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Late Outcome of Direct Vision Urethrotomy in Patients with Urethral Stricture at Kilimanjaro Christian Medical Center (KCMC), Moshi-Tanzania

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Keywords: *urethral stricture, outcome.*

GJMR-I Classification: *NLMC Code: WP 175*

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Methodology: This is a hospital based retrospective cohort study that involved patients who presented to urology department at KCMC with urethral stricture and underwent direct vision urethrotomy from January 2006 to December 2013.

Results: A total of 648 cases of urethral stricture disease were managed at KCMC between January 2006 and December 2013, out of these 365 (56.3%) underwent DVU and 283 (43.7%) underwent urethroplasty. Of the patients who underwent urethroplasty, 191(67.5%) underwent anastomotic urethroplasty, 64 (22.6%) underwent staged urethroplasty and 28 (9.9%) underwent substitutional urethroplasty. Out of 365 patients who underwent DVU during the study period 227 (62.2%) met the inclusion criteria, and 138 (37.8%) did not meet the inclusion criteria. Eighty six point four percent of participants were 40 years or older. One hundred and three participants (45.4%) had urethral strictures from iatrogenic causes. Most strictures were located in the bulbous part of urethra (63.9%). The majority of participants (66.1%) had strictures 1cm long or shorter. Most participants (90.8%) had a single stricture. Out of the 227 participants, 102 (44.93%) needed a re-operation. Of the 102 patients who required re-operation; 59 (57.84%) required the operation within six months; 18 (17.65%) within one year; 9 (8.82%) within two years; 12 (11.76%) within five years; and 4 (3.92%) required the operation beyond five years.

Conclusion: DVU is still the commonest treatment option for patients with urethral stricture at KCMC. Most patients (63%) who underwent DVU were 60 years or above.

The overall long term success rate of DVU was 55.07%

The outcome of DVU was good when stricture was single, the length was 1 cm or less and located in the bulbous urethra.

Recurrence of urethral stricture post DVU is significantly high for strictures which are long, multiple and located in other sites apart from bulbous urethra.

Age of the patient and etiology of the urethral stricture have no influence on the outcome of DVU

Keywords: urethral stricture, outcome.

I. Background and Literature Review

Since the introduction of DVU by Sachse in 1974, the wheel has come a full circle. Earlier studies demonstrated excellent outcomes following DVU and poor success of urethroplasty techniques. However the last two decades have witnessed a revolution in techniques of urethroplasty and many state-of-art centers have reported excellent long-term outcome coupled with the expansion of urethroplasty techniques, studies have highlighted extremely poor long-term outcomes for DVU [Lumen et al, 2009].

Dilatation and DVU are the most common procedures used by the majority of urologists in the United States. Recently, several authors analyzed the trends in male urethral stricture management in the United States using the data from the 1992-2001 Medicare claims. These authors concluded that despite the poor overall efficacy of dilation and DVU, urethroplasty rates were the lowest of all treatments [Barbagli et al, 2012].

Optical urethrotomy is a widely accepted treatment in approximately 80% of patients with urethral strictures. Repeated dilatation and open urethroplasty are other treatment procedures for urethral strictures. Optical urethrotomy (OU) has been performed either under general or spinal anesthesia. There are few excellent reports on use of local anesthesia. Generally

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optical urethrotomy is considered ideal for short segments (less than 2 cm). However, some authors believe that length is not a limiting factor for urethrotomy of anterior urethral strictures. OU has many advantages including day care procedures, early mobilization, shorter period of indwelling catheter and good short term results. However, significant percentage of patients recurs following OU. Most of these patients require either self-dilatation, dilatation by urologist in clinic, repeat OU or open urethroplasty [Zehri et al, 2009].

In a study done in Dar es Salaam a total of 111 patients with urethral strictures were recruited into the study, all were male with age range of 10 – 97 years with a mean of 52.7 years. DVIU was the most performed procedure accounting for 73 (65.8%) of all patients followed by primary urethroplasty at 31 (27.9%) and multistage urethroplasty at 7 (6.3%) [Nyongole et al, 2013].

In a study done at KCMC DVU was done in 50% of cases of urethral stricture [Mteta et al, 2009].

