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A Prospective Study of Patient-reported Pain After Bulbar Urethroplasty



Patrick Evans, Sorena Keihani, Benjamin N. Breyer, Bradley A. Erickson, James M. Hotaling, Sara M. Lenherr, and Jeremy B. Myers

OBJECTIVE	To understand the prevalence of chronic perineal pain, activity limitations, and patient satisfaction after urethroplasty.
METHODS	From 2014 to 2016, we prospectively enrolled men undergoing urethroplasty for bulbar urethral strictures. Patients, before and after surgery, completed questions from the Core Lower Urinary Tract Symptom Score assessing pain frequency in the bladder and penis or urethra, as well as nonvalidated questions assessing perineal pain. Overall satisfaction with their current urinary condition and pain-related activity limitations at home, work, or during exercise were also measured. Patients with <3 months of follow-up were excluded. Pre- and postoperative scores were compared using the Wilcoxon signed-rank test.
RESULTS	Thirty-five men were included in the study. Mean age and body mass index were 44.6 years and 30.9 kg/m ² , respectively. Urethroplasties were anastomotic in 24 (69%) and were single-stage buccal graft substitution in 11 (31%). Median follow-up after surgery was 483 days (range: 90-810 days). A total of 10 patients (29%) reported worsening perineal pain intensity after surgery, whereas 8 (23%) reported improvement and 17 (48%) reported no change. Overall, pain frequency in the bladder, penis or urethra, and perineum improved. Home and exercise pain-related activity restrictions improved significantly after surgery. Satisfaction with current urinary condition also improved with 91% reporting feeling “delighted,” “pleased,” or “mostly satisfied” with their current condition.
CONCLUSION	Patients are highly satisfied with their urinary condition after urethroplasty. Pain frequency in the bladder and the urethra significantly improves after urethroplasty; however, perineal pain intensity can worsen and become chronic after surgery in some patients. UROLOGY 117: 156–162, 2018. © 2018 Elsevier Inc.

Male urethral strictures affect between 200 and 1200 per 100,000 men/year in the United States.^{1,2} It most commonly presents with symptoms of lower urinary tract obstruction and can be associated with high morbidity.³ Lower urinary tract pain (LUTP) is also a common complaint of men with urethral strictures and along with urinary urgency and frequency contributes to diminished quality of life (QoL).^{4,5} Urethroplasty is the gold standard treatment for urethral strictures with higher success rates and cost-effectiveness compared to endoscopic treatments.^{2,6} Most patients experience noticeable relief of

both LUTP and urinary urgency or frequency with successful urethroplasty, and the procedure is well tolerated.⁴ The majority of patients are satisfied with their surgery and when asked are glad they underwent the procedure and would recommend it to others.⁷

Perineal and scrotal sensory neuropathy has been described as a complication of urethroplasty; however, this has been thought to be a transient complication, which universally resolves postoperatively.⁸ There are few investigations of this problem after urethroplasty or other types of perineal surgery and very little is understood about the pathophysiology of the problem. In addition, studies have been retrospective and do not involve preoperative assessment of pain. The effects of LUTP from urethral stricture on activities of daily living and satisfaction of men with the outcomes of surgery have also not been well studied.

We hypothesized that some men have lasting perineal pain after urethroplasty. Thus, we aimed to (1) describe and compare prevalence of LUTP frequency and perineal pain intensity pre- and posturethroplasty; (2) determine

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home, work, and exercise activity limitations due to pain; and (3) analyze the effects of perineal pain upon satisfaction with the surgery.

