**ORIGINAL ARTICLE**

# Clinical significance of cystoscopic urethral stricture recurrence after anterior urethroplasty: a multi-institution analysis from Trauma and Urologic Reconstructive Network of Surgeons (TURNS)

Nima Baradaran[1] · Kirkpatrick B. Fergus[2] · Rachel A. Moses[3] · Darshan P. Patel[3] · Thomas W. Gaither[2] · Bryan B. Voelzke[4] · Thomas G. Smith III[5] · Bradley A. Erickson[6] · Sean P. Elliott[7] · Nejd F. Alsikafi[8] · Alex J. Vanni[9] · Jill Buckley[10] · Lee C. Zhao[11] · Jeremy B. Myers[3] · Benjamin N. Breyer[2]

## Abstract

**Purpose** To assess the functional Queryoutcome of patients with cystoscopic recurrence of stricture post-urethroplasty and to evaluate the role of cystoscopy as initial screening tool to predict future failure.

**Methods** Cases with cystoscopy data after anterior urethroplasty in a multi-institutional database were retrospectively studied. Based on cystoscopic evaluation, performed within 3-months post-urethroplasty, patients were categorized as small-caliber (SC) stricture recurrence: stricture unable to be passed by standard cystoscope, large-caliber (LC) stricture accommodating a cystoscope, and no recurrence. We assessed the cumulative probability of intervention and the quality of life scores in association with cystoscopic recurrence 1-year post-urethroplasty. Patients with history of hypospadias, perineal urethrostomy, urethral fistula, and meatal pathology were excluded.

**Results** From a total of 2630 men in our cohort, 1054 patients met the inclusion criteria: normal ($n=740$), LC recurrence ($n=178$), and SC recurrence ($n=136$) based on the first cystoscopic evaluation performed at median 111 days postoperatively. Median follow-up was 350 days (IQR 121–617) after urethroplasty. Cystoscopic recurrence was significantly associated with secondary interventions (2.7%, 6.2%, 33.8% in normal, LC, and SC groups, respectively). Quality of life variables were not statistically significantly different among the three study groups.

**Conclusions** Many patients with cystoscopic recurrence do not need an intervention after initial urethroplasty. Despite good negative predictive value, cystoscopy alone may be a poor screening test for stricture recurrence defined by patient symptoms and need for secondary interventions.

**Keywords** Urethra · Lower urinary tract symptoms · Urethral stricture · Cystoscopy · Self report · Treatment outcome

✉ Benjamin N. Breyer
benjamin.breyer@ucsf.edu

1. Department of Urology, Ohio State University, Columbus, OH, USA

2. Department of Urology, Zuckerberg San Francisco General Hospital and Trauma Center, University of California San Francisco, 1001 Potrero Suite 3A, San Francisco, CA 94110, USA

3. Division of Urology, University of Utah, Salt Lake City, UT, USA

4. Department of Urology, University of Washington, Seattle, WA, USA

5. Department of Urology, Baylor College of Medicine, Houston, TX, USA

6. Department of Urology, University of Iowa, Iowa City, IA, USA

7. Department of Urology, University of Minnesota, Minneapolis, MN, USA

8. Uropartners, Gurnee, IL, USA

9. Department of Urology, Lahey Hospital and Medical Center, Burlington, MA, USA

10. Department of Urology, University of California San Diego, San Diego, CA, USA

11. New York University School of Medicine, New York, NY, USA

## Introduction

Urethral stricture disease (USD) occurs in 0.6% of the male population and is associated with significant urologic morbidities if left untreated [1, 2]. There has been a paradigm shift in treatment algorithm of USD favoring urethroplasty over less effective endoscopic approaches in recent years. This change is reflected in the most recent update of American Urological Association guideline for treatment of USD [3].

