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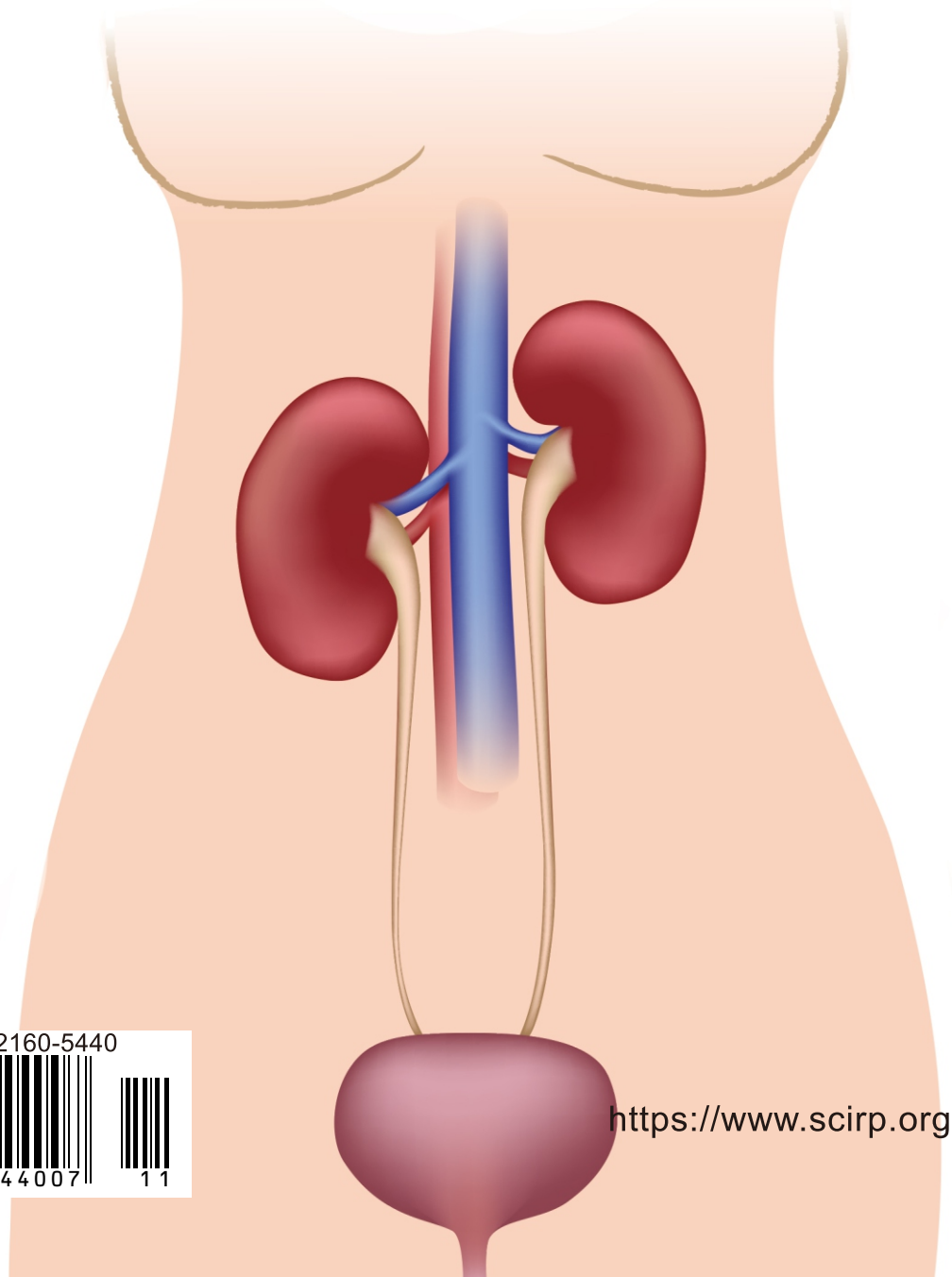

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The Impact of Body Mass on Male Fertility in a Cohort of 127 Patients

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Abstract

Background: Aromatase and leptin are two adipose tissue cytokines. The former converts androgens into estrogens and stimulates adipogenesis. The latter cannot fully stimulate GnRH release as its hypothalamic receptors are reduced in obese men. Thus, obesity which is associated with an adipose tissue increment can interfere with male fertility. Objective: We aim to study the correlation between the body mass index (BMI) of an individual and the quality of semen he produces. Patients and Method: By means of the software R 4.2.1 we performed a retrospective analysis of the relationship between the BMI and the semen alterations in the patients managed at the former Military Teaching Hospital of Cotonou from October 1, 2017, to September 30, 2022: a bi-varied analysis and Fischer's exact test (significance threshold 5%, confidence interval 95%) followed by a logistic regression when a non-significant p-value is below 0.20. Results: 127 males managed for infertility (mean age = 36.2 years) were recorded, including 11.1% obese (BMI > 30 kg/m^2) and 36.5% overweighted (25 kg/m^2 < BMI ≤ 30 kg/m^2). The most frequent semen alterations were: oligoasthenospermia (27.8%), asthenospermia (22.2%), oligoasthenoteratospermia (14.3%), azoospermia (13.5%) and asthenoteratospermia (9.5%). Bi-varied analysis showed no correlation between the BMI and the semen alterations (p-value ranged from 0.086 to 0.9) and no difference in semen alterations between patients with BMI below and above 25 kg/m^2 (p-value ranged from 0.12 to 0.9). Logistic regression demonstrated that asthenoteratospermia were correlated with BMI ≥ 25 kg/m^2 [OR = 2.1, 95% CI (1.50 - 2.70), p = 0.021]. Conclusion: Male obesity and overweight can trigger asthenoteratospermia.

Keywords

Body Mass Index, Male Infertility, Semen Alterations

1. Introduction

Infertility is a public health issue which involves 15% of couples worldwide [1]. In Africa, 43% of couples' infertility is linked to a male factor [2]. Etiologies of male infertility are variable. Obesity can possibly alter the spermatogenesis [3]. In fact, obesity is associated with an increment of fatty tissue [4]. The latter produces aromatase and leptin, two cytokines that interfere with spermatogenesis and testicular steroidogenesis. The aromatase converts testosterone into estrogens. The estrogens exert negative feedback onto the hypothalamus-hypophysis axis. Besides, estrogens stimulate adipogenesis [5] while testosterone inhibits adipogenesis and stimulates myogenesis [6]. Clearly, obesity induces in males a vicious cycle of estrogen excess and androgen deficit. The leptin stimulates the hypothalamus to release GnRH thereby making the hypophysis to release FSH and LH and stimulates testicular spermatogenesis and steroidogenesis [7]. The leptin's effect is reduced in obese males as they do experience a reduction in hypothalamic leptin receptors [8]. In our institution, the prevalence of male infertility is 14.1% among patients aged 15 through 40 years [9]. Elucidating the obesity's fertility-altering effect can insert anti-obesity measures into the therapeutic armamentarium against male infertility.

2. Objective

This study aims to elucidate the correlation between the body mass and male infertility in males whose couples are managed or followed up for infertility. Specifically, we will study the relationship that links a male's body mass index (BMI) to the quality of the semen that he produces.

3. Patients and Method

The study was conducted at the former Military Teaching Hospital of Cotonou from October 1, 2017, to September 30, 2022. It included all patients that were managed in the urological department for infertility, who were living a heterosexual couple life for at least 12 months and who had performed at least one semen analysis. Those patients who performed a premarital medical examination or any form of self-evaluation of fertility status and those patients who had undergone any treatment (inguinal surgery, chemotherapy, etc.) or event that could alter their semen were excluded. Smoker and alcoholic patients were also excluded. We conducted an exhaustive medical-records-based census of all patients who met the above-mentioned criteria. The data collected in each patient were age, weight, height, and semen analysis report. We calculated the body mass index (BMI in kg/m^2) by dividing the weight (kg) by the square of the height (m). The patients were categorized into classes of BMI: less than 18.5, 18.5 to 25, 25 to 30 and more than 30. We used the R 4.2.1. software to analyze the data. By means of a bi-varied analysis and Fischer's exact test, we studied the link between the BMI and the semen alterations that the patients presented on semen analysis. The significance threshold was 5% and the interval of confidence

was 95%. We used logistic regression to further analyze the data when the p-value was non-significant but less than 0.20.

4. Results

Among the 2506 patients managed during the study period, 293 males (11.7%) consulted for infertility. But semen analysis data were fully available in only 127 of them (Table 1). Their age ranged from 23 to 60 years; their mean age was 36.3 years. Their height ranged from 1.62 to 1.90 meters; their mean height was 1.71 meters. Their BMI ranged from 17.9 to 35.9 kg/m^2. The BMI in 62 (48.8%), 47 (37.0%), 14 (11.0%) and 4 (3.1%) of the 127 patients was respectively less than 18.5, between 18.5 and 25, between 25 and 30 and more than 30 kg/m^2.

Table 2 summarizes the semen analysis data. The main semen alterations observed were oligoteratospermia (27.6%), asthenospermia (22%), oligoasthenoteratospermia (14.2%), azoospermia (13.3%), asthenoteratospermia (9.4%), oligospermia (4%) and teratospermia (3.2%). The semen analysis was normal in 2, *i.e.*, 1.6% of patients.

The BMI in most of the patients, *i.e.*, 109 out of 127 patients, ranged from 18.5 to 30 kg/m^2 (Table 3). The bi-varied analysis demonstrated no correlation between the BMI and the semen alterations: the p-value ranged from 0.086 for asthenoteratospermia to 0.9 or more for alterations such as oligoasthenoteratospermia. Resuming the analysis with the 127 patients categorized into two subsets (Table 4), one with BMI < 25 kg/m^2 and the other with BMI ≥ 25 kg/m^2, showed no significant correlation between the BMI and the semen analysis data. Here, the p-value varied from 0.12 for teratospermia to 0.9 or more for alterations such as asthenospermia.

Table 1. Demographic characteristics of the patients.

	Age (years)	Weight (kg)	Height (m)	BMI (kg/m^2)
Minimum	23	54	1.62	17.9
Maximum	60	108	1,9	35.9
Mean	***36.3***	***74.3***	***1.71***	***25.4***

Table 2. Semen alterations.

ALTERATIONS	SIZE	%	ALTERATIONS	SIZE	%
Asthenospermia	28	22	OAS	35	27.6
Oligospermia	5	4	OATS	18	14.2
Teratospermia	4	3.2	OTS	1	0.8
Necrospermia	1	0.8	ONS	1	0.8
Hypospermia	1	0.8	OANS	1	0.8
Azoospermia	17	13.4	ATS	12	9.4
Leucospermia	1	0.8	Normal	2	1.6

Table 3. Correlation between BMI and semen alterations.

SEMEN ALTERATIONS	BMI < 18.5 (*n* = 4)	18.5 ≤ BMI < 25 (*n* = 62)	25≤ BMI < 30 (*n* = 47)	BMI ≥ 30 (*n* = 14)	p-value
Asthenospermia	0 (0.0%)	15 (24.2%)	11 (23.9%)	2 (14.3%)	0.8
Oligospermia	1 (25.0%)	2 (3.2%)	2 (4.3%)	0 (0.0%)	0.3
Teratospermia	0 (0.0%)	4 (6.5%)	0 (0.0%)	0 (0.0%)	0.3
Necrospermia	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	> 0.9
Hypospermia	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	> 0.9
Azoospermia	0 (0.0%)	10 (16.1%)	6 (13.0%)	1 (7.1%)	0.9
Leucospermia	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0.5
OAS*	1 (25.0%)	15 (24.2%)	12 (26.1%)	7 (50.0%)	0.3
OATS*	0 (0.0%)	9 (14.5%)	8 (17.4%)	1 (7.1%)	0.9
OTS*	***0 (0.0%)***	***0 (0.0%)***	***0 (0.0%)***	***1 (7.1%)***	***0.14***
ONS*	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0.5
OANS*	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	>0.9
ATS*	***2 (50.0%)***	***4 (6.5%)***	***5 (10.9%)***	***1 (7.1%)***	***0.086***
Normal	0 (0.0%)	0 (0.0%)	1 (2.2%)	1 (7.1%)	0.2

*OAS = oligoasthenospermia, OATS = oligoasthenoteratospermia, OTS = oligoteratospermia, ONS = oligonecrospermia, OANS = oligoasthenonecrospermia, ATS = asthanoteratospermia.

Table 4. Correlation between BMI and semen alterations.

SEMEN ALTERATIONS	BMI < 25 kg/m^2 (*n* = 66)	BMI ≥ 25 kg/m^2 (*n* = 61)	p-value
Asthenospermia	15 (22.7%)	13 (21.3%)	0.9
Oligospermia	3 (4.5%)	2 (3.3%)	>0.9
Teratospermia	4 (6.1%)	0 (0.0%)	0.12
Necrospermia	1 (1.5%)	0 (0.0%)	>0.9
Hypospermia	1 (1.5%)	0 (0.0%)	>0.9
Azoospermia	10 (15.2%)	7 (11.5%)	0.6
Leucospermia	0 (0.0%)	1 (1.6%)	0.5
OAS*	16 (24.2%)	19 (31.1%)	0.4
OATS*	9 (13.6%)	9 (14.8%)	0.8
OTS*	0 (0.0%)	1 (1.6%)	0.5
ONS*	0 (0.0%)	1 (1.6%)	0.5
OANS*	1 (1.5%)	0 (0.0%)	>0.9
ATS*	6 (9.1%)	6 (9.8%)	0.9
Normal	0 (0.0%)	2 (3.3%)	0.2

*OAS = oligoasthenospermia, OATS = oligoasthenoteratospermia, OTS = oligoteratospermia, ONS = oligonecrospermia, OANS = oligoasthenonecrospermia, ATS = asthanoteratospermia.

