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Original Research / Özgün Araştırma

The impact of age on urethroplasty outcomes: a match pair analysis

Yaşın üretroplasti sonucuna etkisi: eşleştirmeli analiz

Yaşar Pazır[1], Fatih Yanaral[1], Ufuk Çağlar[1], Sedat Çakmak[1], Akif Erbin[1], Ömer Sarılar[1], Faruk Özgör[1]

1 Haseki Training and Research Hospital, Department of Urology, Istanbul, Turkey

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Yazışma / Correspondence
Yaşar Pazır
Aksaray, Dr. Adnan Adıvar Cd. No: 9, 34130 Fatih, Istanbul, Turkey
Email: ypazir@hotmail.com
Phone:+90 212 453 20 00

ORCID

Y.P.	0000-0002-0056-7459
F.Y.	0000-0002-7395-541X
U.Ç.	0000-0002-4832-9396
S.Ç.	0000-0003-1942-4279
A.E.	0000-0001-7147-8288
Ö.S.	0000-0002-1273-1084
F.Ö.	0000-0001-8712-7458

Özet

Amaç: Üretroplasti başarısı iyi vaskülarize bir uretraya, greft uygulanan prosedürlerde ise ayrıca neovaskülarizasyon için sağlıklı ve iyi vaskülarize greft yatağına bağlıdır. Yaşlı hastalar, penil ve uretral kan akışının azalmasına neden olabilecek artan komorbid yüke sahiptir. Bu nedenle, çalışmamızda üretroplasti uygulanan hastalarda yaşın cerrahi başarının bağımsız bir belirleyicisi olup olmadığını araştırmayı amaçladık.

Gereç ve Yöntemler: Kliniğimizde 2015-2020 yılları arasında üretroplasti (Eksizyon-primer anastomoz ve bukkal mukoza greft) uygulanan erkek hastaların verileri geriye dönük incelendi. Üretroplasti başarısı, en az bir yıllık takipte herhangi bir uretral girişim ihtiyacı olmaması olarak tanımlandı. Altmış yaş altı hastalar, darlık uzunluğu ve operasyon tipine göre 60 yaş ve üstü hastalarla 1:1 oranında eşleştirildi. Hasta özellikleri iki yaş grubu arasında karşılaştırıldı. Çok değişkenli lojistik regresyon analizi ile başarıya etki eden faktörler değerlendirildi.

Bulgular: Altmış yaş ve üstü 19 hasta (n= 8 eksizyon-primer anastomoz, n= 11 bukkal mukoza greft), <60 yaş olanlarla eşleştirildi. Ortalama yaş ve takip süresi <60 yaş ve ≥60 yaş grupları için sırayla 41,9±12,6 ve 67,9±4,8 yıl (p= 0,001), 27,3±8,7 ve 24,1±10,9 ay (p= 0,325) idi. Altmış yaş üstü grupta iatrojenik etiyoloji (p= 0,026), komorbidite (p= 0,007) ve koroner arter hastalığı (p= 0,027) varlığı daha yaygındı. Gruplar arasında diyabetes mellitus, vücut kitle indeksi, sigara kullanımı, geçirilmiş uretral cerrahi öyküsü, önceki uretrotomi intern sayısı, darlık yeri ve başarı oranları açısından anlamlı fark saptanmadı. Darlık uzunluğu başarıyı öngörmede anlamlı tek klinik faktördü (p= 0,044).

Abstract

Objective: The success of urethroplasty depends on a well-vascularized urethra, and in graft procedures, also on a healthy and well-vascularized graft bed for neovascularization. Elderly patients have an increased comorbid burden that may result in decreased penile and urethral blood flow. Therefore, we aimed to investigate whether age is an independent determinant of surgical success in patients undergoing urethroplasty.

Material and Methods: The data of male patients who underwent urethroplasty (Excision-primary anastomosis and buccal mucosa graft) between 2015 and 2020 in our clinic were retrospectively analyzed. Urethroplasty success was defined as no urethral intervention required for at least one year of follow-up. Patients under the age of 60 were matched in a 1: 1 ratio with patients aged 60 and over, according to the length of the stricture and the type of operation. Patient characteristics were compared between the two age groups. Factors affecting success were evaluated with multivariate logistic regression analysis.