The definition of "success" after urethroplasty is a point of controversy in the literature [4]. Historically, success has been defined as the absence of secondary interventions after urethroplasty. However, multiple publications have affirmed the importance of patients' perspective when urethroplasty success is being evaluated [5, 6]. In addition there is no consensus on the optimal surveillance protocol after urethroplasty, which has led to significant variability in practice patterns among experts and increased cost [7–9]. Surprisingly the utility of cystoscopy, as the presumed gold standard for diagnosing USD, has never been critically studied as a surveillance tool after urethroplasty.

The present study aimed to evaluate the association between cystoscopic recurrence of USD and the need for secondary intervention as a primary outcome. Secondary goal was to study the association between cystoscopic recurrence and patients' symptoms assessed by standardized questionnaires.

## Materials and methods

### Subjects

We retrospectively reviewed a cohort of 2630 men in the Trauma and Urologic Reconstruction Network of Surgeons (TURNS) that underwent anterior urethroplasty at ten institutions between December of 2006 and May of 2017. Details regarding the study design and database are available in other publications [10]. Patients with history of hypospadias, perineal urethrostomy, urethral fistula, and meatal pathology were excluded ($n = 321$). All postoperative cystoscopic evaluations were performed using standard flexible 17 french (f) cystoscope to the level of stricture. No attempts to pass the cystoscope beyond the area of urethroplasty (regardless of caliber) are routinely performed unless clinically indicated. Total of 1054 patients who had their initial postoperative cystoscopic evaluation between 3 and 6 months after urethroplasty were included. Subjects were classified into three groups according to their first cystoscopy result: normal; large-caliber (LC) stricture recurrence which could accommodate the standard cystoscope; and small-caliber (SC) stricture where a standard cystoscope could not be easily passed.

### Urethroplasty failure and patient-reported outcome measures (PROM)

The primary outcome was failure after anterior urethroplasty, which was classified as the need for re-intervention such as internal urethrotomy, dilation, fistula excision, perineal urethrostomy or repeated urethroplasty. The secondary outcome was PROMs which were assessed during the same follow-up visit for cystoscopy and again > 8 months after urethroplasty. Questionnaires were mailed prior to clinic visit or filled during the same visit but prior to cystoscopy. For patients with primary failure of urethroplasty, the most recent available PROM before re-intervention is reported. Measures included the International Prostate Symptom Score (IPSS), Sexual Health Inventory for Men (SHIM), Male Sexual Health Questionnaire (MSHQ), and Core Lower Urinary Tract Symptom Score (CLSS).

### Statistical analysis

All analyses were conducted using STATA, version 15, with statistical significance set at $p < 0.05$. We provide descriptive statistics to present patient demographics, as well as one-way ANOVA, Kruskal–Wallis, and Chi squared tests to compare patient characteristics according to cystoscopy result. Non-parametric tests were used when the data were not normally distributed. Survival analysis for anterior urethroplasty failure included a Kaplan–Meier curve reporting cumulative incidence of re-intervention (failure) with an accompanying log-rank test for equality. Cox proportional hazards test was used to calculate unadjusted and adjusted hazard ratios (adjusting for age, stricture length, location and etiology). We used descriptive statistics to report PROMs and Kruskal–Wallis test to compare PROMs.

## Results

### Demographic and clinical characteristics

In our cohort, 1054 patients met the inclusion criteria with a mean age of 46.21 (SD = 16.48). Total follow-up time for all participants was a median of 350 days after anterior urethroplasty (IQR 121–617). Baseline comorbidities are presented in Table 1. In total, 18.3% of patients had a previous urethroplasty ($n = 180$). Postoperative cystoscopic evaluation occurred a median of 111 days post-urethroplasty (IQR 99–125). 740 (70.2%) patients had a normal lumen, 136 (12.9%) had SC recurrence, and 178 (16.9%)