Visual internal urethrotomy provides a safe first line therapeutic option for pediatric urethral stricture shorter than 1 cm, independent of etiology and location. For patients with more than one recurrence or with strictures longer than one centimeter, who are at high risk for recurrence after internal urethrotomy, open Urethroplasty remains the treatment of choice [Hafez et al, 2005].

The classical DVIU includes a single cut made at 12 o'clock position in the scar tissue, till the scar is incised completely. Concerns have been raised about the correct position of the incision. Some authors advocate multiple radial incisions for better incision of the scar. However, there is no reported difference in the outcome of single versus multiple incisions [Santucci et al, 2010].

Laser urethrotomy using different lasers has been attempted to improve outcomes. One prospective study demonstrated superior outcomes using a neodymium-doped yttrium aluminium garnet laser. In this study, recurrence rates following laser urethrotomy were 30% compared to 65% with DVIU over 12-month follow up. However other studies have reported similar success rates after laser and cold knife incision [Turek et al, 1992; Kamp et al, 2006].

In a double-blind, randomized, placebo-controlled study it was shown that injection of triamcinolone acetonide did not improve significantly the outcome of DVU. [Tavakkoli et al, 2011].

The reported duration following urethrotomy ranges from one day to three months. As yet there is no convincing evidence that extending the duration of catheterization has an impact on the outcome. Contrary to the popularly held belief, leaving the urethral catheter in place for three days or less is associated with lower recurrence rate (34%), compared to leaving it for four to seven days or more than seven days (recurrence rates of 43% and 65% respectively). Most studies have reported catheterization duration of one to four days [Dubey, 2011].

Various techniques have been employed to follow patients following visual internal urethrotomy. These include urethral calibration with a catheter, uroflowmetry, flexible cystourethroscopy, AUA symptom index, urethrographic studies and the need for a repeat procedure. There is no uniformly accepted method of follow-up. Using a peak flow rate of less than 15 ml/sec, stricture recurrence could be diagnosed in 84% patients who had stricture recurrence [Pandasoro et al, 1996].

A retrospective study done in Detroit, Michigan from January 1994 through March 2009 to assess the success of DVIU in series of 76 patients with simple urethral strictures, in this study Time to Recurrence (TTR) was defined as the time from urethrotomy until first subjective or objective sign of recurrence (if known), or actual date of subsequent repeat urethrotomy. Sign of recurrence included decreased force of stream, incomplete bladder emptying, recurrent urinary tract infections, increased post-void residual urine, obstructive pattern on uroflow study or definitive radiographic or cystoscopic evidence or recurrent stricture [Santucci et al, 2010].

In a study done in Germany including two university hospitals, Mainz university (group 1) and Bonn University (group 2) with a mean follow up of 4.6 years in group 1 and 3.2 years in group 2. The stricture recurrence rate in Group 1 was 26.9%, whereas in Group 2 was 44.6%. Subgroup analysis revealed a higher preponderance of idiopathic stricture in Group 1 and iatrogenic strictures in Group 2. Theses authors concluded that idiopathic strictures have a more favorable prognosis [Albers et al, 1996].

In a study done in Italy, 224 patients were followed for longer than 60 months after optical urethrotomy and a preoperative peak flow of less than 15 millilitres per second. The mean patient age was 62 years. The success rate (peak flow rate of more than 15 millilitres per second) was 32% overall, and 42%, 16% and 11% among patients with bulbar, penile and penile bulbar strictures respectively [Pansadoro et al, 1996].

Stricture recurrence has been shown to be directly proportional to stricture length. It has been shown that recurrence rate is high with strictures longer than 1cm. In a study done in Italy success rate was 71% for strictures shorter than 1cm versus only 18% for longer strictures [Pansadoro et al, 1996].

In a study by Albers et al, 1996 which was done in Germany, stricture length was analyzed by retrograde urethrography. The recurrence was 27.8% for strictures less than 1cm which was less compared to long strictures of which recurrence was 50.5% following internal urethrotomy.

In a study done in Nigeria a total of 23 patients needed a repeat urethrotomy within 48 months of follow up (recurrence of 32.9%) [Ramyil et al, 2007].

