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Effect of Varicocelectomy on Gonadal Function among Patients Reporting with Sexual Dysfunction in Ghana

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Abstract

Background: Long-standing varicocele is often associated with testicular hypoxia and that might worsen Leydig cell function, a significant risk factor for hypogonadism. This may affect both the secretory and endocrine functions of the testis. This study aims to determine the effect of microsurgical sub-inguinal varicocelectomy on gonadal function among men reporting sexual dysfunction in Ghana. **Methods**: This was an intervention study conducted at the Tamale Teaching Hospital from September 2017 to August 2021. A total of 103 participants were randomized into two groups; the surgery group (n = 52) and the observed group (n = 51). Venous blood samples were collected at baseline, varicocelectomy was performed for the surgery group, and no intervention was given to the other. Blood samples were subsequently collected at 12-, 24-, 36-, and 48-month intervals for assay of serum total testosterone, FSH, and LH. The data were analyzed in GraphPad Prism (v8.0) at an alpha value of 0.05. **Results:** All the participants had varicocele and were aged between 55.0 to 69.0 years old. At the baseline of the study, all participants presented with sexual dysfunction but a significant improvement ($p < 0.001$) in the GRISS score, and the subscale was observed 12 months after the surgery. The mean ± SD serum total testosterone ($p = 0.6078$), FSH ($p = 0.6522$) and LH ($p = 0.2281$) between the groups at baseline did not vary but those in surgery group had improved values at 12-, 24-, 36- and 48-month post-surgery (p-trend < 0.0001). The surgery group had an overall percent increase in serum total testosterone (76.3%, 194.0%, 221.0%, and 231.9%) over 12-, 24-, 36- and 48-month and significant percent reduction in both FSH (−14.7%, −29.9%,

−33.8% and −40.8%) and LH (−21.8%, −31.0%, −32.4%, and −36.4%) respectively. These gonadotropins observed annual percentages spike within the first and second year but changes were marginal from the third year onwards in the surgery group. **Conclusions:** Microsurgical sub-inguinal varicocelectomy improved gonadal function among varicocele patients reporting sexual dysfunction. It is recommended to use this choice for similar patients; however, these findings should be verified by a multi-institutional study to provide more evidence for this choice.

Keywords

Varicocele, Sub-Inguinal Varicocelectomy, Gonadal Function, Sexual Dysfunction

1. Introduction

Varicocele is the enlargement of pampiniform venous plexus draining the testicle, with reflux of venous blood [1] [2]. It is a common problem in men who seek medical attention for fertility problems, sexual dysfunction, or complain of continuing scrotal discomfort [3].

Varicocele has been identified in 15% of healthy men [4] but the prevalence ranges from 35% to 45% among men seeking medical attention for primary infertility and 80% among patients seeking care for secondary infertility [5] [6].

Studies involving humans have reported that varicocele causes progressive time-dependent testicular damage [7] [8] [9]. Between the ages of 18 - 20 years, the testicular function is usually normal but declines progressively depending on the duration of the varicocele [10]. Some propositions have sort to explain the lethal effects of varicocele on testicular function with the most accepted postulate related to alterations in the thermal environment of the testicles. The formation of a communicating meshwork of spermatic veins leaving the testicles produces a counter-current heat-exchange mechanism to cool arterial blood [11]. However, persons confirmed with varicocele lack this mechanism, hence, causing elevated scrotal temperature.

Long-standing varicocele might worsen Leydig cell functions and is a significant risk factor for hypogonadism. Lotti *et al.* [12] in a study found that patients with severe varicocele had increased serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) with lowered testicular volume. Increased serum FSH and LH levels in infertile men diagnosed with varicocele have resulted in the hypothesis that varicocele causes Leydig cell dysfunction [13].

Clinical studies suggest that repair of the varicocele may improve gonadal function in men with varicocele [14] [15] [16]. Çayan *et al.* [16] reported that approximately 60% - 80% of men with low serum testosterone had normalized testosterone levels after varicocele repair. Li *et al.* [15] in a meta-analysis found that the mean serum testosterone level increased after varicocelectomy. None-

theless, there are conflicting reports on whether varicocele and varicocelectomy result in changes in serum FSH and LH levels or not. Some studies reported no significant changes in the levels of serum FSH and LH [17] [18], yet others noted decreased serum FSH and LH levels following varicocelectomy [13] [19].

As already known, Leydig cells function to produce testosterone but this is controlled by luteinizing hormone. FSH functions to promote the beginning of testosterone production; in the process, LH is maintained. Hence, there is cross-talk with the changes in serum testosterone, FSH, and LH. This study, therefore, aims to determine the effect of microsurgical sub-inguinal varicocelectomy on serum total testosterone, FSH, and LH levels among patients reporting sexual dysfunction in Ghana.

2. Methods

2.1. Ethical Consideration

This study was approved by the Ethics and Review Board of the Department of Research and Development, Tamale Teaching Hospital (No: TTH/R & D/SR/119), and has therefore been performed following the standards laid down in the 1964 Declaration of Helsinki. Informed consent was obtained from all the participants before the study. Participation in this study was voluntary, participants were kept anonymous, and information obtained remained confidential to the researchers only. Only blood samples intended for the study were drawn and information that was deemed as important to the management of the patient was communicated to the patient.

2.2. Study Design

This was an intervention study design in which participants were randomized into two groups; the surgery group (n = 52) and the observed group (n = 51) (**Figure 1**). The study was conducted at Tamale Teaching Hospital in the Tamale Metropolis from September 2017 to August 2021.

2.3. Study Population

Participants who were eligible for inclusion in this study were given the option of immediately undergoing microsurgical sub-inguinal varicocelectomy or being observed for 12 months with a subsequent reassessment of the management plan and possibly delayed the operation. Based on the willingness to equally accept either option, eligible participants were randomized to the surgery group and observed group. However, neither the investigator nor participants were blinded to the intervention after allocation [20].

2.3.1. Inclusion Criteria

Participants were eligible for inclusion in the study if they had fathered at least one child, and had complained of any form of sexual dysfunction including; weak sex drive, impotency, premature ejaculation, infrequency of sexual intercourse,

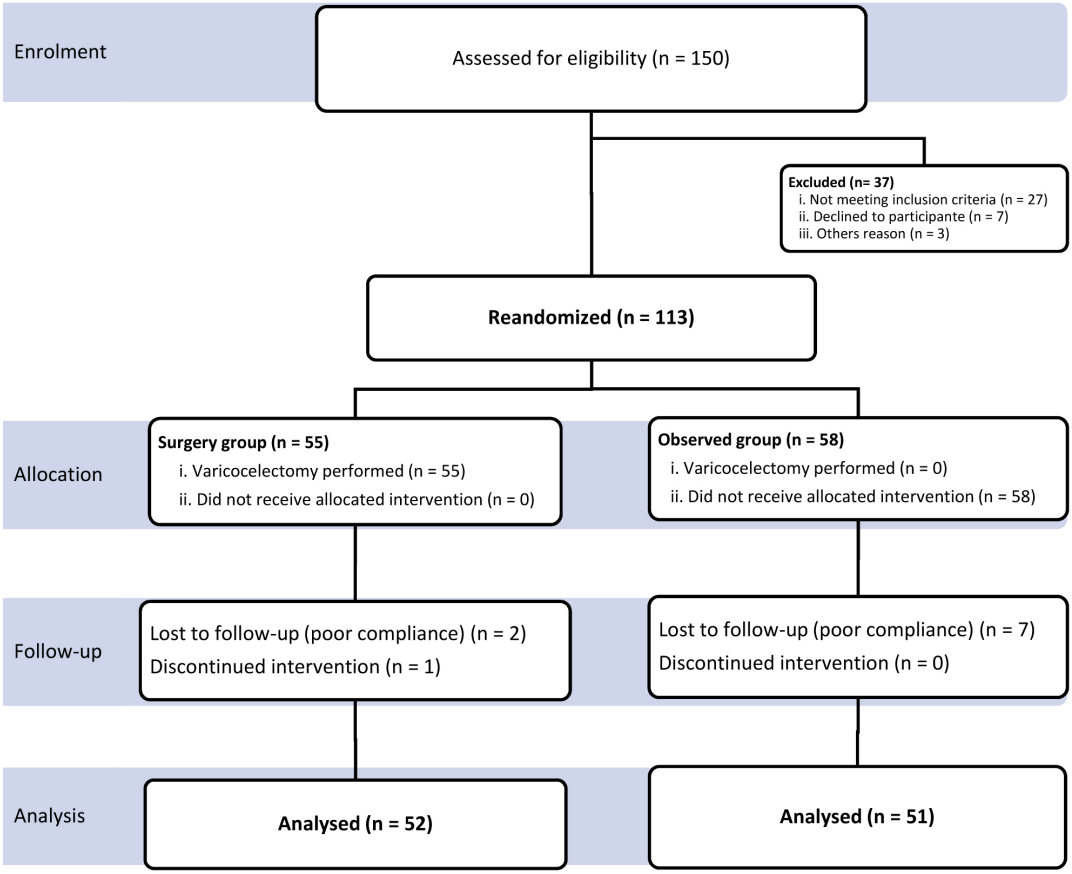

Figure 1. Flowchart diagram.

avoidance of sexual intercourse, non-communication about sex with a partner, and dissatisfaction after sexual intercourse activity [21].