**Table 1** Baseline demographic and clinical characteristics of patients undergoing urethroplasty according to postoperative surveillance cystoscopic evaluation

| | Normal lumen | > 17 French stricture | < 17 French stricture | $p$ value |
|---|---|---|---|---|
| Number variable | 740 | 178 | 136 | |
| Age mean (SD) | 45.6 (16.6) | 48.9 (16.0) | 45.9 (16.0) | 0.05 |
| BMI (SD) | 29.5 (6.7) | 30.3 (6.6) | 30.7 (7.0) | 0.09 |
| Diabetes $n$ (%) | 88 (11.9) | 21 (11.8) | 9 (6.6) | 0.19 |
| Hypertension $n$ (%) | 211 (28.5) | 50 (28.1) | 52 (38.2) | 0.07 |
| Hyperlipidemia $n$ (%) | 155 (21.0) | 31 (17.4) | 29 (21.3) | 0.55 |
| CAD $n$ (%) | 7 (1.0) | 1 (0.6) | 1 (0.7) | 1.00 |
| COPD $n$ (%) | 9 (1.2) | 3 (1.7) | 5 (3.7) | 0.10 |
| Smoking history $n$ (%) | | | | 0.97 |
| Never smoked | 484 (65.4) | 117 (65.7) | 76 (55.9) | |
| Current smoker | 46 (6.2) | 11 (6.2) | 7 (5.2) | |
| Previous smoker | 145 (19.6) | 32 (18.0) | 26 (19.1) | |
| Not reported | 65 (8.8) | 18 (10.1) | 27 (19.9) | |
| Stricture length (cm) | 3.4 (3.2) | 3.9 (3.1) | 4.0 (3.0) | 0.02 |
| Previous urethroplasty $n$ (%) | 129 (18.5) | 30 (18.5) | 21 (17.4) | 0.96 |
| Location of stricture $n$ (%) | | | | |
| Distal penile | 75 (10.1) | 19 (10.7) | 16 (11.8) | 0.84 |
| Mid-penile | 77 (10.4) | 24 (13.5) | 13 (9.6) | 0.44 |
| Proximal penile | 85 (11.5) | 29 (16.3) | 22 (16.2) | 0.11 |
| Distal bulbar | 146 (19.7) | 58 (32.6) | 38 (27.9) | < 0.001 |
| Mid bulbar | 300 (40.5) | 82 (46.1) | 61 (44.9) | 0.32 |
| Proximal bulbar | 384 (51.9) | 85 (47.8) | 56 (41.2) | 0.06 |
| Membranous | 63 (8.5) | 12 (6.7) | 8 (5.9) | 0.48 |
| Prostatic | 7 (1.0) | 1 (0.6) | 0 (0) | 0.85 |
| Stricture etiology $n$ (%) | | | | |
| Lichen sclerosis | 33 (4.5) | 5 (2.8) | 7 (5.2) | 0.54 |
| Idiopathic | 366 (49.5) | 86 (48.3) | 66 (48.5) | 0.95 |
| Failed hypospadias | 37 (5.0) | 6 (3.4) | 2 (1.5) | 0.16 |
| Iatrogenic | 124 (16.8) | 39 (21.9) | 28 (20.6) | 0.20 |
| Trauma | 123 (16.6) | 26 (14.6) | 16 (11.8) | 0.33 |
| Infectious | 14 (1.9) | 3 (1.7) | 2 (1.5) | 1.00 |
| Radiation | 19 (2.6) | 2 (1.1) | 3 (2.2) | 0.61 |
| Primary repair | | | | |
| Substitution dorsal onlay | 200 (27.0) | 63 (35.4) | 42 (30.9) | 0.08 |
| Substitution ventral onlay | 77 (10.4) | 38 (21.4) | 32 (23.5) | < 0.001 |
| Substitution dorsal inlay | 29 (3.9) | 5 (2.8) | 4 (2.9) | 0.70 |
| Augmented anastomotic repair w/buccal dorsal onlay | 54 (7.3) | 14 (7.9) | 9 (6.6) | 0.92 |
| Augmented anastomotic repair w/buccal ventral onlay | 13 (1.8) | 3 (1.7) | 9 (6.6) | 0.01 |
| First stage dorsal onlay with plate excision | 19 (2.6) | 4 (2.3) | 6 (4.4) | 0.42 |
| First stage dorsal onlay | 8 (1.1) | 0 (0) | 2 (1.5) | 0.30 |
| First stage lateral onlay | 3 (0.4) | 1 (0.6) | 3 (2.2) | 0.06 |
| Excision and primary anastomosis | 290 (39.2) | 37 (20.8) | 22 (16.2) | < 0.001 |
| EPA (non-transected) | 17 (2.3) | 5 (2.8) | 3 (2.2) | 0.90 |
| Other | 44 (6.0) | 11 (6.2) | 9 (6.6) | 0.92 |
| Time to first cystoscopy (days) | 110 (101–124) | 113 (98–126) | 113 (95–135.5) | 0.14 |
| Total follow-up length (days) | 344 (118–561) | 374 (121–731) | 319.5 (135.5–714) | 0.13 |

