ORIGINAL PAPER

TRAUMA AND RECONSTRUCTIVE UROLOGY

# Is urethral stricture really so often idiopathic? Exploring the etiology of urethral strictures in males undergoing urethroplasty: a multicenter retrospective cohort study

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**Introduction** The aim of this study was to retrospectively evaluate the etiology of urethral stricture disease (USD) in a large series of patients undergoing urethroplasty.

**Material and methods** The multicenter retrospective cohort study was conducted at two reconstructive urology referral centers in years 2015–2022. Prior to the surgical intervention, all patients underwent diagnostic procedures including retrograde urethrography and voiding cystourethrography. We collected comprehensive demographic and medical data including the length and location of the stricture. We paid particular attention to identifying the underlying causes of USD in the medical records.

**Results** The study included 949 patients meeting criteria, with a mean age of 53. The primary cause of USD was identified as iatrogenic (404 cases, 42.6%), followed by trauma (210, 22.1%), previous hypospadias repair (122, 12.9%), lichen sclerosus (32, 3.4%), and infections (12, 1.3%). Notably, 169 patients (17.8%) did not have a discernible cause for their USD and were thus classified as idiopathic. Furthermore, it was observed that 66% of idiopathic USD cases were localized in the bulbar urethra. The etiology of USD varied significantly based on its localization ($p < 0.01$). The mean stricture length differed among different causes, with the longest in patients with USD due to lichen sclerosus (41 mm), followed by previous hypospadias repair (35 mm), and iatrogenic causes (29 mm), $p < 0.001$.

**Conclusions** Careful medical history-taking can identify the etiology of urethral stricture in over 80% of patients undergoing urethroplasty. The etiology of the USD impacts its location and length and thus can affect surgical treatment strategy and outcomes.

Key Words: urethral stricture ‹› etiology ‹› urethroplasty

## INTRODUCTION

Urethral stricture disease (USD) is a relatively common disease in men, especially in the elderly population, with a marked increase after 55 years of age [1]. It is a very heterogeneous condition as it can occur in different parts of the urethra, vary in length, and have different causes of origin. All these factors significantly affect the management options and the effectiveness of the proposed treatment [2, 3]. The most common management of USD is a minimally invasive treatment, namely dilation or direct visual internal urethrotomy (DVIU). These are simple procedures with little risk of significant complications. However, they are characterized by low long-term effectiveness [2, 4]. Nevertheless,

in the majority of clinical scenarios, urethroplasty should be the golden standard in the treatment of recurrent USD in males [4].
Data on the etiology of USD are scarce and often come from developing countries. In addition, the causes of urethral strictures are known to vary significantly depending on the society from which the data are drawn [5, 6, 7]. At the same time, to the best of our knowledge, such data for Central Europe do not exist.
The aim of this study was to retrospectively evaluate the etiology of urethral stricture disease in a large series of patients undergoing urethroplasty in Poland and to assess the potential impact of USD etiology on the length and location of the stricture.

## MATERIAL AND METHODS

A multicenter retrospective cohort study was conducted in two reconstructive urology centers in Poland which are the referral centers for USD repair. This included patients who underwent urethral reconstruction surgery between 2015–2022. In all patients, the stricture was diagnosed and evaluated prior to surgery by retrograde urethrography combined with voiding cystourethrography. Urethroscopy was performed in the cases where diagnostic uncertainty was present. Patients who underwent DVIU or dilation only were not included in the study as its goal was to evaluate the etiology of USD in the population of males undergoing urethroplasty. The exclusion of those patients from the study to ensures a focused evaluation specifically on those who underwent urethroplasty, aiming for a more targeted analysis of the etiology of USD in the population requiring open surgical reconstruction. We collected basic demographic and medical data including the length and localization of the stricture. Special focus was given to finding information on the potential cause of USD in the medical records. If no identifiable cause was found, the stricture was categorized as idiopathic. For urological surgeries after which a transurethral catheter is routinely left in place such as TURP, prostatectomy, hypospadias repair, the surgery itself rather than the catheter was considered the cause of the USD. Catheterization as a cause of USD was considered in cases where it was the only urethral intervention. Based on the previous studies subanalysis of USD etiology was performed by patient age less than 45 vs 45 and greater [6].
To test the normality of variables the Shapiro-Wilk test was used. Chi-square test and Fisher's exact test were used to examine the association between patients' age group with baseline characteristics and stricture etiology as well as the location of USD and its etiology. The Kruskal-Wallis test was used to assess the association between the etiology and the length of the stricture. The results are presented as means or medians. Statistical analysis was performed using jamovi (Version 2.3).
This was a retrospective non-interventional study, so the informed consent and the Ethical Board approval were waived according to institutional regulations.