Table 5. (a) Correlation between BMI and asthenoteratospermia; (b) Correlation between BMI and oligoteratospermia.

(a)

	OR	95% IC	p-value
BMI			***0.021***
<25	1		
≥25	2.1	1.50 - 2.70	0.019

(b)

	OR	95% IC	p-value
BMI			***0.071***
<25	1		
≥25	1.9	0.20 - 3.60	0.08

The asthenoteratospermia ($p = 0.086 < 0.20$) and the oligoteratospermia ($p = 0.14 < 0.20$) seemed to be associated to the BMI. Nevertheless, submitting those two semen parameters to a logistic regression analysis (**Table 5(a)**, **Table 5(b)**) demonstrated that only the asthenoteratospermia was significantly correlated to the BMI (OR = 2.1, 95% CI = 1.50 - 2.70, $p = 0.021$). The correlation between the oligoteratospermia and the BMI was not significant (OR = 1.9, 95% CI = 0.20 - 3.60, $p = 0.071$).

5. Discussion

The effects of the leptin and the aromatase portend that the fatty tissue increment and leptin resistance associated with obesity can alter the testicular production of spermatozoids. In our population, eleven subsets of patients presented either single or combined alterations on semen analysis. Only 1 case of hypospermia and 2 cases of normal semen analysis were observed.

There was no correlation between the BMI and most of the observed semen parameters' alterations. Only the asthenoteratospermia and the oligoteratospermia were associated with BMI ≥ 25 kg/m^2 (*i.e.*, overweight and obesity): although their risk was respectively 2.1 and 1.9-fold increased, only the asthenoteratospermia was significantly correlated with BMI ≥ 25 kg/m^2.

Studies of the effect of obesity on fertility have so far led to variable and even contradictory results. According to McDonald, there is no link between obesity and sperm volume alteration [10]. Some authors have found that obesity triggers hypospermia [11]. Other authors have shown that BMI is negatively correlated the sperm motility and concentration [12]. Some study has demonstrated a positive correlation between BMI and sperm morphologic anomalies [13]. According to Dubeux, there is no association between obesity and semen alterations [14]. Further, Iliceto has demonstrated that semen parameters' alterations are not linked to obesity [15]. All those divergent results suggest that the relationship between the adipose tissue and fertility may be more complex than the ef-

fects of leptin and aromatase do suggest.

Our study has demonstrated that male obesity or overweight can lead to asthenoteratospermia thereby stressing that men should maintain a BMI below 25 kg/m^2. However, we think that studying the effect of counter-obesity therapeutic measures on asthenoteratospermia in males with no other cause of semen alteration than obesity will further test the link between the body mass index and the asthenoteratospermia.

6. Conclusion

The risk of asthenoteratospermia was 2.1-fold higher in obese and overweighted men. The other semen alterations were not correlated with the body mass.

Limitations of This Study

It is a retrospective study. The population's size is relatively limited. Ideally, the correlation between the body mass index and the sperm count should be studied by comparing two demographically similar populations of men, one set of fertile males and one set of infertile males.

Conflicts of Interest

We have no conflict of interest to declare.

Ethical Issues

The study has been submitted to and approved by our "Comité d'Ethique et de Recherche en Sciences de la Santé" before being carried out.

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Prevalence of Comorbidities in the Urological Patients at the Former Military Teaching Hospital of Cotonou

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Abstract

Background: Comorbidities are additive diseases and care burdens in urological patients. Determining the epidemiologic profile of comorbidities in urological patients in our setting may help us to better the management of urological disease. Objective: To evaluate the prevalence of comorbidities in urological patients. Patient and Method: We collected comorbidity, urological disease and demographic data in all urological patients managed at the former Military Teaching Hospital of Cotonou from January 1, 2012, to December 31, 2020. We used the software R 4.2.2 to perform descriptive and bi-varied data analysis. Student's t test was used to compare means. Results: The prevalence of comorbidities was 14.2%, *i.e.*, 601 comorbidity-affected among 4242 patients. The comorbidities predominantly affected men: the sex ratio was 13:1. The presence of comorbidity was correlated with patients' age ($p < 0.001$). The comorbidities observed in the 601 affected patients were hypertension (84.5%), diabetes (26.5%), asthma (2%), and heart failure (1.2%). Hypertension ($p = 0.001$) and asthma ($p = 0.030$) were correlated with age. No comorbidity was associated with gender. The comorbidities' prevalence was highest in patients aged 40 - 80 years who presented urological diseases such as BPH (68.9%), Erectile dysfunction (ED) and ejaculatory disorders, overactive bladder (OAB) and neurogenic lower urinary tract dysfunction (LUTD), renal cyst (5%), inguinal hernia (4.2%), urinary stones (2.8%), and prostate cancer (2.3%). Conclusion: The comorbidities' prevalence was 14.2% in the urological patients. The main comorbidities were hypertension (84.5%) and diabetes mellitus (26.5%).

Keywords

Comorbidity, Urological Patients, Prevalence

1. Introduction

In urology, comorbidities are diseases coexisting with urological diseases in the same patient. Comorbidities may not interact with the urological disease, but it can negatively impact urological therapy especially urological surgery [1] [2]. The index of Charlson enables the surgeon to mitigate such negative surgical impact [3]. We have previously depicted the prevalence of potentially surgical diseases among our patients [4]: benign prostate hyperplasia (52.03%), prostate cancer (6.49%), urinary stone (3.87%), bladder cancer (0.95%), etc. It is evident that comorbidities may increase the treatment cost, prolong the duration of therapy and hospitalization, or influence therapeutic choices. Although we often cope with situations such as infectious complications in diabetic urological patients for example, very few studies have evaluated the types and the prevalence of comorbidities in our country. In the West African region, few but no studies have dealt with comorbidities in urological patients. A Nigerian study has depicted comorbidities in prostate cancer patients [5]. We need the epidemiology of comorbidities associated with a broader spectrum of urological diseases. Knowing the epidemiologic profile of comorbidities in urological patients in our setting may also help us to better the management of urological disease.

2. Objective

We aim to evaluate the prevalence of comorbidities in urological patients at the former Military Teaching Hospital of Cotonou.

3. Patients and Method

We performed an exhaustive collection of data on diseases managed at the urological department of the former Military Teaching Hospital of Cotonou from January 1, 2012, to December 31, 2020. We recorded in each patient, the age, the gender, the urological disease, and every comorbidity that he presented along with his urological disease. We used the software R 4.2.2 to perform a descriptive analysis of collected data and a bi-varied analysis of the relationship between comorbidities and patients' demographic characteristics. We used Student's t test to compare means. The significance threshold was 5% with the confidence interval being 95%.

4. Results

Among 4242 patients, 601, *i.e.*, 14.2% had one or more comorbidities along with their urological diseases. In the overall population (n = 4242), the presence of comorbidity was significantly associated with the patients' age ($p < 0.001$) and gender ($p < 0.001$).

The comorbidities' frequency increased from 0.6% in patients below 40 years up to 21.9% and 20.4% respectively in patients aged 40 - 80 years and 80 - 102 years (**Table 1**). The risk of comorbidity in the patients aged 40 - 80 years and 80 - 102 years was respectively 47.6-fold and 43.3-fold the risk of comorbidity in the patients aged 27 - 40 years.

Table 1. Demographic characteristics of comorbidity-affected patients.

Patients		Comorbidity-affected patients		p	RC	CI95% RC
Demographics	Number	Frequency (n)	Percentage (%)			
Age				<0.001		
0 - 40	1534	9	0.6		1	
40 - 80	2595	569	21.9		47.6	24.6 - 92.2
80 - 102	113	23	20.4		43.3	19.5 - 96.3
Sex				<0.001		
Female	528	43	8.1		1	
Male	3714	558	15.0		2.0	1.4 - 2.8

The comorbidities were more frequent in the male patients (15.0%) than in the female patients (8.1%). The comorbidity's risk was twofold higher in the male patients than in the female patients (Table 1).

The urological diseases in the comorbidity-affected patients were mainly (Table 2) BPH (68.9%), Erectile dysfunction (ED) and ejaculatory disorders, overactive bladder (OAB) and neurogenic lower urinary tract dysfunction (LUTD, 6.7%), renal cyst (5%), inguinal hernia (4.2%), urinary stones (2.8%), and prostate cancer (2.3%).

The comorbidities observed in the 601 affected patients were chiefly hypertension, diabetes mellitus, asthma, and heart failure (Figure 1). The prevalence of hypertension was 84.5%: hypertension was alone in 70.7% of patients and combined with diabetes mellitus in 13.0% of patients, asthma in 0.3% of patients, heart failure in 0.2% of patients, and diabetes mellitus and asthma in 2 (0.3%) patients. The prevalence of diabetes, asthma and heart failure was respectively 26.5%, 2%, and 1.2%.

The comorbidity-affected patients were aged 27 through 102 years, their mean age was 62.3 years (Table 3, Figure 2 and Figure 3). They were 92.9% male (n = 558) and 7.1% female (n = 43), *i.e.*, the sex ratio was 13:1. The males' mean age was 62.6 years, the females' mean age was 57.8 years, but the difference was not significant (p = 0.05).

Inside the comorbidity-affected population, none of the comorbidities and none of the combination of comorbidities was correlated with patients' gender (Table 4). Each comorbidity and each combination of comorbidities affected more males than females, but the differences were not significant. Similarly, each comorbidity or combination of comorbidities affected more patients aged 60-80 years than patients aged 40-60 years. Nevertheless, only hypertension (p = 0.001) and asthma (p = 0.030) were significantly associated with patients' age. Diabetes (p = 0.508), heart failure (p = 0.073), the combinations hypertension-diabetes (p = 0.431), hypertension-asthma (p = 0.324), hypertension-heart failure (p = 1.000), and hypertension-diabetes-asthma (p = 0.571), were not correlated with patients' age.

Table 2. Urological diseases in the 601 comorbidity-affected among 4242 patients.

Urological diseases	Number (n) of affected patients	Proportion (%) of affected patients
BPH	***414***	***68.9***
ED and Ejaculatory disorders	114	19
OAB and neurogenic LUTD	40	6.7
Renal cyst	***30***	***5***
Inguinal hernia	***25***	***4.2***
Urinary stones	***17***	***2.8***
Prostate cancer	***14***	***2.3***
Acute urinary infections	13	2.2
Other	65	10.8

Table 3. Demographic characteristic of comorbidity-affected patients.

	Patients	Patients' age			Sex-Ratio	p-value
	n (%)	Range	Mean	Standard Deviation		
Female	43 (7.2)	34 - 79	57.8	11.1	13:1	0.05
Male	558 (92.9)	27 - 102	62.6	10.3		
Overall	601 (100)	27 - 102	62.3	10.5		

Table 4. Correlation between comorbidities' presence and patients' demography.

Comorbidities	Comorbidity-affected patients (n = 601): correlation with age				
	n (%) per age range in years				p-value
	20 - 40	40 - 60	60 - 80	80 - 102	
Hypertension	4 (44.4)	183 (81.7)	304 (88.1)	17 (73.9)	***0.001***
Diabetes	3 (33.3)	63 (28.1)	85 (24.6)	8 (34.8)	*0.508*
Asthma	2 (22.2)	3 (1.3)	7 (2.0)	0 (0.0)	***0.030***
Heart failure	0 (0.0)	0 (0.0)	6 (1.7)	1 (4.3)	*0.073*
HT + Diabetes	0 (0.0)	25 (11.2)	52 (15.1)	3 (13.0)	*0.431*
HT + Asthma	0 (0.0)	0 (0.0)	4 (1.2)	0 (0.0)	*0.324*
HT + Heart failure	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	*1.000*
HT + Diabetes + Asthma	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)	*0.571*
	Comorbidity-affected patients (n = 601): correlation with gender				
	n	Frequency (%)	n (%) Female	n (%) Male	p-value
Hypertension	508	84.5	34 (79.1)	474 (84.9)	*0.305*
Diabetes	159	26.5	13 (30.2)	146 (26.2)	*0.560*
Asthma	12	2.0	2 (4.7)	10 (1.8)	*0.209*
Heart failure	7	1.2	1 (2.3)	6 (1.1)	*0.407*
HT + Diabetes	78	13.0	7 (16.3)	73 (13.1)	*0.552*
HT + Asthma	2	0.3	0 (0.0)	4 (0.7)	*1.000*
HT + Heart failure	1	0.2	0 (0.0)	1 (0.2)	*1.000*
HT + Diabetes + Asthma	2	0.3	0 (0.0)	2 (0.4)	*1.000*

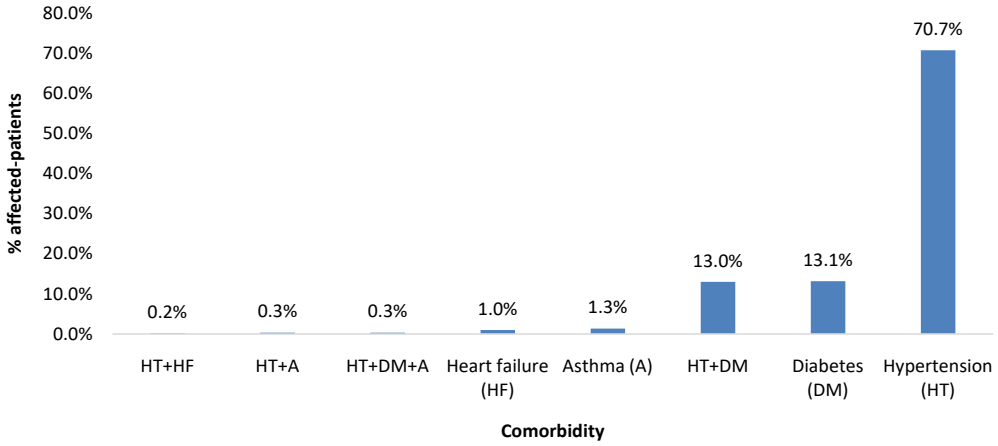

Figure 1. Comorbidity's spectrum.