Used one-way ANOVA and Chi squared tests, fisher's exact, Kruskal–Wallis

*BMI* body mass index, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease
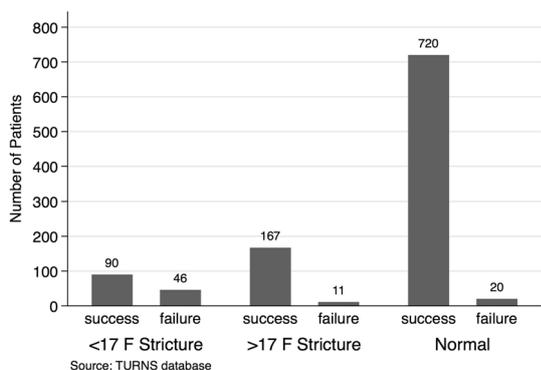
**Fig. 1** Frequency of long-term procedure success and failure according to first cystoscopy result after anterior urethroplasty
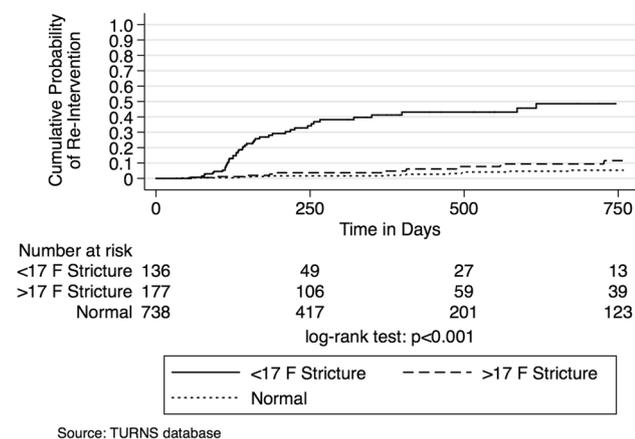


**Fig. 2** Cumulative probability of re-intervention after anterior urethroplasty

had LC recurrence. Patients with recurrence of any kind also had longer preoperative stricture length compared to the normal cystoscopy group. The primary repair for the non-recurrence (normal) group was more likely to be excision and primary anastomosis, whereas the recurrence groups (LC and SC) were more likely to have a graft.

## Objective outcomes

Stricture recurrence requiring re-intervention at any time point is shown in Fig. 1, with frequencies divided according to cystoscopy group. The 1-year overall cumulative incidence for patients with a full year of follow-up was 10.5% in our cohort. The Kaplan–Meier graph shows the post-anterior urethroplasty cumulative probability of re-intervention according to postoperative cystoscopy group (Fig. 2). The 1- and 2-year cumulative probability of intervention was 0.02 and 0.05 for those with normal cystoscopy, 0.41 and 0.49 for those with SC recurrence, and 0.04 and 0.12 for those with LC recurrence. A log-rank test of equality demonstrates the cumulative probability of intervention is not equal among the three groups ($p < 0.001$). Compared to the normal cystoscopy group, the unadjusted hazard ratio was 16.4 (95% CI 9.59–28.04) in the SC group and 2.2 in the LC group, and increased in our adjusted model (Table 2).