METHODS

After institutional review board approval, between December 2014 and June 2016, men undergoing urethroplasty for urethral stricture at the University of Utah Hospital completed a questionnaire, which included 2 questions from the validated Core Lower Urinary Tract Symptom Score (CLSS) questionnaire about the frequency of LUTP in the bladder and the urethra.⁹ QoL was assessed using the final question from the CLSS asking about satisfaction with the current urinary condition on a 7-point scale ranging from “terrible” to “delighted.” Nonvalidated questions about perineal or scrotal pain frequency and intensity, and perineal pain-related limitations in home, work, and exercise activities were added. Questions regarding pain frequency and limitations were on a 4-point scale, ranging from “never” to “often.” We also administered a visual analog scale asking patients to rate the intensity of any perineal or scrotal pain (Supplementary Table S1).

We included patients who underwent either anastomotic or buccal graft substitution urethroplasty within the bulbar urethra for urethral stricture treatment. Patients were excluded if they had <90 days of follow-up or did not have both pre- and postsurgery questionnaires (n = 21), underwent perineal procedures other than urethroplasty (eg, perineal urethrostomy, artificial urinary sphincter placement, etc [n = 70]) or had extensive repairs after radiation or pelvic fracture (n = 17). We collected baseline demographics, body mass index (BMI), type of surgery, postoperative complications within 30 days of surgery (graded by the Clavien-Dindo system¹⁰), and urethroplasty specific outcomes. Information available from the last follow-ups was used for the analyses. When the patients had not followed up, they were contacted and an electronic version of the questionnaire was sent to them. These patients were also asked about interval procedures indicating urethroplasty failure and about whether their urinary flow was better than before the surgery. Anatomic urethroplasty success was defined as the ability to atraumatically pass an adult flexible cystoscope through the area of repair. Clinical success was described as (1) not having had any interval procedures to treat urethral stricture recurrence (urethral dilation, direct vision internal urethrotomy, redo urethroplasty, perineal urethrostomy, and insertion of suprapubic tube); (2) not needing self-dilation or intermittent catheterization; and (3) having stronger urinary flow than before surgery.¹¹

Continuous data are reported as mean (standard deviation [SD]) or median (25-75 interquartile range [IQR]), when appropriate. Categorical data are presented as numbers and percentages. Pre- and postoperative scores were compared using the Wilcoxon signed-rank test to analyze non-normally distributed paired data. Independent *t* test or Wilcoxon rank-sum test were used to compare characteristics of independent groups as appropriate. All the analyses

were performed using STATA-15 software (Stata corp., College Station, TX). Two-sided statistical significance was assessed at the 0.05 level.

RESULTS

Demographics

A total of 35 patients were included in the study. Mean age and BMI were 44.6 years (SD: 14.6) and 30.9 kg/m² (SD: 6.5), respectively. Basic characteristics of the patients are summarized in Table 1.

Urethroplasty Specifics

Urethroplasty types are summarized in Table 1. Thirty-four of 35 patients left the hospital the day after surgery. Three men (8.6%) had Clavien-Dindo grade 1 complications (2 patients requiring repositioning or replacement of their Foley catheters and the third patient needing cauterization of a portion of the wound that bled after discharge). One patient (2.8%) had a grade 3a Clavien-Dindo complication; he experienced hematemesis on postoperative day 1 and required endoscopy which was normal. He also experienced bilateral upper lobe pulmonary emboli requiring anticoagulation and a prolonged hospital stay.

Cystoscopy was performed on 23 patients at a median of 125 days (IQR: 110-363). All 23 patients had open repair and anatomic success. The remaining 12 patients had only clinical follow-up (no cystoscopic exam); all had clinical success. The overall group had a median follow-up of 483 days (IQR: 386-679).

Patient Reported Outcome Measures

Preoperatively, 28 patients (80%) reported that they would feel “terrible,” “unhappy,” or “dissatisfied” if they were to

Table 1. Baseline patient characteristics and pain history

Number of Patients	35
Age, mean (SD), years	44.6 (14.6)
BMI, mean (SD), kg/m ²	30.9 (6.5)
Urethroplasty technique	
Anastomotic	24 (69%)
BMG substitution	11 (31%)
Patients having frequent pain*	
Bladder	7 (20%)
Penile/urethral	19 (54%)
Perineal	6 (17%)
Patients with frequent activity restriction*	
Domestic	4 (11%)
Exercise	4 (11%)
Work	3 (9%)
Patients with negative quality of life [†]	28 (80%)

BMG, buccal mucosa graft; BMI, body mass index; SD, standard deviation.