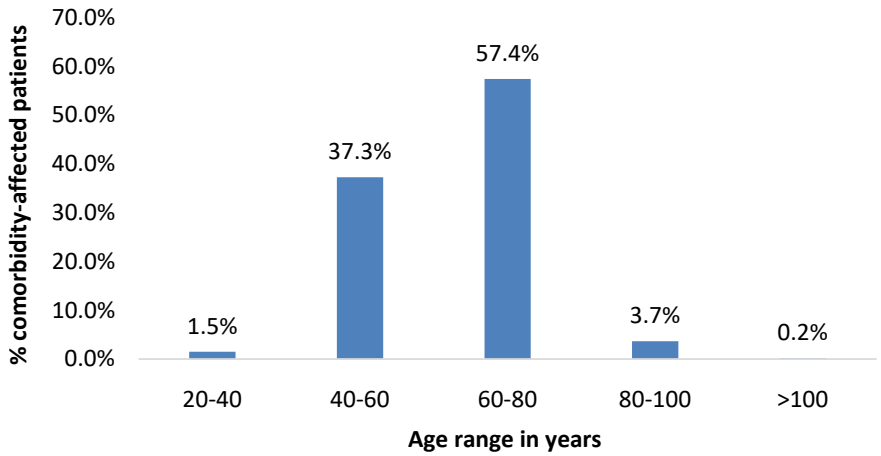

Figure 2. Comorbidities and patients' age.

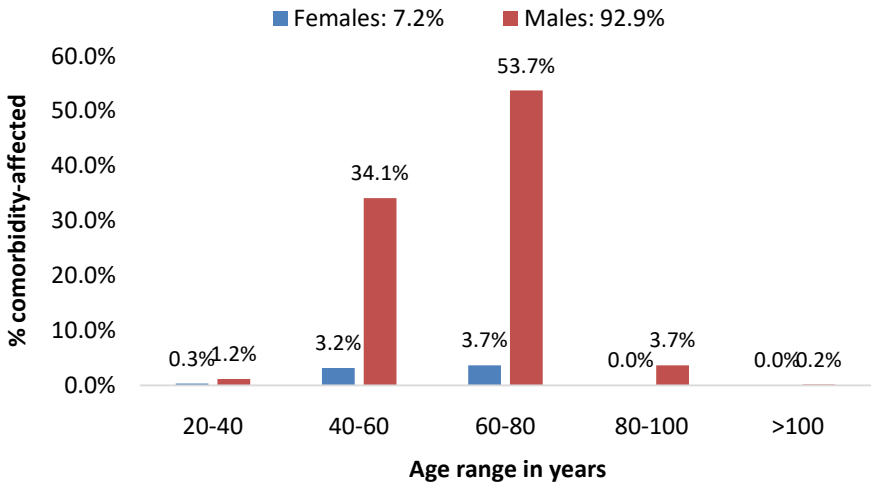

Figure 3. Comorbidities and patients' gender.

5. Discussion

The overall prevalence of comorbidities was 14.2%. Nevertheless, comorbidities'

burden varied according to age and gender. The prevalence of comorbidity was low in patients less than 40 years old. Females were less likely to have comorbidities than the males. Thus, patients below 40 years are less likely to have a comorbidity along with their urological disease. It means less care burden for both the clinician and the patient. For example, presurgical anesthetic evaluation can be swift and simple or possibly omitted in patients below 40 years, which will mean a non-delayed surgery and a reduced treatment cost [6]. The prevalence of comorbidity dropped in patients more than 80 years old while it was highest in patients aged 40-80 years. Certainly, numerous comorbidity-affected patients died before they reached 80 years of age. Urologists should correctly manage comorbidities to lengthen life expectancy in comorbidity-affected patients.

The predominant comorbidities in our patients were hypertension and diabetes. A Nigerian study on prostate cancer patients in which the prevalence of comorbidities was 48.1% (*i.e.*, 3.4 times the 14.2% prevalence in our patients) also found hypertension (39.5%), and hypertension and diabetes (8.6%) as the main comorbidities [5]. Similarly, Garg found among other chronic conditions, 64.6% hypertension and 26.8% diabetes in patients with benign urological diseases, 77.6% hypertension and 29.8% diabetes in patients with urological cancers, the mean age being 58.7 ± 17.6 years in all the patients, 56.9 ± 17.5 in the patients with benign urological diseases, and 71.0 ± 12.1 in the patients with urological cancers [7].

The comorbidities were observed in patients with potentially surgical diseases such as BPH, renal cysts, inguinal hernia, urinary stones, and prostate cancer. According to some authors, comorbidities increase the mortality rate in major urological surgeries such as radical prostatectomy for prostate cancer [1] [8] and radical cystectomy for urothelial cancer [9]. Other authors have insisted on comorbidities' linkage with non-specific cancer death in prostate cancer patients [9] [10]. Frendl, *et al.* have integrated comorbidities into the prediction tool that they have designed to predict death from other causes in localized prostate cancer patients [11]. Comorbidities can promote post-surgery complications, stressing that treating comorbidities is crucial for the prevention of post-surgical complications [12]. Comorbidities also influence non-surgical urological therapy. They increase the toxicity of anti-angiogenic drugs [13] in the treatment of metastatic renal cancer. They also induce a difference in prognosis between two patients managed for the same pathology [3]. Clearly, comorbidities are both life expectancy limiting and post-therapeutic complications promoting factors. Any urological care should encompass comorbidities to achieve full efficacy and maximum benefit for the patient.

6. Conclusion

The comorbidities' prevalence was 14.2% in the urological patients. The main comorbidities were hypertension (84.5%) and diabetes mellitus (26.5%). They predominantly affected the males (sex ratio 13:1) aged 40 - 80 years and pre-

senting mainly BPH or prostate cancer (71.2%).

Limitations to This Study

This a retrospective study carried out in a single hospital. It may not reflect the actual prevalence of comorbidities in urological patients at the national level.

Conflicts of Interest

We have no conflict of interest.

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Laparoscopic Radical Cystectomy in a Low-Middle Income Country: A 5-Year Review of a Single Institution; Operative Data, Oncologic Results and Morbidity

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Abstract

Introduction and Objective: Laparoscopic radical cystectomy (LRC) is an alternative to open approach with lower morbidity and better oncologic outcome. We aim to share our experience on laparoscopic radical cystectomy and to evaluate our morbidity and oncological outcome in our settings. **Methodology:** An observational study in the Douala Medico-Surgical Urology Centre on 5 patients who underwent laparoscopic cystectomy with or without lymph node dissection and external urine diversion between April 2014 to July 2016 was conducted. The overall survival rate was subsequently estimated. **Results:** Four men and one woman underwent laparoscopic radical cystectomy during the 5-year study period with a mean age of 54.5-year-old. Three patients were submitted to ileal conduits, one to neobladders, and one patient to uretero-cutaneostomies. The mean operative time was 300 ± 17 minutes and the mean length of hospital stay was 9 ± 3 days. Three patients had minor complications according to Clavien and Dindon Classification treated conservatively without need for further operation. Four patients had transitional cell carcinoma and one Squamous cell carcinoma types. Everyone had negative resection margin while only two had negative lymph node. The median survival years in our study was 2.5 years, the overall survival rates at 2 years were 60%, 40% at 3 years and 20 at 5years. 2 patients die after one year due to renal failure and intercurrent disease. **Conclusion:** Laparoscopic radical cys-

tectomy carried lower morbidity and cancerological outcome compare to open surgery making it a good alternative for bladder oncologic surgery.

Keywords

Radical Cystectomy, Laparoscopy, Oncology Findings, Bladder Cancer

1. Background

Radical cystectomy (RC) with pelvic lymph node dissection and urinary diversion is the preferred treatment for non-metastatic muscle-invasive bladder cancer (BC), and for some cases of high-risk non-muscle-invasive BC, in patients fit for major surgery [1]. RC is a comprehensive procedure that involves surgery to several organ systems and as a result it is associated with high postoperative morbidity and mortality. This procedure can be performed by laparotomy, laparoscopy or robot-assisted surgery [2].

The classic approach is the open surgery which has evolved since its first description nearly 80 years ago [2] [3]. Perioperative outcomes have slowly improved, but overall, 90-days complication rates have been reported to be as high as 65% [4]. Morbidity can particularly correlate with urinary diversion technique [5]. Laparoscopic techniques were first used for radical cystectomy in 1992 for neurologic bladder then in 1993, Sanchez De Badajoz introduce this approach in the treatment of bladder cancer due to its benefits such as reduce postoperative pain, less blood loss, shorter hospital stays, earlier return to normal activity and cosmetic benefits [6] [7] [8].

The frequency of radical cystectomy worldwide is not-well known. Approximately 2100 cystectomies are performed in each year in England among which 37.9% are Laparoscopic Radical Cystectomy (LRC) [9]. In hospital-based studies, there were 185 cystectomies perform over 4 years in Japan [10]. Whereas, in Africa, from 2007 to 2013 a single South African centre performed Thirty (30) patients LRC and 32 ORCS [11]. In Egypt, LRC was completed for 47 patients [12]. Improvements in perioperative care, anesthesia, and surgical technique have led to a decrease in postoperative mortality with rates from 20% in the late 1970s to currently between 2.5% and 7.9% [13] [14].

Bladder cancer is diagnosed based on a bladder biopsy histologic analysis after white light or fluorescent cystoscopy [15]. The biopsy histology results, combined with the imaging work-up and a detailed exploration of the entire urinary tract, allow to classify patients into 3 main therapeutic and prognostic groups [15]: non-muscle invasive bladder cancer (T * a, T is and T1 lesions 2); Muscle-invasive bladder cancer (T* ≥ 2) and Metastatic bladder cancer. Moreover, this classification allows us to determine the therapeutic management of patients with urothelial bladder carcinoma. Therefore, palliative chemotherapy is indicated in patients with metastatic disease [16]. For Non-muscle-invasive bladder cancer,

treatment will consist of a complete transurethral resection of bladder tumour followed by intravesical therapy with some agents. Under certain circumstances, radical cystectomy may be indicated [17].

Higher surgical volume is associated with improved outcomes [18] [19], but the magnitude of this effect remains controversial. While several studies emphasize the importance of the surgeon's experience [18], the influence of treating institution and perioperative management might be additional key factors to reduce in-hospital morbidity and mortality [19].

Significant worldwide involvement has advanced the Laparoscopic radical cystectomy (LRC) technique from initial single case report to compelling more sophisticated series with reproducible procedures, therefore LRC is enhancing as an acceptable treatment replacement of ORC. In Africa this approach is still very little used due to the cost of surgery and the socio-economic level of the patients [20]. From our literately review, data on LRC series in low-middle income countries are available. Therefore, we will report our centre 5-year experience with LRC and LND and urinary diversion operative results, morbidity and oncological outcome to improve the knowledge gap between our region and the world.

2. Methodology

2.1. Type of Study, Location

A 5 patient's case series was carried out in the Douala Medico-Surgical Urology Centre as an observational descriptive cohort study. This is specialised urology centre, which has 5 urological surgeons among who an experienced laparoscopic surgeon who frequently perform several laparoscopic procedures, including radical cystectomies.

2.2. Study Population, Study Period, Sampling, Inclusion and Exclusion Criteria

In this Case series study, all patients who met the selection criteria during April 2014 to July 2016 were recruited regardless of gender, age and race. Patients with pathologically confirmed bladder cancer who underwent laparoscopic radical cystectomy and pelvic lymph node dissection and urinary diversion were included. We excluded: patients who did not consent, patients who underwent open cystectomy, patients with metastatic disease and those who were lost to follow-up at the end of treatment.

2.3. Procedures

Diagnosis and staging: The diagnosis of bladder cancer was made on the basis of the result of a transurethral bladder biopsy providing oncological evidence of the tumor and histological grading. Patients were staged using the 2017 TNM classification [20]. All patients had abdominal and pelvic CT scans to complete the staging.

Complications: The complications were classified according to the Clavien-

Dindo classification (CDC) of surgical complications. We considered CDC I and II as minor complications and CDC III and above as major complications.

