## Title

Outcomes of Urethroplasty for Synchronous Anterior Urethral Stricture Utilizing the Trauma and Urologic Reconstruction Network of Surgeons Length, Segment and Etiology Anterior Urethral Stricture Classification System



## Authors

Jamil, Marcus L
Hamsa, Alexandra
Grove, Shawn
et al.

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# Outcomes of Urethroplasty for Synchronous Anterior Urethral Stricture Utilizing the Trauma and Urologic Reconstruction Network of Surgeons Length, Segment and Etiology Anterior Urethral Stricture Classification System

**Marcus L. Jamil, Alexandra Hamsa, Shawn Grove, Eric Y. Cho, Nejd F. Alsikafi, Benjamin N. Breyer, Joshua A. Broghammer, Jill C. Buckley, Sean P. Elliott, Bradley A. Erickson, Jeremy B. Myers, Andrew C. Peterson, Keith F. Rourke, Bryan B. Voelzke, Lee C. Zhao, and Alex J. Vanni**

**OBJECTIVE** To describe the characteristics, management, and functional outcomes of patients with synchronous urethral stricture disease (SUSD) utilizing a multi-institutional cohort.

**METHODS** Data were collected and assessed from a prospectively maintained, multi-institutional database. Patients who underwent anterior urethroplasty for urethral stricture disease (USD) were included and stratified by the presence or absence of SUSD. USD location and etiology were classified according to the Trauma and Urologic Reconstruction Network of Surgeons Length, Segment and Etiology Anterior Urethral Stricture Classification System. Anterior urethroplasty techniques were recorded for both strictures. Functional failure was compared between groups.

**RESULTS** One thousand nine hundred eighty-three patients were identified, of whom, 137/1983 (6.9%) had SUSD. The mean primary stricture length for patients with SUSD was 3.5 and 2.6 cm for the secondary stricture. Twelve anterior urethroplasty technique combinations were utilized in treating the 27 different combinations of SUSD. Functional failure was noted in 18/137 (13.1%) patients with SUSD vs 192/1846 (10.4%) patients with solitary USD, $P = .3$. SUSD was not associated with increased odds of functional failure. S classifications: S1b, $P = .003$, S2a, $P = .001$, S2b, $P = .01$ and S2c, $P = .02$ and E classifications: E3a, $P = .004$ and E6, $P = .03$, were associated with increased odds of functional failure.

**CONCLUSION** Repair of SUSD in a single setting does not increase the risk of functional failure compared to patients with solitary USD. Increasing S classification, S1b through S2c and E classifications E3a and E6 were associated with increased functional failure. This reinforces the importance of the Trauma and Urologic Reconstruction Network of Surgeons Length, Segment and Etiology Anterior Urethral Stricture Classification System as a necessary tool in large-scale multi-institutional analysis when assessing highly heterogenous patient populations. UROLOGY 181: 155–161, 2023. 

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*From the Lahey Hospital and Medical Center, Burlington, MA; the University of Minnesota, Minneapolis, MN; the University of California San Diego, San Diego, CA; the Uropartners, Gurnee, IL; the University of San Francisco, San Francisco, CA; the University of Kansas, Kansas City, KS; the University of Iowa, Iowa City, IA; the University of Utah, Salt Lake City, UT; the Department of Urology, Duke University, Durham, NC; the Division of Urology, Department of Surgery, University of Alberta, Edmonton, Alberta, Canada; the Spokane Urology, Spokane, WA; and the New York University, New York City, NY*

*Address correspondence to: Alex J. Vanni, M.D., F.A.C.S., Lahey Hospital and Medical Center, 41 Burlington Mall Rd, Burlington, MA 01805. E-mail: Alex.J.Vanni@Lahey.org*

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The incidence of urethral stricture disease (USD) has been well described, with an estimated prevalence of 229-667 per 100,000 males.[1] The prevalence of synchronous urethral stricture disease (SUSD) however is not well established, with estimations varying from 5% to 10% of all patients presenting with USD.[2,3] SUSD is the presence of two distinct urethral strictures separated by a healthy intervening urethral segment.[3] SUSD can be caused by various etiologies, including trauma, infection, inflammation, or previous urethral surgeries, and vary in severity and length.

