FACTORS ASSOCIATED WITH RECURRENCE OF ANTERIOR URETHRAL STRICTURE FOLLOWING DIRECT VISION INTERNAL URETHROTOMY

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FACTORS ASSOCIATED WITH RECURRENCE OF ANTERIOR URETHRAL STRICTURE FOLLOWING DIRECT VISION INTERNAL URETHROTOMY

By

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Dissertation Submitted In (Partial) Fulfilment of the Requirements for the Degree of Masters of Medicine in Urology.

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CERTIFICATION

The undersigned, certify that they have read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation titled: ***"Factors Associated with Recurrence of Anterior Urethral Stricture Following Direct Vision Internal Urethrotomy"*** in fulfillment of the requirements for Award of the Master of Medicine in Urology of Muhimbili University of Health and Allied Sciences.

_____

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Date:_____

_____

Dr. Isaack Mlatie

(Co-Supervisor)

Date:_____

DECLARATION AND COPYRIGHT

I **Philipo Felix** declare that this dissertation is my original work and has not been presented and will not be presented to any other Higher Learning Institution for a similar or any other degree award.

Signature: …… Date: …….

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DEDICATION

I dedicate my work to my family and classmates, for their support and drive to my dissertation completion.

ABSTRACT

Background: Anterior urethral stricture is a common urological condition that often requires surgical intervention, such as direct vision internal urethrotomy (DVIU), for treatment. Despite the initial success of DVIU, recurrence remains a significant concern. Identifying factors associated with recurrence of anterior urethral stricture can aid in patient management and improve outcomes.

Objective: This study aims at determining factors associated with recurrence of anterior urethral stricture following DVIU among patients attending at Muhimbili National Hospital.

Methodology: Between March 2018 and February 2023, a retrospective evaluation was conducted on 177 patients who underwent DVIU for urethral stricture. Data, including risk factors and preoperative workups were collected. Patients were divided into recurrence and non-recurrence groups based on postoperative outcomes, bivariate and multivariate analysis was done to compare association between sociodemographic factors, clinical factors and recurrence of anterior urethral stricture following DVIU.

Results: In this study, 42 patients (24%) experienced stricture recurrence after DVIU, while 135 patients (76%) did not. Only patient age and stricture length had statistical significant association with recurrence of anterior urethral stricture following DVIU within five years of follow up. Patients with age of 60 years and above had higher chances of stricture recurrence following DVIU than younger ones. (p- value 0.04). The average age of patients with recurrence was 66±15 years, compared to 64±16 years. Recurrence occurred on average 2.6 months after DVIU, ranging from 1 to 49 months.

The results indicated that stricture length above 1 centimeter (p-value < 0.001) exhibited statistically significant associations with recurrence of stricture. After adjusting for confounders, it was found that patient's stricture length and age has an independent

association with recurrence. As patients with strictures equal to 1 cm were five times [aOR=5.19 (2.36 - 11.41)] more likely to have recurrence compared to those with structure less than 1 cm, with the difference being statistically significant (p-value < 0.001)

There was with no statistical significant difference between neutrophil count and neutrophil to lymphocyte ratio among patient recurrence and those without recurrence of anterior urethral stricture.

Conclusion: The findings from this study demonstrated that older patients of age 60 years and above have higher chances of stricture recurrence than younger ones (p-value 0.04) also patients with strictures equal to 1 cm are five times [aOR=5.19 (2.36 - 11.41)] more likely to have recurrence compared to those with stricture less than 1 cm, with the difference being statistically significant (p-value < 0.001).

Keywords: Urethral stricture, Direct vision internal urethrotomy. Stricture recurrence, predictors of stricture recurrence.

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LIST OF ABBREVIATIONS

AUC	Area under the curve
BMI	Body Mass Index
DRP	Director of Research and Publication
DVIU	Direct Vision Internal Urethrotomy
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Science
NLR	Neutrophil to lymphocyte ratio
NPP	Negative Predictive Value
PPV	Positive Predictive Value
ROC	Receiver Operator Characteristics

DEFINITIONS OF TERMS

Urethral stricture refers to fixed anatomic narrowing of the urethra so that the lumen will not accommodate instrumentation without disruption of the urethral mucosal lining.

Anterior urethral stricture refers to a stricture involving the urethra that is surrounded by the corpus spongiosum.

Direct Vision Internal Urethrotomy (DVIU) is a surgical technique employed to address urethral stricture it involves making an endoscopic incision, under sedation or anesthesia (spinal or general), using a cold knife. This incision is performed at the 12 o'clock position with the assistance of a guide wire.

Neutrophil-to-lymphocyte ratio (NLR): - The neutrophil-to-lymphocyte ratio (NLR) is a biomarker that reflects the balance between neutrophils and lymphocytes in the peripheral blood, representing two essential aspects of the immune system: the innate immune response primarily involving neutrophils and the adaptive immunity supported by lymphocytes

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Urethral stricture stands as a prevalent condition affecting the urethral tract, particularly in male patients. Symptoms can vary from being entirely asymptomatic to experiencing reduced urine flow, increased urination effort, a hesitancy, a sense of incomplete urination, and, in severe cases, urinary retention [1]. The phrase ‘urethral stricture’ is customarily used to describe stricture occurring specifically in the anterior segment of the urethra. Essentially, it denotes a narrowing within the urethral passages, secondary to urothelial damage and the subsequent development of fibrous tissue within the urethral passages, situated within the corpus spongiosum [2]. Anterior urethral stricture affects individuals of all ages and has a global prevalence of 0.6% [3]. The prevalence of urethral stricture remains undetermined in Sub-Saharan Africa, although limited epidemiological research suggests it presents a substantial healthcare challenge in the region. Over time, there has been a worldwide shift in the epidemiological patterns and treatment strategies for urethral stricture, with the extent of this transformation influenced by variations in the regional and sub regional economic landscapes [4,5].

Anterior urethral stricture, specifically, can be caused by conditions such as infection from sexually transmitted diseases like gonorrhea and Chlamydia, prostatectomy, urethral catheterization, transurethral resection of the prostate, cystoscopy, brachytherapy, hypospadias surgery, lichen sclerosis, infection, urethral tumor, perineal trauma, pelvic fracture, and, in some cases, the cause may be idiopathic [6]. It’s worth highlighting that approximately 30% of urethral strictures are considered idiopathic. Nevertheless, even minor damage to the urethral lining can result in urine seeping into the spongy tissue, triggering fibrotic responses within that tissue. The incidence of urethral narrowing ranges from 200 to 1200 cases per 100,000 individuals, with a significant rise observed in those aged 55 and above. In most developed nations, the estimated prevalence of urethral stricture stands at approximately 0.9% [7].

Older men and individuals of African-American descent are more prone to developing this condition [8].

In cases of urethral strictures, all available treatments focus on maintaining the patency of the urethral lumen for as long as possible. The two main treatment options currently employed are direct vision internal urethrotomy (DVIU) and urethroplasty [9]. Urethral dilatation and urethral stenting may also be considered for certain patients. The choice of treatment depends on the patient's overall health and the characteristics of the stricture. Urethroplasty is typically preferred for long or recurrent strictures, as it addresses the underlying processes leading to the development of strictures [10][11]. DVIU involves incising the fibrous tissue causing the stricture using endoscopic visualization, providing initial symptom relief and improved urine flow. However, recurrence of urethral stricture remains a significant challenge following DVIU [12–14]. As endoscopic procedures can disrupt the smoothness and integrity of the urethral mucosa and alter the microstructure of the corpus spongiosum, recurrence often occurs [15,16]. The recurrence rates after DVIU have been reported to range from 23% to 92% within the first year, and these rates tend to increase with longer follow-up periods [16–18]. Recurrent strictures often necessitate repeated interventions, impacting the patient's quality of life and healthcare costs. Therefore, there is a pressing need to identify reliable predictive factors that can help urologists stratify patients at higher risk of stricture recurrence and tailor their management accordingly.

