A STUDY TO COMPARE THE SHORT TERM OUTCOME OF URETHRAL STRICTURE DISEASE MANAGEMENT BETWEEN HIV AND NON HIV INFECTED PATIENTS AT UTH.

By

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A dissertation submitted in partial fulfilment of the requirements for the award of master of medicine (urology) degree of the University of Zambia.

THE UNIVERSITY OF ZAMBIA

SCHOOL OF MEDICINE

DEPARTMENT OF SURGERY

DECEMBER 2010.
Declaration

I hereby declare that this dissertation herein presented for the degree of master of medicine (Urology) has not been previously submitted wholly or in part for any other degree at this or any other university nor is it being currently submitted for any other degree. I further declare that all sources I have quoted have been indicated and acknowledged by means of complete references. It has been prepared in accordance with the prescribed guidelines for the post graduate studies Dissertations of the University of Zambia.

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Certificate of Approval

This dissertation of Michael Silumbe has been approved as fulfilling the requirements or partial fulfilment of the requirements for the award of master of medicine (urology) degree by the University of Zambia, school of medicine.

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Abstract

Background: According to Steencamp et al (1997), urethral stricture disease is one of the oldest known urological diseases and remains a common problem with a high morbidity despite earlier predictions to the contrary. In many third world countries with limited medical resources male urethral stricture disease remains highly prevalent.

STIs cause urethritis which is an aetiology for urethral stricture disease and urethritis is a risk factor for HIV transmission (De Schryver and Meheus, 1990).

The outcome of surgery has been found to be affected by the immune status of the patient and HIV has a bearing on the outcome. Urethral stricture disease is thus not an exception.

This study intended to compare short term outcome of treatment of urethral stricture disease between HIV seropositive and HIV seronegative patients at the UTH in Lusaka.

Patients and Methods: This was a prospective cohort study conducted on patients presenting with virgin urethral stricture disease at the University Teaching Hospital (UTH), Lusaka, Zambia, between October 2009 and December 2010. One arm included HIV seropositive patients and the other arm had HIV seronegative patients. The recruited patients underwent urethral dilatation, anastomotic urethroplasty and staged urethroplasty. They were followed up postoperatively for 6 months and recurrence and complication rates were compared between the two groups. Other parameters studied included patients demographics, CD4 cell count in positive patients, HIV WHO stage, stricture aetiology, stricture site and stricture length. The collected data was analysed using SPSS 16.

Results: A total of 71 patients with a mean age of 38.04 years who had urethral stricture disease were recruited in this study.
37% (n=26) were HIV seropositive while 63% (n=45) were seronegative and 53.8% (n=14) of the seropositive patients were on HAART.

45% (n=32) of urethral strictures resulted from urethritis and the prevalence of HIV in patients presenting with post urethritis stricture disease was 50% (n=16/32).

In terms of stricture location, 73.2% (n=52) of strictures were located in the bulbar urethra, 19.7% (n=14) had strictures in the penile urethra and 5.6% (n=4) had strictures located in the membranous urethra.

The operation types included urethral dilatation, anastomotic urethroplasty and staged urethroplasty. 73% (n=52) of the patients had urethral dilatation, 17% (n=12) had anastomotic urethroplasty and 10% (n=7) had staged urethroplasty.

The intraoperative complication rate in this study was 2.8% (n=2) while postoperatively it was 12.7% (n=9).

55.2% (n=32/58) had urethral stricture disease recurrence after being followed up for 6 months. Urethral dilatation accounted for most of the failures as 28% (n=20/58) of the patients who had urethral dilatation had recurrence.

With regard to HIV status, 47% (n=16/34) of the non reactive patients had recurrence while 67% (n=16/24) of the reactive patients had recurrence. However, the 20% difference in recurrence between reactive and non reactive patients was statistically insignificance (p=0.139).

**Conclusions:** Urethral stricture disease affects patients from all age groups. The prevalence of HIV in patients with post urethritis stricture disease is high. Stricture recurrence following treatment is not affected by the HIV status of the patient and CD4cc although it is affected by stricture site and stricture length. Time to recurrence and Cum survival of urethral stricture disease following treatment are also not influenced by the HIV status of the patient.
Dedication

This project is dedicated to my late father Jackson Silumbe, my mother Margret Namwila Silumbe and my daughter Michelle Nalumbe.
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List of Abbreviations and Acronyms

LUTS............................................................ Lower urinary tract symptoms

SPC.............................................................. Suprapubic cystostomy

AUA.............................................................. American urological association

DVIU............................................................. Direct visual internal urethrotomy

HIV............................................................... Human immunodeficiency virus

Fr................................................................. French gauge

TV............................................................... Tunica vaginalis

BXO.............................................................. Balanitis xerotica obliterans

UTH.............................................................. University Teaching Hospital

IPSS.............................................................. International prostate symptom score

HAART.......................................................... Highly Active Anti Retroviral Therapy
Chapter One

INTRODUCTION

According to Steencamp et al (1997), urethral stricture disease is one of the oldest known urological diseases and remains a common problem with a high morbidity despite earlier predictions to the contrary. In many third world countries with limited medical resources male urethral stricture disease remains highly prevalent.

Sexually transmitted infections (STI) are now the commonest group of notifiable infectious diseases in most countries, particularly in the age group of 15 to 50 years and in infants. Their control is important considering their role in increasing transmission of the human immunodeficiency virus (HIV). STIs are hyperendemic in many developing countries and urethral stricture disease and infertility are frequent sequelae in men (De Schryver and Meheus, 1990).

Some STIs cause urethritis which is an aetiology for urethral stricture disease and urethritis is a risk factor for HIV transmission. The aetiology of urethritis, the significance of potential pathogens and the relation of urethritis to HIV infection were determined in 335 men (cases) with and 100 men (controls) without urethral symptoms. The sero-prevalence of HIV was 45% in the patients with urethritis (Sturm et al, 2004).

DEFINITION - The term urethral stricture refers to an abnormal narrowing of the tube (urethra) that carries urine out of the body from the bladder.
ANATOMY OF THE URETHRA (Barbagli G, 2009) - The male urethra is a tubular structure about 18cm in length, originating in the bladder, at the inferior and anterior level. After crossing the pelvic floor and the perineum, it runs along the entire length of the penis, ending at the apex of the glans. The male urethra can be subdivided into various parts based on different criteria.

Prostatic urethra

The prostatic urethra is inside the prostate gland and extends from the bladder neck to the verumontanum. In the adult, the length of the prostatic urethra is about 3cm.

Membranous urethra

The membranous urethra is about 1.5cm long and is located inside the urogenital diaphragm. It is in anatomical relationship with the external urethral sphincter.

Bulbar urethra

The bulbar urethra, located inside the perineum and scrotum, extends from the external distal urinary sphincter to the peno-scrotal junction, and is surrounded by the corpus spongiosum. It contains the opening of the ducts of the Cowper glands, and differs in length from person to person.

Penile urethra

The penile urethra extends from the peno-scrotal junction to the glans and is surrounded by the corpus spongiosum.

Blood supply

The urethra receives its blood supply from the bulbar arteries arising from the pudendal arteries and from the dorsal artery of the penis in retrograde fashion.
AETIOLOGY OF URETHRAL STRICTURES (Bhargava and Chapple, 2005) - Insult to the urethral epithelium or the corpus spongiosum will lead to narrowing of the urethral calibre.

The cause of anterior urethral stricture disease can be classified into congenital or acquired.

Congenital strictures are a rare cause of urethral stricture disease.

Acquired strictures are due to four main causes;

(1) **Iatrogenic:** These are hospital acquired strictures. Traumatic placement of urethral catheters is the most common cause and any part of the urethra can be affected. Prostatic urethral strictures can arise following prostatectomy.

(2) **Infection:** Strictures are mostly due to gonococcal urethritis. They are common in the bulbar and penile urethrae because of the presence of bulbar glands and glands of Littre respectively.

