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LONG-TERM OUTCOMES OF DIRECT VISION INTERNAL URETHROTOMY:

A RETROSPECTIVE STUDY AT A TERTIARY HOSPITAL IN ETHIOPIA

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JULY 2024,

ADDIS ABABA, ETHIOPIA

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JULY 2024,

ADDIS ABABA, ETHIOPIA

I. STATEMENT OF DECLARATION

I confirm that this thesis presented for fellowship fulfilment has been composed solely by my self and the result of my own work not been summited in whole or in part in any previous application for degree or professional qualificaitons, except were stated otherwise by reference or acknowledgment, the work presented is entirely my own.

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II. STATEMENT OF CERTIFICATION

This is to certify award given by TASH surgery department IRB on September 2, 2024 that the research paper submitted by me is an outcome of my independent and original work. I have duly acknowledged all the sources from which the ideas and extracts have been taken. The project is free from any plagiarism and has not been submitted elsewhere for publication.

III. Approval Sheet and panel of oral examiners for research Defense

The research entitled long-term outcomes of direct vision internal urethrotomy: a retrospective study at a tertiary hospital in Ethiopia prepared and submitted by Dr. Samuel Almaw in partial fulfillment of requirement for fellowship had been and recommended or acceptance and approval for oral examination .

Name of Advisor

Dr. Bedri Kazali (MD, General Surgeon and Consultant Urologist)

Signature ———————————

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ABBREVIATIONS

TASH ……... Tikur Anbessa Specialized Hospital

DVIU …… Direct Vision Internal Urethrotomy

USD ……..... Urethral Stricture Disease

SSA ……... Sub-Saharan Africa

BPH ……Benign Prostatic Hyperplasia

CUG ……...Cystourethrography

Abstract

Background *Urethral stricture disease in men is a prevalent urological condition that can significantly affect quality of life and healthcare costs. Despite urethroplasty being the gold standard management for urethral stricture disease, direct vision internal urethrotomy is commonly performed due to its simplicity and lower cost. However, the use of direct vision internal urethrotomy as a definitive management and its long-term outcomes, particularly in Sub-Saharan Africa (SSA), remain unknown.*

Objective: *To assess the long-term outcomes and risk factors for failure in patients with urethral strictures who underwent direct vision internal urethrotomy as a primary intervention.*

Method: *We carried out a retrospective study on patients with urethral stricture disease that underwent direct vision internal urethrotomy at our institution over a course of 5 year period with a minimum postoperative follow-up period of one year. The study included a comprehensive review of medical records from 79 patients who fulfilled the inclusion criteria.*

The Kaplan-Meier curve was used to characterize the recurrence-free survival, and multivariable COX regression analysis was carried out to predict treatment failure. Predictors evaluated included location, length, etiology, number and type of strictures, comorbidities, and age of the patients.

Result *: The Mean age was 59.8 ± 14.9 years.Of the 79 patients, 88.6% had a single stricture, of which 62% had a stricture length between 11 and 20mm while 11.4 % had a stricture length ≤ 10mm. Bulbar urethral strictures accounted for 75.9% of cases. The mean follow up duration after the procedure was 31.1±16.7(range:12 to 69) months.The recurrence rate was 57%,68.4%, 82.3%, and 88.6% at 3,6,12, and 24 months respectively. The mean time to recurrence was 4.4 ± 4.5 (range: 1 to 24) months. Multivariate regression analysis demonstrated, soft non-obliterating stricture type and stricture length ≤10mm were significantly associated with recurrence-free survival with hazard ratio of 14.1 ; 95 percent confident interval (2.78 – 72.0) with P < 0.001 and hazard ratio of 46.9 ,95 percent confident interval, (1.4 - 1568.5) with P=0.032 respectively.*

Conclusion *Direct vision internal urethrotomy is associated with an unacceptible high recurrence rate among out patient population. Soft, non-obliterating strictures and those strictures with less than or equal to10mm length had lower recurrence.Further prospective studies are required in low-income setting to clearly define the patient population that could benefit from this procedure.*

Introduction

Regardless of geography and etiology, urethral stricture disease (USD) has negative impact on physical health and quality of life. The management options for USD includes less invasive methods such as urethral dilation, and direct vision internal urethrotomy (DVIU), and open reconstructive urethroplasty(1).