Treatment of SUSD can be particularly challenging. Previous investigations have described various techniques of treating SUSD to reduce intraoperative and postoperative complications and reduce operative times.[3] A paucity of data exists on the ideal management strategies and functional outcomes of patients with SUSD, with only small, single institutional retrospective reviews investigating the issue.[3,4] Currently, when classifying SUSD in the Trauma and Urologic Reconstruction Network of Surgeons (TURNS) LSE (Length, Segment and Etiology) Anterior Urethral Stricture Classification System, a modifier "m" is utilized when the urethra has two clinically distinct urethral strictures managed by two separate surgical techniques.[5] The outcomes of SUSD have yet to be evaluated utilizing the LSE classification system, and a more developed phenotyping of SUSD has yet to be determined.

Our objective was to describe the unique characteristics and management strategies of patients with SUSD utilizing the multi-institutional, prospectively managed TURNS database. Secondly, we sought to assess the functional outcomes of patients with SUSD compared to solitary USD. Our hypothesis is that patients with SUSD are more complex than solitary USD, and thus likely to have higher stricture recurrence rates.

## METHODS

### Data Source and Study Population

Data were collected and assessed from a prospectively maintained, institutional review board-approved, multi-institutional dataset.[6] Patients who underwent anterior urethroplasty for USD involving the bulbar urethra, pendulous urethra and meatus as outlined by the LSE classification system between 2007 and 2020 were included. Patients were further stratified by the presence or absence of SUSD. Patients with panurethral strictures, bladder neck or prostatic urethral involvement were excluded. Patients who underwent perineal urethrostomy or an endoscopic intervention (urethral dilation or direct visual internal urethrotomy [DVIU]) for either of the urethral strictures in the same setting of the urethroplasty were also excluded.

### Covariates

Patient-specific characteristics included age and body mass index at time of surgery, smoking status (active or never/former) and number of prior DVIUs or dilations. Urethral stricture location and etiology were classified according to the TURNS LSE Anterior Urethral Stricture Classification System. Details regarding the classification system are available in previous publications.[5] Length of both strictures was recorded as a continuous variable. Stricture length and location were determined by the surgeon intraoperatively. The primary and secondary stricture in patients with SUSD were defined as such by surgeon discretion, typically the primary stricture was noted to be the longer of the two strictures. Follow-up was recorded in months with interquartile ranges (IQR). Anterior urethroplasty techniques were recorded for both strictures and stratified into the following categories: (1) graft or flap substitution urethroplasty, (2) augmented anastomotic urethroplasty, (3) anastomotic urethroplasty with or without transection, (4) staged anterior urethroplasty, (5) meatotomy or (6) hypospadias repair/other.

### Endpoint

The primary endpoint was functional failure. Functional failure was defined as undergoing any form of treatment for urethral stricture recurrence, including clean intermittent catheterization, DVIU, dilation or revision urethroplasty at either stricture.[6] Patients who underwent both endoscopic management and revision urethroplasty were documented as a single event. For patients with SUSD, recurrence location, whether at the primary stricture, SUSD or both was assessed.

### Statistical Analysis

Mean and IQRs were reported for continuous variables, while frequencies and proportions were reported for categorical variables. Comparisons were made utilizing *t*-test and analysis of variance (ANOVA) where appropriate. Logistic regression analysis was performed which assessed predictors of retreatment utilizing all the aforementioned covariates in the model. Logistic regression analysis was performed which assessed predictors of retreatment. A time-to-event analysis was performed between patients with SUSD vs solitary USD in assessing time to functional failure. All statistical analyses were performed utilizing R version 4.2.2. Two-sided statistical significance was defined as a $P$-value < .05.