Values are numbers (%) unless otherwise specified.

* Defined as pain or activity restriction scored as “sometimes” or “often.”

[†] Defined as quality of life related to the urinary condition scored as “mostly dissatisfied” or “unhappy” or “terrible.”

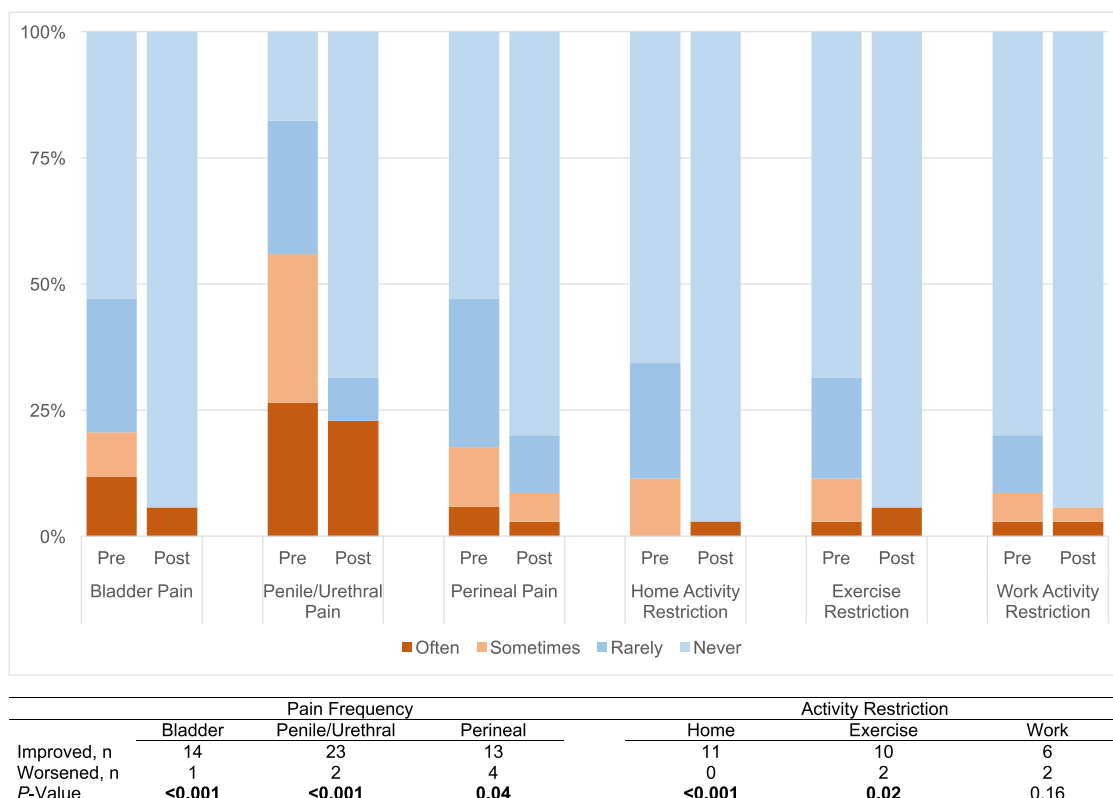


Figure 1. Changes in pain frequency and activity restrictions pre- and posturethroplasty. (Color version available online.)

spend the rest of their lives with their current urinary condition. Overall, 29 patients (83%) reported some LUTP frequency (either bladder, penile or urethral, or perineal); pain frequency was reported as “sometimes” or “often” in 22 patients (63%). Preoperatively, 12 men (34.3%) reported having some degrees of perineal or scrotal pain where median perineal or scrotal preoperative pain intensity (rated on the 0-10 pain scale using visual analog scale) was 4.0 (IQR: 3.0-4.5, range 1-8). Restrictions of activities at home, at work, or during exercise due to pain were rare in the preoperative period (Table 1).