DVIU is a minimally invasive procedure which involves transurethral incision using a cold-knife to cut and release the scar tissue,that promots healing at a wider caliber by secondary intention,which increases the urethral lumen diameter(2). Despite urethroplasty being the gold standard procedure with a superior success rate and favorable long-term outcome(3,4), the use of DVIU remains highly prevalent in contemporary urology practice(3). In fact,in several areas across the globe, DVIU is reported to be preffered over urethroplasty (5).

In the Ethiopian context, a survey of 33 urologists in the country revealed that nearly 76% have access to endourology, with DVIU sets being the second most common resource available(6). However, only a few studies have tried to show the short-term outcomes following DVIU(7,8) with no long-term outcome study for DVIU in Ethiopia.

We report our experience with DVIU in 79 patients with USD who underwent DVIU as the primary intervention, with a minimum post-operative follow-up period of one year. We have done a multivariable analysis to assess success rate and identify predictors of treatment failure. We believe that understanding this is essential for optimizing clinical decision-making and treatment strategies for improved patient outcomes.

Patients and Methods

Study design

The study was an institution-based retrospective analysis of patients with USD who undergone DVIU as their primary treatment during the five-year period between September 1, 2018, and August 31, 2023.

Study setting

The investigation was carried out at Tikur Anbessa Specialized Hospital, Ethiopia's largest academic and tertiary referral hospital.

Sample size

We included all patients meeting the inclusion criteria

Inclusion criteria

All patients who are 18years and older with a documented diagnosis of USD, who undergone DVIU as the primary intervention with complete and accessible medical records containing detailed information about the DVIU procedure and post-operative outcomes, with a minimum post-operative follow-up period of one year were included in our study.

Exclusion Criteria:

We excluded patients who are below the age of 18, those with incomplete or unavailable medical records, patients who underwent prior multiple dilation, DVIU, or urethroplasty, those with other concomitant interventions or procedures at the time of DVIU or having a maximum follow-up duration of less than 12 months.

Data collection and quality management

The data was gathered from surgical logbooks and electroic medical records of patients.Data concerning key variables such as Patient demographics (age, gender), Stricture characteristics (location, length, etiology, complexity), DVIU procedural details (technique, instruments used), and Postoperative follow-up data (symptom recurrence, additional interventions) was extracted. Missing data was checked and identified to ensure the accuracy of the result.

Data sources

The data was extracted from patient electronic medical records using a data abstraction tool that had been designed and validated prior to the start of the study. The data collection tool comprised clinical, outcome, and sociodemographic information.

Measurement/analysis and interpretation

Following data collection , the data was coded, cleaned, and entered into IBM SPSS ver 27 for Windows, (IBM Corp). The same software and both descriptive and inferential statistical models were then used to analyze it. For continuous and categorical variables, the corresponding median, frequency, and proportion were explained. The Kaplan-Meier curve was used to report the recurrence-free survival. Treatment failure was predicted by multivariable COX regression analysis. Predictors included location, length, etiology, number and type of strictures, and

comorbidities. A $P < 0.05$ threshold was used for significance.

Ethical Considerations

The Institutional Review Board (IRB) of Addis Ababa University's College of Health Sciences, which is in charge of health science research within its jurisdiction, granted the ethical approval. The study was carried out in accordance with national and institutional research ethics guidelines as well as the Helsinki Declarations. No one other than the principal investigators had access to the patient data, and all information was managed in a secret manner.

Dependent and Independent variables

Our dependent variable was the long-term success rate of DVIU. Patient Age, comorbidity, stricture characteristics (location, Length, Etiology, Stricture complexity), and follow-up duration post-DVIU were the independent variables.

Results

During the study period ,574 DVIU were done out of which only 79 patients met the criteria for inclusion and included in our study. The 495 Patients were excluded based on exclusion criteria.