All consented participants were sexually active men who had maintained a stable heterosexual relationship for at least 2 years before participating in the study. A stable heterosexual relationship was considered as one in which the man was involved and maintained sexual relations, regardless of marital status.

Selection strategies were adopted depending on the unit at the recruitment center of the Tamale Teaching Hospital. After a patient arrived at the Urology Specialist Clinic, pre-assessment checks were made according to the criteria stated above and those who did not qualify for the study were made to continue with their routine medical examinations. If a patient met the eligibility criteria, informed consent was obtained and a questionnaire was administered to be completed independently. Where participants were not able to read and write, the queries on the questionnaire were translated verbatim in the common dialect. Participants were made to see the urologist for medical examination.

2.3.2. Exclusion Criteria

Participants with sexual dysfunction who had not fathered a child (or children), had no sexual dysfunction complaints, excessive alcohol use (chronic alcoholics), cigarette smoking history, and incomplete/inconclusive questionnaires were ex-

cluded. Again, participants with a history of uncontrolled diabetes, uncontrolled hypertension as well as patients on long term statins, undescended testis, mumps orchitis, use of anti-androgen and/or testosterone replacement therapy, or orchidectomy were all also excluded [22].

2.4. Clinical Evaluation

Each consenting participant was clinically examined by a urologist. The diagnosis was based on physical examination and was confirmed by ultrasound scan examination. All participants had a varicocele. Dubin and Amelar [23] approach was employed to detect, confirm and clinically grade varicocele. Varicocele was categorized into three (3) grades; grade I (first grade), II (second grade), and III (third grade). Grade I was confirmed if the participant had an enlarged venous plexus of spermatic tone evident only by palpation during the Valsalva manoeuvre. Enlargement of the venous plexus of spermatic tone evident only by palpation at the upright position was considered Grade II while enlargement of the venous plexus of spermatic tone evident visually was confirmed Grade III [24]. Scrotal ultrasound was used to diagnose the non-palpable enlargement of the venous plexus of the spermatic tone [25].

Scrotal Ultrasound Evaluation (SUE)

Two phases of scrotal ultrasound scans were carried out on participants who qualified for the study; the first phase was with participants in the supine position (with penis resting on suprapubic region) and the second in an upright position. The examination was conducted with a Samsung Medison Accuvix V20 scan (Samsung Electronics, South Korea) equipped with linear, high-resolution, and high-frequency (7.5 - 14 MHz) probe keen to the study of soft body parts and with color Doppler for detecting slow flows and scanning surface of at least 5 cm [26]. To evaluate testicular malposition, blood reflux along the pampiniform plexus, or the extent of any fluid collections an ultrasound scan was done [22].

2.5. Data Collection

2.5.1. Questionnaire Administration

Sociodemographic data, cigarette smoking, and medical history were gathered with a structured pre-tested questionnaire. Questions on sexual response were assessed using the Golombok Rust Inventory of Sexual Satisfaction (GRISS) questionnaire which measures specific sexual behaviors, attitudes, and beliefs [21]. The GRISS questionnaire has 28 items on a single sheet and it is used for assessing the existence and severity of sexual problems in heterosexual couples or individuals who have a current heterosexual relationship. All the 28 questions were answered on a five (5) point scale from "always" through "usually", "sometimes" and "hardly ever" to "never". This provided overall scores for the quality of sexual functioning within a relationship. In addition, the subscale scores for infrequency, non-sensuality, dissatisfaction, non-communication, and avoidance

were obtained and presented as a profile. The total score and subscale scores were transformed using a standard nine-point scale ranging between 1 and 9, with high scores indicating greater problems. Scores of 5 or more were considered to indicate sexual dysfunction (SD). The GRISS was chosen because it is standardized, easy to administer and score, relatively unobtrusive, and substantially inexpensive [21].

2.5.2. Blood Pressure Measurement

The Omron blood pressure monitor was used to measure the blood pressure of the participant. These included; systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse rate, and categorization of normotension (SBP < 140 mmHg/DBP < 90 mmHg) and hypertension (SBP > 140 mmHg/DBP > 90 mmHg) was based on WHO cut-offs as cited by Mittal and Singh [27]. The Omron blood pressure monitor uses the oscillometric method of blood pressure measurement. This means the monitor detects the blood's movement through the brachial artery and converts the movements into a digital reading (https://www.omron.com/global/en/).

2.5.3. Anthropometric Measurement

Anthropometric measurements were done on all study participants. The Seca 213 portable Stadiometer (Seca Corp., Hamburg, Germany) was used to measure the height of the participants to the nearest 0.1 cm. To measure the height, the stadiometer was set up according to the manufacturer's instructions. Participants were asked to take off footwear including socks and measurements taken in the upright position.

The measurement of weight, calculation of BMI, and the assessment of body fat composition were done using the Omron HBF-516B Body Composition Analyzer and Electronic Scale (Omron Corp., USA). The Omron HBF-516B Body Composition Analyzer and Electronic Scale is a tetra-polar bioelectrical impedance analyzer that measures weight to the nearest 0.01 kg. It has electrodes on the surface of the scale and on a hand-held device that is attached to the scale by a retractable cord. It works by passing a painless, imperceptible electrical current (500 μA) at a fixed frequency of 50 kHz through the body while determining resistance and reactance. Body fat and muscle mass were recorded as percentages of the total body weight at intervals of 0.1% [22].

2.5.4. Blood Samples Collection

Venous blood samples (4 mls) were collected from each participant within the hours of 8:00-11:00 GMT after at least 8 hours of fast by a phlebotomist using standard venipuncture methods. A check-list was given to each consenting participant to tick the number of hours fasted to enable rescheduling those who could not meet the time.

Venous blood samples collected were dispensed into a 5 ml vacutainer containing a gel separator. Blood samples were centrifuged at 8000 rpm for 5 minutes to yield serum and cells. The serum was aliquoted and stored at −20˚C until assay.

2.5.5. Hormonal Measurement

Baseline male fertility hormones (total testosterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH)) were measured by electrochemiluminescence with Hitachi-Roche analyzer (Cobas 6000, Roche Diagnostics, IN, USA).

2.6. Interventions (Sub-Inguinal Microscopy Varicocelectomy)

Participants were counselled about their condition, and the exact nature of the problem was explained to them by a urologist. A microsurgical open sub-inguinal varicocelectomy procedure as described by Marmar *et al.* [28] was performed for the surgery group. Surgery was performed under spinal anaesthesia, using microsurgical instruments and magnification with an operating microscope KARL CAPS SOM 82, Germany. The lymphatic vessels and testicular artery were spared, and both internal and external spermatic veins ligated and divided. The spermatic fasciae were closed using PGA 3/0 running sutures. The wound was closed in layers and a subcuticular skin stitch was applied using 4/0 PGA sutures. Wound dressing was removed after 24 hours. No antibiotics were employed and the pain was managed by using 1-gram of rectal paracetamol during the period of recovery and followed by oral paracetamol 1-gram tid for the next 24 hours [22].

2.7. Follow-Up

Both groups were followed for 48 months (4 years) after the day of surgery (surgery group) or the day of the last baseline hormone analysis (observed group). Participants in the observed group were advised not to use any form of contraceptives during sexual intercourse, and to abstain from tobacco/cigarette smoking. Participants in the operated group were advised to abstain from any form of sexual activity until the surgical wound was properly healed. All participants were reassessed every 90 days to confirm that; the participant was not smoking, and was clinically examined to confirm the absence of genital infection, formation of hydrocele, recurrence of varicocele, and increased testicular size. Participants were asked to revisit the clinic after 6 months and 12 months. Blood samples were drawn for repeated measurement of serum total testosterone, FSH, and serum LH at follow-up months 12, 24, 36, and 48 respectively.

2.8. Statistical Analysis

Data were entered into Microsoft Excel version 10 (https://www.ibm.com/cn-zh) and exported to GraphPad Prism version 8.0 (https://www.graphpad.com/) for analysis. Categorical data were presented as frequency, percent, and charts, and parametric data presented as mean ± standard deviation (SD) or mean ± standard error of the mean (SEM). Kolmogorov-Smirnov test was performed on parametric data to check whether or not the data was normally distributed. To compare two groups, the Chi-square test was used for categorical variables, and the unpaired student t-test was used for parametric data. Variables before and

after the operation in each patient were compared using paired *t*-test. Group means were compared using one-way ANOVA followed by Newman-Keul's test as post hoc. A two-tailed p-value less than 0.05 was considered statistically significant.

3. Results

3.1. Baseline General Characteristics of Study Participants

The general characteristics of the study population are summarized in Tables 1-3. From Table 1, the majority of the participants were married (83.5%), self-employed (60.2%), and were from the Mole-Dagomba tribe (62.1%). About 46.6% of the participants attained formal education and 19.4% were gainfully employed. The majority were confirmed with varicocele grade II (50.5%) with left-sided being the predominant type (94.2%) (Table 1).