## RESULTS

There were 949 male patients who fulfilled the inclusion criteria, with a mean age of 53. Out of them 327 patients who underwent urethroplasty were at the age lesser than 45, and 622 who were 45 or older. The basic patient's characteristics is summarized in Table 1. The major cause of USD was iatrogenic (404 cases – 42.6%) which included 207 patients after transurethral procedures, 127 patients after traumatic or prolonged catheterization, 42 patients after radical prostatectomy, 18 patients with radiation-induced USD. The second most prevalent etiology was trauma (210 patients – 22.1%). Previous hypospadias repair was the reason of USD in 122 cases (12.9%), lichen sclerosus in 32 (3.4%), and infections in 12 (1.3%). In 169 patients no possible cause of USD was found, and they were classified as idiopathic. The USD etiology differed significantly depending on the patients' age group (Table 2). In patients younger than 45 trauma and previous hypospadias repair were the major etiology of USD, while in the group of older patients the most common etiology was iatrogenic.
The most frequent location of the stricture was bulbar urethra (493 patients – 52%), followed by penile urethra (284 patients – 30%) and posterior urethra (106 patients – 11%). Penobulbar strictures

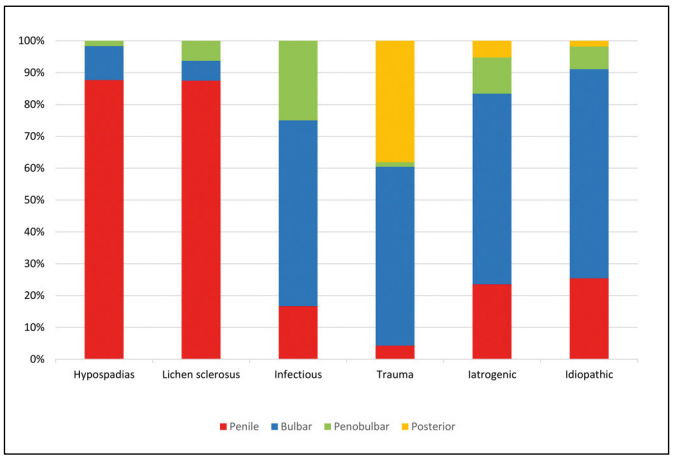


**Figure 1.** *The incidence of localisation of urethral stricture by its etiology.*

were relatively rarely seen and accounted for 7% of strictures. The etiology od USD differed significantly regarding the stricture localization. The penile urethra strictures were mostly caused by previous failed hypospadias repair (38% of all penile urethra strictures) while bulbar urethra strictures' etiology was predominantly iatrogenic or traumatic. The strictures located in the posterior urethra were usually caused by trauma. The most of the penobulbar strictures were iatrogenic. The detailed information about the etiology of USD and its location is summarized in Table 3.

The mean length of the stricture was 26,5mm in the whole cohort. The mean length of the stricture varied significantly depending on the etiology of USD. The strictures were the longest in patients with lichen sclerosus (Table 4).

The cross-sectional structure of patients with idiopathic USD in terms of mean age most closely resembles those with post-traumatic USD (Table 2), and in terms of location of stricture patients with iatrogenic USD (Figure 1).

The following types of surgeries were performed on patients: 385 – excision and primary anastomosis (EPA);

**Table 1.** *Comorbidities*

| | Number of patients | % | Age <45 | % | Age ≥45 | % | p-value |
|---|---|---|---|---|---|---|---|
| Total | 949 | | 327 | | 622 | | |
| DM2 | 90 | 9% | 5 | 2% | 85 | 14% | <0.001* |
| Hypertension | 271 | 29% | 16 | 5% | 255 | 41% | <0.001* |
| CAD | 72 | 8% | 2 | 1% | 70 | 11% | <0.001** |
| RTx | 18 | 2% | 0 | 0% | 18 | 3% | 0.003** |
| SPC | 397 | 42% | 134 | 41% | 263 | 42% | 0.769* |