Operative technique: With the patient under general anaesthesia and Trendelenburg position, a 10 mm umbilical port is placed using lift abdominal technique. This allows introduction of a 10 mm 30˚ lens. Under direct vison pneumoperitoneum is induced. Right and left 5 mm port are placed 4 to 6 cm superior to the pubic symphysis below the camera port, just lateral to the respective rectus muscles bilaterally and symmetrically to allow introduction of 5mm trocars. The fourth port (12-mm right assistance port) is placed approximately 5 cm above the right anterior superior iliac spine in the mid-axillary line. We start with Lymph node dissection to remove bilateral obturator and iliac lymphadenectomies. We then proceeded with identification and dissection of the ureters follow by posterior dissection then anterior dissection to extract the bladder. For urine diversion we did mini-laparotomy under direct visual control. There were not specific criteria for choosing the type of diversion, this choice was made by the surgeon and patients after discussing the risks and benefits of each type of diversion on each individual situation. A 14 French drain is left in the abdominal cavity after surgery.

Outcome Measures and Analysis: The outcome measures evaluated the patients' demographics, cystectomy pathology grading, operative time, conversion rate, urinary diversion method, length of hospital stay, rehospitalisation, adjuvant chemotherapy and complication rates.

Follow-up: Patients were seen in clinic one month postoperatively, then every three months for the first year, then every six months for the next year, then on a yearly basis. Follow-up investigations consisted of transabdominal ultrasound, CT scan and LAB Tests including FBC, Serum electrolyte, CRP, Urine culture and sensitivity, renal and liver functions Tests

Ethical considerations: Before the start of recruitment, we obtained clearance from the ethical review board of the institution. Written informed consent was obtained from patients for publication of this case series and any accompanying images. A copy of the written consent is available for review by the Editorin-Chief of this journal. Any identifying material has been removed, including the patient's name, date of entry, face or any distinctive features on the pictures taken. The collected data has been codified and stored in strict respect for the privacy of patients.

3. Results

3.1. Clinical Manifestations, Risks Factors, Diagnosis, Staging

A total of 5 patients with bladder tumours who underwent LRC were included in the study. The majority of patient were men (4 men to 1 woman) with a mean age of 54.5 years ranging from 34 to 74 years (Table 1). The histologic type for 4 of our patients was Urothelial carcinoma while one who 3 years earlier was diagnosed with a muscle invasive Urothelial tumour had an Urothelial carcinoma with epidermoid differentiation. In this latter, an endoscopic resection was per-

formed, with histologically healthy margins; then, Bacillus Calmette Guerin (BCG) immunotherapy therapy was then initiated. Regarding risk factors, apart from BCG therapy, only 1 patient was a smoker (Table 1). All presented with muscle-invasive form of the disease (T* ≥ 2). One patient presented with a bladder tumour alongside a concurrent renal pelvis tumour. A staging computer tomography proven organ confined tumour cT2N0M0 for 2 patients, lymph node extension for two patients (cT2N1M0) who also had lymph node involvement and the last one had an extravesical tumour cT3N0M0.

3.2. Treatment Protocol, Surgery and Postoperative Follow Up

Base on the preoperative histologic results, RC was practice because of muscular invasive disease (T* ≥ 2) in 100% of the cases; in one patient radical cystectomy was associated with a right ureteronephrectomy (Table 2). All the procedures were done through laparoscopic approach with mini-invasive laparotomy urine diversion, there were no conversion. With respect to the type of urinary derivation, Ileal conduit was performed in 3 patients out 5 patients, while orthotopic

Table 1. Clinical and histological characteristics of patients.

Patient	Age (Years)	Sex	Risks factors	Comorbidities	Clinical manifestations	Grade (G)	TNM	Stage
Patient X	32	M	None	None	Painless gross haematuria	G2	$cT_2N_0M_0$	IIIA
Patient Y	47	F	Tobacco	None	Painless gross haematuria	G3	$cT_3N_1M_0$	IIIA
Patient Z	62	M	None	None	Painless gross haematuria with voiding symptoms	G2	$cT_2N_0M_0$	II
Patient M	62	M	BCG Therapy	PMH of Non-infiltrative bladder cancer	Painless gross haematuria	G3	$cT_2N_0M_0$	II
Patient B	74	M	None	None	Painless gross haematuria	G3	$cT_2N_1M_0$	IIIA

Abbreviations: BCG: Bacillus Calmette-Guérin; PMH: Past Medical History; TNM: Tumour, Node, Metastasis; c: clinical.

Table 2. Distribution and description of surgical intervention, urine diversion, length of stay, operative time and complications.

Patient	Type of resection	Type of urinary diversion	Operative Time (minutes)	Hospital Stay (Days)	Complication (grade)*	Timeframe of complication (days)
Patient X	Cystoprostatectomy	Ileal Conduits (Briker)	260	6	Grade I	8
Patient Y	Anterior pelvectomy and right ureteronephrectomy	Uretero-cutaneoustomy	350	12	Grade IV	10
Patient Z	Cystoprostatectomy	Orthotopic neobladder	310	10	Grade IV	9
Patient M	Cystoprostatectomy	Ileal Conduits (Briker)	270	9	Grade I	7
Patient B	Cystoprostatectomy	Ileal Conduits (Briker)	310	8	Grade II	10

*Graded according to Clavien-Didon classification of surgical complications [25].

Table 3. Distribution and detailed description clinical and pathologic stage, histology result, adjuvant chemotherapy and margin.

Patient	Age (Years)	Clinical stage	Pathological stage	Histology	Margin	Adjuvant chemotherapy	Survival years
Patient X	32	G2cT2N0M0	G2pT2N0M0	Transitional carcinoma	Negative	Gemcitabine-cisplastin	5
Patient Y	47	G3cT3N1Mx	G3PT3N1Mx	Transitional carcinoma	Negative	Gemcitabine-cisplastin	1
Patient Z	62	G2cT2N0M0	G1pT2N1M0	Transitional carcinoma	Negative	G2	1
Patient M	62	G3cT2N0M0	G3pT2N0M0	Transitional carcinoma with epidermoid differentiation	Negative	Gemcitabine-cisplastin	1
Patient B	74	G3cT2N1M0	G2pT3N1M0	Transitional carcinoma	Negative	Gemcitabine-cisplastin	4

neobladder and ureterocutaneostomies. was done for 1 patient each. The mean operative time was 300 min, the mean length of stay was 9 days, no patient dies during the surgery nor was rehospitalise within 30 days postoperatively.

The pathological staging post cystectomy is on (Table 3). Only two patients had similar clinical and pathological stages. However, 3 patients had positive lymph node and received adjuvant chemotherapy with gemcitabine and cisplastin. Transitional cell carcinoma was the histologic diagnosis in the cystectomy specimen, one had an associated epidermoid tumour. All specimens had negative surgical margin.

3.3. Complications and Survival Rates

Minor complications (Clavien-Dindo 1 to 2) within 10 days of cystectomy occurred in all patients, in details grade I: 2 cases of vomiting manage with antiemetic, 2 cases of paralytic ileus manage with fluid rehydration and electrolyte and a case of abdominal sepsis due to Surgical Site infection manage at the bed side with dressing. In regard to late complication, patients with Incontinent urine diversion (Briker), there was no complication such as renal failure or urolithiasis base on clinical and paraclinical continuous evaluation after 4 years follow up.

The patient with orthotopic bladder, reported 80% daytime continence after 6 months.

The follow-up period lasted approximately 30 months. The median survival years in our study was 2.5 years, the overall survival rates (Table 3) at 2 years were 60%, 40% at 3 years and 20 at 5years. 2 patients die after one year due to renal failure and intercurrent disease (gastroenteritis).

4. Discussion

Bladder cancer is a cancer of the elderly. The median age at diagnosis is 73 years [21]. In subSaharan Africa, the age at diagnosis varies between 65 and 75 years for urothelial carcinomas and 45 to 65 years for squamous cell carcinomas (SCC) [22]. In our series, the population was younger, with ages between 34 and 74 years. Even those according to the literature bladder tumour are rare before the age of 40 years accounting only for 1% - 4% of all cases. The ratio of male to

female in the present study was 4:1.

In Africa, Squamous Cell Carcinoma is often encountered in the context of schistosomiasis. The predominant histological type in our series was TCC, only one case of associated SCC was diagnosed in a patient with a history of intravesical Bacillus Calmette-Guerin (BCG) immunotherapy. Indeed, the risk factors identified for SCC are mainly chronic cystitis from various causes: bladder calculi, recurrent urinary tract infections, schistosomiasis, BCG and pelvic irradiation. Smoking and prolonged use of cyclophosphamide have also been cited [23].

Radical Cystectomy with pelvic lymphadenectomy is the gold standard treatment for muscleinvasive bladder cancer [2] [16]. The operative goals of the surgery are to ensure negative surgical margin and an adequate Lymph node dissection (LND) [2]. Other cystectomy indications include non-invasive bladder tumours that are either recurrent, high grade, SCC or multifocal [2] [17].

During radical cystectomy, several procedures may be combined depending on the stage of the disease. Anterior or posterior pelvectomy may be associated, as well as nephro-ureterectomy. In our series one patient presented with a multifocal urothelial tumour diagnosed after a Uroscan. Indeed, patients with pelvic and ureteral urothelial tumours have an associated bladder tumour in 17% of cases at the time of diagnosis [21] [24].

LRC is an emerging technique which has been propose as an alternative to ORC minimally-invasive. The goal of this minimally-invasive approach is to reproduce the oncologic results of an open procedure while reducing postoperative morbidity and length of hospital stay [8]. The laparoscopic approach has various benefits, enclosing less blood loss, a shorter hospital stays, and equivalent complication rates.

However, the longer operating time and having to overcome the learning curveare disadvantage. Since the first laparoscopy procedure a lot of centres have publish their series sharing their experience. Our study report data on our 5-year experience with LRC. Laparoscopy is hardly performed because of its high cost. In our study, only 5 patients underwent the procedure. All of these patients had health insurance, which covered most expenses related to the procedure.

We have no rehospitalisation nor perioperative death in our series, this could be explained by his size and the close monitoring the benefited from our multidisciplinary team. Indeed, the early perioperative mortality rate in RC is relatively low, around 1.2% - 3.2% [17].

In term of surgical management, the reconstruction of the urinary tract either with orthotopic or heterotopic, continent or incontinent urinary diversions represent an important step, which will affect the patient quality of life forever. Therefore, the choice of urine diversion technique should be made in accordance with patient base on the surgeon skills. In our institution we used three types of urine diversion: Briker, neobladder and ureterocutaneoustomy. The ileal conduit was the most practice technique, this choice was drove by the patient option and sur-

geon experience.

Following RC, adjuvant chemotherapy may be introduced for patients. Indications are a pT3 or T4 stage after cystectomy, or a positive node [17]. In our series, 4 of the 5 patients had an indication for adjuvant chemotherapy. No patient benefited from peri-operative radiotherapy.

As stated in previous literature early complications, defined as the ones affecting patients within 30 days of surgery, and their rate ranged from 20% - 57% [2]. In our study, the overall morbidity rate in this series was 100%. A significant decrease in the incidence rate of complications has been shown to occur as the learning curve increases. Therefore, the EAU recommends a minimum of 10 RCs per institution per year [17]. We encounter only minor complications according to Clavien-Didon especially Grade I representing 80% of them which occurred within the 10 postoperative days. The overall postoperative mortality rate was null, the mean follow-up period of 30 months with a median survival rate of 2.5 years. In terms of 5 years survival rate, we report a rate of 60% at 2 years 40% at 3 years and 20% at 5years. This survival rate can be link to the limited number of patients we had and length of our follow-up also knowing that proficiency of the surgeon and hospital volume also relate to survival outcomes. After all, time will tell us the full potential of LRC within our centre and his potential as an alternative to ORC in low-middle income countries as us.

5. Conclusions

RC plays a central role in the multimodal therapy of patients with high risk NMIBC and MIBC. With this study documenting the early experience of LRC in our centre we were able to conclude that LRC is associated less blood loss, less analgesic consumption, reduce morbidity and mortality. ORC is associated with shorter operative time. The two options are similar in terms of complication rates and oncological outcomes. After establishment of an adequate learning curve and equipment, LRC is a feasible and safe option in our setting. Therefore, is should be proposed to patient with bladder cancer as a therapeutic option as an alternative to ORC. However, the cost of this approach remains high in our context.

Knowing the number of patients who subsequently underwent LRC at our centre since the completion of this study, it is clear that the number of potential participants for a future study may allow for more definitive statements to be made regarding which modality may provide better outcomes especially in a comparative study. The volume of RC currently being performed at our centre may allow for a prospective study design, thereby producing more robust evidence, which may guide practice in the future.

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Declarations

What is known about the subject: Laparoscopic radical cystectomy is an emerging minimally invasive approach which has been proposed as an alternative to open radical cystectomy. This procedure is most often performed in high income countries.

What our study brings back: This study brings as addition: The indication, feasibility and outcomes of the treatment of invasive bladder cancer by laparoscopy in a resource-limited environment.

Availability of Data and Materials

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study

Ethical Considerations

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

A copy of the written consent is available for review by the Editor-in-Chief of this journal. Any identifying material has been removed, including the patient's name, date of entry, face or any distinctive features on the pictures taken.

