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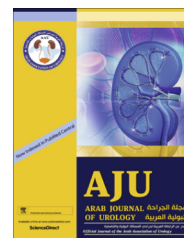


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Is there a way to predict failure after direct vision internal urethrotomy for single and short bulbar urethral strictures?



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KEYWORDS

Direct vision internal urethrotomy;
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ABBREVIATIONS

BMI, body mass index;
DVIU, direct vision internal urethrotomy;
RSD, regular self-dilatation;

Abstract Objective: To identify patient and stricture characteristics predicting failure after direct vision internal urethrotomy (DVIU) for single and short (< 2 cm) bulbar urethral strictures.

Patients and methods: We retrospectively analysed the records of adult patients who underwent DVIU between January 2002 and 2013. The patients' demographics and stricture characteristics were analysed. The primary outcome was procedure failure, defined as the need for regular self-dilatation (RSD), redo DVIU or substitution urethroplasty. Predictors of failure were analysed.

Results: In all, 430 adult patients with a mean (SD) age of 50 (15) years were included. The main causes of stricture were idiopathic followed by iatrogenic in 51.6% and 26.3% of patients, respectively. Most patients presented with obstructive lower urinary tract symptoms (68.9%) and strictures were proximal bulbar, i.e. just close to the external urethral sphincter, in 35.3%. The median (range) follow-up duration was 29 (3–132) months. In all, 250 (58.1%) patients did not require any

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RUG, retrograde urethrography

further instrumentation, while RSD was maintained in 116 (27%) patients, including 28 (6.5%) who required a redo DVIU or urethroplasty. In 64 (6.5%) patients, a redo DVIU or urethroplasty was performed. On multivariate analysis, older age at presentation [odds ratio (OR) 1.017; $P = 0.03$], obesity (OR 1.664; $P = 0.015$), and idiopathic strictures (OR 3.107; $P = 0.035$) were independent predictors of failure after DVIU.

Conclusion: The failure rate after DVIU accounted for 41.8% of our present cohort with older age at presentation, obesity, and idiopathic strictures independent predictors of failure after DVIU. This information is important in counselling patients before surgery.

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Introduction

Urethral dilatation and direct vision internal urethrotomy (DVIU) are feasible and minimally invasive treatment options for men with short anterior urethral strictures. In addition, it represents a valuable option after failed posterior urethroplasty [1,2]. The procedures can be performed under local anaesthesia and as an outpatient procedure with rapid recovery. In the current literature there is a marked variability in reporting of outcomes after DVIU, with stricture-free rates ranging from 10% to 90% [3]. However, in nationwide surveys, urologists prefer to perform DVIU even when the risk of recurrence is virtually 100% [4]. Similarly, DVIU was the most common procedure followed by urethral dilatation, stent/steroid injection in a review of Medicare claims [5]. However, it has been shown that multiple transurethral manipulations increases the complexity and disease duration when patients are referred for definitive urethroplasty [6].

Therefore, identifying patients at risk of recurrence after DVIU is crucial. There is paucity of research regarding factors predicting failure after DVIU, notably with no standardised definition of failure [7]. In the present study, we investigated stricture characteristics and clinical predictors of failure after DVIU performed for single and short bulbar urethral strictures in a large contemporary series.

Patients and methods

After obtaining Institutional Review Board approval, we retrospectively analysed our electronic database for adult patients (aged > 18 years) who underwent DVIU for strictures of the anterior urethra between January 2002 and January 2013. In this analysis, only patients with single and short bulbar urethral strictures (<2 cm) were included. Paediatric patients and patients who underwent DVIU after failed urethroplasty were excluded. The patients' demographics were retrieved and included age, associated comorbidities, and body

mass index (BMI). The cause of stricture was determined to be inflammatory if the patient had had previous episodes of urethral infection or a sexually transmitted disease, iatrogenic if there was history of urethral instrumentation, traumatic if there was a previous history of urethral trauma, and idiopathic if there was no relevant history.

