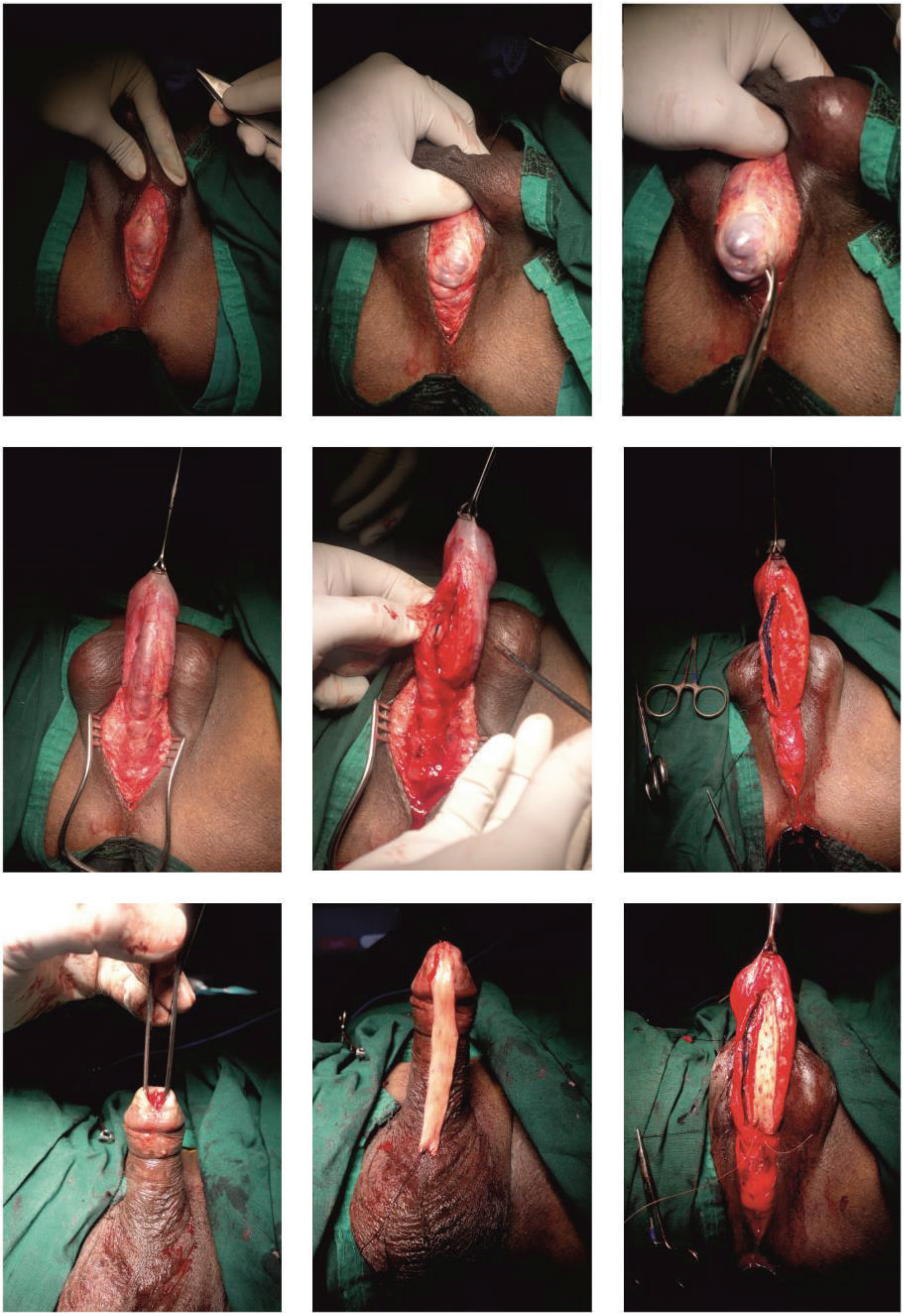


Figure 4: Kulkarni operation.

Postauricular skin has also been used as a good alternative for men with panurethral strictures with high success rate [48–50]. Postauricular skin is thin and has a dense subdermal plexus, and, therefore, graft take and functional outcomes are superior to other nongenital skin grafts. However, Andrich and Mundy cautioned that no skin graft should be used for urethroplasty in LS patients. LS is a skin disease and can also affect any skin graft in due course [49].

Another subject of controversy is the location for graft placement. Ventral graft placement, particularly in the pendulous urethra, is usually associated with poorer results. In the bulbar urethra, similar results can be expected, as long as ventral grafting is not used for long and complex strictures. A flap or a two-stage procedure is advocated by some authors for these strictures [46]. Dorsal graft placement usually produces the best outcomes and, therefore, is the method of choice in panurethral strictures [6, 23, 51–53]. Although doubled-sided dorsal plus ventral oral mucosa grafting has also been suggested for bulbar urethroplasty, the authors did not recommend its use for strictures measuring more than 4 cm in length [54]. Therefore, this technique is not indicated in long-segment or panurethral stricture disease.

Colonic mucosa has been employed for the reconstruction of panurethral stricture disease [55]. This graft is harvested from sigmoid colon using a laparoscopic approach or by a lower abdominal paramedian incision. Full-thickness grafts of 12 to 15 cm in length of sigmoid colon mucosa can be obtained and the colon continuity is immediately restored by an end-to-end anastomosis. An unstretched colonic mucosa graft is trimmed and sized to an appropriate individual need (ranging from 15 to 22 cm in length and 3 cm in width) and is tubularized over a 16 to 18 Fr fenestrated or fluted silicone catheter with interrupted 5-0 absorbable suture to create a neourethra. An end-to-end anastomosis is performed between the neourethra and the proximal end of the native urethra. The distal end of the neourethra is pulled through the glans tunnel to form the neomeatus. Xu et al. reported their experience with 35 patients who underwent colonic mucosal graft urethroplasty for complex, long-segment urethral strictures, ranging from 11 to 21 cm in length (mean 15.1). Five (14.2%) of these patients developed recurrent strictures. However, 3 of the recurrences were not related to the urethroplasty. Therefore, they concluded that tubularized urethroplasty using colonic mucosa grafts was successful and had a lower recurrence rate than patch urethroplasty. Nonetheless, this procedure needs further investigation and confirmation and, therefore, should be reserved as an alternative in complex patients where other options are not available or possible.

5.3. Combination of Flaps and Grafts. The exclusive use of long flaps for complex or panurethral strictures may be a technically challenging ordeal and are usually associated with long operating times and morbidity due to positioning and the surgical procedure itself. Furthermore, sufficient length of skin flaps may not be available, particularly in circumcised men or if LS is present. In such cases, a reasonable treatment option is to combine a shorter flap with a graft, and the graft placed proximally in the bulbar urethra [51]. A penile circular fasciocutaneous flap combined with an oral mucosa graft placed proximally was used by Wessells et al. in 7 patients with a mean stricture length of 18.3 cm [56]. The mean flap length was 12.6 cm (range 10–15) and mean graft length was 6.2 cm (range 3–9). The overall success rate was 88% at 16 months follow-up. Unfortunately, the authors did not mention results specific to panurethral strictures separately. The authors emphasized the importance of avoiding tubed reconstructions as these are associated with high risk of restricture and other flap-related complications.

Oral mucosa has become the graft material of choice for substitution urethroplasty, but at times it may be insufficient to completely reconstruct a long-segment or panurethral stricture. The combined use of oral mucosa and a genital skin flap has proved to be a reliable and durable alternative for single-stage reconstruction of long-segment or panurethral stricture disease [51].

5.4. Staged Procedures. At present, the majority of uncomplicated anterior urethral strictures can be successfully managed with a single-stage procedure. However, complex strictures associated with adverse local conditions, such as extensive scarred tissue formation of the urethra, infection, fistulation, prior multiple failed urethral reconstruction attempts, totally obliterated residual urethra, graft or flap-related factors, or following heavy irradiation, represent a challenge and are more appropriately treated with a staged procedure. A staged reconstruction may also be indicated in some long urethral strictures. All these situations are associated with unhealthy, poorly vascularized, and inelastic urethral and neighbouring tissues for urethral reconstruction. Although LS can be managed with a single-stage reconstruction, in some cases a staged procedure may be a reasonable option, as it may have a beneficial impact on the natural history of the disease [57–60]. A perineal urethrostomy for urinary diversion avoids continuous extravasation into the corpus spongiosum and promotes quicker and better urethral tissue healing.

The classical two-stage method was developed in the 1950s by Johanson [61]. The Johanson procedure is based on marsupialization of the strictured urethra, followed by a second surgical stage approximately 4–6 months after the first stage has healed (Figures 5 and 6). In the past, scrotal or perineal skin was used for urethral reconstruction. The great achievement of Johanson's technique was its use in all types of strictures, apart from initiating an era of urethral reconstructive surgery. The drawbacks of this technique resulted from the use of hair-growing scrotal and perineal skin, which lead to chronic urinary tract infection, abscesses, lithogenesis, fistulation, sacculation, and diverticula formation in the reconstructed urethra.

In the 1980s, Schreiter reported a two-stage mesh graft procedure in an attempt to avoid the use of scrotal or perineal skin by using a hairless skin graft which is transferred to a two-stage procedure [62, 63]. Although this technique can be employed in every type of stricture, apparently its best indication is in complex strictures, especially associated with severe tissue scarring and absence of healthy penile skin for urethral reconstruction.

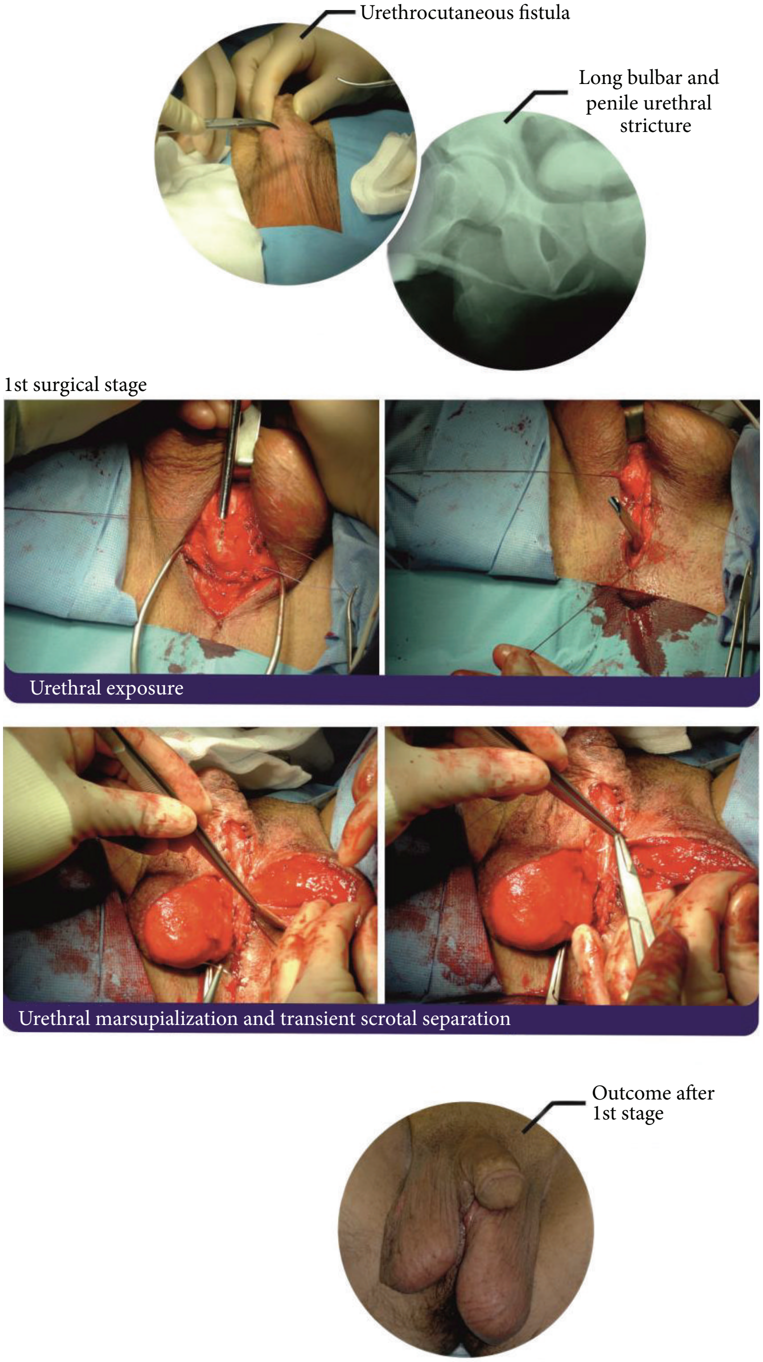


FIGURE 5: First stage of Johanson reconstruction with OMG inlay of panurethral stricture.

More recently, other authors have reported on a two-stage Johanson-type urethroplasty with oral mucosa grafting for anterior urethral strictures. For penile urethral strictures, Patterson and Chapple favor a two-stage procedure with dorsal onlay oral mucosa grafting after complete excision of the scarred urethra [64].

Staged reconstructions are associated with significant inconvenience to some patients, exposing them to an increased risk of morbidity due to multiple general anesthetics. Additionally, revision is common after two-stage operations and in one series half of the patients ended up needing a three-stage repair [65].

5.5. Tunica Albuginea (Monseur) Urethroplasty. In 1969, Monseur described a procedure by which a neourethra was created and its lumen continuity was maintained by the tunica albuginea through a supraurethral or subcavernosal groove without the need of a graft or flap [66]. Recently, there has been some renewed interest in this technique and various

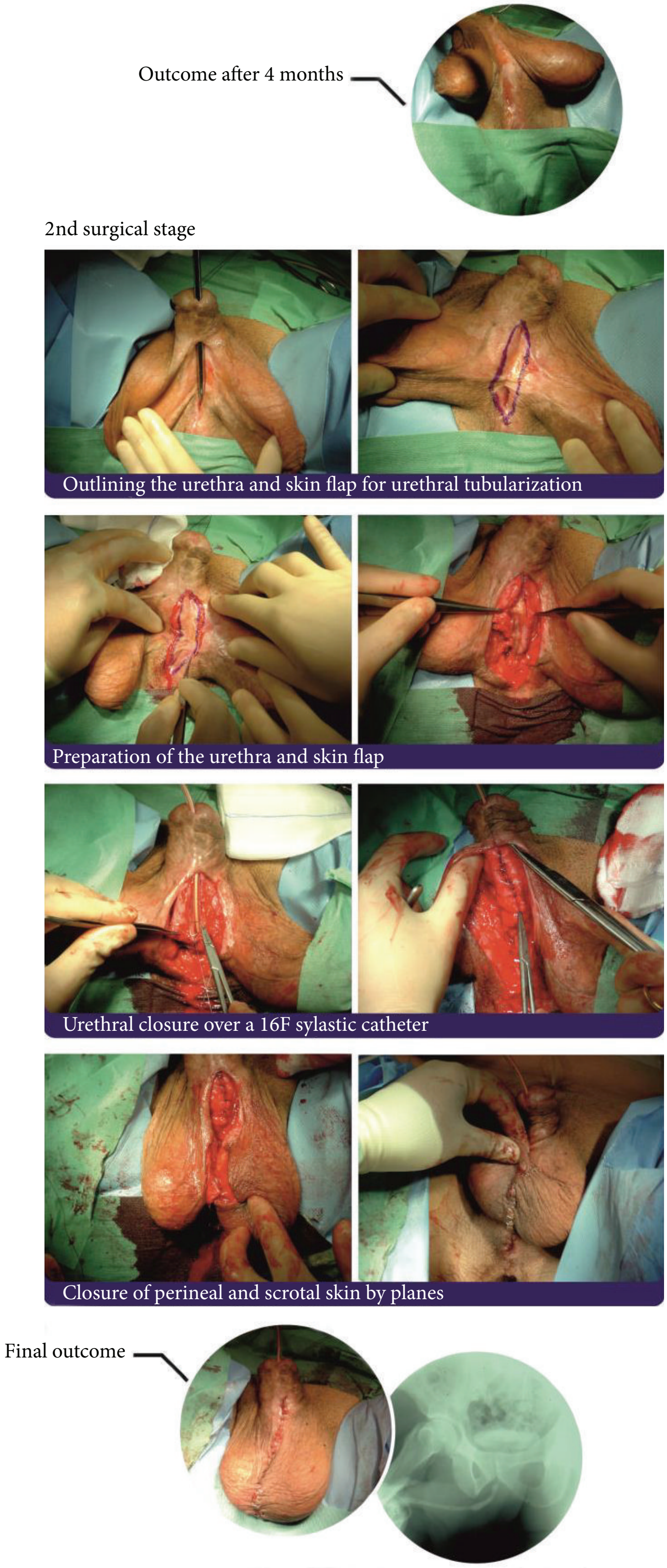


Figure 6: Second stage and closure.

reports have been published on the use of Monseur's tunica albuginea urethroplasty for short- and long-segment urethral strictures with acceptable success rates [67, 68]. The authors reported on the utility of this technique in cases where oral mucosa urethroplasty is not feasible due to lack of healthy oral mucosa associated with tobacco chewing or need of very long grafts to bridge panurethral strictures [69]. The authors described some similarity with the tubularized incised plate (TIP) urethroplasty described by Snodgrass and Bush, where the tunica exposed after incision of the urethral dorsal plate forms the roof of the neourethra and has stood the test of time for that purpose [70]. The authors argue that flap procedures are considered extremely labor-intensive, tedious, and among the most difficult in reconstructive urology [32]. Oral mucosa graft procedures, although very successful in medium-sized strictures, may not be feasible in very long strictures. Because some studies have shown that, even in dorsal onlay grafting, oral mucosa and penile skin grafts have shown similar results, while both proving superior to flaps, these authors concluded that it is not the type of graft, but rather the site of graft that is ultimately responsible for the success of the procedure [71]. Other studies have reported that a ventral onlay graft has a significant disadvantage over a dorsal onlay. It is claimed that complications are decreased if the graft is placed dorsally over the urethral groove [72]. Based on the concept advocated by Monseur, Barbagli et al. introduced the dorsally placed (onlay) graft technique and postulated that dorsal graft placement is superior as it allows better mechanical support for the graft and a richer and predictable vascular blood supply for the graft from the underlying corpora cavernosa [73, 74]. So if it is assumed that dorsal onlay grafts yield results better than ventral, then it must be the site of graft placement rather than the type of graft material that is ultimately responsible for the better success rates [75]. Lastly, the authors claim that Monseur's tunica albuginea urethroplasty is easy to perform, with short learning curve, without graft morbidity, requiring less time and resources, and success rates are comparable to oral mucosa urethroplasty. Tunica albuginea appears to be sufficient to allow regrowth of urethral epithelium and a patent distensible lumen if proved by urethrosccopic biopsy. However, we think that further studies are necessary.

6. Success and Complications

Generally, urethroplasty has excellent success rates and far exceed those found with direct vision internal urethrotomy. Serious complications following urethroplasty are relatively uncommon, 3% of them occurring in the early postoperative period and 18% in a late follow-up period [76]. Most reports in the literature contain heterogeneous data, that is, different types of strictures treated by different modalities and surgeons. When complications are mentioned, they are mixed for all the procedures. Another pitfall found in the literature is in comparing success rates in different series, as these have variable definitions of treatment failure. Therefore, consensus in reconstructive urology needs to be established in the future.

Table 2: Major and minor complications of "panurethroplasty"*.

Major	Minor
Early	Early
Hematuria	Oral numbness
RUG leak	Drooling when eating or Speaking
Oral discomfort	Speech impairment
Wound dehiscence	Perineal hypoesthesia
Wound tightness	Scrotal hyperesthesia
Epididymitis	Stensen's duct squirting
Penile ecchymosis	Penile pain
Penile swelling	Penile shortening
Penile skin ischemia/necrosis	Postvoid dribbling
UTI	Stress incontinence
Wound infection	Urine splaying
Late	Late
Rectal injury	Recurrent stricture
Urosepsis	Sexual dysfunction
	Chordee
	Fistulation

*Generally, similar and common to any urethroplasty.

Generally, complications of urethroplasty are directly related to location of stricture, length of stricture, operative technique, and type of transfer tissue employed (Table 2). Complications after urethroplasty can be divided into major and minor groups, occurring early or late. Most minor complications are usually mild and temporary and may be amenable to simple corrective procedures. Major complications are usually severe and complicated and result in failure of urethroplasty. In this review we will focus on complications associated with the reconstructive procedures of long-segment anterior urethral or panurethral strictures (Table 3).

Oral mucosal grafts are now considered the standard substitution material for urethral surgery. Surgical procedures involving oral mucosa onlay have better success rates and less morbidity compared with fasciocutaneous flaps [23, 46, 73, 74, 76]. One report has mentioned complication rates of fasciocutaneous flaps between 3% and 56% [77]. In a multi-institutional study, Warner et al. reported on the complication rates of different surgical techniques to repair long-segment and panurethral strictures [23]. The complication rate was higher in the fasciocutaneous cohort compared with those without a flap (32% versus 14%, resp.; $P = 0.02$). In this review, a 2-stage Johanson urethroplasty was not as successful as the buccal mucosal graft procedure (BMG) (64% versus 82.5%, resp.). It was found that 2-stage Johanson urethroplasties performed with skin had a higher failure rate than those performed with a BMG (66.7% recurrence rate versus 28.3%, resp.). Meticulous follow-up of patients after long-segment or "panurethroplasty" may show an important percentage of early and late complications. Perineal neuralgia or neuropraxia is a well-known

Table 3: Complications by most common techniques for pan-urethroplasty.

Type of surgery	Early	Late	Recurrence
FC flap	Transient pain and numbness Fistula (resolved)	Fistula	37.5%
OMG	UTI Penile edema Bleeding	Chordee Fistula ED Oral and lip discomfort numbness Cold glans	17.5%
Second-stage Johanson	Wound dehiscence UTI Scrotal abscess Penile numbness Epididymitis	ED Graft contracture Fistula Chordee Cold glans	35.7%
PU and definitive 1st-stage Johanson	Wound dehiscence UTI Transient pain and numbness	Chordee Fistula	24.1%
FC flap + graft	Wound hematoma PE Penile skin ischemia	Fistula Chordee	23.5%

FC: fasciocutaneous; OMG: oral mucosal graft; UTI: urinary tract infection; ED: erectile dysfunction; PU: perineal urethrostomy; PE: pulmonary embolism. Adapted from [23].

complication of bulbar and posterior urethroplasty, or any surgery performed in the exaggerated lithotomy position (i.e., radical perineal prostatectomy and urorectal fistula repair) [78–80]. The most common position-related complications of complex urethroplasty include superficial peroneal nerve neuropraxia, rhabdomyolysis, and lower extremity compartment syndrome. Although several causes of neuropraxia have been identified, the mechanical nerve compression seems to be the most common. It usually resolves spontaneously within 6–8 weeks. Recent studies have reported much lower position-related complication rates not exceeding 3% due to shortening of overall lithotomy position and meticulous protocol of patient protection during this type of surgery. In the authors' personal series, the severe neuropraxia rate has been in accordance with these reports.

Although most complications are minor, with little impact, and easily corrected, they seem to occur in a higher number than previously published (40%) [76]. These complications are important to the patient and should be discussed in the counseling before surgery.

7. Impact on Sexual Function

Impairment of male sexual function (penile sensation, erectile, and ejaculatory dysfunctions) are usually underreported. However, this scenario has been changed recently. In 2001, Coursey et al. reported a study on erectile function after anterior urethroplasty based on a questionnaire evaluation of erectile dysfunction. ED occurred in 19% of patients after OMG and 27% after anastomotic urethroplasty. Although he postulated that men with a long stricture might be at increased risk for transient erectile changes, the overall postoperative sexual dysfunction rate was no higher than circumcision [81]. Based on validated inventory questionnaires, such as the International Index of Erectile Function (IIEF-5) or the O'Leary Brief Male Sexual Function Inventory (BMSFI), the majority of the studies published recently have not shown that urethral reconstructive surgery impairs erectile function and sexual drive. Ejaculatory function was even improved in the younger ages [82–86]. Although erectile dysfunction has been associated with urethroplasty operations, its incidence is largely unknown. A 1% incidence of *de novo* erectile dysfunction after anterior urethroplasty was found in a meta-analysis study by Blaschko et al. However, in most cases the erectile dysfunction was transient and resolved within the first 12 months [85]. Another study reported an incidence of transient erectile dysfunction after anterior urethroplasty in approximately 40%, although recovery was observed in most by 6 months [83]. In 2006, the same authors had described a relationship between older age and a higher incidence of erectile dysfunction after surgery. Nonetheless, overall, men had not reported a decline in erectile dysfunction or sexual drive after urethroplasty [82]. In 2015, Xu et al. published a study dealing specifically with the impact of erectile dysfunction on complex panurethral stricture disease. They concluded that the surgical reconstruction with the use of grafts (buccal, lingual, and colonic mucosa) had limited effect on erectile function. The only adverse factor was extension of the stricture to posterior urethra, in which case an impairment was observed [86]. Ejaculatory dysfunction was reported in patients after ventrally placed flaps or grafts, possibly due to urethrocele formation [87]. However, no ejaculatory dysfunction has been reported in patients after dorsal onlays [77, 87].

8. Conclusion

One-stage repairs with BMG offer an excellent option for patients with long-segment and panurethral stricture disease. In cases with obliterative or absent urethral plate, a 2-stage

Johanson urethroplasty with BMG offers a viable alternative. In cases of LS, 1-stage BMG has better outcomes than a 2-stage repair. If BMGs are not available, FC flaps offer similar success; however, these are associated with higher rates of complications. Skin grafts should be avoided, unless no alternatives exist. Finally, the valuable role of PU cannot be understated in the setting of multiple failed urethroplasties.

The options currently available to reconstruct the urethra are in permanent development and attention should be focused on both old and new concepts. No surgical technique should compromise penile length, cause chordee, and affect cosmesis. Oral morbidity should be given attention after OMG to avoid permanent late sequelae in mouth function. Critical attention should also be given to sexual function as any urethral reconstructive method can eventually cause its occurrence.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Review Article

Posterior Urethral Strictures

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Pelvic fracture urethral injuries are typically partial and more often complete disruptions of the most proximal bulbar and distal membranous urethra. Emergency management includes suprapubic tube placement. Subsequent primary realignment to place a urethral catheter remains a controversial topic, but what is not controversial is that when there is the development of a stricture (which is usually obliterative with a distraction defect) after suprapubic tube placement or urethral catheter removal, the standard of care is delayed urethral reconstruction with excision and primary anastomosis. This paper reviews the management of patients who suffer pelvic fracture urethral injuries and the techniques of preoperative urethral imaging and subsequent posterior urethroplasty.