Authors' Contributions

ASNM, LHD and LWT, contributed in design of the study and writing of the manuscript BNN, LOM, MDB and JPF contributed in critical reading BNN, collected the pictures, and obtained the patient's consent.

All authors have read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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List of Abbreviations

BCG	Bacillus Calmette-Guérin
c	Clinical
CDC	Clavien-Dindo Classification
CT	Computerized Tomography
EAU	European Association of Urology
F	French
LND	Lymph Node Dissection
LRC	Laparoscopic Radical Cystectomy
min	Minute
ORC	Open Radical Cystectomy
p	Pathology
PMH	Past Medical History
RC	Radical Cystectomy
SCC	Squamous Cell Carcinoma
TCC	Transitional Cell Carcinoma
TNM	Tumor, Node, Metastasis
UC	Urothelial Carcinoma

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Surgical Management of Adrenal Tumors: Experience of Three Tertiary Hospitals in Yaounde, Cameroon

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Abstract

Introduction: Surgical management of adrenal tumors has greatly improved over the past years, with laparoscopic adrenalectomy being the gold standard. However, Open adrenalectomy is indicated in large adrenal tumors, malignant tumors and large phaeochromocytomas. We report surgical outcomes of 18 cases of functional adrenal tumors from 2007 to 2022. **Methods:** We conducted a retrospective cross-sectional and descriptive study in three tertiary hospitals in Yaounde, Cameroon. We reviewed files of patients who underwent adrenalectomy over a period of 15 years from July 2007 to July 2022. Clinical and diagnostic components of adrenal tumors, indications and surgical outcomes were analyzed. **Results:** A total of 18 patients were included in our study. The average age of patients was 38.33 years, with a female-to-male sex ratio of 2:1. Weight gain (72.2%) was the most represented clinical sign. The secretory nature of tumor and malignancy represented 55.5% and 33.3% of the operative indications and all 18 (100%) of the patients had open adrenalectomy. Vascular injury was the most common intraoperative complication with 5.63%, while acute adrenal insufficiency (16.7%) was the most common post-operative complication. The average tumor size was 6.22 cm and the mean duration of hospitalization was 11.61 days. Adenoma 7 (38.9%) and adrenocortical carcinoma 5 (27.8%) were the frequent histological types. One patient died two months post-surgery from anemia-related complications. **Conclusion:** The success of adrenal surgery is linked to multidisciplinary patient care

and the experience of the surgeon. Conventional surgery still has indications with satisfactory short- and medium-term results in our context.

Keywords

Adrenal Tumors, Surgical Management, Outcome, Yaounde

1. Introduction

Surgical management of adrenal tumors has greatly improved over the past years. The means of diagnosis are more precise, and management is multidisciplinary, including urologists, endocrinologists, anesthetists, biologists, oncologists, radiologists and pathologist [1].

Adrenal masses are most frequently benign and could be a sign of secondary localization of a primitive tumor or a secondary adrenal tumor. Most often are diagnosed incidentally due to the progress of medical imaging. The prevalence of adrenal tumor is estimated at approximately 5% on abdominal CT scan examinations and autopsy series [2]. These tumors could also be discovered in patients with hormonal hyper secretions. A study conducted in Cameroon by Nouedoui and colleagues in 1990-1997, at the Yaounde General Hospital reported the diagnosis of 7 adrenal incidentaloma following abdominal imaging among which two were benign. Three had tumoral calcifications and four of the tumors were non-secreting [3]. Adrenal tumor diagnosis raises three preoccupations: its benign or malignant nature, its secretory functions and indications for surgical management. Adenomas constitute the most common secretory adrenal tumors with the least common being pheochromocytomas. Morbidity and mortality of these tumors are usually due to cardiovascular risk factors including hypertension and infra-clinical or patent Cushing syndrome. Management of adrenal tumors is multi-disciplinary and most often surgical treatment is indicated when the tumor has functional and malignant characteristics [4].

Open adrenalectomy was the only surgical option for the management of functional adrenal tumors before the introduction of laparoscopic adrenalectomy in the early 1990s. Adrenal gland surgery emerged as part of abdominal surgery in the 19th century, with Knowsley-Thorton reporting the removal of a large adrenal tumor in 1889 [4].

The anterior approach was first described by Cahill, a pioneer adrenal surgeon. The posterior approach was originally described by Young and offered surgical advantages of being sub-diaphragmatic, extra-peritoneal, extra-pleural and clinical advantages of being associated with less post-surgical mobility [5].

Minimal invasive adrenalectomy has become the gold standard for the treatment of most patients presenting with adrenal tumors; notwithstanding, open adrenalectomy still has its indications and is a surgical procedure which is complex and mostly carried out in centralized referral centers. Its main indications include Patients with large tumors (>6 - 8 cm), large pheochromocytomas, and

cortical adrenal tumors suspected of malignancy either because of radiological characteristics or signs of local invasion and tumor [6]. The success of surgical treatment is evaluated biologically by the decrease in plasma cortisol level post-surgery, a hormone which is vital for the normal functioning of the body. This is also a biological marker to evaluate residual adrenal functions [7].

Mbouche *et al.* in a case series of seven functional adrenal tumors reported in Yaounde, three patients with perioperative morbidity including a patient with adrenal insufficiency and two cases of mortality which were due to hypovolemic shock per-operatively and anaphylactic complications during transfusion post-surgery. These patients did not have multidisciplinary consultations and were all operated using the trans-peritoneal approach [8].

Takongmo and colleagues during a 14 years retrospective study reported the diagnosis and management of 9 cases of histologically confirmed pheochromocytoma in Yaounde. However, the management and outcome of other adrenal tumors were not evaluated in this study [9].

It is on this background that we report our experience on the surgical management of adrenal tumors at three tertiary hospitals in Yaounde Cameroon over a period of 15 years.

2. Methods

2.1. Study Design and Participants

We retrospectively reviewed records of 18 patients who had adrenalectomy over the period of 15 years (July 2007 to July 2022) at the urological surgical unit of three referral hospitals in Yaounde; Yaounde Central Hospital (YCH), Yaounde General Hospital (YGH), and Yaounde Gynecology,Obstetrics and Pediatric Hospital (YGOPH). We included all patients who underwent adrenalectomy indicated for functional adrenal tumors. Ethical clearance was approved by the institutional ethics committee. Data on demographics, clinical symptoms, ultrasound and CT scan findings, operative findings and post-surgical outcomes was recorded for each patient. Data collection was achieved using self-designed structured questionnaires. Validity and reliability of the questionnaire were done. The questionnaire is made up of 9 sections (sociodemography, past medical history, clinical features, biological investigations, radiological investigations, surgical management, post-surgery, diagnosis, adjuvant therapy, and surveillance) (see **Appendix**). Data was collected by consulting patient records, post-surgical reports and by carefully viewing videos of the different operative procedures.

The adrenal tumor was diagnosed by doing a clinical examination of patients, hormonal assays, Doppler abdominal ultrasound and abdominal CT scan was done for all patients. Secretory adrenal tumors were defined as patients with adrenal mass presenting with raised hormonal assays and or raised serum or urinary catecholamines.

2.2. Surgical Technique

Open adrenalectomy was done under general anesthesia and endotracheal intu-

bation was in the supine position.

Anterior sub-coastal incision is made 2 cm below the coastal margins extending from mid clavicular line to the mid axillary line (Figure 1). Incision at the line of Toldt with medial mobilization of the descending colon was realized. The spleno-colic ligament is divided, and the splenic flexure is mobilized medially (Figure 2). The retroperitoneum is opened along the inferior border of the pancreas by dividing the leno-renal ligament. Exposure of the left adrenal vein is obtained by retracting the spleen and pancreas superiorly. The left adrenal vein is identified as it courses from the inferio-medial border of the left adrenal gland into the left renal vein and is ligated and divided (Figure 3). The medial attachments to the aorta can now be taken either with monopolar diathermy on a long right-angle instrument or with a harmonic scalpel while applying gentle lateral traction on the gland. The lateral and inferior attachments to the kidney are taken by blunt and sharp dissection off the renal capsule, taking care to avoid the vasculature to the renal upper pole (Figure 4). Excision en monobloc of adrenal tumour is done (Figure 5). Excision of a large adrenal tumor measuring 14 cm on its longest axis was done (Figure 6).

2.3. Statistical Analysis

Data was analyzed using EPI info 7.0. Parametric variables were reported as means and standard deviations and percentages and counts were used to report categorical variables.

Figure 1. Right anterior sub-costal extraperitoneal approach during right adrenalectomy for a massive right adrenal tumor. (*Source*: *Urology service YCH*)

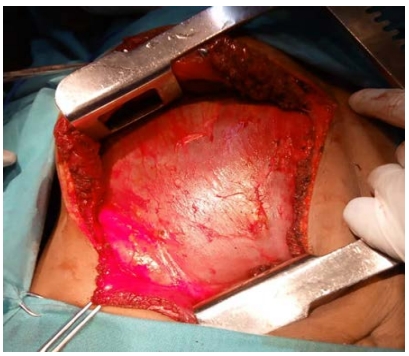

Figure 2. Left subcostal extraperitoneal approach. (*Source*: *Urology service YCH*)

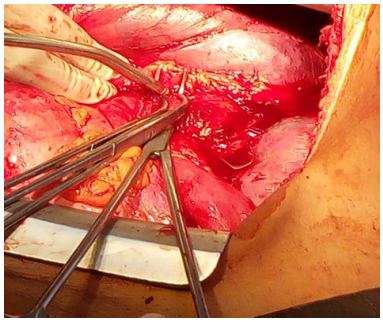

Figure 3. Vascular control with identification and ligature of the adrenal vessels. (*Source*: *Urology service YCH*)

Figure 4. Exposition of right adrenal tumor after kochers maneuver. (*Source*: *Urology service YCH*)

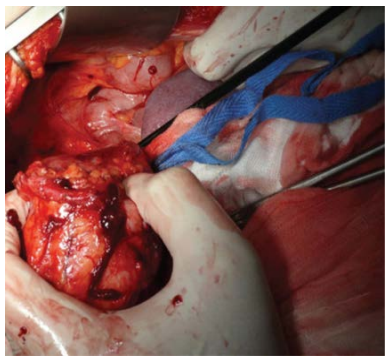

Figure 5. Excision en bloc of right adrenal tumor. (*Source*: *Urology service YCH*)

Figure 6. Large adrenal tumor following surgical excision measuring 14 cm on its longest. (*Source*: *Urology service YCH*)

3. Results

A total of 18 files of patients who had adrenalectomy were collected.

3.1. Socio-Demographic Characteristics

We registered 18 patients operated on for adrenal tumors in 15 years. This corresponds to an incidence of 1.2 cases per year. This included 11 patients from the YCH, 5 patients from the YGH and 2 patients from the YGOPH.

The mean age of patients was 38.33 ± 9.40 years old (range: 17 - 69 years) the predominant age group was 30 to 40 years and we recorded one pediatric case of 17 years. Females were most affected with a female-to-male ratio of 2:1 (Table 1).

3.2. Clinical Features

Weight gain (72.2%) and asthenia (44.4%) were the most reported symptoms at consultation. Throbbing headache (38.9%), palpitation (38.9%), and secondary amenorrhea (33.3%) were also symptoms frequently reported among participants. The triad of hypertension, palpitation and headache was common in most of the patients presenting with pheochromocytoma (Table 2). The physical examination was normal in 10 patients (55.6%). However, we had facial and central obesity among (44.4%) of patients and a palpable mass at the level of the abdomen in 22.2% of patients. Four patients (22.2%) had multiple stretch marks and cutaneous eruptions and 3 patients (16.7%) presented with bruising and a buffalo hump (Table 3).

3.3. Operative Indications

Malignant tumors and secretory adrenal gland tumors presenting clinically as Cushing's syndrome and pheochromocytoma were the main indications for surgical management. Furthermore, the large size of these tumors was also a surgical indication.

Majority of patients (88.9%) had a multidisciplinary consultation before surgery. This was done by a team consisting of urologists, endocrinologists, anesthesiologist,

Table 1. Socio-demographic data.

Socio-demographic parameters	Count (N = 18)	Percentage (%)
Age group (years)		
≤20	2	11.1
[20 - 30[	3	16.7
[30 - 40[	6	33.3
[40 - 50[	3	16.7
≥50	4	22.2
Gender		
Male	6	33.3
Female	12	66.7

Table 2. Functional signs and symptoms.