The Mean age was 59.8 ± 14.9 (range: 28 to 94) years. 48 patients (60.7%) did not have any comorbidities (Table 1).

Table 1. Comorbidities

Number = 79	Frequency	Percentage
With comorbidities	31	39.3%
No comorbidities	48	60.7%

Iatrogenic and infectious urethritis accounted for more than three quarter of the USD cases. The most common stricture location was bulbar urethra follwowed by penile and bulbo-membraneous urethra. Nearly 90% Of the patients, had a single stricture,and just over 60% of the patients had a stricture length between 11 and 20mm. Table 2 (etiology, site and length of USD)

Table 2- stricture etiology,location and length

Stricture characterstics		Frequency	Percentage
Etiology	Iatrogenic	32	40.5%
	Infectious	29	36.7%
	Idiophatic	11	13.9%
	Traumatic	9	8.9%
Location	Bulbar	60	75.9%
	Penile	6	7.6%
	Bulbo-membraneous	6	7.6%
	Penile and bulbar	5	6.3%
	Posterior	2	2.5%
Length	≤10mm	9	11.4%
	11 to 20mm	49	62%
	21 to 30mm	12	15.2%
	Multiple sttrictures	9	11.4%

The mean follow-up duration was 31.1± 14.9 (range: 12 to 69) months. The mean time to recurrence was found to be 4.4 ± 4.5 (range:1 to 24) months . The recurrence rate was 57%, 68.4%, 82.3%, and 88.6% at 3, 6,12, and 24 months respectively.