1. Introduction

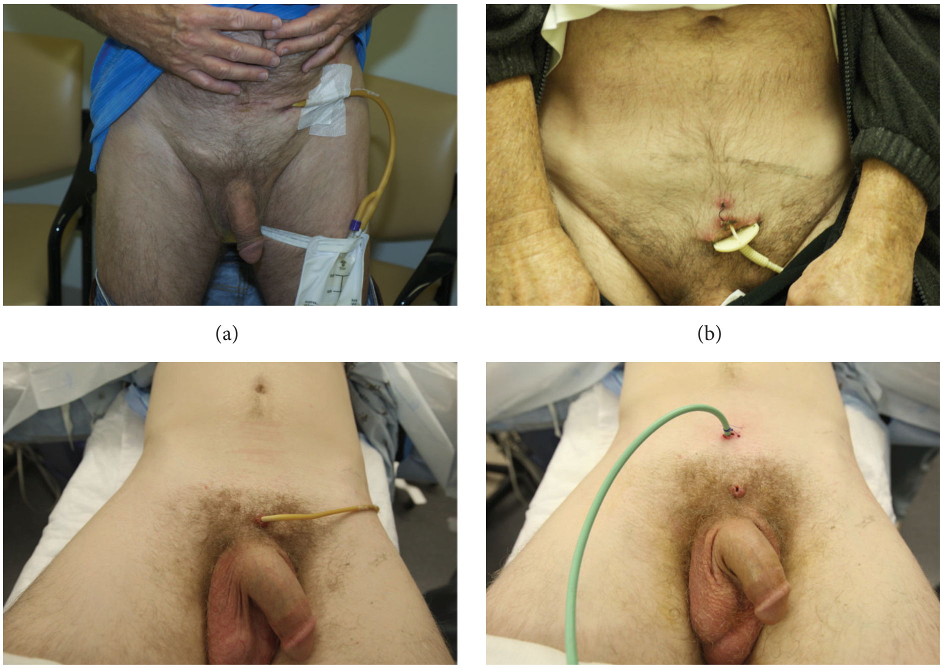
Pelvic fracture trauma in males, often secondary to motor vehicle trauma or pelvic crush injuries, can be associated with injuries to the posterior urethra, especially where there is pubic symphysis diastasis or there are displaced inferomedial pubic bone fractures [1]. The term “prostatomembranous disruption” is often used to describe these injuries, and this terminology suggests that the transection occurs at the junction of the prostatic and membranous portions of the posterior urethra. However, more recent studies, including an autopsy review of male patients who sustained pelvic fracture related urethral injuries and died of associated multiple trauma, revealed that the injuries are generally membranous and distal to the urogenital diaphragm [2]. There can be proximal or distal extension, but the injury generally remains distal to the verumontanum of the prostate. As long as the bladder neck remains intact, continence should be maintained in these patients after repair. Additionally, in many patients, there also remains a significant rhabdosphincter contribution, as demonstrated by video-urodynamic testing after reconstruction [3].

The classic sign of urethral injury in a patient with a pelvic fracture is blood at the urethral meatus, but other symptoms such as bladder distension, inability to void, and perineal hematoma should raise a high index of suspicion as well. Older texts emphasize the finding of a high riding prostate on digital rectal examination, but this is not a reliable finding on physical exam.

2. Initial Evaluation and Management

A retrograde urethrogram (RUG) is indicated when a urethral injury is suspected and will typically reveal significant extravasation due to a partial tear or, more often, a complete disruption (Figure 1). Initial management should be placement of a suprapubic tube as the most effective and immediate way to drain the bladder. The ideal suprapubic tube is no less than 16 French in size and positioned in the midline 2-finger breadth above the pubic symphysis. Subsequently, options include primary realignment or suprapubic diversion for several months followed by posterior urethroplasty.

The purpose of primary realignment is to approximate the severed ends of the urethra to potentially avoid subsequent stricture formation. Historically, this was performed through an open approach with an attempt at immediate repair. This procedure was mostly abandoned due to the prohibitively high rates of erectile dysfunction and incontinence that resulted compared to those who underwent delayed repair [4]. The advancement of endoscopic technology, however, has allowed primary endoscopic realignment (PER) of



(a) (b) (c) (d)

Figure 1: (a) Laterally placed suprapubic tube. (b) Small "pigtail" catheter of inadequate caliber. (c) Suprapubic tube placed below the ideal location. (d) Suprapubic tube repositioned midline 2-finger breadth above the midline pubic symphysis.

the urethra without the potentially damaging extensive manipulation that was required for immediate open repair and is now attempted routinely in some centers.

Stricture formation can potentially be avoided with this approach. However stricture rates remain high after PER and it is essential that these patients be followed in the long term. A recent meta-analysis reported a 49% rate of stricture formation after PER, yet this is likely an underestimate as the literature consists of mostly small case series that are retrospective and have variable follow-up that does not always include cystoscopy to confirm patency [5].

While sometimes successful, PER can have unintended consequences when strictures are not treated appropriately. In a recent study, the mean time to definitive resolution of stenosis was dramatically longer in patients who underwent PER (122 months versus 6 months) because they underwent multiple endoscopic interventions without resolution of their stenosis [6]. Repeated, not only are unsuccessful interventions costly to the healthcare system, but they can also expose the patient to painful self-dilations or office dilations as well as the potential for acute urinary retention requiring emergency management.

The purpose of limiting the immediate management to placement of a suprapubic tube is to allow a successful, definitive repair once the tissues have had time to heal, typically after 3 months. Placement of a suprapubic tube can easily be accomplished in any trauma center without the need for immediate reconstructive expertise, and the patient can subsequently be referred for further management. In this situation, posterior urethroplasty is highly successful, with a patency rate of 97.6% at our own institution.

Although the benefits of primary realignment are the subject of controversy, it should be emphasized that when a stricture develops after primary realignment, the subsequent management is not controversial. The best approach is suprapubic tube urinary diversion for several months followed by urethral reconstruction. Management with dilations, urethrotomies, and/or self-catheterization should not be advised in an attempt to avoid open surgery as these options manage a chronic problem whereas a properly performed urethroplasty is almost always curative.

3. Preoperative Planning

3.1. Three-Month Delay. We wait 3 months from the time of injury or catheter removal in cases of failed primary realignment before performing urethroplasty to allow time for the initial extravasation to heal, hematoma to resolve, and the extent of the injury to become clearly defined. It has been shown that, after manipulation, several months of "urethral rest" is required before anterior urethral strictures become clearly defined [7]. When there is a pelvic fracture associated injury to the posterior urethra, initial imaging reveals extravasation, whereas imaging 3 months after injury typically confirms no extravasation and clear delineation of the location and length of the defect. Recent publications indicate that the delay is often a minimum of 3–6 months. However, the interval between initial injury and urethroplasty can exceed one year when there are associated injuries [8–12].

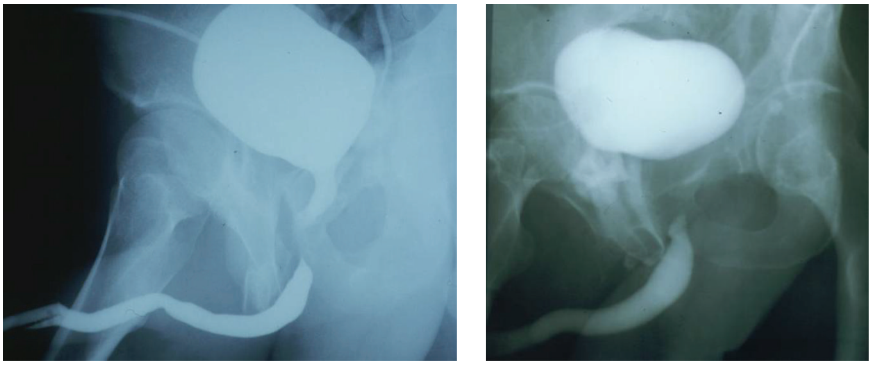
3.2. Suprapubic Tubes. Although the ideal suprapubic tube is at least 16 Fr, midline, and well above the midline pubic symphysis, patients are often initially managed with tubes that are far lateral to the midline or just above the symphysis. In some cases, very small caliber "pigtail" catheters are placed (Figure 1). Small caliber pigtail catheters are especially prone to encrustation and ultimately urinary retention. Moreover, catheters placed just above the symphysis are more uncomfortable than catheters placed in a higher position away from the bone. When patients are referred for posterior urethral reconstruction and have tubes of inadequate caliber, or if the tube is not in the ideal position, it is our preference to percutaneously place a new 16 Fr tube. This is generally done as soon as possible when the caliber is small and in no less than 1 month prior to urethroplasty so there will be an established stable tract at the time of surgery.

The main benefit of having the suprapubic tube midline in the ideal location with an established tract is that this facilitates the surgery and prevents the need for a temporary vesicostomy. During posterior urethroplasty with the patient in the lithotomy position, after perineal exposure is achieved and the urethra is transected, a metal sound is generally advanced through the established tract, and perineal dissection proceeds towards the tip of the sound until the sound can be seen and advanced into the perineum. When the caliber of the tract is inadequate, sounds will not advance without dilation at the time of the surgery. This can be associated with bleeding and compromise of the tract. When the tube is just above the bone, a very acute angle is needed to advance the sound through the bladder neck. Moreover, when the tract is lateral to the midline, the rigid sound cannot be reliably advanced medially towards the midline bladder neck and then distally along the posterior urethra. One option is to create a temporary vesicostomy. However, this adds considerable time and morbidity to the reconstructive surgery and therefore this is not our preference.

3.3. Preoperative Urethral Imaging and Cystoscopy. Prior to definitive urethral reconstruction, urethroscopy, antegrade cystoscopy, and simultaneous antegrade cystourethrogram and retrograde urethrogram (RUG) provide a definitive diagnosis of the exact length and location of the defect. One common imaging technique is for the bladder to be filled with contrast by gravity through the suprapubic tube and for a RUG to be performed as the patient is asked to Valsalva and attempt to void. This attempt to void can open the bladder neck and allow filling of the posterior urethra proximal to the obliteration, and the length of the defect will be determined (Figure 2(a)). However, in many cases, the patient cannot relax to void when the urethra is obliterated and contrast is being injected through the penis. When the bladder neck is intact, the appearance will be as shown (Figure 2(b)). The distance between the bladder and the distal end of the defect is not the length of the distraction defect because the prostatic urethra is not visualized. In a recent study where the goal was to determine if the type of urethroplasty could be predicted based on certain features from the preoperative imaging, 38% of the 100 study patients evaluated with a Valsalva cystourethrogram and RUG were excluded because there was no visualization of the urethra below the bladder neck [7].

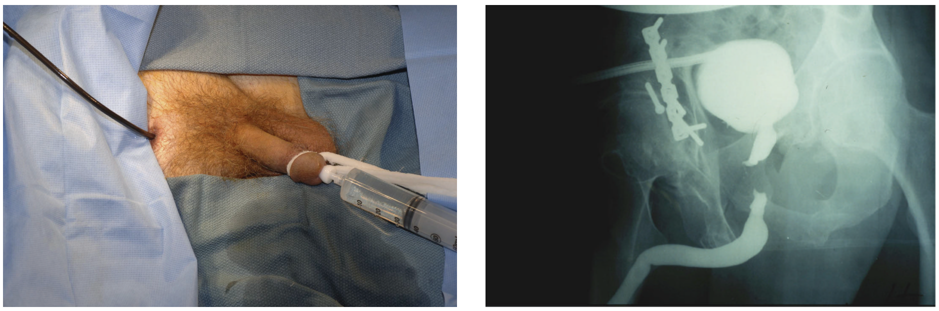
Our preferred approach is to first perform antegrade cystoscopy with the patient prepped and draped in the oblique position after a 14 × 17 scout film is obtained to confirm proper position and penetration. Antegrade cystoscopy is important to inspect for bladder stones that may need to be removed preoperatively and also provides assessment of the bladder neck. An open bladder neck at rest suggests that there may be an increased incidence of incontinence subsequent to urethral reconstruction. Iselin and Webster identified 15 patients who sustained pelvic fracture urethral injuries and had an open bladder neck at rest [13]. Six were continent and 8 were incontinent after urethroplasty. However, MacDiarmid et al. identified 4 patients that had an open bladder neck at rest and all of these patients were continent after surgery [14]. Although some surgeons occasionally perform bladder neck reconstruction at the time of posterior urethroplasty [15], most do not feel this is necessary given the observation that an open bladder neck at rest does not reliably predict postoperative incontinence. When we observe an open bladder neck at rest, the patient is counseled that there may be an increased incidence of postoperative incontinence, but this finding does not influence our management.

3.4. Preoperative Urethral Evaluation: Urethral Imaging. Once the scope is advanced through the bladder neck, the location of the proximal aspect of the injury is noted, and this is almost always distal to the verumontanum of the prostate within the membranous urethra. With the tip of the scope at the level of the obliteration, full-strength contrast is injected, which will then backfill the posterior urethra and bladder. Simultaneously, a RUG is performed. Our preferred technique for performing a RUG is to place a gauze around the coronal sulcus to place the penis on stretch and inject contrast through a cone-shaped Taylor adaptor (Cook Urological) connected to a 60 cc syringe filled with full-strength contrast (Figure 3). Many published textbooks advocate the advancement of a catheter into the fossa navicularis and inflation of the balloon with 1–3 cc of contrast to form a seal. However, the balloon caliber of catheters of several different sizes when inflated with only 2 cc of fluid or air is approximately 59 French and the normal caliber of the adult anterior urethra is approximately 30 French except at the level of the urethral meatus and fossa navicularis where the caliber is approximately 24 French (Figure 4(a)). Therefore, the balloon will dilate the normal distal anterior urethra, which can be associated with considerable pain and even stricture disease of the fossa navicularis. We have seen patients referred for strictures initially limited to the bulbar urethra who then developed narrow caliber fossa strictures after undergoing painful urethral imaging where the technique included balloon inflation within the fossa navicularis (Figure 4(b)).



(a) (b)

Figure 2: (a) After the bladder is filled with contrast through the suprapubic tube, a RUG is performed as the patient is asked to attempt to void. If the bladder neck opens, contrast fills the prostatic urethra, and the membranous urethral defect is seen. (b) When the bladder neck does not open, the length of the defect cannot be determined accurately.



(a) (b)

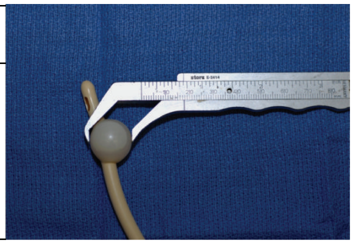
Figure 3: (a) A RUG is performed as contrast is simultaneously injected into the posterior urethra through the flexible cystoscope, with the tip in the distal prostatic urethra. (b) Imaging accurately demonstrating the length and location of the defect.

Simultaneous antegrade and retrograde imaging and endoscopy performed with proper technique will clearly define the exact length and location of the defect. Other imaging modalities that can be used include MRI and ultrasound [16]. However, we have never found an indication to perform these additional tests. Fluoroscopy offers the advantage of dynamic real time imaging. However, disadvantages include a reduced field of view and decreased resolution compared to conventional radiographs. We prefer flat plate imaging using digital cassettes that can be digitized and stored electronically and also printed on 14 × 17 film. Although magnification and positioning can influence the scale, we have observed that the length of the obliteration measured directly on the film very accurately corresponds to the length of the defect at the time of surgery. Most defects are 1 to 3 cm in length.

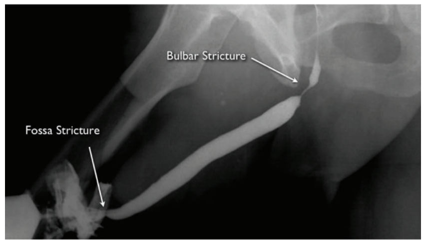
Defining the exact location of a stricture is also critical to management. Although pelvic fracture trauma typically injures the posterior urethra, if there is also straddle trauma at the time of the pelvic fracture, the injury can be to the bulbar urethra, which changes the treatment strategy. For example, a man who sustained pelvic fracture trauma during a race car accident was found to have significant extravasation on a RUG on the day of the injury and managed with a laterally placed suprapubic tube. Delayed imaging and antegrade cystoscopy confirmed a proximal bulbar urethral defect and a normal membranous urethra (Figure 5). Although both traumatic proximal bulbar and membranous disruptions are managed with excision and primary anastomosis, bulbar urethroplasty does not require antegrade access to facilitate identification of the patent proximal segment. If the injury was membranous, then a new midline suprapubic tube would have been placed to facilitate subsequent antegrade access to the proximal segment at the time of posterior urethroplasty. However, since antegrade access is not required for bulbar urethroplasty, the placement of a new midline tube was not required.

3.5. Preoperative Vascular Evaluation. The anterior urethra has a dual blood supply, with an additional minor contribution provided by perforating vessels between the corpora cavernosa and the corpus spongiosum. The bulbar arteries enter the corpus spongiosum at the level of the most proximal bulbar urethra and provide antegrade flow to the corpus spongiosum of the anterior urethra. In addition, the dorsal arteries course within the neurovascular structures along the dorsal aspect of the penis superficial to the corporal bodies and supply the glans penis, which is the distal expansion of

cc	Fr
1	39
2	50
3	56



(a)



(b)

Figure 4: (a) Catheter balloon inflation with only 1–3 cc of air or fluid is associated with balloon inflation well beyond the normal caliber of the normal fossa navicularis. (b) Repeat RUG demonstrating, in addition to the previously seen bulbar stricture, a new fossa navicularis stricture that developed after a RUG was performed using fossa balloon inflation technique.

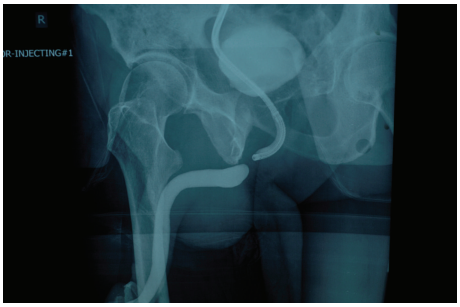
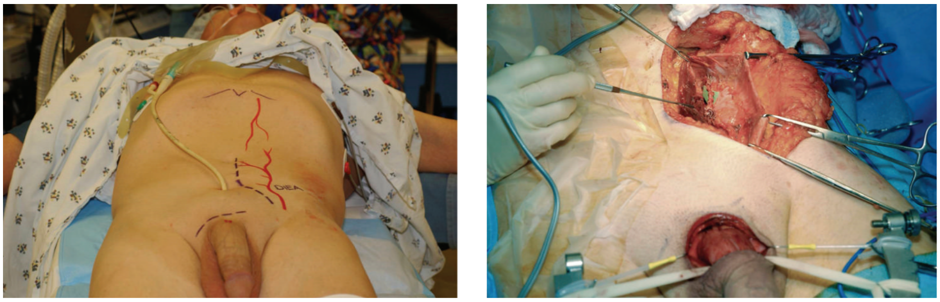


Figure 5: Simultaneous antegrade and retrograde urethral imaging demonstrating a bulbar urethral obliteration, further confirmed with antegrade cystoscopy.

the corpus spongiosum. This provides a secondary blood supply to the anterior urethra as the blood courses in retrograde fashion along the corpus spongiosum. When the urethra is completely transected at the departure of the anterior urethra, any patent bulbar arteries are ligated or cauterized. The anterior urethra then survives as a flap based on the retrograde dorsal artery contribution in addition to perforating vessels. Although unpublished, it has been observed by several reconstructive urologists that, in rare cases, long segment bulbar strictures developed as an ischemic complication of posterior urethroplasty. The mechanism of the ischemic stenosis was presumed to be compromised of the bulbar artery supply during surgery in patients who suffered perineal trauma that compromised dorsal artery supply. We have observed cases of ischemic stenosis in patients with hypospadias who developed discreet bulbar strictures and were treated with a urethral stent [17]. Prior to stent placement, these patients were noted on urethroscopy to have a normal caliber anterior urethra distal to the bulbar stricture. Subsequent to stent placement, they developed severe panurethral disease. This makes sense anatomically as hypospadias and corrective surgery are associated with a compromise of the corpus spongiosum distally and the associated retrograde blood supply to the more proximal anterior urethra. These patients were likely “bulbar dependent,” and stent expansion compromised the antegrade bulbar artery flow distal to the stent. Therefore, in addition to antegrade cystoscopy and contrast imaging, we perform a preoperative vascular evaluation to identify patients who have severe arterial inflow compromise to both dorsal arteries and perform penile revascularization prior to urethral reconstruction in selected cases. Penile revascularization provides a microvascular anastomosis of the inferior epigastric artery to the dorsal artery of the penis (Figure 6).

Erectile dysfunction and pudendal vascular injuries are highly associated with pelvic fracture urethral disruptions. A recent meta-analysis revealed that 34% of all patients with pelvic fracture urethral injury developed erectile dysfunction, even prior to any treatment other than suprapubic tube placemat [18]. In a study by Shenfeld et al., 25 patients who sustained traumatic posterior urethral disruptions were evaluated with nocturnal penile tumescence testing [19]. Eighteen patients (72%) were found to have erectile dysfunction, and these patients underwent a penile duplex with pharmacologic erection that revealed arterial inflow impairment in 5/18 patients. The remaining patients were considered to have a neurogenic etiology of their erectile dysfunction. Davies et al. performed a penile duplex testing on 56 men who sustained posterior urethral disruptions and identified 25 men with vascular compromise. These patients underwent arteriogram. Twenty-one had reconstitution of one or both pudendals, and 4 did not. These 4 patients underwent revascularization prior to urethral reconstruction, and no patient developed ischemic stenosis after surgery [20]. A limitation of this study is that it is not known if any of these patients would have developed stenosis if reconstruction had been performed without prior revascularization. This is an area of controversy. However, we believe vascular testing and revascularization in selected cases are justified based on the anatomic principals and the available data. Moreover, revascularization will often successfully treat the erectile dysfunction associated with pelvic fracture injuries [21].

3.6. Posterior Urethral Reconstruction: Preparation and Patient Positioning. Prior to definitive repair, patients are placed in high lithotomy during a physical examination to assess hip flexion and ability to tolerate this position. Some patients may have unresolved back or other orthopedic problems, which may then be exacerbated by prolonged lithotomy positioning. In our series of 85 patients, the longest delay was 19 months. This patient had severe compromise of hip flexion



(a) (b)

Figure 6: Inferior epigastric artery to dorsal artery penile revascularization, shown subsequent to skin marking (a) and during surgery (b).

(a) (b)

Figure 7: (a) Modified Skytron Custom 6000 Surgical Table with pelvic tilt mechanism (highlighted in yellow). (b) Patient positioned in exaggerated lithotomy.

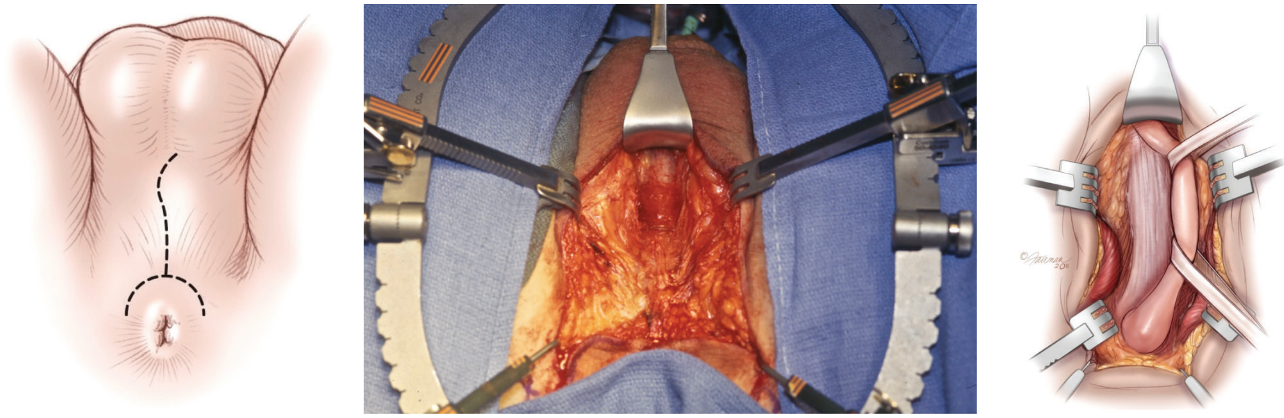
that persisted more than 12 months after the injury. With ongoing physical therapy, mobility returned to normal, and positioning was safely accomplished without compromise. A urine culture is sent the week prior to surgery. The specimen is obtained by clamping the suprapubic tube and then unclamping the tube 20 minutes later over a specimen container. The sample is then obtained directly from the suprapubic tube and not the drainage bag. Any mixed growth is separately cultured. Patients are admitted the day prior to surgery for dual coverage antibiotics. Our protocol is to administer piperacillin/tazobactam and tobramycin but adjust the antibiotics if indicated based on the culture result. To date, no patient suffered the complication of a perineal infection, which can be associated with urethral compromise and stricture development.

Although some reconstructive urologists prefer a low lithotomy position, we prefer the exposure of exaggerated lithotomy. However, this position can be associated with severe complications including neuropraxia, compartment syndrome, and rhabdomyolysis [22–24]. Fortunately, neuropraxia is usually not permanent. Sensory deficits are more common than motor impairment, and the risk of a positioning complication is related to the time in lithotomy. One form of exaggerated lithotomy, often used for perineal prostatectomy, places hips under considerable flexion so that the thighs are parallel to the back and the floor. In a study by Holzbeierlein et al., of 111 men who underwent a radical perineal prostatectomy in this extreme lithotomy position with a mean duration of less than 3 hours, 23 (21%) suffered a positioning complication. Of these 23 patients, 17 had symptoms at the time of discharge, and 6 required physical therapy support for ambulation [25].

