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Risk factors associated with failed EPA urethroplasty in older male patients: A single center experience

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Summary

Introduction & Objectives: Excision with primary anastomosis (EPA) urethroplasty is the gold standard treatment for short-segment urethral strictures; however, recurrence remains a concern. This study aims to evaluate the factors associated with surgical failure in patients aged ≥ 40 years.

Materials and methods: This retrospective study included male patients who underwent EPA urethroplasty between 2013 and 2023 by a single surgeon. Patients were stratified into < 40 years (Group A) and ≥ 40 years (Group B). Comorbidities, stricture characteristics, prior procedures, and time to surgery were analyzed. Univariate and multivariable logistic regression analyses were performed, followed by Firth's penalized logistic regression to account for the small number of outcome events.

Results: A total of 89 patients were included (41 in Group A and 48 in Group B). The success rate was higher in Group A than in Group B (97.6% vs. 85.4%). In patients aged ≥ 40 years, hypertension, diabetes mellitus, and delayed time to surgery were associated with recurrence in univariate analysis. However, in Firth's penalized logistic regression, only delayed time to surgery (> 6 months) remained significantly associated with recurrence (OR 6.59, 95% CI 1.15-68.78, $p = 0.033$). Diabetes mellitus showed a trend toward increased risk but was not statistically significant.

Conclusions: EPA urethroplasty remains an effective treatment for urethral stricture. Delayed time to surgery may be associated with an increased risk of failure in patients aged ≥ 40 years, while the role of metabolic factors remains inconclusive. To establish the clinical utility of these predictors, larger prospective cohorts are essential to overcome the limitations.

KEY WORDS: Age-related surgical outcomes; EPA; Urethral stricture; Urethroplasty.

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INTRODUCTION

Urethral strictures are caused by narrowing of the urethra due to ischemic spongiofibrosis (1). Common causes include trauma from instrumentation, infections, and inflammatory conditions such as balanitis xerotica obliterans. These processes result in epithelial damage followed by fibrosis, leading to reduced urethral diameter and obstructed urinary flow. Urethral strictures can affect

the entire male urethra and are associated with significant physical and psychological morbidity. The prevalence is estimated at 200-1,200 cases per 100,000 men, with a higher incidence in older populations (2-4).

Treatment strategies depend on stricture location, length, and underlying etiology. Excision and primary anastomosis (EPA) urethroplasty is widely regarded as the gold standard for short-segment strictures, with success rates exceeding 85-90% (5-9). Despite these favorable outcomes, recurrence remains a clinically relevant complication, with reported rates ranging from 2% to 36.4%, most occurring within the first six months after surgery (10-11). Several factors have been proposed to influence urethroplasty outcomes, including stricture characteristics, prior interventions, and patient-related comorbidities. Among these, metabolic conditions such as diabetes mellitus and delayed surgical intervention may impair tissue healing and contribute to recurrence. However, findings across studies remain inconsistent, especially in specific patient subgroups.

Importantly, data focusing on patients aged ≥ 40 years remain limited, and the interaction between comorbidities and surgical timing in this population is not well established. Therefore, this study aimed to evaluate factors associated with failure following EPA urethroplasty in patients aged ≥ 40 years.

METHODS

This retrospective study was conducted at Dr. Saiful Anwar General Hospital in Malang, a tertiary referral center and included male patients who underwent EPA urethroplasty between 2013 and 2023. All procedures were performed by a single reconstructive urologist.

Patients were stratified into two age groups: < 40 years (Group A) and ≥ 40 years (Group B). Inclusion criteria were as follows: (1) Male patients with traumatic urethral strictures; (2) Patients with a clear medical history; (3) Patients who had not undergone previous EPA urethroplasty. Exclusion criteria were: (1) Male patients with urethral strictures caused by non-traumatic factors; (2) Patients lost to follow-up before 12 months post-surgery.

Surgical success was defined as the absence of the need for repeat urethroplasty or endoscopic intervention during follow-up. Follow-up evaluation was primarily based

on clinical assessment and the need for re-intervention. Follow-up duration was estimated based on available records and is reported as mean $\pm$ standard deviation due to the lack of precise date information. Uroflowmetry parameters, including maximum flow rate (Q_{max}), were available for all patients; however, these measurements were not incorporated into the primary outcome definition. In patients aged ≥ 40 years, data on educational level, comorbidities, previous procedures, stricture length, and time to surgery were collected. Associations between these variables and recurrence were evaluated. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Saiful Anwar Hospital (Ref No. 400/214/K.3/102/7/2024). Univariate and multivariate logistic regression analyses were performed using IBM SPSS Statistics. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and $p < 0.05$ was considered statistically significant. Given the limited number of outcome events, Firth's penalized logistic regression was subsequently performed as a sensitivity analysis to reduce small-sample bias. This analysis was conducted using R software.