Figure 1- Time to recurrence

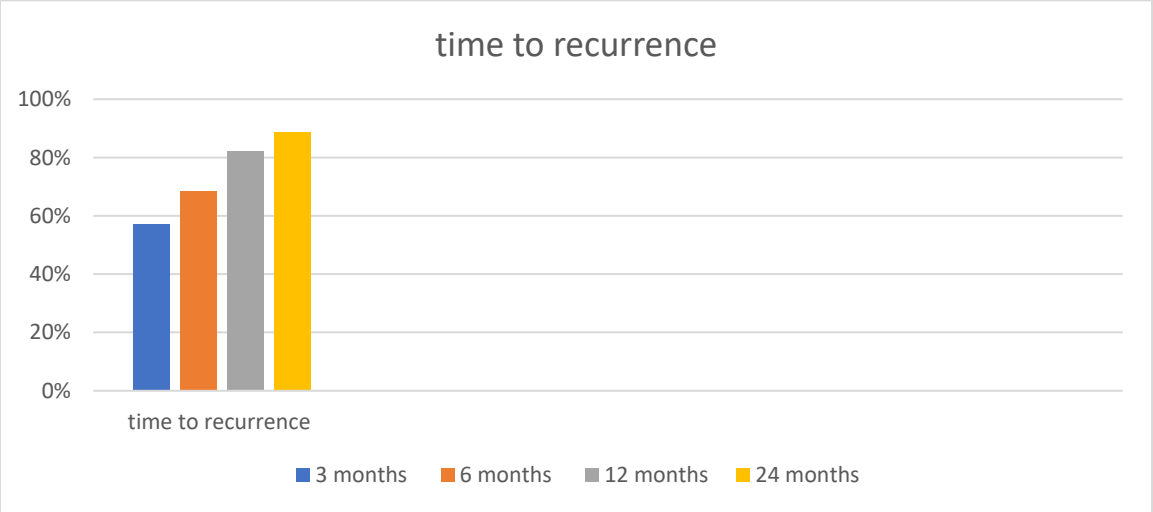


Figure 2 Kaplan-Meier survival curve

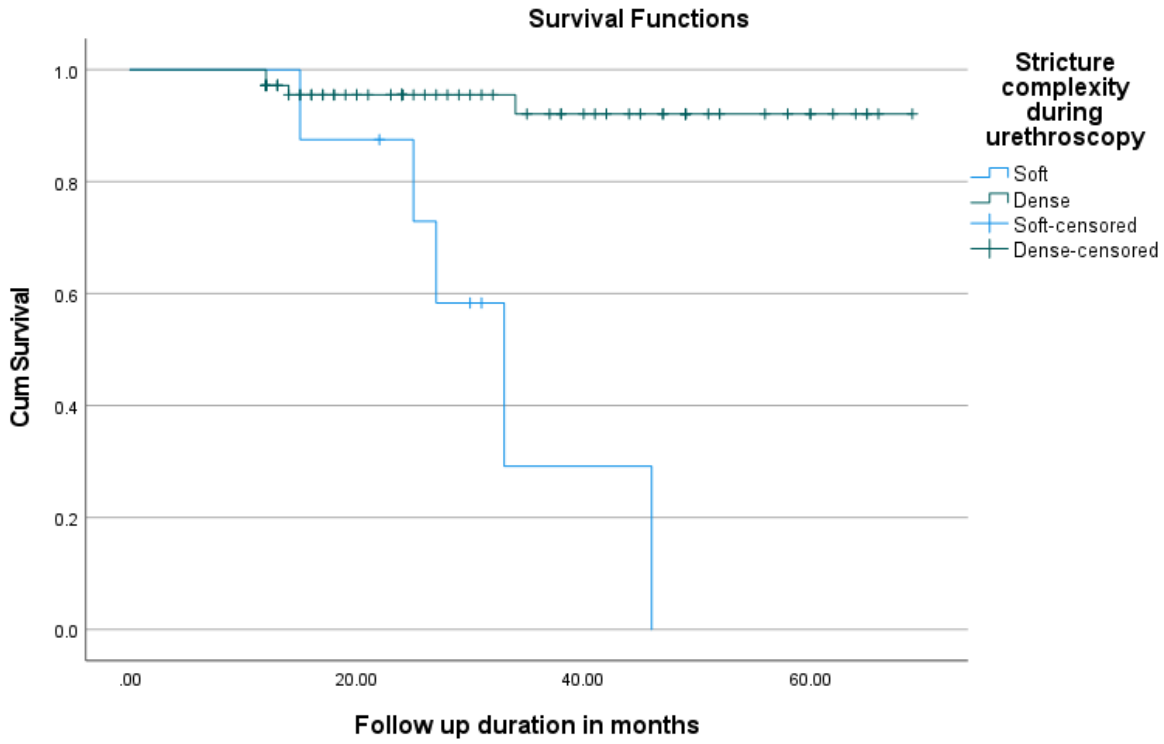
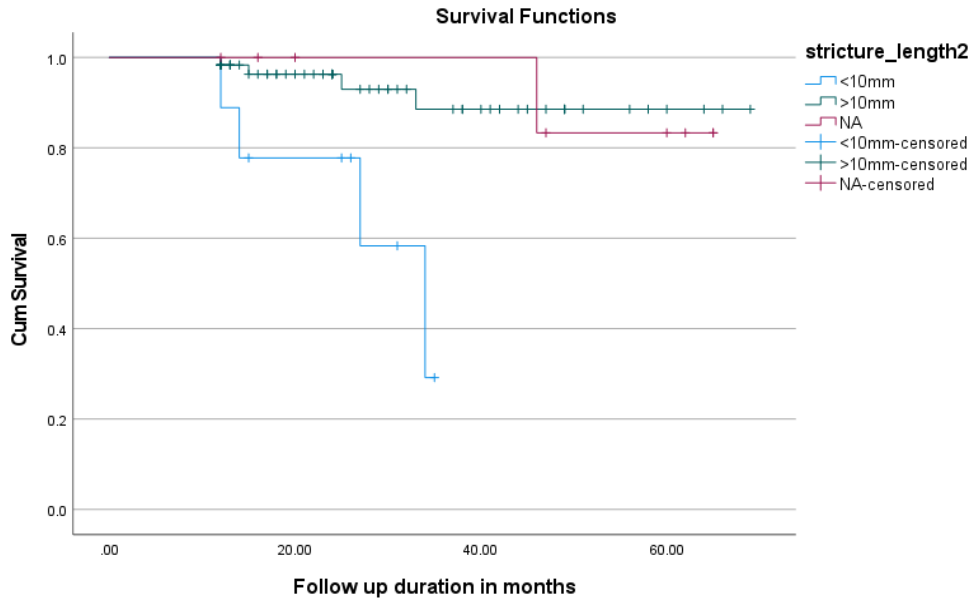