(3) **Inflammation:** Balanitis xerotica obliterans and lichen sclerosis are the causes. It usually begins with inflammation of the glans and inevitably causes meatal stenosis. The cause of this distal penile skin and urethral inflammation is not known.

(4) **Trauma:** Urethral injuries occur mostly in association with pelvic fractures. The membranous urethra is prone to injury in pelvic fractures as it is posterior and inferior to the pubic symphysis. The prostatic urethra can also be affected in pelvic fractures. Balbar urethral strictures can arise following straddle injuries.

CLINICAL FEATURES (Bhargava and Chapple, 2005) - Patients with urethral stricture disease become symptomatic only after the urethral calibre falls to less than 10 Fr. They present with a history of obstructive voiding symptoms (poor flow, straining to void, incomplete bladder
emptying, urinary retention), urinary tract infections, urethral bleeding and now more rarely, urethrocuteaneous fistula and peri-urethral abscess develop.

**INVESTIGATIONS** (Bhargava and Chapple, 2005 and Gordon et al, 1998) - Investigations aim to establish a diagnosis, identify co-existing infection and determine the location and nature of the stricture in order to devise a treatment plan.

(1) **Urine culture:** Urine culture is mandatory to identify infection and to treat it before contemplating treatment.

(2) **Urinary flow rate:** It provides useful information at initial assessment and follow up.

(3) **Flexible Urethroscopy:** This has simplified the evaluation of the urethra.

(4) **The urethrogram:** It is the single most important investigation when evaluating urethral stricture disease. It provides information on the site, length, number, calibre and relation of the stricture to other structures.

The patient is placed in an oblique (45 degrees) or lateral decubitus position. A small-bore urethral catheter (8 - 10 French) is placed un lubricated 1 cm into the fossa navicularis, and the balloon is filled with 1 cm of water to achieve a snug fit. About 25 mL of contrast material is injected gently into the urethra through the catheter and the film is taken during injection.

For a combined cystourethrogram, 40ml of contrast is injected into the bladder through a suprapubic catheter before injecting contrast in the urethra.

(5) **Ultrasonic evaluation:** This is more accurate in determining spongiosis.

The American Urological Association symptoms index combined with maximum urine flow is an accurate, timesaving and cost-effective tool for predicting recurrent stricture in patients with a known urethral stricture. It can be used to direct decision making on further invasive studies and
treatment. The AUA symptom index is classified as mild (0-7), moderate (8-19) and severe (20-35) (Heyns and Marais, 2003).

In the UK, most failures following urethroplasty occur in the first twelve months. Follow-up can be undertaken using flow rates or flexible urethroscopy. Bhargava and Chapple (2005) prefer flexible urethroscopy carried out at three months and then at twelve months, in order to identify those in whom the stricture will recur.

**TREATMENT** (Barbagli G, 2009) - Treatment of urethral strictures is primarily surgery, but the choice of the appropriate treatment is based on the characteristics of the stenosis (site, etiology, length, adverse local factors) and on the patient’s characteristics (age, clinical history, associated diseases, physical and mental condition).

Basically, the treatment types are:

1) Periodical instrumental and clinical evaluation of the patient. This approach is commonly known as watchful waiting.

2) Progressive dilatation of the urethral calibre periodically performed in an outpatient office using soft catheters.

3) Endoscopic opening of the stricture. This procedure is commonly known as internal urethrotomy using a cold knife or holmium laser.

4) Surgical repair of the stricture. This procedure is commonly known as urethroplasty.

The main types of urethroplasty are:

**One-stage urethroplasty**

The urethra is reconstructed using a single surgical step. The most important surgical techniques for one-stage urethroplasty are:
1) **End-to-end anastomosis**: the urethra is transected at the level of the stricture site, the scar tissue is removed and the two urethral edges are sutured together. End-to-end anastomosis may also be performed using oral mucosa grafting.

2) **Urethroplasty using oral graft**: the urethra is fully opened at the level of the stricture site and the canal is widened with a strip of oral mucosa harvested from the cheek or the tongue. This is a true self-transplant because the strip of oral mucosa is removed entirely from the inside of the mouth or from the tongue and sutured to the urethra using different techniques (urethroplasty with dorsal or ventral oral mucosal graft).

3) **Urethroplasty using penile skin flap**: the urethra is opened at the level of the stricture site, and the canal is widened with a strip of penile skin, which is vascularized by a special vascular pedicle.

**Two-stage or multi-stage urethroplasty**

The urethra is repaired using two or more surgical procedures performed within 6 - 8 or 12 months from each other.

1) **In penile urethral strictures**, during the first stage, the urethra is opened or completely removed and replaced by a wide strip of oral mucosa or penile skin, which is sutured directly onto the corpora carvenosa or the glans surface. After 6-8 or 12 months, if the graft is well vascularized, the mucous membrane strip is transformed into a tube and the urethral meatus is positioned on the apex of the gland.

2) **In bulbar urethral strictures**, during the first stage, the urethra is opened at the perineum and urine is discharged from this new stoma, thus obligating the patient to urinate in a seated position. Whenever possible, this perineal stoma may be closed, thus allowing the patient to urinate through the penis again.
In some cases, however, when it is impossible to restore the patient’s ability to urinate through the penis, perineostomy is considered a definitive surgery (Barbagli G, 2009).

Chapter Two

STATEMENT OF THE PROBLEM

The prevalence of urethral stricture disease in Zambia is high. HIV is known to affect outcomes in many surgical procedures. Despite the high prevalence of urethral stricture disease in Zambia, no study has been performed to compare treatment outcome between HIV seropositive and HIV seronegative patients.
Chapter Three

STUDY JUSTIFICATION

An audited review of work at the Urology unit in UTH by Bowa (2004) revealed that the prevalence of urethral stricture disease in Zambia is high hence the need for further studies to improve outcome following treatment. With the advent of HIV, the disease outcome following surgery has changed hence the need to know the effect of HIV on urethral stricture disease (Bayley, 1990). The recurrence rate if a wrong management plan is chosen is high hence patients spend productive time seeking retreatment and HIV may further compound the outcome of urethral stricture disease management. The burden of urethral stricture disease cannot be ignored as it takes long for patients to be treated as operating theatre waiting lists are long.

The knowledge obtained will be used to know at which CD4 cell count treatment outcome would be good in HIV patients.

Therefore, it’s very important to compare the outcome of urethral stricture disease management between HIV seropositive and HIV seronegative patients.
Chapter Four

LITERATURE REVIEW

The aetiology of urethral stricture disease differs between developing and developed countries. According to studies shown below, infection an uncommon cause of urethral stricture disease in developed countries, is the most common aetiology of stricture in the developing world.

As Fenton et al (2005) found out in an evaluation of the aetiology and characteristics of symptomatic anterior urethral strictures, most strictures were idiopathic (34%) or iatrogenic (32%); fewer were inflammatory (20%) or traumatic (14%). Most involved the bulbar urethra (52%). Pendulous strictures were longer on average than those in the fossa navicularis or bulb. Prolonged catheterization and transurethral surgery were common causes of iatrogenic strictures. In the UK, about 20% of patients will have strictures due to iatrogenic causes (Bhargava and Chapple, 2005).

However, most urethral strictures in the developing world are post infective. At the urology unit, Department of Surgery, University College Hospital, Ibadan, Nigeria a study carried out indicated the aetiology of stricture disease as being post-infective in 80% of the cases (Shittu, 2001).

At the Urology Department of the Conakry University Hospital, Republic of Guinea, a study was done to evaluate surgical management of male urethral stricture. The majority of strictures were caused by infection followed by post-traumatic strictures accounting for 84% and 10% respectively. Urethral stricture was associated with other pathologies in 16% of cases (Daillo et
Ramyil and group (2007) did a study which further affirmed infection as being the leading cause of urethral stricture disease in developing countries. Visual Internal Urethrotomy in the Management of Anterior Urethral Stricture was studied at the Jos University Teaching Hospital, Nigeria and all patients were treated as day cases. The main cause of urethral stricture was infection (61%) followed by trauma which was found in 16% of patients. The strictures were bulbar in 89%, non-obliterative in 94%, single in 40% and less than 1cm long in 14% of the patients.