## RESULTS

### Descriptive Characteristics

Descriptive characteristics are noted within Table 1. In all, 1983 patients met all inclusion criteria, of which 137/1983 (6.9%) patients had SUSD. The mean stricture length for patients with solitary USD was 4.4 cm. The mean primary stricture length for patients with SUSD was 3.5 cm. The mean stricture length for the secondary stricture in patients with SUSD was 2.6 cm. The mean total stricture length for patients with SUSD was 5.7 cm. Median (IQR) follow-up was 11.6 (1.4) months in patients with solitary USD vs 12.9 (2.1) months in patients with SUSD. Twelve different anterior urethroplasty technique combinations were utilized in treating the 27 different combinations of SUSD, Figure 1. The most utilized technique combination was graft or flap substitution urethroplasty for both strictures, performed in 24/62 patients (38.7%), followed by augmented anastomotic urethroplasty for the primary USD and graft or flap substitution urethroplasty for the SUSD, 8/62 patients (12.9%) Figure 1. The most common stricture location combination for patients with SUSD were

**Table 1.** Descriptive characteristics of 1983 patients who underwent a urethral stricture repair, grouped by presence or absence of a synchronous urethral stricture.

| | Solitary USD<br>1846 (93.1%) | SUSD<br>137 (6.9%) | Total<br>1983 (100%) |
|---|---|---|---|
| Body mass index (kg/m$^2$) | 29.6 (17.7-56.7) | 30.8 (17.0-56.0) | 29.8 (17.0-56.7) |
| Age at time of surgery (y) | 48.1 | 50.3 | 48.3 |
| Smoking status (%) | | | |
| Active | 189 (10.2) | 14 (10.2) | 203 (10.2) |
| Never/Former | 1657 (90.2) | 123 (898) | 1780 (89.8) |
| Number of prior DVIUs | 0.89 (0.00-10.00) | 1.01 (0.00-7.50) | 0.90 (0.00-10.00) |
| Number of prior dilations | 1.5 (0.00-10.00) | 1.4 (0.00-10.00) | 1.5 (0.00-10.00) |
| Mean operative stricture length #1 (cm) | 4.4 (0.01-25.00) | 3.5 (0.50-14.00) | 4.3 (0.01-25.00) |
| Mean operative stricture length #2 (cm) | - | 2.6 (0.50-12.00) | - |
| S classification for primary USD* (%) | | | |
| S1a | 885 (47.9) | 44 (32.1) | 929 (46.9) |
| S1b | 325 (17.6) | 11 (8.0) | 336 (16.9) |
| S2a | 174 (9.4) | 8 (5.8) | 182 (9.2) |
| S2b | 187 (10.1) | 35 (25.5) | 222 (11.2) |
| S2c | 112 (6.1) | 23 (16.8) | 135 (6.8) |
| S2d | 101 (5.5) | 14 (10.2) | 115 (5.8) |
| S3 | 62 (3.4) | 2 (1.5) | 64 (3.2) |
| S classification for SUSD* (%) | | | |
| S1a | | 71 (51.8) | |
| S1b | | 17 (12.4) | |
| S2a | | 7 (5.1) | |
| S2b | | 26 (19.0) | |
| S2c | | 5 (3.7) | |
| S2d | | 11 (8.0) | |
| E classification† (%) | | | |
| 1 | 195 (10.6) | 12 (8.8) | 207 (10.4) |
| 2 | 869 (47.1) | 40 (29.2) | 909 (45.8) |
| 3a | 236 (12.8) | 16 (11.7) | 252 (12.7) |
| 3b | 198 (10.7) | 21 (15.3) | 219 (11.0) |
| 3c | 92 (5.0) | 4 (2.9) | 96 (4.8) |
| 4 | 28 (1.5) | 0 (0.0) | 28 (1.4) |
| 5 | 105 (5.7) | 16 (11.7) | 121 (6.1) |
| 6 | 98 (5.3) | 24 (17.5) | 122 (6.2) |
| Repair type #1 (%) | | | |
| Graft or flap substitution urethroplasty | 1382 (67.7) | 85 (62.0) | 1467 (74.0) |
| Augmented anastomotic | 35 (1.9) | 13 (9.5) | 48 (2.4) |
| Anastomotic (transecting or nontransecting) | 293 (15.9) | 21 (15.3) | 314 (15.8) |
| Staged anterior urethroplasty | 59 (3.2) | 4 (2.9) | 63 (3.2) |
| Meatotomy | 12 (0.7) | 9 (6.6) | 21 (1.1) |
| Hypospadias/other | 65 (3.5) | 5 (3.6) | 70 (3.5) |
| Repair type #2 (%) | | 40 (29.2) | |
| Graft or flap substitution urethroplasty | | | |
| Augmented anastomotic | | 3 (2.2) | |
| Anastomotic (transecting and/or nontransecting) | | 14 (10.2) | |
| Meatotomy | | 2 (1.5) | |
| Hypospadias/other | | 3 (2.1) | |