As shown in Table 2, participants were aged between 55.0 and 69.0 years old. The mean ± standard deviation (SD) BMI, body fat, muscle mass, and visceral fat were 23.63 ± 2.971, 17.92 ± 7.814, 35.82 ± 4.322, and 7.434 ± 3.467 respectively. The systolic blood pressure (SBP) was between 96.0 and 136.0 mmHg while the diastolic blood pressure (DBP) was between 66.0 and 88.0 mmHg. Before the randomization, the mean ± standard deviations (SD) for the total FSH, LH, and Testosterone were 23.8 ± 7.788, 11.85 ± 3.751, and 2.128 ± 0.811 respectively.

Table 1. General (categorical variables) characteristics of study participants.

Variable	Frequency (n = 103)	Person (%)
Married	86	83.5
Formal education	48	46.6
Consumption of alcoholic beverage	21	20.4
Ethnicity		
Mole-Dagomba	64	62.1
Other tribes	39	37.9
Occupation status		
Gainful employed	20	19.4
Self-employed	62	60.2
Unemployed	21	20.4
Varicocele grade		
I	16	15.6
II	52	50.5
III	35	33.9
Varicocele type		
Left-sided	97	94.2
Bilateral	6	5.8

Data presented as frequency and percent. Other tribes in Ethnicity included; Dagaati, Frafra, Gonja, Ashanti, Ewe, Ga, and Kassena.

Table 2. General (continuous variables), anthropometric characteristics, and baseline hormonal parameters of study participants.

Variable	Minimum	Mean	Std. deviation	Maximum
Age (years)	55.0	60.92	2.487	69.0
Anthropometric measurements				
Weight (kg)	60.1	69.2	15.62	158.0
Height (cm)	82.3	168.9	13.47	183.0
BMI (kg/m^2)	17.9	23.63	2.971	33.0
Body fat (%)	6.9	17.92	7.814	45.8
Muscle mass (%)	22.6	35.82	4.322	44.7
Visceral fat	2.0	7.434	3.467	17.0
Blood pressure				
SBP (mmHg)	96.0	121.1	7.190	136.0
DBP (mmHg)	66.0	73.7	5.787	88.0
Pulse (beat/mins)	58.0	66.77	5.250	97.0
Pre-operative hormones				
S-Follitropin (FSH) (IU/L)	4.8	23.8	7.788	38.1
S-Lutroppin (LH) (IU/L)	2.0	11.85	3.751	25.0
Total Testosterone (nmol/L)	0.4	2.128	0.811	4.1

Data presented as mean and standard deviation (SD); Abbreviation: BMI—Body Mass Index; SBP—Systolic Blood Pressure; DBP—Diastolic Blood Pressure, FSH—Follicle Stimulating Hormone; LH—Luteinizing Hormones.

Table 3. General (continuous variables), age, anthropometric characteristics, and blood pressure at baseline of study participants.

Variable	Observed Group (n = 51)	Surgery Group (n = 52)	p-value
Age (years)	61.35 ± 2.262	60.52 ± 2.666	0.2294
Anthropometry			
Weight (kg)	68.43 ± 19.81	69.93 ± 10.48	0.7300
Height (cm)	166.7 ± 18.23	171.0 ± 5.831	0.2509
BMI (kg/m^2)	22.76 ± 2.857	24.48 ± 2.880	0.0337
Body fat (%)	17.44 ± 8.634	18.38 ± 7.070	0.6648
Muscle mass (%)	36.21 ± 4.142	35.44 ± 4.534	0.5235
Visceral fat	6.538 ± 2.420	8.296 ± 4.103	0.0644
Blood Pressures			
SBP (mmHg)	121.2 ± 13.59	121.0 ± 11.23	0.9697
DBP (mmHg)	72.81 ± 4.77	71.67 ± 4.444	0.1247
Pulse (beat/min)	66.15 ± 5.12	68.22 ± 6.11	0.2986

Data presented as mean ± standard deviation (SD); quantitative variables compared using unpaired *t*-test statistics and a two-tailed p-value less than 0.05 considered statistically significant. Abbreviation: BMI—Body Mass Index; SBP—Systolic Blood Pressure; DBP—Diastolic Blood Pressure.

The eligible participants were randomized into; the observed group and the surgery group (those who had undergone varicocelectomy). At baseline, participants in the surgery group recorded significantly higher BMI ($p = 0.0337$) compared with their counterparts. However, there was no significant difference between the age ($p = 0.2294$), body fat ($p = 0.6648$), muscle mass ($p = 0.5235$) and visceral fat ($p = 0.0644$) (Table 3).

3.2. Baseline Score of Sexual Dysfunctions among Participants according to Golombok Rust Inventory of Sexual Satisfaction (GRISS)

The sexual function scores of the participants for each GRISS scale are shown in Figure 2. The Stanine scale depicting sexual dysfunction for the overall male score ranges from 6 - 9, impotence (5 - 9), premature ejaculation (4 - 9), non-sensuality (5 - 9), avoidance (4 - 9), dissatisfaction (4 - 9), in frequency (5 - 7), and non-communication (6 – 9) with the prevailing value for each of these scales being a score of 5 or above.

3.3. Subscale Score among Participants Using GRISS

As shown in Table 4, all consenting participants had one or more baseline subscale scores reflecting sexual problems as the overall GRISS scale and the score for each subscale was above the upper value of 5. The distribution of the baseline subscale score for each of the groups was almost the same such that there was no significant ($p < 0.05$) difference between their means.

After 12 months of follow-up, the overall male scale (3.259 ± 0.9027), impotence (3.037 ± 1.1260), premature ejaculation (3.481 ± 1.2820), non-sensuality (2.667 ± 0.9199), avoidance (3.148 ± 1.4060), dissatisfaction (2.222 ± 0.8006), infrequency (1.963 ± 0.8077) and non-communication (3.407 ± 1.1180) were significantly ($p < 0.0001$) lower in the surgery group compared with the observed group (Table 4).

3.4. Distribution of Gonadal Function over 48 Months of Follow-Up among Study Participants

The gonadal function was compared to the baseline measurement for over the 48 months follow-up in each group. From the unpaired t-test analysis, before the operation, there was no difference between the serum testosterone ($p = 0.6078$), FSH ($p = 0.6522$) and LH ($p = 0.2281$). After 48 months of follow-up, the serum testosterone increased in 12 months ($p < 0.0001$), 24 months ($p < 0.0001$), 36 months ($p < 0.0001$), and 48 months ($p < 0.0001$) in patients whom had undergone varicocelectomy compared with the observed group whilst the levels of serum FSH and serum LH values decreased ($p < 0.0001$) respectively (Table 5 and Figure 3(a) and Figure 3(b)).

According to the paired t-test statistics showing whether the difference between gonadal hormones among each group was significant; in the surgery group, baseline serum testosterone was 2.185 ± 0.730 but increased in 12 months