Changes in pain frequency and activity restrictions are shown in Figure 1. Overall, patients had statistically significant decreases in bladder, penile or urethral, and perineal or scrotal pain frequency after surgery. Home and exercise activity restrictions significantly improved after surgery; however, the changes in work activity restriction was not statistically significant ($P = .16$). Figure 2 demonstrates the changes in overall patient-reported satisfaction before and after the surgery. Preoperatively, satisfaction was poor in most patients. Of the 33 men who filled out the QoL section of the questionnaire, 12 men (36.4%) reported feeling “terrible,” 12 (36.4%) felt “unhappy,” and 4 (12.1%) felt “mostly dissatisfied.” A significant improvement was observed postoperatively as only 3 men (8.6%) reported feeling either terrible or unhappy or mostly dissatisfied about their current condition, compared to

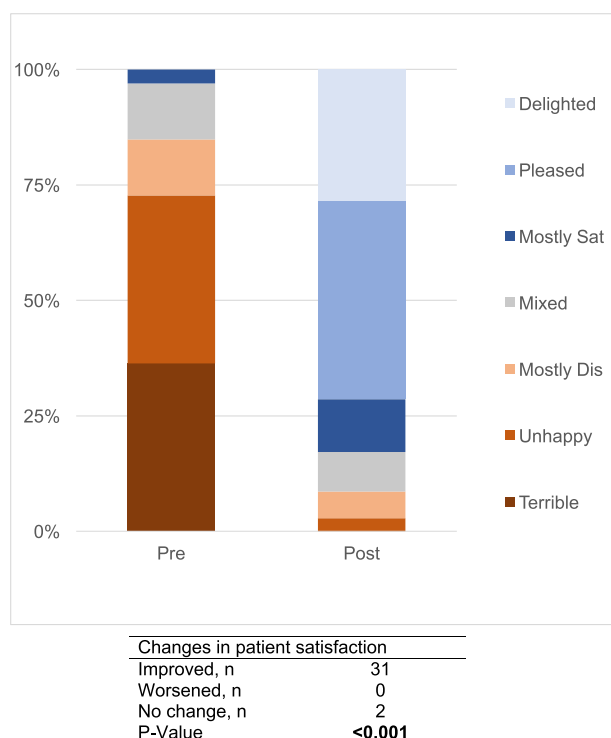


Figure 2. Patient satisfaction (overall feeling about urinary condition) before and after urethroplasty. (Color version available online.)

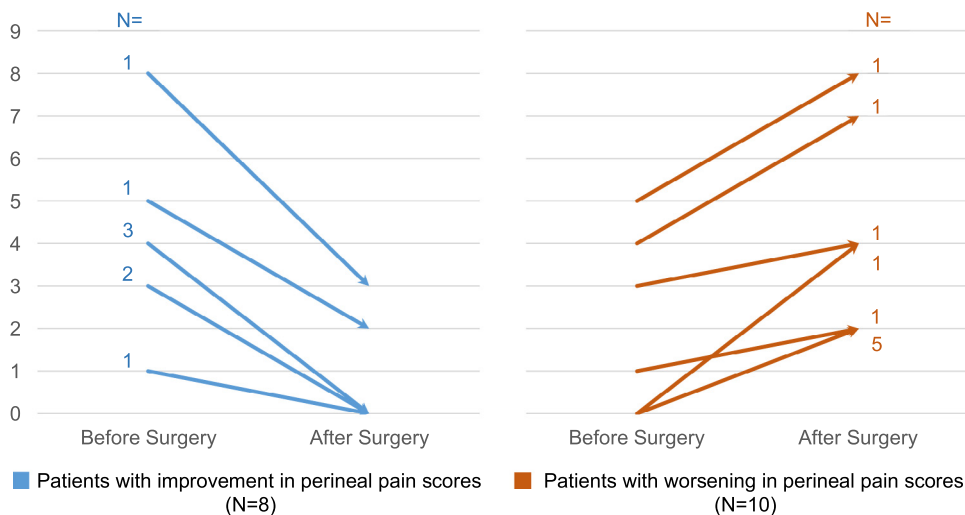


Figure 3. Change in perineal pain score before and after urethroplasty. (Color version available online.)