After receiving an appropriate prophylactic single dose of antibiotic, the procedure was typically performed under spinal anaesthesia in lithotomy position and was accomplished by performing a dorsal cut of the fibrous strictured area at the 12 O'clock position until bleeding and visual confirmation of healthy tissue was confirmed. If required, repetition of cuts in the same incision area was performed. Patients were kept in hospital overnight and were discharged on the first postoperative day with an indwelling urethral catheter. Patients received antibiotics for the duration that the catheter was *in situ*. The catheter was left *in situ* for an average of 10 days. Regular self-dilatation (RSD) was typically performed for a select group of patients based on the complexity of the stricture and the surgeon perspectives. Our routine RSD regimen included regular dilatation three-times weekly for the first month, and then gradually reducing the frequency to once weekly for the following 3 months. All patients were scheduled for the first follow-up at ≤ 3 months of the procedure, with patients' symptoms evaluated and uroflowmetry performed. If indicated, ascending urethrography and cystoscopy were performed if there was a recurrence of obstructive symptoms and an obstructive uroflowmetry pattern. Only patients who completed ≥ 3 months follow-up were included.

The primary outcome of the study was failure of DVIU, defined as the need for further instrumentation, i.e. if patients required maintenance RSD, redo DVIU, or urethroplasty. Failure was tested for association with various preoperative and operative parameters to detect significant variables. For association between categorical variables, the chi-square test was used, while the Student's *t*-test was used for comparing means between

groups. Logistic regression analysis was used to determine independent predictors of failure after DVIU. All statistical analysis was performed using IBM statistical software, with a $P < 0.05$ considered to indicate statistical significance.

Results

In all, 430 patients underwent DVIU for short bulbar urethral strictures within the specified period and met the study eligibility criteria. The mean (SD) age was 50 (15) years and the BMI was 29 (5) kg/m². The main cause of stricture was idiopathic followed by iatrogenic in 51.6% and 26.3% of patients, respectively. Most patients presented with obstructive LUTS (68.9%), while acute urine retention and suprapubic tube fixation were the presenting symptoms in 9.5%. In 21.6% of patients, the stricture at the bulbar urethra was identified during cystoscopy for another indication, e.g. ureteroscopy for ureteric stones and ureteric catheter fixation for percutaneous nephrolithotomy. Therefore, this subset of patients was not evaluated by ascending urethrography before the procedure. Strictures were proximal bulbar, i.e. just close to the external urethral sphincter, in 35.3% of patients. The shape of the

stricture by urethroscopy was determined to be annular in 61.4%, pinpoint in 26%, and undetermined in 12.6% of patients.

The median (range) follow-up duration was 29 (3–132) months. In all, 250 (58.1%) patients did not require any further instrumentation. In 64 (6.5%) patients redo DVIU or urethroplasty was required to treat recurrence. While, RSD was maintained according to the proposed regimen in 116 (27%) patients including 28 (6.5%) who required a redo DVIU or urethroplasty. In all, 88 redo DVIUs and four urethroplasty procedures were performed for the management of recurrence.

Table 1 shows the results of univariate analysis; patients who experienced failure after DVIU were older ($P = 0.002$) and obese ($P = 0.001$), and were more likely to undergo DVIU in association with other pathologies ($P = 0.03$). Also, idiopathic strictures were the most likely to be associated with recurrence ($P = 0.004$). On multivariate analysis, older age at presentation, obesity, and idiopathic strictures were independent predictors for failure after DVIU (Table 2).

Discussion

Recently, more attention has focused on the causes and presentation of male anterior urethral stricture. Palminteri et al. [8] reported that the bulbar urethra was the most common site, while pan-urethral and multiple sites were the least common. In addition, they reported that iatrogenic and unknown strictures were the most common, occurring in 38.6% and 35.8% of patients, respectively. These findings are in concordance with the present study. However, idiopathic strictures were the most common in our present study, while pan-urethral strictures were not included as the focus was on strictures treated by DVIU. Although lichen

Table 1 Univariate analysis for factors associated with failure after DVIU for short bulbar urethral strictures.

