

Parameters predicting the number of recurrences, strictural length and localization in urethral strictures

Üretra darlıklarında nüks sayısı, darlık uzunluğu ve lokalizasyonu öngören parametreler

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Abstract

Purpose: In addition to the known etiological and predisposing factors of urethral stricture, we aimed to examine unknown and not clearly defined factors.

Materials and methods: Medical records of 317 patients who underwent visual internal urethrotome (VIU) surgery in our clinic between 2017 and 2022 were retrospectively reviewed. The parameters affecting the total number of VIU operations were investigated. In addition, the factors affecting the total length and localization of the stricture were investigated.

Results: The presence of history of endourological surgery and history of cardiovascular disease were independently associated with a higher number of VIU operations ($p<0.05$). The age was independently associated with a longer total segment of urethral stricture ($p<0.05$). The history of previous endourological intervention or the presence of cardiovascular disease are significantly increased the rate of distally localized strictures ($p<0.05$).

Conclusion: Endourological interventions and urethral catheter procedures should be avoided as much as possible for people with cardiovascular disease. It will be a useful approach to investigate the status of cardiovascular disease of patients with anterior urethral stricture, as it is done in erectile dysfunction.

Key words: Urethral stricture, visual internal urethrotome, cardiovascular arrest, coronary artery bypass.

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Öz

Amaç: Bu çalışmada üretral darlıkların bilinen etiyolojik ve predispozan faktörlerine ek olarak, bilinmeyen ve net olarak tanımlanmamış faktörler incelendi.

Gereç ve yöntem: Merkezimizde 2017-2022 yılları arasında Vizüel internal üretrotom (VIU) operasyonu geçiren 317 hastanın tıbbi kayıtları geriye dönük olarak incelendi. Total VIU operasyon sayısı üzerinde etkili olan parametreler araştırıldı. Ek olarak total dar segment uzunluğu ve darlık lokalizasyonuna etki eden faktörler araştırıldı.

Bulgular: Geçirilmiş endoürolojik cerrahi öyküsü ve kardiyovasküler hastalık öyküsünün, daha fazla VIU operasyonu sayısı ile ilişkili olduğu görüldü ($p<0,05$). Yaş, daha uzun total üretral darlık segmentiyle ilişkiliydi ($p<0,05$). Daha önce geçirilmiş endoürolojik müdahale öyküsü ve kardiyovasküler hastalık hikâyesi, darlığın daha distalde olma oranını istatistiksel anlamlı şekilde arttırmaktaydı ($p<0,05$).

Sonuç: Kardiyovasküler hastalık hikâyesi olan kişilerde endoürolojik girişim ve üretral kateter yerleştirilmesi işlemlerinden mümkün olduğunca kaçınılmalıdır. Erektile disfonksiyon hastalarında yapıldığı gibi, anterior üretral darlığı olan hastalarda da kardiyovasküler hastalık araştırmasının yapılması faydalı bir yaklaşım olacaktır.

Anahtar kelimeler: Üretral striktür, vizüel internal üretrotomi, kardiyovasküler arrest, koroner arter bypass.

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Introduction

Urethral stricture is a disease that can develop throughout the entire male urethra and has many etiologies. Overall, its incidence is estimated to be 229-627 per 100,000 men [1]. This disease, which is common and frequently recurring worldwide, seriously affects human health and can significantly reduce the quality of life [2]. Urethral stricture, which has many etiologies, imposes serious burdens on the health system and patients [3]. A thorough understanding of the etiology and pathophysiology of urethral stricture may play an active role in preventing this disease and finding new treatment methods. Many predisposing factors related to urethral stricture have been reported in the guidelines of European Association of Urology and American Urological Association [4, 5]. The most common etiology is iatrogenic causes, however idiopathic strictures still constitute a substantial portion of 34% [6]. Based on these informations, it can be concluded that there are still many unknown factors about the etiology of urethral stricture. Mundy and Andrich [7] reported that one of the possible causes of idiopathic urethral strictures in elderly patients may be urethral ischemia, in a review. Yildiz et al. [8] reported that the severity of coronary artery disease is an independent predictive factor in the occurrence of urethral stricture, in a study which they compared patients with and without urethral stricture after urethral catheterization. In this study, we aimed to investigate also the not yet clearly defined etiological factors such as cardiovascular arrest, bypass and patient's age, in addition to well defined etiological and predisposing factors of urethral stricture. New informations related to these factors will be scientifically valuable due to they have the potential to provide a new and different approach to this disease in the literature and guidelines. Our study is one of the limited number of studies examining these new potential etiological factors.