* Chi-square test, ** Fisher's exact test
DM2 – diabetes mellitus type 2; CAD – coronary artery disease; RTx – radiotherapy; SPC – suprapubic catheter

**Table 2.** *Stricture etiology by patient age*

| | Number of patients | % | Age -mean (years) | Age <45 | % | Age ≥45 | % | p-value |
|---|---|---|---|---|---|---|---|---|
| Hypospadias | 122 | 12.9% | 38 | 90 | 27.5% | 32 | 5.1% | <0.001 * |
| Lichen sclerosus | 32 | 3.4% | 42.7 | 20 | 6.1% | 12 | 1.9% | 0.001 ** |
| Infectious | 12 | 1.3% | 56.7 | 1 | 0.3% | 11 | 1.8% | 0.068 ** |
| Trauma | 210 | 22.1% | 46.2 | 97 | 29.7% | 113 | 18.2% | <0.001 * |
| Iatrogenic | 404 | 42.6% | 63.7 | 50 | 15.3% | 354 | 56.9% | <0.001 * |
| Idiopathic | 169 | 17.8% | 49.6 | 69 | 21.1% | 100 | 16.1% | 0.062 * |
| TOTAL | 949 | 100.0% | | 327 | 100.0% | 622 | 100.0% | |

* Chi-square test
** Fisher's exact test

**Table 3.** *The etiology of urethral stricture and its localization*

| | Penile | | Bulbar | | Penobulbar | | Posterior | | p-value |
|---|---|---|---|---|---|---|---|---|---|
| No | 284 | | 493 | | 68 | | 106 | | |
| % | 30% | | 52% | | 7% | | 11% | | |
| Hypospadias | 107 | 38% | 13 | 3% | 2 | 3% | 0 | 0% | <0.001 ** |
| Lichen sclerosus | 28 | 10% | 2 | 0% | 2 | 3% | 0 | 0% | <0.001 ** |
| Infectious | 2 | 1% | 7 | 1% | 3 | 4% | 0 | 0% | 0.083 ** |
| Trauma | 9 | 3% | 118 | 24% | 3 | 4% | 80 | 75% | <0.001 ** |
| Iatrogenic | 95 | 33 | 242 | 49% | 46 | 68% | 22 | 21% | <0.001 * |
| Idiopathic | 43 | 15 | 111 | 23% | 12 | 18% | 4 | 4% | <0.001 ** |

* Chi-square test
** Fisher's exact test

**Table 4.** *The length of the strictures in different etiologies*

| | The length of the stricture (mm) | |
|---|---|---|
| Hypospadias (mean, SD) | 35.1 | 28.3 |
| Lichen sclerosus (mean, SD) | 40.9 | 34.2 |
| Infectious (median, quartiles) | 19.6 | 11.5; 25 |
| Trauma (mean, SD) | 17.1 | 14.1 |
| Iatrogenic (mean, SD) | 28.6 | 24.7 |
| Idiopathic (mean, SD) | 22.9 | 20.3 |

p-value (Kruskal-Wallis test) – <0.001
SD – standard deviation

24 – non-transecting EPA; 50 – bulbo-prostatic anastomosis; 290 – urethral augmentation including 274 patients with oral mucosa graft and 16 patients with preputial graft or flap; 80 – staged procedures using grafts; 45 – penile urethrostomy, 33 – perineal urethrostomy, 42 – other procedures.

## DISCUSSION

Recently, we have seen a change in the characteristics of the causes of urethral strictures. In the 1960s and 1970s, urethritis was the most common cause of USD [8]. In the following decades, there has been a rapid shift towards iatrogenic causes of urethral stricture. In the study by Lumen et al. from the early 20$^{th}$ century urethritis was the cause of urethral stricture in 3.7% of cases [6]. In our study it was even less – 1.3%. This is clearly related, on the one hand, to much more widespread access to antibiotics and greater public awareness of sexually transmitted diseases, and,on the other hand, to the prevalent performance of transurethral procedures and the frequent insertion of catheters.

