Original Article

Relationship between the Severity of Coronary Artery Disease and Catheter-Associated Urethral Stricture in Patients with Acute Coronary Syndrome

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Abstract

Background: *Different arterial segments throughout the vascular system develop similar grades of atherosclerosis concomitantly. Urethral ischemia has been proposed as a cause of urethral stricture. Therefore, we aimed to investigate the relationship between coronary artery disease severity using a SYNTAX score and urethral stricture occurrence after urethral catheterization in patients with non–ST-segment-elevation acute coronary syndrome (ACS).*

Methods: *This retrospective study consisted of 306 men with urethral catheters that were diagnosed with ACS and underwent coronary angiography between January 2016 and January 2018 in Kars Kafkas University and Osmaniye Government Hospital, Turkey. Hospital records were reviewed to collect the follow-up data of the patients regarding the occurrence of urethral stricture after urethral catheterization. The study population was divided into 2 groups according to urethral stricture development, and both groups were compared statistically.*

Results: *SYNTAX scores were significantly higher in patients with urethral stricture than in those without urethral stricture (14.86±7.11 vs. 29.25±9.79; P<0.001). The SYNTAX score (OR=1.27; 95% CI: 1.16–1.39; P<0.001), diabetes, and serum albumin were found to be the independent predictors of urethral stricture. The receiver operating characteristic curve analysis showed that the cutoff value of the SYNTAX score for urethral stricture prediction was greater than 22.5, with 76.7% sensitivity and 85.1% specificity (AUC=0.88, 95% CI: 0.84–0.91; P<0.001).*

Conclusion: *Coronary artery disease severity graded according to the SYNTAX score is an independent predictor of urethral stricture occurrence in ACS patients with a urethral catheter inserted.*

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Introduction

Male urethral stricture disease, defined as the narrowing of the urethral lumen from the urethral meatus to the bladder neck, remains a common condition and one of the challenges facing urologists.[1] Besides the decrease in the quality of life, it is associated with increased rehospitalization rates and costs.[2] Idiopathic, iatrogenic, inflammatory, and traumatic causes are the most common etiologies of urethral stricture.[3] Urethral catheterization, widely used in coronary intensive care units for patients suffering from acute coronary syndrome (ACS) with hemodynamic instability, is one of the leading causes of iatrogenic urethral stricture and poor tissue perfusion in the presence of a urethral catheter, and it is proposed as a significant factor in the causation of such stricture.[4-8] Urethral ischemia has been suggested as one of the possible causes of idiopathic stricture in elderly patients.[9] The incidence of catheter-associated urethral stricture has been reported to be high after coronary artery bypass graft and peripheral vascular surgery.[8, 10-12]

Exposure to common risk factors for atherosclerosis initiates a systemic event occurring simultaneously and causes endothelial dysfunction, intima-media thickening, and vascular stenosis across the entire vasculature.[13] As a part of atherosclerosis processes involving the coronary artery, non–ST-segment-elevation ACS is the primary cause of death in patients with coronary artery disease (CAD).[14] The severity of CAD, which is commonly graded using a SYNTAX score calculated from coronary angiography, is closely correlated with poor prognosis in ACS.[15] We hypothesized that patients with high SYNTAX scores would have a higher incidence of urethral stricture due to greater urethral ischemia, which has been proposed as an etiologic factor in the occurrence of urethral stricture.

The aims of our study were to investigate the prevalence of urethral stricture occurrence after urethral catheterization in patients with ACS that underwent coronary angiography and to evaluate the relationship between its occurrence and CAD severity.

Methods

This study was designed in a retrospective manner. The study recruited 306 male patients with urethral catheters that were diagnosed with non–ST-segment-elevation ACS and underwent coronary angiography between January 2016 and January 2018 in our institutions. Either a 16-F or 18-F silicone-coated latex catheter was inserted into all the patients after admission to the coronary intensive care unit. Urethral catheterization was used in the coronary intensive care unit for the patients with ACS that were hemodynamically unstable and that were not ambulatory because of symptoms and arrhythmia risk. The duration of catheter stay was approximately 2 days.

Patients that had a history of medical treatment for lower urinary tract symptoms; a history of pelvic, urethral, and prostatic surgery; a history of coronary artery bypass graft surgery; a history of urethral catheterization before and 6 months after the index hospitalization; a diagnosis other than urethral stricture; and a positive urine culture during urological evaluations were excluded from the study. We also excluded patients that did not attend follow-up visits in the first 6 months. The diagnosis of non–ST-segment-elevation ACS was made according to the 2014 American College of Cardiology (ACC)/ American Heart Association (AHA) guideline for the management of patients with non–ST-segment-elevation ACS.[16] Hospital records were reviewed to collect the patients' follow-up data regarding lower urinary tract symptoms and urethral stricture. The study protocol was approved by our institutional ethics committee in accordance with the Declaration of Helsinki.