Material and methods

After the ethical approval from local institute's committee on human research obtained on 28.03.2022, medical records of 381 patients who underwent internal urethrotome (VIU) surgery in our clinic between 2017 and 2022 were reviewed retrospectively. All the patients were underwent VIU operation due to urethral stricture disease which had diagnosed

with uroflowmetry and cystourethroscopy. A 20 Fr urethral catheter was inserted after the procedure to all patients. The durations of catheterizations were determined according to the surgeon's foresight. All patients who had a second VIU operation were offered to the option of open urethroplasty operation. Patients who accepted open urethroplasty were excluded the study. Patients younger than 18 years old, with congenital urethral/penile anatomical anomalies (Hipospadias, Epispadias, Posterior urethral valve exc.) or who were operated for these reasons (TIPU, Magpi, Other urethroplasties exc.), with Balanitis xerotica obliterans or lichen sclerosus et atrophicus of the penis, with previous pelvic fracture and postradiation urethral strictures were excluded from the study. Patients older than 18 years, who had undergone VIU surgery and had congenital normal urethral anatomy were included in the study. Patients who wanted to continue their treatment with VIU operation and did not accept urethroplasty after second VIU were included in the study. A total of 381 patients' data were obtained and 317 patients, who met the study criteria were included in the study. Informed consent was obtained from all patients included in the study. The patients' age, number of total VIU operations, history of previous endourological intervention, history of cardiovascular disease, history of cardiovascular arrest/bypass, length of the total strictural segment and stricture localization (Anterior or Posterior urethra) were recorded. Patients who had previously undergone any type of transurethral resection (TUR), cystoscopy, ureterorenoscopy (URS) or percutaneous nephrolithotomy (PNL) surgery were considered as patients with endourological intervention. Patients with chronic hypertension, coronary artery disease affecting cardiac function, previous myocardial ischemia, cardiac arrhythmia, cardiomegaly, chronic heart failure, cardiac thrombus, low ejection fraction, chronic valve diseases, aortic aneurysm and varicose diseases were considered as patients with cardiovascular disease. Cold knife visual internal urethrotomy technique was applied to all patients at 12 o'clock position. The length of the urethral stricture was measured by calculating the ratio of the stricted segments' length to the cold knife length, after the stricture/strictures was incised with the urethrotome. In patients with more than one urethral stricture, the stricture length was calculated as the sum

of the length of all stricture segments. The effect of other parameters on the total number of VIU operations performed on the patients was investigated. In addition, the factors affecting the stricture length and localization were investigated.

The statistical analysis of the data was performed using the SPSS version 22.0 (IBM, New York, USA). Shapiro-Wilk test was used to determine whether the data was normally distributed or not. Qualitative data was expressed as frequencies and percentages. Because the quantitative data in the study was distributed nonparametrically, the results were reported as Median (IQR). Linear regression analysis was applied to investigate which parameters affected the number of total VIU operations and the strictural length. Binary regression analysis was used to assess the relation between the localization of urethral stricture and other parameters. Values of $p < 0.05$ were considered statistically significant.

Results

A total of 317 patients were included in the study. The age range of the patients included in the study was 18-93, and the median (IQR) age was 68 (17.50). The urethral stricture lengths of the patients ranged from 2 to 100 mm, and the

median (IQR) value was 10 (5) mm. The total number of VIU operations performed to the patients ranged from 1 to 23, and the median (IQR) value was 1 (1). The mean VIU values, the number of cardiovascular disease, the number of cardiovascular arrest/surgery history according to age decade of the patients are given in Table 1. Of 317 patients, 162 (51.1%) had a history of previous endourological procedure, 97 (30.6%) had a history of cardiovascular disease, and 28 (8.8%) had a history of cardiovascular arrest or bypass. The stricture was in the posterior urethra in 48 (15.14%) patients and in the anterior urethra in 269 (84.86%) patients. Anterior urethral strictures were localized in the bulber urethra in 176 (55.52%) patients and in the penile urethra in 93 (29.34%) patients.