Results: Nineteen patients (n= 8 excision-primary anastomosis, n= 11 buccal mucosa graft) aged 60 years and older were matched with those <60 years of age. Mean age and follow-up period were 41.9±12.6 and 67.9±4.8 years (p= 0.001), 27.3±8.7 and 24.1±10.9 months (p= 0.325) for <60 years and ≥60 years old groups, respectively. Presence of iatrogenic etiology (p= 0.026), comorbidity (p= 0.007) and coronary artery disease (p= 0.027) were more common in the group over 60 years of age. No significant difference was found between the groups in terms of diabetes mellitus, body mass index, smoking, history of previous urethral surgery, number of previous direct vision

This study has been conducted retrospectively. All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

Sonuç: Üretroplasti başarısı darlık uzunluğundan etkilenmekte ancak yaştan etkilenmemektedir. Üretroplasti, darlık uzunluğu değerlendirildikten sonra yaşlı hastalarda da benzer başarı oranları ile yapılabilir.

Anahtar Kelimeler: Uretra darlığı, üretroplasti, yaş

internal urethrotomy procedures, location of stricture, and success rates. Stricture length was the only significant clinical factor predicting success (p= 0.044).

Conclusion: Urethroplasty success is affected by the length of the stricture, but not by age. Urethroplasty can be performed with similar success rates in elderly patients after evaluating the length of the stricture.

Keywords: Urethral stricture, urethroplasty, age

INTRODUCTION

Urethral stricture is narrowing of the urethral lumen due to fibrosis of the urethral epithelium and corpus spongiosum. Urethral stricture can cause lower urinary tract symptoms, recurrent urinary tract infections, stone formation, and kidney failure, which can significantly affect the quality of life (1). The estimated incidence of male urethral stricture disease is about 1% and this rate increases significantly with age (2, 3). Because older men are more commonly exposed to urethral instrumentation and transurethral interventions due to diseases such as benign prostatic hyperplasia or prostate cancer (4-6). Consequently, they have higher rates of urethral stricture-related procedures, outpatient visits, and hospitalizations (2).

Male urethral strictures can be treated with urethral dilatation, direct visual internal urethrotomy (DVIU), or urethroplasty. However, poor long-term results and high recurrence rates of 40-75% have been reported after endoscopic procedures such as urethral dilatation and DVIU (7-9). Urethroplasty is the gold standard treatment method with long-term high success rates of up to 90% (10). Current guidelines recommend urethroplasty after failure of a single endoscopic treatment or in patients at high risk for stricture recurrence (11).

The success of urethroplasty depends on the well-vascularized urethra. In transection procedures such as excision-primary anastomosis, due to the interruption of antegrade urethral blood flow, retrograde spongiosal blood flow occurs from the dorsal penile arteries through the glans and the circumflex branches of the dorsal arteries (12, 13). In grafting procedures, a healthy and well-vascularized graft bed is required for neovascularization. Elderly patients have an increased comorbid burden that can result in decreased penile and urethral blood flow and subsequent ischemia (14). In this context, there are concerns about performing urethroplasty in elderly patients due to the possible low success and high complication rates. Therefore, in clinical practice, these patients are mostly treated endoscopically and repeated procedures are required due to the high recurrence rate of the disease (3, 15, 16). With the increase in human life expectancy in developed countries, most elderly patients want a more durable solution for urethral stricture disease (17).

The impact of age on the success of urethroplasty is not clear. There is limited evidence in the literature regarding the outcomes of urethroplasty in older men because most urethroplasty series have reported outcomes in populations consisting mostly of young men (15, 18, 19). Therefore, in the present study, we aimed to investigate whether age is an independent predictor of surgical success in patients undergoing urethroplasty.

MATERIAL AND METHODS

Study Design and Population

The data of male patients who underwent urethroplasty in a tertiary academic center between January 2015 and December 2020 were retrospectively analyzed. During this period, a total of 77 urethroplasty procedures were performed on 75 patients. Patients older than 18 years of age who had at least one year of follow-up data and underwent single-stage urethroplasty were included in the study. The exclusion criteria were non-compliance with the postoperative follow-up program and pelvic radiation history. Informed consent forms were obtained from all patients included in the study and the study was conducted according to the principles of the World Medical Association Declaration of Helsinki 'Ethical Principles for Medical Research Involving Human Subjects'.

