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Trends in Urethral Stricture Disease Etiology and Urethroplasty Technique from a Multi-Institutional Surgical Outcomes Research Group

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Abstract:

Objectives
To analyze contemporary urethroplasty trends and urethral stricture etiologies over a seven-year study period amongst urologists from a large multi-institutional surgical outcomes group.

Methods
Review of a multi-institutional, prospectively maintained urethroplasty database was performed on 2,098 anterior urethroplasties done between 2010 and 2017 by 10 surgeons. Stricture characteristics, including etiology, length and anatomic location were analyzed and compared to urethroplasty type over the study period using chi-squared analysis to assess for linear trends within the group and by surgeon.

Results
Average stricture lengths for bulbar (2.8 ± 1.8 cm), penile (3.6 ± 2.6 cm), and penile-bulbar strictures (8.7±5.0) remained stable. The most common stricture etiology was idiopathic/unknown in all study years (63%). In the bulbar urethra, the group performed significantly 1) fewer excisional repairs (-31%) and more substitutional repairs (+78%); 2) of substitutional repairs, more grafts are being placed dorsally (+95%) versus ventrally (-75%) (3) of the bulbar excisional repairs, more are being performed without transection of the bulbar urethra (+430%); and in the penile urethra, 4) the
fasciocutaneous flap is in decline (-86%), while single stage dorsal repairs are increasing (+280%).

**Conclusions**

Anterior urethroplasty techniques continue to evolve in the absence of robust clinical data or randomized controlled trials, with a general movement in this cohort towards an initial dorsal approach for most strictures. Inter and intra-surgeon variability in the surgical management of similar strictures was noted, and the feasibility of any future randomized controlled trials, without apparent surgical equipoise, must be questioned.
Introduction

Urethroplasty is well-established as the gold standard treatment for urethral stricture disease. Recent investigations cite a significant rise in urethral reconstruction, versus serial dilation/urethrotomy\(^1\)\(^{-}\)\(^3\), amongst newer generations of urologists\(^2\)\(^,\)\(^4\)\(^{-}\)\(^6\). Reviews of surgical case logs by the American Board of Urology (ABU) show that urethroplasty comprised 11% of all male urethral stricture cases for newly certified urologists versus 3% for those undergoing recertification\(^4\). Burks et al\(^2\) also highlighted that urologists who have recently completed postgraduate training are three times more likely to perform urethroplasty than their more experienced counterparts. Factors driving this trend have been attributed to changes in patient referral patterns, evidence-based clinical guidelines built on the long-term durability of urethral reconstruction\(^7\)\(^{-}\)\(^9\), and a greater number of urologists with fellowship training in reconstructive surgery\(^2\),\(^10\). These findings indicate a gradual shift in the treatment paradigm for anterior urethral stricture disease.

While these studies demonstrate a welcome trend showing a shift towards urethroplasty, studies that describe how urethroplasty techniques have changed over time have not been conducted. As new techniques continue to be developed and old techniques continue to evolve – all without the benefit of randomized controlled trials (RCT) – trend analyses can offer insights into current surgical preferences, presumed surgical effectiveness, and importantly, whether surgical equipoise can ever be achieved to a degree that would allow for sufficient recruitment into an RCT. If trend
data suggests that surgeons believe one technique to be superior to another, even without robust clinical data to prove it, the assumptions necessary to perform an RCT will never be met.

The purpose of the present study is to analyze surgical trends of anterior urethroplasty techniques from a large, multi-institutional, observational cohort study. We hypothesize that techniques for anterior urethroplasty will change significantly over the study period and that these changes will occur independent of stricture etiology, length or location – though we expect individual differences in technique choice to persist.

Methods

A retrospective analysis of a prospectively maintained, IRB approved, multi-institutional urethroplasty database was performed for all adult men undergoing anterior urethroplasty between 2010 and 2017 from one of ten institutions. All urethral strictures were classified into one of three length categories (<2 cm, ≥2 to <7 cm, or ≥7 cm) and one of three anatomic categories: penile (including urethral meatal and fossa navicularis strictures), bulbar, or penile-bulbar for strictures spanning both segments of the urethra and/or with non-contiguous strictures in separate locations. Because penile and penile-bulbar strictures are mostly managed using similar techniques, for the purposes of analysis they were analyzed together.