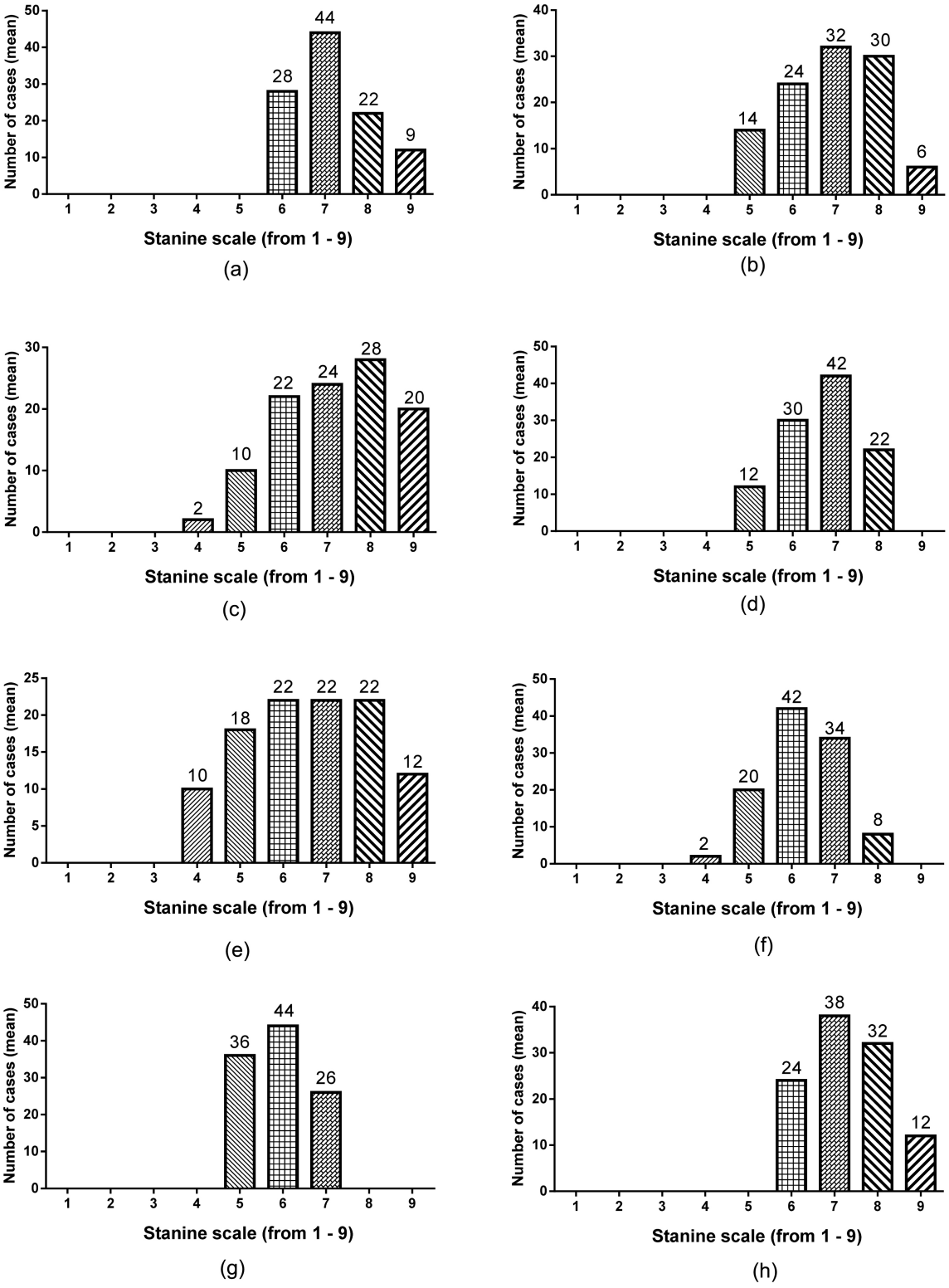

Figure 2. Score of sexual dysfunctions among participants according to Golombok Rust Inventory of Sexual Satisfaction (GRISS) questionnaire. Graphs show the number of participants (y-axis) and Stanine scale (from 1 - 9 on the x-axis) for each GRISS subscale. Normal scores range from 1 - 4 and 5 - 9 indicate the abnormal score. (a) Overall male score; (b) Impotence; (c) Premature Ejaculation; (d) Non-sensuality; (e) Avoidance; (f) Dissatisfaction; (g) Infrequency; (h) Non-communication.

Table 4. Subscale score among participants using GRISS.

GRISS SCALE	Observed Group (n = 51)	Surgery Group (n = 52)	p-value
Baseline (Onset)			
Overall male scale	7.115 ± 1.033	7.222 ± 0.891	0.6882
Impotence	6.769 ± 1.142	7.037 ± 1.126	0.3941
Premature Ejaculation	6.846 ± 1.287	7.519 ± 1.312	0.0654
Non-sensuality	6.615 ± 0.983	6.778 ± 0.892	0.5312
Avoidance	6.231 ± 1.478	6.963 ± 1.480	0.0775
Dissatisfaction	6.308 ± 0.970	6.185 ± 0.879	0.6318
Infrequency	5.846 ± 0.732	5.963 ± 0.808	0.5840
Non-communication	7.269 ± 0.919	7.333 ± 1.000	0.8092
12 Months			
Overall male scale	7.269 ± 0.8744	3.259 ± 0.9027	<0.0001
Impotence	7.231 ± 0.7646	3.037 ± 1.1260	<0.0001
Premature Ejaculation	7.077 ± 0.8910	3.481 ± 1.2820	<0.0001
Non-sensuality	6.692 ± 1.1580	2.667 ± 0.9199	<0.0001
Avoidance	6.500 ± 1.0680	3.148 ± 1.4060	<0.0001
Dissatisfaction	6.692 ± 1.0110	2.222 ± 0.8006	<0.0001
Infrequency	6.846 ± 0.8339	1.963 ± 0.8077	<0.0001
Non-communication	7.000 ± 0.9381	3.407 ± 1.1180	<0.0001

Data presented as mean ± standard deviation (SD); quantitative variables compared using unpaired t-test statistics and p-value < 0.05 considered statistically significant.

Table 5. The distribution of gonadal function over 48 months of follow-up among study participants.

Variable	Baseline	12 months	24 months	36 months	48 months	One-way ANOVA; p-value	p-trend
FSH (IU/L)							
Observed group	23.30 ± 8.642	24.91 ± 8.446****	25.52 ± 8.339**	26.31 ± 8.257**	27.03 ± 8.799***	F (4,125) = 0.7348; p = 0.5699	0.0949
Surgery group	24.28 ± 7.001	20.69 ± 6.947****	16.59 ± 5.197****	15.57 ± 4.512****	13.87 ± 4.019****	F (4,130) = 14.99; p < 0.0001	<0.0001
p-value	0.6522	0.0518	<0.0001	<0.0001	<0.0001		
LH (IU/L)							
Observed group	11.21 ± 3.168	12.00 ± 3.335****	13.07 ± 3.850****	13.91 ± 4.368****	14.94 ± 4.439****	F (4,125) = 3.823; p = 0.0058	0.0002

Continued

Surgery group	12.46 ± 4.207	9.419 ± 2.410****	7.970 ± 1.668****	7.752 ± 1.313****	7.323 ± 1.452****	F (4,130) = 19.80; p < 0.0001	<0.0001
p-value	0.2281	0.0021	<0.0001	<0.0001	<0.0001		
Testosterone (nmol/L)							
Observed group	2.069 ± 0.899	1.931 ± 1.931**	1.977 ± 0.9052	1.773 ± 0.8488***	1.869 ± 1.333	F (4,125) = 0.3298; p = 0.8575	0.3654
Surgery group	2.185 ± 0.730	3.644 ± 1.239****	5.915 ± 2.101****	6.444 ± 2.211****	6.667 ± 2.202****	F (4,130) = 32.17; p < 0.0001	<0.0001
p-value	0.6078	<0.0001	<0.0001	<0.0001	<0.0001		

The data were presented as mean ± SD. The presence of significant differences among means of the groups was determined by one-way ANOVA followed by Newman-Keul's test as post hoc. Significantly different from baseline (Ctrl): *p < 0.05, **p < 0.01, ***p < 0.001 by Newman-Keuls test.

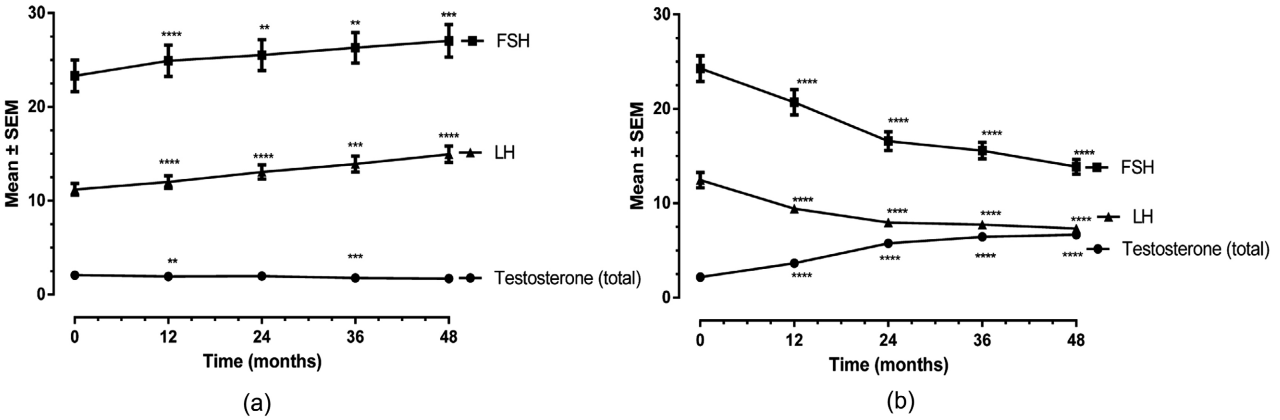

Figure 3. Mean difference in the hormones for each of the groups; data presented as means ± standard error of mean. (a) For the observed group; (b) For the surgery group.

(p < 0.0001) through to 48 months (p < 0.0001) whilst serum FSH (baseline: 24.28 ± 7.001) and LH (baseline: 12.46 ± 4.207) decreased significantly (p < 0.0001) throughout the 48 months of follow-up. On the other hand, the baseline serum testosterone was 2.069 ± 0.899 but reduced in 12 months (p = 0.001) and 36 months (p < 0.0001) whilst serum FSH (baseline: 23.30 ± 8.642) and LH (baseline: 11.21 ± 3.168) continued to increase (p < 0.0001) for the 48 months of follow-up in the observed group (Table 5).

For the one-way ANOVA statistics, serum FSH increased significantly (p < 0.05) in the observed group for every 12 months of follow-up through to the 48 months, but the group means did not vary statistically (F (4,125) = 0.7348, p = 0.5699; p-trend = 0.0949). However, after 48 months of follow-up, the serum FSH values were significantly lowered and the linear trend indicated a significant reduction (F (4,130) = 14.99, p < 0.0001; p-trend < 0.001) for each year among

participants who had the surgery. The serum lutropin (luteinizing hormones) generally showed a significant difference between the observed group and the varicocelectomy group. Luteinizing hormones (LH) significantly ($F(4,125) = 3.823$, $p = 0.0058$) increased in the observed group with the linear trend showing the rise (p-trend = 0.002) but decreased ($F(4,130) = 19.80$, $p < 0.0001$) in the operated group with a lowered linear trend ($p < 0.0001$). Furthermore, total testosterone increased significantly ($F(4,130) = 32.17$, $p < 0.0001$) in the operated group with a linear trend ($p < 0.0001$) depicting the increase but was moderately decreased in the observed group although this was not statistically significant (Table 5).