The prevalence of urethral stricture disease in Zambia is high. In an audited review of work at the Urology unit in UTH by Bowa (2004), the prevalence of urological diseases at UTH was: benign prostatic hypertrophy-33%, urethral stricture disease-17%, vesico-vaginal fistula-11%, prostate cancer-8%, bladder cancer-7%, urological stone disease-6%, paediatric urology-8% and others-10%.

A study by Zulu Robert (2003) at UTH revealed that 80.6% of urethral strictures were due to infection while 8.3% were as a result of trauma. However, the aetiology was unknown in 11.1% of the patients.

An exception in the aetiological pattern was noted in one study by Nwofor and Ugezu (2004). A study to evaluate the aetiological pattern, treatment and outcome of urethral strictures was carried out at Nnewi, South East Nigeria. Strictures resulting from infection accounted for 49% while trauma was responsible for 52% with road traffic accident topping the list at 29%. Iatrogenic trauma was responsible for 2%. The strictures were located in the anterior urethra in 52%, posterior urethra in 37% while in 11% both the anterior and posterior portions of the
urethra were involved. The conclusion was that urethral stricture was still a major urological problem and trauma was the leading cause.

Stack and Schlossberg (1998) in Virginia, USA devised two arms of consideration in the evaluation and treatment of urethral stricture disease. The first is to attempt to cure the patient of urethral stricture disease and the second is to simply manage the patients’ urethral stricture disease without intent of cure. Urethroplasty is still regarded as the gold standard for treatment of urethral strictures but it requires surgical expertise, adequate operating room facilities and relatively long hospitalization, while the cost to the economy is further increased by the often prolonged absence from work. In many third world countries with limited medical resources male urethral stricture disease remains highly prevalent. Urethroplasty for all strictures is not feasible due to the lack of adequate operating room and hospital facilities. Urethral dilation can be performed on an outpatient basis with local anesthesia by an adequately experienced surgeon with relatively inexpensive equipment. Internal urethrotomy requires surgical expertise, the appropriate endoscopic equipment and operating room facilities (Steencamp et al, 1997).

The following study further reaffirms how superior urethroplasty is when compared to other treatment modalities. A study to evaluate the aetiological pattern, treatment and outcome of urethral strictures was carried out at Nnewi, South East Nigeria. 75% had urethral dilatation, 23% had urethroplasty while 2% had urethrotomy. Urethroplasty gave better results with a 17% recurrence rate and a 25% overall complication rate, while in those treated by dilatation, 62% required repeated dilatations between 6 and 12 months in order to maintain a satisfactory urine flow. The conclusion was that urethral stricture is still a major urological problem. Urethroplasty gives a much better result than dilatation and should be the treatment of choice where the skill is available. Man power development in this regard is recommended (Nwofor and Ugezu, 2004).
The efficacy of dilatation and urethrotomy is not different as shown by the following studies; Urethral dilatation and urethrotomy can be effective treatments of the stricture disease in selected patients when the spongy tissue is not severely damaged. Reports in Italy comparing urethrotomy and dilatation indicated that there was no significant difference between the two (Pansadoro and Emiliozzi, 1998). A current randomized clinical trial in the United Kingdom has shown no difference in the efficacy between urethral dilation and urethrotomy that relies upon the use of a cold knife or laser to incise the urethra. Both techniques carry a success rate after urethral dilation of about 50% with further success with urethrotomy of 10% (Bhargava and Chapple, 2005). A study from the Department of Urology, Faculty of Medicine, University of Stellenbosch and Tygerberg Hospital, Tygerberg, South Africa compared the efficacy of dilation versus internal urethrotomy as initial outpatient treatment for male urethral stricture disease. It was concluded that there is no significant difference in efficacy between dilation and internal urethrotomy as initial treatment for strictures. Both methods become less effective with increasing stricture length. Dilation or internal urethrotomy was recommended for strictures shorter than 2 cm, primary urethroplasty for those longer than 4 cm. and a trial of dilation or urethrotomy for those 2 to 4 cm. long (Steenkamp et al, 1997). In a study carried out at the urology unit, department of surgery, University College Hospital, Ibadan, Nigeria, 75% of the patients had maintained a satisfactory flow rate of between 15 ml/sec and 28 ml/sec with a mean flow rate of 23 ml/sec after a single attempt at urethrotomy and over a period of follow-up of between 6 months and 5 years. Internal optical urethrotomy can be effective in the management of patients with post-infective urethral strictures that do not involve the membranous urethra, and should be attempted in the first instance where the facility exists, particularly as a failed urethrotomy does not jeopardize the management of the stricture by other techniques (Shittu,
2001). At the department of urology, Christian Medical College and hospital, Vellore, India, it was concluded that self intermittent catheterization following internal urethrotomy resulted in a lower restructure rate and better stream when compared to regular urethral dilatations (Gnanaraj et al, 1999).

The outcome of surgery has been found to be affected by the immune status of the patient and HIV has a bearing on the outcome. Harrison et al (2002) performed a prospective, blind, controlled study on wound infection after implant surgery at the College of Medicine and Queen Elizabeth Hospital, Blantyre, Malawi involving 41 procedures in patients infected with the human immunodeficiency virus (HIV) and 141 in HIV-negative patients. The patients were staged clinically and the CD4 cell count determined. They concluded that when there was preoperative contamination, the incidence of wound infection in HIV-positive patients increased markedly (42%) compared with that in HIV-negative patients (11%; p = 0.084).

Bayley (1990) at the Department of Surgery, University of Zambia, Lusaka found that Human immunodeficiency virus had resulted in a major change in the presentation and behaviour of certain common diseases in Africa. The experience of surgeons in Africa with patients infected with human immunodeficiency virus (HIV) suggests 5 trends: 1) an increased incidence of surgical sepsis--most commonly in the female genital tract, the pleural cavity, large joints, and the anorectal area--in HIV-infected patients; 2) an increase in surgical tuberculosis of spine, bone joints, lymph nodes, and the peritoneal cavity concomitant with an increased incidence of pulmonary tuberculosis in high-incidence countries; 3) impaired healing of wounds, wound breakdown, and the development of skin lesions and ulcers; 4) tumors whose aggressiveness is accelerated by HIV infection; and 5) new pathologies such as nonspecific cystitis, chronic
osteitis and vascular disease. In many cases, HIV infection has not been identified until after hospital patients have demonstrated a rapid, progressive decline after routine surgery.

Karpelowsky et al (2009) carried out a prospective study at the Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa. The aim of this study was to prospectively document outcomes of human immunodeficiency virus-infected and exposed children undergoing surgery. They concluded that Human immunodeficiency virus-positive and exposed patients present a unique challenge in management which is complicated by concomitant disease and poor nutrition.

However, No known studies have been done to compare the outcome of urethral stricture disease management between HIV and non HIV patients.
Chapter Five

RESEARCH QUESTIONS

(1) What’s the short term outcome of urethral stricture disease management (urethral dilatation, optic urethrotomy and urethroplasty) in HIV negative patients?

(2) What’s the short term outcome of urethral stricture disease management (urethral dilatation, optic urethrotomy and urethroplasty) in HIV positive patients?

(3) What’s the difference in urethral stricture disease management short term outcome between HIV seropositive and HIV seronegative patients?

(4) What’s the minimum CD4 cell count in HIV positive patients at which treatment outcome is expected to be good?

OBJECTIVES

GENERAL OBJECTIVE
The study intends to compare short term outcome of treatment of urethral stricture disease between HIV seropositive and HIV seronegative patients at the UTH in Lusaka.