We use Skytron Custom 6000 Table modified by Jordan to offer an electronic pelvic tilt mechanism to cradle the pelvis as an alternative to raising the buttocks and placing a beanbag support (Figure 7(a)). In addition, stirrups are modified to provide additional extension so that hip and knee flexion is reduced. Foam padding is placed along the dorsal feet and anterior legs to evenly distribute the pressure (Figure 7(b)). We previously used gel pads but found that use of the softer foam pads reduced the incidence of temporary (24–28 hours) dorsal foot numbness. Extreme flexion of the hips and knees is avoided, and the boots are tilted so that there is no pressure on the calves.

3.7. Posterior Urethral Reconstruction: Surgical Technique

3.7.1. Exposure. A midline perineal incision is one option. We prefer an inverted "Y" shaped lambda incision to obtain generous exposure (Figure 8(a)). This is carried medial to the ischial tuberosities posteriorly and along the median scrotal raphe. Dissection then proceeds sharply through the subcutaneous fat longitudinally along the midline until the bulbospongiosus muscle is encountered. The Jordan-Simpson perineal retractor is used to facilitate exposure as shown (Figure 8(b)). Although other retractors are commercially available such as the Lone Star retractor, advantages of the Jordan retractor include the fixation of the ring and



(a) (b) (c)

Figure 8: (a) Lambda incision with the patient in the exaggerated lithotomy position. (b) Jordan-Simpson perineal retractor is used to facilitate exposure of the corpus spongiosum. (c) The corpus spongiosum is circumferentially mobilized along the bulbar urethra.

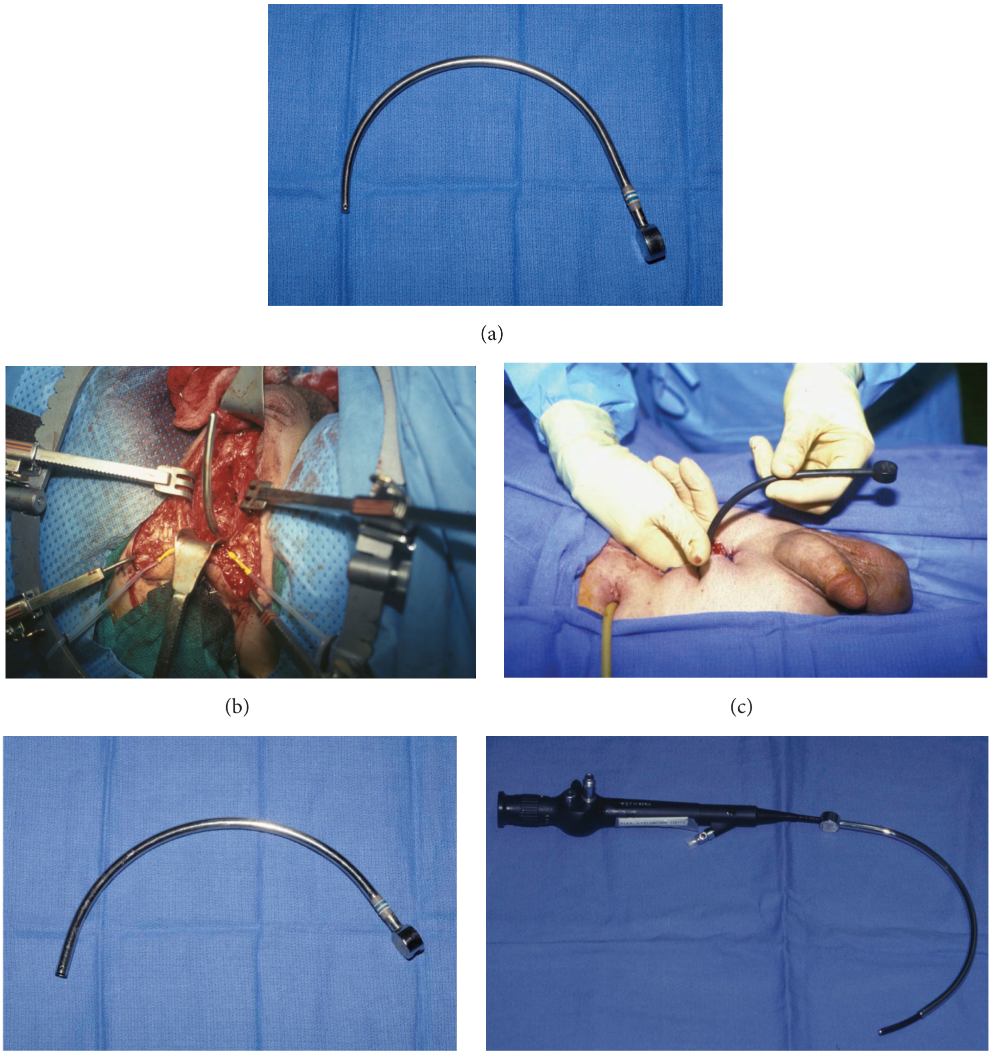
the ability to use a variety of different specialized blades in addition to the hooks used in the Lone Star system. In addition, tilt ratchets facilitate lateral retraction to facilitate exposure. The bulbospongiosus muscle is then divided and retracted laterally to expose the bulb. The bulb is detached from the perineal body and we find that the use of a bipolar cautery facilitates this dissection and maintains hemostasis to the extent that suction is seldom required. The urethra is then circumferentially mobilized from the penoscrotal junction distally to the departure of the anterior urethra proximally (Figure 8(c)). This is done sharply without the use of right angle clamps, which can tear the corpus spongiosum. The bulbar arteries are transected and cauterized if patent.

Several recent papers describe bulbar artery sparing anastomotic anterior urethroplasty [26, 27]. Although the use of artery sparing surgery during posterior urethral reconstruction has not been published, an abstract recently presented described the successful use of this technique in 9 patients [28]. Intraoperative ultrasound was performed, and the artery with the strongest signal was preserved. No patient developed a recurrent stricture with a mean follow-up of 10 months. This may possibly represent a future modification of operative technique.

3.7.2. Proximal Exposure and Scar Excision. Once the urethra has been adequately mobilized, it is transected at the distal aspect of the defect, which can be accurately located intraoperatively with the use of a 16 Fr catheter or bougie á boule. Subsequently, unless preoperative imaging suggests very short segment obliteration, we routinely separate the corporal bodies at the level of the triangular ligament and retract them laterally to improve proximal exposure and facilitate excision of the scar tissue, which is generally whitish in color and firm.

The suprapubic tube is then removed and a curved metal sound is advanced through the established tract into the bladder and then through the bladder neck, guided by feel, until the impulse of the tip of the sound can be palpated in the perineum as the sound is manipulated. This guides the dissection in the appropriate direction towards the patent proximal urethra. One option is to advance a Van Buren sound. Although these instruments are often readily available and familiar to most urologists, the fact that the instrument is curved only at the tip and tapered to a more pointed tip relative to the shaft of the instrument renders these instruments poorly suited to use in posterior urethroplasty, especially when an exaggerated lithotomy position is used. However, the semicircular Haygrove sound is designed to best follow the path from the suprapubic access to the membranous urethra (Figures 9(a) and 9(b)). The tip is curved and smooth, and the caliber is not greater than 16–18 Fr and, therefore, no tract dilation is required if the indwelling suprapubic tube was 16 Fr.

There are cases, however, when the tip of the sound may not be palpable. This may be due to the presence of very dense scar or malposition of the sound. This presents a significant challenge because if dissection proceeds in the wrong direction, what is entered may be the bladder or the posterior urethra proximal to the distal aspect of the patent urethra. This could essentially "bypass" the bladder neck and may lead to severe postoperative incontinence. This is a major limitation of using a solid sound that is guided blindly. A flexible cystoscope can be used in these cases, but since the active scope deflection is limited only to the tip of the scope, it may be difficult to advance the tip of the scope to the proper position, especially when the patient is in high lithotomy and the surgeon is positioned at the level of the perineum. To prevent the possibility of false passages, some surgeons perform rigid antegrade cystoscopy before the patient is prepped and draped in the exaggerated lithotomy position, advance the scope through the bladder neck and prostatic urethra, and then palpate the perineum to determine if the tip of the scope is palpable or not [29]. When the tip of the scope is not palpable, or if the suprapubic tube is laterally located, a temporary vesicostomy is created prior to lithotomy positioning and then taken down subsequent to the completion of the repair (Figure 9(c)). It was determined that the creation



(a)

(b) (c)

(d) (e)

Figure 9: (a) Solid Haygrove sound. (b) After dissection of the obliterative scar, the tip of the sound (placed through the suprapubic tract) can then be advanced through the patent proximal urethra into the perineum. (c) Temporary vesicostomy in a patient with a laterally placed suprapubic tube. (d) Gelman visualizing posterior urethral sound. (e) Flexible scope advanced through the hollow visualizing sound.

of the vesicostomy allows the surgeon to palpably identify the bladder neck before instrumentation of the posterior urethra and that this maneuver eliminates the occurrence of false passages and the misanastomosis of the anterior urethra to sites other than the apical prostatic urethra. While this maneuver can be effective, it adds considerable time and morbidity to the surgery.

It is for this reason that we prefer to always proceed with a midline suprapubic tube, even if this requires placement of a new tube no less than 1 month prior to urethroplasty to allow time for the tract to mature and use a new visualizing sound (Gelman Urethral Sound, CS Surgical) (Figure 9(d)). This sound has a contour similar to the Haygrove sound but is hollow, allowing a flexible cystoscopy to be advanced through the sound (Figure 9(e)). The tip of the sound and/or the tip of the cystoscope can then be directed to the obliteration under direct vision. An additional advantage is that the light from the scope can be seen to further guide the dissection. Prior to the development of the visualizing sound, 2/9 patients at our institution required a temporary vesicostomy at the time of reconstruction. Subsequently, 76 patients (ages 4–77 years) underwent reconstruction (including 6 pediatric patients and 14 patients who had unsuccessful procedures prior to referral), and 0/76 patients required a temporary vesicostomy. In every case, the sound could be directed to the proper position under direct vision. It is our experience that the visualizing posterior urethral sound greatly facilitates the reliable identification and dissection of the proximal segment during posterior urethral reconstruction. With the use of this device, the open dissection can be limited to the perineal exploration, even in pediatric and difficult cases. One disadvantage of the sound is that the outside diameter (OD) is greater than the OD of the solid Haygrove sound, and the solid sound can be manipulated more easily.

Therefore, we continue to use the solid sound when the tip can be readily palpated in the perineum. Although the larger diameter hollow sound will not advance as easily through the suprapubic tract when 16–18 Fr indwelling tubes are used prior to surgery, the tip of the flexible cystoscope can be first advanced into the bladder, and the sound can then be advanced over the scope using the scope as the equivalent of a guide wire.

The most complex portion of posterior urethral reconstruction is the proximal exposure and dissection subsequent to transection of the urethra. One option is to sharply incise scar tissue, advance a nasal speculum through the scar, and place "J" shaped sutures through the speculum to initiate the anastomosis [30]. It is our preference to excise the scar tissue until normal healthy tissue is encountered. Supple tissue more readily everts, bringing the mucosa forward from deep within the pelvis during the placement of the first several sutures, and this facilitates the placement of subsequent sutures. Our objective is to achieve the proximal preplacement of 10-12 3-0 absorbable monofilament sutures. We alternate using violet PDS and clear Monocryl to help maintain orientation at the time of the completion of the anastomosis.

3.7.3. Infrapubectomy. In cases where the scar is especially dense and the defect is long, it is possible that the tip of the sound will not be palpable, and the light of the cystoscope will not be seen even when using the visualizing sound. In these cases, scar tissue just below the midline symphysis is excised sharply in a 1-2 cm diameter area. As the dissection extends deep into the pelvis, infrapubectomy is often required to facilitate the proximal scar excision. The corporal bodies, which have already been separated, are retracted laterally exposing the dorsal vein, which is then mobilized and ligated to expose the midline symphysis pubis. Periosteal elevators are then used to sweep the medial crura laterally and free the undersurface of the bone from adherent tissue. Kerrison rongeurs provide controlled bone removal, which widens the exposure and facilitates further proximal dissection. Moreover, the separation of the corpora and infrapubectomy provide a more direct route for the urethra to course, and this facilitates a tension-free repair.

3.7.4. Additional Maneuvers. Some authors have reported that, in addition to distal mobilization, crural separation, and infrapubectomy, supracrural corporal rerouting was required to achieve an acceptable amount of tension in selected cases [31]. This technique appears to be associated with a high rate of restenosis. In a recently published combined series of 142 cases, 4 underwent rerouting and 3 of these patients (75%) developed restenosis [12]. Other surgeons never find supracrural rerouting to be a beneficial maneuver. It is often stated that the objective is a "tension-free" anastomosis. This is not necessary as there is normally a certain amount of innate tension along the corpus spongiosum. It is for this reason that when the urethra is transected, there is generally some retraction of the distal segment. Our goal is not a tension-free anastomosis, but rather an anastomosis without unacceptable tension that would lead to tethering of the penis during erections or separation of the anastomosis. To date, we have never encountered a case where supracrural rerouting was required.

Another option in complex cases where there is a large defect is a transpubic approach [32–34]. This is a technique we have never found necessary, and more recent reports confirm that infrapubectomy generally provides adequate proximal exposure in complex cases [35].

Another tool that has been reported to bridge longer defects is the use of tissue transfer with flaps or grafts [31]. This appears to have been performed mostly in older series, and recent reports do not support the use of or need for tissue transfer. It is fortunate that excision and primary anastomosis can reliably be achieved during posterior urethral reconstruction given that tube flaps and grafts are generally associated with a high failure rate, and the tissues surrounding the membranous urethra deep within the pelvis proximal to the triangular ligament do not represent an excellent bed for graft spread fixation.

3.7.5. Anastomosis. Once the proximal sutures are placed along a widely patent proximal segment surrounded by pink healthy mucosa proximally, and flexible cystoscopy further confirms that the opening is distal to the verumontanum at the appropriate location, the distal segment is dorsally spatulated and calibrated using bougie á boule. The caliber should be greater than 30 Fr. The anastomosis is then completed as a stenting catheter is placed. It is our preference to use a 14 Fr soft silicone catheter. A small round drain is placed deep adjacent to the corpus spongiosum deep to the bulbospongiosus muscle, which is then reapproximated along the ventral midline, and a second flat 7 mm drain is placed superficial to the muscle. The incision is then closed in 2 layers with absorbable suture and a clear dressing is placed. No compressive dressing is required.

3.8. Postoperative Care. Our protocol is to maintain the stenting urethral catheter and the suprapubic tube urinary diversion for 3 weeks and then perform a VCUG by removing the stenting catheter, filling the bladder with contrast by gravity installation and then obtaining a film during urination. In the rare case of extravasation, a new stenting catheter is replaced and a repeat study is performed the following week. Other surgeons favor catheter removal without postoperative imaging [36]. In most cases, the force of stream will be excellent, and the suprapubic tube is then removed. If the stream is weak, the tube is plugged and the patient is instructed to unplug the tube at home, if unable to urinate, to check residuals by unplugging the tube after micturition. One possible reason for voiding difficulty is neurogenic bladder dysfunction related to the initial injury, especially if there is associated back trauma. Several months after tube removal, flexible urethroscopy is performed to definitively confirm wide patency of the repair. Patients are then encouraged to have a baseline flow rate and postvoid residual assessment and then to have this repeated annually. There is currently a lack of consensus regarding appropriate follow-up after surgery.

3.9. Outcomes. In our series of 85 patients, prior to referral, 17 underwent failed endoscopic treatment and 17 underwent failed open surgery. At the time of surgery, 19 patients underwent infrapubectomy, and no patient required supracrural rerouting. No patient required transfusion, and the only persistent neuropraxia was in one patient who had persistent tingling of the toes that resolved after several months. At the time of urethroscopy 4 months after surgery, 2 patients were noted to have medium caliber narrowing. One of these patients underwent dilation 2 years after surgery and the other was observed and never required treatment. This corresponds to a success rate of 97.6% success, using the strict definition of maintaining durable wide patency of the repair and with no further treatment required.

Other series report a similar success rate for adults, adolescents, and children, and this indicates that a stricture recurrence after a properly performed posterior urethroplasty should be a rare event [35, 37]. Of the patients who presented to our center after failed surgery, the recurrence was often within days or weeks, suggesting that these were technical failures, likely due to inadequate scar excision. Further suggesting that technical inexperience of the surgeon is likely the most common cause of failure is the fact that these patients usually have a successful outcome with the same technique of excisional repair when the revision surgery is performed by a specialist in urethral reconstruction. Published papers from referral centers confirm that when open repair fails, excision and primary anastomosis still remains the procedure of choice, and when properly performed, it offers a very high success rate [38, 39]. In conclusion, delayed posterior urethral disruption injuries are highly amenable to successful reconstruction with excisional posterior urethroplasty via a perineal approach.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Review Article

The Use of Flaps and Grafts in the Treatment of Urethral Stricture Disease

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The use of various grafts and flaps plays a critical role in the successful surgical management of urethral stricture disease. A thorough comprehension of relevant anatomy and principles of tissue transfer techniques are essential to understanding the appropriate use of grafts or flaps to optimize outcomes. We briefly review these principles and discuss which technique may be best suited for a given anterior urethral stricture, depending on the location and length of the stricture, the presence or absence of an intact corpus spongiosum, and the availability of adequate and healthy penile skin.

1. Introduction

1.1. Principles of Tissue Transfer. The two broad categories of tissue transfer are flaps and grafts. A flap refers to tissue that is transferred with its native blood supply intact, while a graft refers to tissue removed from its donor site without its native blood supply and relies on establishing new circulation through a process termed "take." This process consists of two separate 48-hour phases: imbibition is the initial phase in which the graft is directly absorbing nutrients from the graft recipient bed; this is followed by inosculation, during which new blood supply is established.

1.2. Blood Supply to the Urethra and Penile Skin. Detailed knowledge of the blood supply to the penile skin and corpus spongiosum is mandatory for successful tissue transfer. The healthy urethra within the corpus spongiosum has dual blood supply: it receives antegrade flow directly from the paired bulbar arteries and retrograde flow from the terminal branches of the dorsal arteries, which communicates with the corpus spongiosum in the glans penis (Figure 1). Although there are also small perforating vessels between the corpora cavernosa and corpus spongiosum, this is a minor contribution. This robust dual blood supply all within the corpus spongiosum allows aggressive mobilization of the spongiosum off of the corporal bodies without compromising the blood supply to the urethra. However, the distal blood supply to the corpus spongiosum is compromised in cases of hypospadias, especially more severe forms, or after prior repair and after urethroplasty. In these cases, wide mobilization may compromise the blood supply to the urethra and create ischemic stenosis.

The penile skin receives its blood supply from branches of the superficial external pudendal artery. These branches travel just underneath the dartos fascia in an axial pattern, which provides reliable blood flow to skin flaps that are elevated on this fascial layer; hence these are referred to as fasciocutaneous flaps. There is also random blood supply achieved through the subdermal plexus, although this is much less dependable and not ideal for the survival of the flap (Figure 2).

1.3. Graft Material. The use of grafts in urethral reconstruction has been described since the late 19th century but was not popularized until Devine et al. began using full thickness penile skin grafts in 1961 [1]. This "patch graft" technique was historically the substitution procedure of choice, although it has now largely been supplanted by buccal mucosal grafts (BMG), split thickness skin grafts, and, in some cases, lingual grafts.

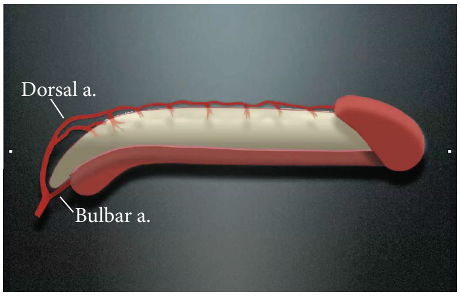


Figure 1: The dual blood supply to the urethra.

Buccal mucosal grafts have many advantages over penile skin and other materials which have led to their widespread use in recent years. These grafts are readily available and easily harvested and have more favorable vascular characteristics, including a rich submucosal plexus that facilitates good take. Additionally, buccal mucosa is nonhirsute and has an epithelial surface that is already well suited to a "wet" environment. As would be expected, long-term success rates with the use of BMG appear to be superior to penile skin grafts [2]. The use of lingual mucosa, while not as commonly used, is very similar in histology to buccal mucosa and has been described with very similar success rates [3].

1.4. Flap Techniques. Penile skin flaps, when used correctly, are a reliable and time-tested tool for urethral reconstruction. In the absence of prior flap surgery, penile skin (foreskin and distal penile skin in particular) is nonhirsute, has reliable axial vascular supply, and can be well mobilized and used to cover long urethral defects. Various flaps have been described, which can be elevated from ventral or dorsal skin and taken in either the longitudinal or transverse direction.

Orandi first described his ventral, longitudinal flap for penile urethral strictures using a lateral pedicle in 1968 with good results [4]. One disadvantage of this type of flap, however, is that if the stricture involves the proximal part of the pendulous or any part of the bulbar urethra, hair-bearing skin is involved in the reconstruction which can lead to recurrent infections and stone formation. For strictures isolated to the fossa, Jordan reported the use of a smaller, ventral penile skin flap that can be rotated onto the incised urethral opening [5].

For longer strictures, Quartey and McAninch have both described methods of obtaining transverse penile/preputial island flaps [6, 7]. These transverse flaps are versatile and hairless and can supply enough tissue to cover near panurethral defects. Furthermore, they involve a circumcision type incision with minimal disfigurement of the penis.

1.5. Grafting Techniques. Several techniques have been described, the two most common of which are the dorsal and ventral onlay grafts. The dorsal onlay approach was first described by Monseur in 1980 in which he incised the dorsal surface of the strictured urethra and sutured the edges directly to the corpora cavernosa to heal by secondary intention; this was later modified by Barbagli who used a penile skin or buccal graft to fill the defect [8, 9]. The ventral onlay graft was first described by Devine with the use of a full-thickness "patch graft" of penile skin and then later was modified to use with buccal mucosa [1, 10]. Several other grafting techniques have been described and will be detailed throughout this paper.

2. Selecting the Right Technique

Selecting the appropriate technique for each patient is highly individualized and dependent on multiple factors. The optimal repair will depend on the length and location of the stricture, the presence or absence of healthy, abundant penile skin, and whether or not the corpus spongiosum is intact. Incorporating all of these considerations can make the decision-making process quite complex; however, the proper selection of tissue transfer technique is paramount to success. Our aim is to provide a logical, easily comprehensible approach to the appropriate selection of grafts and flaps in urethral reconstruction.

3. Tissue Transfer to the Glans and Fossa Navicularis

Our approach to strictures of the glans and fossa navicularis is summarized in Figure 3. If a stricture is truly limited to the glans penis alone (meatal stenosis), a simple meatotomy is the procedure of choice. However, distal strictures often either extend into the fossa navicularis or are limited to the fossa. These strictures are often best treated with a one-stage flap repair as long as there is abundant and healthy penile skin. When this is not the case, as in cases of prior penile flap surgery or in cases of lichen sclerosus (LS) also known as balanitis xerotica obliterans (BXO), then a two-stage repair with buccal mucosa grafting is more appropriate given the prohibitively high recurrence rates when using skin in these situations [11, 12]. Alternatively, the patient may simply elect for an extended meatotomy if he believes that the resulting ventral displacement of the meatus is cosmetically acceptable and prefers a simple procedure.

Although multiple flap techniques have been described, we prefer the ventral transverse island flap as initially described by Jordan for this location [5]. This technique involves incising the urethra ventrally through the stricture, elevating a transverse skin island on a broad pedicle of dartos fascia, and inverting the flap onto the defect prior to closure (Figure 4). This technique has been demonstrated to be highly successful, with Jordan reporting success in all 23 patients who did not have LS with an average follow-up of 10 years. Of note, the success was only 50% (6/12 patients) in those who had LS, reaffirming the recommendation against using penile skin in these cases [12].

Grafts are used by some authors for one-stage repairs of strictures involving the glans and fossa navicularis with dorsal graft placement [13]. Others place buccal mucosa grafts as ventral onlays using the glans wings as the graft bed [14, 15]. However, we do not believe that these techniques in our hands obtain the same caliber of patency (24–30 French)

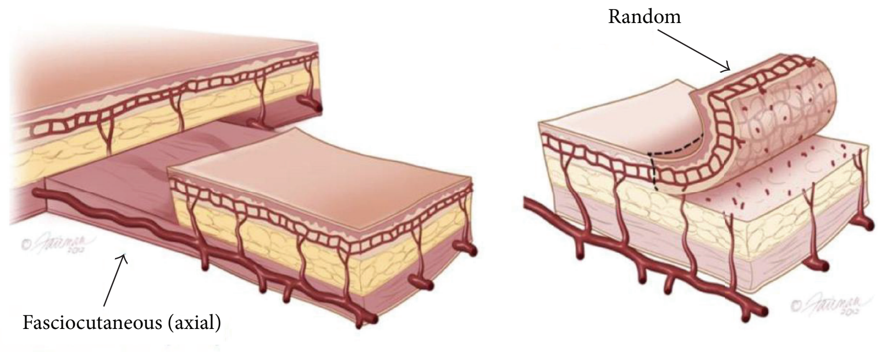


FIGURE 2: Axial and random flaps.

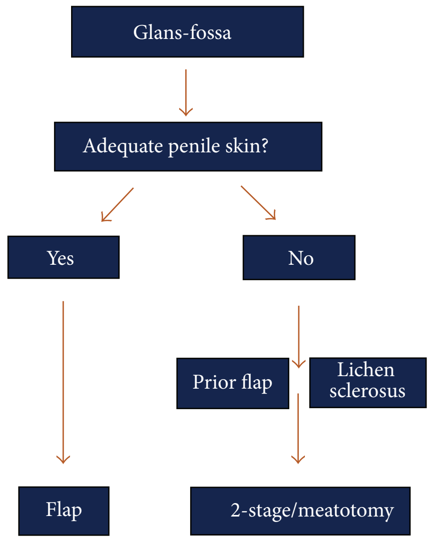


FIGURE 3: Treatment algorithm for strictures of the fossa navicularis.

that can be achieved with ventral flaps or staged repairs. Most importantly, however, it should be emphasized that the priority of the repair is relief of obstruction; thus the caliber of the repair, regardless of technique, should not be compromised by aggressively attempting to bring the meatus all the way to the tip of the glans.