The presence of history of endourological surgery and history of cardiovascular disease were independently associated with a higher total number of VIU operations in linear regression analysis ($p < 0.05$), (Table 2). The age was independently associated with a longer total segment of urethral stricture in regression analysis ($p < 0.05$), (Table 3). In addition, it was observed that the presence of a previous endourological intervention or cardiovascular disease significantly increased the probability of the stricture being at more distal (anterior urethra) ($p < 0.05$), (Table 4).

Table 1. The mean VIU values, the number of cardiovascular disease, the number of cardiovascular arrest/surgery history according to age decade of the patients

Decade of Age	Frequency (number of patients)	Mean number of VIU operations	Presence of history of cardiovascular disease (Ratio to decade population)	Presence of history of cardiovascular arrest/surgery (Ratio to decade population)
18-20	2	1.00	0 (0.00 %)	0 (0.00 %)
21-30	10	1.40	0 (0.00 %)	0 (0.00 %)
31-40	14	1.42	0 (0.00 %)	0 (0.00 %)
41-50	23	1.60	5 (21.73 %)	3 (13.04 %)
51-60	49	1.95	11 (22.44 %)	0 (0.00 %)
61-70	87	1.93	24 (27.58 %)	7 (8.04 %)
71-80	97	2.28	40 (41.23 %)	13 (13.40 %)
81-90	33	1.66	16 (48.48 %)	5 (15.15 %)
91-93	2	2.50	1 (50.00 %)	0 (0.00 %)
Total	317		97	28

Table 2. Linear regression analysis results in which total IUT number was assumed as independent variable and other factors as dependent variable ($p < 0.05$)

	B value	Standard Error	Beta(β) value	<i>p</i> value	95% Confidence Interval	
					Min	Max
Age	0.003	0.008	0.024	0.664	-0.012	0.018
History of previous endourological surgery	1.148	0.225	0.275	0.000	0.706	1.590
History of cardiovascular disease	1.081	0.282	0.239	0.000	0.526	1.635
History of cardiovascular arrest/ bypass	-0.371	0.439	-0.050	0.399	-1.235	0.493

Table 3. The age was independently associated with a longer total segment of urethral stricture ($p < 0.05$)

	B value	Standard Error	Beta(β) value	<i>p</i> value	95% Confidence Interval	
					Min	Max
Age	0.138	0.053	0.150	0.010	0.033	0.243
History of previous endourological surgery	-2.253	1.558	-0.083	0.149	-5.319	0.813
History of cardiovascular disease	-1.486	1.956	-0.051	0.448	-5.334	2.362
History of cardiovascular arrest/bypass	0.017	3.048	0.000	0.995	-5.980	6.015

Table 4. Binary regression analysis with the localization of urethral stricture as the dependent variable and the other parameters as the independent variables ($p < 0.05$)

	β value	<i>p</i> value	Odds ratio	95% Confidence Interval for β	
				Min	Max
Age	0.010	0.450	1.010	0.985	1.035
History of previous endourological surgery	0.938	0.012	2.555	1.230	5.308
History of cardiovascular disease	1.600	0.000	4.951	2.297	10.668
History of cardiovascular arrest/bypass	0.294	0.560	1.341	0.500	3.597

Discussion

Urethral stricture is a common disease that can affect men of all ages and seriously reduce the quality of life all over the world [2]. The mean age at diagnosis of urethral stricture in men is 45.1, with a significant increase in incidence after 55 years of age [1, 9]. Many etiological factors have been reported about urethral stricture, which is known to impose serious burdens on the patient and the health system, and all causes are still not fully clarified [3, 5]. Obtaining more clear data about the etiological and predisposing factors will play an active role in the management of this disease and in the prevention of its recurrence. Therefore, in addition to the identified etiological factors of urethral stricture, we aimed to investigate the factors that have not yet been defined or for which sufficient data has not been obtained in the literature. Therefore, we collected the data of all our patients who had VIU operation in our clinic in the last 6 years, and we investigated how these factors are effective on urethral stenosis.