DVIU, direct visual internal urethrotomy; SUSD, synchronous urethral stricture disease; USD, urethral stricture disease.
* (S): S1a, proximal bulb; S1b, distal bulb; S2a, bulbar/penile; S2b, penile only; S2c, penile/fossa; S2d, fossa only; S3, bulb/penile/fossa.
† (E): E1, external trauma; E2, idiopathic; E3a, internal trauma; E3b, urethroplasty failure; E3c, radiation; E5, hypospadias; E4/6, inflammatory/Lichen Sclerosus.

two separate S1a strictures, 27/137 (19.7%), followed by patients with a S2b and S1a stricture, 18/137 (13.1%), Figure 2.

### Functional Failure

Functional failure was noted in 18/137 (13.1%) of patients with SUSD vs 192/1846 (10.4%) in patients with solitary USD, $P = .3$, Supplementary Table 1. The mean recurrence length was 1.3 cm in SUSD vs 2.1 cm in men with solitary USD, $P = .1$, Supplementary Table 1. Figure 2 details the failure locations and management strategies for patients with SUSD and functional failure.

On multivariable analysis the presence of SUSD was not associated with increased odds of functional failure, odds ratio [OR] = 1.17, 95% confidence interval [CI] = 0.65-2.12, $P = .6$, Table 2. Previous DVIU, OR = 1.1, CI = 1.01-1.18, $P = .01$ was associated with increased odds of functional failure. Decreasing age, OR = 0.99, CI = 0.98-0.99, $P = .02$, was noted to decrease the odds of functional failure. Active smoking status was noted to be protective, with an increased odds of functional failure in patients with no history or previous history of smoking, OR = 2.65, CI = 1.40-5.03, $P = .002$. S classification S1b through S2c and E classifications 3a (internal trauma following