Hospital records were used to determine the clinical, demographic and laboratory characteristics of the patients. Records showed that blood biochemical parameters and a complete blood count were measured in all the patients after admission to the coronary intensive care unit. Blood samples for troponin were repeated until peak levels were detected. The left ventricular ejection fraction (LVEF) was assessed by applying the modified Simpson method.

The patients with ACS having received a urethral catheter were questioned as regards lower urinary tract symptoms and if necessary, asked to attend urology outpatient clinics for further evaluations when they attended their cardiac checkup within 6 months after discharge. In the urology outpatient clinics, all the patients were evaluated in terms of the international prostate symptom score (IPSS), urinalysis, urine culture, urinary ultrasound, post-micturition residual volume measurement, and urethrography.[17] Finally, the patients with a prediagnosis of urethral stenosis underwent urethrocystoscopy for accurate decision-making.

Selective coronary angiography was carried out using standard Judkins percutaneous transfemoral or transradial technique for all the patients. The decision to treat with stent implantation and/or balloon angioplasty according to the patients' needs did not affect the choice of patients included in the study. Coronary angiograms were recorded in digital media (Dicom-viewer; MedCom GmbH, Darmstadt, Germany), and then quantitative analysis was performed. Two external and experienced interventional cardiologists evaluated the digital angiograms and used an online calculator (www.syntaxscore.com) to calculate the SYNTAX score. In the case of conflicting results, the digital angiograms were evaluated with a third independent cardiologist to obtain a consensus.

All the statistical analyses were performed using the SPSS program, version 22.0, (SPSS Inc., Chicago, Illinois, USA). The mean ± the standard deviation, the median (the interquartile range), and percentages were used for the description of normally and non-normally distributed data and categorical variables, respectively. For the continuous variables, a t-test or the Mann–Whitney U test was used to compare the differences between the characteristics of patients with and without urethral stricture. The χ^2 test was used for the categorical variables. Multivariate logistic regression (stepwise backward elimination) analysis was performed to determine the independent predictors of urethral stricture. According to the univariate analysis, variables with a P value of less than 0.2 were incorporated in the multivariate model. The cutoff value of the SYNTAX score for the prediction of urethral stricture was identified using the receiver-operating characteristics (ROC) curve analysis. A P value of less than 0.05 was considered statistically significant.

Results

The study population comprised 306 male patients with ACS (mean age=61.19±11.67 years) with a urethral catheter inserted that underwent coronary angiography. In 276 (90.2%) cases, there was no urethral stricture in the outpatient clinic controls within 6 months of catheter removal, and in 30 (9.8%) patients urethral stricture was diagnosed. Mild symptoms score (IPSS 0-7) in 3 patients, moderate symptoms score (IPSS 8-19) in 12 patients, and severe symptoms score (IPSS 20-35) in 15 patients were detected. The site of stricture was pure bulbar in 8 patients, pure membranous in 4 patients, pure penile in 12 patients, and penile and bulbar in 6 patients with a stricture length of less than 2 cm in 16 patients and greater than 2 cm in 14 patients. Table 1 shows the demographic, clinical, laboratory, and coronary angiographic characteristics of all the patients, with and without urethral stricture. The SYNTAX score was significantly higher in the patients with urethral stricture than in those without urethral stricture (14.86±7.11 vs. 29.25±9.79; P<0.001). The patients with urethral stricture had a significantly higher incidence rate of diabetes mellitus, left main CAD, multivessel disease, bifurcation lesion, lesion length over 20 mm, chronic total occlusion, and severe tortuosity compared with those without urethral stricture (P<0.05). The white blood cell (WBC) count, the platelet count, and the peak troponin level were significantly lower, whereas the high-density lipoprotein cholesterol level was significantly higher in the patients with urethral stricture than in those without urethral stricture (P<0.05). There was no difference between the groups in terms of age; levels of hemoglobin, glucose, creatinine, C-reactive protein, serum albumin, total cholesterol, low-density lipoprotein cholesterol, and triglyceride; weight; height; the body mass index; the left ventricular ejection fraction; urethral catheterization duration; heavy calcification; coronary artery ectasia; and hypertension incidence (Table 1).

Multivariate logistic regression analysis was utilized to define the independent predictors of urethral stricture, using variables that were found to be related to urethral stricture development in the univariate analysis with a P value of less than 0.2 (ie, the SYNTAX score, diabetes, peak troponin, WBC, high-density lipoprotein cholesterol, hypertension, platelet, glucose, serum albumin, left main CAD, multivessel disease, bifurcation, lesion length, chronic total occlusion, heavy calcification, severe tortuosity, and coronary artery ectasia). The SYNTAX score (odds ratio [OR]=1.27; 95% confidence interval [CI]: 1.16–1.39; P<0.001), diabetes (OR=12.70; 95% CI: 2.61–61.85; P=0.002), serum albumin (OR=0.10; 95% CI: 0.02–0.49; P=0.005), and peak troponin (OR=0.99; 95% CI: 0.99–1.00; P=0.010) were found to be the independent predictors of urethral stricture development (Table 2). The median for the SYNTAX score was 15, and the median for peak troponin was 853 pg/mL. The patients were divided into 2 groups according to the median SYNTAX score (15) and the median peak troponin value (853) and compared with each other according to urethral stricture occurrence (Table 3).