In another study by Zehri et al, 2009 it was shown that strictures length more than two centimetres was significantly associated with recurrence following DVU, (P Value 0.0001).

A study by Javier et al, 2014 in patients who underwent urethrotomy, the procedure was performed a mean of 1.32 ± 0.94 times; in 20% of the subjects, the treatment included urethroplasty due to the poor results of the previous endoscopic treatment. Analysis of the studied parameters revealed that the length of the stricture was the only factor that influenced sole treatment or treatment with urethrotomy and subsequent urethroplasty.

In a study by Mandhani et al, 2005 the degree of spongiofibrosis associated with strictures may also predict stricture recurrence. However, spongiofibrosis is difficult to quantify. Percentage narrowing on retrograde urethrography can be used to predict stricture recurrence. From January 1991 to June 2002 patients with primary bulbar urethral strictures who underwent DVU were selected for the study. Patients with a history of intervention, complete block of the urethral lumen and stricture greater than 2 cm were excluded from study. Urethral diameter at the area of maximum stenosis and at the normal distal urethra was measured on RGU with Vernier caliper and percentage narrowing was derived. Patients were followed 3 times monthly with symptoms, calibration and whenever required with RGU. Recurrence of symptoms, failure to self-calibrate and the need for secondary procedure were considered treatment failure. Complete follow up data were available in 105 patients (44 grade 1 and 61 grade 2). Mean bulbar urethral stricture length was 0.86 cm. Inflammation was the cause of stricture in 83 (79%) and trauma the cause in 22 (21%) patients. In the Cox proportional hazards model only grade of narrowing had a significant impact on outcome. There were 41 cases of treatment failure in the total follow up of 46 +/- 9 months. Mean recurrence-free duration +/- SD was 13 +/- 15 and 44.52 +/- 19 months in cases of treatment failure and success, respectively ($p < 0.0001$). Mean percentage narrowing was significantly higher with treatment failure (69.9% +/- 16.1% vs 48.55% +/- 17.3%, $p < 0.0001$). A cutoff of 74% for urethral narrowing was derived to predict the outcome with 78% probability.

In a study done by Albers et al, 1996 in Germany strictures were in bulbous urethra in 52.6% of the cases and multiple in 21.9%. Penile strictures (28.6%) had the highest recurrence rates (42.5%), bulbar strictures had the lowest recurrence rate (34.3%). Location did not significantly influence recurrence rate.

The location of the stricture did not influence outcome of DVU. Among short strictures those in the bulbar showed lower recurrence rates than, for example, those in the penile urethra, which may be explained by the better vascularization of the proximal urethra. Nonetheless, the process and scarring certainly depend more on aetiology than stricture location [Albers et al, 1996].

In a systematic review by Dubey, some studies have found that iatrogenic strictures had higher recurrence rates than inflammatory or traumatic strictures, whereas another study showed better results for iatrogenic strictures. Inflammatory strictures occurring after long-term catheterization or genital infection were found to be associated with higher chance of recurrence. Others have found no relationship between stricture etiology and risk of recurrence. There is no consensus on whether stricture etiology predicts recurrence, as different studies have proposed different aetiologies as poor responders to DVU.

In a study by Heyns et al, 1998 a single dilatation or a DVU, not followed by restricturing at 3 months, the stricture recurrence rate was 55-60% at 24 months and 50-60% at 48 months. After a second DVU for stricture recurrence at 3 months, the stricture-free rate was 30-50% at 24 months and 0-40% at 48 months. After a third dilatation or DVU for stricture recurrence at 3 and 6 months, the stricture –free rate at 24 months was 0. Urethrotomy has no role when stricture recurrence occurs within 3 months of DVU or recurs after a second urethrotomy.

In a study by Pansadoro et al, 1996 only 2 of the 47 patients treated with multiple urethrotomies achieved a good result and a third or fourth urethrotomy always failed. In a study involving 126 patients who underwent internal urethrotomy and got recurrence underwent either a subsequent urethrotomy or urethroplasty. It was demonstrated that repeat urethrotomy was neither cost-effective nor clinically effective.

In a study by Kjaergard et al, 1988 43 patients were randomized to either weekly CISC for one year or no CISC. The stricture recurrence was 68% in those who did not perform CISC versus 19% in those who did, clearly demonstrating the beneficial effects for CISC.