Variable	Failure*		P
	No	Yes	
Mean (SD)			
Age, years,	48.4 (15.6)	53 (14)	0.002
Haemoglobin, g/dL	13.8 (1.6)	13.4 (1.6)	0.05
N (%)			
Presentation			0.03
LUTS	181 (61.1)	115 (38.9)	
Urinary retention	26 (63.4)	15 (36.6)	
Incidental	43 (46.2)	50 (53.8)	
Diabetes mellitus			0.9
No	226 (58.1)	163 (41.9)	
Yes	24 (58.5)	17 (41.5)	
Hypertension			0.6
No	210 (58.7)	148 (41.3)	
Yes	40 (55.6)	32 (44.4)	
Stricture cause			0.004
Inflammatory	22 (81.5)	5 (18.5)	
Iatrogenic	70 (61.9)	34 (38.1)	
Traumatic	45 (66.2)	23 (33.8)	
Idiopathic	113 (50.9)	109 (49.1)	
Obesity (BMI > 30 kg/m ²)			0.001
No	154 (65.3)	82 (34.7)	
Yes	96 (49.5)	98 (50.5)	
Urine culture			0.1
Negative	176 (55.9)	139 (44.1)	
Positive	74 (64.3)	41 (35.7)	
Stricture site			0.017
Bulbo-membranous	100 (65.8)	52 (34.2)	
Distal bulbar	150 (54)	128 (46)	

* Failure includes RSD and/or operative intervention.

Table 2 Multivariate analysis of recurrence predictors for patients undergoing DVIU for short bulbar urethral strictures.

	OR (95% CI)	P
Age	1.017 (1.002–1.032)	0.03
Stricture site		
Bulbo-membranous	Referent	
Distal bulbar	1.482 (0.963–2.278)	0.073
Stricture cause		
Inflammatory	Referent	
Idiopathic	3.107 (1.022–11.72)	0.035
Iatrogenic	1.969 (0.503–6.524)	0.227
Traumatic	2.750 (1.559–20.076)	0.079
Presentation		
LUTS	Referent	
Urinary retention	1.124 (0.547–2.310)	0.7
Incidental	1.710 (1.048–2.790)	0.05
Obesity (BMI > 30 kg/m ²)		
No	Referent	
Yes	1.664 (1.105–2.504)	0.015

OR, odds ratio.

sclerosis and radiation therapy contribute significantly to the spectrum of causes of stricture, none of our patients underwent DVIU because of either cause.

Despite the common belief that urethral stricture presents with LUTS, there is paucity of studies describing the spectrum of presentation, notably for those requiring DVIU. This information is critical in defining patients reported outcome after treatment [9]. Rourke et al. [10] have reported the presenting symptoms in 611 patients with anterior urethral stricture. They reported that LUTS and acute urinary retention were the most common in 54.3% and 23.4% patients, respectively; while other symptoms were reported in 22.3%. In the present study, the most common presentation was LUTS in 68.9%, while 9.5% of patients presented with acute urinary retention. In our present cohort, a significant proportion (21.6%) of strictures was incidentally discovered while performing an endoscopic procedure for other indications, e.g. percutaneous nephrolithotomy and ureteroscopic stone extraction. This information confirms the necessity to include the whole spectrum of urethral stricture disease while developing questionnaires to assess the outcome.

After defining RSD as failure, the failure rate after the initial DVIU in the present study was 41.8%. A recent review has shown that the stricture-free rates after urethral dilatation and DVIU ranged from 10% to 90%, with a potential benefit of RSD [3]. In another review, the success rate in studies reporting short-term results was up to 85%, while long-term results ranged from 6% to 28% [7]. This wide range of outcome is most probably due to the diversity of methods and outcome measures among the different studies. Although there is no consensus about the definition of failure after urethral surgery, failure was defined in the present study as the need to perform a secondary procedure. This definition was the most commonly used in 60% of surgeons surveyed for urethroplasty practice and surveillance patterns [11].