The receiver operating characteristic (ROC) curve analysis showed that the cutoff value of the SYNTAX score for urethral stricture prediction was greater than 22.5, with 76.7% sensitivity and 85.1% specificity (area under the curve [AUC] =0.88, 95% CI: 0.84–0.91; P<0.001) (Figure 1).

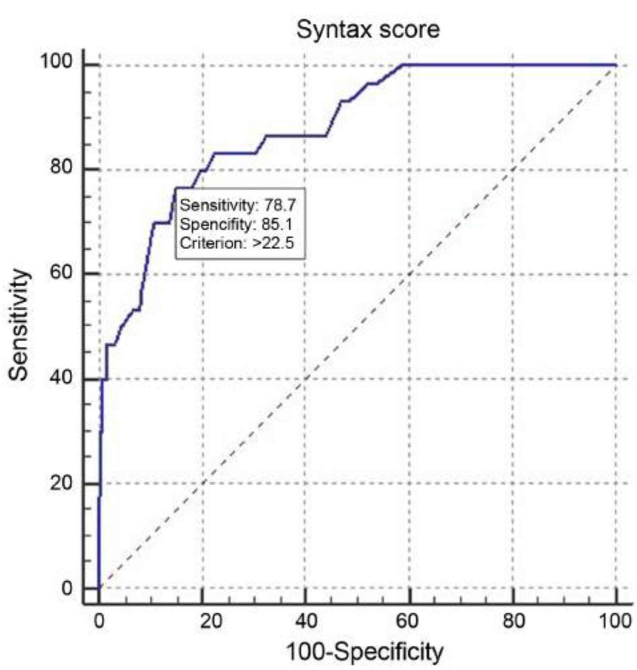

Figure 1. Receiver operating characteristic graphic to detect the best cutoff value of the SYNTAX score for urethral stricture prediction
The cutoff value of the SYNTAX score for urethral stricture prediction was greater than 22.5 with sensitivity of 76.7% and specificity of 85.1% (area under the curve=0.88, 95% confidence interval: 0.84-0.91; P<0.001).

Table 1. Demographic, clinical, laboratory, and coronary angiographic characteristics of the patients with and without urethral stricture*

Variable	Patients without Urethral Stricture (n=276)	Patients with Urethral Stricture (n=30)	P
Age (y)	61.00±11.70	62.90±11.43	0.234
Diabetes mellitus	83 (30.1)	16 (53.3)	0.010
Hypertension	124 (44.9)	19 (63.3)	0.055
Weight (kg)	76.04±11.78	76.90±11.82	0.740
Height (m)	1.66±0.08	1.65±0.07	0.439
Body mass index (kg/m^2)	27.65±3.77	28.32±4.22	0.605
Hemoglobin (g/dL)	14.19±1.62	14.23±1.91	0.619
WBC count (10^3/µL)	11.47±3.74	9.24±2.27	0.001
Platelet count (10^3/µL)	245.55±75.36	208.00±63.02	0.007
Glucose (mg/dL)	142.68±73.53	143.80±47.44	0.170
Creatinine (mg/dL)	0.92±0.23	0.95±0.34	0.679
C-reactive protein (mg/dL)	7.20 (3.4-15.4)	5.50 (3.8-7.2)	0.225
Serum albumin (g/dL)	4.00±0.35	3.88±0.45	0.089
Total cholesterol (mg/dL)	179.99±32.81	240.40±72.87	0.240
HDL-C (mg/dL)	37.96±9.13	44.60±10.38	<0.001
LDL-C (mg/dL)	105.12±30.22	110.50±39.86	0.688
Triglyceride (mg/dL)	174 (106-256)	144 (105-192)	0.299
Peak troponin (pg/mL)	961 (195-2410)	183 (152-442)	<0.001
Left ventricular ejection fraction (%)	52.87±5.76	52.00±6.64	0.559
Urethral catheterization duration (d)	2 (2.0-2.0)	2 (2.0-2.0)	0.907
LMCA disease	4 (1.4)	5 (16.7)	<0.001
Multivessel disease	184 (66.7)	29 (96.7)	0.001
Bifurcation	148 (53.6)	25 (83.3)	0.002
Lesion length	139 (50.4)	23 (76.7)	0.006
Chronic total occlusion	19 (6.9)	13 (43.3)	<0.001
Heavy calcification	25 (9.1)	5 (16.7)	0.184
Severe tortuosity	30 (10.9)	9 (30.0)	0.003
Coronary artery ectasia	68 (24.6)	11 (36.7)	0.153
SYNTAX score	14.86±7.11	29.25±9.79	<0.001