Functional signs and symptoms	Count (N = 18)	Percentage (%)
Presenting complaint		
abdominal distension/pains	4	22.2
Amenorrhea	4	22.2
weight gain	13	72.2
weight loss	3	16.8
Asthenia	8	44.4
Palpitation	7	38.9
Headache	7	38.9
profuse sweating	5	27.8
Secondary amenorrhea	6	33.3
Decrease libido	6	33.3
Ascending constrictive pain	6	33.3

Table 3. Physical signs of adrenal tumours.

physical signs	Count (N = 18)	Percentage (%)
Performance status index (WHO)		
GRADE I	12	66.7
GRDE II	6	33.3
Facial and trunkal obesity	8	44.4
Easy bruising	3	16.7
Cutaneous eruptions	4	22.2
Signes of virilism	2	11.1
Amyotrophie of lower limbs	1	5.6
Cardiac arrhythmias	1	5.6
Palpable tumor in the abdomen	4	22.2
Gallactorrhoea	1	5.6
Stretch marks	4	22.2
Bufallo hump	3	16.7
Palpable flank mass	2	11.1
Clitoral hypertrophy	1	5.6
Hirsutism	1	5.6

pathologist and radiologists. All patients had anesthetic evaluation and 61.1% of patients were staged ASA I. All patients were operated using general anesthesia and oro-tracheal intubation

3.4. Operative Results

1) Techniques used

All patients had open total adrenalectomy using the anterior sub-coastal ap-

proach in 16 (88.9%) of patients and the anterior midline approach in 2 (11.2%) of patients in our study. The surgeon's approach was extra peritoneal among 10 (56.6%) patients and trans-peritoneal with 8 (44.4%) patients. The different intraoperative findings encountered include localized tumors in 13 patients, two large adrenal tumors without peri-renal infiltration, a large renal tumor with ipsilateral adrenal extension, one large right adrenal tumor with extension to the right kidney and inferior vena cava (Table 4).

2) Per operative complications

We recorded 5 patients with per-operative complications in the current study. This included bleeding, breech of peritoneum, hypertension and persistent hypovolemic instability in one patient who later died following persistent hypovolemic shock despite resuscitation and reanimation. The deceased patient was operated using the trans-peritoneal approach (Table 5).

Table 4. Type of surgical intervention.

Type of surgical intervention	Count (N = 18)	Percentage (%)
Type of surgical intervention		
Laparoscopic	0	0
open surgery	18	100.0
Patient installation		
Decubitus dorsal	18	100
Decubitus ventral	0	0
Decubitus lateral	0	0
Surgical technic		
Total adrenalectomy	18	100.0
Partial adrenalectomy	0	0
Surgical approach		
anterior midline	2	11.2
Anterior Subcostal	16	88.9
Surgical attitude		
Trans-peritoneal	8	44.4
Extra-peritoneal	10	55.6
Findings		
Large adrenal tumour without perirenal infiltration	2	11.1
Renal tumour with adrenal involvement	1	5.6
Large tumour with extension to the kidney and ivc	1	5.6
Large adrenal tumour with infiltration of para-renal	1	5.6
Localised	13	72.2

Table 5. Per-operative surgical complications.

Surgical complications	Count (N = 18)	Percentage (%)
Per-operative complications		
Yes	**5**	**27.8**
No	**13**	**72.2**
Hypertension	1	5.6
Hypotension	2	11.1
Bleeding	2	11.1
Cardiac arrest	1	5.6
Peritoneal breech	1	5.6
Pleural breech/injury	0	0
IVC injury	1	5.6
Adjacent organ injury	0	0

3) Blood loss and transfusion:

The average blood loss was estimated at 300 cc with extremes ranging from 200 cc to 2500 cc. 4 patients were transfused preoperatively. 1 patient received 4 units of blood preoperatively due to excessive bleeding following a major vascular injury.

4) Duration of intervention:

The mean duration of surgical intervention was 165.3 ± 43.1 mins with extremes ranging from 150 mins to 265 mins

5) Size of tumor excised:

The average size of the tumor excised was 7.11 ± 5.1 cm with tumor sizes ranging from 3 cm to 25 cm. One patient had a right radical nephrectomy due to a right large adrenal tumor with ipsilateral renal extension (Table 6).

3.5. Outcomes

Post-operative care was multidisciplinary including endocrinologists management which began immediately post-surgery. Most of these patients were placed on hydrocortisone supplement to prevent adrenal insufficiency which is usually common among these patients post-surgery.

Post-operative evolution was favorable in 13 (72.2%) patients. However, we recorded 5 (27.8%) patients with post-surgical complications among which 3 (16.7%) had acute adrenal insufficiency, 1 (5.6%) had superficial surgical site infection and 1 patient had retroperitoneal abscess. We recorded 1 case of post-operative mortality 5 weeks following surgery from anemia-related complications (Table 7).

The mean duration of hospitalization following surgery was 8.6 ± 3.8 days with extremes ranging from 6 to 21 days. The hospitalization for 21 days was observed in a patient who presented with right retroperitoneal abscess post-surgery. Ultrasound guided percutaneous drainage of the retroperitoneal abscess was done

Table 6. Duration of surgery, specimen size and duration of hospitalization.

Parameters	Mean SD	Median (IIQ)	Min—max	Mode
Duration of surgery	165.3 ± 43.1	182 (150 - 190)	150 - 265	150
Specimen size	7.11 ± 5.1	5.5 (4 - 7.5)	3 - 25	4
Drain duration	5.01 ± 1.2	4 (3 - 5.5)	3 - 10	5
Hospital stay duration	8.6 ± 3.8	7(7 - 9.5)	6 - 21	7

Table 7. Post-surgical complications.

Post-surgical complications	Count (N = 18)	Percentage (%)
Post-surgical complications	**5**	**27.8**
Anemia	2	11.1
Surgical site infection	1	5.6
Acute adrenal insufficiency	3	16.7
Conn disease	0	0
Hypovolemic shock	0	0
Retroperitoneal abscess	1	5.6
Death	1	5.6

with favorable outcome. The delay period for patients to return to their normal activity was 30 ± 4.34 days (range: 3 - 45 days).

13 (72.2%) of patients received steroid supplement therapy using hydrocortisone. This was begun on day 1 post-surgery. 2 patients received adjuvant chemotherapy using mithotane. These patients were those with histopathologic confirmation of adrenocortical carcinoma (ACC) (Table 8).

All patients had histopathological analysis of specimens (100%). Adrenal adenoma 7 (38.9%) and adrenocortical carcinoma 4 (22.2%) were the most frequent histologic type (Table 9).

4. Discussion

This study on characteristics, indications and surgical outcomes of patients with adrenal tumors has shown that all tumors present intra-abdominally, are located in the adrenal gland and were mostly benign tumors. Complete recovery was documented in the majority of the patients, and, despite the high rate of perioperative complications, the overall mortality was low. Clinical presentation in most patients included weight gain, asthenia and the classical triad (headache, palpitation and excessive sweating) associated with hypertension was present in most patients who presented with pheochromocytoma.

Laparoscopic technique was the first treatment modality of most adrenal tumors [6]. However, open surgery is still indicated in large and malignant adrenal tumors. In our context (developing countries and low technical platforms), minimally invasive surgery is not always available and accessible [8] [9].

Table 8. Clinical surveillance post-surgery.

Adjuvant treatment	Count (N = 18)	Percentage (%)
Hydrocortisone supplementation	13	72.2
Chemotherapy	2	11.1
Clinical surveillance		
Resolution of initial clinical signs	14	77.8
Appearance of new signs	5	27.8
Relapse	2	11.1
Control abdominal CT scan	8	44.4

Table 9. Histopathological results.

Histopathological result	Count (N = 18)	Percentage (%)
Cushing's adenoma	7	38.9
Adrenocortical carcinoma	4	22.2
Myelolipoma	2	11.1
Phaeochromocytoma	3	16.7
Conn's adenoma	1	5.6
Renal tumour with extension to the adrenal gland	1	5.6

We recorded 18 patients who had adrenalectomy for adrenal tumors over 15 years during this study, giving an incidence of 1.2 cases per year. This finding is higher than that reported by Takongmo *et al.* (0.06) and lower than that of Zorgani *et al.* who had an incidence of (2 - 4) [9] [10]. Studies in developed countries have shown an increased prevalence and incidence of adrenal tumors [8] [11] [12] [13]. This could be attributed to the availability of social security, diagnostic and therapeutic means such as minimally invasive surgery which is not easily accessible in our context. The mean of patients was 38.33 years with a female predominance of 66.3%. These findings are similar to that reported in the literature [8] [10] [13]. The reasons for these gender disparities are not well established.

Clinical presentation in most patients included weight gain (72.6%) and asthenia (44.4%) with an average BMI of 31 among participants.

The classic pheochromocytoma triad (headache, 38.9%; palpitations, 38.9%; and sweating, 27.8%) associated with hypertension were presenting symptoms in the majority of patients, especially those who presented with pheochromocytoma, confirming the classical hyper-adrenergic spells of adrenal tumors. This is lower compared to the available literature, which reports headaches in 55% - 90%, palpitations in 50% - 77% and sweating in 40% - 74% of patients with pheochromocytoma [14] [15] [16]. This could be explained by the fact that our study did not only include patients with pheochromocytoma, but rather included all patients presenting with different types of adrenal tumors.

Arterial hypertension was the most frequently presenting clinical finding, found in 55.6% of the current study, which is quite close to the figures (90% - 100%) from most available reports [14] [15], except one study that reported a low rate (45%) [16]. About 9 patients (50.0%) had grade I hypertension while one (5.6%) patient had grade II hypertension and no patient presented with grade III arterial hypertension. Furthermore, in our study, sustained hypertension (44.4%) was more common than paroxysmal hypertension (11.2%), which is similar to studies from Asia and Europe [14] [15] [16], but higher than other studies, which report similar proportions for both types [17] [18]. Hypertension persisted in 22.2% after successful resection of the tumor (as defined biochemically and radiologically); similar findings have been reported from centers in Asia [14] [15] and Sweden [19], with rates of 10% - 35%. This may be related to the late presentation with target organ (renal) involvement from hypertension or the coexistence of essential hypertension in this study.

Incidental adrenal tumors (Incidentalomas) can be discovered by chance on an imaging assessment. The notion of fortuitous discovery of adrenal mass is common and has been reported in different series (1% to 8.7%) [20] [21]. In our series, one incidental adrenal tumor was discovered by chance (5.6%). This result is similar to that reported in the literature [22] [23].

A palpable adrenal mass is highly suspicious of adrenal malignancy or secondary malignant extension. This is because most adrenal tumors are not palpable. In our series, 4 (22.2%) patients had a palpable abdominal mass.

Cushing's adenoma accounted for the majority in this study (38.9%). Available reports are variable with some studies reporting high rates [24].

Consistent with the available literature [19] [25], benign tumors (72.2%) were far more common than malignant in our setting; however, the frequency of malignant adrenal tumors (27.8%) is higher than the 4% - 15% reported [16] [25]; and probably accounts for the high proportion of large tumors found in this study.

Contrary to other studies [11] [26] [27], familial syndromes were not diagnosed in our study. In our setting, no patient reported a family history of MEN2A. This could be explained by the fact that unlike other studies where genetic tests were used to diagnose inherited cases [15] [19], in this study familial tumors were screened primarily on the basis of the positive family history of adrenal tumor and the presence of biochemical and radiological features of other components of inherited tumors such as bilateral adrenal tumors, renal cell carcinoma, or medullary thyroid carcinoma. Selective genetic testing is not still available at our centers.

In the current study, 57.1% of patients were diagnosed based on biochemical results following positive hormone secretion in 10 (55.6%) of patients. This is much lower than that reported (88.8% - 96.5%) in other studies [11] [28], and is probably accounted for by the low sensitivity and specificity of the tests used.

Similar to other studies [29] [30], anatomical imaging (CT) was able to correctly localize all tumors preoperatively. This is higher than that reported from a

Chinese study (79%) [18], but similar to other studies (88% - 98%) [21] [25], and may be related to large tumor sizes in this study.

Indications and surgical technique

Treatment of functional adrenal tumors is essentially surgical. The goal is to achieve total excision of adrenal tumors without damage to neighboring organs. Minimally invasive surgery precisely laparoscopic adrenalectomy remains the goal standard of adrenal tumor management [2] [6] [31]. However, open adrenalectomy is indicated in large adrenal tumors (>5 cm), malignant adrenal tumors and large pheochromocytomas [2] [32]. In our study, open surgery was performed on all patients. This could be explained by the unavailability of adequate working platform to perform laparoscopic adrenal (LA) surgeries in our centers. In addition, the surgeons are skilled in performing open adrenal surgery. The secretory nature of the tumor (38.8%), Cushing's syndrome (27.8%) and malignant suspicion (22.2%) were the most common indication for surgical management. These indications are similar to other studies reported in the literature [4] [21] [26]. However, our results are higher than those of Mbouche *et al.* where Cushing's syndrome was reported in 15% - 20% of patients [8]. This difference could be explained by the fact that not all the patients had hormonal assays done.

An anterior subcostal surgical approach was used in the majority of our patients (88.9%), given the fact that large tumors were identified with preoperative localization. This is compatible with the study by Lo *et al.* [18] (mean tumor size 6.4 cm), but higher than in other studies (mean tumor size 4.8 cm) [6] [21] [23]. The mean operative duration in our study was 165.3 days results similar to that of Musina *et al.* [33].

55.6% of patients were operated on using the anterior extra-peritoneal approach while the trans-peritoneal approach was used in 44.4% of patients. This could be explained by the fact that the patients in our study were operated on by two different surgical teams and each of the surgeons used the technique which they mastered best.

The mean tumor size in our study (7.11 cm) was larger than that recorded in other studies (mean 5.2 cm) [27] [34]. This may be accounted for by the late presentation at consultation or delayed referral for specialized care. However, in concordance with other studies [14] [30], malignant tumors (mean size 9 cm) were larger than benign (mean size 4.5 cm).