24 prior to surgery ($P < .001$). Of those 3 men, 2 had new onset erectile dysfunction and 1 had severe incontinence after surgery.

The changes in perineal or scrotal pain score pre- and postoperatively were not statistically significant (1.4 vs 1.1, $P = .98$). In the entire group of patients undergoing urethroplasty, 10 patients had worsening of pain after the surgery and 8 patients had improvement in pain intensity; the remaining patients indicated no perineal or scrotal pain on the Likert scale preoperatively and did not develop pain postoperatively (Fig. 3). We compared the 10 patients—whose perineal pain scores got worse after surgery—with the 25 patients who got better or did not have pain. There were no significant differences in their baseline age, BMI, type of urethroplasty, preoperative perineal pain, or postoperative satisfaction with their urinary condition.

A total of 17 patients filled out the questionnaires both at an early follow-up (approximately 3 months) and then at subsequent longer follow-ups. The median time for the early and late follow-ups were 113 days (IQR: 106-120) and 514 days (IQR: 465-704), respectively. There was no significant change in the bladder, urethral or penile, and perineal pain frequency or perineal or scrotal pain Likert scores. Additionally, patient satisfaction did not change from the early to late follow-up in this group of patients (data not shown).

DISCUSSION

In this prospective study, using patient reported outcome measures, we found patients experienced fewer activity restrictions at home or during exercise after urethroplasty. However, perineal pain intensity did not improve after surgery and approximately a third of men reported worsened pain in the perineum, which persisted postoperatively. Despite this observation, patients reported a high level of QoL and satisfaction with their urination.

LUTP is often underappreciated as an important symptom of urethral stricture compared to obstructive

symptoms.⁴ Bertrand et al reported that around 40%-70% of patients have some degrees of LUTP at presentation with urethral strictures.⁴ Similarly, we found that >80% of men reported some LUTP before surgery, and 63% reported this pain to be frequent (sometimes or often). In our study, both the bladder, and the urethra or penis pain frequency improved after surgery. Similarly, Bertrand et al found that most patients had improvement or resolution of pain after urethroplasty and only 4% and 5% had worsening pain in the bladder, and the urethra or penis pain frequency, respectively.⁴ Our findings were almost identical (3% and 6% worsening pain in the bladder, and urethra or penis pain frequency, respectively). Resolution of LUTP also appears to be durable; our study nearly doubles the follow-up period compared to the Bertrand et al study⁴ (median follow-up 483 days vs mean follow-up of 216 days) with no apparent return of LUTP in this longer follow-up.

Very few prior studies have examined the incidence of perineal pain after urethroplasty. In 2015, Granieri et al reported that 14% of patients experienced postoperative scrotal or perineal neuralgia after bulbar stricture repair; they suggested that perineal neuralgia is a temporary phenomenon with a 100% resolution by 271 days after surgery.⁸ In contrast, we found that 12 patients (34%) reported some degrees of pain (ie, perineal pain Likert score >0) even at a median follow-up of 483 days. Although 2 of these patients had improvements compared to their preoperative pain, it is noteworthy that 6 patients developed de novo lingering pain after the surgery. Additionally, up to 25% of our patients had frequent LUTP postoperatively; a finding in agreement with Maciejewski et al who reported about 20% rate of postoperative pain after urethroplasty.¹² The subtle differences in these rates might be attributable to the use of different questionnaires to assess LUTP, as well as different patient cohorts. Nevertheless, these findings indicate the possibility of chronic neuropraxia in the perineum after urethroplasty.