Figure 3 Kaplan-Meier survival curve



Multivariate COX regression analysis showed that soft, non-obliterating stricture and stricture length ≤10mm were significantly associated with recurrence-free survival, with P <0.01 and 0.032 respectively.

Table 3-Univariate and multivariable COX regression analysis predicting recurrence-free survival

Variable		Univariate analysis		Multivariable analysis	
		HR	P-value	HR	P-value
Stricture length	≤ 10mm	9.129	.65	46.9	.032
	11 to 20mm	1.387	.775	3.65	.331
	21 to 30mm	0.001	.979	0.018	.746
Stricture location	Penile	0.947	.997	4.692	0.990
	Bulbar	30.7	.814	8.128	0.982
	Bulbo-membraneous	0.943	.997	3.951	0.991
Stricture etiology	Iatrogenic	10.272	.950	3.951	0.806
	Idiopathic	9.909	.952	4.591	0.775
	Infectious	10.173	.950	4.937	0.758
Stricture type	Soft, non-obliterating	2.546	< .001	14.16	< .001
comorbidity	No	9.370	0.960		
	One or more	10.279	0.956		

Table 4 -univariate and multivariable COX regression analysis predicting treatment failure

Variable		Univariate analysis		Multivariable analysis	
		HR	P-value	HR	P-value
Stricture length	≤ 10mm	2.116	.211	3.437	.151
	11 to 20mm	2.359	.033	3.080	.096
	21 to 30mm	1.448	.429	1.778	.410
Stricture location	Penile	0.449	.335	1.024	.981
	Bulbar	0.412	.227	0.920	.930
Stricture etiology	Iatrogenic	1.056	.898	1.801	.180
	Idiopathic	1.116	.825	0.703	.306
	Infectious	0.797	.601	1.104	.825
Stricture type	Soft, non-obliterating	1.889	0.286	0.483	.241
Comorbidity	No	0.826	0.717	0.492	.591
	One or more	0.210	0.410	0.188	.041

Definition of Terms

Adult patient: In this study adults' patients are those patients above the age of 18 years.

The Success of DVIU: The absence of signs or symptoms of recurrence during a minimum follow-up period of one year (as documented in medical records) will define the success.

Recurrence: Patients will be categorized as having "failed" DVIU if they report symptomatic recurrence (reappearance of symptoms) or if there is a need for additional intervention.

Time-to-Recurrence: is defined as a period in months or years between the date of DVIU and the appearance of a subjective or objective sign of recurrence (if known), or the actual date of the next intervention.

Postoperative Follow-up Duration: Duration of follow-up will be calculated as the period in months or years from DVIU date to the recorded last follow-up visit. The endpoint of the follow-up should be at least one year after the initial urethrotomy.

Discussion

Stricture etiology and location

In the developed world USD is predominantly attributed to trauma(9). Ameta-analysis involving 732 patients ,on etiology of USD found that iatrogenic and idiopathic subtypes were beyond a doubt the most common etiologies, each responsible for 33% of all cases(10). Similarly, in our study, Iatrogenic causes were responsible for a great proportion of strictures (40.5%), while infectious urethritis accounted for 36.7% of cases. This finding is similar to a study in South Africa where iatrogenic causes accounted for the majority(11). However studies from Cameroon and Kenya showed that infectious causes were the commonest etiologies(12,13).

In our study Bulbar urethra was found to be the commonest site of strictures accounting for 75.9% of cases; this is in line with the previous study in Ethiopia by Hagos et. Al. (8) and also most studies we reviewed(14,15).