Recurrence risk assessment models for anterior urethral stricture following procedures like DVIU often involve a combination of clinical and demographic variables. While there are no universally accepted models specifically for anterior urethral stricture recurrence, clinicians may utilize elements from related studies and adapt them to their patient populations [16]. Common variables like age, comorbidities, complications and urodynamic testing may be included in such models. Older individuals may have a higher risk of recurrence [11]. Certain medical conditions, such as diabetes or chronic urinary tract infections, may increase the risk of stricture recurrence [12,19,20].

Complications during or after DVIU, such as bleeding or infection, can influence recurrence risk [18]

An important part of managing urethral strictures is identifying patients who are susceptible to developing recurrent strictures or who are at risk of doing so. By identifying the risk factors, the processes that lead to stricture can be stopped before they start or worsen. Our goal was to look into how patients with primary anterior urethral strictures measuring less than 1 cm responded to traditional treatment during their follow-up period. In patients with recurrent urethral stricture, we also assessed potential predictors of recurrence

1.2 Problem Statement

Anterior urethral stricture is a frequently encountered urological condition, often requiring surgical intervention in the form of urethral dilatation, DVIU or urethroplasty. While DVIU can provide initial relief from obstructive symptoms, the persistent challenge of stricture recurrence remains a substantial concern within urological practice. In Tanzania prevalence of anterior urethral stricture at Muhimbili national hospital was observed to be 74.3% by Nyongole et al[5].

In a study done in Turkey by Aydemir the prevalence of recurrence of anterior urethral stricture following DVIU was 27.6% after one year of follow-up.[21].

Reconstructive urologists with experience managing strictures should handle male anterior urethral stricture disease, as it presents a complex surgical challenge. Anatomic narrowing and patient symptoms found on validated questionnaires are both necessary for the diagnosis of recurrence, with little room for intervention in cases of asymptomatic treatment "failures." When it comes to recurrence, endoscopic management plays a very specific role, and pre-operative urethrography and cystoscopy determine the best urethroplasty technique.

Due to the tendency of stricture recurrence post DVIU A study done by wright et al recommended that urethroplasty should be treatment of choice if an individual has a total of two consecutive failed DVIU or if the success rate of endoscopic procedures is less than 35%[22].

1.3 Conceptual Framework

The conceptual relationship centers on evaluating factors associated with recurrence of anterior urethral strictures following DVIU. It evaluates how factors such as stricture length, location, etiology, age and patient comorbidity influence stricture recurrence among patients who have received DVIU as a treatment modality of urethral stricture at Muhimbili National hospital.

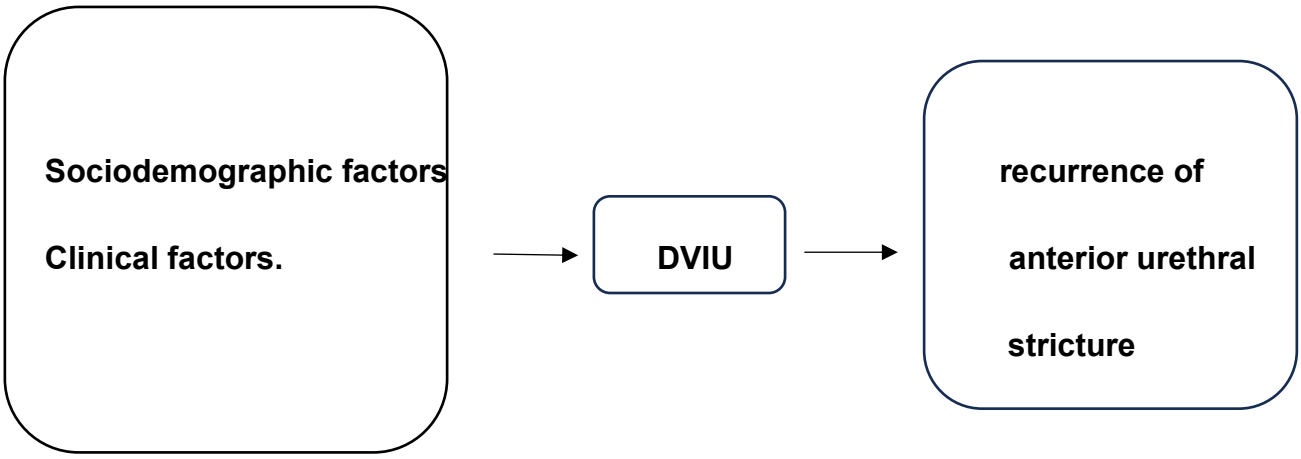


Figure 1: Conceptual Framework Illustration by the researcher

The conceptual relationship between these variables can be described as follows:

Sociodemographic factors such as patient age,patient clinical factors such as stricture length, com comorbidities, etiology of stricture nutritional status contributes in recurrence of anterior urethral stricture. Furthermore elevation of inflammation based

prognostic markers such as NLR could be used to predict stricture recurrence following DVIU. The study aims to identify the correlation between these factors and to give clinicians foundation of making jugdement in managing urethral stricture.

1.4 Rationale

This study will provide highlight to clinicians on the factors which predict recurrence of anterior urethral stricture and also help clinicians in preventing recurrence. The study seeks to contribute valuable insights into risk assessment and the optimization of postoperative care in the management of anterior urethral strictures and also to alert surgeons on the presence of factors which may lead to stricture recurrence e.g. stricture length, age and inflammatory status so that they take measures to minimize chances of recurrence. This will help clinicians to understand when to do and when not to do DVIU.

1.5 Research Questions

1.5.1 Primary Research Question

What are the factors associated with the recurrence of anterior urethral stricture following DVIU among patients treated at Muhimbili National Hospital?

1.6 Research Objectives

1.6.1 Broad Objective

To describe factors associated with the recurrence of anterior urethral stricture following DVIU among patients treated at Muhimbili National Hospital.

1.6.2 Specific Objectives

1. Describing sociodemographic characteristics of patients with anterior urethral stricture recurrence following DVIU among patients treated at Muhimbili National Hospital.
2. To determine the prevalence of recurrence of anterior urethral stricture following DVIU among patients treated at Muhimbili National Hospital.
3. To determine clinical factors associated with recurrence of anterior urethral stricture following DVIU among patients treated at Muhimbili National Hospital.

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CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Sociodemographic characteristics of patients with anterior urethral stricture recurrence following DVIU among patients treated at Muhimbili National Hospital

A number of studies have shown that sociodemographic characteristics of patients such as age has great influence on recurrence of anterior urethral stricture.

In a study done by Galves it revealed that 56.7% of patient with recurrence of anterior urethral stricture had age above sixty years[23]. Another study by Aydemir showed that patient with anterior urethral stricture had a mean age of 67.2 [21]. Another study done by Issack was in alignment with this findings whereby it was observed that patient with anterior urethral stricture had a mean of fifty four years and median age of fifty eight years[22].

2.2 Prevalence of recurrence of anterior urethral stricture following DVIU in the study population among patients treated at Muhimbili National Hospital.

Stricture recurrence has been the most embarrassing challenge to both patients and urologist attending these cases with varying prevalence among different studies**.** One of the major challenges in managing anterior urethral stricture is the recurrence of the condition, which can significantly impact patients' quality of life and healthcare costs. This literature review provides an overview of the prevalence of anterior urethral stricture recurrence, highlighting key findings from relevant studies.