Currently, the most common cause of USD is iatrogenic, as confirmed by our analysis. Of these, the main group is made up of patients after transurethral procedures, most of which involve transurethral procedures performed within the prostate gland [7, 9]. USD after transurethral procedures is not common and, according to a recent systematic review, affects 1.7% of patients after enucleation procedures, 2.1% after ablation and up to 3.8% after TURP [10]. Nevertheless, due to the large number of procedures of this type performed worldwide, especially in developed countries, patients who are affected by this complication constitute a large group. Various hypotheses have been put forward for the origin of urethral stricture after transurethral surgery. It has been postulated that the cause could be an inappropriate relationship between the size of the instrument and the diameter of the urethra, improper traumatic insertion of the resectoscope with perforation of the urethral bulb, prolonged friction of the instrument in the penoscrotal angle or leakage of monopolar power caused due to insufficient insulation of the resectoscope [11]. It should also be borne in mind that in the early postoperative period, patients undergoing transurethral procedures may develop complications, such as bladder clots, which may require additional catheterization or prolonged catheter maintenance. These factors can also have a significant impact on the subsequent development of USD [12].

An important, and often forgotten, group of patients with USD are those who have undergone radical prostatectomy. It has been proven that USD can affect up to 16% of those patients, and in addition, early urinary retention after catheter removal and the leakage of the vesicourethral anastomosis with the need for prolonged catheter maintenance are direct risk factors for USD [13, 14]. In these patients, the issue of further treatment may be additionally significantly complicated by the fact that many of them are also treated with radiotherapy, which can worsen the effects of afterwards urethroplasty [15].

In more than one in five patients in our study, the cause of USD was trauma, which was the second most common group of patients. This is higher than in other recently published series from developed countries [6, 9]. It is a cause that primarily affects young patients <45 years of age and is the leading cause of USD in this age group. Moreover, in patients with post-traumatic USD, posterior urethra involvement is very common. This is the primary cause of stenosis in this location both in our study and those of other authors [16, 17].

Patients with lichen sclerosus are a rare group of USD etiology and accounted for less than 4% of patients undergoing urethroplasty in our study which is in line with global data in developed countries [6, 18]. Patients with lichen sclerosus had longer strictures on average, similarly to other studies [19]. Although these patients may benefit from primary urethroplasty before endoscopic treatment [20], still most urologists consider direct visual internal urethrotomy as a first-line treatment option for USD associated with lichen sclerosus [21]. On the other hand, these patients pose a major therapeutic challenge, as they experience more frequent complications and surgical treatment failure [18], thus conservative management with endoscopic procedures with self-dilation may serve as a safe alternative to most of the patients as it leads to avoiding invasive surgery and permanent indwelling catheters in even 84% of patients [22].

In our study, we were unable to determine the cause of USD in 17.8% of patients. This number is significantly lower than in other studies, where it was about 30–40% [6, 23], and even 63% in the study by Cotter et al. which assessed trends in the etiology of USD based on a multi-institutional, prospectively maintained urethroplasty database in the USA [24]. Moreover, this study did not report a significant effect of USD etiology on its localization. We strongly believe that proper medical history taking is the key in truly assessing the cause of urethral stricture.

The length and location of the urethral stricture define the type of surgical treatment that can be offered to the patient [2]. Although no single, clear definition of success after urethroplasty has emerged so far, it is clear that the length of urethral stricture and its location affect it [25, 26]. Hence, trying to determine the cause of the USD is vital because it can potentially affect the treatment modality and the risk of treatment failure. While there is still a large group of patients in whom we will not find the cause, we will be able to do so in the vast majority of patients.

The study has several strengths, such as its multicenter design, a large sample size, and a comprehensive evaluation of USD etiology. However, certain limitations should be acknowledged. Firstly, the retrospective nature of the study may introduce inherent biases, and reliance on medical records for etiological information could result in incomplete data. Additionally, the study primarily focuses on patients undergoing urethroplasty, excluding cases managed with less invasive interventions. The exclusion of patients undergoing dilation or direct visual internal urethrotomy might limit the applicability of results to the broader population with USD. Lastly, the study's geographical scope is limited to Poland, which may impact the generalizability of findings to other regions with potentially distinct USD etiologies. Despite these limitations, the study provides valuable insights into USD etiology and its implications for surgical management.

## CONCLUSIONS

The etiologies of USD differ regarding patients age group. The most prevalent etiology of USD in younger patients are trauma and previous hypospadias repair and in older patients iatrogenic strictures. Careful medical history-taking can reveal the cause of urethral stricture in more than 80% of patients undergoing urethroplasty. The etiology of the USD impacts its location and length and thus can affect surgical treatment strategy and outcomes.

### CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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