It is stated in the EAU and AUA guidelines that previous endourological interventions and iatrogenic causes are serious predisposing factors for urethral stricture [4, 5]. However, there is no detailed data about the factors that are affecting the recurrence and re-VIU operation requirement. Based on these lack of data, we tried to find out which parameters affect the recurrence of urethral stricture and the need for re-VIU. According to our study results, it was observed that the history of previous endourological interventions increased the total number of VIUs performed and urethral stricture recurrences significantly ($p<0.05$), (Table 2). In a retrospective study of 224 patients by Kizilay et al. [10], it was observed that the rate of recurrence of urethral stenosis increased statistically significantly in patients with a previous history of endourological intervention.

The studies investigating the relationship between cardiovascular diseases and urethral stenosis are limited. However, urethral catheterization and poor tissue perfusion due to cardiovascular pathologies are said to be the cause of urethral stenosis, which occurs frequently in patients with hemodynamic instability due to acute coronary syndrome or other cardiovascular pathologies [7, 11-13]. In a

retrospective study of 306 patients, Yildiz et al. [8] reported that; There is a positive correlation between the SYNTAX score, which indicates the severity of coronary artery disease, and the risk of urethral stenosis in patients with urethral catheterized acute coronary syndrome. According to the results of this study; It was observed that the SYNTAX score was statistically significantly higher in the group of patients who were hospitalized for acute coronary syndrome and developed urethral stenosis during the follow-up period, compared to those who did not develop urethral stenosis. In addition, it was also reported in the same study that the SYNTAX score and severity of coronary artery disease are independent predictors for urethral stricture development ($p<0.001$). In our study, the presence of cardiovascular disease was found to be an independent risk factor for increased number of previous VIUs and recurrence of urethral stenosis ($p<0.05$) (Table 2). There is no detailed information about the effects of cardiovascular diseases on urethral strictures in the actual urology guidelines we use. Avoiding endourological interventions or urethral catheter procedures in people with cardiovascular disease may have a potential role in the prevention of this disease. Condom catheters may be used as an alternative method in such patients. If invasive urinary diversion is absolutely necessary, using percutaneous cystostomy may be more appropriate to reduce the risk of urethral stricture [14].

It is known that the risk of urethral stricture increases with age [1, 2, 9, 15]. In a comprehensive demographic study of Santucci et al. [16]; It has been reported that the incidence of urethral stenosis increases significantly especially after the age of 55, and the prevalence of urethral stenosis increases in correlation with increasing age. There is no study primarily investigated the relationship between age and the length of the urethral stricture. However, in a study by Levy et al. [17]; It has been reported that the mean urethral stricture length in patients over 60 years of age is higher than under 60 years of age, although not statistically significant. In our study, age was found to be the only independent factor that had a statistically significant increase effect in urethral stricture length ($p<0.05$) (Table 3). We think that avoiding endourological interventions or urethral catheterization as much as possible especially in elderly patients will be a serious

prevention in terms of reducing the risk of urethral stricture development [11].

In a retrospective cohort study in which Stein et al. [3] compared two different urethral stricture groups; It was reported that in the patient group with a higher rate of iatrogenic stenosis, the rate of the urethral stricture segment being more distally was statistically significantly higher. Also in our study, the probability of the urethral stricture segment being more distally (anterior urethra) was statistically significantly higher in the patient group with a previous history of endourological intervention ($p < 0.05$) (Table 4). In addition, according to the results of our study, the possibility of distal urethral stenosis increased in patients with cardiovascular disease ($p < 0.05$) (Table 4). Lumen et al. [18] reported that most urethral strictures after major cardiac surgery or neurosurgery occurred in the anterior urethra. They stated that the cause of these strictures were increasing ischemia of the corpus spongiosum during the systemic blood circulatory failure and the hypothermia.