SPECIFIC OBJECTIVES
(1) To establish the demographical characteristics of patients presenting with urethral stricture disease and its aetiology at the UTH.

(2) To determine the prevalence of HIV in a cohort of patients presenting with post urethritis urethral stricture disease at the UTH.

(3) To compare the short term treatment outcome of urethral stricture disease management in HIV negative and HIV positive patients over a period of 6 months using recurrence and complication rates.
(4) To determine if CD4 cell count and HIV stages affect the outcome of treatment among HIV positive patients.

Chapter Six

METHODOLOGY

STUDY DESIGN
This was a prospective cohort study conducted on patients who presented with virgin urethral stricture disease.

SETTING
Urology units I and II in the department of surgery at the University teaching hospital in Lusaka, Zambia.

CASE DEFINITION
A case was defined as a patient with an acquired virgin urethral stricture confirmed by a retrograde urethrogram or combined cystourethrogram and urinary flow rate less than 15mls/sec.

DURATION OF THE STUDY
Patients recruited were followed up for a maximum period of about 6 months, from the date of study approval.

STUDY SITE
This study was carried out at clinic VII / urology and the male urology admission ward (GO1) at the University Teaching Hospital in Lusaka, Zambia. This is the largest referral hospital and receives patients from all corners of the country.

PATIENT SELECTION
Inclusion criteria
Participants were patients irrespective of age with a virgin urethral stricture disease confirmed by
a urethrogram and with a urinary flow rate less than 15mls/min. They also had an HIV test done and had no complications on recruitment. HIV positive patients had CD4 cell counts done.

**Exclusion criteria**

Patients with unconfirmed urethral stricture disease and who declined to have an HIV test done were excluded. Patients who refused to give consent and those with complications were also excluded.

**SAMPLING AND SAMPLE SIZE**

Convenient sampling was employed were all patients meeting the inclusion criteria were recruited. The sample size was calculated using openEpi software and was 71 (25 exposed and 46 nonexposed). This was based on the assumptions outlined below;

**Assumptions;**

(i) HIV negative patients = 65%  
(ii) HIV positive patients = 35%  
(iii) HIV negative with outcome = 35%  
(iv) HIV positive with outcome = 70%  
(v) Confidence level = 95%  
(vi) Power = 80%

**DATA COLLECTION**

Data was collected using a standard data collecting sheet at the time of patient enrollment into the study and postoperatively at day 21, 1 month, 3 months, 6 months and when necessary.

**METHOD**

Patients with strictures less than 1cm long underwent urethral dilatation while anastomotic urethroplasty was done for strictures between 1 and 3cm. Staged substitution urethroplasty was used for strictures longer than 3cm.

**Urethral dilatation:** This was performed on an outpatient basis in clinic 7. The patient was
positioned in lithotomy position, cleaned and draped. Intraurethral lignocaine gel was applied and a urethral clamp placed. Anaesthesia took effect after about 5 minutes and serial urethral dilatation was done using bougies in an increasing order of size. The patient was catheterized with F16 2-way catheter, catheter balloon inflated with 10mls saline and discharged on ciprofloxacin and paracetamol.

**Anastomotic urethroplasty**: This was performed from phase III theatre on an inpatient basis.

The patient was positioned in lithotomy position and the procedure was done under spinal or general anaesthesia. The surgeon scrubbed and the patient was cleaned and draped.

The distal extent of the stenosis was identified using a size 14 nasogastric tube and marked. The urethra was then freed from the bulbocavernosus muscle and dissected from the corpora carvenosa. The urethra was transected at the stricture site and the stricture removed. The urethra was spatulated on both ends and about 10 vicryl or chromic cat gut 3/0 interrupted sutures were placed without tying. The anastomosis was completed on the roof and a size F16 foleys catheter inserted. The anastomosis was then completed and the wound closed in layers using vicryl or chromic cat gut 3/0.

**Staged substitution urethroplasty**: This was done in two stages and both stages were done under general or spinal anaesthesia from phase III theatre. The patient was placed in lithotomy position and surgical preliminaries done.

**First stage**: the distal extent of the stenosis was identified using a size 14 nasogastric tube and marked. The urethra was then freed from the bulbocavernosus muscle and dissected from the corpora carvenosa. The strictured urethra was excised and substituted with skin and a proximal and distal urethrostomy created. Vicryl or chromic cat gut 3/0 suture was utilized. The patient was followed up on an outpatient basis and second stage was performed 6 – 8 months later if
there were no complications.

**Second stage:** the patient was catheterized with a size F 16 foleys catheter and the skin was tubularised and used to create a urethral plate around the catheter. Vicryl or chromic cat gut 3/0 was used to close the urethral plate and a glove drain inserted. The wound was then closed in layers using the same suture.

**VARIABLES**

**Dependant variables** - Recurrence of urethral stricture disease and post operative complications.

**Independent variables** - Patient HIV status, CD4 cell count in positive patients, HIV WHO stage, patient age, patient education, patient social status, patient occupation, patient’s family support, stricture aetiology, stricture site and stricture length.

**DATA ANALYSIS**

The data obtained was entered into windows excel 2007 and then exported to SPSS version 16. Assessment of the association between dependent and independent variables was done using the chi square. Multivariable logistic regression analysis was used to determine the factors associated with stricture recurrence and time to recurrence analysis was performed using Kaplan-Meier plots and log rank score.

**ETHICAL CONSIDERATION**

Approval was obtained from the University of Zambia Biomedical and Research Ethics committee (UNZAREC). An informed consent was obtained from all the participants, security and confidentiality of all the information obtained was guaranteed and maintained throughout the study duration and after. The study made sure that the participation of participants in the study
was purely voluntary and participants were assured that they could withdraw from the study at any time if they felt injured or inconvenienced with no consequence of their treatment.

Chapter seven

DATA PRESENTATION/RESULTS

7.1: Socio-demographic characteristics of patients

A total of 71 patients were recruited in this study. 36.6% (n=26) were aged below 30 years, 31% (n=22) were aged 31 – 40 years and 32.4% (n=23) were aged above 41 years.

The minimum age was 4 years and the maximum age was 84 years with 38.04 years being the mean.

7.2: Stricture characteristics and HIV

Figure 1; Stricture aetiology

Figure 1 shows that urethritis is the commonest cause of urethral stricture disease as 45.1% (n=32) had post urethritis urethral stricture disease. 25.4% (n=18) had stricture disease resulting from external trauma while 25.4% (n=18) had urethral stricture disease resulting from unknown
aetiologies. Iatrogenic trauma was the least common aetiology and was an aetiology in 12.7% (n=9) of the patients.

Table 1; Stricture location

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulbar urethra</td>
<td>52</td>
<td>73.2</td>
<td>73.2</td>
<td>73.2</td>
</tr>
<tr>
<td>Bulbo-membranous urethra</td>
<td>1</td>
<td>1.4</td>
<td>1.4</td>
<td>74.6</td>
</tr>
<tr>
<td>Membranous urethra</td>
<td>4</td>
<td>5.6</td>
<td>5.6</td>
<td>80.3</td>
</tr>
<tr>
<td>Penile urethra</td>
<td>14</td>
<td>19.7</td>
<td>19.7</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 illustrates that the bulbar urethra is the commonest location of urethral stricture disease accounting for 73.2 % (n=52). 5.6% (n=4) had strictures located in the membranous urethra and 19.7% (n=14) had strictures in the penile urethra. The stricture was located in the bulbo-membranous urethra in 1.4% (n=1) of the patients.

Figure 2; stricture length
Figure 2 shows that 76.1% (n=56) of the patients had strictures less than or equal to 1cm in length. 14.1% (n=10) had strictures between 1.1cm and 3cm. 9.9% (n=7) had strictures longer than 3cm.