Studies investigating the prevalence of anterior urethral stricture recurrence have reported varying rates. Basaif and colleagues in their systematic review illustrated that the stricture recurrence rate following interventions involving internal urethrotomy and direct vision internal urethrotomy reached 65% within a three-year timeframe [24]. Aydemir et al. conducted a retrospective study and found that approximately 27.6% of

patients experienced stricture recurrence within the first year following DVIU [21]. Additionally, other studies have indicated recurrence rates of approximately 14% at the six-month mark post-internal urethrotomy, with figures climbing to as high as 27% after 12 months [14,18]. Another retrospective study was done over seven years by Galves et al whereby prevalence of recurrence of stricture following DVIU was 37% [23]. Another similar study was done in Nigeria by Okpani to to asses disease course of urethral stricture following DVIU whereby and 7.6% of patients had recurrence [25]. In the context of Sub-Saharan Africa, addressing urethral stricture has presented an enduring clinical complexity, particularly due to the persistent issue of recurrent strictures.

Most of the available studies on this topic are conducted in different geographic regions with potentially varying patient populations, healthcare systems, and risk factors. Therefore, it is essential to establish a Tanzanian-specific understanding of stricture recurrence rates to tailor treatment approaches and patient counseling more effectively.

2.3 Determining clinical factors associated with recurrence of anterior urethral stricture following DVIU among patients treated at Muhimbili National Hospital.

History of urethral instrumentation like urethral catheterization or prior history of endoscopic surgery like TURP was observed to be a risk factor in stricture recurrence in a number of studies.

. It was also observed that there was a significant correlation between stricture length and increase in number of DVIU[21]. One of the pivotal findings in Pallares-Méndez et al's study contributes valuable insights into the multifaceted landscape of urethral stricture recurrence prediction. Age, obesity, and a history of previous urethral surgery emerge as pivotal factors that clinicians should consider when assessing recurrence risk. Recognizing these variables empowers healthcare providers to offer more accurate prognostic information to patients and guide treatment decisions that align with the unique characteristics and needs of each individual. Nonetheless, further research is essential to validate these findings and refine risk assessment models for

improved stricture recurrence [26]. Aging leads to tissue changes, including reduced elasticity and regenerative ability. These age-related alterations may increase vulnerability to fibrosis and stricture formation in the urethra.

Kay et al. conducted a comprehensive analysis and identified obesity as a substantial prognostic factor for recurrence, demonstrating its significance within both the entire patient cohort and specifically among individuals who underwent anterior anastomotic urethroplasty [27]. This finding aligns with existing evidence highlighting the well-established perioperative risks and comorbidities associated with a body mass index (BMI) exceeding 30 [28]. Notably, Chapman et al., in their study encompassing 596 patients undergoing isolated bulbar urethroplasty, also ascertained obesity as an autonomous predictor for the recurrence of urethral stricture [29]. While a singular causative mechanism for the heightened perioperative risk observed in obese individuals remains elusive, the correlation between obesity and systemic chronic low-grade inflammation, compromised collagen regeneration, and vascular inadequacies has been documented [30]. Obesity could potentially compromise surgical visibility and consequently hinder the technical feasibility of a procedure, particularly in cases involving proximal bulbar strictures [31]. These factors collectively may contribute to the susceptibility of treatment complications and the recurrence of strictures.

Per findings from Kay et al., it's noteworthy that both stricture length ≥ 5 cm and recurrence maintained their status as significant indicators of postoperative complications. The predictive value of stricture length is intuitive, as longer strictures frequently necessitate more intricate surgical interventions and present a larger potential area for recurrence [27]. Conversely, other studies have indicated an association between stricture lengths exceeding 4 cm and the recurrence of strictures following urethroplasty [32].

In their study, Kay and colleagues added to the complexity by demonstrating that patients with penile strictures exhibited significantly reduced likelihood of stricture recurrence[27]. This finding diverges from earlier studies, some of which reported no

discernible influence of stricture location on recurrence [33], while Meeks et al. suggested that bulbar strictures were less prone to recurrence [34]. The considerable divergence in the literature regarding the impact of stricture location might be attributed to the inherent challenges of controlling for all potential confounding variables in this complex field. Variables such as surgical technique, cohort sizes, and unaddressed confounding factors have contributed to the inconsistency in findings across studies [29], making it challenging to derive definitive conclusions regarding the role of stricture location in recurrence.

The most common cause of urethral stricture was found to be inflammatory followed by traumatic cause by 52.4% and 42.6% respectively Okpani et al[25].

Another factor which may be used to predict recurrence of anterior urethral stricture is neutrophil to lymphocyte ratio obtained from routine full blood picture taken one day prior to DVIU.

Krane et al. showcased in their research that in contemporary times, there is mounting evidence indicating that the NLR can serve as an indicator of chronic systemic inflammation and is closely linked with prognostic outcomes across a spectrum of cardiovascular diseases, malignancies, and chronic inflammatory conditions [35]. Furthermore, Grimes et al. highlighted that these biomarkers have previously been examined in diverse uro-oncological scenarios, revealing their significant utility in predicting postoperative surgical margin status and influencing progression-free survival [36]. In another study where an NLR threshold of 2.7 was considered, findings indicated that the amalgamation of tumor stage and NLR could be employed for evaluating the recurrence risk among non-metastatic renal cell carcinoma patients [37]. Similarly, another research demonstrated that within non-clear-cell kidney tumors, NLR emerged as an autonomous prognostic determinant influencing disease-free survival following curative surgery. Consequently, NLR has been identified as a noteworthy indicator guiding patient counseling and informing the structure of clinical trial protocols [38].

Inflammation has the ability to trigger fibrotic processes that ultimately lead to stenosis and blockage, especially when chronic inflammation persists inside luminal organs. Inflammatory indicators have been proposed as feasible predictive variables in the development of restenosis and blockage based on this concept. An analysis by Qian et al. examined inflammatory markers in cohorts with and without restenosis in a study comprising 261 individuals with coronary artery problems. The results of the study highlighted the viability of using these markers as independent prediction biomarkers for the emergence of restenosis [39]. A study investigating the link between inflammation and peripheral artery disease was undertaken in 2019 by Velioglu and Yuksel. Their research led them to the conclusion that the severity of peripheral artery disease and an increased NLR, a well-known inflammatory measure, are directly correlated [40]. The degree of inflammation in tissues that contain lumens was used by Urkmez et al. in their study as a predictor of luminal disease, particularly in patients having internal urethrotomy. The use of NLR allowed for the prediction of tissue inflammatory features and the estimate of probable post-surgical recurrences, especially in situations of frequent and recurring stricture [11]

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

A retrospective cohort study was conducted at MNH to assess the factors associated with recurrence of anterior urethral stricture following DVIU from March 2018 to February 2023.

3.2 Study Area

This study took place at MNH which is located in Dar es salaam, Tanzania. The hospital serves as a major healthcare institution in the region and is renowned for its comprehensive medical services as well as teaching hospital for Muhimbili University of Health and Allied Science (MUHAS). The Department of Urology at MNH is equipped with state-of-the-art medical facilities and equipment required for the diagnosis, treatment, and research related to urological conditions. These facilities include operating rooms, diagnostic imaging equipment, outpatient clinics, and laboratories. Urology clinic serves around 21860 patients annually, and about 168 DVIUs are performed every year. The department houses a team of highly skilled urologists, surgeons, nurses, and support staff with expertise in the management of urological disorders. They play a critical role in patient care, surgical interventions, data collection, and the overall conduct of the research study.

3.3 Study Population

The primary focus of the study is patients diagnosed with anterior urethral stricture. This population includes individuals who have previously undergone DVIU as part of their treatment for urethral stricture. Specifically target patients are those who have experienced recurrence of anterior urethral stricture after their initial DVIU procedure.

3.4 Inclusion and Exclusion Criteria

3.4.1 Inclusion Criteria

i. Participants with a confirmed diagnosis of anterior urethral stricture. This diagnosis can be based urethroscopy findings, urethrogram or prior medical records.
ii. Those who have undergone a DVIU procedure as part of their treatment for anterior urethral stricture.
iii. Patients with full blood picture results taken before their DVIU procedure mainly for obtaining Neutrophil count and lymphocyte count in order to obtain Neutrophil to lymphocyte ratio.