Surgical repair types for urethral stricture disease were categorized into anastomotic, substitutional, and miscellaneous (e.g., perineal urethrostomy, urethrocutaneous fistula
repair, first-stage Johanson). Anastomotic repairs were further stratified into transecting and non-transecting excision and primary anastomosis. Non-transecting included both Heineke-Mikulicz repairs (i.e., no resection of strictured urethral tissue) and repairs that included excision of the scarred urethral mucosa with sparing of the ventral spongiosum\textsuperscript{11}. The onlay group was further divided into ventral and dorsal onlay of mucosal grafts or flaps.

To determine the effect of individual surgeons on overall trend data for repairs, individual percentages of the repairs were compared by surgeon over time (transecting vs non-transecting and dorsal vs ventral bulbar repairs). Urethral stricture etiologies were classified into: traumatic, idiopathic/unknown, iatrogenic, radiation-induced, inflammation, or failed hypospadias repair. Within each category, to determine if a linear trend was observed in a procedure over time, a chi-squared test for trend in proportion was applied to the years 2010 to 2017 for each individual repair. To correct for multiple comparisons and control the family-wise error rate, the Holm-Bonferroni method was used\textsuperscript{12}.

**Results**

*Patient/Stricture Demographics*

Ten fellowship-trained urologic surgeons that contribute clinical data to the Trauma and Urologic Reconstruction Network of Surgeons (TURNS) were included. Of the 2,343 eligible patients who underwent anterior urethroplasty between 2010 and 2017, a total
of 2,152 patients met full inclusion criteria. Reasons for exclusion included missing surgery date (n=49) and/or stricture location (n=142). Mean stricture length remained statistically similar over the study period with the average bulbar stricture measuring 2.8 (+1.8 SD) cm, penile stricture 3.6 (+/- 2.6) cm, and strictures spanning both segments (i.e. penile-bulbar strictures) measuring 8.7 (+/- 5.0). The most common stricture location in the overall cohort was the bulbar urethra (isolated; 65.2%), ranging from 59.7% to 79.2% by year.

**Stricture Etiology Trends**

The most common bulbar stricture etiology was idiopathic/unknown, representing 63% (1356/2152) of the overall cohort, with traumatic (17%) and iatrogenic (13%) being the next most common. Idiopathic/unknown (34%) was also the most common etiology for penile strictures, followed by iatrogenic (23%) and infectious/lichen sclerosus (20%). There were no significant differences in stricture etiology distribution over the study period for either bulbar (Figure 1A) or penile strictures (Figure 1B).

**Bulbar Urethroplasty Trends**

Trends in bulbar urethroplasty repair types are shown in Figure 2. Overall, the percentage of excisional repairs of the 1336 total bulbar repairs declined by 28% (50 to 36%), while substitution repairs increased 78% (35 to 58%). Within the excisional repair cohort, the overall percentage of non-transecting repairs increased from 0% to 42%, though percentages amongst group individuals in the most recent calendar year varied widely (0 to 90%) (Figure 3A). The overall trend of excisional versus non-excisional
repairs was not statistically significant (p=0.12). Within the substitutional repair cohort, the percentage of repairs in which the graft was placed dorsally (versus ventrally) increased from 2-fold (44% to 88%), though again, the use of the dorsally placed graft varied significantly amongst the group in 2017 (70 to 100%) (Figure 3B). The overall trend of dorsal versus ventral graft placement was highly statistically significant (p=0.001). A median of seven (range: 2-10) different techniques were used by individual surgeons to manage bulbar strictures, which remained unchanged over the study period.

Penile/Penile-Bulbar Urethroplasty Trends
The trends in penile urethroplasty repair types of the study period are shown in Figure 4. Overall, the procedure performed on the 816 total penile repairs with the greatest decline was the fasciocutaneous flap, decreasing by 86% (14% to 5%). Single-stage dorsal onlay (14 to 27%) and inlay repairs (0 to 10%) increased significantly, while two stage repairs and perineal urethrostomy rates remained stable. A median of eight (range: 3-11) different techniques were used by individual surgeons to manage their penile/penile-bulbar urethral stricture practice, which remained unchanged over the study period.
Discussion

The purpose of our study was to describe etiology and surgical trends for the management of anterior urethral stricture disease within a multi-institutional urethroplasty outcomes group over an 8-year period. The majority of urethral stricture etiologies remain classified as idiopathic/unknown, with over 50% of all men with strictures not knowing how they obtained their stricture. The most significant overall surgical trends included: 1) a transition away from excisional/anastomotic repairs in the bulbar urethra towards dorsal buccal substitutional repairs; 2) greater use of non-transecting, vessel-sparing anastomotic bulbar urethral repairs and; 3) a shift away from fasciocutaneous flaps and two stage repairs towards single stage dorsal (both onlay and inlay) repairs in the penile urethra. Surgical trends in individual surgeons were more heterogeneous.