*Data are presented as mean±SD, n (%), or median (IQR $_{25-75\%}$).
WBC, White blood cell; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; LMCA, Left main coronary artery disease

Table 2. Multivariate analysis of urethral stricture

	Odds Ratio	95% CI	P
SYNTAX score	1.27	1.16-1.39	<0.001
Diabetes mellitus	12.70	2.61-61.85	0.002
Peak troponin	0.99	0.99-1.00	0.010
Serum albumin	0.10	0.02-0.49	0.005

Table 3. Comparison of urethral stricture between the SYNTAX score and peak troponin subgroups

	Patients without Urethral Stricture (n=276)	Patients with Urethral Stricture (n=30)	P
Low SYNTAX score	146 (52.9)	2 (6.7)	<0.001
High SYNTAX score	130 (47.1)	28 (93.3)	
Low peak troponin	129 (46.7)	24 (80.0)	0.001
High peak troponin	147 (53.3)	6 (20.0)	

Discussion

In our study, urethral stricture was observed more often in patients with severe CAD, and the SYNTAX score was an independent predictor of urethral stricture occurrence in patients suffering from ACS with a urethral catheter inserted.

The presence of a catheter is a cause for the development of urethral stricture.10 Post-catheterization urethral stricture in patients undergoing cardiovascular surgery has been reported with an incidence ranging from 10% to 50%.[8, 10-12] Although there is no clear established information in patients with ACS undergoing coronary angiography, urethral stricture was seen in 9.8% of the study population.

Urologic factors responsible for the development of catheter-associated urethral stricture are the type of lubricant used in catheterization, catheter material, catheter size, prolonged catheterization, traumatic catheterization, and urinary infection.[18-20] In our series of urethral stricture, traumatic catheterization and urinary infection were excluded as etiological factors since a responsible and experienced hospital staff member performed the catheterization and patients with urinary infection according to their medical report history were excluded from the study. The average duration of catheterization was similar between the groups, and same-sized silicone-coated latex Foley catheters were inserted into all the patients with the use of lidocaine 2% jelly. Therefore, prolonged catheterization, type of lubricant, catheter material, and catheter size as the contributing factors to urethral stricture occurrence were excluded.

Although idiopathic and iatrogenic factors are defined as the main reasons, several other factors have been implicated in the development of urethral stricture. Urethral ischemia has been implicated as a cause of both idiopathic and catheter-associated urethral stricture.[7-9] The role of ischemia in catheter-associated urethral stricture could be considered a manifestation of severe atherosclerosis, affecting the entire vascular system, including the pelvic arterial trees. It is well-known that erectile dysfunction is more common in patients with CAD; moreover, the severity of CAD correlates with the severity of erectile dysfunction.[21-23] There is limited information regarding the relationship between urethral stricture and ischemia in the literature. A study found that urethral stricture developed in 22% of patients that underwent cardiovascular surgery within an average of 3 months after surgery. Of these patients, 86.6% complained of erectile dysfunction and had a penile-brachial index of 0.6 or less, which is a criterion of lowered penile blood flow.[8] Considering the common blood supply of the penis and the urethra from the internal pudendal artery, the relationship between urethral stricture and urethral ischemia could be attributed to the relationship between erectile dysfunction and imperfect erectile perfusion. In accordance with the abovementioned knowledge, in our study, patients that developed urethral stricture had more severe CAD. Although there is no information about erectile dysfunction in our study, urethral stricture may be caused by severe pelvic artery atherosclerosis in patients with severe CAD.

In our study, diabetes mellitus was an independent predictor of the occurrence of urethral stricture in patients suffering from ACS with a urethral catheter inserted. Urethral stricture due to urethral ischemia and diabetes may be closely related as a result of endothelial dysfunction, which affects different vascular beds of various diameters and, as a result, gives rise to the development of systemic atherosclerosis.[24, 25] Further, in a study conducted by Kumsar et al.,[26] increased HbA1c levels were found to be associated with urethral stricture development after the transurethral resection of the prostate. Although troponin was also found to be statistically significant for urethral stricture prediction when evaluated in the multivariate analysis, odds ratios showed that troponin was not clinically significant.

Our study has some limitations, the most notable among which are its small sample volume and its retrospective nature.

Conclusion

The severity of CAD as graded on the basis of a SYNTAX score is associated with the occurrence of urethral stricture in ACS patients with a urethral catheter inserted. Among patients with ACS, the potential for subsequent urethral stricture and urogenital symptoms should be considered when planning to insert a urethral catheter.

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