3.4.2 Exclusion Criteria

i. Participants with missing or incomplete NLR measurements were excluded.
ii. Individuals with comorbid medical conditions that could significantly impact NLR values or stricture recurrence were excluded. These include conditions such as malignancies, active urinary infection and uncontrolled DM.
iii. Individuals who have previously undergone urethroplasty were excluded since these procedures may confound the study results.

3.5 Sampling Strategy and Calculation

3.5.1 Sampling Technique

Given the nature of the study, consecutive sampling was employed. Eligible patients who have previously undergone DVIU for anterior urethral stricture were identified from the patient population at the Department of Urology at MNH. Patients who met the inclusion criteria were consecutively enrolled in the study depending on availability of their records within the study period.

3.5.2 Sample size and technique

The minimum sample size was determined using a formula below. The formula incorporates a number of key parameters, including the desired level of statistical significance, expected effect size, power of study and variability of the outcome measure. By systematically accounting for these factors it was aimed to calculate a sample size that optimally balances statistical rigor with practical considerations such as feasibility and resource constraints.

$$n = 2\frac{x\ (Z\alpha/2 + Z\beta)^2 x \sigma^2}{\delta^2}$$

Where

n = desired sample size

Zα/2= Z value corresponding to the desired level confidence interval

Zβ = Z value corresponding to the desired power of study

σ²= variance (or standard deviation) of the outcome variable in the population (equal to 2)

δ= minimum clinically relevant difference (effect size) to be detected (0.5)

substituting the values;

$$n = \frac{2x(1.96+0.84)^2x2}{0.5^2} = 125$$

Through calculation, the minimum sample size of 125 patients was concluded, but in this study 177 patients meeting the inclusion criteria were obtained.

3.6 Study Variables

Independent Variable:

i. Sociodemographic factors.
ii. Clinical features of urethral stricture.
iii. Measurement: NLR was measured from full blood picture results from samples taken before the DVIU procedure.

Scale: Continuous numerical scale.

Dependent Variable: Anterior Urethral Stricture Recurrence

i. Measurement: The occurrence or absence of stricture recurrence following DVIU within a specified follow-up period.
ii. Scale: Binary (1 for recurrence, 0 for no recurrence).

Prevalence of Recurrence

i. Measurement: Proportion of patients who experience stricture recurrence within the defined follow-up period.
ii. Scale: Percentage (0-100%).

Preoperative Clinical Parameters

i. Measurement: Various patient-specific clinical parameters such as age, comorbidities, and other relevant characteristics.
ii. Scale: Continuous numerical scale for age; categorical for comorbidities (e.g., yes/no).

3.7 Data Collection Methods

Data from all individuals who meet criteria to be included in the study were collected using a standardized questionnaire. Since the study was retrospective, waiver for consent was obtained from Director of Research and Publication (DRP) MUHAS. Relevant medical records and patient histories were reviewed to gather baseline information, including demographic data, medical history, and details of the initial DVIU procedure. NLR measurements were obtained through patient records obtained from Jeeva system. This measurement serves as a key variable for the study. All collected data, including demographic information, NLR measurements, clinical findings, and recurrence status, were recorded in a structured database for analysis.

In this study, the main aim was to identify factors associated with recurrence of anterior urethral stricture following direct vision internal urethrotomy. This involved sociodemographic factors as well as clinical factors and to describe how they contribute in the recurrence of anterior urethral stricture in patients who underwent Direct vision internal urethrotomy as treatment.

In this study, the gold standard model for calculating the accuracy of NLR as a predictive factor for the recurrence of anterior urethral stricture post-DVIU was typically the clinical assessment and diagnosis of stricture recurrence by healthcare professionals. This means that the gold standard is the clinical judgment made by experienced urologists or medical practitioners based on a combination of diagnostic criteria, including symptoms, physical examinations, imaging studies (e.g., urethrography), and possibly additional procedures (e.g., cystoscopy) to confirm stricture recurrence. Results of NLR-based predictions of stricture recurrence were compared with the clinical diagnosis made by healthcare professionals.

DVIU was done under spinal anaesthesia using a 21F urethrotome, the urethrotomy was performed under vision with a cold-knife incision of the stricture at the 12 o’clock position according to the technique described by Sachse. A 16–18Fr. indwelling

catheter was left for 2-7 days. Patients were evaluated postoperatively by clinical improvement of symptoms and with uroflowmetry monthly for the first 3 months, every 3 months during the first year and every 6 months during the second year. After year 2 most patients were followed annually. When the peak flow was less than 15ml per second, urethrogram or urethrocystoscopy was performed to exclude recurrent stricture. Patients who had low maximum flow rate on uroflowmetry (Q max) less than 10ml per second required repeat direct vision internal urethrotomy or urethroplasty basing on the assessment of the treating urologist.

3.7.1 Recruitment of Research Assistants

Two assistants were hired for the research work during the data gathering exercise, both with experience in the clinical field. They received instruction on the purpose of the study and the protocols to be followed during data collection from the primary investigator, who also supervised them throughout that time. The training provided to the research assistants covered the data collecting instrument as well as ethical issues in research.

3.8 Investigation tool Validity and Reliability

Using a sample of male patients from the Urology department at MNH, the validity and reliability of research tool was assessed. A preliminary evaluation involving ten adult males was conducted to gauge the accuracy and internal consistency of the checklist. The responses from the pilot test provided valuable insights into the level of consistency and accuracy of the questionnaire’s questions. Any identified discrepancies led to adjustments in the instrument.

3.9 Data Management and Analysis

3.9.1 Data Management

Microsoft Excel was used to process the data after it has been collected. Before beginning the analysis, quality control checks were done to make sure the data was obtained accurately and completely.

3.9.2 Statistical Analysis

The statistical analysis was conducted using IBM SPSS Statistics 27 software. The study data underwent evaluation via the Shapiro-Wilks test to assess distribution, revealing that the parameters were determined to be non-normally distributed.

A. **Objective I:** Bivariate and multivariate analysis was used to compare the influence of age of patient between the two groups of recurrences and non-recurrence of urethral stricture following DVIU.
B. **Objective II:** The prevalence of recurrence was determined by calculating the proportion of patients who experienced recurrence out of the total number of patients included in the study. This calculation was performed by dividing the number of patients with recurrence by the total number of patients and expressing the result as a percentage.
C. **Objective III** Chi-square test was used to assess correlations between preoperative clinical parameters (e.g., age, stricture length, NLR, comorbidities) and stricture recurrence. Multivariate regression analysis was performed to identify independent predictors of stricture recurrence while controlling for potential confounders. $P < 0.05$ and 95% confidence intervals determined the statistical significance of associations and correlations. Summary statistics (mean, median, standard deviation) for NLR values were calculated in both groups (recurrent and non-recurrent). Mann-Whitney U tests was performed to compare NLR values between the two groups.

3.10 Ethical considerations and Approval

The MUHAS research and publications committee was responsible for obtaining ethical approval, and the MNH administration granted permission to conduct the study. We ensured the confidentiality of all data generated during the research, and only the individuals directly involved in the study had access to the information. The gathered data were used solely for research purposes and for publishing the results.

3.11 Limitation of the study

The procedure books may not have comprehensive documentation of DVIU procedures, which could result in missing information. To address this, a comparison was conducted between the procedure books, the hospital's operation listing in the Jeeva system, and the operating notes present in the files. This comparison aims to identify any gaps or discrepancies in the documentation of DVIU procedures and ensure a comprehensive understanding of the performed surgeries. Since this was a retrospective study some of patients might lost to follow up if they won’t return to clinic for follow-up or if they receive treatment of recurrent stricture in other health facilities. Also, the number of participants found in the study was relatively lower compared to previous studies. This led to significant difference in findings and expected outcomes.