4. Tissue Transfer to the Penile Urethra and Bulbar Urethra

The repair of penile and bulbar urethral strictures that are not amenable to EPA can be performed with grafts, flaps, or staged procedures, depending on whether the corpus spongiosum is intact and whether there is sufficient penile skin, as summarized in the algorithm in Figure 5. There is some debate about at what length an EPA should be avoided in favor of a tissue transfer technique, as lengthy excisions can lead to a tethered penis and tension on the anastomosis. In general, strictures in the penile urethra and distal bulbar urethra are only highly amenable to EPA when they are short (i.e., less than 2 cm), whereas primary repairs without undue tension can be achieved for longer proximal bulbar strictures. In this location, maneuvers including separation of the corporal bodies and detachment of the bulb from the perineal body are options, and EPAs have been described for strictures up to 5 cm long in this location [16].

4.1. *When the Corpus Spongiosum Is Intact.*

There is general consensus that strictures of the penile urethra not amenable to excisional repair are best repaired with a dorsal onlay graft, as the spongiosum even when intact is tenuous in this area and does not supply a reliable vascular bed to a ventrally placed graft [17]. Prior to the popularization of BMG, skin flaps were preferred as the most reliable approach when available. Dorsally placed buccal grafts, however, have also been demonstrated in multiple studies to provide very reliable results and are more durable and better suited to the "wet" environment than penile skin [17, 18]. Moreover, with the use of dorsal buccal grafting, the dorsal aspect of the urethra is supported by the corporal bodies, and the ventral and lateral native urethra is supported by intact corpus spongiosum, which will likely prevent both fistula formation and diverticular change.

Strictures of the bulbar urethra have generated considerably more debate as to the optimal location and technique of graft placement. There is an anatomical difference between the penile urethra and bulbar urethra with regard to the ventral spongiosum. As the urethra moves proximally, it becomes more dorsally located so that the spongiosum becomes thicker and more robust ventrally, thus providing a potentially suitable vascular bed for graft take.

Some authors prefer the ventral approach as it limits urethral mobilization with preservation of cavernosal-spongiosal perforating arteries [19]. In addition, the ventral approach is often considered to be less technically challenging with shorter operative times. Even Barbagli, who developed the dorsal onlay graft, has noted preference for the ventral approach in certain situations: if the dorsal aspect of the urethra is scarred down to the corpora from prior surgery or if the stricture extends proximally beyond the triangular ligament [20].

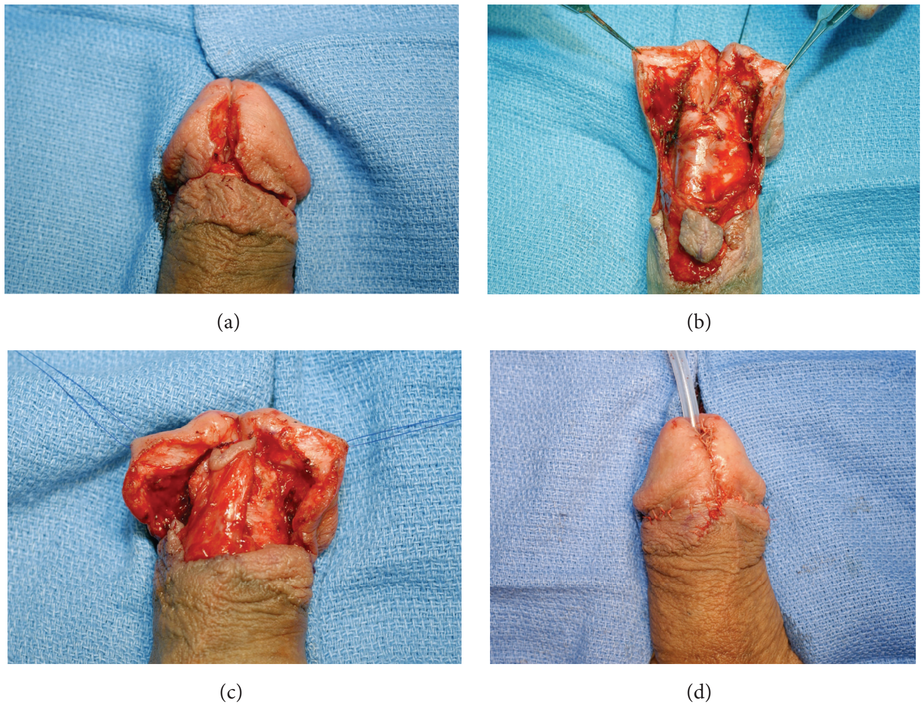


Figure 4: (a) An extended meatotomy is made through the stricture. (b) Glans wings are mobilized and a ventral flap is isolated. (c) The ventral flap has been rotated onto the defect. (d) Immediate appearance after closure.

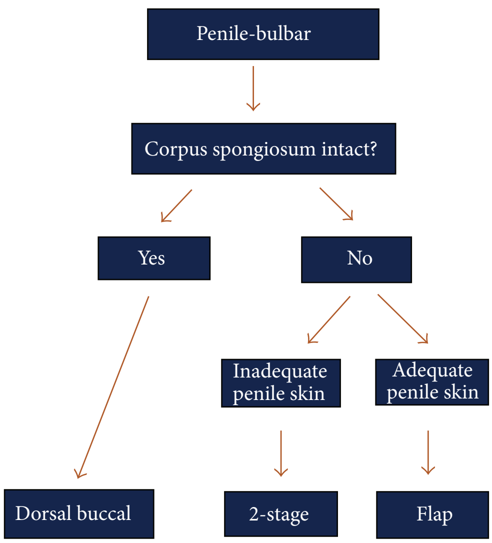


Figure 5: Treatment algorithm for strictures of the penile urethra and bulbar urethra.

However, several advantages exist to the dorsal approach, including the fact that the graft can be spread fixated to the corpora cavernosa, which supplies a consistently reliable graft bed that is not affected by spongiofibrosis. This spread-fixation, which cannot be accomplished with the ventral approach, also maximizes the surface area of the graft that is in direct contact with its vascular bed. This optimizes the conditions for graft take and allows for a widely patent lumen, ideally up to 30 French. Additionally, the use of a dorsal approach may reduce the incidence of postvoid dribbling, which has been shown in at least one retrospective study to be more prominent with the ventral approach [21].

Fueling the controversy is the fact that there have not been any randomized controlled trials to compare these two techniques, and the evidence that does exist is limited by its retrospective nature and conflicting results. One early comparison of 71 patients concluded that the dorsal onlay method was superior (5% versus 14% failure rates), but no statistical analysis was performed [22]. In contrast, Barbagli et al. retrospectively compared 17 ventral, 27 dorsal, and 6 lateral bulbar urethroplasties and found a success rate (defined by lack of subsequent treatment at mean follow-up of 42 moths) of 83%, 85%, and 83%, respectively [21]. More recently, a group of authors published a multicenter series with extended follow-up (median of 118 months) and found very similar success rates between the two techniques (80.2% of 81 patients with dorsal onlay compared to 81.5% of 130 patients with ventral onlay ($n = 130$)) [2]. However, we advise caution before concluding that these results are equivalent because each patient was carefully selected for the procedure they received and therefore the inherent selection bias prohibits this study from providing a decisive comparison. Another large retrospective study compared 62 ventral onlay cases with 41 dorsal onlay cases and reported equivalent outcomes with failure rates of 19% and 17%, respectively, at a mean follow-up of 36 months. However, the authors admit a selection bias as dorsal onlay procedures are reserved for more complicated strictures at their institution [19]. A recent systematic review of published series showed very little difference between the two techniques. The published ventral onlay series success rates ranged from 83% to 100% with an average of 88.84%, while the reviewed dorsal onlay series successes ranged from 73% to 100% with an average of 88.37% [17].

An additional technique was described in 2001 by Asopa et al., in which they were able to access the dorsal aspect of the urethra via a ventral urethrotomy and then excise an elliptical portion of the dorsal urethra and apply a dorsal "inlay" graft in its place before retubularizing the urethra [23]. The benefit of this approach is to combine the advantages of having a dorsally placed graft laying on the corporal graft bed while avoiding division of the perforating arteries that occurs during urethral mobilization to maintain maximal blood supply. This technique has been evaluated by several authors with results that compare to the historical results for the ventral and dorsal onlay approaches [17].

While the debate between these techniques is likely to continue until higher level evidence emerges, we prefer the dorsal approach at our institution for the variety of reasons mentioned above.

4.2. When the Corpus Spongiosum Is Not Intact. In cases where the spongiosum is not intact, such as in hypospadias, a one-stage graft is not recommended as the blood supply to the urethra will be severely compromised once it is fully mobilized. In these cases, whether it involves the penile or bulbar urethra, a skin flap is more appropriate as long as there is adequate and healthy penile skin. Transverse fasciocutaneous penile/preputial skin flaps can provide excellent coverage and have achieved good to excellent results in the published literature. In his initial description, McAninch obtained flaps up to 15 cm with no stricture recurrence in 10 patients with strictures which are 8–21 cm long and a mean follow-up of 14 months [24]. A subsequent publication of his long-term data revealed a success rate of 87% in 54 patients [25]. A review by Wessells and McAninch evaluated nine studies, all with at least one year of follow-up, and found that success rates ranged from 77% to 95%, with an average of 85.5% [18].

When there is not enough healthy skin, such as in cases of LS or prior flap surgery, a two-staged approach is more appropriate (Figure 6).

5. Special Situations

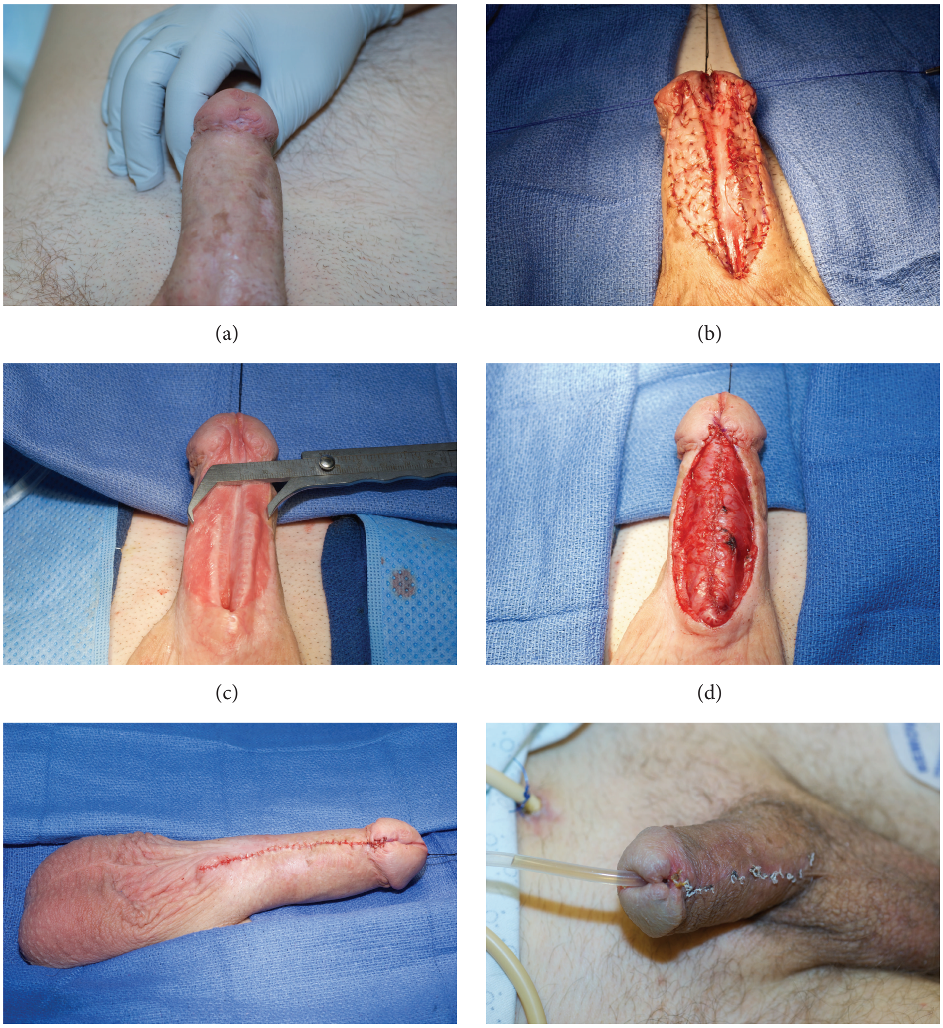
In certain complex cases with a segment of obliterated or near-obliterated urethra, there is not an adequate urethral plate to perform a ventral or dorsal onlay graft. If these are short strictures, they are best treated by excision with primary anastomosis (EPA). However, in such cases when the stricture is too long for an EPA, an augmented anastomosis can be considered. This technique, initially described by Turner-Warwick, involves excising the stricture, placing a graft dorsally, and then reanastomosing the native urethral edges ventrally [26]. Yet even this technique can be limited by length, with the longest stricture treated with this technique in one prominent series being of only 2 cm [27].

In patients with longer obliterative segments, an EPA or augmented anastomotic repair may not be feasible. Additionally, in patients who have already failed urethroplasty or have a history of hypospadias, strictures that would otherwise be technically amenable to one of these repairs may be at risk of urethral ischemia with urethral transection. For this small subset of patients, a more involved and creative approach may be necessary. Tabularized grafts and flaps have been attempted but have significantly high failure rates, reportedly up to 58%; therefore other techniques are needed to repair these challenging cases [14, 28].

5.1. Graft/Flap Combination. A more successful method to treat these strictures is with the combination of a dorsal buccal graft to augment or replace the inadequate urethral plate, followed by a penile skin flap onlay reconstruction (Figure 7). This was initially described by Morey in 2001 for single stage circumferential tissue transfer in 2 patients with penile urethral strictures [29]. A larger series of 12 patients was subsequently published with a success rate of 92% defined as wide patency documented by cystoscopy 4 months after surgery with subsequent follow-up that averaged 39 months [30].

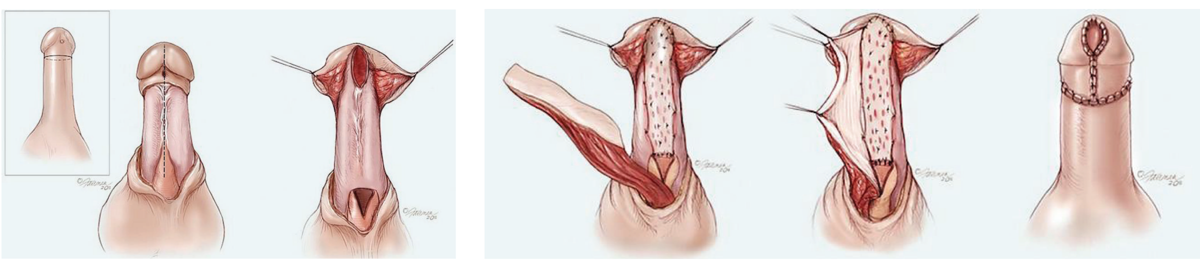
The graft and flap combination can also be used for panurethral strictures that are too long for repair with BMG even when bilateral grafts are harvested. This technique typically involves using as much BMG as possible in the proximal aspects of the stricture and then using a penile skin flap to repair the remainder of the stricture distally [31, 32].

5.2. Combined Dorsal/Ventral Buccal Grafting. If penile skin is not available for a flap, then a combination of a dorsal and ventral BMG may be used. Such a combination approach was initially described by Palminteri et al. who used the Asopa technique to place a dorsal inlay graft and then place a ventral onlay graft in the ventral urethrotomy to obtain additional area within the new lumen [33]. However, this description was not targeted to obliterative strictures as the technique relies on a native urethra wide enough to be sutured to both grafts. Gelman and Siegel recently reported results from our institution on a series of 18 patients who had segments of total or near-total obliteration of their urethras and underwent combined ventral and dorsal buccal grafting for a 1-stage repair. The technique involves a dorsal incision without transection of the mobilized urethra, thereby preserving the continuity of the blood supply within the spongy tissue. Buccal mucosa is quilted dorsally to the corporal bodies in the standard dorsal onlay fashion. Additional buccal mucosa can then be quilted to the dorsally incised, nontransected corpus spongiosum in continuity with the distally and proximally spatulated urethra. The repair is then completed by approximating dorsal and ventral buccal mucosal graft segments (Figure 8). We feel the strengths of this technique include being able to leave the robust ventral spongy tissue intact and being able to place quilting sutures to secure the graft firmly to its bed. In this series with a mean follow-up of 50 months, the success rate was 94% (100% after the single failure underwent an internal urethrotomy) [34]. Although this needs to be



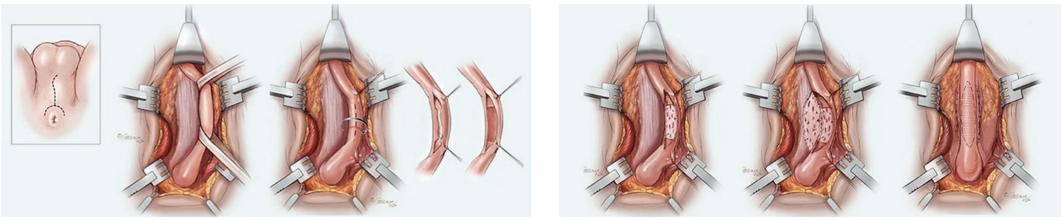
(a) (b) (c) (d) (e) (f)

Figure 6: A 2-stage repair performed for a patient with a fossa and penile urethral stricture. (a) Demonstration of inadequate penile skin. (b) BMG quilted on either side of the opened urethral plate. (c) The urethral plate is now very adequate after healing of 1st stage. (d) Tubularization of new urethral plate. (e and f) Postoperative appearance immediately after closure and 3 weeks postoperatively.



(a) (b)

Figure 7: Graft/flap combination. (a) The obliterated urethra is incised proximally until a healthy, widely patent lumen is encountered. (b) The buccal graft is spread fixated to the corpora cavernosa, after which a penile skin flap is rotated ventrally onto the graft to create a new lumen. In cases where there is a deficiency of urethra within the fossa and a lack of a groove within the glans penis, a defect is created and the BMG is extended into the glans.



(a) (b)

Figure 8: Dorsal and ventral buccal graft combination. (a) The urethra is mobilized and incised dorsally and healthy ventral spongiosum is exposed. (b) A buccal graft is spread fixated to the spongiosum where the obliterated segment was located, and an additional buccal graft is applied to the corpora cavernosa before the edges are anastomosed for retubularization.

validated by other studies, it remains a promising technique for some of the most challenging cases.

6. Summary

The use of grafts and flaps in the treatment of urethral stricture disease remains an indispensable tool in the armamentarium of the reconstructive urologist. While success rates are very difficult to compare between various techniques at this time, all of the current techniques mentioned appear to be highly successful for appropriately selected patients. The decision on which technique to use is dependent on a variety of factors. For strictures involving the fossa navicularis, the use of a penile skin flap provides excellent coverage while leaving a widely patent lumen. A meatotomy or two-stage repair should be considered if the penile skin is unhealthy or deficient. For strictures of the penile or bulbar urethra, we prefer the dorsal buccal approach as long as the corpus spongiosum is intact and reserve the use of a flap for when the spongiosum is not intact or a two-stage repair if the penile skin will not allow a flap to be used. Randomized controlled trials will likely be necessary to definitively recommend one technique over another, but until that time, it is imperative for the surgeon to be comfortable with all of the described techniques to individualize the treatment approach for each patient.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Review Article

Surgical Repair of Bulbar Urethral Strictures: Advantages of Ventral, Dorsal, and Lateral Approaches and When to Choose Them

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Objectives. To review the available literature describing the three most common approaches for buccal mucosal graft (BMG) augmentation during reconstruction of bulbar urethral strictures. Due to its excellent histological properties, buccal mucosa graft is now routinely used in urethral reconstruction. The best approach for the placement of such a graft remains controversial. *Methods*. PubMed search was conducted for available English literature describing outcomes of bulbar urethroplasty augmentation techniques using dorsal, ventral, and lateral approaches. Prospective and retrospective studies as well as meta-analyses and latest systematic reviews were included. *Results*. Most of the studies reviewed are of retrospective nature and majority described dorsal or ventral approaches. Medium- and long-term outcomes of all three approaches were comparable ranging between 80 and 88%. *Conclusion*. Various techniques of BMG augmentation urethroplasty have been described for repairs of bulbar urethral strictures. In this review, we describe and compare the three most common "competing" approaches for bulbar urethroplasty with utilization of BMG.

1. Introduction

Buccal mucosa graft (BMG) is now routinely used in urethral reconstruction since its popularization by Burger et al. in 1992 in pediatric reconstruction [1] and subsequently by El-Kasaby et al. in 1993 for adult urethroplasty [2]. Its use in urethroplasty is arguably the gold standard for treatment of medium- and long-length strictures [3]. The first use of buccal mucosa in urethral reconstruction is attributed to Professor Sapezhko who by 1894 had performed 4 operations on humans [4, 5]. In 1941, Humby, a British surgeon, described using buccal mucosa in hypospadias repair [6]. The excellent histological properties of buccal mucosa were subsequently described by Duckett et al. [7]. In comparison to skin, buccal mucosa holds the distinct advantage of being hairless and accustomed to a moist environment. Moreover, it has a thicker epithelial layer, thinner lamina propria, and a greater density of capillaries with an abundance of Type IV collagen. All these qualities are thought to improve graft inosculation and survival after transplantation.

Various techniques of BMG augmentation urethroplasty have been described for repairs of bulbar urethral strictures. In this review, we describe and compare the three most common "competing" approaches for bulbar urethroplasty with utilization of BMG.

2. Technique

2.1. Indications. Before describing the approach to bulbar stricture in detail, it is important to reiterate the indications for the use of oral mucosa in urethral reconstruction. The authors follow a traditional algorithm, where bulbar strictures <2 cm in length can mostly be treated with excision and primary anastomosis, whereby strictures longer than 2 cm may require adjunct maneuvers and the use of graft tissue to augment the caliber of the urethra. These maneuvers may include augmented anastomotic urethroplasty typically used for strictures between 2 and 5 cm in length or, for longer strictures, "pure" urethral augmentation in order to establish a larger gauge urethra. The choice of where and how to augment the urethra is discussed here in further detail.

2.2. Dorsal Onlay. This technique was first described by Barbagli et al. in 1998 and involved circumferential bulbar urethral dissection, dorsal stricturotomy followed by augmentation of the stricturotomy by a penile skin graft (in the first 31 patients) or by BMG (in the last 6 patients) [8]. The key step of the procedure was "quilting" or spread-fixation of the graft on the tunica albuginea overlying the corpora cavernosa prior to suturing the edges of urethral mucosa to the edges of the graft. Even spread-fixation has a range of implementation techniques; some surgeons prefer a "traditional" manner of suturing through the graft to the underlying tunica albuginea, while others advocate for use of a biologic "glue." The advantage of suture quilting the graft includes microfenestration of the graft resulting from the surgical needle, which may aid in allowing any trapped blood to escape, preventing hematoma under the graft, and increasing the likelihood of proper buccal mucosa engraftment. This maneuver is critical in fostering sufficient graft apposition to the well-vascularized tissue of the corpora cavernosa and minimizing the risks of graft contracture and pseudodiverticula formation.

One of the advantages of the dorsal approach is that it yields a relatively bloodless operation. This is because the bulbar urethra is eccentrically located in the corpus spongiosum, with only thin dorsal coverage by corpus spongiosum that requires incision. Another advantage of the dorsal approach is its versatility and applicability for strictures of any length and location. The dorsal stricturotomy in the bulbous urethra can be extended proximally towards the membranous urethra or distally into penile urethra if required by intraoperative findings without dramatically altering the plan for reconstruction. In the event that complete or near-complete obliteration is identified after committing to dorsal stricturotomy, several solutions are described. These include (a) excision of the obstructed segment and conversion to augmented anastomotic urethroplasty [9], (b) removal of ventral mucosal strip and addition of ventral BMG onlay [10], and (c) ventral stricturotomy and addition of elliptical ventral inlay [11].

One of the disadvantages of the original dorsal approach is the need to circumferentially mobilize the urethra. Kulkarni et al. addressed this with their modification where mobilization is undertaken unilaterally and carried just across the midline dorsally, preserving the lateral blood supply on the contralateral side [12].

There have been numerous studies examining the success of BMG bulbar urethroplasty over the last two decades, with a wide range of follow-up and varying definitions of success. The Société Internationale d'Urologie (SIU) with the International Consultation on Urological Disease (ICUD) published a systematic review of 66 studies, describing outcomes of a total of 934 patients after dorsal onlay urethroplasty with average follow-up of 42 months and mean success rates of 88.3% [13]. Soon after, Barbagli et al. published a long-term retrospective paper on the deterioration rate of augmentation urethroplasty [14]. In this study, only patients with follow-up of greater than 6 years were included, totaling 81 patients after dorsal onlay BMG urethroplasty. At a median follow-up of 111 months, the authors reported an 80.2% success rate, defined as requiring absolutely no further instrumentation including dilation. This compared to 81.5% and 83.3% for ventral and lateral onlay techniques, respectively, with similar lengths of follow-up. The overall conclusion drawn from these reviews is that no significant difference exists in recurrence rates between dorsal, ventral, and lateral approaches to bulbar urethroplasty [13, 14].

2.3. Ventral Onlay. The ventral "patch" onlay urethroplasty came to the forefront of urethral reconstruction in 1996 when, encouraged by the use of BMG in complex pediatric hypospadias repair, Morey and McAninch applied the graft to repair strictures of the bulbar urethra [15]. The authors describe direct saggittal ventral urethrotomy through the diseased bulbar urethra, followed by sewing of the graft to each edge of the native urethral mucosa. Subsequently, the corpus spongiosum is closed over the graft in a second layer and the bulbospongiosus muscle over this. While there is no separate tissue to which the graft can be "quilted," the spongiosal closure typically incorporates a small "bite" of the graft, to increase proper apposition to the spongiosum that will provide its blood supply. The technique was introduced contemporarily with Barbagli's dorsal onlay technique, and the advantages and superiority of each have been the subject of intense debate ever since.