![Figure 3; HIV status](image)

According to figure 3, 63% (n=45) of the patients were HIV positive while HIV negative patients accounted for 37% (n=26). All HIV seropositive patients had HIV WHO stage I disease.

<table>
<thead>
<tr>
<th>Stricture etiology</th>
<th>HIV status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-reactive</td>
<td>Reactive</td>
</tr>
<tr>
<td>Urethritis</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Iatrogenic trauma</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>External trauma</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>32</strong></td>
<td><strong>21</strong></td>
</tr>
</tbody>
</table>

As illustrated by table 2, 50% (n=16/32) of patients with post urethritis stricture disease were HIV positive.
Table 3; HIV patients on HAART

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>On HAART</td>
<td>14</td>
<td>19.7</td>
<td>53.8</td>
<td>53.8</td>
</tr>
<tr>
<td>Not on HAART</td>
<td>12</td>
<td>16.9</td>
<td>46.2</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>36.6</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Of the patients who were reactive, 53.8% (n=14) were on HAART while 46.2% (n=12) were not on HAART. This is as shown in table 3 above.

7.3 : Operations and outcome

Figure 4; Operation types performed
Figure 4 shows that 73% (n=52) of the patients had urethral dilatation while 17% (n=12) underwent anastomotic urethroplasty. 10% (n=7) had staged urethroplasty performed.

### Table 4; Intra Operative Complications

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No complication</td>
<td>69</td>
<td>97.2</td>
<td>97.2</td>
</tr>
<tr>
<td>Pain &amp; minimal bleeding</td>
<td>1</td>
<td>1.4</td>
<td>98.6</td>
</tr>
<tr>
<td>Mild haemorrhage</td>
<td>1</td>
<td>1.4</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>71</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

2.8% (n=2) of the patients had intraoperative complications as shown by table 4. The complications included pain and minimal bleeding and mild haemorrhage.

### Table 5; Post Operative complications

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound infection</td>
<td>3</td>
<td>4.2</td>
<td>33.3</td>
<td>33.3</td>
</tr>
<tr>
<td>Fistula</td>
<td>6</td>
<td>8.5</td>
<td>66.7</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>9</td>
<td>12.7</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>No complication</td>
<td>62</td>
<td>87.3</td>
<td></td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>71</td>
<td>100.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

12.7% (n=9) of the patients had postoperative complications as shown in table 5. 4.2% (n=3) had postoperative wound infections and 8.5% (n=6) had urethrocutaneous fistulas.
Table 6; Stricture recurrence

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No recurrence</td>
<td>26</td>
<td>36.6</td>
<td>44.8</td>
</tr>
<tr>
<td>Recurrence</td>
<td>32</td>
<td>45.1</td>
<td>55.2</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>81.7</td>
<td>100.0</td>
</tr>
<tr>
<td>Lost to follow up</td>
<td>13</td>
<td>18.3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Table 6 illustrates postoperative urethral stricture disease recurrence. 44.8% (n=26/58) of the patients had no recurrence after being followed up for 6 months. 55.2% (n=32/58) had recurrence while 18.3% (n=13/71) were lost to follow up.

Figure 5; Stricture recurrence by procedure

According to fig 5, 28% (n=20/58) of the patients who had urethral dilatation had recurrence whereas 6% (n=4/58) who had anastomotic urethroplasty had recurrence. Of the patients who had staged urethroplasty, 10% (n=7/58) had urethral stricture disease recurrence.

Table 7; HIV status versus stricture recurrence

<table>
<thead>
<tr>
<th>HIV</th>
<th>No recurrence</th>
<th>Recurrence</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-reactive</td>
<td>18</td>
<td>16</td>
<td>34</td>
</tr>
</tbody>
</table>
47% (n=16/34) of the non reactive patients had recurrence while 67% (n=16/24) of the reactive patients had recurrence as shown in table 11 above.

7.4 : Association between dependent and independent variables

Table 8; chi square tests

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Chi Square Statistic</th>
<th>DF</th>
<th>P value</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence and HIV status</td>
<td>2.187</td>
<td>1</td>
<td>0.139</td>
<td>Accept the H0</td>
</tr>
<tr>
<td>Recurrence and age</td>
<td>1.454</td>
<td>2</td>
<td>0.483</td>
<td>Accept the H0</td>
</tr>
<tr>
<td>Recurrence and education</td>
<td>2.244</td>
<td>3</td>
<td>0.508</td>
<td>Accept the H0</td>
</tr>
<tr>
<td>Recurrence and occupation</td>
<td>2.412</td>
<td>1</td>
<td>0.120</td>
<td>Accept the H0</td>
</tr>
<tr>
<td>Recurrence and family support</td>
<td>2.954</td>
<td>1</td>
<td>0.086</td>
<td>Accept the H0</td>
</tr>
<tr>
<td>Recurrence and stricture length</td>
<td>10.009</td>
<td>2</td>
<td>0.002</td>
<td>Reject the H0</td>
</tr>
<tr>
<td>Recurrence and stricture aetiology</td>
<td>2.388</td>
<td>2</td>
<td>0.296</td>
<td>Accept the H0</td>
</tr>
<tr>
<td>Recurrence and stricture location</td>
<td>6.568</td>
<td>3</td>
<td>0.047</td>
<td>Reject the H0</td>
</tr>
<tr>
<td>Recurrence and CD4cc</td>
<td>4.195</td>
<td>2</td>
<td>0.109</td>
<td>Accept the H0</td>
</tr>
</tbody>
</table>

Chi square tests were carried out to know the association between dependent and independent variables and results are shown in table 8. The null hypothesis was rejected on association between recurrence and stricture length and stricture location.

7.5 : Multivariable logistic regression analysis

Table 9; Regression analysis

<table>
<thead>
<tr>
<th>Valuable</th>
<th>OR</th>
<th>P</th>
<th>(c – i)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stricture location</td>
<td>0.407</td>
<td>0.008</td>
<td>0.210-0.789</td>
</tr>
<tr>
<td>Stricture length</td>
<td>1.946</td>
<td>0.199</td>
<td>0.705-5.377</td>
</tr>
<tr>
<td>Stricture aetiology</td>
<td>0.534</td>
<td>0.167</td>
<td>0.219-1.301</td>
</tr>
<tr>
<td>CD4cc</td>
<td>0.633</td>
<td>0.598</td>
<td>0.116-3.457</td>
</tr>
<tr>
<td>HAART</td>
<td>1.745</td>
<td>0.675</td>
<td>0.129-23.548</td>
</tr>
</tbody>
</table>
Multivariable logistic regression analysis as shown in table 9 was used to know the effect of independent variables on stricture recurrence. There was no statistically significant result.

### 7.6: Kaplan-Meier plots

**Table 10: Kaplan-Meier percentiles**

<table>
<thead>
<tr>
<th></th>
<th>25</th>
<th>Std. Error</th>
<th>50</th>
<th>Std. Error</th>
<th>75</th>
<th>Std. Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>non-reactive</td>
<td>55.000</td>
<td>34.641</td>
<td>35.000</td>
<td>4.961</td>
<td>21.000</td>
<td>4.330</td>
</tr>
<tr>
<td>reactive</td>
<td>98.000</td>
<td>31.177</td>
<td>56.000</td>
<td>35.000</td>
<td>22.000</td>
<td>6.062</td>
</tr>
<tr>
<td>Overall</td>
<td>93.000</td>
<td>11.635</td>
<td>35.000</td>
<td>7.778</td>
<td>22.000</td>
<td>3.062</td>
</tr>
</tbody>
</table>

Time to recurrence analysis was done using Kaplan-Meier plots. Table 10 shows that 25% of the non-reactive patients took 55 days for stricture recurrence to occur while 25% of the reactive patients took 98 days for stricture recurrence to take place.
Figure 6 above shows the cum survival at 50 days for non reactive patients as being 0.3 and for reactive patients as being 0.55. The cum survival in most parts of the curve is higher in reactive patients.