Outcome:

Complications following open adrenalectomy for adrenal tumors vary in different reported studies (5.6% - 28.6%) [6] [33] [35]. In our study, we had a perioperative complication rate of 22.2%. It was principally vascular injury, the reason for blood transfusion. Post-operative complications observed were acute adrenal insufficiency and surgical site infections. The adrenal insufficiency was due to non-observance to corticosteroid supplementation therapy. The surgical site infection included one parietal suppuration and retroperitoneal abscess which occurred in a patient with diabetes. The average hospitalization days

post-surgery was 8.6 days higher than that reported by Musina *et al.* [33]. This was probably due to the fact that in other studies, the laparoscopic approach was associated with early recovery.

In the present study, chemotherapy (5.6%) was used as adjunctive therapy for patients with metastatic tumors. No patient benefited from adjuvant radiotherapy and this is lower than that for use of chemotherapy (16% - 30%) in other studies [2] [16] [27]. This could be explained by the high cost and scarcity of chemotherapeutic drugs which are sensitive to adrenal tumors in our milieu.

In the current study, 72.2% were deemed as cure (biochemically and/or radiological) and is lower compared to results reported in other studies (79% - 92.6%) [2] [35]. This is probably due to the high rate of adrenocortical carcinoma in our series (**Table 9**).

Available information on mortality rates is variable. The mortality of 11.1% found in this series is lower than that reported by Modigliani *et al.* (13%) [26] whose results may be related to the high proportion of familial cases of adrenal tumors (all patients had either MEN I2A or MEN I2B) in that study. By contrast, low mortality rates have also been reported in the Johannesburg study (5.9 - 7.4%) [10] [23] [35].

Limitations: This study was retrospective with a small sample size. We therefore propose large prospective studies in order to confirm the results of this study.

5. Conclusions

Adrenal tumors despite being rare urological tumors have been encountered during our urological consultations with an increased incidence during recent years. The principal clinical manifestations of these tumors include weight gain, hypertension and asthenia. A high index of suspicion at primary health care levels, surgeons' experience and a multidisciplinary approach are necessary to effectively treat these rare tumors. Laparoscopy remains the gold standard for the management of most adrenal gland tumors. However conventional surgery still has indications with satisfactory short-term and medium-term results in our context.

What is already known on this topic:

- Adrenal tumors are rare urological tumors.
- Laparoscopic adrenalectomy is the gold standard for the treatment of functional adrenal tumors, and it is associated with reduced post-operative complications.

What this study adds:

- Laparoscopic adrenalectomy is a new surgical technique in Cameroon, and it is less practiced.
- Conventional open surgery still has indications with satisfactory short-term and medium-term outcomes in our context.

Conflicts of Interest

The authors declare no competing financial or personal interests.

Authors' Contribution

All the authors contributed to the research work. They read and agreed to the final version of the manuscript.

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Data Collection Form

Questionnaire N0: |_|_| **code**: |_|_|_| Contact Tel Number:……
Date: …. /…. /…. (dd/mm/yy)

SECTION 1: SOCIO-DEMOGRAPHIC DATA		
1	SEX: M = Male, F = Female	|_|
2	Age (in years)	
3	Marital status: S = single, M = married, D = Divorced	|_|
4	Residence	
5	Region of origin: EN = Extreme North, N = North, A = Adamawa, C = Centre, W = west, NW = North west, SW = South west, E = East, L = Littoral	|_|
6	Profession	
SECTION 2: PAST MEDICAL AND FAMILY HISTORY		
7	Chronic pathologies: Y = Yes, N = No	|_|
8	If yes, what type; HTN, diabetes = D, Nephropathy = N, Endocrinopathy = Endoc to precise, Neoplasia = precise, Others (precise)	|_|
9	Use of Medications Y = Yes, N = No	|_|
10	Past surgery Y = Yes, N = No	|_|
11	If yes, precise	|_|
12	Smoking Active = A, passive = P, Non = N	|_|
13	Alcohol comsuption Y = Yes, N = No	|_|
14	If yes, IE = number × volume × % × alcohol density/day	|_|
15	Sedentary life style Y = Yes, N = No	|_|
16	Socio-professional stress Y = Yes, N = No	|_|
17	Similar cas in family, Y = Yes, N = No	|_|
18	Phaeochromocytoma, Y = Yes, N = No	|_|
19	Thyroid medullary carcinoma, Y = Yes, N = No	|_|
20	MEN type I Y = Yes, N = No	|_|
21	Von Hipple—Lindau disease Y = Yes, N = No	|_|
22	Neurofibromatosis Y = Yes, N = No	|_|
23	Other tumor Y = Yes, N = No	|_|
24	If yes precise	|_|
SECTION 3: CLINICAL EXAMINATION		
A-Functional Signs		
25	Presenting complaint or circumstance of diagnosis	
26	Duration of evolution since presentation of first symptom	
27	Weight gain Yes |_|, No |_|	|_|
28	Secondary ammenorrhoea Yes |_|, No |_|	|_|

Continued

29	Decrease libido Yes |_|, No |_|	|_|
30	Bone signs (non mechanical lumbar or pelvic pains) Yes |_|, No |_|	|_|
31	Immunity disorders Yes |_|, No |_|	|_|
32	Psychiatric disorders/problems Yes |_|, No |_|	|_|
33	HTN Yes |_|, No |_|	|_|
34	Neuromuscular signs Yes |_|, No |_|	|_|
35	Constipation Yes |_|, No |_|	|_|
36	PUPD syndrome Yes |_|, No |_|	|_|
37	Cramps and paresthesia of extremeties Yes |_|, No |_|	|_|
38	Dyspnea on effort Yes |_|, No |_|	|_|
39	Intense pulsatile headache Yes |_|, No |_|	|_|
40	Palpitations Yes |_|, No |_|	|_|
41	Profuse sweating Yes |_|, No |_|	|_|
42	Orthostatique hypotension	|_|
43	Ascending constrictive pains:abdomen and thorax Yes |_|, No |_|	|_|
B-Physical Signs		
44	General state: performance status index (WHO)	……
45	Blood pressure	……mm/Hg
46	Pulse	…….Bpm
47	Respiratory rate	……cpm
48	Temperature	……..˚C
49	BMI: weight……(Kg)/Height…….(m)	|_| |_|kg/m^2
50	Waist circumference	…..cm
51	Facial and trunkal obesity Yes |_|, No |_|	|_|
52	Easy bruising Yes |_|, No |_|	|_|
53	Cutaneous eruptions (pupural at pertechies) Yes |_|, No |_|	|_|
54	Signs of virilism Yes |_|, No |_|	|_|
55	Amyotrophie of lower limbs Yes |_|, No |_|	|_|
56	Pseudoparalytic crises Yes |_|, No |_|	|_|
57	Cardiac arrhythmias Yes |_|, No |_|	|_|
58	Gynaecomastia Yes |_|, No |_|	|_|
59	Palpable tumour at the level of the abdomen	|_|
60	Presence of goiter, exolpthalmos and signes of thyroid dysfunction Yes |_|, No |_|	|_|
61	Gallactorrhoea Yes |_|, No |_|	|_|
62	Presence of breast nodule Yes |_|, No |_|	|_|
63	Peculiarities of rest of physical examination …… …… ……	

Continued

SECTION 4: BIOLOGICAL INVESTIGATIONS		
Investigation	**Results**	**Normal value**
Aldosterone		
Plasma renin activity		
24 hrs CLU		
Freinage minute test		
• Midnight cortisol		
• 8 h cortisol		
ACTH		
DHEAS		
Testosterone		
17OHP		
Plasma metanephrines		
24 hrs urinary metanephrines		
Creatinnuria		
Creatinine (mg/l)		
Urea (g/l)		
FBS		
$Na^+/K^+/Cl^-$ (meq/l)		
$Ca^{2+}/PO_4/Mg^{2+}$		
Albuminemia (g/l)		
EPPS		
TSH (IU/l)		
Free T4 pmol/L		
CT/HDL/LDL/TG (g/l)		
FBC, WBC		
Hb		
Platelets		
CRP		
ASAT/ALAT/GGT		
Abdominal ultrasound…….		
……		
……		
Abdominal CT scan:		
• Tumour location: left |_|, right |_|		
• Size of tumour: …….cm		
• Content: homogenous |_|, heterogeneous|_|		
• Spontaneous density: <10 HU |_|, >10 HU |_|		
• Wash out: absolute……..%, Relative…….%		
• Limits: Regular irregular		
• Necrosis: Yes |_|, No |_|		
• Calcifications: Yes |_|, No |_|		
• Infiltration of pararenal fats: Yes |_|, No |_|		
• Hemorrhagic Yes |_|, No |_|		
• Metastasis Yes |_|, No |_|		
Chest X-Ray:…….		
Others: ……..		

Continued

SECTION 6: SURGICAL MANAGEMENT	
A-Pre-surgical preparation	
Pre-anesthetic consultation: ASA……., Altemier	
Pre-surgical investigations:	
FBC, WBC	
Hb	
Platelets, TP	TCK
Urea	creatinine
64	Multidispinary consertations (RCP) Yes |_|, No |_|
65	Medications Yes |_|, No |_|
66	If yes which type of medications?
67	Blood transfusion Yes |_|, No |_|
B-Per operative	
Day of surgical intervention……	
Duration with respect to onset of symptoms	
Type of Anesthesia:……	
Installation of patient:…….	
68	Indications:
69	Type of surgical intervention: Laparoscopic open surgery
70	Surgical technic: 1-Total adrenalectomy, 2-Partial adrenalectomy,
71	Surgical approach: 1-anterior midline, 2-Anterior Subcostal, 3-Anterior bisubcostal 4-thoracoabdominal
72	Surgical attitude: 1 = transperitoneal, 2 = extraperitoneal
73	Intraoperative findings:
74	Per-operative complications: HTN: Yes |_|, No |_| Hypotension Yes |_|, No |_| Bleeding Yes |_|, No |_| Cardiac arrest Yes |_|, No |_| Peritoneal breech Yes |_|, No |_| Pleural effraction Yes |_|, No |_| IVC injury Yes |_|, No |_| Adjacent organ injury Yes |_|, No |_|
75	Duration of surgery:
76	Specimen size……(cm) and weight……..(g)
C-Post surgery	
77	Immediate …… ……
78	Complications: Hemorrhage: Yes |_|, No |_| Anemia: Yes |_|, No |_| Surgical site infection: Yes |_|, No |_|

Continued

	Acute adrenal insufficiency: Yes |_|, No |_| Paralytic ileus: Yes |_|, No |_| Fistulas: Yes |_|, No |_| Death: Yes |_|, No |_| Others
79	hospital stay duration
SECTION 7: DIAGNOSIS (Anatomopathological diagnosis)	
80	Anatomopathological results:…… ……
SECTION 8: ADJUVANT TREATMENT	
Hydrocortisone supplementation Yes |_|, No |_| Chemotherapy Yes |_|, No |_|	
SECTION 9: SURVEILLANCE	
81	CLINICAL: Resolution of initial clinical signs Yes |_|, No |_| Appearance of new signs: Yes |_|, No |_| …… …… Relapse
82	Paraclinical: ● Cortisol 8 h Base 0 - 3 months 3 - 6 months >6 m ● Cortisol 1 H after synacthene test
83	Control abdominal CT scan

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Traumatic Penile Amputation Post Circumcision: A Series of 3 Cases

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Abstract

Circumcision remains a frequently performed surgical procedure and could be associated with various complications, ranging from mild to catastrophic. Penile amputation is a rare and severe complication usually complex and challenging to manage. We describe three cases of penile amputation injuries following circumcision referred within a week at the urological service of the Yaoundé Central Hospital. The first case was a 5-year-old who had complete penile amputation during circumcision by a nurse assistant at a rural health center. The second was a 7-year-old boy who sustained total penile glans amputation while undergoing circumcision by a nurse under local anesthesia at a rural health facility. The third involved a 6-year-old who had total penile amputation with loss of the amputated stump during circumcision by a traditional practitioner at home. Non-microsurgical penile re-implantations were done with diverse outcomes. The preservation of the amputated stump, the ischemic time and the severity of injury are factors affecting surgical outcome. The aim of this study is to evaluate our management experience and outcome of penile amputation injuries in resource-limited settings. Microsurgical replantation remains the gold standard in the management of penile amputation injuries. However, in resource-limited settings macroscopic replantation could be used as an alternative remedy to salvage the amputated penis.

Keywords

Circumcision, Penile Amputation, Surgical Management, Complications

1. Introduction

Circumcision is among the oldest and most frequently performed surgical procedures. Unfortunately, this procedure when performed by inexperience persons could result in various complications which could be mild or even catastrophic [1]. Penile amputation remains a rare and serious complication which is cumbersome and challenging to manage even in the hands of experienced urologists. The first penile replantation was described by Ehrlich and colleagues in 1929 following a macro surgical penile anastomosis [2]. Microsurgical replantation was later reported in 1977 by Cohen *et al.* and since then it has become the gold standard of management. The largest documented case series of penile amputation injuries was reported in Thailand following penile amputation injuries on 18 men by their spouses as a result of infidelity in the late 1970s. A Literature review of 80 cases of penile amputation injuries from 1996 to 2007 reported only 37.5% of successful replantation. However, there were considerable variations in the patient's surgical techniques used and the outcome [3]. Penile reconstructive and implantation surgeries remain very challenging generally and specifically in infants due to the scarcity of adapted equipment [4]. We describe our management experience of three cases of penile amputation injuries following circumcision received within a week in July 2022 at the urological service of the Yaoundé Central Hospital in Cameroon. Non-microsurgical penile re-implantations were done with diverse outcomes.

