The effect of recurrent direct vision internal urethrotomy for short anterior urethral strictures on the disease course and the predictors of treatment failure

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Abstract

Introduction:

Urethral stricture is a condition characterized by narrowing of the urethral lumen due to fibrosis during the healing process following epithelial injury. After endoscopic internal urethrotomy, which is the most commonly preferred treatment modality, recurrence rates range from 20% to 80%, depending on the number of prior operations, stricture length, localization, and number of strictures. The aim of this study was to evaluate whether demographic characteristics, laboratory parameters, and stricture-related features can predict disease prognosis in patients with recurrent urethral stricture, and to assess the impact of postoperative follow-up and treatment modalities on recurrence.

Methods:

A total of 154 patients who underwent more than one internal urethrotomy procedure with a preliminary diagnosis of urethral stricture between November 2021 and November 2023 at Süleyman Demirel University Faculty of Medicine Hospital were retrospectively analyzed. Demographic data, height, weight, body mass index (BMI), comorbidities, lifestyle factors (smoking, alcohol use), clinical and laboratory findings, follow-up duration, and treatment modalities were recorded. Patients with and without recurrence during follow-up were compared in terms of age, BMI, lifestyle factors, comorbidities, and number of previous failed procedures. Additionally, stricture characteristics including number, length, localization, calibration, and etiology were analyzed. Postoperative treatment methods used in our clinic to prevent recurrence were also compared, including medical therapy, intermittent self-dilatation, and follow-up alone.

Results:

In our study population of patients who underwent multiple internal urethrotomy procedures due to urethral stricture, the recurrence rate was 45%. Comparative analysis between patients with and without recurrence demonstrated that the number of previous operations, uroflowmetry pQmax value, stricture calibration, and stricture length were significant predictors of recurrence. Among laboratory parameters, red cell distribution width (RDW) was also identified as a significant predictor. Comparison of postoperative

treatment modalities showed no statistically significant difference in terms of recurrence prevention. However, patients receiving losartan therapy had a longer time to recurrence.

Conclusions:

Our findings provide important insights into the factors associated with urethral stricture recurrence and treatment approaches that may delay recurrence. These results may serve as a basis for future studies.

Introduction

Urethral stricture (US) is a condition characterized by narrowing of the urethral lumen, most commonly resulting from fibrosis secondary to epithelial injury [1,2]. Clinically, it presents with lower urinary tract symptoms such as weak urinary stream, straining during voiding, hesitancy, increased urinary frequency, a sensation of incomplete bladder emptying, and post-void dribbling, all of which may significantly impair patients' quality of life [3]. The clinical manifestation of symptoms may vary depending on the localization and severity of the stricture.

Urethral stricture may develop due to various etiological factors, including idiopathic causes, iatrogenic interventions, infections, trauma, and lichen sclerosus [4]. Its prevalence in the general population has been reported to be approximately 0.9% [5]. Treatment options include mechanical dilatation, endoscopic internal urethrotomy (IU), and open urethroplasty. Although mechanical dilatation is one of the oldest treatment modalities, its use has decreased with the advancement of endoscopic techniques, and it is now mainly utilized as an adjunctive method.

Endoscopic internal urethrotomy is a minimally invasive procedure aimed at enlarging the urethral lumen by incising the stricture segment. Due to its ease of application, short learning curve, and feasibility under local anesthesia, it remains one of the most commonly preferred treatment modalities in clinical practice. However, recurrence rates following IU have been reported to range between 20% and 80% in the literature [6]. Particularly after repeated interventions, increased recurrence rates and progression of fibrosis within the stricture segment are major factors limiting the long-term success of this technique. Consequently, unsuccessful endoscopic treatments may necessitate open urethroplasty [4]. However, urethroplasty is not always the first-line option for all patients due to its longer learning curve, higher cost, and limited availability in specialized centers.

Currently, there is no clear consensus on the optimal management of urethral stricture disease. The high recurrence rates observed after internal urethrotomy, which is the most commonly performed procedure, highlight the need to identify predictive factors that may determine disease course and to develop strategies aimed at reducing recurrence. Early

identification of patients at high risk of recurrence is clinically important for selecting the most appropriate treatment modality and avoiding unnecessary repeated interventions.

The aim of this study was to evaluate clinical, demographic, and laboratory parameters that may predict recurrence of urethral stricture following internal urethrotomy, and to investigate the impact of postoperative follow-up and treatment modalities on recurrence.