Chapter Eight

DISCUSSION

8.1: Socio-demographic characteristics of patients

The mean age of patients presenting with urethral stricture disease in this study is 38.04 years. This mean age is close to what is reported in other African studies. O.B. Shittu (2001) in Nigeria reported the mean age as being 42.2 years. Another study by Ramyil et al (2007) found the mean age to be 30.6 years. C. F. Heyns and D. C. Marais (2002) showed in their study that the mean age of patients presenting with urethral stricture disease was 48 years.
Most patients were below 30 years old. This is the most sexually active age group and most strictures can be attributed to urethritis.

8.2: Stricture characteristics and HIV

8.2.1 Stricture aetiology

In this study, urethritis was the commonest cause of urethral stricture disease as 45.1% (n=32) of the patients had post urethritis urethral stricture disease. 25.4% (n=18) had stricture disease resulting from external trauma while 25.4% (n=18) patients had stricture disease resulting from unknown aetiologies. Iatrogenic trauma was the least common aetiology and was an aetiology in 12.7% (n=9) of the patients.

This is in conformity with other studies done in Africa which have shown urethritis as the commonest cause of urethral stricture disease. At the urology unit, Department of Surgery, University College Hospital, Ibadan, Nigeria a study carried out indicated the aetiology of stricture disease as being post-infective in 80% of the cases (Shittu, 2001). At the Urology Department of the Conakry University Hospital, Republic of Guinea, the majority of strictures were caused by infection followed by post-traumatic strictures accounting for 84% and 10% respectively (Daillo et al, 2006).

The pattern is however different in developed countries. A study by Fenton et al (2005) in the United States of America found that most strictures were idiopathic (34%) or iatrogenic (32%); fewer were inflammatory (20%) or traumatic (14%).

The high prevalence of post urethritis urethral stricture disease is due to the high prevalence of untreated STIs whose sequelae is urethral stricture disease.

The lower percent of post infective strictures in this study compared to other African studies may be because some participants felt stigmatized to mention urethritis as an aetiology. Such
participants’ aetiology thus falls under unknown causes.

8.2.2 Stricture location
The commonest location of urethral stricture disease in this study was the bulbar urethra accounting for 73.2% (n=52). 5.6% (n=4) had strictures located in the membranous urethra and 19.7% (n=14) had strictures in the penile urethra. The stricture was located in the bulbo-membranous urethra in 1.4% (n=1) of the patients.

Ramyil and group (2007) showed that strictures were bulbar in 89%. The pattern was similar in the United States of America where Fenton et al (2005) found that most strictures involved the bulbar urethra (52%).

Therefore, the pattern of stricture location in this study is similar to what is seen in other developing and developed countries.

8.2.3 Stricture length
Stricture length in this study was important as it determined the type of operation to undertake. 76.1% (n=56) of the patients had strictures less than or equal to 1cm in length. 14.1% (n=10) had strictures between 1.1cm and 3cm while 9.9% (n=7) had strictures longer than 3cm. The average urethral stricture length in this study was 1.4cm.

In a study by M A Abdalla (2008), the average stricture length was 7cm. The average stricture length in a study by Fenton et al (2004) was 4.1cm.

The average stricture length in this study was lower than in the two studies above and this may be because most strictures in this study were bulbar and mostly less than 1cm.
**8.2.4 HIV status and WHO stage**

The number of HIV seropositive and HIV seronegative patients was predetermined when calculating the sample size. 63% (n=45) of the patients were HIV positive while 37% (n=26) were HIV negative.

The 2011 WHO HIV classification system as shown in the appendix 5 was used and all the patients who were HIV positive had stage I disease. Patients in this stage were either asymptomatic or had persistent generalized lymphadenopathy.

Patients with WHO stages II, III and IV may not be fit for surgery. However, patients with WHO stages II, III and IV were not excluded but were not just available.

The 2011 CDC HIV classification which is shown in the appendix 5 was not used in this study as it is based on the lowest documented CD4 cell count and on previously diagnosed HIV-related conditions whose details the questionnaire was not capturing.

**8.2.5 Stricture aetiology and HIV status Crosstabulation**

In this study, 50% (n=16/32) of patients with post urethritis urethral stricture disease were HIV positive. This corresponds to a study done by Sturm et al (2004) who found the sero-prevalence of HIV to be 45% in patients with urethritis. However, the study by Sturm et al only considered urethritis and not urethral stricture disease which is a sequelae of urethritis. This shows that the prevalence of HIV in patients with urethritis is high as urethritis is a risk factor for HIV acquisition. STIs cause urethritis which is an aetiology for urethral stricture disease and there is thus an association between urethritis and HIV.

**8.2.6 HIV patients on HAART**
Of the patients who were reactive, 53.8% (n=14/26) were on HAART while 46.2% (n=12/26) were not on HAART. HAART improves the immune status of patients by improving CD4cc and this is a good predictor of a good surgical outcome (Kumar P and Clark M, 2002).

8.3: Operations and outcome

8.3.1 Operation types performed
Operations done included urethral dilatation, anastomotic urethroplasty and staged urethroplasty. 73% (n=52) of the patients had urethral dilatation while 17% (n=12) underwent anastomotic urethroplasty. 10% (n=7) had staged urethroplasty.

8.3.2 Complications
In a study by M.A Abdalla (2008), the postoperative complication rate was 19% and complications included secondary haemorrhage, ischemia and sloughing of the penile skin and urethrocutaneous fistula.

In this study, only 2.8% (n=2) of the patients had intraoperative complications which included pain, minimal bleeding and mild haemorrhage. However, postoperative complications were seen in 12.7% (n=9) of the patients and included wound infection and urethrocutaneous fistulas. The postoperative complication rate was lower than that highlighted in the study by Abdalla.

8.3.3 Stricture recurrence
After following up patients postoperatively for 6 months, the overall urethral stricture recurrence rate was 55.2% (n=32/58).
28% (n=20) of the patients who had urethral dilatation had urethral stricture recurrence while 6% (n=4) of the patients who had anastomotic urethroplasty had urethral stricture recurrence. Of the patients who underwent staged urethroplasty, 10% (n=7) had urethral stricture recurrence.

In a 5-year retrospective study by Nwofor and Ugezu (2004), 51 patient records were reviewed and it was found that urethroplasty gave better results with a 16.7% recurrence rate. 61.5% of the patients who had urethral dilatation required repeated dilatations between 6 and 12 months in order to maintain a satisfactory urine flow.

The recurrence rate following urethroplasty in this study was 16% (6% for anastomotic urethroplasty and 10% for anastomotic urethroplasty) and this is similar to the recurrence rate in the study by Nwofor and Ugezu. The recurrence rate following dilatation was lower in this study probably because the follow up period was shorter.

8.3.4 HIV status versus recurrence

No known study has been done to compare urethral stricture disease management between HIV seropositive and seronegative patients. The overall urethral stricture recurrence rate in this study irrespective of HIV status was 55.2% (n=32/58).

With respect to HIV status, 47% (n=16/34) of the non-reactive patients had urethral stricture recurrence while 67% (n=16/24) of the reactive patients had urethral stricture recurrence. The difference in urethral stricture recurrence rate between reactive and non-reactive patients was 20%. There were more non-reactive patients (n=34) than reactive patients (n=24) and this
contributed to the difference. However, this difference was also not statistically significant as there was no association in this study between urethral stricture recurrence and HIV status \( (p=0.139) \).

### 8.4: Association between dependent and independent variables

Chi square tests were carried out to know the association between dependent and independent variables. The null hypothesis was rejected on association between recurrence and stricture length and stricture location.

The association between stricture recurrence and stricture length gave a chi-square test of 10.009 with 2 as the degree of freedom. The p value was 0.002 hence rejecting the null hypothesis.

In the association between stricture recurrence and stricture location, the chi-square test was 6.568 and the p value was 0.047. The degree of freedom was 3 hence rejecting the null hypothesis.