In a study by Bubey, 2011 it was shown that biweekly intermittent self-dilation (ISD) when continued for longer than 12 months, had a much lower rate of stricture recurrence (16%) when compared with the group that performed ISD for 6 months (40%). There is no role for short-term ISD following urethrectomy.

II. Methods

a) Study design

This was a retrospective hospital based cohort study conducted at KCMC, which is a tertiary referral hospital receiving patients from districts and regional hospitals from the Central and northern zone of Tanzania but also from other zones and neighboring

countries. It involved all patients who had urethral stricture and underwent DVU with a follow of at least six months at KCMC from January 2006 to December 2013.

Patients with incomplete information (incomplete investigation, incomplete surgical operation report) and those who were lost to follow up were excluded from the study.

b) Ethical issues

Ethical clearance was approved by KCMU College Research and Ethics Review Committee for ethical clearance. All patients' information were kept confidential and not to be accessed by people not involved in the study

c) Data processing and analysis

All the collected data were recorded into the extraction form and were checked by the researcher for completeness and consistency. Data from patient record extraction forms were entered into excel spreadsheet and then transferred into SAS (version 9.3) statistical software (SAS Institute, Cary, NC, USA) for analysis. Proportions were used to describe the basic characteristics of the study participants and the patient long term outcomes. Statistical significance was considered when the respective p value was less than 0.05.

III. Results

A total of 648 cases of urethral stricture disease were managed at KCMC between January 2006 and December 2013, out of these 365 (56.3%) underwent DVU and 283 (43.7%) underwent urethroplasty. One hundred ninety one (67.5%) patients underwent anastomotic urethroplasty, 64 (22.6%) underwent staged urethroplasty and 28 (9.9%) underwent substitutional urethroplasty. Out of 365 patients who underwent DVU during the study period 227 (62.2%) met the inclusion criteria, and 138 (37.8%) did not meet the inclusion criteria. Sixty three percent of participants were aged 60 years or above 60 years as shown in **Figure 1**;

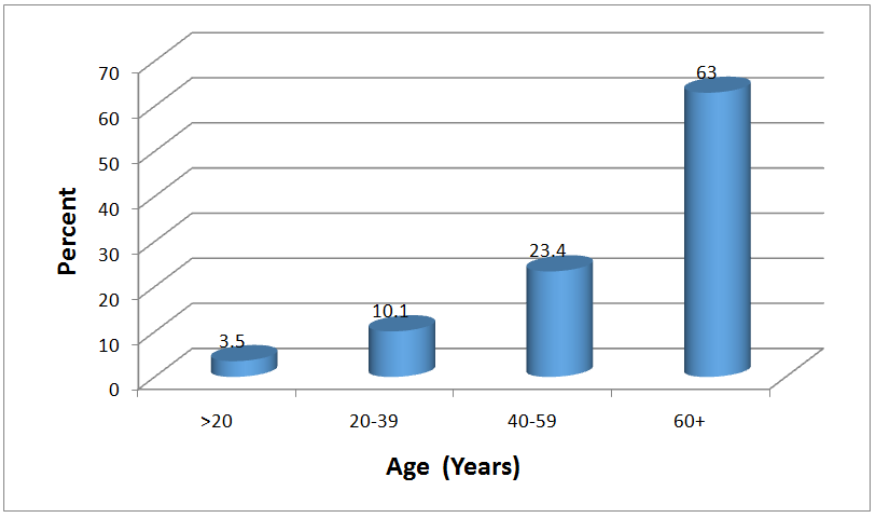

Figure 1: Bar chart showing age distribution of patients who underwent DVU (N=227).