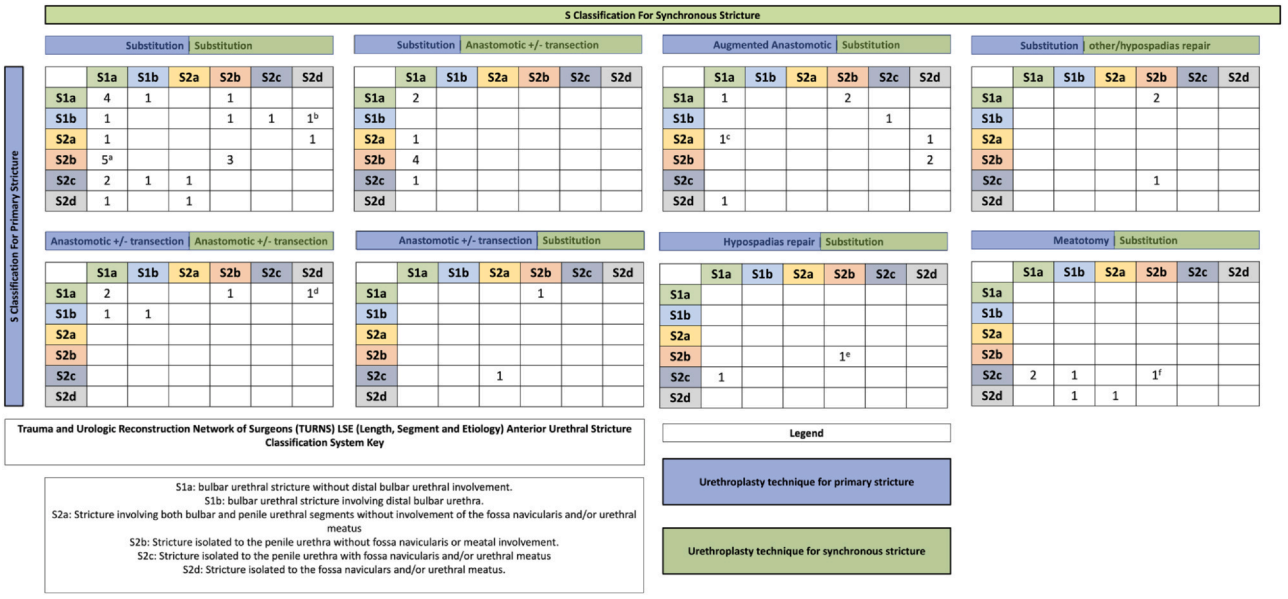


**Figure 1.** Anterior urethroplasty technique combinations for both the primary stricture and the synchronous stricture stratified by "S" Stage in all patients with synchronous urethral stricture. [a]1/5 patients underwent substitution urethroplasty for primary stricture and augmented anastomotic urethroplasty for synchronous urethral stricture. [b]Patient underwent substitution urethroplasty for primary stricture and augmented anastomotic urethroplasty for synchronous urethral stricture. [c]Patient underwent augmented anastomotic urethroplasty for both strictures. [d]Patient underwent anastomotic urethroplasty +/− transection for primary stricture and meatotomy for synchronous urethral stricture. [e]Patient underwent hypospadias repair for primary stricture and anastomotic urethroplasty +/− transection for synchronous urethral stricture. [f]Patient underwent extended meatotomy for both strictures. (Color version available online.)

endoscopic procedure ie, transurethral resection of the prostate or bladder tumor) and E6 (Lichen Sclerosus) were also associated with increased odds of functional failure, Table 2.

No difference was noted in time to functional failure when comparing patients with SUSD vs solitary USD, $P = .4$, Supplementary Figure 1.

## Discussion

The present investigation is the largest study evaluating the rates of SUSD utilizing a large contemporary (2007-2020) cohort of 1983 patients within a multi-institutional database. Our findings reveal that the rate of SUSD was 6.9%, which falls within previously reported ranges from single institutional investigations.[3,4] Historically, SUSD has been classified as a "complex" urethral stricture and has been grouped in retrospective single institutional series with other "complex" urethral strictures, such as long segment USD or in patients with both anterior and posterior urethral involvement.[3,4,7-9] Such lack of standardization has made comparisons between investigations challenging. Contrary to previous studies, we utilized the TURNS LSE Anterior Urethral Stricture Classification System which allowed for improved standardization and stratification of an extremely heterogenous patient population. To our knowledge, this is the first investigation to assess patients with SUSD utilizing both a multi-institutional dataset and a standardized classification system.

As initially discussed, SUSD is defined as presence of two distinct urethral strictures separated by a healthy intervening urethral segment and therefore could be present in any two locations with the male urethra. Utilizing the TURNS LSE Anterior Urethral Stricture Classification System we were able to demonstrate 27 different combinations of SUSD, Figure 2. The most common stricture location combination for patients with SUSD was two separate proximal bulbar urethral strictures (S1a). This is to be expected given the bulbar urethra is the most commonly involved urethral segment in USD.[10,11] Moreover, unique to our investigation, we were able to demonstrate 12 different anterior urethroplasty technique combinations utilized in treating the various combinations of SUSD, Figure 1. Such findings demonstrate that there is no "one size fits all" approach when managing patients with SUSD, and that in order to effectively treat patients with SUSD, urologists much be equipped with a broad armamentarium of reconstructive and urethroplasty techniques.