Methods

Data from patients who underwent more than one internal urethrotomy (IU) with a preliminary diagnosis of urethral stricture between November 2021 and November 2023 at Süleyman Demirel University Faculty of Medicine Hospital were prospectively evaluated. Only patients aged ≥18 years with anterior urethral stricture confirmed intraoperatively were included in the study. Patients with posterior urethral stricture, those who continued follow-up and treatment at another center, those with missing data, those who did not attend routine follow-up visits, those who underwent additional surgical procedures other than IU during the same session, and those with uncontrolled diabetes mellitus, lichen sclerosus, metastatic cancer, or hematological malignancies were excluded. In addition, patients who required further urological surgery such as cystectomy or radical prostatectomy during the follow-up period were also excluded. After applying the exclusion criteria, a total of 154 patients were included in the study.

No additional diagnostic tests or interventions were performed during the study period. Demographic data, height, weight, body mass index (BMI), comorbidities, smoking and alcohol use, clinical and laboratory findings, follow-up duration, and treatment modalities were recorded. Medical records were reviewed to determine the number of previous failed IU procedures and potential etiological factors, including history of transurethral interventions, catheterization, trauma, and idiopathic causes.

Preoperative laboratory parameters obtained within a maximum of 30 days prior to surgery were recorded, including complete blood count parameters, C-reactive protein (CRP), albumin, creatinine, and fasting blood glucose levels. Comorbidity burden was assessed using the Charlson Comorbidity Index (CCI). Patients were also classified individually in terms of diabetes mellitus, hypertension, coronary artery disease, chronic obstructive pulmonary disease/asthma, malignancy, chronic kidney disease, cerebrovascular disease, congestive heart failure, and other comorbid conditions.

Stricture characteristics were evaluated based on hospital information system records and operative notes. Stricture length was categorized as 0–2 cm, 2–4 cm, and >4 cm; the number of strictures was classified as single or multiple. Localization was recorded as bulbar, penile, or penobulbar. Stricture calibration was assessed according to the European Association of Urology (EAU) stricture classification.

The minimum follow-up period was defined as 6 months. Patients were scheduled for follow-up visits at the 3rd and 12th months. During follow-up, patients requiring repeat internal urethrotomy were defined as having recurrence, while those without recurrence were considered as the successful treatment group. Postoperative treatment modalities were also recorded and categorized as medical therapy, intermittent self-dilatation, and follow-up alone.

Statistical analyses were performed using SPSS Statistics version 21. Categorical variables were expressed as number and percentage, while continuous variables were presented as mean ± standard deviation or median (minimum–maximum), as appropriate. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Comparisons between recurrence and non-recurrence groups were performed using appropriate parametric or non-parametric tests for continuous variables, and the Pearson chi-square test for categorical variables. The effect of postoperative treatment modalities on recurrence-free survival was evaluated using Kaplan–Meier analysis. A p-value <0.05 was considered statistically significant.

Ethical approval for the study was obtained from the Clinical Research Ethics Committee of Süleyman Demirel University Faculty of Medicine (decision no: 180, dated 21.09.2023).

Results

A total of 154 patients were included in the study. The mean age was 70.9 ± 10.7 years and the mean body mass index (BMI) was 25.7 ± 3.6 kg/m². A history of smoking was present in 46.8% of the patients, and the mean Charlson Comorbidity Index (CCI) score was 1.87 ± 1.43. The demographic characteristics, comorbidities, and lifestyle factors of the study population are summarized in Table 1.

Table 1. Baseline demographic characteristics, comorbidities, and lifestyle factors of the study population

General characteristics of all patients	**n=154**
Age, years, mean (±SD)	70.9 ± 10.7
Body mass index, kg/m², mean (±SD)	25.7 ± 3.6
Charlson comorbidity index, mean (±SD)	1.87 ± 1.43
Smoking, n (%)	72 (46.8)
Alcohol use, n (%)	16 (10.4)

Regarding stricture characteristics, 64.9% of patients had a stricture length of 0–2 cm, and the majority of strictures were single (83.8%). The most common localization was the bulbar urethra (53.2%). According to the European Association of Urology (EAU) classification, grade 3 strictures were the most frequent (61.0%). The most common etiology was transurethral interventions (62.3%). The mean preoperative pQmax value was

6.57 ± 2.70 mL/s. Detailed stricture characteristics and clinical findings are presented in Table 2.