Although the main etiological causes of urethral stricture are idiopathic and iatrogenic factors, it is a fact that many other factors may play a role in the development of stricture. It is well known that patients with coronary artery disease (CAD) are more likely to have erectile dysfunction (ED) [19, 20]. In addition, the severity of CAD is related to the severity of ED [19, 20]. There is a limited number of study which investigated the relationship between urethral stricture and local ischemia and vascular pathologies. However, the possibility that local tissue ischemia and vascular pathologies causing erectile dysfunction, may cause also urethral strictures occurred after urethral catheter or endourological interventions, should not be ignored. Also it should not be ignored that urethral strictures may be the first sign of a generalized systemic atherosclerosis that affects the pelvic end arteries, like erectile dysfunction. Considering the common perfusion of the penis and urethra from the internal pudendal artery, the relationship between urethral stricture and urethral ischemia may be correlated with the relationship between erectile dysfunction and defective erectile perfusion. In our study, it was observed that the urethral strictures of patients with CAD were mostly localized in the anterior urethra, which is more difficult to perfusion. These results are also consistent with previous

literature. Based on all these results; It may be beneficial to evaluating patients with anterior urethral stricture in terms of cardiovascular disease, also like in patients with erectile dysfunction. For example, a grading system like "cardiac risk stratification based on Princeton Consensus" which used in erectile dysfunction may also be used in urethral strictures [4].

Our study has some limitations. These were natural shortcomings due to the retrospective planning. The number of factors investigated to find out which parameters affect the total number of VIU operations performed, the length and localization of the urethral stricture, were limited. Because of our study was of a retrospective nature, we had to investigate only the parameters that could be accessible. In addition, the erectile function status of the patients was not recorded, and its relationship with other parameters could not be investigated. This is another limitation of our study.

Although our study has a retrospective nature, we think that it gave meaningful results, because of its large number of participants. In addition, because of our study was single-centered, it has a more homogeneous nature in terms of surgical equipment, demographic factors and surgeon factors. In our study, factors that have not been fully investigated before or factors about which there is a limited data investigated, and meaningful results were obtained about these factors. This is another superiority of our study.

In conclusions, the avoidance of endourological interventions or urethral catheter insertions in people with cardiovascular disease may have a potential role in prevention of urethral stricture disease. Condom catheters may be used as an alternative method in such patients. If invasive urinary diversion is absolutely necessary, using percutaneous cystostomy may be more appropriate to reduce the risk of urethral stricture. It may be beneficial to evaluating patients with anterior urethral stricture in terms of cardiovascular disease, also like in patients with erectile dysfunction. Adding a directive about this subject to the guidelines may be a useful practice in terms of early diagnosis and treatment of urethral stricture and cardiovascular diseases. More comprehensive and prospective studies are needed to support our results.