Our investigation found that functional failure occurred in 18/137 (13.1%) of patients with SUSD vs 192/1846 (10.4%) in patients with solitary USD, $P = .3$, Supplementary Table 1. Additionally, despite the opportunity for failure at two different surgically repaired sites, we did not identify a significant difference in time to retreatment between our cohorts, Supplementary Figure 1. On multivariate analysis, the presence of SUSD did not increase the odds of functional failure. Despite the inherent heterogenicity in patients with SUSD and complexities in treating these strictures, our investigation further confirms the findings, that repair of SUSD in a single setting does not carry an increased risk of functional failure.[3,4]

To date, only small, single-institution series have been published regarding SUSD. In 2009, Langston et al specifically evaluated patients with SUSD.[3] The authors performed a single institution retrospective review over a 11-year period. The authors reported that 30/482 (6.2%) patients had SUSD. Similar to the present study, the authors noted that the most commonly

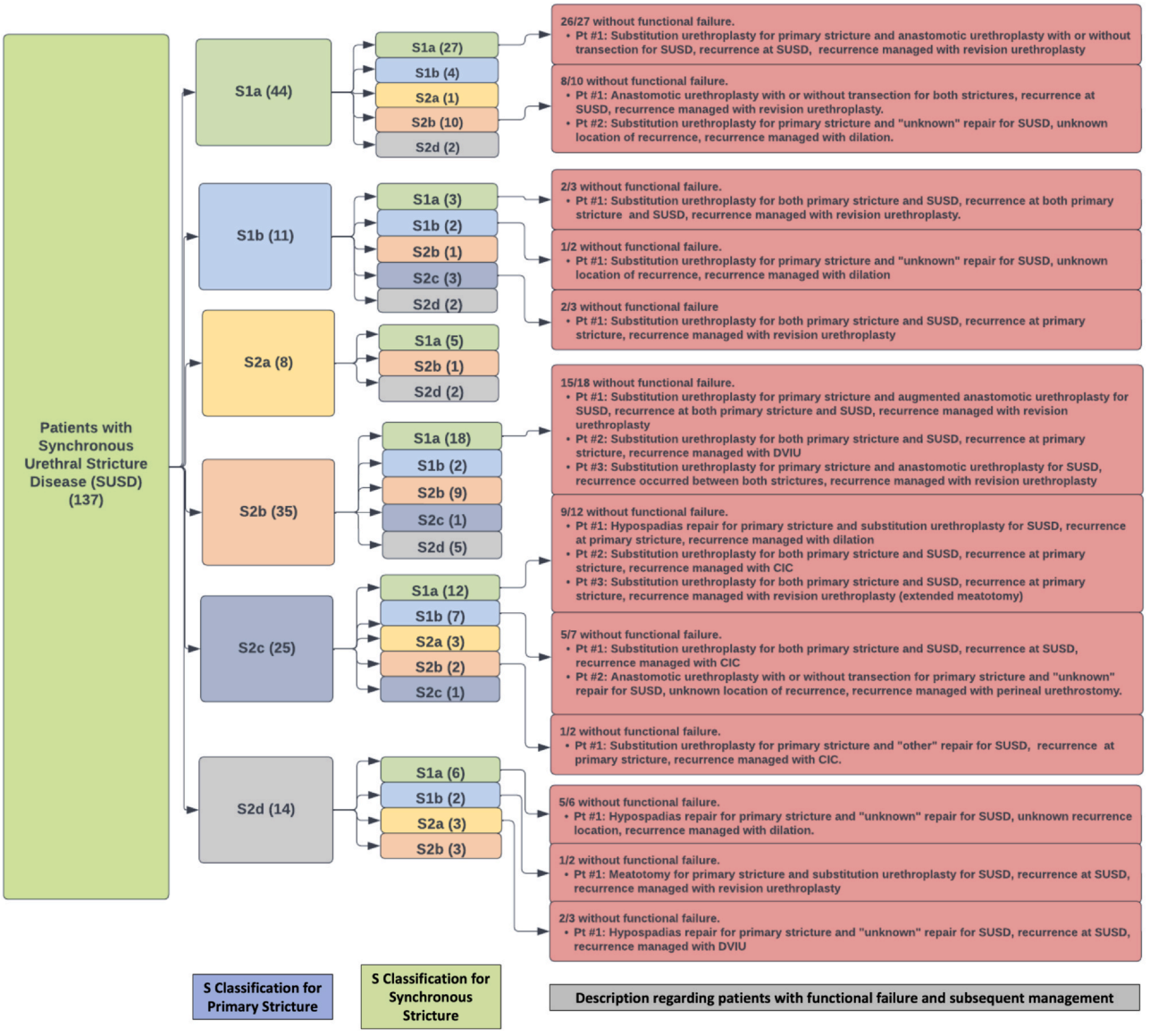


**Figure 2.** Synchronous urethral stricture location combinations stratified according to "S" stage with associated outcomes. Trauma and Urologic Reconstruction Network of Surgeons (TURNS) LSE (Length, Segment and Etiology) Anterior Urethral Stricture Classification System Key. S1a: Bulbar urethral stricture without distal bulbar urethral involvement. S1b: Bulbar urethral stricture involving distal bulbar urethra. S2a: Stricture involving both bulbar and penile urethral segments without involvement of the fossa navicularis and/or urethral meatus. S2b: Stricture isolated to the penile urethra without fossa navicularis or meatal involvement. S2c: Stricture isolated to the penile urethra with fossa navicularis and/or urethral meatus. S2d: Stricture isolated to the fossa naviculars and/or urethral meatus. (Color version available online.)

utilized technique to repair both strictures was graft or flap substitution urethroplasty. The authors noted that 3/30 (10%) patients had recurrence. Additionally, in 2003, Elliott et al assessed the success rates of ventrally placed buccal mucosa grafts in patients with bulbar USD.