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: The objective of this study was to investigate the disease course after direct vision internal urethrotomy (DVIU) for short anterior urethral strictures.

Methods: We retrospectively analyzed 94 patients who underwent DVIU of the anterior urethra. Patients' age, etiology, length and localization of the strictures, total number of DVIU procedures, comorbidities, and other data were evaluated.

Results: The mean age of the patients was 67.2 years. The mean followup duration was 27.1 months. Recurrence was observed in 27.6% of the patients. Recurrence had occurred in these patients at a mean of 12 months. Both the comorbidity score (rs=0.395; p<0.001) and the urinary tract infection (UTI) score (rs=0.492; p<0.001) had significant correlation with the recurrence. In patients with recurrent urethral stricture, as the number of DVIU increased, the length and number of the urethral stricture increased as well. Patients with recurrence had a single stricture in the first DVIU procedure, while the number of strictures increased to a mean of two in the second and/or third DVIU procedures.

Conclusions: DVIU is an effective treatment method in short anterior urethral stricture if it has been applied as a first intervention. However, if the stricture recurs, repeated DVIU application appears to be a negative predictive factor. The presence of perioperative treated UTI, smoking, and total number of comorbidities were negative predictive factors for the recurrence of urethral stricture. The disadvantages of our study are that it is retrospective, it includes a low number of patients, and the followup period is short.

Introduction

Although urethral stricture is one of the longest recognized urological diseases, its management is still challenging. The most important reason for this is the high recurrence rate of stricture despite various modern treatment modalities.

The incidence and epidemiology of urethral strictures vary according to age, race, gender, geographical location, and socioeconomic status.[1] The simplest definition of the urethral stricture is narrowing of the urethral lumen with scar tissue. Obstructive voiding symptoms occur in relation to the severity of this constriction. Urethral stricture is not only a pathology affecting patients' quality of life, but it is also associated with life-threatening conditions (urethral abscess, necrotizing fasciitis, kidney failure, etc.) in approximately 7% of patients.[2] All treatment options in cases with urethral stricture aim to keep the urethral lumen open as long as possible. Currently, direct vision internal urethrotomy (DVIU) and urethroplasty are the main treatment options for urethral stricture.[3] Additonal treatment modalities in select patients incude urethral dilatation and urethral stenting. Treatment method is selected according to the general condition of the patient and the characteristics of the stricture.[4,5] The generally accepted approach is to perform DVIU in short urethral strictures and urethroplasty in long and frequently recurring strictures.[3] However, most urologists prefer DVIU as the first-line treatment option for all urethral strictures,[6,7] as DVIU is associated with a shorter hospital stay, lower cost, early mobilization of the patient, shorter urethral catheterization duration, and better early outcomes. In fact, short-term success rates are high in all treatment options;[8] however, due to recurrent stricture development, long-term treatment success rates are lower and repetitive treatment interventions are required.[8-11]

Identification of patients who are prone to recurrent urethral stricture development or those at risk for recurrence is an important issue in the management of urethral stricture. Defining the risk factors will help prevent the onset or progression of the processes that cause strictures.

In this study, we aimed to investigate the course of the disease in patients with primary anterior urethral stricture of less than 1 cm under classical treatment and followup period. We also evaluated the potential predictive factors of recurrence in patients with recurrent urethral stricture.