Overall Failure rate/ Success rate

In this study involving patients with USD who underwent DVIU as a primary intervention, the overall failure rate was found to be 88.6% at a mean follow-up duration of 31.1 months. This is

fairly comparable to studies from Cameron(13) and Egypt(14), where the stricture recurrence rates following DVIU were 85.7% and 91.7% respectively. This is also comparable to a report by Santucci et al(15), where stricture-free survival was only 8% ,after the first urethrotomy.

The success rate in our study is lower than in a study by Barbagli from Italy(2), where the overall failure rate was reported to be 37.5%. This significant outcome difference may be explained by differences in patient selection criteria where they included patients with strictures only in the bulbar urethra. In our study, even though the majority are bulbar urethral strictures, we have also included those in the penile and posterior urethra, which may negatively influence DVIU outcomes, and 89.8% of strictures in our study are obliterating types.

The recurrence rate was also high compared to those reported in Tanzania(16) and two prior studies done in our country by Hagos(8) and Isack(9) showed a failure rate of 12.8% and 35%,respectively. These differences could be explained by the shorter follow-up duration compared to ours, which was one year. Duration of postoperative follow-up is an important element that should be considered when explaining the differences in various DVIU success rates .Success rates close to 10-30%, and 80% with long and short-term follow up respectively had been reported(13).

Association between stricture complexity, length, and success rate of DVIU

Much literature has described that the recurrence rate after urethrotomy is affected by certain stricture characteristics such as stricture length, location, and etiology(17). Our study has clearly showed a statistically significant association between stricture complexity, length, and success rate of DVIU. Soft, non-obliterating strictures and strictures length of ≤10 mm were significantly associated with recurrence-free survival with $P< 0.001$ and 0.032 respectively.

In our study, a stricture length of 11 to 20 mm has shown a statistically significant association with recurrence on univariate COX regression analysis. However, we failed to show a significant association between stricture length, location, etiology, and complexity, and stricture recurrence on multivariable regression analysis. This could be because of our small sample size as opposed to the previously mentioned studies which used large sample sizes.

In their analysis of 450 patients with USD, Pansadoro et al. found that strictures longer than 1 cm had a significant recurrence rate (18). For USD shorter than 1 cm, the success rate was 71%, but

for longer strictures, it was only 18%.Steenkamp et al.(19) showed recurrence rate of approximately 40%,50%, and 80% at 12 months for those USD, less than 2 cm, 2 to 4 cm, and greater than 4cm respectively. In the same context, Barbagali et al. reported 71% success rate for short strictures (1–2 cm) and 47.6% for longer strictures(2).

In our, study Only 4.2% of patients undergo urethroplasty after failed DVIU, while, 62.8% and 32.9 % of patients undergo dilation and repeat DVIU respectively. Further 10.3 % undergo urethroplasty after multiple failed DVIU and dilation. The remaining 89.7 % are still on dilation or having multiple DVIU or discontinued Follow-up.

Limitations of the study

Due to the retrospective and uncontrolled nature of the study, a sizable portion of patients were not included since the stricture characteristics were not adequately described, which reduced the sample size.Patients with clear indications of urethroplasty were included in the study which can contribute to a high failure rate

Conclusion

DVIU has a high failure rate and should be used as a temporary or palliative measure until definitive urethroplasty is performed or in selected patients when they are at high risk for undergoing a definitive procedure**.** We recommend that DVIU be performed only when the stricture is soft, non-obliterating, and has a length ≤ 10mm.

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Authors' contributions

S.A: prepaired the proposal and tool for data collection ,collected the data, wrote the manuscript, and analyzed the study. B.K: proofread the manuscript. AM: assisted with the reviewing of final manuscript

Funding

There was no funding utilized for the study.

Availability of data and materials

Source data will be available upon reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate

We obtained ethical approval for the study from Addis Ababa University, College of Health Sciences, institutional review board. Data extracted from the patient's medical records were kept confidential. This was a retrospective study utilizing patients electronic medical records, and no direct written consent was needed as there was no contact with the patients themslves.

Consent for publication

Not applicable since no direct written consent was needed to this study.

Competing interests

The authers declare that there were no competing interests

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