Therefore, there is an association between stricture recurrence and stricture location and length. However, there is no association between stricture recurrence and HIV status.

In the association between urethral stricture disease recurrence and CD4cc, the chi-square statistic was 4.195 and the p value was 0.109. Therefore, there is no association between urethral stricture recurrence and CD4cc.

### 8.5: Multivariable logistic regression analysis

Multivariable logistic regression analysis was used to know the effect of independent variables on stricture recurrence.
All the independent variables could not fit into the model at once. The independent variables were fed into the model in batches and the results obtained were assembled into one table. This could be attributed to a small sample size.

However, there was no statistically significant result.

8.6: Kaplan-Meier plots
Analysis of time to recurrence was carried out using Kaplan-Meier plots. 25% of the non reactive patients took 55 days to have stricture recurrence while 25% of the reactive patients took 98 days for the stricture to recur.

This shows that HIV status in this study was not significant in determining stricture recurrence. This is further affirmed by the survival function curve which showed the cum survival at 50 days for non reactive patients as being 0.3 and for reactive patients as being 0.55.

Chapter Nine

CONCLUSIONS AND RECOMMENDATIONS

9.1: CONCLUSIONS

Urethral stricture disease affects patients from all age groups as the youngest patient in this study is 4years old and the oldest is 84years old. The commonest aetiology of urethral stricture disease at UTH is urethritis.

The prevalence of HIV in patients presenting with post urethritis stricture disease is high.
The recurrence rate of urethral stricture disease following treatment is not affected by the HIV status and the CD4cc of the patient. However, urethral stricture disease recurrence is affected by the location of the stricture as well as the length of the stricture.

Time to recurrence and Cum survival of urethral stricture disease following treatment are also not influenced by the HIV status of the patient.

### 9.2: RECOMMENDATIONS

HIV should always be suspected in patients presenting with post urethritis urethral stricture disease and direct counselling and testing should be offered if their HIV status is not known.

There is need to increase awareness of the association between Urethritis and urethral stricture disease.

In the management of urethral stricture disease, more attention should be paid to stricture length and stricture location as these variables have been found to be associated with urethral stricture disease recurrence.
A similar study needs to be carried out with a bigger sample size and with patients recruited being followed up over a longer period of time to ascertain the factors that affect urethral stricture disease recurrence.

Appendix-1

**BUDGET**

**FIXED ASSETS**

- Purchase of laptop .......................................................... K5, 600,000=00
- Purchase of printer and accessories ................................. K487, 000=00
- Stationary purchase .......................................................... K1, 000, 000=00
- Printer cartridge .............................................................. K3, 000, 000=00
- Document binding ............................................................ K800, 000=00
- Flash disc ........................................................................... K250, 000=00
- SPSS software ................................................................. K400, 000=00
RECURRENT EXPENDITURE

Client transport fees .................................................. K2, 000,000=00
Communication .............................................................. K2, 000,000=00
Ethics committee ........................................................... K500, 000=00
Administrative fees ....................................................... K1, 000,000=00
Supporting personnel ..................................................... K5, 000,000=00
Secretarial services ....................................................... K1, 000,000=00
Researcher training in SPSS ............................................ K2, 000,000=00
CD4 cell counts ................................................................ K2, 600,000=00

TOTAL ........................................................................ K27, 637,000=00

Appendix-2

EVALUATION FORM

PERSONAL DETAILS

Hospital identification number................................................. Age..........years
Tribe.............................................................. Date seen in clinic VII....../....../201....
Highest level of Education attained.................................................................
Occupation................................. Residence.........................................
Married {   }    Single {   }     Divorced {   }

HISTORY

LUTS after urethral discharge/urethritis {   }
LUTS preceded by urethral catheterization or instrumentation/iatrogenic trauma {   }

LUTS after pelvic or perineal trauma/external trauma {   }

Unexplained LUTS {   } Virgin stricture {   }

Are you on HAART?  Yes {   }    No {   }

Others………………………………………………………………………………………………

……………………………………………………………………………………………………

EXAMINATION

External urethral meatus patent {   }                                Non patent external urethral meatus {   }

Firm, palpable areas along the length of the urethra {   }                             Distended bladder {   }

Spc present {   } Urethral discharge/pus present {   }             Blood urethral discharge {   }

Pelvic fracture present {   }                                    WHO HIV stage; I {   } II {   } III {   } IV {   }

Others………………………………………………………………………………………………

……………………………………………………………………………………………………

INVESTIGATIONS

HIV test;      Reactive {   }                        Nonreactive {   }                      Refused HIV test {   }

CD4 cell count (if HIV positive)....................... Residual urine volume..............mls

Routine urine m/c/s..............................................................................................

..........................................................................................................................

..........................................................................................................................

International prostate symptom score....................... Flow rate;.......................mls/min

Retrograde urethrogram/cystourethrogram;

Stricture location; prostatic urethra {   } membranous urethra {   } bulbar urethra {   }

Penile urethra {   }
Stricture length: ...........cm.

DIAGNOSIS

Virgin urethral stricture disease with the following aetiology;

Urethritis {  } External Trauma {  } Iatrogenic Trauma {  } Unknown {  }

Others.................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................

OPERATIVE DETAILS

Date of operation:......./......./201......

Operation site: Phase V theatre {  }, Phase III theatre {  }, Clinic VII {  }

Surgeon: Consultant {  }, Senior Registrar {  }, Registrar, Year II, III, IV {  }

Type of operation:

Urethroplasty; End to end anastomosis {  } Urethroplasty with tunica vaginalis {  }

Second stage urethroplasty {  }

Optic urethrotomy {  }

Urethral dilatation {  }

Catheterized {  } Not catheterized {  } Catheter size.................................
Complications during the procedure:

Hemorrhage {   }

Others…………………………………………………………………………………………

………………………………………………………………………………………………

Date of discharge……./……/201……

POST OPERATIVE FOLLOW UP

First review date……./……/201……

Catheter removal; Yes {   } No {   } International prostate symptom score………………

Flow rate ............mls/min Residual urine volume.......mls

Retrograde urethrogram/cystourethrogram (if applicable):

Stricture location; prostatic urethra {   } membranous urethra {   } bulbar urethra {   }

Penile urethra {   } Stricture length;.............cm.

Complications during the first review:

Urinary extravasation {   } Wound infection {   }

Forneurs gangrene {   } Urethrocutaneous fistula {   }

Others…………………………………………………………………………………………

………………………………………………………………………………………………

Second review date……./……/201....

International prostate symptom score……………… Flow rate ............mls/min

Residual urine volume.......mls

Retrograde urethrogram/cystourethrogram (if applicable):
Stricture location; prostatic urethra { } membranous urethra { } bulbar urethra { }

Penile urethra { }

Stricture length:............cm.

Complications during the first review:

Urinary extravasation { } Wound infection { }

Forneurs gangrene { } Urethrocutaneous fistula { }

Others........................................................................................................................................

........................................................................................................................................

........................................................................................................................................

........................................................................................................................................

Third review date; ....../....../201....

International prostate symptom score................. Flow rate.................mls/min

Residual urine volume........mls

Retrograde urethrogram/cystourethrogram (if applicable):

Stricture location; prostatic urethra { } membranous urethra { } bulbar urethra { }

Penile urethra { }

Stricture length:............cm.

Complications during the first review:

Urinary extravasation { } Wound infection { }

Forneurs gangrene { } Urethrocutaneous fistula { }

Others........................................................................................................................................

........................................................................................................................................

........................................................................................................................................

........................................................................................................................................
Fourth review date……/……/201…

International prostate symptom score………… Flow rate…………mls/min

Residual urine volume………mls

Retrograde urethrogram/cystourethrogram (if applicable):

Stricture location; prostatic urethra {   } membranous urethra {   } bulbar urethra {   }
Penile urethra {   }

Stricture length:…………cm.