From the patients' demographics, older age and obesity were identified as independent predictors of recurrence after DVIU, while for stricture characteristics, idiopathic strictures were independent predictors of recurrence. We identified older age as an independent predictor for recurrence in the present study. Although there is a well-recognised decline in fibroelasticity with ageing, and consequently less expected deposition of collagen and elastic tissues, other factors should be considered for the association with recurrence. Older age at presentation might reflect a delay in requesting treatment and therefore longer stricture duration, which would contribute to more fibrosis. The relationship between obesity and recurrence should be taken cautiously. As patients with a high BMI usually have comorbidities, minimally invasive rapid procedures are preferred. The same rationale applies to older patients.

A recent analysis of urethroplasty procedures in the USA showed that age and obesity were significantly associated with postoperative complications, albeit the relation to outcome was not mentioned [12]. In addition, there might be a causal relationship between obesity and the extent of fibrosis and wound healing that necessitates further investigation. Recently, obesity has been identified as an independent predictor of delayed wound healing [13]. In skeletal muscles, a high-fat diet has been shown to increase TGF- β 1 protein expression, Smad-3 activation, and collagen deposition, consequently increasing fibrosis [14].

Idiopathic strictures might involve unnoticeable minor trauma or urethral infection, which develops over a long period to a stricture and hence more spongiofibrosis. Nevertheless, idiopathic stricture is a potentially unmodifiable factor at the time of surgery. Therefore, it should be considered while counselling patients before surgical intervention of the possibility of recurrence and the need for definitive surgery.

We considered RSD in the present study as a failure based on previous reports suggesting that RSD might delay recurrence but that it did not prevent it, and even that it might be associated with more complex corrective urethroplasty [15–18]. Recently, the Société Internationale d'Urologie and the International Consultation on Urologic Disease (SIU/ICUD) consultation guidelines on urethral strictures recommended RSD might be used as a palliative procedure for patients unwilling to undergo definitive intervention or in medically unfit patients [16].

Although retrograde urethrography (RUG) is the cornerstone in identifying the site, number, and extent of the stricture, it is blind to the extent of the spongiofibrosis, which is considered the main cause of recurrence. Osman et al. [19] have shown a superior detection rate with magnetic resonance urethrography vs RUG for detection and determining the extent of spongiofibrosis. In addition, El-ghar et al. [20] have shown that RUG combined with sono-urethrography had a comparable detection rate to magnetic resonance urethrography for detecting the site and extent of the spongiofibrosis of anterior urethral strictures. Therefore, further studies are warranted to evaluate the extent of spongiofibrosis in addition to RUG in determining failure after DVIU.

We acknowledge several limitations of the present study including primarily its retrospective nature. Most of our present patients were evaluated using RUG and hence, the degree of spongiofibrosis was not investigated. In addition, the variable follow-up duration might reflect patients with missed follow-up. However, all of the included patients had completed the 3-month follow-up visit. The recurrence rate in the present study might be underestimated, as we counted only patients who underwent repeat procedures at our institution. Nevertheless, our routine policy is to provide life-long

follow-up for any admitted patient in our institution. In addition, our institution is a main referral centre covering a large geographical area; therefore minimising the odds of missing patients. The impact of DVIU on quality of life and sexual function has been previously reported [21]. However, no validated tool was used to assess such items in the present study. Lastly, there are local factors that might contribute to the outcome after DVIU but not tried in our patients e.g. intralesional triamcinolone and hyaluronic acid combined with carboxymethylcellulose [22] and [23].

In conclusion, the failure rate after DVIU accounted for 41.8% of our present cohort with older age at presentation, obesity, and idiopathic strictures being independent predictors of failure. This information is important for counselling patients before surgery. The present study is a step forward towards identifying which patients and what stricture characteristics are eligible for corrective surgery to minimise frequent patient procedures.

Conflicts of interest

None.

Source of funding

None.

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