CHAPTER FOUR

4.1 ANALYSIS AND PRESENTATION OF FINDINGS

4.1.1 Patients Demography and Prevalence of Stricture Recurrence Post DVIU

A total of 177 patients were enrolled in the research study. The youngest respondent was 20 while the oldest one was a 94 years old man. The average age of patients who experienced recurrence following DVIU was 65±15 years, while for those who did not experience recurrence, it was 64±16 years. There was no statistically significant difference in the average ages between these two groups. The follow-up period for patients without recurrence after DVIU averaged 49±1.4 months, spanning from 6 to 60 months, with a median follow-up of 30 months. Conversely, for patients who experienced recurrence, the average follow-up duration after DVIU was 33.2±8.1 months, ranging from 3 to 60 months, with a median follow-up of 9 months. Throughout the follow-up period after the initial DVIU procedure, 40 patients (22.6%) had recurrences, while 137 patients (77.4%) did not experience recurrences. The mean duration until recurrence after DVIU was 2.6 months, with a range from 1 to 49 months, and a median of nine months. Neutrophil and lymphocyte levels were measured in all patients as part of routine anesthesia assessment and pre-operative preparation.

Table 1: Patient Demography and Prevalence of Stricture Recurrence after DVIU, N=177

Variable	Frequency (%)
Age (years)	Mean 65 (20-94)
Recurrence	
Yes	42(24)
No	135 (76)
Follow up duration (months)	Mean 49 (1-60)
Recurrence period	Mean 2.6 (1-49)
Comorbidities	
Hypertension	68 (38.4)
Diabetes	24 (13.6)
Previous urethral surgery	
Yes	75 (42.3)
No	102 (56.7)

Regarding comorbidities, 38.4% of participants had hypertension, 3.6% had diabetes. Additionally, 42.4% (75 out of 177 patients) had a prior history of urethral surgery before undergoing DVIU.

4.1.2 Prevalence of anterior urethral stricture recurrence post-DVIU among participants

Among the 177 participants, the majority (n=135; 76%) had no recurrence of stricture with only (n=42; 24%) of patients who underwent DVIU has a recurrence. Among those who experienced recurrence, the average duration until recurrence was 11.3 ± 12.1 months, with an average initial stricture length of 1.36 ± 0.33 cm."

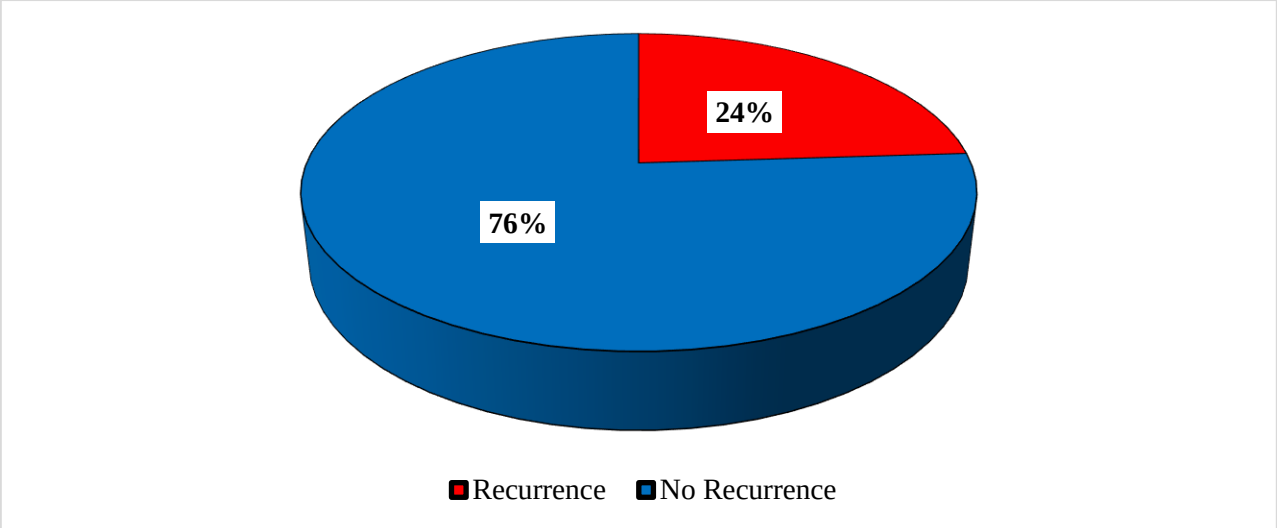


Figure 2: Proportion of patients with anterior urethral stricture recurrence post-DVIU

4.1.3 Factors associated with recurrence of stricture post-DVIU

The relationship between recurrence of stricture after DVIU and several social and clinical characteristics was analyzed using a chi-square test at a statistically significant level of $p < 0.05$. These factors including include patient age, comorbidities, stricture length, stricture location and stricture etiology. The results indicated that only stricture length (p-value < 0.01) and patient age of 60years and above (P-value = 0.04). exhibited statistically significant associations with recurrence of stricture. After adjusting for confounders, it was found that patient's stricture length and age has an independent association with recurrence. As patients with strictures longer or equal to 1 cm were five times [aOR=5.19 (2.36 - 11.41)] more likely to have recurrence compared to those with structure less than 1 cm, with the difference being statistically significant (p-value < 0.01). With those aged 60 years or above were two times [aOR=2.75 (1.02 - 7.40)] more likely to have recurrence compared to those aged below 60 years

Table 2: Factors associated with recurrence of stricture after DVIU

	Recurrence Status		Bivariable Analysis	Multivariable analysis	
Variables	**Reccur (n=42)**	**No Reccur (n=135)**	**Crude OR**	**aOR(95% CI)**	**P-value**
Age Category					
≥60 years	35	94	2.18 (0.89 - 5.31)	2.75 (1.02 - 7.40)	P = 0.04
<60 years	7	41	*Reference*	*Reference*	
Stricture length					
≥ 1 cm	29	41	5.11 (2.42 - 10.83)	5.19 (2.36 - 11.41)	P < 0.01*
<1 cm	13	94	*Reference*	*Reference*	
Stricture Location					
Bulbar Urethra	36	126	0.71 (.133 - 3.84)	0.59 (0.07 - 4.85)	P = 0.63
Bulbar and Membranous	3	4	1.88 (0.20 - 17.27)	1.19 (0.09 - 16.43)	P = 0.89
Penile and Bulbar Urethra	2	5	1	1	
Penile Urethra	1	0	*Reference*	*Reference*	
Stricture etiology					
Iatrogenic	21	62	0.47 (.14 - 1.66)	0.40 (0.09 - 1.73)	P = 0.22
Idiopathic	16	57	0.39 (0.11 - 1.41)	0.42 (0.09 -1.78)	P = 0.24
Inflammatory cause	0	9		1	
Trauma	5	7	*Reference*	*Reference*	

≥ 60 years; Above or equal to 60 years, <60 years; Below 60 years, ≥ 1 cm; Longer or equal to 1 cm, < 1cm; Less than 1cm,

4.2 Factors associated with recurrence of anterior urethral stricture following DVIU

4.2.1 Pre-Operative Stricture characteristic characteristics

Pre-operation the majority of participants were diagnosed through cystoscopy (n=106; 59.9%), with only (n=71; 40.1%) receiving imaging-based diagnoses. The average length of strictures among patients was 1.2 ± 0.28 cm, with the majority of strictures located in the bulbar region (n=162; 91.5%). The most common etiology of strictures was iatrogenic (n=83; 46.9%), followed by idiopathic cases (n=73; 41.2%)