All patients were preoperatively evaluated with detailed history, physical examination, urine culture, uroflowmetry, residual urine measurement, and retrograde urethrography. Patient demographics and clinical data, including age, body mass index (BMI), comorbidities, smoking status, previous treatment, etiology, and characteristics of the strictures were recorded. Urethral stricture length and anatomic location were characterized by preoperative imaging and confirmed intraoperatively. Follow-up was defined at the period from surgery to the last clinic encounter.

Forty-five patients with regular follow-up and meeting the study criteria were eligible for match pair analysis. Patients were divided into two groups according to their age (Group 1 <60 years, Group 2 ≥60 years). Finally, 19 patients aged 60 and over were matched in a 1:1 ratio with patients under 60, according to the length of the urethral stricture and the type of surgery. Patient characteristics were compared between the two age groups. Multivariate logistic regression analysis was performed to determine the factors (including age, previous DVIU history, length of stricture, and the presence of comorbidity) effective in predicting the success of urethroplasty. The primary outcome of the study was to determine whether age is an independent predictor of urethroplasty success. The secondary outcome was to evaluate the success rates of urethroplasty between groups of patients <60 years and ≥60 years of age.

Intervention

All procedures were performed by the same surgeon using urethroplasty techniques including standardized excision-primary anastomosis (EPA) and urethroplasty with buccal mucosa graft (BMG) as described by Barbagli et al. (20). Considering the patient and stricture characteristics, EPA or BMG procedures were applied to the patients according to the surgeon's preference. A suprapubic catheter was used routinely in all urethroplasty cases.

Follow-up

The urethral catheter was left in place for two weeks after excision-primary anastomosis urethroplasty and three weeks after buccal mucosa graft urethroplasty. Following the removal of the urethral catheter, retrograde urethrography was performed. The suprapubic catheter was removed when there was no extravasation on the urethrography. The suprapubic catheter was left in place an additional one week when extravasation was present. Patients were discharged from the hospital 3-5 days after surgery and cystourethroscopy was performed one month after removal of the urethral catheter.

In the postoperative period, patients were followed up at three-month intervals for the first two years and then annually. Symptomatic assessment, physical examination, uroflowmetry, and post-void residual urine measurement were routinely carried out at each follow-up visit. Retrograde urethrography and/or urethroscopy were repeated in the presence of lower urinary tract symptoms and when a low flow rate was detected in uroflowmetry (Qmax<15ml/s). Urethroplasty failure was defined as the need for any surgical intervention such as DVIU, urethral dilation, or urethroplasty for at least one year of follow-up.

Statistical Analysis

The Statistical Package for the Social Sciences version 22 (SPSS IBM Corp., Armonk, NY, USA) program was used. The normality of the distribution of the variables was checked by Shapiro-Wilk test and Q-Q plots. Paired samples t-test was used for comparison of the normally distributed variable between the groups, and Wilcoxon test was used for nonnormally distributed data. Quantitative data are showed as mean ± standard deviation values. The data were analyzed at a 95% confidence level and P value of less than 0.05 was accepted as statistically significant.

RESULTS

Nineteen patients aged 60 years and older were matched with patients under 60 years of age, depending on the length of the urethral stricture and the type of surgery. In each group, eight patients underwent EPA, and 11 patients underwent BMG urethroplasty procedures. The mean age of <60-year-old and ≥60-year-old groups were 41.9±12.6 and 67.9±4.8 years, respectively (p= 0.001). The mean follow-up time was 27.3±8.7 months (range 21-42) in the <60-year-old group and 24.1±10.9 months (range 23-47) in the ≥60-year-old group (p= 0.325).

The ≥60-year-old group had statistically significant higher rates of iatrogenic etiology (p= 0.026), comorbidity (p= 0.007) and coronary artery disease (p= 0.027). There was no significant difference between the groups in terms of the presence of diabetes mellitus, body mass index, smoking history, history of previous urethral surgery, number of previous urethrotomy intern procedures, and urethral stricture location. The main characteristics of the two groups are shown in Table 1.