Table 2. Stricture characteristics and preoperative clinical parameters of the study population

Stricture characteristics	**n (%)**
Stricture length	
0–2 cm	100 (64.9)
2–4 cm	39 (25.3)
>4 cm	15 (9.7)
Number of strictures	
Single	129 (83.8)
Multiple	25 (16.2)
Localization	
Penile urethra	33 (21.4)
Bulbar urethra	82 (53.2)
Penobulbar	39 (25.3)
Stricture calibration (EAU classification)	
Grade 2	6 (3.9)
Grade 3	94 (61.0)
Grade 4	45 (29.2)
Grade 5	9 (5.8)
Etiology	
Post-TUR	96 (62.3)
Idiopathic	33 (21.4)
Radiotherapy	7 (4.5)
Catheter-related	18 (11.7)

During the follow-up period, recurrence was observed in 69 patients (45%). Comparison between patients with and without recurrence showed no significant differences in terms of age, BMI, smoking, alcohol use, or comorbidity burden ($p>0.05$ for all).

However, the number of previous failed internal urethrotomy procedures was significantly higher in patients with recurrence ($p=0.001$). Among preoperative uroflowmetry parameters, pQmax values were significantly lower in the recurrence group ($p=0.018$). Among laboratory parameters, only red cell distribution width (RDW) was significantly associated with recurrence ($p=0.032$).

In terms of stricture characteristics, both stricture length and EAU stricture grade were significantly associated with recurrence (both $p=0.001$). Recurrence rates increased markedly with increasing stricture length. In contrast, no significant association was found

between recurrence and stricture number, localization, or etiology (p>0.05 for all). Comparisons of variables associated with recurrence are presented in Table 3.

Table 3. Comparison of clinical, laboratory, and stricture-related variables between patients with and without recurrence

Variable	No recurrence (n=85)	Recurrence (n=69)	p
Stricture length, n (%)			**0.001**
0–2 cm	66 (66.0)	34 (34.0)	
2–4 cm	15 (38.1)	24 (61.9)	
>4 cm	4 (26.7)	11 (73.3)	
Stricture number, n (%)			0.058
Single	73 (56.6)	56 (43.4)	
Multiple	12 (48.0)	13 (52.0)	
EAU stricture grade, n (%)			**0.001**
Grade 2	6 (100)	0 (0)	
Grade 3	57 (60.6)	37 (39.4)	
Grade 4	18 (40.0)	27 (60.0)	
Grade 5	4 (44.4)	5 (55.6)	
Localization, n (%)			0.075
Penile	17 (51.5)	16 (48.5)	
Bulbar	51 (62.2)	31 (37.8)	
Penobulbar	17 (43.6)	22 (56.4)	
Etiology, n (%)			0.522
Post-TUR	53 (55.2)	43 (44.8)	
Idiopathic	20 (60.6)	13 (39.4)	
Radiotherapy	2 (28.6)	5 (71.4)	
Catheter-related	10 (55.7)	8 (44.3)	
Preoperative pQmax (mL/s)	higher	lower	**0.018**
Voiding time (sec)	NS	NS	0.596
RDW	lower	higher	**0.032**
Previous DVIU number	lower	higher	**0.001**

BMI: body mass index, CCI: Charlson Comorbidity Index, RDW: red cell distribution width, DVIU: direct vision internal urethrotomy

No statistically significant difference was observed between postoperative treatment modalities in terms of recurrence rates (p=0.242). However, Kaplan–Meier analysis demonstrated that patients receiving medical therapy with losartan had a longer recurrence-free survival time.

Table 4. Kaplan–Meier analysis of recurrence-free survival according to postoperative treatment modalities

Treatment group	Median recurrence-free survival (months)	SE	95% CI
Intermittent self-dilatation	8	1.117	9.071–14.923
Medical treatment (losartan)	18	1.493	14.620–18.622
No treatment	14	1.021	13.549–17.926
Overall	15	0.741	14.205–17.108

Discussion

Internal urethrotomy (IU), one of the most commonly used treatment modalities for urethral stricture disease, is widely preferred due to its minimally invasive nature and ease of application. However, the high recurrence rates reported in the literature remain one of the most important factors limiting its long-term success [7–11]. Therefore, identifying predictive factors for recurrence is of great clinical importance.