Table 3: Pre-operative Stricture characteristic characteristics among patient

Variable		Freq (n=177)	Proportion (%)
Stricture Length			
	Less than 1 cm	107	60.45
	Longer than 1 cm	70	39.55
Stricture Location			
	Bulbar Urethra	162	91.53
	Penile Urethra	1	0.56
	Bulbar & Membranous Urethra	7	3.95
	Penile and Bulbar Urethra	7	3.95
Stricture Etiology			
	Iatrogenic	83	46.89
	Idiopathic	73	41.24
	Inflammatory causes	9	5.08
	Trauma	12	6.78

In the group without recurrences, the average neutrophil levels stood at 18.0 ± 22.6, with a median of 3.9. On the other hand, in the group experiencing recurrences, the average neutrophil levels were higher, at 20.8 ± 17.8, with a median of 31.8. Comparing lymphocyte levels, the mean values in the non-recurrence and recurrence groups were 12.9 ± 16.5 (median: 2.67) and 20.8 ± 17.8 (median: 28.6) respectively. The mean NLR was 1.7 ± 1.2 (median: 1.4) in the non-recurrence group and 2.1 ± 1.9 (median: 1.5) in the recurrence group. There was no statistical significance observed between the two groups regarding neutrophil count and NLR (*p*: > 0.05 – both). See Table 4

Table 4 Recurrence of stricture according to NLR

	Recurrence		
	Yes	**No**	***p*-value**
Variables	**Mean ± SD**	**Mean ± SD**	
Patient age (year)	65 ± 15	64 ± 16	0.860
Mean follow up (months)	18 ± 20 (3-60)	49 ± 1	
Time to recurrence (months)	12 ± 12		
Neutrophil	30.7 ± 26.0	18.0 ± 22.6	0.311
Lymphocyte	20.8 ± 17.8	12.9 ± 16.5	0.423
Neutrophil/Lymphocyte	2.1 ± 1.9	1.7 ± 1.2	0.076
Stricture length (cm)	1 ± 0.5	1 ± 0.5	0.571

CHAPTER FIVE

5.0 DISCUSSION

In this study, the recurrence rate of anterior urethral strictures following direct vision internal urethrotomy (DVIU) was 24%. This indicates that a significant portion of patients experienced a return of symptoms after the procedure. Factors such as previous urethral surgeries and the complexity of the strictures may have contributed to this outcome. The recurrence rate of 24% observed in this study is slightly lower than the 27.6% reported by Aydemir et al. and the 37% recurrence rate found in Zehri's study [21,41]. However, it is significantly lower than the 65% recurrence rate reported by Basaif et al. within a three-year period following DVIU [24]. In Sub-Saharan Africa, where urethral stricture management poses specific challenges, the 25% recurrence rate observed in Ofoha et al [42].'s study is almost similar to that of this study, reflecting the persistent clinical challenge of recurrent strictures in the region. The mean duration until recurrence in this study was shorter (2.6 months) compared to the 5.3 months reported by Ofoha et al [42]. Overall, while this study's recurrence rate aligns with some reported rates, it is notably lower than others, likely due to differences in patient populations, treatment methods, and follow-up durations.

Age was found to be a significant predictor of anterior urethral stricture recurrence in this study, with patients aged 60 years and above having a higher likelihood of recurrence after DVIU compared to those under 60 years ($P = 0.04$). This finding aligns with research by Harraz et al [14]., which indicated that older age at presentation was associated with a higher risk of stricture recurrence. Additionally, Aydemir et al [21]. in Turkey reported a mean patient age of 67.2 years; furthermore, their study found significant correlations between comorbidity, urinary tract infections, and recurrence, further suggesting that older patients may have a higher prevalence of such factors. In Ethiopia, Issack et al [22]. noted that 41.25% of their cohort was aged 61–78, indicating a greater incidence of strictures among older populations. In contrast, Zehri et al [41].

in Pakistan found a median patient age of 54 years. Scientific evidence suggests that aging induces tissue changes, including reduced elasticity and regenerative capacity, which may heighten susceptibility to fibrosis and subsequent stricture formation in the urethra [44]. The collective evidence emphasizes the importance of age as a risk factor for urethral stricture recurrence, warranting further urological studies to explore the mechanisms behind this association and to refine treatment approaches for older patients.

Building on the understanding that stricture length plays a critical role in the recurrence of anterior urethral strictures, this study found a strong association between longer strictures and increased recurrence rates. Specifically, patients with strictures measuring 1 cm or more had a significantly higher likelihood of experiencing recurrence compared to those with shorter strictures. This finding is consistent with other studies, such as those by Galvez et al and Aydemir et al, which also identified stricture length as a crucial predictor of recurrence following direct vision internal urethrotomy (DVIU) [21,23]. Steenkamp et al further supported this by noting a direct correlation between stricture length and recurrence, suggesting that even small increments in length could notably impact patient outcomes [45].

In this study, a substantial majority of patients experiencing stricture recurrence underwent DVIU, highlighting the treatment's commonality despite the challenges it presents. The most frequent diagnosis method prior to the procedure was cystoscopy, which reflects standard practice, while a significant proportion of strictures were located in the bulbar urethra—similar to the findings of Okpani et al and Galvez et al, indicating a consistent pattern in stricture location across various populations [23,25]. The predominant etiology of strictures in this study was iatrogenic, predominantly due to previous urethral interventions, followed by idiopathic cases, further emphasizing the challenge of managing stricture disease.

Interestingly, while the study identified diabetes mellitus and hypertension as common comorbidities among participants, these conditions did not significantly influence stricture recurrence. This finding contrasts with other studies that suggest a potential link between systemic health issues and postoperative outcomes, pointing to the need for further investigation into the interplay between comorbidities and stricture management [47,48].

Moreover, the role of inflammatory markers, particularly the neutrophil-lymphocyte ratio (NLR), in predicting postoperative outcomes warrants attention. Although the study did not find a statistically significant relationship between neutrophil count, NLR, and recurrence, previous research suggests that chronic inflammation may contribute to stricture development and recurrence. Studies by Urkmez et al and Qian et al have proposed that elevated NLR values could reflect a heightened inflammatory state, potentially guiding treatment decisions [11,39].

The findings imply that addressing inflammation through anti-inflammatory therapies or interventions targeting fibrosis may reduce recurrence rates in patients with urethral strictures [39,40]. Therefore, as clinicians navigate the complexities of urethral stricture management, it becomes imperative to consider not only the anatomical characteristics of strictures but also the broader biological and inflammatory contexts in which they occur. These insights may pave the way for more personalized treatment strategies that address both structural and inflammatory components of urethral strictures, ultimately improving patient outcomes in this challenging field.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The findings from this study suggest that sociodemographic factors and clinical factors have impact on recurrence of anterior urethral stricture following DVIU.

Patient age is a strong predictor of recurrence of anterior urethral stricture whereby individuals with age of 60 years and above have higher risk compared to younger age group.

Stricture length is a great factor in predicting recurrence of anterior urethral stricture. So, when stricture length is more than 1-centimeter chances of recurrence after DVIU are higher compared to stricture less or equal to one centimeter. There was no significant association between comorbidities, NLR and stricture recurrence.

6.2 Recommendations

Prospective studies can be conducted to validate the findings of this study in a larger and more diverse patient population. Prospective studies allow for real-time data collection and minimize biases associated with retrospective analyses, thereby providing stronger evidence for the clinical and demographic factors.

In this study it was observed that NLR had no statistical significance in predicting recurrence of anterior urethral stricture this could have been due to the fact that number of patients found in the study (177) was smaller compared to other similar studies so further studies with larger sample size or longer follow up period could be done to asses this factor. Also, comparative studies involving other predictive markers may be done in assessing stricture recurrence following DVIU.