Table 1. Patient Characteristics

	Age <60 (N= 19)	**Age ≥60 (N= 19)**	**P value**
Mean age (year)	**41.9±12.6**	**67.9±4.8**	**0.001**
Etiology			0.026
Infectious	5	0	
Iatrogenic	7	14	
Trauma	4	1	
Idiopathic	3	4	
Comorbidities	8	16	0.007
Diabetes	1	3	0.604
Coronary Artery Disease	2	8	0.027
Body Mass Index (kg/m^2)	27.0±3.9	27.0±3.6	0.970
Smoking status	6	3	0.411
Prior urethral intervention history			0.562
No	4	4	
DVIU	12	14	
Urethroplasty	3	1	
Number of previous DVIU			0.103
0-1	6	11	
>1	13	8	
Location of stricture			0.838
Penile	2	4	
Bulbar	12	10	
Membranous	2	2	
Panurethral	3	3	
Stricture length (cm)	6.0±4.2	5.9±4.1	0.908
Stricture length			1.000
<2.5cm	4	4	
>2.5cm	15	15	
Surgery type			1.000
EPA	8	8	
BMG	11	11	
Follow-up duration (month)	27.3±8.7 (range 21-42)	24.1±10.9 (range 23-47)	0.325

**Continuous variables are presented as mean ± SD*

BMG, buccal mucosa graft; DVIU, direct vision internal urethrotomy; EPA, excision-primary anastomosis

The urethroplasty success rates of <60-year-old and ≥60-year-old groups were 63.1% and 52.6%, respectively (p= 0.511). Also, there was no significant difference in urethroplasty success rates when age groups were compared according to the surgical approaches. EPA was successful in 75% of the patients in both groups (p= 1.00); similarly, BMG was successful in 54.5% of men <60 years old and in 36.3% of men ≥ 60 years (p= 0.392) (Table 2).

A multivariate analysis was performed with variables such as age, previous DVIU history, length of stricture, and the presence of comorbidity. Stricture length was the only significant clinical factor predicting urethroplasty success (Table 3).

Table 2. Urethroplasty success rates stratified by age group

	Age <60 (N= 19)	**Age ≥60 (N= 19)**	**P value**
Success rate n, (%)			
Overall	12/19 (63.1%)	10/19 (52.6%)	0.511
EPA	6/8 (75%)	6/8 (75%)	1.000
BMG	6/11 (54,5%)	4/11 (36,3%)	0.392

BMG, buccal mucosa graft; EPA, excision-primary anastomosis

Table 3. Evaluation of factors affecting success with multivariate logistic regression model

	Odds ratio	**%95 CI**	**P value**
Age <60 vs. Age ≥60	1.978	0.42-9.26	0.387
Prior DVIU vs. No Prior DVIU	0.353	0.06-2.01	0.239
Stricture Length <2.5cm vs. ≥2.5cm	10.910	0.95-124.62	0.044
Comorbidities (Yes vs. No)			
Diabetes	5.196	0.40-66.87	0.206
Coronary artery disease	0.721	0.11-4.45	0.726

DVIU, direct vision internal urethrotomy

DISCUSSION

There are theoretical concerns about performing urethroplasty in the elderly. Because vascular insufficiency due to increased comorbidities in this population may lead to lower success rates and higher complication rates (14, 21). More than half of the ≥60-year-old men in our cohort were stricture-free for two years following urethroplasty and urethroplasty is generally well tolerated. Also, when age groups were compared according to the surgical approaches, EPA success rates were the same. Although BMG urethroplasty success was slightly lower in the elderly patient group, there was no statistically significant difference. We find these success rates acceptable given the low associated morbidity and long-term benefits of urethral reconstruction. These observations highlight the efficacy and safety of urethroplasty in older men when meticulous patient selection is made.

The effect of age on urethroplasty outcomes has been investigated in various series (13, 22, 23). Breyer et al. demonstrated that over 65 years of age was not predictive for urethroplasty failure (22). The most commonly used surgical approaches in their study cohort were anastomotic urethroplasty, BMG, and fasciocutaneous flap. Similar findings were reported by Levy

et al. in patients over 60 years of age who underwent EPA and BMG urethroplasty (13). In the present study, we did not find a correlation in patients treated with EPA and BMG urethroplasty between age and urethroplasty failure, consistent with the findings of the aforementioned studies. In contrast, Viers et al. reported that advancing age per decade beyond 50 years was independently associated with the risk of urethroplasty failure in patients who underwent EPA and substitution urethroplasty (23). However, they found that although the failure rate increased with age, about 75-80% of men over the age of 60 remained stricture-free for 5 years and they concluded that advanced age alone should not be a contraindication to open urethral reconstruction. Overall, according to the available evidence, urethroplasty with various surgical approaches is well tolerated by elderly men.