Among the factors associated with urethral stricture recurrence, stricture length has consistently been reported as one of the strongest predictors. Several studies have demonstrated that longer stricture segments are associated with higher recurrence rates [9,12,13]. Similarly, in our study, recurrence rates increased significantly with increasing stricture length. In particular, the marked increase in recurrence in strictures longer than 2 cm supports the role of stricture length as a critical determinant of treatment success.

The detrimental effect of repeated IU procedures on stricture pathophysiology has also been emphasized in previous studies. It has been shown that with each repeated intervention, the stricture segment tends to lengthen and the fibrotic process extends further [11,14]. In line with the literature, our findings demonstrated that the number of previous failed procedures was significantly associated with recurrence. This suggests that repeated endoscopic interventions may contribute to additional damage in healthy urethral tissue, thereby exacerbating fibrosis.

Stricture calibration also emerged as an important factor associated with recurrence. Higher-grade strictures with narrower luminal diameter have been reported to have higher recurrence rates [9,15]. This finding highlights that not only the length but also the severity of the stricture plays a crucial role in determining treatment outcomes.

The finding that preoperative pQmax values were significantly lower in patients with recurrence suggests that the degree of functional obstruction may also be an important prognostic indicator. Patients with lower urinary flow rates may have more advanced underlying stricture pathology, which could increase the likelihood of recurrence following treatment.

From a laboratory perspective, RDW was identified as a significant predictor of recurrence in our study. RDW has been associated with systemic inflammation and impaired tissue

healing processes [16–18]. Therefore, elevated RDW levels may reflect chronic inflammation and an altered healing response, potentially contributing to stricture recurrence. Given the limited number of studies evaluating the relationship between RDW and urethral stricture recurrence, this finding appears to be particularly noteworthy.

In contrast, no significant association was observed between recurrence and age, body mass index, smoking, alcohol use, or comorbid conditions. The literature reports conflicting results regarding these factors. While some studies have identified advanced age and higher comorbidity burden as risk factors for recurrence, others have failed to demonstrate a significant relationship [10,19–21]. These discrepancies may be explained by differences in patient populations and study designs.

The impact of postoperative treatment modalities on recurrence remains controversial. Intermittent dilatation has been suggested to delay recurrence by mechanically maintaining urethral patency [22,23]. However, in our study, no significant difference was observed between postoperative treatment modalities in terms of recurrence rates. Nevertheless, the longer recurrence-free survival observed in patients receiving losartan is a notable finding. This may suggest that angiotensin receptor blockers, known for their antifibrotic properties, could potentially slow stricture progression.

Limitations

This study has several limitations. First, its single-center design and relatively limited sample size may restrict the generalizability of the findings. In addition, the relatively short minimum follow-up period may have limited the evaluation of late recurrences.

Although the study was prospectively designed, no intervention was made in the treatment or follow-up processes of the patients, which resulted in heterogeneity among postoperative treatment modalities. This may have made it more difficult to clearly determine the effect of different treatment strategies on recurrence.

Furthermore, recurrence was defined based on the need for repeat surgical intervention. Therefore, patients with symptomatic recurrence who did not yet require surgical treatment may have been overlooked. Some patients may have considered their current voiding patterns acceptable and may not have sought further treatment despite recurrence.

Finally, the lack of routine use of invasive diagnostic methods (such as retrograde urethrography or endoscopic evaluation) in all patients may have limited the objective detection of recurrence. However, applying these evaluations to all patients would not be practical due to their invasive nature and associated costs.

Conclusions

According to our findings, stricture length, stricture calibration, the number of previous failed internal urethrotomy procedures, and preoperative pQmax value emerged as

significant predictive factors for urethral stricture recurrence. In addition, the association between RDW levels and recurrence supports the potential role of inflammation in the pathophysiology of urethral stricture.

Although internal urethrotomy is an effective treatment modality in appropriately selected patients, repeated interventions may increase the risk of recurrence and negatively affect stricture complexity. Therefore, early identification of patients at high risk of recurrence is essential, and alternative treatment options, particularly reconstructive surgery, should be considered at an earlier stage in these patients.

While no significant difference was observed between postoperative treatment modalities in terms of recurrence rates, certain medical therapies may prolong recurrence-free intervals. These findings highlight the importance of individualized treatment strategies in the management of urethral stricture disease.

No conflicts of interest were declared by the authors.

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