3.5. Comparison of Overall Percentage Change in Gonadal Function over 48 Months Follow-Up

As shown in Figure 4, the baseline serum total testosterone ($p = 6078$), serum FSH ($p = 6522$) and LH ($p = 6078$) did not vary significantly among the two groups (Figure 4(a)). However, a 76.3% increase in testosterone was observed in 12 months, 194.0% in 24 months, 221.0% in 36 months, and 231.9% increase in 48 months among participants who had surgery compared with a percentage reduction in the observed group. The percentage variations between these two groups were statistically significant (Figure 4(b)).

A significant ($p < 0.0001$) reduction in FSH was observed in the surgery group over the 48 months with the percentage change of 14.7% in 12 months, 29.9% in 24 months, 33.8% in 36 months, and 40.8% in 48 months. While a steady increase in FSH in the observed group with a percentage change of 8.6%, 13.2%, 18.1%, and 20.6% in the first year, second, third, and fourth-year respectively (Figure 4(c)).

Again, LH reduced significantly ($p < 0.0001$) in the surgery group with the change of 21.8% in 12 months, 31.0% in 24 months, 32.4% in 36 months, and 36.4% in 48 months. Whilst among the observed group, LH increased with a change from the baseline values of 8.6% in 12 months, 23.4% in 24 months, 30.2% in 36 months, and 39.8% in 48 months (Figure 4(d)).

3.6. Comparison of Annual Percentage Change in Gonadal Function over the 48 Months Follow-Up

A comparison of annual percentage change in the gonadal function between the two groups is shown in Figure 5. Among participants who had undergone varicocelectomy, serum total testosterone increased by 76.3% in the first year from the baseline, reduced to 69.7% in the second year, and 11.2% in the third year and further to 5.2% in the fourth year. While in the observed group, a decrease of 6.3% was observed in year one, an increase to 3.1% annually from the first year, then a decrease to 10.2% in the third year and finally increase to 0.3% in the fourth year. The annual variations in percentage change were statistically significant ($p < 0.05$) (Figure 5(a)).

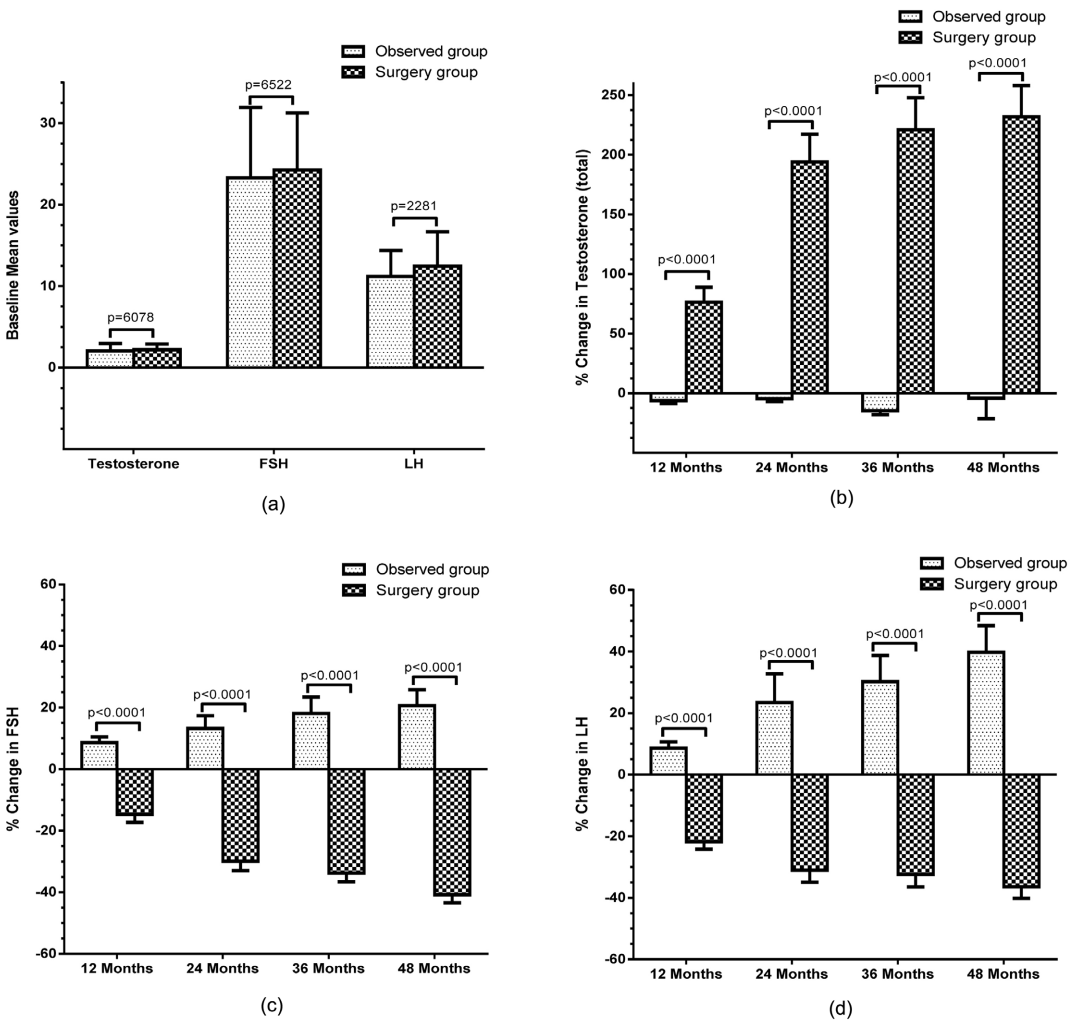

Figure 4. Comparison of overall percentage change in gonadal function between the observed group and operated group over 48 months. (a) = a graph of mean values of total testosterone, FSH, and LH between the two groups; (b) = a graph % change in Testosterone; (c) = a graph % change FSH; and (d) = a graph % change in LH. Data presented as group means (SEM). Significantly different between observed group and the surgery group at: *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.

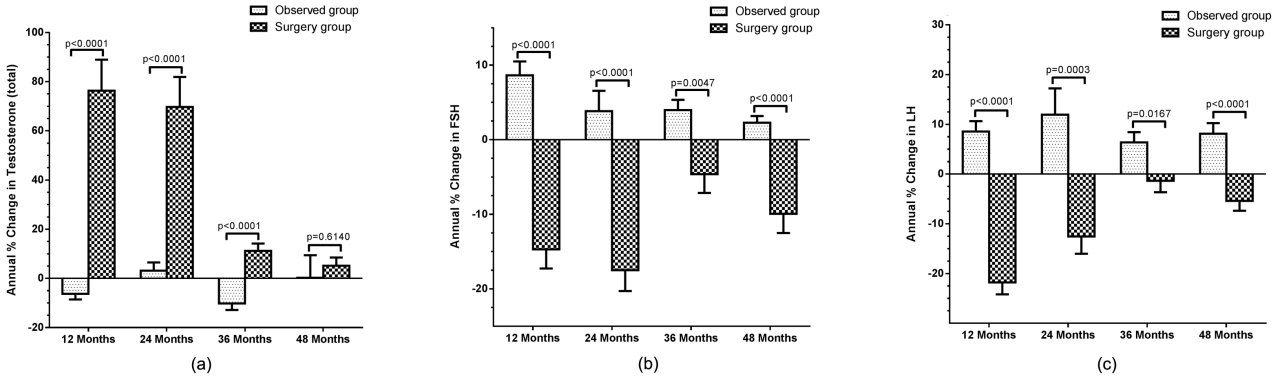

Figure 5. Comparison of annual percentage change in gonadal function between the observed group and operated group. (a) = a graph of Annual % change in Testosterone; (b) = a graph of Annual % change in FSH; (c) = a graph of Annual % change in LH respectively. Data presented as group means (SEM). Significantly different between observed group and surgery group at: *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.

As shown in Figure 5(b), serum FSH decreased by 14.7% in the first year from the baseline, decreased further by 17.5% in the second year, an annual decrease of 4.6% in the third year, and in the fourth year, a downward increase by 9.9% in the surgery group. In the observed group, a percentage change of 8.6 was observed in year one, 3.8% in year two, 4.0% in year three, and finally to 2.3% in year four (Figure 5(b)).

In the surgery group, serum LH had reduced significantly by 21.8% in the first year, and a year after, changed to 12.5%, further reduced by 1.3% in the third year, and finally to 5.4% in the fourth year. Whilst in the observed group, a percentage change of 8.6% in the first year was observed, then increase to 11.9% the following year, 6.4% in the third year, and further to 8.1% in the fourth year. For each year, the percentage change was statistically significant ($p < 0.05$) (Figure 5(c)).

In the surgery group, 5 patients recorded postoperative pain requiring strong opioids, 3 patients experienced severe pains that was not relieved by paracetamol after 24 hours, and 2 patients had postoperative erythema which was noticed on the 3rd and 4th day after the surgery (Table 6).