There is no clear explanation why urethroplasty can cause chronic perineal or scrotal pain. In our study, no baseline demographic factor was different among those who experienced worsening of perineal pain compared to those without pain or those who had improvement in pain. However, our ability to detect differences is no doubt limited by the small sample size of our study. Innervation of the perineum is complex and arises from the pudendal and the lateral femoral nerve; these nerves arise posteriorly and travel anteriorly through the buttock and inner thigh toward the midline in the perineum and the scrotum. A common belief is that fixed retraction may injure these nerves during urethroplasty. If this is the case one could hypothesize that perhaps different retractor configurations might decrease postoperative pain (Supplementary Fig. S1). Alternatively, nerves may be entrapped or injured during surgery and an incision such as a lambda or inverted “Y” incision, compared to a midline incision, might lead patients to be more prone to pain due to the proximity of larger proximal nerve trunks laterally and posteriorly.

Patient satisfaction in our study did not appear to be affected by pain postoperatively. Satisfaction with the results of urethroplasty has been previously reported in several studies. In 2013, Jackson et al reported that 87% of patients were either “satisfied” or “very satisfied” with the outcome of their urethroplasty.¹³ A more recent study by Bertrand et al found that 89.4% of patients were satisfied with their surgery.⁷ Our results are very similar with these findings as we demonstrated a 71.4% increase in men feeling pleased or delighted with their urinary condition. Bertrand et al reported that the only factors associated with dissatisfaction after urethroplasty were erectile dysfunction and failed surgery. Others have found similar results with dissatisfaction associated with de novo sexual dysfunction after urethroplasty.^{12,14} In our study, the 3 patients who reported dissatisfaction with their urinary condition had either new onset erectile dysfunction or incontinence postoperatively. Comparing the 10 men with worsened pain intensity in the perineum or scrotum to those with improved or without pain did not show any difference in satisfaction between the groups. We can surmise that the degree of postoperative pain did not affect the patients’ perception of their urinary function negatively. The QoL question at the end of the CLSS, however, is specific to satisfaction with urinary function, and a broader question, such as “did the surgery have any negative impact on your health or quality of life?” might better demonstrate the impact of chronic pain on QoL after urethroplasty.

The strengths of our study are the prospective design and our inclusion of preoperative assessment of pain, as well as the relatively long follow-up of the patients. In addition to pain frequency, we also assessed perineal pain severity in this study. However, our study is underpowered for subgroup analyses and to identify factors that predict perineal pain after surgery. Because of the small number of dissatisfied patients, we were unable to evaluate the factors associated with patient dissatisfaction. The study also may have a selection bias as 100% of the patients had a successful

urethroplasty outcome, which is not representative of the success in larger series; this may limit the generalizability of the results. In addition, a number of men in our study reported they had pain postoperatively in the perineum or scrotum “sometimes” or “often” but rated this pain as a 0 on the Likert scale; this discrepancy might stem from the wording of the question that may have indicated to the patient that the scale is meant to assess current pain, not as our intention that was to assess pain in the perineum and scrotum when the pain is present. Use of nonvalidated questions to assess perineal pain frequency and intensity and activity limitations is another limitation of this study. Additionally, we did not attempt to make any statistical or clinical interpretation of the significance of small changes in pain scores (eg, perineal pain score changing from 3 to 4). Despite these limitations, this study is hypothesis generating and the next step is to use this information to prospectively and systematically analyze factors that could be modified to decrease chronic postoperative pain after urethroplasty.

CONCLUSION

Pain is a common preoperative finding in patients with urethral stricture. We found that after urethroplasty, LUTP frequency improves and that patients experience fewer limitations at home or during exercise due to perineal pain. However, in approximately one-third of patients, perineal or scrotal pain intensity worsens after urethroplasty and does not appear to moderate over time. Despite this finding, satisfaction with urinary condition is high. There remains a clear need for multicenter prospective studies to investigate possible causes of long-term perineal pain and identify any modifiable factors, in an effort to prevent postoperative chronic pain.