Methods

The data of 674 patients who had undergone DVIU between July 2012 and July 2017 in our department were retrospectively evaluated. The patients whose current data were missing and those who were not followed up by us or continued the treatment process in another center were excluded from the study. Patients with a history of previous urethroplasty operation, with strictures longer than 1 cm, those with posterior urethral stricture, and those with less than one year of followup were excluded from the study. After expulsion of patients having any of the exclusion criteria, a total of 94 male patients were enrolled in the study. Uroflowmetry and retrograde urethrography (RUG) were carried out on patients with clinical findings consistent with urethral stricture. Urine samples were obtained for culture from all patients scheduled for DVIU. Surgical treatment was performed on patients without urinary tract infection (UTI). Antibiotic prophylaxis was administered to the patients with a single dose of ceftriaxone 1 g. DVIU was applied using a 21 Fr Storz urethrotome under general anesthesia with a cold knife incision at the 12 o'clock line. After the DVIU operation, 16–18 Fr urethral catheters were inserted in all patients and removed on the third to fifth day postoperatively. The duration of urinary catheter stay was determined by the number and length of the stricture, as well as the surgeon's preference. Periodic urethral dilatation was performed according to the individual features of the patient, characteristics of the stricture, and surgeon preference. Patients were routinely checked at the end of the first week and third month after removal of the urinary catheter. Patients who had no recurrence of stricture were called for control visits annually. Urine culture, uroflowmetry, and RUG (if necessary) were performed at each control visit. Data regarding the patients' age, etiology, length, and localization of the stricture, total DVIU count, urinary catheterization duration, results of preoperative and postoperative urine cultures, postoperative urethral dilatation application, concomitant diseases, body mass index (BMI), and smoking status were noted. The Charlson comorbidity index (CCI) was used for the definition and grading of comorbidities. The patients were divided into two groups: those who had undergone DVIU only once without any recurrence, and those who had undergone multiple DVIUs.

Patients with a history of multiple DVIUs were further evaluated in terms of urethral stricture characteristics.

Statistical analysis

Due to the fact that the parametric test assumptions were not provided as descriptive statistics in the study, the numerical variables are given as median (minimum–maximum) and the categorical data are given as frequency (n) and percentage (%). Any difference between the recurring and non-recurring groups in terms of numerical variables was analyzed using the Mann-Whinty U-test, since the parametric test assumptions were not provided; the difference between the repetition times in terms of numerical variables was analyzed using the Wilcoxon test. The effect of categorical variables on recurrence was tested between the groups using the Pearson Chi-square test or Fisher's exact test, as appropriate. The relationship between the number of recurrences and the numerical variables was examined by the Spearman's rank correlation coefficient. For all tests, the type I error probability was determined as α=0.05.

Results

The median age of the patients was 67.2 years. The median followup duration was 27.1 months. The most common etiological factor was iatrogenic causes (84%). All of the strictures were in the anterior urethra and shorter than 1 cm in length. The majority (54.4%) of patients included in the study had at least one accompanying disease. The mean CCI of the participants was 1.4. General patient characteristics are shown in Table 1.

Recurrence of the urethral stricture was observed in 26 patients (27.6%). DVIU was performed twice in 26 patients, three times in 12 patients, and four times in five patients. Recurrence occurred in these patients at a mean of 12 months (range 2–19). Periodic urethral dilatation was applied to 31 patients. Recurrence was observed in 41.9% of the patients who underwent dilatation. We isolated bacteria from the perioperative urine culture of 23 patients. Recurrent stricture was observed in 65.2% of these patients. There was a statistically

Table 1. General characteristics of whole study population patients

General characteristics of all patients		n=94
Age, years, median (range)		67.2 (26–86)
Etiology, n (%)	Iatrogenic	79 (84.04)
	Infectious	13 (13.82)
	Idiopathic	2 (2.12)
Localization, n (%)	Penile urethra	39 (41.48)
	Bulbar urethra	55 (58.51)
Periodical dilatation		31 (32.9)
Postoperative infection, n (%)		23 (24.46)
Smoking, n (%)		20 (21.27)
Body mass index, n (%)	<25 kg/m^2	39 (41.5)
	≥25 kg/m^2	55 (58.5)
Comorbidity, n (%)	Diabetes mellitus	9 (9.57)
	Hypertension	33 (35.10)
	Coronary artery disease	21 (22.34)
Charlson comorbidity index, median (range)		1.40 (0–8)
Followup duration (months), median (range)		27.1 (12–58)
Recurrence period (months), median (range)		12.07 (2–19)

significant moderate relation between the number of recurrences and the presence of UTI (rs=0.492; p<0.001).

When the patients included in the study were evaluated as those who experienced recurrence and those who did not, there was no significant difference in the etiology, localization of stricture, and followup duration (p>0.05 for all). Diabetes, hypertension, BMI, and smoking were not significantly related to the recurrence. A history of coronary artery disease (CAD) was found to be 13.3% in patients without recurrence and 46.2% in patients with recurrence; there was a statistically significant moderate relation between the recurrence number and CAD (rs=0.404; p<0.001). There was a weak but statistically significant relationship between the number of recurrences and smoking habit (rs=0.265; p=0.01). When the CCI of the patients was evaluated, there was a weak but statistically significant relation between the comorbidity score and stricture recurrence (rs=0.395; p<0.001), that is, more frequent recurrence was observed in patients with higher CCI (Fig. 1). The comparative data of the patients who had recurrent disease and those who did not are shown in Table 2.