4. Discussion

Erectile dysfunction is commonly reported among mature and aging men [29] [30] with an estimated prevalence of 66% among the Ghanaian populace [31] and rates varying from 12% to 71% in other parts of the world [32] [33].

All enrolled participants in this study were clinically diagnosed [23] and confirmed with varicocele [26]. Earlier studies have reported extreme rarity of isolated right-sided varicocele with reported incidence rates between 2.5% to 6.5% depending on the diagnosis [34] [35]. From the results of this study, 94.0% of the respondents by laterality of varicocele were left-sided while the rest were bilateral, which finding is in consonance with reported rarity of isolated right-sided varicocele.

Baseline analysis of the data showed that all the men had sexual dysfunction based on the GRISS scale with subscale scores above 5 [21]. We observed improved erectile function among study participants who had undergone varicocelectomy 12 months post-operation. Prior to the surgeries, pre-operative hormonal concentrations were recorded which allowed a comparative analysis to post-operative hormonal concentrations to reveal improvements in testosterone

Table 6. Post-surgery complications.

Postoperative complications	Frequency (n)	Percent (%)
Postoperative pain	5	9.6
Severe postoperative pain that was not relieved by paracetamol.	3	5.8
Postoperative erythema	2	3.8

concentration among the surgery group. This finding suggests that induced Leydig cell dysfunction attributed to varicocele can be reversed by varicocelectomy which is consistent with reportedly improved erectile function post varicocelectomy by Sathya Srini and Belur Veerachari [19]. The observed improvement in total testosterone levels plays an important role in the male sexual characteristics controlling the timing of the erectile process as a function of sexual desire [36].

There is still a debate on the effect of varicocele on Leydig cell function and testosterone biosynthesis. Some researchers have reported no significant effect of varicocelectomy on testosterone levels [37] [38] with fewer studies reporting significant improvement in gonadal function following varicocelectomy [17] [19] [39]. Sathya Srini and Belur Veerachari [19] reported a significant rise in serum total testosterone from 1.77 ± 0.18 ng/mL pre-varicocelectomy to 3.01 ± 0.43 ng/mL 12 months after surgery and this was associated with insignificant reductions in serum FSH and LH. Su *et al.* [17] also found that serum total testosterone increased post microsurgical varicocelectomy but serum LH and FSH levels did not vary.

Sakamoto and Ogawa [9] reported an association between varicocele and relative testicular hypotrophy. Patients with severe varicocele showed lower testicular volume and increased FSH levels [12] and management of the varicocele reduced this negative effect [9]. A systematic review and meta-analysis of five studies including 312 patients by Tian *et al.* [13] showed that serum FSH levels (95% CI: 0.19 - 0.77; p = 0.001) and serum LH levels (95% CI: 0.25 - 0.91; p = 0.0005) were higher pre-varicocelectomy compared to post-varicocelectomy. In this study, serum FSH and serum LH decreased significantly after varicocelectomy among the surgery group over the 48 months of follow-up whilst no significant changes were recorded for respondents in the observed group. The observed percent decrease in FSH and LH could be attributed to negative feedback on the hypothalamus-pituitary-gonadal axis as a result of increased serum total testosterone stemming from improvements in Leydig cell function.

Few clinical studies have reported on the effects of varicoceles on serum testosterone and sexual dysfunction. Comhaire and Vermeulen [40] reported decreased testosterone levels and erectile dysfunction in 30% of men with varicoceles and both symptoms improved after varicocelectomy. In 2011, a study conducted by Tanrikut *et al.* [41] demonstrated that men with varicocele had lower serum total testosterone levels compared with controls, and about 79% of cases post-varicocelectomy reported with normal serum total testosterone levels. Cayan *et al.* [42] found that men with varicoceles exhibit decreased free testosterone levels and increased plasma FSH levels but after microsurgical varicocelectomy, the total plasma and free testosterone levels significantly increased and FSH level decreased which findings are consistent with what is reported in this study.

In a meta-analysis of seven studies involving 712 patients to compare pre-and post-surgical serum testosterone levels, Chen *et al.* [43] found that the mean

post-operative serum testosterone concentration improved by 34.3 ng/dL compared with pre-treatment concentrations representing an increase by 105.65 ng/dL in the hypogonadal men, favoring those who had undergone varicocele repair. After the microsurgical sub-inguinal varicocelectomy, sharp increases in serum total testosterone by 76.3% in the first year and subsequent, diminishing change by 69.7% in the second year, 11.2% in the third year, and 5.2% in the fourth year. Contrary to the observations for testosterone concentration, sharp decreases in serum FSH and LH (annual percentage change) was observed post-operatively. The possible explanation may be due to the fact that within the first two years of post-varicocele repair by microsurgical sub-inguinal varicocelectomy, serum testosterone concentration increases whilst serum FSH and LH reduce significantly. From the third year, variations in the annual percent changes in gonadotropin concentration will be marginal as a result of hormonal down regulation.

The following postoperative complications were observed in the surgery group: 1) Postoperative pain requiring strong opioids 5/52 (9.6%); After the surgery, all patients received paracetamol 1000 mg tid for 24 hours with the majority not experiencing pain. However, three patients experienced severe postoperative pain that was not relieved by paracetamol. They, therefore, were given IM Pethidine 50 mg tid to control the pain. 2) Postoperative erythema 2/52 (3.8%); a mild form of surgical site infection which was noticed on postoperative days 3 and 4. Wound swab for culture and sensitivity yielded negative cultures. The wound healed spontaneously without the need for antibiotics.

A major limitation of the study was drop-outs during follow-up, especially among the observed group due to the 48 months long (4 years) duration of follow-up. We recommend the use of microsurgical sub-inguinal varicocelectomy for similar categories of patients with further studies in large sample sizes to provide significant evidence for such therapy.

5. Conclusion

Long-standing varicocele may cause Leydig cell damage and this may be seen by causing a further decrease in total testosterone and a concomitant rise in follicle-stimulating hormone (FSH) and luteinizing hormone (LH). This study found that serum total testosterone, FSH, and LH observed spike changes within the first and second year in the surgery group but changes were marginal from the third year onwards. Microsurgical sub-inguinal varicocelectomy improved serum total testosterone, decrease both serum FSH and LH levels, and improve sexual dysfunction in patients reporting with varicocele.

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Authors' Contributions

This work was carried out in collaboration with all authors. Authors YA, AAA, and NA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors YA, SBB, VA, and PPMD carried out the sample collection and immunoassays. Authors YA, LQ, SBB, and PPMD managed the analysis of the study, and software and did the validation. Authors YA, AAA, PPMD, and LQ managed the literature searches. All authors read and approved the final manuscript.

Approval of the Research Protocol

This study was approved by the Ethics and Review Board of the Department of Research and Development, Tamale Teaching Hospital (No: TTH/R & D/SR/119).

Informed Consent

All patients provided written informed consent before the start of the study.

Data Availability

The data that support the findings of this study are available on request.

Conflicts of Interest

All authors declare no competing interests.

References

[1] Clavijo, R.I., Carrasquillo, R. and Ramasamy, R. (2017) Varicoceles: Prevalence and Pathogenesis in Adult Men. *Fertility and Sterility*, **108**, 364-369. https://doi.org/10.1016/j.fertnstert.2017.06.036

[2] Bertolotto, M., Freeman, S., Richenberg, J., Belfield, J., Dogra, V., Huang, D.Y., *et al.* (2020) Ultrasound Evaluation of Varicoceles: Systematic Literature Review and Rationale of the ESUR-SPIWG Guidelines and Recommendations. *Journal of Ultrasound*, **23**, 487-507. https://doi.org/10.1007/s40477-020-00509-z

[3] Paick, S. and Choi, W.S. (2019) Varicocele and Testicular Pain: A Review. *The World Journal of Men's Health*, **37**, 4-11. https://doi.org/10.5534/wjmh.170010

[4] Alsaikhan, B., Alrabeeah, K., Delouya, G. and Zini, A. (2016) Epidemiology of Varicocele. *Asian Journal of Andrology*, **18**, 179-181. https://doi.org/10.4103/1008-682X.172640

[5] Jarow, J.P., Coburn, M. and Sigman, M. (1996) Incidence of Varicoceles in Men with Primary and Secondary Infertility. *Urology*, **47**, 73-76. https://doi.org/10.1016/S0090-4295(99)80385-9

[6] Gorelick, J.I. and Goldstein, M. (1993) Loss of Fertility in Men with Varicocele. *Fertility and Sterility*, **59**, 613-616. https://doi.org/10.1016/S0015-0282(16)55809-9

[7] Lipshultz, L.I. and Corriere Jr., J.N. (1977) Progressive Testicular Atrophy in the Varicocele Patient. *The Journal of Urology*, **117**, 175-176. https://doi.org/10.1016/S0022-5347(17)58387-1

[8] Russell, J. (1957) Varicocele, Age, and Fertility. *The Lancet*, **270**, 222. https://doi.org/10.1016/S0140-6736(57)91599-4

[9] Sakamoto, H. and Ogawa, Y. (2009) Does a Clinical Varicocele Influence the Relationship between Testicular Volume by Ultrasound and Testicular Function in Patients with Infertility? *Fertility and Sterility*, **92**, 1632-1637. https://doi.org/10.1016/j.fertnstert.2008.08.105

[10] Agarwal, A., Sharma, R., Harlev, A. and Esteves, S.C. (2016) Effect of Varicocele on Semen Characteristics According to the New 2010 World Health Organization Criteria: A Systematic Review and Meta-Analysis. *Asian Journal of Andrology*, **18**, 163-170. https://doi.org/10.4103/1008-682X.172638

[11] Lü, Y.Q. and Chen, B. (2008) Progress in Researches on the Mechanism of Varicocele-Induced Male Infertility. *National Journal of Andrology*, **14**, 454-458.