Complications during the fourth review:

   Urinary extravasation {   } Wound infection {   }
   Forneurs gangrene {   } Urethrocutaneous fistula {   }

Others……………………………………………………………………………………………………

Appendix-3
<table>
<thead>
<tr>
<th>Patient's Name</th>
<th>Date of Birth</th>
<th>Date Completed</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>1. Incomplete emptying</th>
<th>Less Than 1 Time in 5</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Frequency</th>
<th>Less Than 1 Time in 5</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month, how often have you had to urinate again less than two hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Intermittency</th>
<th>Less Than 1 Time in 5</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Urgency</th>
<th>Less Than 1 Time in 5</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Weak stream</th>
<th>Less Than 1 Time in 5</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. Straining</th>
<th>Less Than 1 Time in 5</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 3-1. INTERNATIONAL PROSTATE SYMPTOM SCORE (Continued)

<table>
<thead>
<tr>
<th>7. Nocturia</th>
<th>Less Than 1 Time in 5</th>
<th>Less Than Half the Time</th>
<th>About Half the Time</th>
<th>More Than Half the Time</th>
<th>Almost Always</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Total I-PSS Score

<table>
<thead>
<tr>
<th>Quality of Life Due to Urinary Symptoms</th>
<th>Delighted</th>
<th>Pleased</th>
<th>Mostly Satisfied</th>
<th>Mostly Dissatisfied</th>
<th>Mostly Dissatisfied</th>
<th>Unhappy</th>
<th>Terrible</th>
</tr>
</thead>
<tbody>
<tr>
<td>If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

CONSENT FORM

Introduction

This form is given to let you know more about the study. After understanding it, you can decide whether to take part in the study or not.

Who is carrying out this study?

The study is being conducted at the UTH by Dr Silumbe Michael a University of Zambia post graduate urology student. This is part of the requirement for obtaining a specialist qualification in urology.

The purpose of the study

The study is about patients with narrowing of the urethral tube (urethral stricture), a common condition seen in the urology clinic of the UTH but whose outcome after treatment has not been established. The study will look at surgical interventions used in managing acquired urethral stricture disease at the UTH according to the protocol outlined above. Patients fulfilling the inclusion criteria will be directly counseled and tested for HIV. Those found reactive will have blood immediately collected to determine their CD4 cell counts. 25 seropositive and 46 seronegative patients will be routinely followed up postoperatively at 21 days, 1 month, 3 months and 6 months. Ipss, flow rates, residual urine, urethrogram when indicated and complications will be determined at each review. Stricture recurrence and complication rates will be compared between HIV positive and HIV negative patients using information obtained during the reviews.

Benefits
All patients who agree to be included in the study will be seen immediately and managed according to the protocol within the shortest possible time. They will be regularly followed up to monitor their disease at no additional cost. All patients will have easy access to the study team should they have any questions or problems.

**Risks**

The study will not perform any additional treatments other than what any other patient with stricture disease will be exposed to at the UTH. Any injury which the patient suffers during the course of treatment will be treated expeditiously by the research team.

**Confidentiality**

Taking part in this study is voluntary, as such, you may choose to participate or not. Your name and other personal identifiers will not be used in this study. The information of this may be revealed by the study investigator to the examiners appointed by the University of Zambia.

You are free to ask any questions regarding the study.

**Questions**

Should you seek any clarifications concerning this study or your rights as a research participant, feel free to contact;

**Address:**
Dr. Michael. Silumbe,  
Department of Surgery,  
University Teaching Hospital,  
P/B RW 1X, Lusaka.

**Tel no:** +260977817645  

**Have been informed about the study and accept**
to be entered for a project ‘To compare the short term outcome of urethral stricture disease management between HIV and non HIV infected patients at UTH.

Signed .................................. Thumbprint........................................

Witness .................................

Date ........................................

................................................................................................................................................

Signature and name of investigator

Appendix-5
### WHO Clinical Staging of HIV/AIDS

<table>
<thead>
<tr>
<th><strong>Primary HIV Infection</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Acute retroviral syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Clinical Stage 1</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Persistent generalized lymphadenopathy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Clinical Stage 2</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate unexplained weight loss (&lt;10% of presumed or measured body weight)</td>
</tr>
<tr>
<td>Recurrent respiratory infections (sinusitis, tonsillitis, otitis media, and pharyngitis)</td>
</tr>
<tr>
<td>Herpes zoster</td>
</tr>
<tr>
<td>Angular cheilitis</td>
</tr>
<tr>
<td>Recurrent oral ulceration</td>
</tr>
<tr>
<td>Papular pruritic eruptions</td>
</tr>
<tr>
<td>Seborrheic dermatitis</td>
</tr>
<tr>
<td>Fungal nail infections</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Clinical Stage 3</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexplained severe weight loss (&gt;10% of presumed or measured body weight)</td>
</tr>
<tr>
<td>Unexplained chronic diarrhea for &gt;1 month</td>
</tr>
<tr>
<td>Unexplained persistent fever for &gt;1 month (&gt;37.6°C, intermittent or constant)</td>
</tr>
<tr>
<td>Persistent oral candidiasis (thrush)</td>
</tr>
<tr>
<td>Oral hairy leukoplakia</td>
</tr>
<tr>
<td>Pulmonary tuberculosis (current)</td>
</tr>
<tr>
<td>Severe presumed bacterial infections (e.g., pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)</td>
</tr>
<tr>
<td>Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis</td>
</tr>
<tr>
<td>Unexplained anemia (hemoglobin &lt;8 g/dL)</td>
</tr>
<tr>
<td>Neutropenia (neutrophils &lt;500 cells/µL)</td>
</tr>
<tr>
<td>Chronic thrombocytopenia (platelets &lt;50,000 cells/µL)</td>
</tr>
</tbody>
</table>

| **Clinical Stage 4** |
**Pneumocystis pneumonia**  
Recurrent severe bacterial pneumonia  
Chronic herpes simplex infection (orolabial, genital, or anorectal site for >1 month or visceral herpes at any site)  
Extrapulmonary candidiasis (or candidiasis of trachea, bronchi, or lungs)  
Extrapulmonary tuberculosis  
Kaposi sarcoma  
Cytomegalovirus infection (retinitis or infection of other organs)  
Central nervous system toxoplasmosis  
HIV encephalopathy  
Cryptococcosis, extrapulmonary (including meningitis)  
Disseminated nontuberculosis mycobacteria infection  
Progressive multifocal leukoencephalopathy  
Candida of the trachea, bronchi, or lungs  
Chronic cryptosporidiosis (with diarrhea)  
Chronic isosporiasis  
Disseminated mycosis (e.g., histoplasmosis, coccidioidomycosis, penicilliosis)  
Recurrent nontyphoidal *Salmonella* bacteremia  
Lymphoma (cerebral or B-cell non-Hodgkin)  
Invasive cervical carcinoma  
Symptomatic HIV-associated nephropathy  
Symptomatic HIV-associated cardiomypathy  
Reactivation of American trypanosomiasis (meningoencephalitis or myocarditis)

---

**CDC Classification System for HIV-Infected Adults and Adolescents**

<table>
<thead>
<tr>
<th></th>
<th><strong>A</strong></th>
<th><strong>B</strong></th>
<th><strong>C</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asymptomatic, Acute HIV, or PGL</td>
<td>Symptomatic Conditions, not A or C</td>
<td>AIDS-Indicator Conditions</td>
</tr>
<tr>
<td>(1) ≥500 cells/µL</td>
<td>A1</td>
<td>B1</td>
<td>C1</td>
</tr>
<tr>
<td>(2) 200-499 cells/µL</td>
<td>A2</td>
<td>B2</td>
<td>C2</td>
</tr>
<tr>
<td>(3) &lt;200 cells/µL</td>
<td>A3</td>
<td>B3</td>
<td>C3</td>
</tr>
</tbody>
</table>
Appendix-6

REFERENCES