In this study, we found that the length of preoperative urethral stricture (>2.5cm) was associated with urethroplasty failure in patients who underwent EPA or BMG urethroplasty. In line with our findings, most previous studies reported that stricture length was associated with recurrence in multivariate analysis (10, 22). Stricture length plays an important role in preoperative planning, such as the type of procedure required, the need for graft and flap use. While short strictures can be corrected with anastomotic urethroplasties, longer strictures require the use of grafts or flaps. As the stricture length increases, the graft and flap surface used will also increase. Therefore, the rate of stricture recurrence increases.

In the current study, iatrogenic etiology, coronary artery disease, and comorbidities were more common in patients over 60 years old. Elderly patients are more exposed to urological instrumentation (5). Therefore, urethral strictures are mostly due to iatrogenic causes, as in our cohort. However, there is no clear consensus in the literature about the relationship between stricture etiology and success rates. Also, it is not surprising that comorbidities such as coronary artery disease and diabetes mellitus are more common in the elderly population. In our cohort, coronary artery disease was more common in elderly patients. Despite the known negative effects of diabetes and coronary artery disease on vascularization and wound healing, we did not find a relationship between these comorbidities and urethroplasty success in multivariate analysis.

The effect of previous urethral interventions on urethroplasty outcomes is controversial. There are concerns that urethral manipulations may increase inflammation and spongiofibrosis, resulting in longer and more complex strictures and could negatively impact success rates after definitive urethroplasty. In the present study, prior DVIU history was not found to negatively impact urethroplasty success on multivariate analysis. Similarly, in a study by Chapman et al, they reported that the previous DVIU did not affect the success of the urethroplasty at a mean follow-up of 5.4 years (24). By contrast, Viers et al found that each DVIU procedure was associated with an incremental 19% increased risk of urethroplasty failure (25). The discrepancy in the findings can be explained by selection bias since the strictures of patients undergoing endoscopic treatment are less severe and therefore more prone to endoscopic treatment. Patients with severe strictures may not be candidates for the first attempt of endoscopic treatment and are at higher risk for urethroplasty failure.

Testosterone plays a crucial role in the development of the urethra. While serum testosterone levels were not available in this study, the reported prevalence of low testosterone in men >60 approaches 30-40% (26). Due to the decrease in testosterone levels in old age, androgen receptors in the urethra and periurethral vascularity decrease (27). In the study of Hofer et al., a significant increase in the risk of urethral atrophy and artificial sphincter erosion was reported due to the decrease in serum testosterone level (28). Therefore, it has been suggested that the reduction of androgens in the elderly may lead to an increase in urethral stricture and worse reconstructive outcomes.

This study showed that urethroplasty success rates were similar in men <60 and ≥60 years old (p= 0.511). Also, we analyzed the impact of several preoperative variables including age, previous DVIU history, length of stricture, and the presence of comorbidity to identify factors associated with urethroplasty success. Multivariate analysis failed to demonstrate age as a predic-

tive variable for stricture recurrence. The length of the stricture was the only significant predictor. These data support the feasibility of EPA and BMG urethroplasty procedures in patients over 60 years of age and that the decision to perform urethroplasty should not be made solely by age.

The limitations of the present study include its retrospective nature and small sample size. Additionally, the single-center nature of the study limits the strength of our conclusions.

CONCLUSION

Urethroplasty success is affected by the length of the stricture, but not by age. Advanced age alone should not be considered as a barrier for urethroplasty. Urethroplasty can be performed with similar success rates in elderly patients after evaluating the length of the stricture.

Conflict of Interest

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Ethical Approval

This study has been conducted retrospectively. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

Author Contributions

Conception and design; YP, FY, UÇ, SÇ, FÖ, ÖS, AE, Data acquisition; YP, FY, UÇ, FÖ, ÖS, Data analysis and interpretation; YP, FY, UÇ, SÇ, AE, Drafting the manuscript; YP, FY, SÇ, Critical revision of the manuscript for scientific and factual content; FY, SÇ, FÖ, ÖS, Statistical analysis; UÇ, Supervision; YP, ÖS, AE.

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