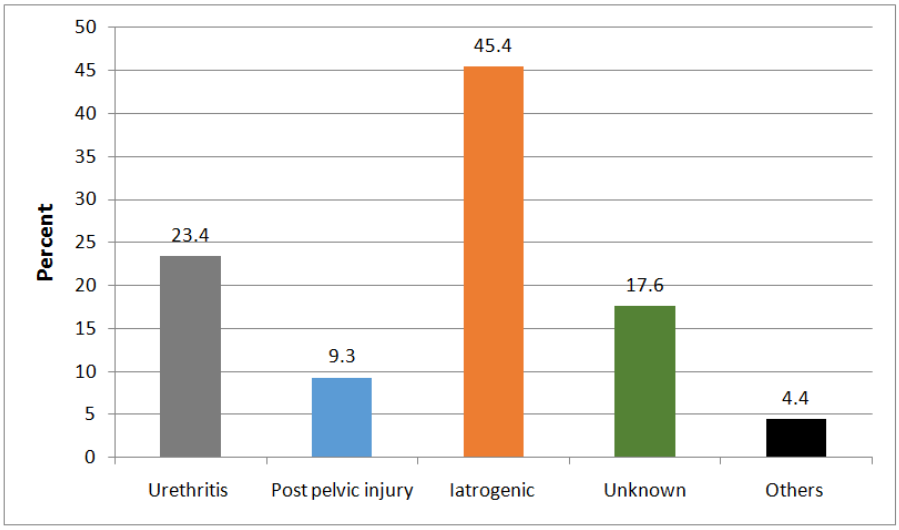

Figure 3 : Aetiologies of urethral stricture in patients who underwent DVU (N=227).

Iatrogenic urethral injuries were found to be the main cause of urethral strictures in 45.4% cases as shown in Figure 3.

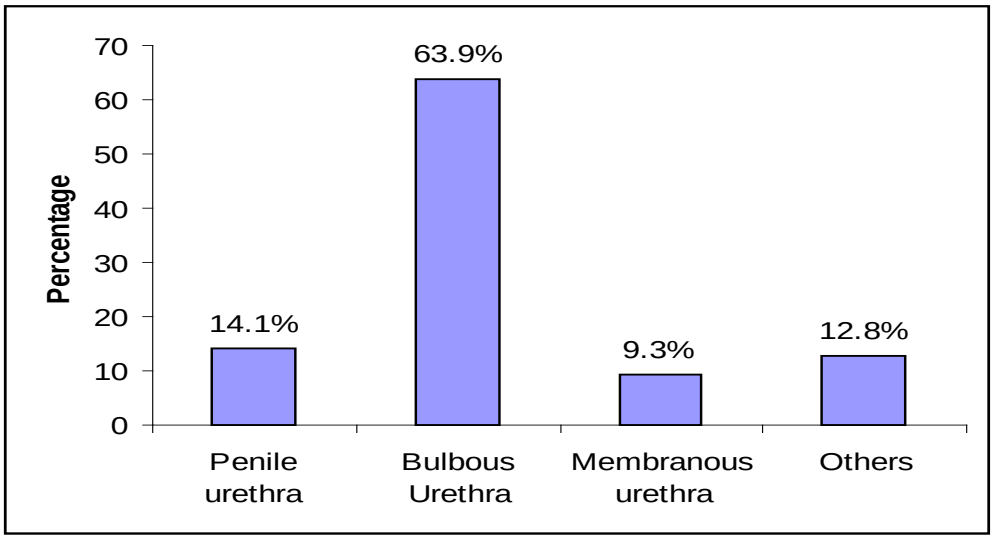

Figure 4 : Site of urethral strictures in patients who underwent DVU (N=227).

One hundred forty five (63.9%) of those who underwent DVU had strictures located at the bulbous part of urethra as shown in figure 4 above.