The patients' parents gave consent for the publication of this case series.

2. Case Presentations

2.1. Case 1

The 5-year-old boy was referred to our urological service for complete penile amputation during circumcision by a nurse at a rural health facility 5 hours prior to arrival at the hospital. The amputated penis was packed with a compressive gauze dressing and the amputated stump was preserved in saline solution which was placed in an ice bag upon arrival at our health service.

Following the primary and secondary survey, the patient had vital parameters; heart rate: 118 beats/min, respiratory rate: 26 breathes/min, hemoglobin: 9 g/dl, blood group: O Rhesus+. After anesthetic assessment, the patient was immediately taken to the operating room for surgical exploration under general anesthesia. Examination in the operating room revealed complete transection at the mid 2/3 of the penile shaft 2 cm from the base of the penis, with sectioning of the corporal bodies and the bulbar urethra (**Figure 1(a)**, **Figure 1(b)**). Hemorrhage was controlled by placing a rubber band as a tourniquet at the base of the penile shaft. Firstly urethral catheterization was done using a 10Fr silicon catheter which was introduced through the meatus of the distal amputated penile segment and then the urethra of the proximal amputated penile stump into the urinary bladder which was verified by the presence of urine in the catheter. Secondly, Anastomotic urethroplasty was done using PDS 6/0 over a 10Fr silicon transurethral catheter

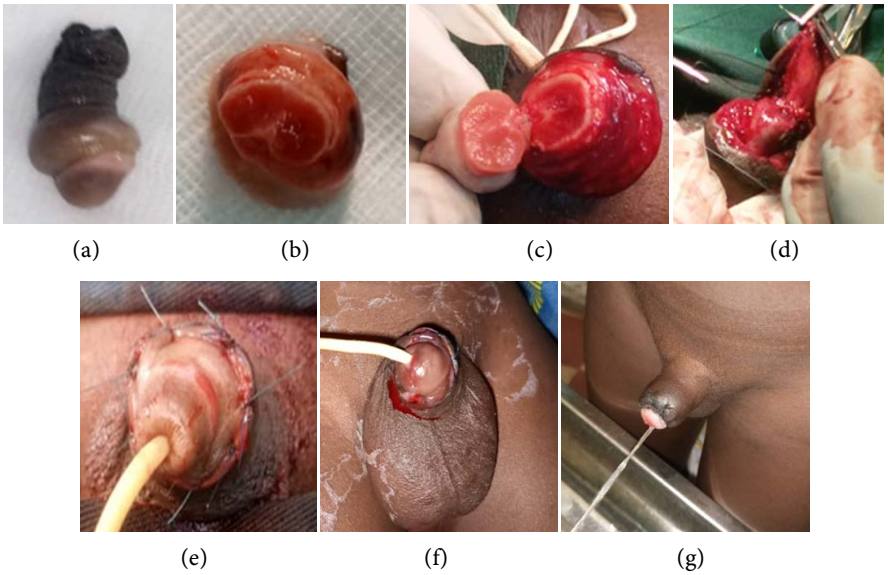

Figure 1. (a) Pre-operative complete amputated penis. (b) Transverse view of amputated penis showing the section copora carvenosa bodies dorsally with section spongiosum and urethra ventrally. (c) Intra-operative anastomotic urethroplasty. (d) Intraoperative anastomosis of corpus cavernosum. (e) Penis appearance at end of re-implantation with change in coloration from blue to pink. (f) Postoperative venous congestion on 5th day post penile replantation. (g) Patient voiding with good urinary stream 5th month post re-implantation.

with the help of 2.5× magnifying surgical loupes (**Figure 1(c)**). Thirdly Carvenoplasty and spongioplasty were realized by approximating the sectioned corporal bodies using PDS 6/0 continuous sutures (**Figure 1(d)**). The dorsal venous complex could not be repaired due to a lack of adapted microscopic resources. Penile skin reconstruction was then achieved using monocryl 4/0 interrupted sutures. Glans coloration was observed to change from purple to pink at the end of surgery after the tourniquet had been removed (**Figure 1(e)**). The patient was placed on broad-spectrum antibiotics (3rd generation cephalosporins), analgesics, anti-cholinergic and was immunized for tetanus. He later had psychosocial support from a psychotherapist after recovery from surgery. Evolution was marked on the 4th day post-surgery by bluish discoloration of the glans and penile edema (**Figure 1(f)**). The urinary catheter was removed 14 days post-surgery with the patient voiding with the good urinary stream. The patient was reviewed 6 months later and had a glans sensation and voids normally and his father reports noticing occasional nocturnal erection (**Figure 1(g)**). However, the parents expressed concerns about the child's sexual and reproductive functions when he becomes an adult.

2.2. Case 2

The 7-year-old boy was referred from a rural health center following total penile glans amputation while undergoing circumcision by a nursing assistant using local anesthesia. Following injury, hemorrhagic control was achieved by compressive dressing using gauze and crepe bandage. The amputated glans was wrapped with

gauze and placed in a polythene bag upon arrival at the hospital 7 hrs post injury. Following primary and secondary surveys with heart rate: 110 beats/min, respiratory rate: 25 cycles/min blood group A rhesus+, an anesthetic assessment was done and the patient was immediately taken to the operating room. Surgery was done under general anesthesia and tracheal intubation. Hemorrhagic control was achieved using a vessel loop placed at the base of the amputated penis. The amputated stump was placed in normal saline after non-viable tissues were debrided. Urethral catheterization was done using a 12Fr silicon catheter which was introduced through the meatus on the amputated glans and then the urethra of the proximal stump of the amputated shaft into the urinary bladder which was verified by the presence of urine in the catheter. Termino-terminal urethral anastomosis was done using vicryl 6/0. Macro-surgical approximation of the glandular epithelium to the distal penile shaft was done using monocryl 5/0 interrupted sutures. Glans coloration was observed to change to purple at the end of surgery after the loop vessel had been removed. The patient was placed on antibiotics (amoxicillin/Clavulanic acid) anticholinergic and the urinary catheter was removed 14 days post-surgery. Evolution was marked by partial glans necrosis on the 5th day post-surgery which was managed by local wound care and sitz bath (**Figure 2(a)**). The urinary catheter was removed on the 12th day post-surgery and the patient voided with a good urinary stream. Eschar formation at the glans dropped spontaneously following continuous sitz bath and local wound care on the 14th day post replantation (**Figure 2(b)**). The patient was evaluated 5 months following surgery and had a good urine stream, preserved glans sensation and nocturnal erection (**Figure 2(c)**).

2.3. Case 3

The 6 year-old was brought to the emergency following the amputation of his penis with loss of the amputated stump which he sustained during a circumcision procedure performed by a traditional practitioner at home.

The patient arrived at the hospital 4 hours post-injury in a state of haemorrhagic shock with a blood pressure of 65/45 mmHg and heart rate of 128 beats/min. Following resuscitation, blood transfusion and anaesthetic evaluation he was taken to the operating room. Surgical exploration revealed a complete penile transaction located 0.5 cm from the penoscrotal junction with a complete section of the corporal bodies and the urethra. There was no amputated stump available for replantation. Management included control of haemostasis by ligation of bleeding vessels from the corporal stumps using Vicryl 3/0 sutures. The sectioned urethra was identified and catheterized using a 10Fr silicon catheter and penile skin closure was done using vicryl 4/0 interrupted sutures (**Figure 3**). Evolution was remarkable for the poor cosmetic appearance of genitalia and retraction of the residual urethral segment. The urinary catheter was removed after 21 days during which the patient voided with a poor urinary stream necessitating intermittent urethral catheterisation. Patient carers were being counselled on future

(a) (b) (c)

Figure 2. (a) Penile glans necrosis on 5th day post replantation. (b) Penis appearance of 14th day post replantation after removal of eschar and urinary catheter. (c) 5th month post penile glans replantation.

Figure 3. Urinary diversion in patient with penile amputation sustained during circumcision with loss of amputated stump.

penile reconstruction procedures but unfortunately patient became unreachable during subsequent follow-up appointments.

3. Discussion

Circumcision remains a common surgical procedure in urology, usually safe, simple and with low morbidity. Nonetheless, serious complications can result when this procedure is performed by unskilled persons. Circumcision-related complications could be diverse ranging from bleeding, and urethra-cutaneous fistulas to even penile amputation as it was in our cases presented [5].

Penile amputation remains a rare, complex and devastating injury which is usually challenging even to experienced urologists. In addition, it has a huge psychological and social impact on both the patient and caregivers coupled with associated long-term morbidity [6]. It requires emergent multidisciplinary surgical management and adequate postoperative care and follow-up. Reported penile amputation mechanisms include trauma, domestic violence, industrial accidents, self-mutilation, failed circumcision and animal bites [7].

The first successful penile replantation was documented in 1929. Since then, more than 100 cases have been reported with varying complications and salvage rates.

Morrison and colleagues reported that following penile replantation, 97.4% of the victims conserved their normal urinary function with the most common complication reported after penile replantation being skin necrosis (54.8%) and venous congestion (20.2%) [8]. Other replantation-related complications include; erection disorders, poor sensation, and poor cosmetic appearance of the genitalia [9]. We report our management experience and outcome of three patients with circumcision-related penile amputation injuries received at the Yaounde central hospital in Cameroon.

Reported factors which may influence the success of penile replantation surgeries include among others; the degree of injury, surgical technique used for replantation, preservation of the amputated stump and surgeon's experience. The length of ischemia endured by the amputated penile segment is a key factor that may influence surgical outcome with cold ischemia having a better prognosis [9]. Microsurgical replantation with anastomosis of the dorsal neurovascular bundles of the penis is the gold standard of management for these injuries. This technique increases the chances of graft survival and reduces postoperative complications. Unfortunately, this technique requires high training even more complex in the pediatric group due to the scarcity of adapted equipments in our setting. The return of normal color is a good intraoperative and postoperative indicator of graft survival [10] [11].

In situations of penile glans amputation or when instrumentation for microscopic surgery is not available, macroscopic replantation may be another reconstructive option to salvage the amputated penis [2] [12]. The first two patients presented had macroscopic replantation of the amputated glans and the penis with a favorable outcome with regards to voiding function and sensation during 8 months period of follow-up.

Penile stump replantation without repair of dorsal vessels of the penis could be considered as a graft. Thus the replanted graft will survive by imbibition by obtaining nutrients from the adjacent graft by diffusion [12]. The penile graft is successful because the dorsal and urethral arteries serve as an excellent source of blood supply to the corpus spongiosum and the glans. Blood circulation at macroscopic replantation could be reinstalled through the spongy tissue of the grafted penis [13]. Furthermore, the corporal sinusoidal blood flow could also act as diffusion for the composite graft in macro-surgical penile replantation. Complications such as fistula formation, loss of sensations, erectile dysfunction and skin necrosis have been reported with this technic [14].

Micro-vascular replantation is the current recommended treatment choice for penile amputation injuries because it yields better physiological micturition, good cosmetic restoration, preservation of sensation, and erectile function. Nonetheless complications including skin necrosis, urethral stenosis and fistulas have also been reported with this technique [11] [15].

In our third case, replantation was not attempted given the severity of the trauma and lack of the amputated segment which was lost. The extensive loss of penile tissue in this patient makes management decisions even more challenging.

Penile replantation will also depend on the condition of both the stump and the amputated segment. In patients with significant tissue loss including loss of amputated stump or poor wound conditions, debridement and stump closure followed by differed secondary penile reconstruction is usually preferred. Such patients may be candidates for phallic replacement. Microsurgical free forearm flap phalloplasty techniques have been used to manage patients who suffered from total penile amputation with loss of the amputated segment [16].

4. Conclusion

Penile amputation injuries are very rare but devastating circumcision-related complications. Management is urgent penile replantation. The preservation of the amputated stump, the ischemic time, the severity of injury and the surgeon's experience are some factors affecting penile replantation surgical outcome. Microsurgical replantation remains the gold standard in the management of penile amputation injuries. However in resource-limited settings macroscopic replantation by an experienced urologist could be used as an alternative remedy to salvage the amputated penis.

Conflicts of Interest

The authors declare no competing interests.

Consent for Publication

Informed consent was obtained from the parents of the patients for the publication of this case series.

Authors' Contributions

Patient management: Mbassi Aurele Achille, Owon Abesolo, Orock Agbor Tanyi and Pierre Joseph Fouda. Data collection: Nwatchap Jean jeaques, Awoundja Christain. Manuscript drafting: Orock Agbor Tanyi. Manuscript revision: Mekeme Mekeme, Fouda Jean Cedrick. All authors read and approved the final manuscript.

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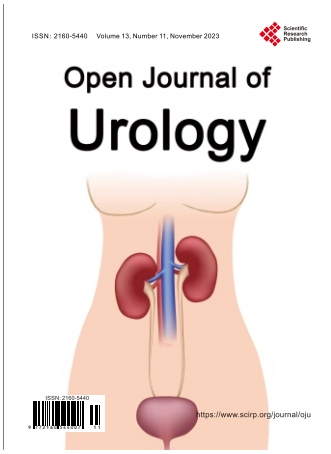

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