Urethral Stricture Etiology

Stricture etiologies remained consistent throughout the study period, with idiopathic and unknown strictures making up the vast majority of strictures. The high percentage of patients undergoing urethroplasty that do not know why they have it is consistent with other series\textsuperscript{13} and should serve as a reminder of just how little we know about this disease process. Our ability to repair these strictures, regardless of etiology, perhaps prevents our efforts towards pursuing a better understanding of pathophysiology. A recent study by the TURNS group that showed an association with systemic disease
and the development of LS\textsuperscript{14}, as well as a separate study that revealed a higher than expected percentage of isolated bulbar strictures with characteristics of LS, suggests that a yet unexplained chronic inflammatory process in the urethra may be responsible for a significant percentage of these idiopathic strictures\textsuperscript{15}.

\textit{Bulbar Urethroplasty Trends}

There were three primary changes that took place for bulbar repairs over the study period. First, fewer anastomotic repairs are now being performed than at the study onset despite stable stricture lengths. While the excisional urethroplasty remains the gold-standard repair for bulbar strictures of less than 2 cm, with reported success rates of over 90\%, the evolving definition of success, which takes a more patient-centered approach to determining outcomes\textsuperscript{10}, may be influencing the change towards more substitution urethroplasties. For example, regardless of how the graft is placed (i.e. dorsally, ventrally or laterally), these repairs typically require less urethral dissection, preserve the bulbar arteries, and in many situations, are technically easier operations than excisional repairs. All of these surgical advantages have the theoretical potential to minimize post-operative sexual side effects and post-operative pain, both known to be strong predictors of patient satisfaction\textsuperscript{16}.

The second major change seen in bulbar urethroplasties was the group’s shift from ventrally to dorsally placed buccal grafts. Though the ventrally placed graft is technically easier, the dorsally placed graft offers the following hypothetical advantages – 1) the
ability to spread fix the graft onto the corporal bodies, which may decrease graft contraction, 2) fewer problems with graft sacculation as has been described with ventral repairs, and 3) the ability to extend the urethral reconstruction distally into the penile urethra without relying on the thinner spongiosum to provide graft support. To our knowledge, a study that directly compares the outcomes of the two types of graft placements has not been performed, and efforts by the TURNS group to recruit into a randomized controlled trial have largely failed (NCT02634619), with poor recruitment potentially being the result of a lack of perceived surgical equipoise between the two procedures.

The third major change in bulbar repairs was the significantly higher percentage of excisional repairs performed using a non-transecting, spongiosum/bulbar artery sparing approach. First described by Jordan et al in 2007 as a way to preserve the bulbar arteries in patients that would likely undergo a post-urethroplasty artificial urinary sphincter placement, the technique, which starts by identifying the urethral stricture dorsally via urethrotomy, was simplified by Mundy et al in 2010 and has since become a staple in many reconstructive urologist's armamentarium after initial reports suggested equal anatomic surgical outcomes to transecting repairs and possibly fewer sexual side effects. The advantages to the non-transecting excisional repair include 1) preservation of the bulbar arteries (and thus, a potential for less sexual morbidity), 2) less need for distal urethral dissection of the urethra to perform the anastomosis without tension (perhaps from the lack of bulbar artery vasospasm once transected), and 3) the ability to perform a dorsal onlay buccal urethroplasty on any part of the urethra if
anastomotic repair is not possible, if for example, the stricture extends more proximally or distally than anticipated by retrograde urethrogram.

**Penile Urethroplasty**

Penile strictures are less common than bulbar strictures, making up only 23% of the present cohort, but are generally more difficult to repair with success rates ranging from 80-85%\(^2\). These success rates are likely related to a less robust blood supply, less ability to mobilize the urethra for excisional repairs given the high risk of chordee, and the association of penile urethral strictures with lichen sclerosus (LS) and hypospadias failures, both of which can independently affect tissue healing after urethroplasty.

Traditionally, much like long-segment repairs in pediatrics, these repairs were managed with local fasciocutaneous flaps, most commonly the penile fasciocutaneous flap popularized by McAninch et al\(^2\) in the 1990s, and the Orandi flap\(^2\)\(^2\). The advantage of these flaps is the generally abundant supply of well-vascularized penile tissue supplied by the dartos, the ability to take many of the flaps into the bulbar urethra for long-segment penile-bulbar strictures (McAninch flap), and the ability to perform complex single stage urethral reconstructions. However, use of fasciocutaneous flaps is contraindicated for LS, and long-term studies have demonstrated high recurrence rates when they are used in this setting, ranging from 50%\(^2\)\(^3\) to 100%\(^2\)\(^4\). In addition, cosmetic and functional concerns with the remaining, post-graft harvest penile shaft skin, as well
as the tendency for ventrally placed flaps to sacculate, have likely led surgeons to seek other options.