[4] The authors also included nine patients who underwent simultaneous repair of penile SUSD utilizing a circular penile fasciocutaneous flap or an end-to-end anastomotic urethroplasty. Only 1/9 patients underwent retreatment. Similar to the present investigation, the authors concluded that concomitant repair was not associated with increased risk of retreatment. Despite the similar conclusions, the present investigation benefits from a much larger sample size (n = 137), generated from multiple institutions, allowing for a far broader assessment of different stricture locations and technique combinations. Historically, SUSD has been defined as a "complex" urethral stricture. However, the present investigation demonstrates that functional failure is driven primarily by elements within the LSE classification system (S classification S1b through S2c and E classification 3a [internal trauma following endoscopic procedure ie, transurethral resection of the prostate or bladder tumor] and E6 [Lichen Sclerosus]) and not by the presence of SUSD, Table 2. This further illustrates the importance of the LSE classification system which allows the evaluation of a highly heterogenous patient population.

Our investigation is not without limitations. First, despite the utilization of a large prospectively maintained multi-institutional

**Table 2.** Multivariable analysis and odds ratios of all 1983 patients assessing predictors of retreatment.

| | OR | CI | *P*-Value |
|---|---|---|---|
| Stricture type | | | |
| SUSD | 1.17 | 0.65-2.12 | .6 |
| Solitary USD | ref | ref | |
| Age | 0.99 | 0.978-0.998 | .02 |
| Smoking status | | | |
| Never/Former | 2.65 | 1.40-5.03 | .002 |
| Active | ref | ref | |
| Operative stricture length | 0.97 | 0.92-1.04 | .4 |
| Number of prior dilations | 1.03 | 0.98-1.09 | .2 |
| Number of prior DVIUs | 1.10 | 1.01-1.18 | .01 |
| S classification[a] | | | |
| S1a | ref | ref | |
| S1b | 1.90 | 1.25-2.89 | .003 |
| S2a | 2.43 | 1.40-4.19 | .001 |
| S2b | 1.97 | 1.17-3.30 | .01 |
| S2c | 2.11 | 1.10-4.00 | .02 |
| S2d | 1.05 | 0.47-2.33 | .9 |
| E classification[a] | | | |
| 1 | ref | ref | |
| 2 | 1.43 | 0.79-2.60 | .2 |
| 3a | 2.64 | 1.35-5.14 | .004 |
| 3b | 1.68 | 0.84-3.36 | .1 |
| 3c | 0.86 | 0.29-2.55 | .8 |
| 4 | 2.05 | 0.54-7.78 | .3 |
| 5 | 1.16 | 0.47-2.85 | .7 |
| 6 | 2.48 | 1.07-5.77 | .03 |
| Repair type | | | |
| Anastomotic (transecting or nontransecting) | ref | ref | - |
| Graft or flap substitution urethroplasty | 1.67 | 0.97-2.88 | .06 |
| Augmented anastomotic | 0.94 | 0.26-3.45 | .9 |
| Staged anterior urethroplasty | 1.47 | 0.50-4.34 | .5 |
| Meatotomy | 1.33 | 0.26-6.86 | .7 |
| Hypospadias/other | 1.52 | 0.44-5.27 | .5 |