## Subjective outcomes

Patient-reported outcomes for sexual and urinary function were available in 440 patients, including 26 in SC recurrence, 80 in LC recurrence, and 334 in normal categories. Median follow-up time to questionnaires was 438 days (IQR 370–747). The median score and interquartile range of IPSS, SHIM, MSHQ, and CLSS scales are presented in Table 3. There was no statistically significant difference in IPSS, SHIM or MSHQ scores according to cystoscopy category. Among those that required re-intervention and had available PROMs, the average IPSS 8.2 ($n = 5$), SHIM 18.8 ($n = 9$), and MSHQ 12.4 ($n = 8$) scores were numerically worse-off than those that did not require re-intervention; however, our sample was not large enough to test this hypothesis.

## Comments

The findings of this multi-institution study confirm that the lack of small-bore recurrence of stricture 3-months after urethroplasty significantly obviates the need for future secondary interventions. Some patients report no significant urinary

**Table 2** Adjusted and unadjusted hazard ratios for post-urethroplasty re-intervention

| | Follow-up time (days) median (IQR) | 1-year cumulative incidence (%) | HR unadjusted (95% CI) | Adjusted HR (95% CI)[a] |
|---|---|---|---|---|
| Normal lumen | 342 (118–530) | 2.6 | Ref | Ref |
| > 17 French | 368 (118–696) | 5.2 | 2.2 (1.05–4.63) | 3.1 (1.35–7.29) |
| < 17 French | 167.5 (118–386) | 53.2 | 16.4 (9.59–28.04) | 23.7 (12.44–45.15) |

[a]Adjusted for age and stricture length, location, and etiology

**Table 3** Most recent quality of life score for each category of cystoscopy (IPSS, SHIM, MSHQ, CLSS)[†]

| PROM median (IQR) | IPSS n=130 | SHIM n=322 | MSHQ n=327 | CLSS n=93 |
|---|---|---|---|---|
| <17f | 4 (2 – 19) | 23 (18 – 24) | 16 (11 – 18) | 4 (0 – 15) |
| >17f | 5 (1 – 11.5) | 24 (17 – 25) | 16 (11 – 19) | 4.5 (1 – 10) |
| Normal | 3 (1 – 5.5) | 23 (17 – 25) | 16 (12 – 20) | 4 (1 – 7) |
| *p* value | 0.22 | 0.59 | 0.93 | - |

*CLSS* core lower urinary tract symptom score, *IPSS* core lower urinary tract symptom score, *MSHQ* core lower urinary tract symptom score, *PROM* patient reported outcome measures, *SHIM* core lower urinary tract symptom score

[†]All patients with available data are included, regardless of outcome; if the patient required reintervention, the most recent quality of life score before failure is reported

and sexual bother despite their cystoscopic recurrence and many forego a repeat intervention.

The discrepancy between the patient's reported symptoms, cystoscopic findings and re-intervention rate can have several explanations. One is that some men are truly asymptomatic from their USD. It has been suggested that men do not demonstrate subjective obstructive symptoms until urethral lumen is less than 10 french [11]. However, certainly other factors that drive a patient's aversion towards a repeat reconstruction should be considered which may include cost, frustration from previous failed attempt, difficult postoperative experience, pain, inconvenience, or other social considerations. Another important point is the realization that patients might be asked the wrong questions despite our best efforts at using standardized PROMs highlighting the need for improvement in this area.

Multiple tools have been used for initial screening of USD recurrence including: voiding symptom questionnaires, retrograde urethrogram, uroflowmetry parameters, and urethral calibration with variable predictive abilities to detect recurrence of USD [12–14]. Our results confirm that, even in the presence of a SC recurrence on cystoscopy, not all patients opt for a repeat intervention and decide to live with their USD. Another significant finding of our results is that all quality of life measures of those with anatomic recurrence were comparable with patients with large bore recurrence or even no recurrence. This highlights the fact that patients' symptoms should come into consideration when an anatomic recurrence is encountered and a treatment decision is to be made according to his goals and expectations. Important to note that potential consequences of delayed treatment of USD in patients with low post-void residual or bladder stones are unknown [4]. Also most patients with otherwise normal voiding dynamics do not report significant bother with urethral caliber of larger than 10 french [11]. Despite