[12] Lotti, F., Corona, G., Mancini, M., Biagini, C., Colpi, G.M., Degli Innocenti, S., *et al.* (2009) The Association between Varicocele, Premature Ejaculation and Prostatitis Symptoms: Possible Mechanisms. *The Journal of Sexual Medicine*, **6**, 2878-2887. https://doi.org/10.1111/j.1743-6109.2009.01417.x

[13] Tian, D., Huang, W., Yan, H., Zong, H. and Zhang, Y. (2018) Effect of Varicocelectomy on Serum FSH and LH Levels for Patients with Varicocele: A Systematic Review and Meta-Analysis. *Indian Journal of Surgery*, **80**, 233-238. https://doi.org/10.1007/s12262-016-1571-1

[14] Tiseo, B.C., Esteves, S.C. and Cocuzza, M.S. (2016) Summary Evidence on the Effects of Varicocele Treatment to Improve Natural Fertility in Subfertile Men. *Asian Journal of Andrology*, **18**, 239-245. https://doi.org/10.4103/1008-682X.172639

[15] Li, F., Yue, H., Yamaguchi, K., Okada, K., Matsushita, K., Ando, M., *et al.* (2012) Effect of Surgical Repair on Testosterone Production in Infertile Men with Varicocele: A Meta-Analysis. *International Journal of Urology*, **19**, 149-154. https://doi.org/10.1111/j.1442-2042.2011.02890.x

[16] Çayan, S., Akbay, E., Saylam, B. and Kadıoğlu, A. (2020) Effect of Varicocele and Its Treatment on Testosterone in Hypogonadal Men with Varicocele: Review of the Literature. *Balkan Medical Journal*, **37**, 121-124. https://doi.org/10.4274/balkanmedj.galenos.2020.2020.1.85

[17] Su, L.M., Goldstein, M. and Schlegel, P.N. (1995) The Effect of Varicocelectomy on Serum Testosterone Levels in Infertile Men with Varicoceles. *The Journal of Urology*, **154**, 1752-1755. https://doi.org/10.1097/00005392-199511000-00047

[18] Salem, H. and Mostafa, T. (2009) Preserved Testicular Artery at Varicocele Repair. *Andrologia*, **41**, 241-245. https://doi.org/10.1111/j.1439-0272.2009.00926.x

[19] Sathya Srini, V. and Belur Veerachari, S. (2011) Does Varicocelectomy Improve Gonadal Function in Men with Hypogonadism and Infertility? Analysis of a Prospective Study. *International Journal of Endocrinology*, **2011**, Article ID: 916380. https://doi.org/10.1155/2011/916380

[20] Abdel-Meguid, T.A., Al-Sayyad, A., Tayib, A. and Farsi, H.M. (2011) Does Varicocele Repair Improve Male Infertility? An Evidence-Based Perspective from a Randomized, Controlled Trial. *European Urology*, **59**, 455-461. https://doi.org/10.1016/j.eururo.2010.12.008

[21] Rust, J. and Golombok, S. (1985) The Golombok-Rust Inventory of Sexual Satisfaction (GRISS). *British Journal of Clinical Psychology*, **24**, 63-64. https://doi.org/10.1111/j.2044-8260.1985.tb01314.x

[22] Adams, Y., Afoko, A.A. and Amidu, N. (2022) Effect of Varicocelectomy on Semen Parameters of Men Seeking Infertility Treatment in Tamale, Ghana. *Open Journal of Urology*, **12**, 7-26. https://doi.org/10.4236/oju.2022.121002

[23] Dubin, L. and Amelar, R.D. (1970) Varicocele Size and Results of Varicocelectomy

in Selected Subfertile Men with Varicocele. *Fertility and Sterility*, **21**, 606-609.

[24] WHO (1992) The Influence of Varicocele on Parameters of Fertility in a Large Group of Men Presenting to Infertility Clinics. *Fertility and Sterility*, **57**, 1289-1293. https://doi.org/10.1016/S0015-0282(16)55089-4

[25] Marsman, J. and Schats, R. (1994) The Subclinical Varicocele Debate. *Human Reproduction*, **9**, 1-8. https://doi.org/10.1093/oxfordjournals.humrep.a138294

[26] Hussein, A.F. (2006) The Role of Color Doppler Ultrasound in Prediction of the Outcome of Microsurgical Subinguinal Varicocelectomy. *The Journal of Urology*, **176**, 2141-2145. https://doi.org/10.1016/j.juro.2006.07.009

[27] Mittal, B.V. and Singh, A.K. (2010) Hypertension in the Developing World: Challenges and Opportunities. *American Journal of Kidney Diseases*, **55**, 590-598. https://doi.org/10.1053/j.ajkd.2009.06.044

[28] Marmar, J.L., DeBenedictis, T.J. and Praiss, D. (1985) The Management of Varicoceles by Microdissection of the Spermatic Cord at the External Inguinal Ring. *Fertility and Sterility*, **43**, 583-588. https://doi.org/10.1016/S0015-0282(16)48501-8

[29] Ayta, I., McKinlay, J. and Krane, R. (1999) The Likely Worldwide Increase in Erectile Dysfunction between 1995 and 2025 and Some Possible Policy Consequences. *BJU International*, **84**, 50-56. https://doi.org/10.1046/j.1464-410x.1999.00142.x

[30] Feldman, H.A., Goldstein, I., Hatzichristou, D.G., Krane, R.J. and McKinlay, J.B. (1994) Impotence and Its Medical and Psychosocial Correlates: Results of the Massachusetts Male Aging Study. *The Journal of Urology*, **151**, 54-61. https://doi.org/10.1016/S0022-5347(17)34871-1

[31] Amidu, N., Owiredu, W.K., Woode, E., Addai-Mensah, O., Gyasi-Sarpong, K. and Alhassan, A. (2010) Prevalence of Male Sexual Dysfunction among Ghanaian Populace: Myth or Reality? *International Journal of Impotence Research*, **22**, 337-342. https://doi.org/10.1038/ijir.2010.24

[32] Lyngdorf, P. and Hemmingsen, L. (2004) Epidemiology of Erectile Dysfunction and Its Risk Factors: A Practice-Based Study in Denmark. *International Journal of Impotence Research*, **16**, 105-111. https://doi.org/10.1038/sj.ijir.3901184

[33] Braun, M., Wassmer, G., Klotz, T., Reifenrath, B., Mathers, M. and Engelmann, U. (2000) Epidemiology of Erectile Dysfunction: Results of the 'Cologne Male Survey'. *International Journal of Impotence Research*, **12**, 305-311. https://doi.org/10.1038/sj.ijir.3900622

[34] Matsuda, T. (1993) Varicocelectomy. *The Japanese Journal of Urology*, **84**, 797-813. https://doi.org/10.5980/jpnjurol1989.84.797

[35] Onozawa, M., Endo, F., Suetomi, T., Takeshima, H. and Akaza, H. (2002) Clinical Study of Varicocele: Statistical Analysis and the Results of Long-Term Follow-Up. *International Journal of Urology*, **9**, 455-461. https://doi.org/10.1046/j.1442-2042.2002.00501.x

[36] Corona, G. and Maggi, M. (2010) The Role of Testosterone in Erectile Dysfunction. *Nature Reviews Urology*, **7**, 46-56. https://doi.org/10.1038/nrurol.2009.235

[37] Segenreich, E., Shmuely, H., Singer, R. and Servadio, C. (1986) Andrological Parameters in Patients with Varicocele and Fertility Disorders Treated by High Ligation of the Left Spermatic Vein. *International Journal of Fertility*, **31**, 200-203.

