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ORIGINAL CONTRIBUTIONS

Changes in Sex Hormones After Laparoscopic Sleeve Gastrectomy in Chinese Obese Men: a 12-Month Follow-Up

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Abstract

Background To examine changes in sex hormones after laparoscopic sleeve gastrectomy (LSG) in Chinese obese male patients and their correlation with metabolic parameters including serum uric acid (SUA)

Methods A total of 56 obese men with body mass index (BMI) 41.9 ± 5.8 kg/m^2 undergoing LSG were selected. Thirty-one healthy men with normal BMI were included as controls. Levels of total testosterone (TT), estradiol (E2), sex hormone-binding globulin (SHBG), follicle-stimulating hormone (FSH), luteinizing hormone (LH), SUA, and other metabolic indices were compared pre- and 12 months post-LSG. Calculated free testosterone (cFT) was calculated from TT and SHBG using an empirical equation.

Results At baseline, low TT and hyperuricemia (HUA) were common in obese men. Twelve months after LSG, statistically significant reduction in weight, BMI, and glucolipid metabolism indices was noted. SUA levels declined remarkably from 474.9 ± 94.6 to 338.8 ± 81.9 μmol/L and the percentage of HUA decreased from 76.8 to 54.1% (all $P < 0.001$). Additionally, significant increases in TT, SHBG, and cFT as well as a decrease in percentage of low TT were observed after LSG (all $P < 0.05$), while E2, FSH, and LH did not change significantly. Moreover, changes in TT levels were more pronounced than those of other sex hormones. After age and BMI were adjusted, increased TT levels were correlated significantly with decreased SUA ($\beta = -1.077$, $P < 0.05$), BMI ($\beta = -0.712$, $P < 0.001$), and HOMA-IR ($\beta = -0.652$, $P < 0.05$), as well as increased SHBG ($\beta = 0.759$, $P < 0.001$).

Conclusions LSG promotes a significant increase in TT levels in Chinese obese men, which may be mediated by substantial weight loss, SUA reduction, and improved insulin resistance (IR).

Keywords Obesity · Laparoscopic sleeve gastrectomy · Uric acid · Total testosterone · Sex hormone-binding globulin

Introduction

Obesity has reached a global epidemic [1], which is associated with numerous comorbidities, including type 2 diabetes mellitus (T2DM), hypertension, insulin resistance (IR), and cardiovascular diseases. Male hypogonadism has been documented in obesity [2]. It can be noted in 33% of obese men referred to obesity therapies and in more than 50% of individuals with superobesity [3]. Recent studies have demonstrated hypogonadism may occur in men with metabolic disorders [4, 5]. Low testosterone levels have been documented in patients with metabolic syndrome (MetS) [6]. Also, the relationship between hypogonadism and IR has been revealed [7]. The underlying mechanism may be states of hyperinsulinemia, which causes a decline of testosterone production [8].

Uric acid is the metabolic end product of purine metabolism. Increased serum uric acid (SUA) has been associated

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with a variety of metabolic diseases, such as T2DM, hypertension, and lipid disorders, as well as cardiovascular diseases [9–11]. Epidemiological studies have shown that hyperuricemia (HUA) is more common in males than in females and the association of uric acid and sex hormones has been demonstrated. Cao et al. [12] and Hurina et al. [13] have revealed a significant negative correlation of SUA and total testosterone (TT) level among male patients with T2DM, demonstrating that SUA levels may be risk factors for male hypogonadism. These findings suggest that HUA and hypogonadism are common in obese men and there is an association between SUA and TT. Thus, it is reasonable to assume that effective treatment of obesity may reduce those risk factors.

Currently, bariatric surgery has become the most effective treatment option for patients with severe obesity based on substantial and durable weight reduction and metabolic improvement in obesity-related comorbidities, such as T2DM, hypertension, and hyperlipidemia [14, 15]. Recently, bariatric surgery has been reported to reverse testosterone levels and hypogonadism in obese male patients [16–18]. Also, recent studies have revealed significant reduction in SUA levels and prevalence of HUA after bariatric surgery [19, 20]. Another prospective longitudinal study of 154 obese patients demonstrated an 18% reduction of SUA levels in patients with HUA, compared with a 10% reduction in the entire obese population [21]. Laparoscopic sleeve gastrectomy (LSG) as a successful and safe bariatric procedure is associated with an improvement in both parameters [18, 22].

However, data evaluating changes in sex hormones after LSG in Chinese obese male patients and their correlation with related metabolic parameters especially SUA remain limited. Therefore, we aimed to investigate the changes of sex hormones after LSG in obese men and to examine their correlations with related metabolic parameters and SUA over a 12-month period following this procedure in Chinese obese male patients.