Proponents of the ventral onlay cite a straightforward approach, not requiring extensive circumferential mobilization and the technical demand of dorsal graft placement. This allows urologists who treat strictures only occasionally to still feel comfortable in performing urethroplasty for strictures that may not be amenable to excision and primary anastomosis. Moreover, the argument may be made that the thicker, ventrally placed corpus spongiosum provides a more robust vascular bed for buccal mucosa engraftment. Another anatomic consideration is specific location of the bulbar stricture. Patterson and Chapple, in a comparison of surgical techniques, note that, for very proximal bulbar strictures, ventral onlay poses a clear advantage in exposure and technique and is the appropriate choice [16]. Palminteri et al. also contend that ventral placement of BMG in bulbar urethroplasty has no significant impact on sexual quality of life and in fact improved most measures of sexual life, aside from postejaculatory dribbling [17]. An additional benefit is that the ventral approach is amenable to use in complex situations, including recurrent stricture [18], after radiation [19], and with adjunct maneuvers such as gracilis muscle flap coverage in particularly high risk, long segment strictures [20]. The ventral approach has also been used as a direct route to the dorsal aspect of the urethra, allowing preservation of bilateral vascular supports to the urethra [21].

Opponents of the ventral technique point to the need to make incision through the thicker ventral corpus spongiosum in order to reach the eccentrically located bulbar urethra, resulting in a bloodier operation. There is also a concern about increased risk of sacculation, diverticulum, or pouch formation, as well as more frequent irritative voiding symptoms and urine infection [22]. In their review of 11 series, Patterson and Chapple note several groups with higher incidence of sacculation or diverticulum formation with resultant worse postvoid dribbling in ventral onlays. They go on, however, to document that an equal number of series found no significant anatomic or clinical difference in these findings in comparing ventral or dorsal onlay [16]. What is ultimately evident is that, in experienced hands and with meticulous technique, these issues can be minimized; furthermore, the issue of sacculation seems dramatically higher in older series based on the use of skin, versus the more modern use of BMG [3].

This being said, there are certain disadvantages to the ventral approach. Several authors [23, 24] have noted finite incidence of urethrocutaneous fistulae after ventral stricture repair with BMG, which is essentially unheard of in the dorsal approach. Reiterating an advantage of the dorsal approach mentioned earlier here, the ventral approach is less versatile, as it does not lend itself to extension of the urethrotomy distally into the penis should intraoperative findings require it.

While the global definition of success varies, a common criterion in most if not all series is the patency rate. The International Consultation on Urological Disease (ICUD) reviewed techniques in management of anterior strictures and found the success rate of ventral onlay to range from 43 to 100%. The authors summarize these series, generating a total number of 563 patients treated at a mean follow-up of 34.4 months, yielding a mean success rate of 88.8%, comparable with dorsal onlay urethroplasty. A number of smaller series, including a recent prospective randomized study, have compared dorsal and ventral techniques and reached a similar conclusion to the ICUD group: that there is no significant difference in success rates based on graft placement [13, 25, 26].

2.4. Lateral Onlay. Lateral onlay BMG augmentation urethroplasty is described but not well established in the literature. It is utilized infrequently and this is reflected by its limited description in the literature. The procedure resembles the ventral onlay technique described above; however, the urethrotomy is made laterally after unilateral urethral mobilization. The graft is similarly sutured in place and the spongiosum is closed over the graft.

As described above, the various locations of the urethrotomy in substitution urethroplasty afford different benefits and can also result in varying consequences. The lateral urethrotomy was described by Barbagli et al. in 2005 [27]. This actually preceded the description of the modified dorsal onlay technique where dissection remains unilateral. In a similar vein to the one-sided dissection technique described by Kulkarni et al. [12], it was felt that eliminating circumferential dissection would help preserve the contralateral urethral blood supply. Furthermore, avoiding urethrotomy through the robust ventral spongiosum may decrease intraoperative blood loss.

While the advantages of one-sided dissection are shared with the modern dorsal onlay technique, several advantages are lost with a lateral onlay procedure. There is a stronger potential for sacculation and diverticulum formation. Additionally, the corpora cavernosa, which are used as a structured vascular bed in dorsal onlay urethroplasty, are not utilized in the same manner in the lateral technique. And while it may seem easier to carry lateral urethrotomy as compared to a dorsal urethrotomy proximally into the membranous urethra, there is no actual data to support the use of lateral onlay in this setting.

In both lateral and ventral onlay, the spongiosum is closed over the BMG. However, in the case of lateral closure, the spongiosum can be rotated dorsally to protect the suture line. Unfortunately, the lateral spongiosal tissue is not as thick and vascular and accordingly may serve as a lower-quality bed for buccal mucosa engraftment. Like ventral grafting, lateral onlay urethroplasty should not be utilized in repair of pendulous urethral strictures. Aside from the similar concerns for sacculation, there is also a conceptual concern for lateral curvature. This is not specifically documented in the literature, likely because it is a technique already not employed in this arena.

One study describes outcomes in 6 patients undergoing lateral onlay urethroplasty. The nonreintervention rate at a mean of 42 months was 83%. Keeping in mind the context of a small sample size and the retrospective nature of the analysis, the lateral technique was comparable to dorsal (85%) and ventral (83%) onlay techniques [27].

The lateral approach offers few advantages, and those too are largely outweighed by its own disadvantages and the advantages of the dorsal and ventral approaches. This technique should be used sparingly and reserved for special circumstances when intraoperative limitations compromise the ability to complete dorsal mobilization.

3. Complications

The complications of bulbar urethral augmentation relate ostensibly more to the surgery itself, rather than any specific technique, although, as discussed in each of the sections above, particular techniques may predispose patients to specific postoperative concerns. Complications can include wound and/or urine infection, urethrocutaneous fistula, perineal hematoma, blood loss requiring transfusion, or nerve injuries related to positioning. The overall incidence is low, and, in their series comparing these 3 approaches, Barbagli et al. noted no such complications amongst 50 patients [27].

4. Conclusion

Because the ventral, dorsal, or lateral placement of BMG is typically determined based on location and length of stricture and surgeon preference, comparative studies are limited. This review outlines the best available evidence supporting each technique. Aside from one randomized trial and one systematic review, the remainder of the studies referenced in this paper are retrospective reviews. While the best data suggest that patency outcomes are similar for each technique, appropriate patient selection is paramount to utilize the strengths of a given technique and avoid its shortcoming.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Clinical Study

Bipolar Transurethral Incision of Bladder Neck Stenoses with Mitomycin C Injection

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Introduction. To determine the efficacy of bipolar transurethral incision with mitomycin C (MMC) injection for the treatment of refractory bladder neck stenosis (BNS). *Materials and Methods*. Patients who underwent bipolar transurethral incision of BNS (TUIBNS) with MMC injection at our institution from 2013 to 2014 were retrospectively reviewed. A total of 2 mg of 40% mitomycin C solution was injected in four quadrants of the treated BNS. Treatment failure was defined as the need for subsequent intervention. *Results*. Thirteen patients underwent 17 bipolar TUIBNS with MMC injection. Twelve (92%) patients had failed a mean of 2.2 ± 1.1 prior endoscopic procedures. Median follow-up was 16.5 months (IQR: 14–18.4 months). Initial success was 62%; five (38%) patients had a recurrence with a median time to recurrence of 7.3 months. Four patients underwent a repeat procedure, 2 (50%) of which failed. Overall success was achieved in 77% (10/13) of patients after a mean of 1.3 ± 0.5 procedures. BNS recurrence was not significantly associated with history of pelvic radiation (33% versus 43%, $p = 0.9$). There were no serious adverse events. *Conclusions*. Bipolar TUIBNS with MMC injection was comparable in efficacy to previously reported techniques and did not result in any serious adverse events.

1. Introduction

Bladder neck stenosis (BNS) is a known complication of prostatectomy, prostate radiotherapy, and transurethral resection of the prostate (TURP) [1]. Although the majority of patients can be treated successfully with one to two endoscopic procedures, approximately 27% develop refractory bladder neck stenoses requiring multiple and increasingly complex treatments, potentially culminating in open reconstruction [2–6]. Many go on to require intermittent self-dilation to avoid major reconstruction, which has been shown to decrease quality of life [7]. More effective endoscopic treatments for refractory BNS are therefore needed.

There has been recent enthusiasm for the use of scar modulators such as mitomycin C to help increase success rates of transurethral incision of bladder neck stenoses (TUIBNS). Mitomycin C is a DNA cross-linker that decreases collagen deposition and leads to fibroblast apoptosis [8]. Patency rates for TUIBNS alone in the setting of recurrent stenoses are around 17% per procedure [2]. In contrast, TUIBNS with MMC injection has urethral patency rates ranging from 58 to 72% per procedure [9, 10]; however, MMC injection has also been associated with severe complications including rectourethral fistula, osteitis pubis, and bladder neck necrosis in a minority of patients [9]. Deep cuts into the fat with high dose MMC injection may be the culprit for these complications.

Monopolar electrocautery has greater depth of tissue penetration than bipolar technology [11, 12]. We hypothesize that bipolar cutting current could be associated with increased success following TUIBNS with MMC since less adjacent tissue damage could decrease scar reformation. We also hypothesize that avoiding deep incisions with bipolar electrocautery with MMC could minimize adverse events. To examine these hypotheses, we reviewed our institutional series of bipolar TUIBNS with intralesional MMC injection.

2. Materials and Methods

2.1. Data Collection. Following institutional review board approval, a retrospective review of all patients who underwent bipolar TUIBNS by a single surgeon (Mang L. Chen) at our institution from January 1, 2013, to December 31, 2014, was completed. Demographic information was collected including age, race, BNS etiology, number and type of prior interventions, and whether or not the patient had previously received pelvic radiation. Operative time and total dose of mitomycin C used were recorded. Postoperative complications were categorized according to the Clavien-Dindo classification [13]. Data were censored as of March 6, 2015.

Postoperatively, patients were monitored every 3 months for stricture recurrence using a combination of serial postvoid residuals, uroflowmetry, and self-reported obstructive voiding symptoms. Flexible cystoscopy was performed as indicated. Recurrence was defined as the need for any subsequent BNS procedure.

2.2. Operative Technique. Rigid cystoscopy was performed and guidewire passed through the stenotic lumen into the bladder. Scar resection was accomplished utilizing either a bipolar PK button electrode or PK Plasma-CISE (Gyrus ACMI, Southborough, MA). The PK Plasma-CISE was placed through a traditional 22-French cystoscope; the PK button electrode required use of a 26-French continuous flow resectoscope. The decision as to which instrument to use was made intraoperatively by the attending surgeon on a case-by-case basis. Severe stenosis required cannulation first with the smaller Plasma-CISE. Less severe but symptomatic stenoses were treated first with the Plasma-CISE, and if scar tissue ablation was unsatisfactory for cystoscopic passage into the bladder, the button was used. Scar incision and sometimes resection were accomplished using a cutting current at the 3, 9, and 12 o'clock positions and were continued until the lumen easily permitted the passage of the operating instrument into the bladder. We avoided 6 o'clock incisions to minimize risk of rectal injury. No fat was identified after the incision and/or resection was complete.

Mitomycin C was injected into four quadrants of the treated BNS following incision and/or resection. The needle was advanced approximately 5 mm into the tissue at the 1, 4, 8, and 11 o'clock positions for injection. A total dose of 2 mg of 40% mitomycin C in saline solution was used in all patients. Foley catheter was left in place for 3 days postoperatively.

2.3. Data Analysis. Demographic information is reported as frequencies and percentages. Means and standard deviations (SD) are reported for normally distributed data and medians with interquartile ranges (IQR) for nonnormal data. Fisher's exact test was used to compare the likelihood of recurrence between patients who did and did not receive pelvic radiation. Time to recurrence following the initial procedure was modeled with the Kaplan-Meier method. Success rates for initial and repeat procedures were analyzed separately so as not to compare MMC-naïve patients with those who had previously received MMC. Statistical significance was defined at the $p < 0.05$ level using two-tailed tests. Data was analyzed using SPSS software, version 20 (IBM Corp., Armonk, NY).

Table 1: Patient demographics.

	$n = 13$
Age, years, mean ± SD	67 ± 8.0
BMI, kg/m^2, mean ± SD	31 ± 6.0
Charlson comorbidity index (%)	
0-1	4 (31)
2	5 (38)
3	4 (31)
Etiology (%)	
RRP	5 (33)
RALP	3 (20)
TURP	3 (20)
Brachytherapy	2 (13)
Prior BNS treatment (%)	12 (92)
Number of prior interventions, mean ± SD	2.2 ± 1.1
Prior radiation (%)	6 (46)

SD: standard deviation, RRP: radical retropubic prostatectomy, RALP: robot-assisted laparoscopic prostatectomy, TURP: transurethral resection of prostate, and TUIBN: transurethral incision bladder neck.

3. Results

Thirteen consecutive patients underwent seventeen bipolar TUIBNS with MMC procedures over the study period. Median follow-up was 16.5 months (IQR: 14–18.4 months). Patient characteristics are summarized in Table 1. Stenosis etiology included radical prostatectomy in 8, prostate brachytherapy in 2, and TURP in 3. Four radical prostatectomy patients received postoperative radiation. Ninety-two percent of patients had failed a mean of 2.2 ± 1.1 prior endoscopic BNS procedures, but all were MMC-naïve.

Success following a single bipolar TUIBNS with MMC injection was 62% (8/13), as shown in Figure 1. Five patients (38%) had a recurrence with a median time to recurrence of 7.3 months (IQR: 3.7–10.9 months). Of the five patients who had a recurrence, one was retreated with TUIBNS alone due to a pharmacy shortage and 4 underwent a repeat TUIBNS with MMC procedure. Retreated patients were given the same MMC dosage of 2 mg. Two of the four (50%) repeat MMC procedures failed, one at four months and one at eight months, and these patients did not receive any further MMC with subsequent treatment. Both patients who failed a repeat procedure had a history of pelvic radiation whereas the two patients with successful repeat procedures did not; further the patients who failed repeat procedures had higher Charlson comorbidity index scores (2 and 3 versus 1) than the patients who responded to a second round. Overall, 77% (10/13) of patients had a patent bladder neck after a mean of 1.3 ± 0.5 procedures. Success rate per procedure was 59% (10/17).

Five of thirteen patients (38%) had some degree of stress urinary incontinence prior to undergoing TUIBNS. Incontinence was significantly worsened in two patients (15%) with preexisting incontinence; one subsequently underwent artificial urinary sphincter placement after BNS resolution and the other was managed with a Cunningham clamp per patient preference. Both of these patients had a history

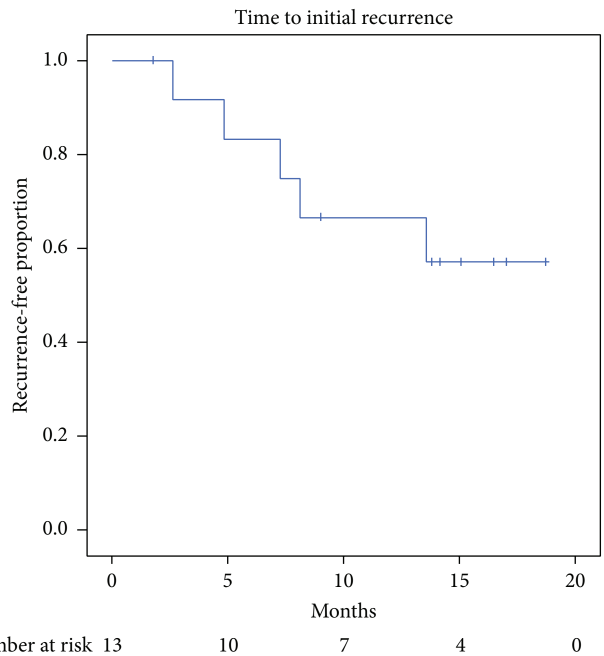

Figure 1: Time to stenosis recurrence following first transurethral incision of bladder neck stenosis with intralesional mitomycin C (MMC) injection in MMC-naïve patients. Censored cases marked by vertical line.

of pelvic radiation. De novo incontinence occurred in one patient (8%), which was mild and required one pad/day.

BNS recurrence was not significantly associated with a history of pelvic radiation (33% versus 43%, $p = 0.9$). One postoperative complication occurred, namely, urinary retention after catheter removal necessitating clean intermittent catheterization, classified as Clavien 1.

4. Discussion

Management of refractory BNS is a vexing problem for urologists and patients given its high recurrence rates following endoscopic treatments. Approximately 27% of patients with BNS develop refractory stenoses highly resistant to traditional therapy, with success rates of 0–20% following dilation or urethrotomy alone [2, 4]. Injection of mitomycin C as an inhibitor of scar formation has gained some traction for use in this subset of patients. Also, previous work has shown that use of electrocautery over cold knife incision may increase success rates [9]. In this paper we reviewed our institutional series of bipolar TUIBNS with MMC injection to determine whether the addition of bipolar electrocautery could maintain or improve upon previously reported patency rates. Using this approach, we report an initial success rate of 62% (8/13) and an overall patency rate of 77% (10/13) at a median follow-up of 16.5 months, which is consistent with recently reported results [9, 10].

Two previous studies have examined the efficacy of intralesional MMC injection in the treatment of refractory BNS. Vanni and colleagues report a series of 18 patients—all of whom had failed prior endoscopic therapy for BNS—treated with cold knife TUIBNS followed by injection of 0.3–0.4 mg/mL MMC [10]. At a median follow-up of 12 months, they report patency rates of 72% after a single procedure and 89% after two procedures. These are confounding results as other reports have suggested superiority of monopolar TUIBNS over cold knife incision [9, 14]. MMC injection may explain the higher than expected patency rates. Building upon this study, Redshaw et al. (TURNS study) reported a multi-institutional series of 55 patients treated with TUIBNS plus MMC [9]. Eighty percent of included patients had failed prior endoscopic treatment, and mean MMC dose was 3.5 mg. Initial and overall success rates in their series were 58% and 75%, respectively. Patients in the TURNS study had TUIBNS by either cold knife or monopolar incision depending on individual surgeon preference. Interestingly, use of electrocautery was associated with success on univariate analysis (OR 10.7 [95% CI 1.2–197], $p = 0.03$), although the confidence interval was wide and no multivariable risk adjustment was possible due to sample size. Our initial and overall success rates of 62% and 77% compare favorably with these two series. It should be noted, however, that our definition of treatment failure as based on clinical symptoms may be causing us to overestimate success relative to the TURNS experience, which defined recurrence based on urethral caliber noted on cystoscopy regardless of whether obstructive voiding symptoms were present.

Two of four patients in our series who failed an initial TUIBNS with MMC responded to a second round of treatment. Subsequent procedures were performed in an identical manner with the same MMC dosage as initial treatments. Both patients who responded to a second procedure had no history of pelvic radiation and a Charlson comorbidity index of 1; conversely the two patients who failed had both received pelvic radiation and had higher Charlson scores of 2 and 3. Unfortunately comparative statistics were not possible in this subset of patients due to the small overall numbers; however our data suggest that a history of pelvic radiation and greater number of comorbidities may be associated with decreased success rates for subsequent TUIBNS with MMC procedures. This finding needs to be validated in a larger sample size before this statement can be definitively made, however.

It is not clear from the literature that concomitant MMC injection is necessary to achieve high success rates following TUIBNS. In contrast to the above, Ramirez and colleagues were able to demonstrate an overall patency rate of 86% after 2 procedures at a mean follow-up of 13 months in 50 patients who underwent TUIBNS with electrocautery alone [14]. It is also not clear whether our ability to achieve similar success to this is due principally to the use of electrocautery, MMC injection, or a combination of the two. Unfortunately the present study is not designed or powered to delineate these differences.

Data from TURP procedures has shown that bipolar current is associated with a more superficial depth of tissue penetration than monopolar electrocautery, ranging from 0.5–1 mm in bipolar procedures to 3–5 mm in monopolar cases [11, 12]. As such, we hypothesized that bipolar cutting current would be associated with increased success following TUIBNS with MMC as there would theoretically be less adjacent tissue damage and therefore less of an impetus for scar reformation. However, with initial success in 62% of our patients compared to 58% in a series of mixed cold and hot knife procedures [9], we are unable to conclude that bipolar electrocautery meaningfully improved success. Due to our small sample size, the power to detect a true difference between techniques is low, and it is possible that with a larger sample a significant difference between the two techniques could emerge.

No patients in our study required diversion, and the only postoperative complication was one case of retention following catheter removal, requiring clean intermittent catheterization. The TURNS group noted 4 adverse events with 3 patients needing cystectomy [9]. There are two key protocol differences that may account for this discrepancy. First, our study exclusively used a 2 mg dose of mitomycin C, lower than the doses ranging from 0.4 to 10 mg in their series. Second, no perivesicular fat was visualized after incision in our series. This is in stark contrast to nearly every other research protocol where, as a prerequisite to injection, incisions were routinely made until the fat was visualized [9, 10, 14, 15]. These deeper incisions may account for the prevalence of serious complications observed in prior studies by allowing extravasation of MMC into the perivesicular fat, resulting in instances of rectourethral fistula, osteitis pubis, and bladder neck necrosis. It should be noted that our series achieved equivalent urethral patency rates to the TURNS study without requiring deep bladder neck incision into the perivesicular fat.

This study has several significant limitations. As with all retrospective studies, the potential for a selection bias exists. The small number of patients included limits statistical power to find differences in outcome. Follow-up was relatively short with a median of 16.5 months and long-term outcomes in these patients are not known. All patients included in this study were Caucasian, which limits generalizability to those of other racial backgrounds. The makeup of our cohort was heterogeneous, including patients who did and did not receive pelvic radiation as well as those with stenosis developing after varying treatments for both benign and malignant prostatic diseases. Unfortunately, the uncommon nature of this problem is a barrier to reaching a large enough sample size to compare these discrete groups directly, and this is reflected in the sample sizes of 18 and 55 seen in the Vanni and Redshaw papers, respectively [9, 10].

Despite these limitations, our results are meaningful for several reasons. We report the first series to our knowledge using bipolar TUIBNS with concomitant MMC injection for the treatment of refractory BNS. We achieved initial success in 62% and overall success in 77% of patients after a mean of 1.3 procedures, which is comparable to prior studies. Importantly, none of the serious adverse events that have previously been reported with the use of MMC were found in our series, possibly due to the previously described alterations in dosage and technique. Although the sample size is small, our results indicate that TUIBNS with MMC can achieve reasonable success without major morbidity. Further study with larger sample size, less patient heterogeneity, and longer follow-up is needed both to determine whether the use of bipolar electrocautery can confer an advantage over other techniques and to confirm that serious morbidity can effectively be avoided without compromising treatment success.

5. Conclusions

Bipolar TUIBNS with MMC done without deep incisions into the perivesicular fat can achieve comparable success to previously published techniques while also avoiding serious adverse events. A prospective, randomized study is needed to determine which factors (dilation, cold knife DVIU, monopolar/bipolar electrocautery, and scar modulator injection) are the most important in decreasing BNS recurrence.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Review Article

Treatment of Urethral Strictures from Irradiation and Other Nonsurgical Forms of Pelvic Cancer Treatment

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Radiation therapy (RT), external beam radiation therapy (EBRT), brachytherapy (BT), photon beam therapy (PBT), high intensity focused ultrasound (HIFU), and cryotherapy are noninvasive treatment options for pelvic malignancies and prostate cancer. Though effective in treating cancer, urethral stricture disease is an underrecognized and poorly reported sequela of these treatment modalities. Studies estimate the incidence of stricture from BT to be 1.8%, EBRT 1.7%, combined EBRT and BT 5.2%, and cryotherapy 2.5%. Radiation effects on the genitourinary system can manifest early or months to years after treatment with the onus being on the clinician to investigate and rule-out stricture disease as an underlying etiology for lower urinary tract symptoms. Obliterative endarteritis resulting in ischemia and fibrosis of the irradiated tissue complicates treatment strategies, which include urethral dilation, direct-vision internal urethrotomy (DVIU), urethral stents, and urethroplasty. Failure rates for dilation and DVIU are exceedingly high with several studies indicating that urethroplasty is the most definitive and durable treatment modality for patients with radiation-induced stricture disease. However, a detailed discussion should be offered regarding development or worsening of incontinence after treatment with urethroplasty. Further studies are required to assess the nature and treatment of cryotherapy and HIFU-induced strictures.

1. Introduction

Radiation therapy (RT) is a well-known and effective means of treating pelvic malignancies. External beam radiation therapy (EBRT), brachytherapy (BT), photon beam therapy (PBT), high intensity focused ultrasound (HIFU), and cryotherapy are forms of noninvasive treatments for malignancy. Although an effective form of cancer treatment, radiation therapy is not without complication. Urethral stricture disease is an underrecognized and poorly reported complication that can cause severe morbidity for cancer survivors [1, 2]. Radiated urethral tissue in particular poses a challenge for the reconstructive urologist. It is our goal to provide a comprehensive discussion of etiology, incidence, and available treatment options for urethral stricture disease following pelvic radiation.

2. Epidemiology

The term stricture has previously been the nomenclature applied to any narrowing along the entirety of the urethra. Updated terminology now uses *stenosis* and *stricture* to more appropriately localize the abnormality along the urethra. Narrowed segments of the urethra surrounded by spongiofibrosis have been deemed *stricture*. In contrast, constrictions that occur within the posterior urethra are deemed *stenosis* [3]. It is import to differentiate between the two as treatments can differ depending on location [4].

Radiation effects on the genitourinary system can manifest early after treatment or present months or years after. Acutely, radiation treatment can cause lower urinary tract symptoms (LUTS) such as frequency, urgency, and dysuria requiring symptomatic management [5, 6]. Late urinary toxicity is a prolonged sequelae that can present with hesitancy, retention, stricture, and hematuria [5]. The timing of late toxicity is highly varied and can declare itself decades after initial radiation treatment [7]. Although narrowing can theoretically form at any location along the course of the urethra, bulbomembranous stenosis accounts for 90% of reported strictures after RT [8]. A study investigating the CaPSure registry reported the incidence of stricture from four separate categories of treatment. Their study found the incidence of stricture from BT to be 1.8%, EBRT 1.7%, combined EBRT and BT 5.2%, and cryotherapy as 2.5% [9]. A more recent study documented ranges of bulbomembranous stricture incidence from BT at 1 to 8% versus 2 to 4% for EBRT [2]. Data reporting the incidence of cryotherapy-related stricture disease is also limited; however a recent study comparing 10-year propensity-weighted adverse urinary events after treatment for prostate cancer found incidence of stricture to be 1.05% ($n = 2115$) [10].