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APPENDIX

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.urology.2018.02.046>.

EDITORIAL COMMENT



The authors reviewed the quality of life as well as the occurrence or persistence of perineal pain in a series of men who are underwent urethroplasty, with primary anastomosis or using single-stage buccal graft repair, for bulbar urethral strictures.

Most of the men had either no change in pain or improved perineal pain while 10 out of the 35 men studied has worsening perineal pain as determined by their questionnaire used. Preoperatively, 12 men of 29 reporting some lower urinary tract pain complained of perineal/scrotal pain.

Interestingly, although some men still complained of perineal pain after surgery, the majority of the men were much happier with their quality of life after urethroplasty than before repair despite the persistence of pain with only 8.6% who felt “terrible” or “unhappy” after surgery. Those factors expressed as causing dissatisfaction with the repair in only 3 patients were either failed surgery or development of erectile dysfunction post-operatively and not pain specifically.

Determining the cause of persistent postoperative pain is difficult as there may have been a chronic pain cycle that developed after the occurrence of the bulbar stricture itself that was not addressed by surgical repair or possibly by traction during the repair, although the duration of follow up was of reasonable duration (median follow up of 483 days).

The only criticism of the review was that success was objectively determined in only 23 patients, although, absence of follow up of 12 patients may indicate satisfaction with the urethroplasty results since patients that did not return to be evaluated may indeed be happy with their surgical results.

This study showed that improved urinary stream after urethroplasty overcame persistence or worsening of perineal/ scrotal pain or other lower urinary tract pain as the improved quality of life with improved home, work and exercise parameters may have been more important to the patient outweighing any persistence of pain after surgery.

The authors’ point out, as have other authors, that, currently, there is no specific questionnaire to assess the quality of life or outcome measures in patients suffering from or treated for urethral strictures.¹

The authors’ plan to develop a specific quality of life questionnaire for urethroplasty patients is to be commended as is their clinically successful urethroplasty results of moderate duration where only 3 out of 35 patients expressed some dissatisfaction with their surgical results.

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AUTHOR REPLY



An optimal definition for urethroplasty success should include both anatomic and functional outcomes.¹ To objectively assess anatomic success, ideally all patients should undergo cystoscopy at follow up. However, previous data show that about half of the patients will not return for a cystoscopic follow-up at 1 year.² Factors such as lack of symptoms, being remote from the clinic, lack of time, and unwillingness to undergo another cystoscopy are among the reasons for low follow-up rates.¹ Lack of cystoscopic follow-up in 12 of 35 (34%) patients in our study is in line with this. However, all these patients were interviewed and met the criteria for clinical and functional success as previously described.² Although it is known that up to 35% of asymptomatic patients may have strictures at cystoscopy (anatomic failure), the significance of anatomic failure in an asymptomatic and satisfied patient is unknown. This also raises the question if becoming aware of an asymptomatic cystoscopic stricture would negatively affect a patients’ conception about success and his satisfaction with the surgery, thereby affecting his quality of life.

Erectile or sexual dysfunction is an important and underappreciated factor in patient satisfaction after urethroplasty.³ The only available validated questionnaire on patient-reported outcomes (PROMs) after urethroplasty combines different voiding and quality of life questions but does not include questions about sexual or erectile function.⁴ Ideally, a PROM should be developed using patient input and include questions that matter the most to these patients. We hope that the PROM being developed by the TURNS group (turnresearch.org) would fill this gap and provide a thorough patient-centered tool to assess urethroplasty outcomes.⁵ Meanwhile, more studies are needed to assess factors affecting patients’ pain and satisfaction after surgery and the potential role of different urethroplasty techniques.

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