RESULTS

A total of 89 male patients underwent EPA urethroplasty during the study period. 41 patients (46%) were aged < 40 years (Group A) and 48 (54%) were aged ≥ 40 years (Group B). The mean age was 41.2 ± 15.6 years, and the mean follow-up duration was 16.3 ± 3.2 months. Baseline characteristics are presented descriptively, and no formal statistical comparison between groups was performed. The success rate was higher in Group A than in Group B [40/41 (97.6%) vs. 41/48 (85.4%)] (Table 1). Overall, 7 patients (8.9%) experienced recurrence during follow-up.

Among patients aged ≥ 40 years, univariate logistic regression analysis showed no association between recurrence and educational status ($p = 0.563$), body mass index ($p = 0.516$), smoking status ($p = 0.389$), prior urethrotomy ($p = 0.310$), or injury type ($p = 0.772$) (Table 2). Hypertension (OR 5.4, 95% CI 0.92-31.55, $p = 0.044$), diabetes mellitus (OR 6.48, 95% CI 1.18-35.58, $p = 0.020$), and delayed surgery (> 6 months) (OR 11.57, 95% CI 1.27-105.82, $p = 0.010$) were associated with recurrence in univariate analysis.

Table 2.

Univariate logistic regression analysis of factors associated with recurrence in patients aged ≥ 40 years old.

Table 1.

Baseline characteristics of patients.

	< 40 years old	≥ 40 years old
Number of Patients, n	41	48
Age (year), mean (SD)	27.30 ± 7.85	53.10 ± 9.39
Mean follow-up (months) (SD)	16.3 ± 3.15	
BMI (kg/m^2), mean (SD)	23.05 ± 2.57	22.59 ± 5.42
Higher Education, n (%)	35 (85.4%)	31 (64.6%)
Current smoker, n (%)	12 (29.3%)	14 (29.2%)
Diabetes mellitus, n (%)	0	9 (18.8%)
Hypertension, n (%)	7 (17.1%)	8 (16.7%)
Stricture length, n (%)		
< 1 cm	21 (51.2%)	23 (47.9%)
> 1 cm	20 (48.2%)	25 (52.1%)
Time to operation (month), mean (SD)	6.67 ± 4.07	
Cystostomy tube, n (%)	38 (92.6%)	42 (87.5%)
Previous urethrotomy, n (%)		
Yes	26 (63.4%)	35 (72.9%)
No	15 (36.6%)	13 (27.1%)
Type of Surgery, n (%)		
Bulbar mobilization	9 (22%)	35 (72.9%)
More than bulbar mobilization	32 (78%)	28 (58.3%)
EPA outcome, n (%)		
Success	40 (97.6%)	41 (85.4%)
Recurrence	1 (2.4%)	7 (14.6%)

Parameter	EPA urethroplasty (≥ 40 yo)				P-value	OR	95% CI	
	Failed		Success					
	Freq	%	Freq	%			Lower	Upper
Education					0.563	1.62	0.31	8.29
Low	3	42.9%	13	31.7%				
High	4	57.1%	28	68.3%				
BMI					0.516	1.70	0.34	8.60
Normal/Underweight	4	47.1%	18	43.9%				
Overweight/Obese	3	42.9%	23	56.1%				
Current Smoker					0.389	2.05	0.39	10.64
Yes	3	42.9%	11	26.8%				
No	4	57.1%	30	73.2%				
Hypertension					0.044	5.40	0.92	31.55
Yes	3	42.9%	5	12.2%				
No	4	57.1%	36	87.8%				
Diabetes mellitus					0.020	6.48	1.18	35.58
Yes	4	57.1%	7	17.1%				
No	3	42.9%	34	82.9%				
Time to surgery				0.010	11.57	1.27	105.82	
> 6 months	6	85.7%	14	34.1%				
≤ 6 months	1	14.3%	27	65.9%				
Type of injury					0.772	0.77	0.13	4.49
Non PFUI	2	28.6%	14	34.1%				
PFUI	5	71.5%	27	65.9%				
Number of urethrotomy					0.310	2.33	0.44	12.20
No	4	57.1%	10	24.4%				
Yes	3	42.9%	31	75.6%				
Type of surgery					0.848	0.85	0.17	4.33
More than bulbar	4	57.1%	25	61.0%				
Bulbar mobilization	3	42.9%	16	39.0%				

Table 3.

Firth penalized logistic regression analysis for risk factors of EPA urethroplasty failure (≥ 40 years old).

Variable	OR	95% CI	P-value
DM	4.30	0.73-27.99	0.105
Hypertension	1.77	0.24-10.91	0.55
Delayed time to surgery (> 6 months)	6.59	1.15-68.78	0.033

In conventional multivariable logistic regression analysis, diabetes mellitus and delayed time to surgery were associated with recurrence. However, given the limited number of outcome events, Firth's penalized logistic regression was performed. In the Firth regression model, only delayed time to surgery (> 6 months) remained significantly associated with recurrence (OR 6.59, 95% CI 1.15-68.78, $p = 0.033$). Diabetes mellitus showed an increased odds ratio (OR 4.30, 95% CI 0.73-27.99) but did not reach statistical significance ($p = 0.105$), while hypertension was not associated with recurrence (Table 3).