3. Etiology

Radiation therapy causes damage on living cells in two main ways: directly, inflicting damage to cellular DNA initiating DNA mutation and apoptosis, and indirectly, interacting with free water within the cell to form hydroxyl free radicals that are highly unstable within the cell. Furthermore, cells that are actively dividing are more sensitive to ionizing radiation than those more stagnant in the cell cycle [11]. Data reviewing the pathophysiology behind urethral stricture in inflammatory, autoimmune, and infectious processes is well-understood and well-described [8]. Unfortunately, studies investigating the underlying mechanism causing stricture after radiation therapy are limited.

Ballek and Gonzalez have studied and described the pathophysiology pertaining to radiation-induced strictures in great detail. Through the aforementioned mechanisms, basement membranes of vascular tissues supplying the urethra become damaged, resulting in occlusion, thrombosis, and impaired neovascularization. Vascular compromise leads to inadequate tissue perfusion and poor wound healing. The result is fibroblasts that are rendered incapable of producing collagen to meet the demands of the healing wound. Collagen maturation is also compromised by poorly functioning fibroblasts leading to contraction and scar formation [12]. Studies have demonstrated this effect to be long lasting and even transmitted to daughter fibroblasts within tissue [13]. Over time, the corpus spongiosum is replaced with fibrotic tissue and subsequent occlusion of the urethral lumen occurs [12].

Healing of these compromised tissues should also be a consideration of the urologist when considering surgical intervention such as reconstructive urethroplasty. Patients receiving radiation therapy weeks to months prior to undergoing surgical intervention experience poor wound healing compared to those who receive similar doses of radiation 6 months or more before surgery [13, 14]. Gorodetsky further found this effect to be dose-dependent; as radiation dose was increased, wound strength decreased. Tissue planes can be distorted making urethroplasty with primary anastomosis or tissue substitution a difficult task [15, 16]. Further complicating the characteristics of these strictures is their location in the bulbomembranous urethra, higher incidence of postoperative urinary incontinence, erectile dysfunction, and fistula formation [16]. Therefore, these patients should be meticulously informed of the risks and benefits of pursuing surgical intervention.

The overall incidence of urethral stricture disease is also dependent on radiation dosage and the type of radiation used [9, 12]. Merrick et al. found the magnitude and extent of high dose radiation, mean membranous urethral dose, dose 20 mm proximal to the prostatic apex, and the duration of hormonal manipulation to be predictive of stricture formation after radiation therapy [17]. Compared with other side effects of radiation, stricture/stenosis is a relatively uncommon occurrence but is difficult to treat effectively.

4. Diagnosis and Evaluation

Patients presenting with LUTS following pelvic radiotherapy should undergo a thorough history and physical examination with special attention to the patency of the urethral meatus, suprapubic exam, and digital rectal examination. Furthermore, inquiries should be made regarding the dose and type of therapy the patient has received. When indicated, postvoid residual by ultrasound can assess bladder emptying [8, 17].

Cystourethroscopy and retrograde urethrogram provide further detail on the location and length of the urethral stricture [12, 17]. However, exact delineation of the anatomy may be difficult due to distortion from the previously administered therapy. Assessment of external sphincter involvement and the length of the strictured segment are essential [8]. Retrograde urethrography offers the ability to determine the length and location of the obstruction (Figure 1).

If retrograde urethrogram is inconclusive, voiding cystourethrogram allows for full evaluation of the posterior urethra as well as the urethra proximal to the stricture. If a suprapubic tube is present, simultaneous antegrade endoscopy and retrograde urethrography can be performed [12].

Because of the potential deleterious effects of radiation therapy on the bladder, urodynamics can be helpful in evaluating bladder capacity prior to any potential surgery [12, 17]. For patients with bladder volumes less than 200 mL or severe detrusor instability, conservative measures to increase bladder volume may be attempted before reconstruction. However, other options such as bladder augmentation before reconstruction or urinary diversion can be discussed with the patient [12].

5. Treatment

Radiation induces an obliterative endarteritis that results in ischemia and fibrosis of the irradiated tissue. In the perioperative setting, these changes lead to compromised wound healing, altered tissue planes, and impaired blood supply of irradiated tissue [18]. Indeed these pathophysiologic changes induced by radiation are the underlying reasons why treatment can present a challenge.

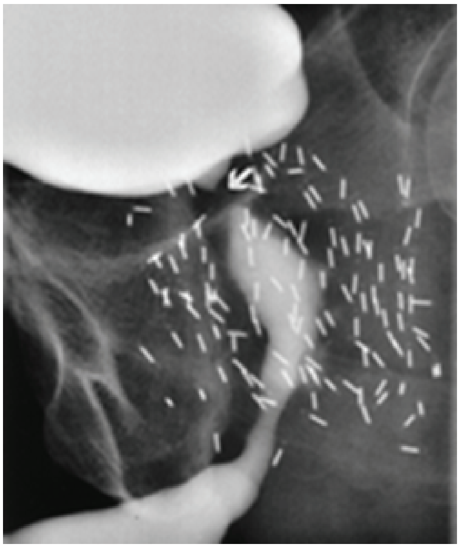

Figure 1: Bulbar and bladder neck stricture from combined EBRT and brachytherapy. *Credit to R. Santucci.*

Typical urethral stenosis after single-modality radiation treatment begins at the proximal bulbar urethra and extends through the membranous urethra and prostatic apex [2]. According to the experience of Mundy and Andrich, strictures after EBRT have an average stricture length of approximately 2 cm. Moreover, they report strictures secondary to combination of BT and EBRT are typically longer with nearly half being obliterative [8]. Short strictures are rare and when they happen, anastomotic repairs are rarely successful. Compared with strictures in BT patients, EBRT strictures are not commonly obliterative; they are less complicated to treat and therefore are theoretically amenable to anastomotic urethroplasty. Alternatively, tissue transfer repairs, such as grafts and/or flaps, are more likely to be appropriate and successful in those nonobliterative strictures which are not controlled by interval urethral dilatation [8, 19].

The gold standard for treatment of urethral strictures is urethroplasty with primary anastomosis or substitution urethroplasty being effective techniques depending on the stricture length [19]. Substitution urethroplasty can be accomplished with a graft and/or flap. The difference between the two methods is contingent on the presence (or lack thereof) of the grafted tissue's native blood supply. A graft is tissue that is moved from a donor site to a recipient site without its native blood supply. In contrast, flap tissues maintain their native blood supply on a pedicle that is transferred onto the recipient site [3, 19]. In the previously irradiated patient, several studies have shown urethroplasty to be efficacious. In general, direct-vision internal urethrotomy (DVIU) and dilation carry much higher failure rates than urethroplasty. Urethral stents have been studied in the setting of prostate cancer related urethral stricture disease and their application is discussed below though their use has fallen out of favor.

6. Urethral Dilation and Direct-Vision Internal Urethrotomy

The increased rate of complications associated with reconstruction of the radiated urethra underlies the initial selection of endoscopic therapy for the management of RT induced strictures, regardless of radiation modality. Endoscopic treatment of radiation-induced posterior urethral stenosis [PUS] has been associated with recurrences of approximately 40–60% regardless of the location or etiology [20]. In a study of 76 patients, Santucci and Eisenberg reported a stricture-free rate after first DVIU of 8% with median time to recurrence of 7 months. Subsequent urethrotomies were associated with decreased success rates with 0% stricture-free rate after the fourth and fifth procedures. As such, dilation and DVIU are advocated as temporizing measures, reserved for a select group of patients who have been counseled on the high likelihood of stricture recurrence until definitive curative reconstruction can be planned [1, 21].

Sullivan et al. assessed the nature and outcomes of urethral stricture disease in 38 patients who received high dose rate BT administered either as a boost to EBRT or as monotherapy. 92.1% of these patients experienced a stricture located in the bulbomembranous urethra with a mean time to diagnosis of 22 months. All strictures were initially managed with either dilation (n = 15) or DVIU (n = 20) with second-line therapy being performed in 17 cases (49%) via repeat dilation, DVIU, or intermittent self-catheterization. Only three cases (9%) required third-line therapy with one patient undergoing urethroplasty. While only one patient underwent invasive surgery with urethroplasty, nearly half of those who initially experienced a urethral stricture subsequently had second-line therapy to treat their stricture disease. However, as the study only provided a median follow-up time after treatment of the initial stricture of 16 months, long-term outcomes of treatment of BT-induced stricture disease cannot truly be reliably assessed based on this data alone [22].

Recently, Hudak et al. investigated the utility and counterproductive effects of repeat DVIU by reviewing 340 consecutive urethroplasties performed by a single surgeon to assess the association of repeat transurethral treatment with stricture complexity. Of 101 urethroplasties meeting inclusion criteria, it was discovered that repeat transurethral manipulation was associated with an eightfold increase in disease duration from stricture diagnosis to curative urethroplasty between patients who had undergone 0 to 1 prior DVIUs versus 2 or more ($p < 0.001$). Moreover, those who had undergone 2 or more previous DVIUs had significantly longer strictures ($p = 0.001$) and were more likely to undergo substitution urethroplasty. Furthermore, though not statistically significant, failure was more common in these patients versus those with 0 or 1 DVIU (12% versus 2%, $p = 0.11$) [23].

Intralesional injection of mitomycin C (MMC) has been assessed as an adjunct to DVIU owing to its ability to mitigate scar formation via inhibition of fibroblast proliferation. Farrell et al. reported a case series prospectively evaluating their experience with DVIU with intralesional MMC and short-term (1 month) clean intermittent catheterization (CIC). 37

patients were enrolled in the study and subsequently underwent DVIU with MMC and once daily CIC for treatment of refractory urethral stricture disease or bladder neck contracture. Radiation-induced urethral strictures were identified in 11 patients with 9 patients (81.8%) having received BT and the other 2 patients receiving EBRT and BT. Though no difference in stricture length was noted between patients with radiation-induced strictures and those without (mean 2.0 cm, $p = 0.651$), patients with prior radiation were noted to have deeper spongiofibrosis. Postoperatively, those with radiation-induced strictures did not experience a significant improvement in flow rate ($p = 0.158$) or PVR ($p = 0.813$) while those with strictures not related to radiation did experience significant improvements in these categories. The overall success rate was found to be 75.7% over the median follow-up period of 23 months. Recurrence-free success was 54.5% in the radiation cohort with a mean time to recurrence of 8 months [24]. The success rate of DVIU with MMC and CIC in patients with radiation-induced strictures is poorer compared to published data assessing urethroplasty [2, 18, 25–30] in this population and is within the estimated overall 40–60% success rate of DVIU/urethral dilation without MMC [20]. Therefore, while conceptually interesting, further large-cohort studies are necessary to the safety and efficacy of intralesional MMC in those with recalcitrant radiation-induced stricture disease.

7. Urethral Stents

The use of urethral stents have been described in the management of urethral stricture disease secondary to prostate cancer therapy. Eisenberg et al. described their experience with urethral stents for treatment of urethral stricture disease in 13 patients, of which 11 had previous history of prostate cancer therapy. The primary indication for urethral stenting versus reconstruction in these patients was to avoid the morbidity of surgery. Of these 11 patients, 3 received EBRT adjuvantly after radical prostatectomy and 4 received combined EBRT and BT with 2 also having undergone concomitant TURP. Overall, 6 of the 13 patients who underwent a urethral stent required additional procedures for stricture recurrence including 5 in previously irradiated patients. Furthermore, 8 of the 13 patients were subsequently rendered incontinent and willing patients underwent AUS placement [31].

In a subsequent study from the same institution, Erickson et al. assessed the efficacy of Urolume stents in 38 men with posterior urethral strictures secondary to prostate cancer treatment. 24 men (63%) received radiation therapy as either the primary treatment (16) or adjuvantly after radical prostatectomy (8). The modalities undertaken to administer radiation treatment were adjuvant EBRT in 8 patients, EBRT with salvage prostatectomy in 2 patients, BT in 8 patients, and BT with EBRT in 6 patients. After a mean follow-up of 2.3 ± 2.5 years, the authors reported an initial success rate of 47% improving to a final success rate of 89% after a total of 33 secondary procedures (including stent placement) in 19 men. Moreover, men who had received radiation therapy experienced recurrence sooner and required more secondary procedures. However, multivariate analysis failed to implicate radiation therapy as an independent risk factor for failure. The overall postoperative incontinence rate was found to be 82% with a higher rate in men who did versus did not receive previous radiation therapy (96% versus 50%, $p < 0.001$) [32].

Urolume stents are no longer commercially available in the United States and have globally fallen out of favor. However, the aforementioned studies advocate that urethral stenting is a reasonable treatment option for radiation-induced urethral strictures particularly when considering the significant postoperative morbidity patients may experience secondary to open excision. While initial success rates were dismal, secondary procedures led to vast improvements in urethral patency though many required yet further procedures to manage continence. Though incontinence and need for secondary procedures is expected, urethral stenting is a reasonable option for men unwilling or unable to undergo open urethral reconstruction.

8. Urethroplasty

Though urethroplasty is the most invasive approach to the treatment of urethral stricture disease, numerous studies have supported its use given the high rates of success. According to a review by Meeks et al., substitution urethroplasty using a buccal mucosal graft (BMG) has become the primary surgical treatment for long segment bulbar urethral strictures that are not suitable for anastomotic urethroplasty. The success rate for urethroplasty with BMG is between 81% and 96% with an estimated overall 15.6% failure rate for substitution urethroplasty [7]. Furthermore, as previously discussed, repeat DVIUs and/or dilation are destined to fail and may in fact reduce the efficacy of subsequent definitive therapy. In a review of 443 patients who underwent urethroplasty, Erickson et al. determined that a previous history of DVIU ($p = 0.04$) or urethroplasty ($p = 0.03$) was a significant factor predictive of urethroplasty failure [32].Therefore, it stands to reason that further DVIUs and/or dilation should be avoided in favor of more definitive therapy.

Elliott et al. established this notion in 2006 when they prospectively assessed their management of 48 patients presenting with urethral stenosis or rectourinary fistula secondary to prostate cancer therapy. Of the 32 cases of stenosis, 14 occurred secondary to primary radiation therapy while 7 cases involved radical prostatectomy plus EBRT. 23 of 32 patients (73%) experienced successful repair of urethral stenosis, which involved anastomotic urethroplasty (19), flap urethroplasty (2), perineal urethrostomy (2), and urethral stent (9). Regardless of the location of the stricture (i.e., anterior versus posterior), success rates were nearly equal at 70% versus 73%. Moreover, the authors highlight prior EBRT as being a risk factor for urethral reconstruction failure as 9% of RP treated versus 50% of RP plus EBRT treated patients experienced failure after posterior urethroplasty. Of note, the authors excluded patients that had previous treatment with dilation, DVIU, or TUR and also did not subsequently manage any of the patients enrolled in the study with these treatment strategies. However, the study demonstrates that urethroplasty and urethral stenting are viable treatment options with acceptable rates of failure for patients presenting with radiation-induced stricture disease [25].

To further assess the efficacy urethroplasty for treatment of radiation-induced strictures, Meeks et al. performed a review of 30 men undergoing urethroplasty at three separate institutions. EBRT for prostate cancer was etiology of stricture disease in 15 men (50%) with brachytherapy in 7 and a combination of the two in 8. All strictures were noted to be in the proximal bulbar or membranous urethra and on average were 2.9 cm in length. At a mean follow-up of 21 months, 22 men (73%) experienced successful urethral reconstruction with the majority of individuals undergoing excision with primary anastomosis (80%). Incontinence was transient in 10% and persistent in 40%, with 13% subsequently undergoing placement of an artificial urinary sphincter [26].

Glass et al. retrospectively reviewed 29 men with urethral stricture following radiation treatment of prostate cancer of which 11 (38%) were treated with EBRT alone, seven (24%) had radical prostatectomy followed by adjuvant EBRT, seven (24%) had combined EBRT and brachytherapy, and four (14%) were treated with brachytherapy alone. The average stricture length was 2.6 cm. 22 of the cases were reconstructed with excision and primary anastomosis (EPA) (76%), substitution urethroplasty with buccal mucosa in five (17%), and fasciocutaneous flap onlay in two (7%). The overall success rate was 90% at a median follow-up of 40 months (range 12–83 months) with time to stricture recurrence ranging from 6 to 16 months. New onset of urge urinary incontinence was reported in two patients (7%) with one patient opting for an artificial urinary sphincter. Of note, one-third of the patients in this cohort underwent either DVIU or dilation, both of which have been previously shown to contribute to subsequent failure of urethroplasties [18, 33]. Therefore, despite previous treatment, urethroplasty was found to be highly successful in this series.

Further support for the efficacy of excision and primary anastomosis (EPA) for radiation-induced strictures was provided by a 2014 retrospective study conducted by Hofer and colleagues. Of the 72 men identified with radiation-induced urethral strictures, 66 (91.7%) underwent urethral reconstruction with EPA and the remaining 6 (8.3%) were treated with substitution urethroplasty using a graft or flap. Mean stricture length, which was determined intraoperatively, was 2.4 cm. Furthermore, stricture length was 2 cm or less in 37 of 65 men (56.1%) and greater than 2 cm in 28 men (42.4%). Stricture lengths were greater in those who underwent substitution urethroplasty (mean length 4.25 cm, range 3 to 7 cm). 46 (69.7%) men ultimately experienced successful reconstruction. Mean time to recurrence was found to be 10.2 months and was associated with stricture length greater than 2 cm ($p = 0.013$). Moreover, 12 (18.5%) men experienced new onset incontinence while the rate of ED remained stable. Radiotherapy type did not affect stricture length ($p = 0.41$), recurrence risk ($p = 0.91$), postoperative incontinence ($p = 0.88$), or erectile dysfunction ($p = 0.53$). Overall, EPA was found to be a successful treatment strategy for patients with radiation-induced strictures of the bulbomembranous urethra. Furthermore, the study indicates that men should be counseled on the development of de novo incontinence and the possible need for secondary procedures to provide adequate management [27].

In a 2015 study, Rourke et al. retrospectively reviewed outcomes in 35 patients undergoing urethroplasty for radiation-induced bulbomembranous stenosis. Of the 35 patients, 20 and 15 had stenosis related to EBRT and BT, respectively, with a mean stricture length of 3.5 cm. Nearly half of the patients enrolled in the study presented preoperatively with an indwelling suprapubic catheter indicating baseline. Reconstruction was performed using anastomotic urethroplasty in 23 patients (65.7%) with 12 patients requiring tissue transfer via buccal mucosa graft (20.0%) or penile island flap (14.3%). With 50.5 months of follow-up, thirty patients (85.7%) achieved cystoscopic patency with no significant difference between techniques ($p = 0.32$). 31.4% of patients experienced a reportable 90-day complication all of which were Clavien Grades I-II [2].

The work of Rourke et al. indicates that urethroplasty is efficacious in radiation-induced urethral stenosis. However, even in well-selected patients (i.e., those without extensive prostatic necrosis, cavitation, prostatosymphyseal fistula, osteomyelitis, or small functional bladder capacity) minor complications were fairly common albeit acceptable and manageable. Despite achieving urethral patency many patients continued to experience bothersome LUTS as well as ED and incontinence. This suggests that even though commendable urethral patency rates may be attained, urethroplasty cannot alone mitigate and may even exacerbate, many of the concomitant complaints experienced by this patient population [2].

While the aforementioned studies have largely assessed the efficacy of anastomotic urethroplasties, long-term outcomes reported in men undergoing substitution urethroplasty have demonstrated higher recurrence rates than anastomotic techniques. The failure of substitution urethroplasties is further exacerbated by the use of donor graft or flap tissue that has been irradiated, which can compromise the effects of the previous radiation exposure.

An abstract published by Kuhl et al. specifically assessed the outcomes of buccal mucosa graft (BMG) urethroplasties for the treatment of radiation-induced urethral strictures. Of the 20 patients enrolled in the study with available data, 75% of treated strictures were within the bulbomembranous urethra and less than 6 cm in length. The success rate was found to be 60% after 25 months of follow-up. Postoperatively, patients experienced an improvement in flow rate from 8.4 to 25.6 mL/s, which trended towards significance ($p < 0.07$) in flow rate. Furthermore, 29% and 10% of the patients with preoperative incontinence experienced worsening or de novo incontinence, respectively. However, despite these postoperative changes in continence, BMG substitution urethroplasties were deemed to be successful with high rates of patient satisfaction [28].

Long segment strictures have been found to be challenging to treat. When treated with traditional dorsal or ventral onlay approaches, these strictures carry a high risk of recurrence due to the lack of a well-vascularized graft bed. Moreover, previously irradiated fields are often poorly vascularized thereby impeding wound healing [12, 29, 30]. In order to promote neovascularity and healing of these reconstructions, Palmer et al. assessed the use of a gracilis muscle flap to provide a well-vascularized graft bed for buccal graft substitutions. After performing a ventral buccal graft onlay, the authors describe harvesting and rotating gracilis muscle onto the perineum and buttressing the muscle to the graft. 20 patients with long segment urethral strictures secondary to various etiologies including radiation therapy in 45% (9 of 20) were retrospectively reviewed. Before surgery, 18 patients (90%) had undergone dilatation and/or endoscopic incision. Strictures were located in the posterior urethra with or without bulbar urethral involvement in 50% of cases (10), the bulbomembranous urethra in 35% (7), the bulbar urethra in 10% (2), and the proximal pendulous urethra in 5% (1) with a mean stricture length of 8.2 cm. Urethral reconstruction was found to be successful in 16 cases (80%) at a mean follow-up of 40 months. Mean time to recurrence was observed to be 10 months with 5 patients (25%) experiencing postoperative incontinence requiring an artificial urinary sphincter. Despite significant preoperative risk factors, the authors demonstrate the efficaciousness of substitution urethroplasty with gracilis flap thereby supporting its use in complex patients with a previous history of radiation therapy. However, despite the encouraging results, the study is limited by its retrospective nature and small sample size [30].

Ahyai et al. recently published their experience with ventral onlay buccal mucosa graft urethroplasties in patients with radiation-induced strictures. 35 of the 38 men (92.1%) included in the study underwent radiotherapy for treatment of prostate cancer with 64.9% exclusively undergoing EBRT. BT was performed in 8 patients (21.6%) with EBRT and BT being performed in combination in 6 patients (13.5%). The median length of strictures treated was 3.0 cm. The mean length of implanted buccal graft was 4.9 cm. 27 patients had undergone previous urethral dilation or DVIU. After a median follow-up of 26.5 months, the overall success rate was 71.1% with 4 patients (10.5%) experiencing de novo incontinence and 11 patients (28.9%) experiencing recurrence. Though limited by its retrospective design and small sample size, the study indicates that ventral onlay buccal mucosa urethroplasty is an acceptable treatment strategy with results similar to EPAs particularly for patients with strictures greater than 1 cm [34].

9. Conclusions

Men with urethral strictures secondary to nonsurgical forms of treatment for prostate cancer represent a challenging cohort to treat. Published data suggests that radiation-induced strictures are best treated with urethroplasty via anastomic or substitution techniques. Patients should be counseled on the high likelihood of stricture recurrence after DVIU or dilation. Moreover, a detailed discussion should take place regarding development or worsening of incontinence after treatment with urethroplasty. Further studies are required to assess the nature and treatment of cryotherapy and HIFU-induced strictures.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Research Article

Impact of Short-Stay Urethroplasty on Health-Related Quality of Life and Patient's Perception of Timing of Discharge

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Objective. To evaluate health-related quality of life in patients after a short-stay or outpatient urethroplasty. *Methods.* Over a 2-year period a validated health-related quality-of-life questionnaire, EuroQol (EQ-5D), was administered to all patients after urethroplasty. Postoperatively patients were offered to be sent home immediately or to stay overnight. Within 24 hours after discharge they were assessed for mobility, self-care, usual activities, pain or discomfort, and anxiety and depression. An additional question assessing timing of discharge was added to the survey. Clinical and operative characteristics were examined. *Results.* Forty-eight patients after anterior urethroplasty completed the survey. Mean age and mean stricture length were 51.6 years (21–78) and 60 mm (5–200 mm), respectively. Most etiologies were idiopathic (50% $n = 24$), trauma (19%, $n = 9$), and iatrogenic (19%, $n = 9$). Forty-one patients (85%) stayed overnight, while 7 patients (15%) chose to be discharged the same day. Overall, ninety-six percent were discharged within 23 hours of surgery. In the short-stay and the outpatient cohorts, 90% and 86%, respectively, felt they were discharged on time. No patient reported a severe problem with postoperative pain or mobility. *Conclusions.* The majority of patients discharged soon after their procedure felt that discharge timing was appropriate and their health-related quality of life was only minimally affected.

1. Introduction

Urethroplasty is recognized as the gold standard treatment of anterior urethral stricture disease, given the reasonably high long-term success rates and acceptable morbidity [1–3]. While, traditionally, urethroplasty was followed by inpatient hospital stay, there has been an increasing trend for urological procedures to be performed on an outpatient basis [4], a pattern reflected in urologic reconstruction as well [5, 6]. While numerous studies have been published reporting the clinical outcomes of urethroplasty, patient perception, satisfaction, and subjective outcomes are not well studied. There is also a paucity of data examining patient perception of early return home from the hospital. The purpose of this study was to examine the patient's perception of appropriateness of timing of discharge and to evaluate immediate health-related quality of life immediately after discharge.

2. Methods

With institutional board review approval, electronic charts of 80 consecutive patients who underwent anterior urethral reconstruction at our institution from August 2012 to May 2014 were analyzed. Patients under 18 years of age, those with documented intellectual disability, incarcerated patients, and transgender patients were excluded, as were patients with planned multistage procedures.

All patients underwent preoperative evaluation with retrograde urethrogram and/or voiding cystourethrogram, uroflowmetry, and AUA symptom scores. All patients were counseled at the time of the preoperative evaluation of possible immediate postoperative discharge or overnight stay based on their postoperative condition and desire. Patients were assured that from our previous experience most prior patients safely returned home either immediately following urethroplasty or after an overnight stay providing pain is controlled and there are no other health concerns. Patients were educated on proper use of all postoperative medications and care for Foley catheter. Each patient was given contact information for the clinic and additionally a mobile phone number of the surgeon and were encouraged to call with additional questions or concerns before or after the surgery. The same points were reiterated immediately before the surgery in the Preoperative Unit.