REFERRENCES

1. Mundy AR, Andrich DE. Urethral strictures. BJU Int. 2011 Jan;107(1):6–26.
2. Fenton AS, Morey AF, Aviles R, Garcia CR. Anterior urethral strictures: Etiology and characteristics. Urology. 2005;65(6):1055–8.
3. Alwaal A, Blaschko SD, McAninch JW, Breyer BN. Epidemiology of urethral strictures. Transl Androl Urol. 2014 Jun;3(2):209–13.
4. Eshiobo I, Ernest U. A Review of the Epidemiology and Management of Urethral Stricture Disease in Sub-Saharan Africa. Curr Med Issues [Internet]. 2019;17(4). Available from: https://journals.lww.com/cmii/fulltext/2019/17040/a_review_of_the_epidemiology_and_management_of.6.aspx
5. Nyongole O V., Akoko LO, Mwanga AH, Mkony CA. Urethral Stricture as seen in Dar es Salaam, Tanzania. East Cent Afr J surg. 2013;18(1):84–9.
6. Stein MJ, DeSouza RA. Anterior urethral stricture review. Transl Androl Urol. 2013;2(1):32–8.
7. Shahsavari R, Bagheri SM, Iraji H. Comparison of Diagnostic Value of Sonourethrography with Retrograde Urethrography in Diagnosis of Anterior Urethral Stricture. Open access Maced J Med Sci. 2017 Jun;5(3):335–9.
8. Simhan J, Ramirez D, Hudak SJ, Morey AF. Bladder neck contracture. Transl Androl Urol. 2014;3(2):214–20.
9. Baskin LS, Constantinescu SC, Howard PS, Mcaninch JW, Ewalt DH, Duckett JW, et al. BIOCHEMICAL CHARACTERIZATION AND QUANTITATION OF THE COLLAGENOUS COMPONENTS OF URETHRAL STRICTURE TISSUE. J Urol [Internet]. 1993;150(2):642–7. Available from: http://dx.doi.org/10.1016/S0022-5347(17)35572-6
10. Zhang P, Shi M, Wei Q, Wang K, Li X, Li H, et al. Increased expression of connective tissue growth factor in patients with urethral stricture. Tohoku J Exp Med. 2008;215(3):199–206.
11. Urkmez A, Artuk I. Is neutrophil to lymphocyte ratio a predictive factor for

recurrence of urethral stricture ? 2019;65(12):1448–53.

12. Kluth LA, Ernst L, Vetterlein MW, Meyer CP, Reiss CP, Fisch M, et al. Direct Vision Internal Urethrotomy for Short Anterior Urethral Strictures and Beyond: Success Rates, Predictors of Treatment Failure, and Recurrence Management. Urology [Internet]. 2017;106:210–5. Available from: http://dx.doi.org/10.1016/j.urology.2017.04.037
13. Smith TG 3rd. Current management of urethral stricture disease. Indian J Urol. 2016;32(1):27–33.
14. Harraz AM, El-assmy A, Mahmoud O, Elbakry AA, Tharwat M, Omar H, et al. Is there a way to predict failure after direct vision internal urethrotomy for single and short bulbar urethral strictures ? Is there a way to predict failure after direct vision internal urethrotomy for single and short bulbar urethral strictures ? Arab J Urol [Internet]. 2019;13(4):277–81. Available from: http://dx.doi.org/10.1016/j.aju.2015.07.007
15. Sukumar S, Elliott SP, Myers JB, Voelzke BB, Smith TG, Carolan AMC, et al. Multi-Institutional Outcomes of Endoscopic Management of Stricture Recurrence after Bulbar Urethroplasty. J Urol [Internet]. 2018;200(4):837–42. Available from: https://doi.org/10.1016/j.juro.2018.04.081
16. Mershon JP, Baradaran N. Recurrent anterior urethral stricture: Challenges and solutions. Res Reports Urol. 2021;13:237–49.
17. Nnabugwu II, Onuh AC, Anyimba SK, Mgbor SO. Comparing complications of urethral stricture across various ages: a retrospective analysis of findings from retrograde urethrogram and voiding cysto-urethrogram over 10 years. BMC Med Imaging. 2019 Oct;19(1):84.
18. Afandiyev F, Ugurlu O. Factors predicting the development of urethral stricture after bipolar transurethral resection of the prostate. Rev Assoc Med Bras. 2022;68(1):50–5.
19. Furman D, Campisi J, Verdin E, Carrera-Bastos P, Targ S, Franceschi C, et al. Chronic inflammation in the etiology of disease across the life span. Nat Med

[Internet]. 2019;25(12):1822–32. Available from: http://dx.doi.org/10.1038/s41591-019-0675-0

20. Azab B, Chainani V, Shah N, McGinn JT. Neutrophil-lymphocyte ratio as a predictor of major adverse cardiac events among diabetic population: A 4-year follow-up study. Angiology. 2013;64(6):456–65.
21. Aydemir H, Sağlam HS, Köse O, Erdik A, Halis F, Gökçe A. The effect of recurrent direct vision internal urethrotomy for short anterior urethral strictures on the disease course and the predictors of treatment failure. Can Urol Assoc J. 2019;13(11).
22. Issack FH, Hassen SM, Tefera AT, Teshome H, Gebreselassie KH, Mummed FO. Short-term recurrence rate of male urethral stricture and its predictors after treatment with optical internal urethrotomy : Prospective Cohort Study at a tertiary center in Ethiopia. :4715–9.
23. Redón-Gálvez L, Molina-Escudero R, Álvarez-Ardura M, Otaola-Arca H, Alarcón Parra RO, Páez-Borda Á. Predictors of urethral stricture recurrence after endoscopic urethrotomy. Actas Urológicas Españolas (English Ed. 2016;40(8):529–33.
24. Basaif WS, Alamri HH, Mousa HW, Alsayed RA, Almohammadi AM, Altulayqi WH, et al. Types of urethral stricture and their recurrence rates post urological treatments. Int J Community Med Public Heal. 2021;8(7):3634.
25. Okpani C.P EN. Short Term Effects of Direct Vision Internal Urethrotomy on Uroflowmetry Parameters in Male Anterior Urethral Stricture Treatment in Port Harcourt.pdf. 2024.
26. Pallares-Méndez R, Cota-Agüero JA, Gutierrez-Gonzalez A, Cervantes-Miranda DE, Hernández-Aranda KL, Ochoa-Arvizo M, et al. Risk factors associated with urethral stricture recurrence after end-to-end urethroplasty and buccal mucosal graft urethroplasty. Urologia. 2022 May;89(2):268–73.
27. Kay HE, Srikanth P, Srivastava A V., Tijerina AN, Patel VR, Hauser N, et al. Preoperative and intraoperative factors predictive of complications and stricture

recurrence following multiple urethroplasty techniques. BJUI Compass. 2021;2(4):286–91.

