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.
Conclusion: 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 is 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 oldest diseases of urology, its management is still challenging. The most important reason for this is the high recurrence rates of stricture despite various modern treatment modalities. The incidence and epidemiology of urethral strictures vary according to age, race, gender, geographical location and the 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 operations are the main treatment options of urethral stricture.[3] Urethral dilatation and urethral stenting are other preferred treatment modalities in selected patients. Each treatment method is preferred according to the general condition of the patient and the characteristics of the urethral stricture.[4,5] The generally accepted approach is to perform DVIU in short urethral strictures and to prefer urethroplasty in long and frequently recurring strictures.[3] However, most of the urologists prefer DVIU as the first line treatment option for all urethral strictures.[6,7] The most important reasons for this are that 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, the short-term success rates are high in all treatment options.[8] However, due to recurrent stricture development, long-term treatment success rates reduce 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 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 follow-up 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 not included in the study. Patients with a history of previous urethroplasty operation, patients with strictures longer than 1 cm, those with posterior urethral stricture and those with less than 1 year of follow-up period were excluded from the study. Follow-up evaluations of the patients included in the study were made according to the time of the last clinical visit. Phone calls were made to patients who had no clinical visit in the last 3 months. In this interview, patients were asked whether the stricture had been repeated. The patients who were continued the treatment process in another center were not included in the study. After the

expulsion of patients having any 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. Antibiotic prophylaxis was administered to the patients with a single dose of 1 g ceftriaxone. 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 3rd to5th day postoperatively. The duration of urinary catheter stay was determined according to the number and length of the stricture, and the surgeon's preference. Periodic urethral dilatation was performed according to the individual features of the patients, characteristics of the stricture and the surgeon's preference. Patients were routinely checked at the end of the first week and 3rd month after the urinary catheter was removed. Patients who had no recurrence of stricture were called for control visits annually. Urine culture, uroflowmetry and RUG (if necessary) were performed on each control visit. Data regarding the patient's age, etiology, length, and localization of the stricture, total DVIU count, urinary catheterization duration, the 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 as the patients who had undergone DVIU only once without any recurrence, and those who had undergone multiple DVIU. The findings of the study groups have been presented in Table 2. In addition, patients with history of multiple DVIU were evaluated among themselves 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 recurrent 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 recurrence and the numerical variables was examined by the Spearman's Rank Correlation Coefficient. For all tests, the Type I error probability was determined as $\alpha = 0.05$.

Results

The median age of 94 patients was 67.2 years. The median follow-up 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. 54 (54.4%) of the patients included in the study had at least one accompanying disease. The mean CGI score of

the participants was 1.4 points. The general characteristics of the patients have been displayed in Table 1.

Recurrence of the urethral stricture was observed in 26 patients (27.6%). DVIU was performed twice in 26 patients, 3 times in 12 patients and 4 times in five patients. Recurrence had occurred in these patients at a mean of 12th month (at the 2nd month in the earliest case and at the 19th month in the latest one). Periodic urethral dilatation was applied to 31 patients. Recurrence was observed in 41.9% of the patients who had undergone dilatation. The isolated bacteria from the perioperative urine culture of 23 patients. Recurrent stricture was observed in 65.2% of these patients. There was a statistically significant moderate relation between the number of recurrences and the presence of urinary infection ($r_s = 0.492$, $p < 0.001$).

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 the follow-up duration between these two groups ($p > 0.05$, for all). Diabetes, hypertension, BMI and smoking were not significantly related to the recurrence. The 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 ($r_s=0.404$, $p<0.001$). There was a weak but statistically significant relationship between the number of recurrence and smoking habit ($r_s=0.265$, $p=0.01$). When the CCI score of the patients was evaluated, there was a weak but statistically significant relation between the comorbidity score and stricture recurrence ($r_s = 0.395$, $p < 0.001$). There was more frequent recurrence observed in patients with higher comorbidity score (Chart 1). The comparative data of the patients who had recurrent disease and who did not, have been presented in Table 2.

There was a significant difference between the DVIU surgeries regarding the length of the stricture ($p < 0.001$). 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 following repetitions of the DVIU procedure (Table 3). There was an increase in the stricture length with the increase in the number of DVIU procedure (Graph 2). In addition, there was a significant difference between the recurrences in terms of the number of strictures.

As the number of recurrence increased, the number of strictures also increased. According to the results, patients with recurrence had a single stricture in the first DVIU procedure, while the number of strictures increased to a mean of 2 in the second and / or third DVIU procedures (Table 4).

Discussion

Some risk factors have been striking in previous studies examining the predictive risk factors for the recurrence of urethral strictures. One of them is the length of the stricture.[12,13] A positive correlation between the recurrence and the length of strictures has been shown previously.[14] The stricture length is a negative predictive factor for recurrence. Steenkamp et

al. have found that every 1 cm increase in the stricture length increased the risk of recurrence by 1.22 fold.[13] Pansadoro et al. reported a higher rate of recurrence in the strictures longer than 1 cm in length. 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 repetition number of DVIU procedure. 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 tissues. At this point, repetitive trauma to the healthy tissue of the urethra during instrumentation or due to effects of the inserted foley catheter can be blamed. 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] On the other hand, it is also 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 follow-up of DVIU procedures performed in any number (once-to-5 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 the first DVIU procedure.