The type of urethroplasty performed was dependent on stricture length, location, and etiology as well as surgeon preference. For substitution or augmentation urethroplasties, only buccal mucosal grafts (BMG) were used. The BMG was harvested as described by Morey and McAninch [7]; however, the harvest site was left open after harvest. The midline perineal incisions were closed in layers and no wound drains were used. A urethral catheter was left in place in all patients. When present, a suprapubic catheter remained capped on discharge.

In the postanesthesia recovery area all patients were assessed and given a choice of immediate discharge or an overnight hospital stay. Patients who elected to return home on the day of surgery were placed in the "outpatient cohort" while those who stayed overnight were a "short-stay" group. Discharge criteria in both groups included hemodynamic stability, adequate pain control with oral analgesics, and sufficient mobility to ambulate without difficulty. Patients were routinely sent home with prescriptions for nonsteroidal anti-inflammatory agents, oral narcotic medications for breakthrough pain, anticholinergics, stool softeners, and anesthetic/antiseptic mouthwash.

Within 24 hours of discharge, a routine postoperative check was conducted over the phone by a nurse or nonmedical administrative assistant. The assessment included questions from the EuroQol (EQ-5D), a validated health-related quality of life (QOL) questionnaire [8, 9]. The questions are designed to assess mobility, self-care, usual activities, pain or discomfort, and anxiety/depression. The choices were scored from 1 to 3 as having "no problems," "moderate," or "severe problems," respectively. An additional question assessing perception of the timing of discharge as "right on time," "too soon," or "too late" was added to the interview.

We also reviewed the charts for hospital readmissions, emergency room visits, and unplanned clinic visits to capture any additional potential burden on patients or the healthcare system due to early postoperative discharge.

3. Results and Discussion

A total of 48 patients who underwent anterior urethroplasty between August 2012 and May 2014 were included. Mean age of the group was 51.6 years (21–78). Mean stricture length was 59.7 mm (5–200 mm). Preoperative patient characteristics and stricture etiology are shown in Table 1. The most common type of repair was a single stage, one sided dissection, dorsal onlay buccal urethroplasty in 13 (27%) patients as described by Kulkarni [10], followed by excision and primary anastomosis in 11 (23%) and augmented anastomotic urethroplasty in 10 (21%) patients (Table 2). Overall, 37 of the 48 patients (77%) had buccal mucosa harvest for augmentation or substitution urethroplasty of which 8 required bilateral buccal mucosa harvest.

Table 1: Patient characteristics.

	Mean (Std. Dev.)	Range
Age (years)	51.6 (±15.65)	21–78
BMI (kg/m^2)	30.6 (±6.2)	18.6–44.7
Stricture length (mm)	60 (±51)	5–200
Stricture etiology	Number	%
Idiopathic	24	50
Trauma	9	19
Iatrogenic	9	19
Infectious	2	4
Radiation	2	4
Lichen sclerosis	2	4
Stricture location	Number	%
Bulbar	20	42
Bulbomembranous	12	25
Panurethral	9	18
Pendulous	5	10.4
Fossa navicularis	2	4

Table 2: Type of urethroplasty.

Repair type	Number (%)
One sided dissection, dorsal onlay (Kulkarni)	13 (27%)
Excision and primary anastomosis (EPA)	11 (23%)
Augmented anastomotic urethroplasty (AAU)	10 (21%)
Dorsal onlay	9 (19%)
Ventral onlay	4 (8%)
Others	1 (2%)

Forty-one patients made a postoperative decision to stay overnight, while seven elected to return home the same day. All except two patients (96%) were discharged within 23 hours of surgery.

Forty-six out of 48 patients (96%) responded to the EuroQuol-5 questionnaire as well as the question on timing of discharge within 24 hours of discharge. Overall, 89.1 % of all patients felt they were discharged on time (Figure 1).

With regard to the 5 dimensions on the EuroQuol-5, severe problems with "mobility" were not reported by any patient: 26 (56%) patients reported moderate problems with mobility compared to 20 (44%) that reported no problems (Figure 2). Only 2 patients (4%) reported severe problems in the "self-care" domain; a majority of patients, 31 (67%), reported no problems with self-care. Eleven patients (24%) reported severe problems with "usual activities," while 23 (50%) reported moderate problems. When asked about "pain or discomfort," no patients reported severe problems, but the majority 38 (83%) did indicate having moderate problems with pain or discomfort. On the question of "anxiety/depression," only one patient (2%) reported severe problems with anxiety or depression, while the majority of

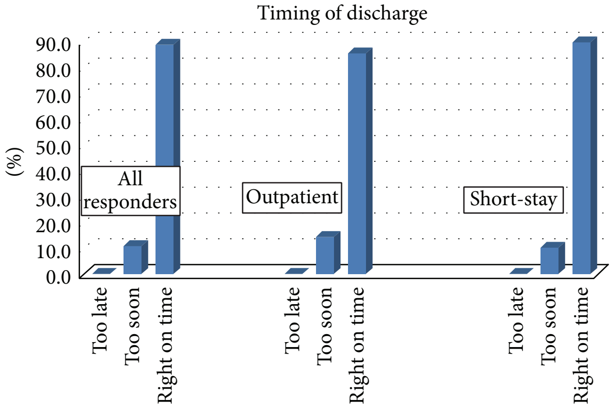

Figure 1: Timing of discharge.

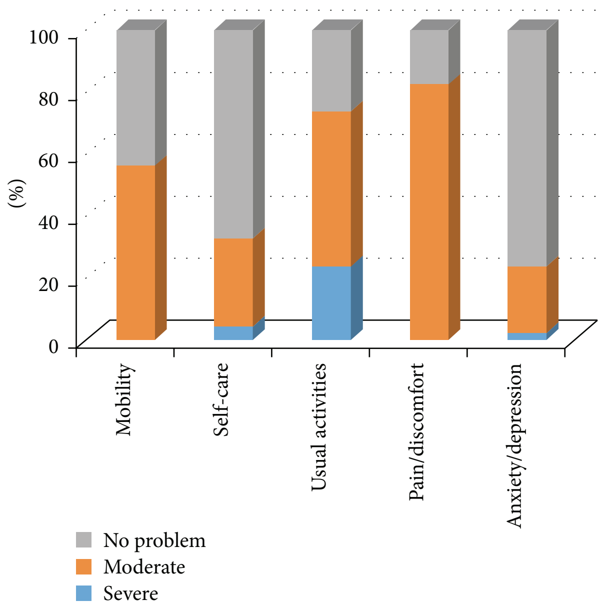

Figure 2: EQ-5 patient responses (all patients).

patients, 35 (76%), reported no problems. Table 3 summarizes the EQ-5 data collected from each group.

There were two Emergency Room visits recorded, one of which was readmitted to the hospital for incision and drainage of a perineal hematoma. No unscheduled clinic visits were identified.

In light of increasing emphasis on patient reported outcome measures (PROMs), a concerted effort has been made to have a questionnaire specific to urethral stricture disease. This has culminated in Jackson et al. developing the validated urethral stricture PROM, part of which assesses health-related quality of life [11]. Prior to that, various tools developed for other disease states were utilized for the urethral stricture patient [12]. We utilized the EuroQuol-5 validated questionnaire as it seeks to identify general health-related difficulties these patients may face, particularly in the context of an elective procedure (urethroplasty) intended to improve quality of life. Most patients, 82.6%, did report

Table 3: EQ-5 patient responses by group.

EQ-5D dimension	All responders (%)	Outpatient (%)	Short-stay (%)
Mobility			
1 = no problem	20 (44%)	3 (43%)	17 (56%)
2 = moderate	26 (56%)	4 (57%)	22 (44%)
3 = severe	0	0	0
Self-care			
1 = no problem	31 (68%)	6 (86%)	25 (64%)
2 = moderate	13 (28%)	1 (14%)	12 (31%)
3 = severe	2 (4%)	0	2 (5%)
Usual activity			
1 = no problem	12 (26%)	3 (43%)	9 (23%)
2 = moderate	23 (50%)	3 (43%)	20 (51%)
3 = severe	11 (24%)	1 (14%)	10 (26%)
Pain/discomfort			
1 = no problem	8 (17%)	1 (14%)	7 (18%)
2 = moderate	38 (83%)	6 (86%)	32 (82%)
3 = severe	0	0	0
Anxiety/depression			
1 = no problem	35 (76%)	7 (100%)	28 (72%)
2 = moderate	10 (22%)	0	10 (26%)
3 = severe	1 (2%)	0	1 (2%)

moderate problems with pain and discomfort. However, despite the added morbidity of buccal harvest in most of the patients, none reported severe pain within 24 hours after discharge. In this population the donor site was left open; however, there are several studies with contradicting conclusions on effect of donor site closure on postoperative pain [13–16].

In this cohort, the majority of patients reported moderate and severe problems in performing usual activities (74%). This was expected as the patients were sent home with an indwelling catheter for 3 weeks and strict instructions to avoid strenuous physical activity and abstain from any sexual activity. Given the varying types of urethroplasty performed in this small population it is difficult to ascertain whether the type of procedure correlates with the increased perception of pain postoperatively. One patient reported severe problems with anxiety or depression, which was unexpected considering that the procedure was performed with a goal of improving the patient's quality of life. This finding highlighted an important limitation of this study, a lack of preoperative data on patients' baseline health-related quality of life. We have since changed our practice and administer all PROM questionnaires pre- and postoperatively.

To our knowledge, there are no published studies on patient-reported perception of appropriateness of timing of discharge after anterior urethroplasty. The only studies on short-stay or outpatient urethroplasty published by Lewis et al. and MacDonald et al. have concentrated on clinical outcomes [5, 6].

Results of anterior urethroplasty performed in the outpatient setting were first described in 2002 by Lewis et al. [5]. The authors described a cohort of patients who underwent bulbar urethroplasty and were then discharged home within 23 hours of surgery. In 2006, MacDonald et al. published outcomes of the "same day urethroplasty," which he defined as being discharged home within 4 hours after surgery [6]. In both series the outcomes of the surgery were excellent but the cohorts were small.

In detail, the first study described 78 bulbar urethroplasties of which 54 (69%) were performed on a short-stay basis (patients discharged <24 hours after surgery) [5]. Overall success in the short-stay cohort was 93% compared with 88% of the admitted inpatient cohort. The authors noted that the short-stay status depended on the type of urethroplasty (90% after EPA, 64% after penile skin flaps, and 45% after buccal mucosal grafts), younger patient's age (36 versus 46 years), and shorter stricture length (3.1 versus 6.6 cm.). The study did not comment on readmissions, ER visits, or unscheduled clinic visits.

In the second study, MacDonald et al. retrospectively describes 54 patients after anterior urethroplasty performed over 4 consecutive years [6]. Over the study period, the rate of the outpatient (same day) urethroplasty increased from 27% to 85%. In this study the outpatient and the admitted inpatient cohorts had similar stricture length, but the outpatient cohort was slightly younger age (42 versus 49 years of age). Over the 27 months of follow-up the success rate was similar in both groups (94% versus 97% in the inpatient group) as were the long-term complications (19% versus 18%, resp.). The authors reported that no readmissions or emergency room visits occurred in this study.

For both studies, overall clinical outcomes were similar between the outpatient or short-stay group and admitted patients. These two studies represent the only studies published on "minimal-impact urethroplasty" and further evaluation of outpatient urethroplasty, as far as patient reported outcome measures have been lacking.

In our series, the majority of patients were comfortable with the timing of discharge in both the outpatient and short-stay cohorts. Given the relative small size of the outpatient cohort, we did not attempt further statistical comparison of the two groups. Additionally, the decision to leave or stay was made by the patient and as might be expected the majority of patients later agreed with their own choices. We surmised that the few "too soon" responses represented a later regret of their original decision. Overall, majority of patients were satisfied with leaving the hospital within 23 hours after urethral reconstruction, even for long or panurethral strictures requiring extensive dissection and bilateral BMG harvest. This data is reassuring as it shows that majority of patients did not feel rushed out of the hospital. This study can serve for a future counseling of patients considering a short-stay urethroplasty showing it as a reasonable option from patients' perspective.

With prompt postoperative discharge, there is a concern about increased readmission rates; this failed to materialize in this series [17]. In our cohort there were two ER visits, one of which was related to patient's concern of scrotal bruising and another for perineal hematoma. The latter resulted in the only readmission to the hospital and subsequent incision and drainage. There were no unscheduled visits to the outpatient clinic in this group showing that early discharge from the hospital did not shift the burden of care from the inpatient to outpatient setting.

Some limitations of the study include its retrospective nature and the nonrandomization of the two groups, which led to an uneven distribution of the outpatient versus short-stay groups. This limited the ability to perform a multivariate or comparative analysis for each group. No preoperative EuroQuol-5 questionnaires were administered making it difficult to identify patients with preexisting problems in any of the 5 dimensions. This study is limited by the assumption that every patient was in sufficiently good health prior to surgery. However, even with this assumption, the majority of patients did not report severe changes in the health-related quality of life shortly after urethroplasty.

4. Conclusion

Early return home after urethroplasty seems to be well tolerated by patients as reported on their health-related quality of life questionnaire. When using EQ-5 as a quality of life indicator in the early postoperative period, the patient's QOL was only minimally affected, except when otherwise expected in domains of "pain" and "usual activities." Most patients are satisfied with timing of their discharge from the hospital after a short-stay or outpatient urethroplasty. Early discharge did not result in numerous catastrophes leading to ER visits, readmissions, or unscheduled office visits.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Clinical Study

Visual Internal Urethrotomy for Adult Male Urethral Stricture Has Poor Long-Term Results

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Objective. To determine the long-term stricture-free rate after visual internal urethrotomy following initial and follow-up urethrotomies. *Methods*. The records of all male patients who underwent direct visual internal urethrotomy for urethral stricture disease in our hospital between July 2004 and May 2012 were reviewed. The Kaplan-Meier method was used to analyze stricture-free probability after the first, second, third, fourth, and fifth urethrotomies. *Results*. A total of 301 patients were included. The overall stricture-free rate at the 36-month follow-up was 8.3% with a median time to recurrence of 10 months (95% CI of 9.5 to 10.5, range: 2–36). The stricture-free rate after one urethrotomy was 12.1% with a median time to recurrence of eight months (95% CI of 7.1–8.9). After the second urethrotomy, the stricture-free rate was 7.9% with a median time to recurrence of 10 months (95% CI of 9.3 to 10.6). After the third to fifth procedures, the stricture-free rate was 0%. There was no significant difference in the stricture-free rate between single and multiple procedures. *Conclusion*. The long-term stricture-free rate of visual internal urethrotomy is modest even after a single procedure.

1. Introduction

Male urethral stricture continues to be a common and challenging urologic condition. Despite the high failure rate of visual internal urethrotomy (VIU), it remains the most commonly performed procedure for the treatment of urethral strictures [1–7]. Even when VIU is initially performed selectively for short bulbar strictures under optimal conditions, the recurrence rate at 12 months was approximately 40% for strictures shorter than 2 cm. VIU and/or urethral dilation is usually the initial treatment approach offered in most cases of male urethral stricture, with no difference in efficacy between urethral dilation and urethrotomy [8–10]. Repeated urethrotomies were not associated with an improved success rate, and VIU for longer strictures usually failed [11, 12]. Urethral reconstruction is usually offered only after repeated failed transurethral stricture treatments, which in some cases span several years [13]. Unfortunately, repeated transurethral manipulation of bulbar strictures is associated with increased stricture complexity, stricture length, and a marked delay to curative urethroplasty [14]. Few studies have shown long-term follow-up of patients after VIU [11].

The purposes of this study are to report the overall success rate of VIU and to analyze whether repeated VIUs are associated with a long-term stricture-free rate. This study reflects urologic practice in real-life situations by multiple urologists in a busy tertiary care hospital.

2. Materials and Methods

This is a retrospective study of male patients who presented to the Department of Urology and underwent VIU for urethral stricture disease between July 2004 and May 2012. We evaluated the long-term stricture-free rate after visual internal urethrotomy following initial and subsequent urethrotomies.

We extracted data from medical records and our Integrated Clinical Information System on ascending urethrogram findings, including the site and length of stricture, number of previous urethrotomies, and presence of complex stricture (after urethroplasty or after radiation). All patients with symptoms or signs suggestive of urethral stricture underwent a urethrogram to confirm the diagnosis and determine urethral stricture length. All patients underwent cystourethroscopy before urethrotomy, confirming the diagnosis.

Four urologists performed the urethrotomies using a single incision at the 12 o'clock position or using a modified procedure including multiple radial incisions at the 3, 9, and 12 o'clock positions; the incisions were made with a cold knife or laser. Associated fossa navicularis stricture was treated with meatotomy prior to urethrotomy. Penile urethral strictures were treated with cold knife urethrotomy.

Follow-up data included subjective and objective results and whether subsequent intervention was needed. Symptoms of recurrence included decreased force of the urine stream, feelings of incomplete bladder emptying, or recurrent urinary tract infections. Signs of recurrence were a significant increase in postvoid residual urine on bladder ultrasound or bladder scan, decreased urine flow rate (<15 mL/second), or stricture as determined by diagnostic cystoscopy or retrograde urethrogram. Absence of symptoms or signs of recurrent stricture in any patient at last follow-up defined the success of the procedure. The end point of the follow-up was the last visit that showed failure of treatment or being recurrence-free for 36 months. Only data up to the fifth recurrence after repeated urethrotomy were included.

The Kaplan-Meier method was used to evaluate the stricture-free rate (survival function) after the first, second, third, fourth, and fifth urethrotomies. We used the Statistical Package of Social Science (SPSS, version 20, IBM Corporation, NY, USA). The log-rank test was used to compare survival differences between procedures.

3. Results and Discussion

3.1. Results. The mean age was 37 years (range: 17–82). A total of 446 male patients with urethral stricture disease were identified in the computerized records of the Department of Urology. Sixty-three patients were lost during follow-up. We excluded 82 patients who had complex urethral strictures, strictures longer than 5 cm, or dense palpable spongiofibrosis. This left 301 eligible patients who continued follow-up until the failure of urethrotomy was observed, at which point an alternative management plan was offered to them. We reported the duration of follow-up and time to failure of urethrotomy as the same duration. Further management and follow-up are excluded from this paper.

The stricture characteristics are shown in Table 1. The most common location is bulbar urethral stricture in 227 (75%) patients, penile urethral stricture in 36 (11%) patients, combined penile and bulbar urethral stricture in 24 (8%) patients, and fossa navicularis stricture in 14 (5%) patients. The mean stricture length was 13 mm (range: 4–42). The overall stricture-free rate at the 36-month follow-up was 8.3% with a median time to recurrence of 10 months (95% CI 9.5 to 10.5, range: 2–36). The success rate following single urethrotomy was modest and dropped significantly after repeated urethrotomies (Table 2).

Table 1: Stricture characteristics.

Stricture length	Location	Number of patients
<1 cm	Penile	14
	Bulbar	75
	Penile and bulbar	0
	Fossa navicularis	2
1-2 cm	Penile	16
	Bulbar	87
	Penile and bulbar	10
	Fossa navicularis	4
>2 cm	Penile	6
	Bulbar	65
	Penile and bulbar	14
	Fossa navicularis	8

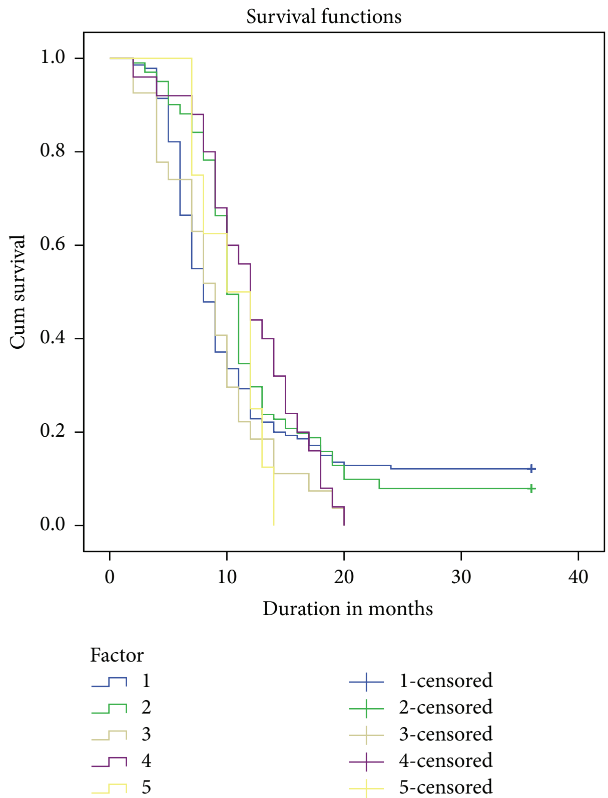

Figure 1: Stricture-free probability after the first, second, third, fourth, and fifth urethrotomies (Kaplan-Meier survival analysis).

Most recurrences occurred within the first postoperative year. Survivors or patients without recurrence were only those with a stricture length of <1 cm and in the bulbar urethra. There was no significant difference in the survival analysis of duration to recurrence among patients undergoing single or multiple procedures ($p = 0.181$, Figure 1). There was no significant difference in the outcome based on the length of the stricture or the type of treatment.

3.2. Discussion. Urethral strictures are often treated with urethrotomy, most commonly direct visual internal urethrotomy [15]. With the introduction of lasers, holmium laser

Table 2: Urethrotomy and stricture-free rate.

Number of urethrotomies	Stricture-free rate	Median time to failure (months)	Number of stricture-free patients	Total number of patients (%)
First	12.1%	8 (95% CI 7.1 to 8.9)	17	140 (46.5%)
Second	7.9%	10 (95% CI 9.4 to 10.6)	8	101 (33.6%)
Third	0%	9 (95% CI 7.3 to 10.7)	0	27 (9%)
Fourth	0%	12 (95% CI 10.4 to 13.6)	0	25 (8.3%)
Fifth	0%	10 (95% CI 6.3 to 13.7)	0	9 (3%)
Overall	8.3%	10 (95% CI 9.5 to 10.5)	25	301 (100%)

urethrotomy was subsequently used in many centers with equal recurrence outcomes as achieved with VIU [16, 17]. Many urologists prefer VIU over urethral reconstruction because of its ease to perform, low cost, short hospital stay, and perceived low complication rate. They may opt to repeat VIU several times to avoid complex urethral reconstruction, which requires significant surgical experience. This trend continues despite the moderate success rate reported in the selected patients. To reduce the stricture recurrence rate, several investigators evaluated different intralesional adjuvant injections with variable success [18–23]. We set out to report the results of VIU of our patients, including a wider inclusion base and strict criteria of success in a long follow-up period. We felt that these patients constitute a real patient group that tempts urologist to repeatedly administer VIU for the management of their stricture.

Our stricture-free rate of 8.3% at a median of 10 months (range: 2–36) is much lower than that reported by others on long-term follow-up [24]. Heyns et al. found that, after a single dilation or urethrotomy in patients who did not experience restricture within 3 months, the estimated stricture-free rate was 50–60% at 48 months [24]. The higher success rate in that study might be related to the exclusion of patients who failed the treatment in the first three months from the analysis and the shorter stricture length. Another study reported a 32% recurrence-free rate after a median follow-up of 98 months following a single internal urethrotomy. The prognostic characteristics of bulbar urethral strictures associated with good results included single or primary strictures and length shorter than 10 mm [11, 25]. The inclusion of strictures from 1 to 4 cm and the strict success criteria in our study might explain a more realistic success rate of 12.1% after single VIU. Comparison of studies that evaluate the outcome of stricture urethra treatment is greatly affected by the success criteria. This heterogeneity of the definition of success has been clearly shown in a meta-analysis of urethroplasty outcome involving more than 300 articles [26]. We did not separately report the details of the differences in outcome between different stricture lengths, associated location, or type of treatment because there was no significant difference. A focus on these comparisons would have been extremely relevant if we had a significant success rate. However, the overall success rate was poor. Only 25 patients remained stricture-free at 10 months. Compared to the total of 301 patients, subgroup analysis did not show a significant difference because of the small number of successful cases in each comparison cell.

Repeated VIU was associated with more dismal outcomes. This is in accordance with the previously reported data [11, 24, 27]. We found no significant advantage of single versus repeated VIU. We think that the inclusion of long strictures at different sites masks the claimed advantage of single VIU. Our findings stress that an early attempt at urethroplasty is warranted. This is particularly important because repeated urethrotomies have a negative impact on the success of subsequent urethroplasty [28].

Several studies have examined the cost-effectiveness of managing anterior urethral strictures. Urethroplasty as the primary therapy was cost-effective only when the expected success rate of the first VIU was less than 35% [29], whereas VIU became more favorable when the long-term risk of stricture recurrence was less than 60% [30]. If a repeat urethrotomy is required, open urethroplasty is the treatment of choice for recurrent urethral stricture.

4. Conclusions

Visual internal urethrotomy is a simple and popular treatment for male urethral stricture; however, the long-term stricture-free rate is modest even after only a single procedure. Most of the recurrences were found to occur within one year. Thus, definitive curative reconstruction should be planned as early as possible. Repeated visual internal urethrotomies should be considered only in patients who are poor surgical candidates and not because of the convenience of performing a simple procedure.

Conflict of Interests

The authors report no conflict of interests.

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Clinical Study

Anastomotic Repair versus Free Graft Urethroplasty for Bulbar Strictures: A Focus on the Impact on Sexual Function

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Objectives. To evaluate alterations in sexual function and genital sensitivity after anastomotic repair (AR) and free graft urethroplasty (FGU) for bulbar urethral strictures. *Methods*. Patients treated with AR ($n = 31$) or FGU ($n = 16$) were prospectively evaluated before, 6 weeks and 6 months after urethroplasty. Evaluation included International Prostate Symptom Score (IPSS), 5-Item International Index of Erectile Function (IIEF-5), Ejaculation/Orgasm Score (EOS), and 3 questions on genital sensitivity. *Results*. At 6 weeks, there was a significant decline of IIEF-5 for AR (−4.8; $p = 0.005$), whereas there was no significant change for FGU (+0.9; $p = 0.115$). After 6 months, differences with baseline were not significant overall and among subgroups. At 6 weeks, there was a significant decline in EOS for AR (−1.4; $p = 0.022$). In the FGU group there was no significant change (+0.6; $p = 0.12$). Overall and among subgroups, EOS normalized at 6 months. After 6 weeks and 6 months, respectively, 62.2 and 52% of patients reported alterations in penile sensitivity with no significant differences among subgroups. *Conclusions*. AR is associated with a transient decline in erectile and ejaculatory function. This was not observed with FGU. Bulbar AR and FGU are likely to alter genital sensitivity.