28. Ozer K, Horsanali MO, Gorgel SN, Horsanali BO, Ozbek E. Association between benign prostatic hyperplasia and neutrophil-lymphocyte ratio, an indicator of inflammation and metabolic syndrome. Urol Int. 2017;98(4):466–71.
29. Chapman D, Kinnaird A, Rourke A. Independent predictors of stricture recurrence following urethroplasty for isolated bulbar urethral strictures. J Urol. 2017;179:1107– 12.
30. Quante M, Dietrich A, ElKhal A, Tullius SG. Obesity-related immune responses and their impact on surgical outcomes. Int J Obes (Lond). 2015 Jun;39(6):877–83.
31. Breyer BN, McAninch JW, Whitson JM, Eisenberg ML, Master VA, Voelzke BB, et al. Effect of obesity on urethroplasty outcome. Urology. 2009 Jun;73(6):1352–5.
32. Breyer B, Mc Aninch J, Whitson J. Multivariate analysis of risk factors for long-term urethroplasty outcome. J Urol. 2010;183(2):613617.
33. Kinnaird A, Levine M, Ambati D, Zorn J, Rourke K. Stricture length and etiology as preoperative independent predictors of recurrence after urethroplasty: a multivariate analysis of 604 urethroplasties. Can Urol Assoc J. 2014;8:E296.
34. Meeks JJ, Erickson BA, Granieri MA, Gonzalez CM. Stricture recurrence after urethroplasty: a systematic review. J Urol. 2009 Oct;182(4):1266–70.
35. Krane LS, Richards KA, Kader AK, Davis R, Balaji KC, Hemal AK. Preoperative neutrophil/lymphocyte ratio predicts overall survival and extravesical disease in patients undergoing radical cystectomy. J Endourol. 2013 Aug;27(8):1046–50.
36. Grimes N, Hannan C, Tyson M, Thwaini A. The role of neutrophil-lymphocyte ratio as a prognostic indicator in patients undergoing nephrectomy for renal cell carcinoma. Can Urol Assoc J = J l'Association des Urol du Canada. 2018 Jul;12(7):E345–8.
37. Shao Y, Wu B, Jia W, Zhang Z, Chen Q, Wang D. Prognostic value of

pretreatment neutrophil-to-lymphocyte ratio in renal cell carcinoma: a systematic review and meta-analysis. BMC Urol. 2020 Jul;20(1):90.

38. de Martino M, Pantuck AJ, Hofbauer S, Waldert M, Shariat SF, Belldegrun AS, et al. Prognostic impact of preoperative neutrophil-to-lymphocyte ratio in localized nonclear cell renal cell carcinoma. J Urol. 2013 Dec;190(6):1999–2004.
39. Qian H, Luo Z, Xiao C, Chen J, Li D, Xu H, et al. Red cell distribution width in coronary heart disease: prediction of restenosis and its relationship with inflammatory markers and lipids. Postgrad Med J. 2018 Sep;94(1115):489–94.
40. Velioglu Y, Yuksel A. Complete blood count parameters in peripheral arterial disease. aging male Off J Int Soc Study Aging Male. 2019 Sep;22(3):187–91.
41. Zehri AA, Ather MH, Afshan Q. Predictors of recurrence of urethral stricture disease following optical urethrotomy. Int J Surg [Internet]. 2009;7(4):361–4. Available from: http://dx.doi.org/10.1016/j.ijsu.2009.05.010
42. Ofoha CG, Ramyil VM, Dakum NK, Shu'aibu SI, Akpayak IC, Magnus FE, et al. Predictors of urethral stricture recurrence following urethroplasty: a retrospective review at the Jos University Teaching Hospital, Nigeria. Pan Afr Med J. 2019;32:190.
43. Zehri AA, Ather MH, Afshan Q. Predictors of recurrence of urethral stricture disease following optical urethrotomy. 2009;7:361–4.
44. Sherratt MJ. Tissue elasticity and the ageing elastic fibre. Age (Dordr). 2009 Dec;31(4):305–25.
45. Steenkamp JW, Heyns CF, de Kock MLS. Internal Urethrotomy Versus Dilation as Treatment for Male Urethral Strictures. J Urol. 1997;98–101.
46. Ekerhult TO, Lindqvist K, Grenabo L, Kåbjörn Gustafsson C, Peeker R. Sclerosis as a predictive factor for failure after bulbar urethroplasty: a prospective single-centre study. Scand J Urol. 2018 Aug;52(4):302–8.
47. Yu J, Sun N, Song H, Li M, Li L, Gong C, et al. Analysis in the influence factors of urethroplasty in DSD. BMC Urol. 2022 Aug;22(1):124.

48. Lee D, Lee R, Gowda NB, Probasco W V, Stake S, Ibrahim G, et al. Impact of diabetes mellitus on surgical complications in patients undergoing revision total knee arthroplasty: Insulin dependence makes a difference. J Clin Orthop trauma. 2020;11(1):140–6.

APPENDICES

Appendix II: Data Collection Tool

Checklist

Section 1: Patient Demographics

1. Patient unique ID: ……...
2. MR number: ……
3. Age: ……. years
4. Gender: Male
5. Date: ……

Section 2: Stricture Recurrence Information

6. Has the patient experienced a recurrence of anterior urethral stricture following your DVIU procedure?
    a. Yes [ ]
    b. No [ ]
7. If yes, please specify the date of recurrence:
    a. Date: ……
    b. How was the recurrence diagnosed?
        i. Clinical symptoms [ ]
        ii. Imaging [ ]
        iii. Cystoscopy [ ]

Section 3: Neutrophil to Lymphocyte Ratio (NLR)

8. Has the patient undergone blood tests to measure your NLR levels before and after DVIU procedure?
    a. Yes [ ]
    b. No [ ]
9. If yes, please provide the NLR value(s) before DVIU procedure:
    a. WBC …….
    b. ANC …….

c. LYM …….
d. HB ……
e. PLT ……

10. NLR value(s) after DVIU procedure:
    a. WBC ……...
    b. ANC ……...
    c. LYM ……...
    d. HB ……
    e. PLT ……
11. Have you experienced a recurrence of anterior urethral stricture following your DVIU procedure? (Yes/No)

Section 4: Preoperative Clinical Parameters

12. Stricture Length (in centimeters): ……...cm
13. Presence of Comorbidities
    a. Diabetes [ ]
    b. Hypertension [ ]
    c. Lichen Sclerosus [ ]
14. History of Previous Urethral Surgery?
    a. Yes [ ]
    b. No [ ]
15. Other Relevant Preoperative Clinical Parameters (please specify):

……

Appendix III: Ethical Clearances

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATION

Ref. No.DA.282/298/01.C/1952 Date: 23/10/2023

MUHAS-REC-10-2023-1952
PHILIPO FELIX
COLLEGE OF MEDICINE
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: NEUTROPHIL TO LYMPHOCYTE RATIO AS A PREDICTIVE FACTOR FOR RECURRENCE OF ANTERIOR URETHRAL STRICTURE POST DIRECT VISION INTERNAL URETHROTOMY

Reference is made to the above heading,

I am pleased to inform you that the Chairperson has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 23/10/2023
EXPIRATION DATE OF APPROVAL: 23/10/2024

STUDY DESCRIPTION:
Purpose:

The purpose of this retrospective cohort study is to assess the efficacy of the neutrophil-to- lymphocyte ratio as a predictive factor for the recurrence of anterior urethral stricture following direct visual internal urethrotomy (DVIU).

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided:
https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014801.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country,
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Dr. Kasusu Nyamuryekung'e

Ag. Chairperson, MUHAS Research and Ethics Committee

Muhimbili University of Health and Allied Sciences
DIRECTOR
Research, Publications & Innovations
Box 65001

Appendix IV: Permission Letter

THE UNITED REPUBLIC OF TANZANI

MINISTRY OF HEALTH

MUHIMBILI NATIONAL HOSPITAL

In reply please quote;

Ref. No.: MNH/CRTCU/Perm/2023/545 Date: 01st November, 2023

Head of Department

Urology

Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH.

Name of Student	**Philipo Felix**
Title	**"Neutrophil to Lymphocyte ratio as a Predictive Factor for Recurrence of Anterior urethral Stricture Post Direct Vision Internal Urethrotomy".**
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Prof. Obadia Nyongole (MUHAS)
Co – Supervisors	Dr. Isaack Mlatie (MNH)
Period	01st November, 2023 to 30th January, 2024

Approval has been granted to the above principal investigators to collect data at MNH. Dissemination of study findings at MNH shall be overseen by **Dr. Isaack Mlatie** (MNH) supervisor.

Kindly ensure the named principal investigator abide to the ethical principles and other conditions of the research approval.

Sincerely,

Dr. Jessie Mbwambo
Head of Clinical Research, Training and Consultancy Unit

c.c DSS

c.c Dr. Isaack Mlatie

c.c **Philipo Felix**

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