In our study, recurrence of the urethral stricture was detected in 27.6% of the patients. Another remarkable point of our results was that 72.4% of the patients included in our study had undergone DVIU procedure only once. This shows that DVIU has significant success rates in short urethral strictures. Periodic dilatation was applied to 26.5% of these patients. The effect of urethral dilatation on recurrence of stricture is not clear yet.[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 DGIU intervals. In many previous studies, it has been reported that recurrent strictures develop in about half of the patients in the first year after the DVIU procedure.[13,14,20,21]

In our study, the mean follow-up period was 27.1 months and 54% of the patients with recurrent stricture had experienced the 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 urinary infection and the number of stricture recurrence ($rs = 0.492$, $p < 0.001$). There was urethral stricture recurrence in 65.2% of the patients with perioperative urinary tract infection. Perioperative urinary tract infection was determined in more than half of the patients after each repeated DVIU, which suggests that urinary tract infection 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. In our results, there was also no significant difference between the recurrent and non-recurrent patients in terms of DM, HT, BMI and smoking. However, there was a statistically significant weak relationship between the number of recurrence and smoking. Besides, CAD was approximately 3 times more frequent in patients with recurrence. This suggests that factors that may cause ischemia may also adversely affect the wound healing in the urethral tissue. Previous studies have not revealed the relation of smoking and CAD with urethral strictures.[24,25] However, 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] Moreover, the relationship between total comorbidity and urethral stricture recurrence in our study was remarkable. As the CCI score increased, the risk of stricture recurrence also increased. This warns clinicians to be more careful in the management of urethral stricture patients with multiple comorbidities. 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, they could not detect any relation between stricture recurrence and both smoking and DM. They 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]

Limitations

The disadvantages of our study include retrospective design, low number of patients and short follow-up period. In addition, some patients did not need additional medical/surgical treatment although they had obstructive voiding patterns. They considered the current urine flow rates as sufficient. Despite the recurrence of the urethral stricture, they do not search for treatment before they suffer from severe obstructive voiding. We could not estimate to what extent the urethral dilatation affected our results, which was applied to approximately 26% of our patients. It is difficult to ensure that patients who were considered as 'non-recurrent' did not actually have recurred urethral stricture. To ensure this, all patients should have undergone retrograde urethrography and endoscopic evaluation, but this would be an extra invasive and cost-increasing application. On the other hand, the individual characteristics of each patient and the lack of a homogeneous study population made it difficult to have an objective conclusion.

Conclusion

According to our findings, the presence of perioperative urinary tract infection, smoking, CAD, and having increased number of co-morbidities 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 effect on the length and number of urethral strictures. Reconstructive surgery options should be planned earlier in such patients.

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Figures and Tables

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

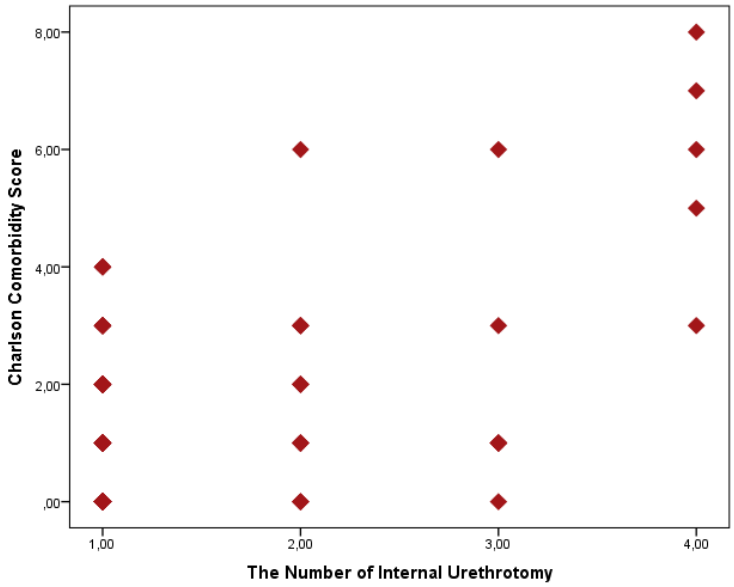

Fig. 2. The length of the stricture increases as the number of direct vision internal urethrotomy procedures increase in patients with recurrent urethral stricture.

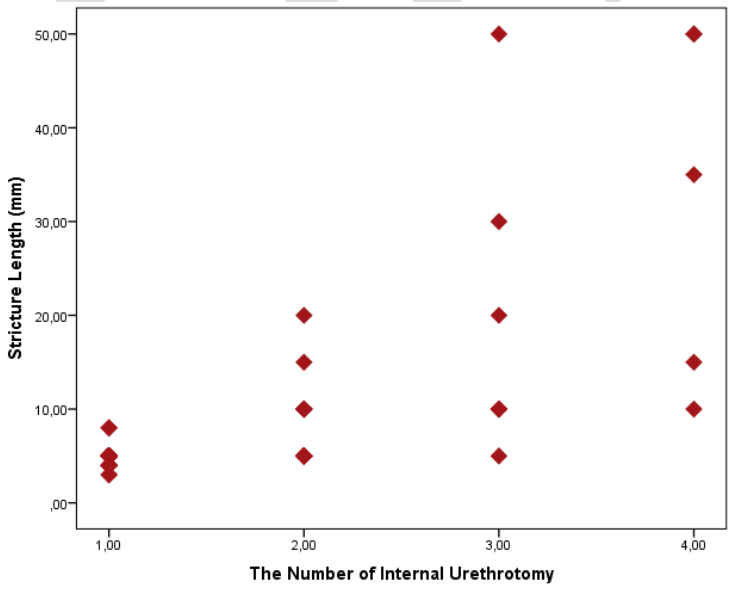

Table 1. General characteristics of whole study population patients		
General characteristics of all patients		**n=94**
Age, years, median (range)		67.2 (26–86)
Etiology, n (%)	Iatrogenic	79 (84.04)
	Infectious	13 (13.82)
	Idiopathic	2 (2.12)
Localization, n (%)	Penil urethra	39 (41.48)
	Bulbar urethra	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)

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/m^2	32 (82.1%)	7 (17.9%)	0.076[c]
	≥25 kg/m^2	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.

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.