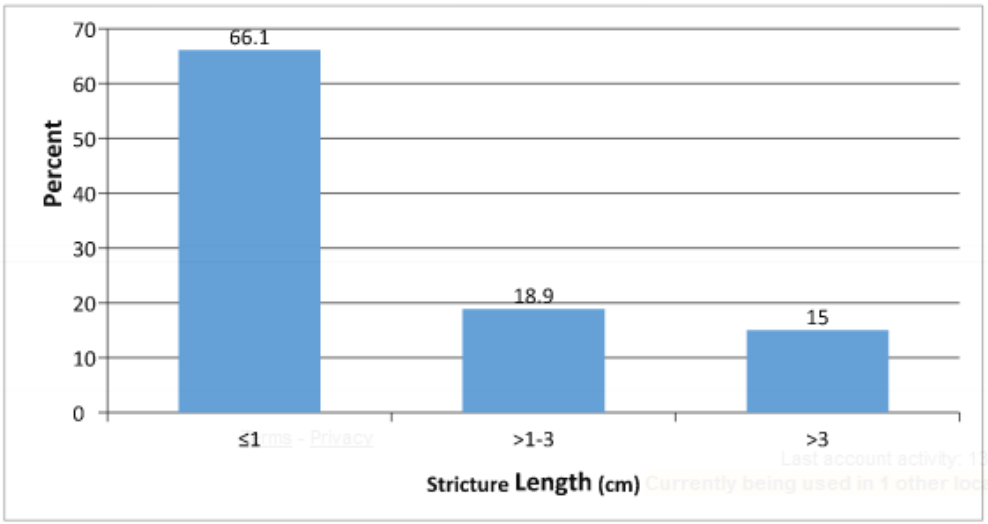

Figure 5 : Length of urethral strictures in patients who underwent DVU (227).

Sixty six point one participants had strictures of 1 cm long or less than 1cm as shown in figure 5 above.

Table 1 : Late DVU outcome among Patients Undergoing DVU at KCMC (227).

	Number	Percent
DVU Outcome		
Need re-operation	102	44.9
No re-operation	125	55.1
Need of re-operation		
Within six months	59	57.8
Within one year	18	17.7
Within two years	9	8.8
Within five years	12	11.8
Beyond five years	4	3.9

Out of the 227 participants, 102 (44.9%) needed a re-operation. Of the 102 patients who required re-operation; 59 (57.8%) required the operation within six months; 18 (17.7%) within one year; 9 (8.8%) within two years; 12 (11.8%) within five years; and 4 (3.9%) required the operation beyond five years as shown in table 1 above.

Table 2 : Outcome of DVU with age

Age group	Outcome of DVU		
	Recurrence	No Recurrence	Total
<20	5 (62.5%)	3 (37.5%)	8 (3.52%)
20-39	10 (43.48%)	13 (56.52%)	23 (10.13%)
40-59	25 (47.17%)	28 (52.83 %)	53 (23.35%)
≥60	62 (43.36%)	81 (56.64%)	143 (63.00%)
Total	102 (44.93%)	125 (55.07%)	227 (100%)

There was no statistical significant difference in the outcome of DVU in the different age groups (using Fisher's Exact Test P value 0.77)

Table 3 : Outcome of DVU with length of urethral stricture

Length of stricture (cm)	Outcome of DVU		
	No Recurrence	Recurrence	Total
<1	76 (80.00%)	19 (20.00%)	95 (41.85%)
1-3	45 (37.5%)	75 (62.5%)	120 (52.86%)
>3	4 (33.33%)	8 (66.67%)	12 (5.29%)
Total	125 (55.07%)	102 (44.93%)	227 (100%)

The recurrence of stricture following DVU increased proportionally to stricture length. Stricture recurrence rates were 20%, 62.5% and 66.67% for strictures less than 1 cm, 1 to 3 cm and above 3 cm respectively. The difference was statistically significant. (Chi-Square 41.1251, DF 2, P value < 0.0001)

Table 4 : Outcome of DVU with stricture location

Stricture Location	Outcome of DVU		
	No Recurrence	Recurrence	Total
Bulbous	90 (62.07%)	55 (37.93%)	145 (63.88%)
Others	35 (42.68%)	47 (57.32%)	82 (36.12%)
Total	125 (55.07%)	102 (44.93%)	227 (100%)

Bulbous urethral strictures showed a better outcome compared to strictures at other sites. Recurrence of stricture following DVU for bulbous stricture was 37.93% while for other sites was 57.32% as shown in Table 4. This difference is statistically significant. (Chi-Square 7.9557, DF 1, P value 0.005)

Table 5 : Outcome of DVU with number of urethral strictures

Number of strictures	Outcome		
	No Recurrence	Recurrence	Total
Single	118 (57.28%)	88 (42.72%)	206 (90.75%)
Multiple	7 (33.33%)	14 (66.67%)	21(9.25%)
Total	125 (55.07%)	102 (44.93%)	227 (100%)