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References

1. Alwaal A, Blaschko SD, McAninch JW, Breyer BN. Epidemiology of urethral strictures. *Transl Androl Urol* 2018;3:209-3213. <https://doi.org/10.3978/j.issn.2223-4683.2014.04.07>
2. Lubahn JD, Zhao LC, Scott JF, et al. Poor quality of life in patients with urethral stricture treated with intermittent self-dilation. *J Urol* 2014;191:143-147. <https://doi.org/10.1016/j.juro.2013.06.054>
3. Stein DM, Thum DJ, Barbagli G, et al. A geographic analysis of male urethral stricture aetiology and location. *BJU Int* 2013;112:830-834. <https://doi.org/10.1111/j.1464-410X.2012.11600.x>
4. EAU Guidelines. Edn. presented at the EAU Annual Congress Milan 2021. ISBN 978-94-92671-13-4.
5. Wessells H, Angermeier KW, Elliott S, et al. Male urethral stricture: American Urological Association guideline. *J Urol* 2017;197:182-190. <https://doi.org/10.1016/j.juro.2016.07.087>
6. Cotter KJ, Hahn AE, Voelzke BB, et al. Trends in urethral stricture disease etiology and urethroplasty technique from a multi-institutional surgical outcomes research group. *Urology* 2019;130:167-174. <https://doi.org/10.1016/j.urology.2019.01.046>
7. Mundy AR, Andrich DE. Urethral strictures. *BJU Int* 2011;107:6-26. <https://doi.org/10.1111/j.1464-410X.2010.09800.x>
8. Yildiz I, Gokalp F, Burak C, et al. Relationship between the severity of coronary artery disease and catheter-associated urethral stricture in patients with acute coronary syndrome. *J Tehran Heart Cent* 2020;15:113-118. <https://doi.org/10.18502/jthc.v15i3.4221>
9. Palminteri E, Berdondini E, Verze P, et al. Contemporary urethral stricture characteristics in the developed world. *Urology* 2013;81:191-196. <https://doi.org/10.1016/j.urology.2012.08.062>
10. Kizilay F, Şimşir A, Özyurt C. Analysis of recurrent urethral strictures due to iatrogenic urethral trauma. *Turk J Med Sci* 2017;47:1543-1548. <https://doi.org/10.3906/sag-1701-36>
11. Meddings J, Saint S, Fowler KE, et al. The ann arbor criteria for appropriate urinary catheter use in hospitalized medical patients: results obtained by using the RAND/UCLA appropriateness method. *Ann Intern Med* 2015;162:1-34. <https://doi.org/10.7326/M14-1304>
12. Aoki T. Appropriate use of urinary catheter in acute heart failure patients. *Circ J* 2018;82:1505-1506. <https://doi.org/10.1253/circj.CJ-18-0447>
13. Latini JM, McAninch JW, Brandes SB, Chung JY, Rosenstein D. SIU/ICUD consultation on urethral strictures: epidemiology, etiology, anatomy, and nomenclature of urethral stenoses, strictures, and pelvic fracture urethral disruption injuries. *Urology* 2014;83:1-7. <https://doi.org/10.1016/j.urology.2013.09.009>
14. Niels Peter B, Riehmman M, Gasser TC. Absence of urethral strictures with suprapubic urinary drainage during extracorporeal circulation. *J Urol* 1993;150:337-339. [https://doi.org/10.1016/s0022-5347\(17\)35478-2](https://doi.org/10.1016/s0022-5347(17)35478-2)
15. Zumrutbas AE, Ozlulerden Y, Celen S, Kucuker K, Aybek Z. The outcomes of Kulkarni's one-stage oral mucosa graft urethroplasty in patients with panurethral stricture: a single centre experience. *World J Urol* 2020;38:175-181. <https://doi.org/10.1007/s00345-019-02758-y>
16. Santucci RA, Joyce GF, Wise M. Male urethral stricture disease. *J Urol* 2007;177:1667-1674. <https://doi.org/10.1016/j.juro.2007.01.041>
17. Levy M, Gor RA, Vanni AJ, et al. The impact of age on urethroplasty success. *Urology* 2017;107:232-238. <https://doi.org/10.1016/j.urology.2017.03.066>
18. Lumen N, Hoebeke P, Willemsen P, Troyer BD, Pieters R, Oosterlinck W. Etiology of urethral stricture disease in the 21st century. *J Urol* 2009;182:983-987. <https://doi.org/10.1016/j.juro.2009.05.023>
19. Andrade WS, Oliveira P, Laydner H, Ferreira EJP, Barreto Filho JAS. Severity of erectile dysfunction is highly correlated with the syntax score in patients undergoing coronariography. *Int Braz J Urol* 2016;42:123-131. <https://doi.org/10.1590/S1677-5538.IBJU.2015.0002>
20. Hamur H, Duman H, Keskin E, et al. The relation between erectile dysfunction and extent of coronary artery disease in the patients with stable coronary artery disease. *Int J Clin Exp Med* 2015;8:21295-21302.

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Authors' contributions to the article

M.C.T. constructed the main idea and hypothesis of the study, developed the theory of the study. M.C.T. edited the material and method section. M.C.T. and S.O. made the evaluation of the data in the results section. Discussion part of the article was written by M.C.T. Discussion part of the article reviewed by S.O., made necessary corrections and approved. In addition, all authors discussed the entire study and approved the final version.