There was a significant difference between DVIU surgeries in regards to the length of the stricture (p<0.001); in particular, there was a significant difference between the first and second DVIU in terms of stricture length in these patients. Similarly, there was also a significant difference in the stricture length between the second and the third DVIU, whereas there was no difference between the subseqent DVIU procedures (Table 3). There was an increase in the stricture length with the increase in the number of DVIUs (Fig. 2). In addition, there was a significant difference between the recurrences in terms of the number of strictures.

As the number of recurrences increased, the number of strictures also increased. According to our results, patients with recurrence had a single stricture in the first DVIU procedure, while the number of strictures increased to a mean of two in the second and/or third DVIU procedures (Table 4).

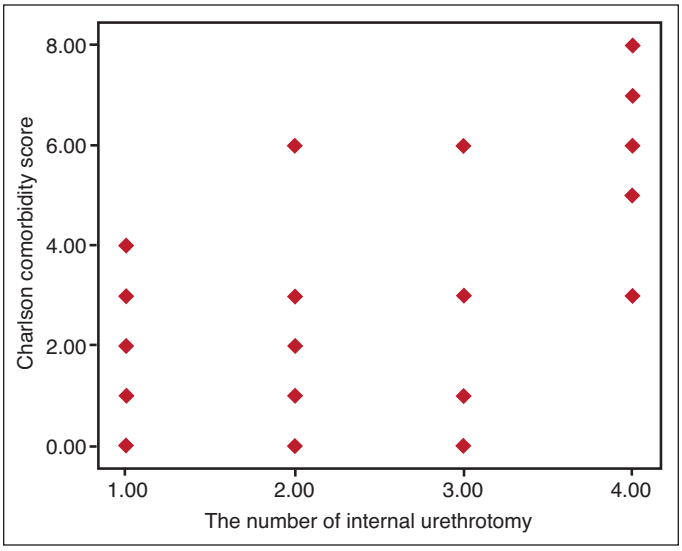

Fig. 1. The patients with a higher Charlson comorbidity index score were more likely to experience stricture recurrence.

Discussion

Strong risk factors have been identified in previous studies examining predictive risk factors for the recurrence of urethral strictures. One of them is stricture length.[12,13] A positive correlation between recurrence and length of stricture has been previously shown.[14] Steenkamp et al found that every 1 cm increase in stricture length increased the risk of recurrence 1.22-fold.[13] Pansadoro et al also reported a higher rate of recurrence in strictures longer than 1 cm. In their study, the success rate of DVIU procedure was 71% for strictures shorter than 1 cm and 18% for longer strictures.[15]

In our study, there was a linear relationship between the length of the stricture and the number of repeat DVIU procedures. We found that the mean length of the stricture increased after the first three DVIU interventions. This suggests that healthy urethral tissue at the neighboring stricture is injured during DVIU and that the fibrotic process extents to these regions. It is noteworthy that the number of strictures doubled after repeated DVIUs; this may indicate that these patients are prone to poor wound healing in the urethral

Table 2. Comparison of the clinical data between the recurrent and non-recurrent groups

		Non-recurrent group n=68	Recurrent group n=26	p
Age, years, median (range)		69.5 (26–86)	69.5 (42–84)	0.872[a]
Etiology, n (%)	Iatrogenic	55 (69.6%)	24 (30.4%)	0.453[b]
	Infectious	11 (84.6%)	2 (15.4%)	
	Idiopathic	2 (100%)	0	
Localization, n (%)	Penile urethra	26 (66.7%)	13 (33.3%)	0.300[c]
	Bulbar urethra	42 (76.4%)	13 (23.6%)	
Length (mm), median (range)		5(3–8)	5 (3–8)	0.451[a]
DVIU number		1	2–4	—
Periodical dilatation		18 (26.5%)	13 (50.0%)	0.030 [c]
Perioperative infection, n (%)		8 (34.8%)	15 (65.2%)	<0.001[c]
Smoking, n (%)		11 (55.0%)	9 (45.0%)	0.051[c]
Body mass index, n (%)	<25 kg/m²	32 (82.1%)	7 (17.9%)	0.076[c]
	≥25 kg/m²	36 (65.5%)	19 (34.5%)	
Comorbidity, n (%)	Diabetes mellitus	5 (55.6%)	4 (44.4%)	0.256[b]
	Hypertension	23 (69.7%)	10 (30.3%)	0.673[c]
	Coronary artery disease	9 (42.9%)	12 (57.1%)	0.001[c]
Charlson comorbidity index, median (range)		0 (0–4)	2 (0–8)	<0.001[a]
Followup duration (months), median (range)		24 (12–52)	25.5 (12–54)	0.198[a]