[38] Pasqualotto, F.F., Sundaram, A., Sharma, R.K., Borges Jr., E., Pasqualotto, E.B. and Agarwal, A. (2008) Semen Quality and Oxidative Stress Scores in Fertile and Infertile Patients with Varicocele. *Fertility and Sterility*, **89**, 602-607. https://doi.org/10.1016/j.fertnstert.2007.03.057

[39] Hurtado de Catalfo, G.E., Ranieri-Casilla, A., Marra, F.A., De Alaniz, M.J. and Marra, C.A. (2007) Oxidative Stress Biomarkers and Hormonal Profile in Human Patients Undergoing Varicocelectomy. *International Journal of Andrology*, **30**, 519-530. https://doi.org/10.1111/j.1365-2605.2007.00753.x

[40] Comhaire, F. and Vermeulen, A. (1975) Plasma Testosterone in Patients with Varicocele and Sexual Inadequacy. *The Journal of Clinical Endocrinology & Metabolism*, **40**, 824-829. https://doi.org/10.1210/jcem-40-5-824

[41] Tanrikut, C., Goldstein, M., Rosoff, J.S., Lee, R.K., Nelson, C.J. and Mulhall, J.P. (2011) Varicocele as a Risk Factor for Androgen Deficiency and Effect of Repair. *BJU International*, **108**, 1480-1484. https://doi.org/10.1111/j.1464-410X.2010.10030.x

[42] Cayan, S., Kadioglu, A., Orhan, I., Kandirali, E., Tefekli, A. and Tellaloglu, S. (1999) The Effect of Microsurgical Varicocelectomy on Serum Follicle Stimulating Hormone, Testosterone and Free Testosterone Levels in Infertile Men with Varicocele. *BJU International*, **84**, 1046-1049. https://doi.org/10.1046/j.1464-410x.1999.00353.x

[43] Chen, X., Yang, D., Lin, G., Bao, J., Wang, J. and Tan, W. (2017) Efficacy of Varicocelectomy in the Treatment of Hypogonadism in Subfertile Males with Clinical Varicocele: A Meta-Analysis. *Andrologia*, **49**, e12778. https://doi.org/10.1111/and.12778

Appendix

QUESTIONNAIRE adopted from Adams *et al.* [22]

To be completed by each subject participating in the study

Tel.: ……..... Code: ……..

Please tick [√] the appropriate box where applicable

Pre-assessment check for exclusion in the study

1) *Are you a known hypertensive patient*? [ ] *Yes* [ ] *No*

2) *Are you a known diabetic patient*? [ ] *Yes* [ ] *No*

3) *Have you ever been diagnosed of tuberculosis*? [ ] *Yes* [ ] *No*

4) *Do you have past history of any of this; mumps orchitis, undescended testis, or orchidectomy*? [ ] *Yes* [ ] *No*

5) *Are you on/or ever been administered with anti-estrogen and/or testosterone replacement therapy*? [ ] *Yes* [ ] *No*

Sociodemographic characteristics of study participants

1) Age: ……

2) Sex: [ ] male [ ] female

3) Marital status [ ] single [ ] married [ ] divorced [ ] widowed

4) Highest Education level [ ] none [ ] primary [ ] secondary [ ] tertiary

5) Occupation: [ ] unemployed [ ] trader/self-employed [ ] gainful employed

6) Ethnicity: [ ] Mole-Dagomba [ ] other ethnic

Lifestyle

7) Do you consume alcoholic beverages? [ ] yes [ ] no

If yes to question 6, how many alcoholic beverages do you consume on an average per day? [ ] 1 bottle [ ] 2 - 3 bottles [ ] >3 bottles

8) Do you smoke cigarette? [ ] yes [ ] no

If yes, [ ] 1 pack/day [ ] 2 pack/day [ ] >2 pack/day

9) Number of sexual partners? [ ] one [ ] two [ ] three [ ] four [ ] more than four

Anthropometric measurement

10) Height (cm): i.……ii.……average (i & ii)…….

11) Weight (kg): i.……ii.……average (i & ii)…….

12) BMI (kg/m^2): i.……ii.……average (i & ii)…….

13) body fat (%): i.……ii.……average (i & ii)…….

14) Muscle mass (%): i.……ii.……average (i & ii)…….

15) Visceral fat: i.……ii.……average (i & ii)…….

Blood pressure measurement

16) SBP (mmHg): i.……ii.……average (i & ii)…….

17) DBP (mmHg): i.……ii.……average (i & ii)…….

18) Pulse (beat/minutes): i.……ii.……average (i & ii)…….

Brief Medical history

19) How long have you and partner been trying to conceive with unprotected sexual intercourse?

Months: …….. Years: ……

20) Have you ever had a pregnancy with your current partner? [ ] Yes [ ] No

If yes to question 10, how many pregnancies? ……

How many did your partner successfully give birth to? …...

21) Have you ever had a pregnancy with another partner? [ ] Yes [ ] No

If yes to question 11, how many pregnancies? ……

How many did your partner successfully give birth to? …...

22) If you have children, how many are boy ……

And how many are girls? ……..

23) Has your current partner ever been pregnant with another partner? [ ] Yes [ ] No

If yes to question 13,

How many pregnancies? ……

How many did your partner successfully give birth to? …...

24) Have you had any problems with erection? [ ] Yes [ ] No

25) How often do you have sex with your partner?

per/day ……. per/week ……. per/month …….

26) Have you ever been treated for a sexually transmitted infection? [ ] Yes [ ] No

If yes, what infection? ……..…… when?.....

27) Did you ever have a surgery where your testes' was brought into the scrotum when you were a child? [ ] Yes [ ] No

If so, did it affect your testes? ……..... which sides(s)? …….

28) Did you ever have a surgery of your testes? [ ] Yes [ ] No

If so, did it affect your testes? …….. which side(s)? …….

Post-surgery questions (Please tick [√] the appropriate box where applicable)

29) Have you had any problems with erection post-surgery? [ ] Yes [ ] No

30) Have you started having sexual intercourse with your partner? [ ] Yes [ ] No

31) How often do you have sex with your partner?

per/day …….. per/week ……..per/month ……..

32) Do you use lubricant(s) during sexual activity? [ ] Yes [ ] No

If so, what type/brand? ……..

33) Are you currently taking any medications on a regular basis? [ ] Yes [ ] No

If so, what medication? ……..

34) Has your current partner complained of not seeing her menses (monthly period)? [ ] Yes [ ] No

If so, when? ……..

35) Is your partner pregnant? [ ] Yes [ ] No

If so, when did she disclose this information to you? ……..

36) Any other complication(s) after your surgery? ……

MALE (GRISS-M) QUESTIONAIRE adopted from Rust, J. and S. Golombok [21]

Instructions: Each question is followed by a series of possible answers:

N—NEVER
H—HARDLY EVER
O—OCCASIONALLY
U—USUALLY
A—ALWAYS

Read each question carefully and decide which answer best describes the way things have been for you recently; then circle the corresponding letter.

Please answer every question.

If you are not completely sure which answer is most appropriate, circle the answer which you feel is most appropriate.

Please answer this questionnaire without discussing any of the questions with your partner. In order for us to obtain valid information it is important for you to answer each question as honestly and as accurately.

1	Do you have sexual intercourse more than twice a week?	N	H	O	U	A
2	Do you find it hard to tell your partner what you like and dislike about your sexual relationship?	N	H	O	U	A
3	Do you become easily sexually aroused?	N	H	O	U	A
4	Are you able to delay ejaculation during intercourse if you think you may be "coming" too quickly	N	H	O	U	A
5	Are you dissatisfied with the amount of variety in your sex life with your partner?	N	H	O	U	A
6	Do you dislike stroking and caressing your partner's genitals?	N	H	O	U	A
7	Do you become tense and anxious when your partner wants to have sex?	N	H	O	U	A
8	Do you enjoy having sexual intercourse with your partner?	N	H	O	U	A
9	Do you ask your partner what she likes and dislikes about your sexual relationship?	N	H	O	U	A
10	Do you fail to get an erection?	N	H	O	U	A
11	Do you feel there is a lack of love and affection in your sexual relationship with your partner?	N	H	O	U	A
12	Do you enjoy having your penis stroked and caressed by your partner?	N	H	O	U	A
13	Can you avoid ejaculating too quickly during intercourse?	N	H	O	U	A
14	Do you try to avoid having sex with your partner?	N	H	O	U	A
15	Do you find your sexual relationship with your partner satisfactory?	N	H	O	U	A
16	Do you get an erection during foreplay with your partner?	N	H	O	U	A
17	Are there weeks in which you don't have sex at all?	N	H	O	U	A

Continued

18	Do you enjoy mutual masturbation with your partner?	N	H	O	U	A
19	If you want sex with your partner, do you take the initiative?	N	H	O	U	A
20	Do you dislike being cuddled and caressed by your partner?	N	H	O	U	A
21	Do you have sexual intercourse as often as you would like?	N	H	O	U	A
22	Do you refuse to have sex with your partner?	N	H	O	U	A
23	Do you lose your erection during intercourse?	N	H	O	U	A
24	Do you ejaculate without wanting to almost as soon as your penis enters your partner's vagina?	N	H	O	U	A
25	Do you enjoy cuddling and caressing your partner's body?	N	H	O	U	A
26	Do you feel uninterested in sex?	N	H	O	U	A
27	Do you ejaculate by accident just before your penis is about to enter your partner's vagina?	N	H	O	U	A
28	Do you have feelings of disgust about what you and your partner do during lovemaking?	N	H	O	U	A

Abbreviations and Acronyms

ANOVA = Analysis Of Variance
BMI = Body Mass Index
DBP = Diastolic Blood Pressure
FSH = Follicle-Stimulating Hormone
GRISS = Golombok Rust Inventory of Sexual Satisfaction
LH = Luteinizing Hormone
RCT = Randomize Control Trials
SBP = Systolic Blood Pressure
SUE = Scrotal Ultrasound Evaluation
TTH = Tamale Teaching Hospital
WHO = World Health Organization