Similar to strictures in the bulbar urethra, this study demonstrated our group’s migration towards a dorsally placed buccal graft, commonly in a single stage, to manage penile urethral strictures. Specifically, the Kulkarni technique was commonly used by group members, which is a single-stage technique that emphasizes one-sided urethral dissection (and thereby maximizing preservation of blood supply) that still allows for spread-fixing of the graft onto the corpora\textsuperscript{25}. While long-segment, single stage dorsal urethroplasties in this setting have been known to lead to fistulas, segmental recurrences and/or other complications that require additional procedures 13-25\% of the time\textsuperscript{25}, this overall rate of reoperation remains significantly lower than the 100\% rate required for a second (and sometimes third, occurring up to 50\% of the time\textsuperscript{26}) urethroplasty for planned two-stage repairs.

**Surgeon Technique Heterogeneity**

Overall, there was a trend towards initially approach all strictures in the anterior urethra dorsally. However, heterogeneity in surgeon management of both bulbar and penile urethral strictures remained, with a greater range observed for penile strictures. While reconstructive urologists learn a wide array of urethroplasty techniques and require expertise in most of them to manage stricture of all types and all locations in the anterior urethra, this study highlights how the search for the “perfect” surgical approach is a
continually evolving process. The inherent nature of a reconstructive operation leads to subjectivity in what is considered a surgical “success”, leading surgeons to different surgical preferences that work best for them. While randomized controlled trials may help solve the issue of “what technique is best?,” the heterogeneity of stricture disease itself and our fundamental lack of knowledge about stricture pathophysiology, highlighted again here by the fact that over 50% of the repaired strictures lacked a definitive cause, will likely mean that there will never be a single superior type of urethroplasty. In addition, the variation in individual practices seen in this study, as well as the rapid adoption of newer techniques, calls into question the ability for individual surgeons to achieve the clinical equipoise necessary to conduct a rigorous surgical trial. In their absence, the need for a reconstructive urologist to understand when and why a particular urethroplasty should and should not be used will be paramount to the overall successful outcomes and perhaps as responsible for the learning curve noted previously in this group as surgical skill. Importantly, while many procedures decreased in numbers over the study period, none disappeared from the armamentarium completely, suggesting that the vast majority of procedures retain some utility in the right clinical situation.

Limitations to this study include potential bias regarding surgical approaches, which may be attributed to similarities in fellowship training and/or discussion regarding surgical techniques, thus driving trends for the group. However, significant differences in management of similar strictures amongst the group without data supporting why these differences might occur, suggests that much of what the individual surgeon does is
based on preference, experience, and anecdote. Similarly, while this study does show migrations from one type of urethroplasty to another over time, this does not necessarily suggest superiority of the newer technique.

Conclusions

This observational study of surgical trends for urethral stricture disease in a large, multi-institutional longitudinal study suggests a migration away from ventrally placed grafts, urethral transection, and the use of fasciocutaneous flaps towards a dorsal approach that allows for non-transecting repairs when possible, or dorsal grafts when necessary for all types of strictures in all segments of the urethra. Objective data to support these changes are still lacking, but lack of perceived surgical equipoise amongst reconstructive urologists may prevent these studies from being performed. The etiology for the majority of urethral strictures continues to be “idiopathic/unknown,” suggesting the continued need for improved efforts at understanding of stricture pathophysiology so to improve overall disease management.
References


Figure Legends:

Figure 1A: Trends in Stricture Etiology for Bulbar Urethral Strictures

![Etiology of Stricture in Bulbar Repairs](image-url)
Figure 1B: Trends in Stricture Etiology for Penile/Penile-Bulbar Urethral Strictures
Figure 2: Trends in the Repair of Bulbar Urethral Strictures
Figure 3A: Individual Surgeon Trends for Proportion of Transecting vs Non-transecting Repairs for Bulbar Urethral Strictures (p value represents statistical change in median (black line) over time)

\[ p = 0.12 \]
Figure 3B: Individual Surgeon Trends for Proportion of Dorsal Onlay vs. Ventral Onlay Buccal Graft Repairs for Bulbar Urethral Strictures (p value represents statistical change in median (black line) over time)
Figure 4: Trends in the Repair of Penile and Penile-Bulbar Urethral Strictures