CI, 95% confidence interval; DVIU, direct visual internal urethrotomy; OR, odds ratio; Ref, Reference; SUSD, synchronous urethral stricture disease; USD, urethral stricture disease.

[a](S): S1a, proximal bulb; S1b, distal bulb; S2a, bulbar/penile; S2b, penile only; S2c, penile/fossa; S2d, fossa only; S3, bulb/penile/fossa.

[b](E): E1, external trauma; E2, idiopathic; E3a, internal trauma; E3b, urethroplasty failure; E3c, radiation; E4, inflammatory; E5, hypospadias; 6, Lichen Sclerosus.

* Retreatment described as undergoing any form of treatment for recurrence, includes clean intermittent catheterization, DVIU, dilation or revision urethroplasty.

database, approximately 50% of patients with SUSD had an unknown repair type for the SUSD, therefore resulting in an inability to draw any conclusions on the effects of repair type on functional failure. Such a finding is the result of a lack of early standardization in the reporting of the presence of SUSD and prior to the development and adoption of the TURNS LSE Anterior Urethral Stricture Classification System. Secondly, given the relatively small sample size of patients with SUSD and functional failure, no definitive conclusions could be made on predictors of retreatment in this patient population, specifically as to which repair type could lead to higher rates of failure in patients with SUSD. Additionally, all urethroplasties were performed by high-volume urethroplasty surgeons and therefore generalizability to all SUSD repair outcomes encountered in the community may be limited. At the present moment, a standardization in the reporting of which stricture is truly the primary stricture and which is the SUSD does not exist.[5] A majority of the primary strictures were labeled as such if they were the longer of the two strictures, however, this was not universal. Our study demonstrates that this may not be important from a research perspective as the outcomes of each individual stricture performs according to its individual LSE classification. Furthermore, as the TURNS LSE Anterior Urethral Stricture Classification System is more widely adopted and refined, a standardized approach as to how to classify which stricture is defined as primary and which stricture is defined as the synchronous stricture may allow for further reduction of the potential number of "s" classification combinations, as noted in Figures 1 and 2. Moreover, given that the TURNS LSE Anterior Urethral Stricture Classification System was adopted during the study period, some degree of contamination may exist, as some patients who may have been categorized as SUSD may potentially have had a long segment solitary USD, as could explain patients with two separate s1a strictures or a s1a and s1b stricture. Similarly, patients with true SUSD may have been categorized as a solitary long segment urethral stricture. Although this potential for reclassification is possible, it should be noted that all patients with SUSD did undergo separate anterior urethroplasties for each stricture. Ultimately, this reinforces the importance of standardization in reporting the specific phenotypes of strictures to improve comparative analyses.

This investigation provides physicians with the necessary information to counsel patients on the risk of functional failure

in the setting of SUSD and that being concomitant repair of SUSD in a single setting does not carry an increased odds of functional failure. Furthermore, the present investigation further reinforces the importance of the TURNS LSE Anterior Urethral Stricture Classification System as a necessary tool in large-scale multi-institutional analysis when assessing a highly heterogeneous patient population.

## Declaration of Competing Interest

No conflict.

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.urology.2023.08.017.

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