[a]Mann-Whitney U-test; [b]Fisher's exact test; [c]Pearson Chi-square test. DVIU: direct vision internal urethrotomy.

Table 3. Comparison of the stricture lengths between repetitive direct vision internal urethrotomies

	Length of the stricture (mm)		p[1]
	Preoperative median (range)	Postoperative median (range)	
1st DVIU–2nd DVIU	5 (3–8)	10 (5–30)	<0.001
1st DVIU–3rd DVIU	5 (3–8)	20 (5–50)	0.003
1st DVIU–4th DVIU	5 (3–8)	35 (10–50)	0.043
2nd DVIU–3rd DVIU	10 (5–30)	20 (5–50)	0.017
2nd DVIU–4th DVIU	10 (5–30)	35 (10–50)	0.068
3rd DVIU–4th DVIU	20 (5–50)	35 (10–50)	0.655

[1]Wilcoxon test; Bonferroni correction α^*=0.008. DIVU: direct vision internal urethrotomy.

tissues. Repetitive trauma to the healthy tissue of the urethra during instrumentation or due to effects of the inserted foley catheter can be a cause. A significant increase in the length and the number of the strictures after repeated DVIUs makes the stricture more complex. This complicates the reconstructive urethral surgery and decreases the success rate.[16]

It has also been suggested that DVIU performed for the treatment of urethral stricture may be a negative predictive factor in the case of stricture recurrence. Santucci et al found that the success rate was not higher than 9% after repeated DVIUs in their series comprising 76 patients.[17] Moreover, they stated that the success rate had approached 0% at the end of the long-term followup of DVIU procedures performed in any number (one to five times). In this context, the authors emphasized that DVIU was a temporary measure before the curative reconstructive treatment. This is a critical conclusion in the management of patients with recurrence after first DVIU procedure.

In our study, recurrence of the urethral stricture was detected in 27.6% of the patients, with 72.4% of our patients having undergone DVIU procedure only once, thus showing DVIU has significant success rates in short urethral strictures. It is important ot note that periodic dilatation was applied to 26.5% of these patients. The effect of urethral dilatation on recurrence of stricture is not yet clear;[18,19] however, it is thought that it ensures the patency of the urethra lumen through a mechanical effect and delays the recurrence of the stricture or prolongs the DVIU intervals.

Many previous studies have reported that recurrent strictures develop in about half of patients in the first year after a DVIU procedure.[13,14,20,21] In our study, the mean followup period was 27.1 months and 54% of the patients with recurrent stricture had experienced recurrence in the first year. The role of urinary bacteria in the pathogenesis of urethral stricture is not clear; however, it is thought to have unfavorable effects on wound healing by causing inflammation.[19] In particular, the presence of perioperative infection in urethroplasty operations was found to be a negative predictive factor.[22] According to our results, there was a significant relationship between UTI and the number of stricture recurrence