1. Introduction

Although a short bulbar stricture can be treated by dilation or endoscopic urethrotomy, longer or recurrent strictures are best treated by urethroplasty as it provides the best chance of success [1–3]. Anastomotic repair (AR) and free graft urethroplasty (FGU) are established treatments for bulbar strictures with the choice of technique mainly depending on stricture length [1, 3, 4]. The main goal of urethroplasty is to restore urethral patency, and, as a consequence, most papers have focused on this criterion to evaluate success of urethroplasty [1, 3, 5]. In the past decade, there is an upcoming concern that especially bulbar urethroplasty might affect sexual functioning [6–8]. The aim of this paper is to evaluate and compare sexual function after AR and FGU for bulbar strictures in a prospective fashion.

2. Materials and Methods

2.1. Patient Recruitment. Out of 258 male patients who underwent urethroplasty between October 2010 and February 2014, 90 patients with a bulbar stricture only were planned to be treated with AR or FGU and eligible to participate in this prospective study. Only native Dutch speaking patients who signed the informed consent (Institutional Review Board Approval EC UZG 2008/234) and who filled in the preoperative questionnaires and at least one postoperative questionnaire (at 6 weeks and/or 6 months) were included in this analysis. Finally, 47 patients were included for further analysis and divided into two groups: AR ($n = 31$) versus FGU ($n = 16$) (Figure 1). Prepuce and oral mucosa was used as graft in, respectively, 12 and 4 patients. Stricture location and stricture length were evaluated by retrograde

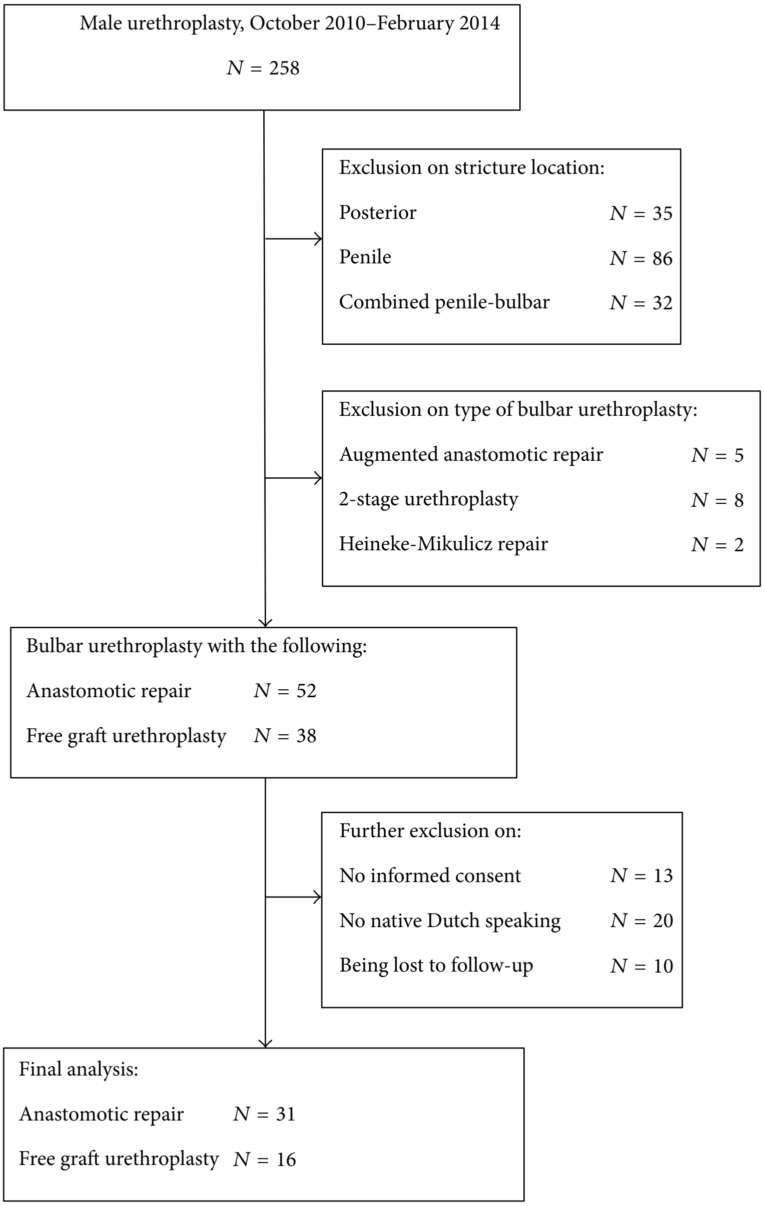


Figure 1: Flowchart of patient inclusion.

urethrography. This study included the following evaluations:

(i) urinary symptoms: maximum urinary flow (Q_{max}) and the International Prostate Symptom Score (IPSS) questionnaire; the IPSS ranges from 0 (no lower urinary tract symptoms) to 35 (severe lower urinary tract symptoms);

(ii) erectile function: the abridged 5-item version of the International Index of Erectile Function (IIEF-5) [9]; this score ranges from 1 (no sexual intercourse) to 25 (no erectile dysfunction);

(iii) ejaculation/orgasm: the sum of questions 9 and 10 from IIEF (long version) [10]; this Ejaculation/Orgasm Score (EOS) ranges from 2 (no ejaculation/orgasm) to 10 (normal ejaculation and orgasm);

(iv) postoperative genital sensitivity: a nonvalidated in-house questionnaire containing 3 dichotomous questions on glans tumescence, alterations in genital sensitivity, and cold feeling in the glans; further analysis of glans tumescence was only done in patients reporting normal erectile function (IIEF-5 $\geq$ 20) in order to avoid contamination of diminished glans tumescence due to globally diminished penile tumescence.

Patients were evaluated preoperatively, after 6 weeks and 6 months. In the first six months, no phosphodiesterase-5 inhibitors were prescribed to stimulate sexual rehabilitation. In case of suspicion of stricture recurrence ($Q_{max} <$ 15 mL/s and/or IPSS > 19), retrograde urethrography and urethroscopy were done. A functional definition of failure

Table 1: Patients' characteristics (SD = standard deviation; FGU = free graft urethroplasty; AR = anastomotic repair; DVIU = direct vision internal urethrotomy; Q_{max} = maximum urinary flow; IPSS = International Prostate Symptom Score; IIEF = International Index of Erectile Function; EOS = Ejaculation/Orgasm Score).

		All (n = 47)	FGU (n = 16)	AR (n = 31)	p value
Age (years)	Mean (SD)	40 (16)	48 (18)	37 (13)	*0.018*
Follow-up (months)	Mean (SD)	23.3 (10.9)	25.2 (12.5)	22.2 (10)	0.376
Stricture length (cm)	Mean (SD)	3 (2.4)	5.4 (2.6)	1.8 (0.8)	*<0.001*
Stricture etiology					
Traumatic	Number (%)	4 (8.5)	0 (0)	4 (12.9)	0.071
Inflammatory	Number (%)	1 (2.1)	0 (0)	1 (3.2)	
Iatrogenic	Number (%)	14 (29.8)	8 (50)	6 (19.4)	
Idiopathic	Number (%)	28 (59.6)	8 (50)	20 (64.5)	
Previous interventions					
None	Number (%)	4 (8.5)	2 (12.5)	2 (6.5)	0.877
DVIU/dilation(s)	Number (%)	34 (72.3)	11 (68.8)	23 (74.2)	
Urethroplasty(ies)	Number (%)	9 (19.1)	3 (18.8)	6 (19.4)	
Preop Q_{max} (mL/s)	Mean (SD)	6.3 (4.6)	6.9 (4)	6 (5)	0.629
Preop IPSS (.../35)	Mean (SD)	22 (8)	23 (7)	21 (8)	0.368
Preop IIEF-5 (.../25)	Mean (SD)	20 (7)	18 (8)	22 (6)	0.202
Preop EOS (.../10)	Mean (SD)	8 (3)	7 (4)	9 (3)	0.135
Suprapubic catheter					
Yes	Number (%)	8 (17)	2 (12.5)	6 (19.4)	0.697
No	Number (%)	39 (83)	14 (87.5)	25 (80.6)	

was used which includes the need for any additional urethral manipulation (including dilation) [11].

2.2. Surgical Technique. Patients were operated on in a single center (GUH) by two surgeons (Nicolaas Lumen and Willem Oosterlinck). AR was preferred whenever a tension-free anastomosis could be made (stricture length < 3 cm on urethrography and/or peroperative findings). For longer strictures, FGU was performed. For both techniques, a midline perineal incision is made; the bulbospongiosus muscle is incised at the midline and dissected away from the corpus spongiosum. In case of AR, the corpus spongiosum is circumferentially freed at the level of the stricture. The corpus spongiosum and urethra are transected at this site. The fibrotic urethra and spongiosus edges are resected until healthy urethra is present at both the distal and proximal ends. The urethra is then spatulated in order to obtain a broad oblique anastomosis, which is finalized by 8–10 interrupted resorbable 4.0 sutures. In case of FGU, the stricture is opened ventrally on the tip of the catheter. The stricture length is measured and a graft is taken accordingly. The graft is sutured into the urethra in a ventral onlay fashion. The corpus spongiosum is closed over the graft for vascular supply and mechanical support (spongioplasty). The urethral catheter is maintained for 14 days and a voiding cystourethrogram is made upon removal.

2.3. Statistical Analysis. Descriptive statistics were performed to evaluate the whole population and both subgroups. To compare both groups, continuous variables were evaluated by independent-samples t-test or the Welch modified t-test for, respectively, equal and unequal distributions. Categorical variables were evaluated by chi-square or Fischer's exact test. The 2-year recurrence-free survival was estimated by Kaplan-Meier statistics and groups were compared by log rank statistics. To evaluate changes in IPSS, IIEF-5 score, and EOS between baseline and at 6 weeks and 6 months, mean differences were calculated by paired-samples t-test.

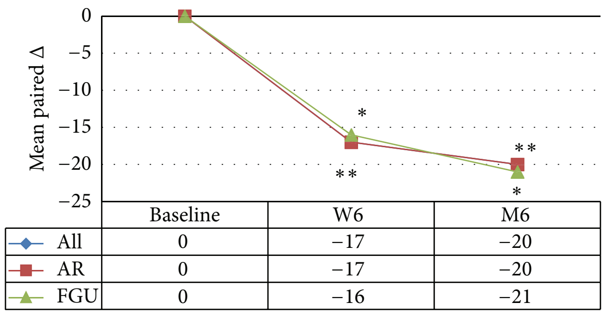
3. Results

Patients treated by AR were significantly younger (37 versus 48 years; $p = 0.018$) and strictures were shorter with AR compared to FGU (1.8 versus 5.4 cm; $p < 0.001$). Both groups were comparable for follow-up duration, stricture etiology, previous interventions, and presence of suprapubic catheter and for preoperative urinary flow, IPSS, IIEF-5, and EOS (Table 1). After a mean follow-up of 23 months, 6 patients (12.8%) suffered a recurrence: 3 (9.7%) patients treated with AR and 3 (18.8%) patients treated with FGU ($p = 0.395$). Estimated 2-year recurrence-free survival rate was 93% and 72%, respectively, for AR and FGU ($p = 0.347$). Overall and in both groups, there was a significant improvement of the urinary flow at latest follow-up. Accordingly, there was a significant improvement in IPSS after 6 weeks and 6 months overall and in both groups (Table 2; Figure 2(a)).

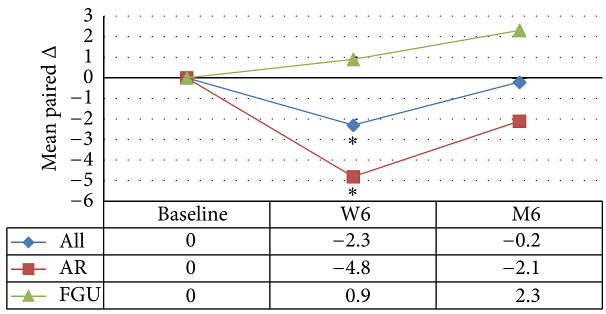
Thirty-three patients, respectively, 19 and 14 patients in the AR- and FGU-group, reported to have sexual intercourse

Table 2: Mean paired differences (Δ) of the maximum urinary flow (Q_{max}) and International Prostate Symptom Score (IPSS). The standard deviation is provided between brackets (FGU = free graft urethroplasty; AR = anastomotic repair).

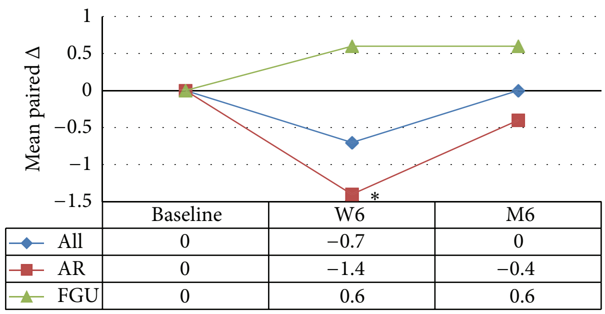
	ΔQ_{max} (mL/s)	p value	ΔIPSS (6 weeks versus preop)	p value	ΔIPSS (6 months versus preop)	p value
All	+19.8 (13.9)	<0.001	−17 (8)	<0.001	−20 (9)	<0.001
FGU	+13.8 (11.7)	0.007	−16 (10)	<0.001	−21 (8)	<0.001
AR	+22.3 (14.3)	<0.001	−17 (7)	<0.001	−20 (9)	<0.001



(a) IPSS



(b) IIEF-5



(c) EOS

Figure 2: Evolution of International Prostate Symptom Score (a), International Index of Erectile Function-5 (b), and Ejaculation/Orgasm Score (c) for all patients and subdivided for anastomotic repair (AR) and free graft urethroplasty (FGU) ($^* p < 0.05$).

and filled in the IIEF-5 (Table 3; Figure 2(b)). Overall, there was a significant decline in IIEF-5 score after 6 weeks (−2.3; $p = 0.026$). This decline remained significant for AR (−4.8; $p = 0.005$). However, for FGU, there was no significant change in IIEF-5 score (+0.9; $p = 0.115$). After 6 months, there were no longer significant changes in IIEF-5 score overall (−0.2; $p = 0.907$), for AR (−2.1; $p = 0.263$) and for FGU (+2.3; $p = 0.313$).

Thirty-seven patients, respectively, 23 and 14 patients in the AR- and FGU-group, tried to have ejaculation/orgasm (by masturbation or sexual intercourse) and completed the EOS (Table 3; Figure 2(c)). Overall, there was no significant postoperative change in EOS at 6 weeks (−0.7; $p = 0.111$). However, in the AR-group there was a significant decline in EOS (−1.4; $p = 0.022$). This was not the case in the FGU-group (+0.6; $p = 0.12$). After 6 months, EOS returned to baseline. The decline for AR (−0.4; $p = 0.431$) was no longer significant.

At 6 weeks and 6 months, respectively, 45 and 25 patients filled in the questionnaire on genital sensitivity and on cold feeling in the glans. At 6 weeks, 28 patients (62.2%) reported to have altered genital sensitivity. This proportion was not significantly different between AR and FGU (66.7 versus 53.3%; $p = 0.517$). Only one patient, treated by AR, had a cold feeling in the glans. At 6 months, 13 patients (52%) reported to have altered genital sensitivity. Again, this proportion was not significantly different with AR compared to FGU (58.8% versus 37.5%; $p = 0.411$). At 6 months, no one reported a cold feeling in the glans. Of 20 patients with IIEF-5 ≥ 20 at 6 weeks 1/10 (10%) and 4/10 (40%) of patients in, respectively, the AR- and FGU-groups reported no glans tumescence ($p = 0.303$). At 6 months, 1/6 (16.7%) and 3/5 (60%) patients with IIEF-5 ≥ 20, respectively, treated by AR and FGU reported no glans tumescence ($p = 0.242$). Of the 4 patients treated with oral mucosa, 2 had altered genital sensitivity and no glans tumescence at 6 weeks and 6 months.

4. Discussion

Although this series is a prospective study, no randomization was done between AR and FGU because the use of AR is limited by the stricture length. The limit for AR is usually

Table 3: Mean paired differences (Δ) of the 5-Item International Index of Erectile Function (IIEF-5) and Ejaculation/Orgasm Score (EOS). The standard deviation is provided between brackets (FGU = free graft urethroplasty; AR = anastomotic repair).

		ΔIIEF-5 (6 weeks versus preop)	p value		ΔIIEF-5 (6 months versus preop)	p value
All	$n = 33$	−2.3 (5.8)	*0.026*	$n = 18$	−0.2 (6)	0.907
FGU	$n = 14$	+0.9 (2)	0.115	$n = 8$	+2.3 (5.8)	0.313
AR	$n = 19$	−4.8 (6.5)	*0.005*	$n = 10$	−2.1 (5.6)	0.263
		ΔEOS (6 weeks versus preop)	p value		ΔEOS (6 months versus preop)	p value
All	$n = 37$	−0.7 (2.5)	0.111	$n = 22$	0 (1.9)	1
FGU	$n = 14$	+0.6 (1.3)	0.12	$n = 8$	+0.6 (2.2)	0.448
AR	$n = 23$	−1.4 (2.8)	*0.022*	$n = 14$	−0.4 (1.6)	0.431

set at 2-3 cm [4, 12]. This also explains why strictures treated with AR were significantly shorter compared to FGU in this series. Another difference between both groups was younger patient's age with AR. For this observation, we have the following explanation: patients treated with AR have shorter strictures (cf. supra) and short bulbar strictures are predominantly idiopathic/congenital in origin and thus occurring at a younger age [13]. Despite these differences in age and stricture length between AR and FGU, preoperative erectile and orgasmic function was not significantly different between these groups. It has been reported that longer stricture length and more advanced patient age are more likely to be associated with postoperative erectile dysfunction (ED) [14–16]. The observed difference in patient age and stricture length would thus be in favor of AR in terms of postoperative erectile function. This has not been observed in this series, on the contrary.

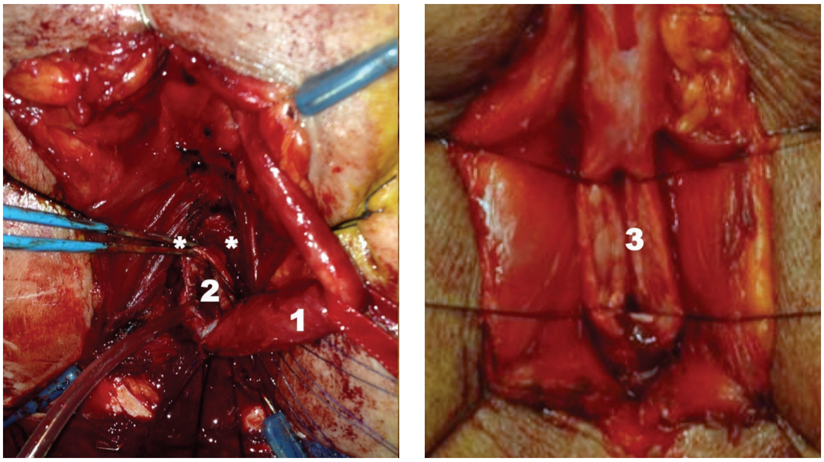
The success rate of 90.3% for AR in this series is in line with the 93.8% composite success rate reported by the SIU/ICUD consultation [1]. For longer strictures at the bulbar urethra, FGU is the preferred technique of substitution urethroplasty as flaps are associated with more morbidity [3]. Our 81.2% success rate of ventral FGU is again in line with the overall 88.8% success rate reported by the SIU/ICUD consultation [3]. Because of its excellent success rate, the SIU/ICUD consultation recommends AR as optimal treatment for short bulbar strictures [1]. This recommendation is questioned because of a potential higher risk of sexual dysfunction related to AR [17].

An increasing number of papers report on sexual dysfunction after urethroplasty [6–8, 18]. Although the results are far from uniform, there is a trend for a higher incidence of sexual dysfunction after AR compared to FGU. Palminteri et al. found that 35% and 65% of patients treated by FGU reported improvement in erectile and ejaculatory function [8]. This is in line with our results revealing a trend to improvement in erectile and orgasmic function in the FGU-group. Al-Qudah and Santucci reported ED as late complication in 17% of patients after AR but no ED after FGU [18]. In their prospective study, Erickson et al. found the highest incidence of ED (50%) in the group treated by AR, compared to FGU, where only 26% of patients suffered from ED. However, these differences were not statistically significant [7]. In their logistic regression model, Xie et al. reported that the method of treatment is a significant factor to predict for postoperative ED, with the highest risk of ED for AR [6].

Other authors did not find a significant decline in erectile function [19, 20] nor did they find a difference between AR and FGU [15, 16, 21, 22]. These contradictory results can be explained by several factors. First, timing of evaluation seems to be very important. Erickson et al. found a significant worse erectile function when evaluation is done <1 year after urethroplasty [15]. Xie et al. found a significant decline of erectile function with AR after 3 months but a normalization after 6 months [6]. This was also noted by Mundy, who found ED in 53% and 33% of patients after AR and FGU, respectively, at a 3-month follow-up. This decreased to 5% and 0.9% after longer follow-up [23]. In the AR-group, we also found a transient decline in erectile function after 6 weeks with recuperation after 6 months. Therefore, it is likely that if erectile function is at earliest assessed >3 months after urethroplasty [19, 22], a transient decline in erectile function might have been missed. Secondly, the evaluation tool to assess erectile function might be important. The IIEF-5 is a validated questionnaire to assess erectile function and was therefore used in this series. Other authors, however, used an in-house questionnaire with dichotomous answers (erectile dysfunction present or absent) [16, 19, 22]. Other factors that might be important to explain contradictory findings among studies are retrospective evaluation (with risk of recall bias) [9, 16, 19, 22] and small patient groups [21].

We speculate that the observed transient decline in erectile function with AR might be related to the following:

(i) more extensive and circumferential dissection of the corpus spongiosum containing the bulbar urethra; proximal dissection and mobilization of the corpus spongiosum nearby the urogenital diaphragm and in the intracrural space might provoke neuropraxia and/or thermal damage (coagulation) of erectile nerves penetrating the corporal bodies at that location (Figure 3); this hypothesis is supported by neuroanatomical findings reported by Yucel and Baskin [24] and Akman et al. [25];



(a) (b)

Figure 3: Peroperative photographs of AR (a) and FGU (b): a more extensive dissection with AR can be appreciated; 1: circumferentially mobilized bulbar urethra; 2: transected urethra; ∗: region where erectile nerves are expected; and 3: ventrally opened bulbar urethra.

(ii) complete transection of the corpus spongiosum that might be associated with a higher risk of bleeding and with postoperative haematoma and inflammation; this needs some time to recover; this might withhold patients to have satisfactory sexual activity or might provoke psychological problems.

In this series, ventral FGU was performed, with no significant decrease in sexual functioning at 6 weeks and 6 months. It would be interesting to know whether dorsal FGU affects sexual functioning. One would expect a higher incidence of sexual dysfunction if the hypothesis of more extensive and circumferential dissection of the bulbar corpus spongiosum is (in part) responsible for sexual dysfunction.

In this series, a transient decline in EOS was seen with AR, whereas there was no significant difference observed with FGU. Erickson et al. found an improvement of ejaculatory function after urethroplasty (mix of AR and FGU) [15], but a later prospective study failed to show any significant changes in ejaculatory function after urethroplasty (also mix of AR and FGU) [26]. Improvement of ejaculatory function after urethroplasty might be related to desobstruction of the urethra [26]. However this cannot explain the transient decline in ejaculatory function after AR that was seen in our series. Barbagli et al. also reported postoperative ejaculatory dysfunction in 23.3% of patients treated with AR [19]. We hypothesize that the higher rate of ejaculatory dysfunction associated with AR is because of the more extensive detachment of the bulbospongiosus muscle in AR needed for a full mobilization of the bulbar urethra. This detachment can indeed interfere with ejaculatory function. Timing of questioning might again be important: recovery of postoperative ejaculatory dysfunction can be expected once the bulbospongiosus muscle has recovered from the surgical trauma. This cannot be expected after 6 weeks but can be expected after 6 months. Another explanation is that ejaculatory and orgasmic dysfunction is related to ED, which was also more frequent after AR.

In this series, postoperative changes in genital sensitivity were present in approximately 2 out of 3 and 1 out of 2 patients after, respectively, 6 weeks and 6 months. Changes in genital sensitivity were not significantly different among subgroups. Palminteri et al. found a change in genital sensitivity after FGU in 50% of patients [8]. This is in line with our findings, but substantially higher than the 18.3% reported rate by Barbagli et al. [19]. However, this was a retrospective series with a possible risk of underreporting. In the same series [19], only one patient (1.6%) reported a cold glans, which is in concordance with the finding in our series. Postoperative changes in genital sensitivity might be explained by postoperative haematoma formation, oedema, and inflammation. Furthermore, in the majority of patients treated by FGU, a preputial skin graft was used. These factors might certainly explain the high rate of early (6 weeks) changes in genital sensitivity. However, even after 6 months, changes in genital sensitivity were still frequently reported, and this occurs also in patients treated with oral mucosa. This might be explained by damage to some sensory branches of the perineal nerves that supply the ventral surface of the penis [24]. By transecting the entire corpus spongiosum, one would expect a higher rate of impaired glans tumescence after AR. This was not observed in this series. However, interpretation of the results is hampered by the small number of patients.

This series again underlines the concern of possible alterations in sexual functioning and genital sensitivity after bulbar urethroplasty. Therefore it should be part of the evaluation of patients treated by urethroplasty. Jackson et al. recently validated patient reported outcome measures (PROMs) for urethroplasty [27]. However, this PROM lacks a section on sexual functioning.

Furthermore, it would be interesting to evaluate whether modifications in urethroplasty techniques such as muscle- and nerve-sparing bulbar urethroplasty [28] and vessel-sparing anastomotic repair [29] will be associated with less sexual dysfunction.

Important limitations of the present series are the small sample size and the missing data in the postoperative questionnaires.

5. Conclusions

AR is associated with a transient decline in erectile and ejaculatory function. This was not observed with FGU. Bulbar urethroplasty is likely to provoke changes in genital sensitivity. Further prospective studies with validated and internationally accepted patient reported outcome measures (PROMs) are needed for further confirmation.

Conflict of Interests

The authors have no conflict of interests.

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