Single strictures had better outcome after DVU compared to multiple strictures. Stricture recurrence was 42.72% for single strictures compared to 66.67% for multiple strictures and the difference is statistically significant. (Chi Square 4.4172, DF 1 P value 0.04)

IV. Discussion

In this study patients with urethral stricture treated by DVU at KCMC had age range from 4 years to 93 years with a mean age of 61.9 years. Age distribution of patients who underwent DVU at KCMC is similar to the findings in most studies done in developed countries (Italy, the mean age of patients was 62 years, range 11 to 90 years, Pansadoro et al, 1996)

The mean age is higher compared to findings in other African countries whereby the mean age was younger. In Nigeria the mean age was 30.6 years [Ramyil et al, 2007] and in Ethiopia the median age was 43 years [Hagos, 2008].

The difference in mean age between this study and the ones done in other African countries could be explained by the etiological factors of urethral strictures, whereby in these other African countries infection was the leading cause of urethral stricture (61.4% in Nigeria and 82.4% in Ethiopia). In this study infection contributed only 23.4% of urethral strictures while majority of urethral strictures were caused by iatrogenic injuries (45.4%). These findings are similar to the ones in

studies done in developed world where iatrogenic causes accounted for 45% of urethral strictures while urethritis accounted for 20% of cases [Tritschler et al, 2013]. In another study done in Europe iatrogenic causes accounted for 45.5% of strictures. In patients younger than 45 years the main causes were idiopathic, hypospadias surgery and pelvic fracture. In patients older than 45 years the main causes were transurethral resection and idiopathic [Lumen et al, 2009].

Most patients in this study had strictures located in bulbous urethra (63.9%) which is higher compared to results found in other studies, (Pansadoro and Emilliozi 49%, Albers 52.6% and Tritschler et al 50%).

In this study it was found that overall stricture recurrence rate was 44.9% which is similar to what was found by a study by Albers et al (44.8%) and Tritschler et al (50%). Other studies had very high stricture recurrence rates of up to 93% to 94%. In a study by Santucci et al stricture free rate (SFR) at five years was 7% and in the one done by Pansadoro et al it was 6%. In both these two studies the sample sizes were small, 76 cases and 47 cases respectively.

The long term outcome of DVU was found to be better for strictures located in bulbous urethra and this difference was statistically significant (P value 0.005). Albers et al found less recurrence with bulbous urethral strictures but without statistical significance. This is explained by more cases of urethral stricture in this study being bulbous and most of them were short compared to other studies and which explains the better results in this site.

In this study length of urethral stricture was associated with recurrence following DVU and this finding was statistically significant (P-Value less than 0.0001). The chance of urethral stricture recurrence is directly proportional to stricture length. This finding is similar to the ones found in other studies [Albers et al, 1996; Pansadoro et al, 1996].

Urethral stricture aetilogy was found not to influence the outcome of DVU in this study (P value 0.21), this is similar to what other studies found. Albers et al found that iatrogenic strictures had less recurrence rate with statistical significance.

Patients with multiple strictures who underwent DVU showed poorer outcomes compared to those with a single stricture, this difference was found to be statistically significant (P value 0.04). This is similar to what Pansadoro et al found.

a) Study limitations

Inadequate documentations of patients' case notes especially on the symptoms/ clinical findings at surgery, significant number of patients were lost to follow up post operatively and some of the urethrogram reports were very deficient.

V. Conclusion

DVU is still the commonest treatment option for patients with urethral stricture at KCMC. Most patients (63%) who underwent DVU were 60 years or above.

The overall long term success rate of DVU was 55.07%

The outcome of DVU was good when stricture was single; the length was 1 cm or less and located in the bulbous urethra.

Recurrence of urethral stricture post DVU is significantly high for strictures which are long, multiple and located in other sites apart from bulbous urethra.

Age of the patient and etiology of the urethral stricture have no influence on the outcome of DVU

VI. Recommendation

DVU should be the first line treatment only for short urethral strictures, single and located in the bulbous urethra.

Prospective studies are needed to assess the long term outcome post DVU in patients with urethral stricture including validation of a tool for outcome measure.

Competing interests

The authors declare no competing interests.

VII. Acknowledgement

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