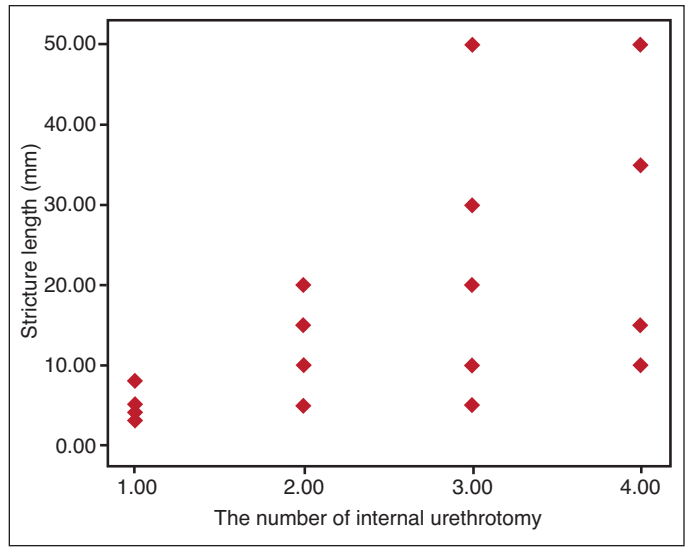

Fig. 2. The length of the stricture increases as the number of direct vision internal urethrotomy procedures increase in patients with recurrent urethral stricture.

(rs=0.492; p<0.001). Urethral stricture recurred in 65.2% of patients with perioperative UTI. Perioperative UTI was determined in more than half of the patients after each repeated DVIU, which suggests UTI is a negative predictive factor for stricture recurrence.

In some previous publications, advanced patient age was reported as another risk factor for recurrence of urethral stricture.[23] However, in our study, there was no relationship between the recurrence and patient age. Our results also showed no significant difference between the recurrent and non-recurrent patients in terms of diabetes, hypertension, BMI, and smoking. However, there was a statistically significant weak relationship between the number of recurrences and smoking. Furthermore, CAD was approximately three times more frequent in patients with recurrence. Although previous studies have not revealed the relationship between urethral strictures and smoking or CAD,[24,25] it is known that ischemia negatively affects wound healing and plays a role in the pathogenesis of stricture by impairment of urethral tissue perfusion.[19]

Table 4. Comparison of the number of strictures between repeated direct vision internal urethrotomies

	Number of the urethral strictures, n		p[1]
	Preoperative median (range)	Postoperative median (range)	
1st DVIU–2nd DVIU	1 (1–1)	1 (1–2)	0.046
1st DVIU–3rd DVIU	1 (1–1)	1.5 (1–2)	0.014
1st DVIU–4th DVIU	1 (1–1)	2 (1–2)	0.083
2nd DVIU–3rd DVIU	1 (1–2)	1.5 (1–2)	0.083
2nd DVIU–4th DVIU	1 (1–2)	2 (1–2)	0.317
3rd DVIU–4th DVIU	1.5 (1–2)	2 (1–2)	0.317

[1]Wilcoxon test; Bonferroni correction α^*=0.008. DIVU: direct vision internal urethrotomy.

The relationship between total comorbidity and urethral stricture recurrence in our study was remarkable. As the CCI increased, the risk of stricture recurrence also increased. Similarly, Chapman et al reported a higher frequency of recurrence in patients with high comorbidities in their large-series study evaluating the results of urethroplasty.[22] In the same study, although they could not detect any link between stricture recurrence and smoking or diabetes, investigators reported that obesity was a risk factor for recurrence. Harranz et al reported that patient age and obesity were independent risk factors for recurrence of strictures.[23] Taken together, thse studies suggest clinicians need to be more cautious in the management of urethral stricture patients with multiple comorbidities.

Limitations

The disadvantages of our study include its retrospective design, the low number of patients, and the short followup period. In addition, some patients did not obtain additional medical/surgical treatment, although they had obstructive voiding patterns. They may have considered the current urine flow rates sufficient and despite recurrence of the urethral stricture, may not have sougt treatment until they suffered from severe obstructive voiding. Furthermore, we could not estimate to what extent the urethral dilatation, applied to approximately 26% of our patients, affected our results. Finally, it was difficult to ensure patients who were considered "non-recurrent" did not actually have recurrent urethral stricture. To guarantee this, all patients would have had to undergo RUG and endoscopic evaluation, which would have been an extra-invasive and cost-prohibitive exercise.

Conclusions

According to our findings, the presence of perioperative UTI, smoking, CAD, and having an increased number of comorbidities are negative predictive factors for the recurrence of urethral stricture. DVIU is an effective and successful method in short anterior urethral stricture if it succeeds at the first application. However, if the stricture recurs, repetitive DVIU procedures have unfavorable effects on the length and number of urethral strictures. Reconstructive surgery options should be planned earlier in such patients.

Competing interests: The authors report no competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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