these findings we still continue the anatomic assessment of urethra postoperatively as it provides the most consistent and reliable metric to compare surgical techniques among different surgeons that is crucial to advance the field of urethral reconstruction. It is also a valuable tool in patient counseling where, as confirmed in this report, lack of early recurrence can predict longer-term success. Another advantage is for young surgeons to critically evaluate their results and modify their technique. We also critically evaluate our follow-up protocol as a group to achieve one that is safe, cost-conscious and acceptable by patients without sacrificing predictive yield. Given the cost and discomfort associated with cystoscopy and as longer-term follow-up of asymptomatic patients with anatomic recurrence becomes available, we can determine the utility of such vigorous screening in the future.

The only disease-specific PROM for urethral stricture has been introduced by Jackson et al. (Urethral Stricture Surgery PROM) in 2011 which showed excellent psychometric parameters and correlation with uroflow measurements [8]. The 2-year interval publication showed improvement in all domains assessed following urethroplasty [15]. Efforts at developing a comprehensive disease-specific instrument are underway by members of TURNS. In the process and during qualitative interviews to prioritize items from patients' and surgeons' standpoint, Breyer et al. showed that patients and clinicians agreed on only 8 of the 15 items (53%) that they independently rated of highest importance. Items that patient's perceived high on the bother list that clinicians failed to recognize included having trouble aiming urine stream, need to sit down to void and the need for planning ahead during daily activities due to voiding function. As urologists continue to increase incorporating patients' perspective into the decision-making process, complaints that most reliably render a patient to accept the morbidity of a secondary procedure after recurrence stricture will continue to emerge. Future research should identify those domains and provide surgical solutions at the time of initial reconstruction or medical solutions postoperatively to specifically address those issues to achieve the ultimate goal of patient satisfaction.

Our study has several limitations. Despite our overall large sample size the nature of our database is conducive to retrospective interpretation only. In addition, the number of patients available to include in our analysis was limited by incomplete follow-up for cystoscopy and PROMs data and this could introduce selection bias as the clinical characteristics of patients who are more likely to adhere to the follow-up protocol is unknown. The choice of 3-month interval as the initial screening period is to identify recurrence early on to individualize follow-ups and also possibly improve patient's compliance with follow-up as they are not too far out from their operation. The correlation between

this time-interval and stricture recurrence is unknown and it is plausible that some patients develop strictures later than 3-month interval. We have relatively poor compliance with completion of cystoscopy. This maybe attributed to lack of symptoms by treated patients who don't see a need for follow-up. It could also be related to cost, inconvenience or fear of cystoscopy. Our survival analysis assumes individuals with follow-up data are representative of our population of interest. Given the study population demographics and the 10.5% cumulative incidence of intervention at 1 year, this assumption seems reasonable. Further, we assume the result of the index test (cystoscopy) does not determine the outcome (re-intervention), which agrees with current practice in reconstructive urology. Another limitation is that comparable IPSS and CLSS scores in patients with recurrence who decide not to have a repeat procedure with patients with no anatomic recurrence does not necessarily mean that these patients are satisfied with their current situation. In addition, although the overall follow-up of our database is longer, excluding patients without complete cystoscopy and PROM data limited the follow-up duration to about 1 year and we know clinically meaningful strictures can present beyond this time.

## Conclusions

Early recurrence of urethral stricture detected on cystoscopy after anterior urethroplasty is a significant predictor for a need for re-intervention. Despite high sensitivity and specificity of direct visualization as a screening test for re-intervention, cystoscopic findings and patient-reported symptoms do not always correlate. Therefore, patients' symptoms should always be incorporated in any decision regarding a repeat intervention. In addition, our findings highlight the need for a comprehensive disease-specific PROM that incorporates patients' symptoms when defining the success of the urethroplasty outcome.

## Compliance with ethical standards

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