Discussion

This study evaluated predictors of failure following EPA urethroplasty in patients aged ≥ 40 years. Although overall outcomes were favorable, success rates were lower in this group compared with younger individuals. Within the ≥ 40 -year cohort, diabetes mellitus and delayed time to surgery were associated with recurrence in univariate logistic regression analysis. However, after adjustment using Firth's penalized logistic regression, only delayed time to surgery remained significantly associated with recurrence. These findings suggest that both disease chronicity and patient-related factors may influence outcomes, although the strength of these associations remains uncertain.

EPA urethroplasty remains the gold standard treatment for short-segment traumatic urethral strictures, with reported success rates exceeding 85-90% in multiple series (6, 12). Long-term studies have demonstrated sustained durability of anastomotic repair, although recurrence rates vary depending on follow-up duration and patient selection (13, 14). Variability across studies may reflect differences in stricture etiology, surgical expertise, and surveillance protocols. Our findings align with previously published success rates while highlighting that recurrence remains clinically relevant, particularly in patients with comorbid conditions.

Diabetes mellitus was associated with recurrence in univariate analysis but did not retain statistical significance after Firth regression. This attenuation suggests that the observed association may be influenced by small-sample bias or confounding. Nevertheless, several biological mechanisms may plausibly link diabetes to impaired healing. Chronic hyperglycaemia is associated with endothelial dysfunction, impaired collagen remodelling, and delayed wound healing, which may compromise anastomotic integrity and promote fibrosis (15-17). Advanced glycation end products (AGEs) accumulate in diabetic tissues and promote cross-linking of collagen fibers, resulting in reduced tissue elasticity and altered extracellular matrix remodelling (18, 19). Additionally, diabetes is associated with chronic low-grade inflammation and oxidative stress,

which may exacerbate fibrotic pathways and promote recurrent spongiositis. Impaired wound healing in diabetic patients has been well documented in other surgical fields and may similarly affect urethral reconstruction outcomes.

Previous studies have suggested a possible association between diabetes and stricture recurrence, particularly following endoscopic management (6). However, evidence in the context of open EPA urethroplasty remains limited and inconsistent. Our findings suggest that the role of metabolic factors in this setting remains inconclusive and warrants further investigation.

Delayed time to surgery was also independently associated with recurrence after Firth regression. Prolonged obstruction may permit progressive spongiositis and chronic inflammatory changes within the corpus spongiosum, potentially increasing tissue rigidity and tension at the time of anastomosis (20, 21). Chronic urinary extravasation and repeated instrumentation may further exacerbate local inflammation and scar formation. From a surgical perspective, increased fibrosis may compromise vascular supply and impair healing, thereby predisposing to recurrence. Early referral and timely definitive reconstruction may therefore reduce fibrotic burden and improve surgical outcomes.

Hypertension showed an association with recurrence in univariate analysis but was not independently associated after adjustment, suggesting potential confounding. Given the frequent coexistence of hypertension with diabetes and other metabolic conditions, its independent role remains unclear.

Interestingly, factors such as smoking status, prior urethrotomy, and injury type were not significantly associated with recurrence. While these factors have been implicated in other studies, their effects may be context-dependent and influenced by sample size and patient selection.

The overall recurrence rate in our cohort was comparable to previously reported series of anastomotic urethroplasty (12, 13). However, the median follow-up duration of approximately 16 months may not be sufficient to capture late recurrences, which are known to occur several years after urethroplasty (13, 14). Therefore, the true recurrence rate may be underestimated, and longer follow-up is required.

Several limitations should be considered. First, the small number of recurrence events ($n = 7$) resulted in a low events-per-variable ratio, which may lead to unstable estimates and reduced statistical power. Although Firth's penalized logistic regression was used to mitigate small-sample bias, the findings should be interpreted as exploratory and hypothesis-generating rather than confirmatory. Second, the follow-up duration was relatively short and may not fully capture late failures. Third, the use of an age cutoff of ≥ 40 years is arbitrary and does not necessarily reflect biological aging; this should be considered when interpreting the results. Finally, no formal sample size or power calculation was performed due to the retrospective design.

From a clinical perspective, these findings highlight the importance of timely surgical intervention in patients undergoing EPA urethroplasty. Minimizing delay to definitive repair may improve outcomes. Although metabolic fac-

tors such as diabetes mellitus may contribute to impaired healing, their impact remains inconclusive in this study. Future research should explore whether metabolic optimization or earlier surgical referral can reduce recurrence rates. Prospective studies investigating the underlying mechanisms of urethral fibrosis and healing are warranted.

CONCLUSIONS

EPA urethroplasty remains a safe and effective treatment for urethral stricture. Delayed time to surgery may be associated with an increased risk of failure in patients aged ≥ 40 years. Although diabetes mellitus showed a potential association, this was not statistically significant after adjustment and should be interpreted with caution. Given the limited number of outcome events, these findings should be considered hypothesis-generating and require validation in larger studies with longer follow-up.

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DECLARATIONS

Ethical approval and consent for participate: Ethical approval was granted by the Ethics Committee of Dr. Saiful Anwar General Hospital, Malang, Indonesia (Ref No. 400/214/K.3/102/7/2024). The study was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

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