Materials and Methods

Participants

A total of 56 male obese patients aged 30.8 ± 7.8 years who underwent the standard LSG at the Department of Gastrointestinal Surgery in Shanghai Tenth People's Hospital of Tongji University were enrolled in this study from June 2012 to March 2018. Thirty-one healthy men with normal BMI (average BMI 23.1 ± 1.6 kg/m^2) were included as controls. The inclusion criteria were as follows: obesity was defined as patients with BMI ≥ 28 kg/m^2 according to the guidelines of prevention and control of overweight and obesity in Chinese adults [23], and age ranged from 18 to 65 years old. They were often accompanied by two or more obesity-related comorbidities such as T2DM, hypertension, hypertriglyceridemia, or non-alcoholic fatty liver disease. Exclusion criteria were as follows: a history of any malignant tumor, genetic disease, hypogonadism, renal dysfunction, severe liver dysfunction (aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels more than 2.5 times the normal value), preexisting heart disease, any use of current or previous testosterone products or treatment for hypogonadism, any medical treatment for diabetes, any UA-lowering therapy for HUA, and inability to understand and comply with the study protocol. Prior to surgery, most of the patients were likely to consume meats, seafood, alcohol (even beer), fructose-rich foods, or animal protein which have been known to increase the risk of HUA and gout. After surgery, all the patients were instructed by a licensed nutritionist to consume a liquid diet with vegetable protein at the first week and soft solid vegetable food for the next 3 weeks, followed by a low-purine diet (LPD), which consisted of soy protein and eggs to replace animal proteins as well as avoided meats, seafood, alcohol, and fructose-rich foods. Such diet choices are based on the guideline for the management of gout [24].

Written informed consent was obtained from each of the participants according to the Declaration of Helsinki prior to enrolment, and the study protocol was approved by the hospital ethnics committee. The Clinical Registration Number is ChiCTR-OCS-12002381.

Measurements

Anthropometric Measurements

All the anthropometric parameters were measured prior to the operation and during the follow-up visits. Height, weight, waist circumference (WC), hip circumference (HC), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were directly measured by trained physicians. BMI was calculated as weight in kilograms divided by height in meters squared. Waist/hip ratio (WHR) was calculated as WC in centimeters divided by HC in centimeters. Percentage of total weight loss (%TWL), the most appropriate value for expressing weight loss [25], was calculated using the formula %TWL = [(initial weight − current weight)/(initial weight)] × 100.

Clinical Biochemical Measurements

General biochemical data including glucose, lipid profiles, and SUA as well as sex hormones were measured at baseline and during the follow-up period. Morning venous blood was drawn from the study participants after a 12-h overnight fast before and after surgery. Blood samples were taken and the following parameters were measured: fasting plasma glucose (FPG), fasting insulin (FINS), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and SUA. Sex hormones including serum total testosterone (TT), sex hormone-binding globulin (SHBG), estradiol (E2), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were measured by electro-chemiluminescent immunoassay. Calculated free testosterone (cFT) was calculated from TT and SHBG using an empirical equation described by Sartorius et al. [26]. All the laboratory measurements were conducted in our department using standard methodologies.

IR was calculated using HOMA-IR as described by Matthews et al. [27]: FPG (mmol/L) × FINS (mU/L)/22.5. HUA was defined as SUA ≥ 420 μmol/L for obese men according to the guideline of HUA [28]. The low TT concentration was defined as TT < 10.5 nmol/L [29].

Statistical Analysis

All statistical analyses were performed using SPSS 20.0 software. Continuous variables were expressed as means ± standard deviation (SD) or percentages for categorical variables. Non-normally distributed data were logarithmically transformed to normality, when needed. Differences between groups were tested for significance using independent Student's *t* test for normal distributions or non-parametric test for non-normal distributions. Paired-sample *t* test was used to compare the data before and after surgery. Differences between groups regarding categorical variables were evaluated using chi-squared test. Pearson's correlation analysis was used to investigate the relationship of two indices. Multivariate linear regression analyses were used to assess the statistical associations of variation in SUA and changes in sex hormones and related metabolic parameters before and after surgery. All reported *P* values are two-sided and considered statistically significant at < 0.05.

Results

Baseline Clinical Characteristics and Changes in Metabolic Parameters of Study Participants

Fifty-six obese male patients with average BMI 41.9 ± 5.8 kg/m^2 and 31 healthy males with average BMI 23.1 ± 1.6 kg/m^2 were enrolled in this study. Baseline clinical characteristics of the study population are presented in Fig. 1. At baseline, obese men had significantly higher SUA levels (474.9 ± 94.6 μmol/L vs. 341.1 ± 81.6 μmol/L, $P < 0.001$) and prevalence of HUA (76.8% vs. 16.1%, $P < 0.001$) in comparison to the control group. Hormonal analysis showed remarkably lower TT levels and higher incidence of low TT in obese men than in the control group (7.9 ± 4.2 nmol/L vs. 18.0 ± 4.9 nmol/L, $P < 0.001$; 80.3% vs. 13.3%, $P < 0.001$) while no significant differences were observed in E2, FSH, and LH levels between the two groups. Twelve months after surgery, participants' weight, BMI, WC, HC, WHR, SBP, and DBP decreased significantly (all $P < 0.01$). The %TWL reached 30.9 ± 6.1% over a 1-year period. We detected a significant improvement in glucose metabolism and insulin sensitivity, as evidenced by significant reductions in FPG, FINS, and HOMA-IR after LSG ($P < 0.05$, $P < 0.001$, $P < 0.001$, respectively). In terms of lipid profiles, we also observed a significant reduction in TC, TG, and LDL-C and an increase in HDL-C levels at 12 months post-LSG (all $P < 0.05$) (shown in Table 1).

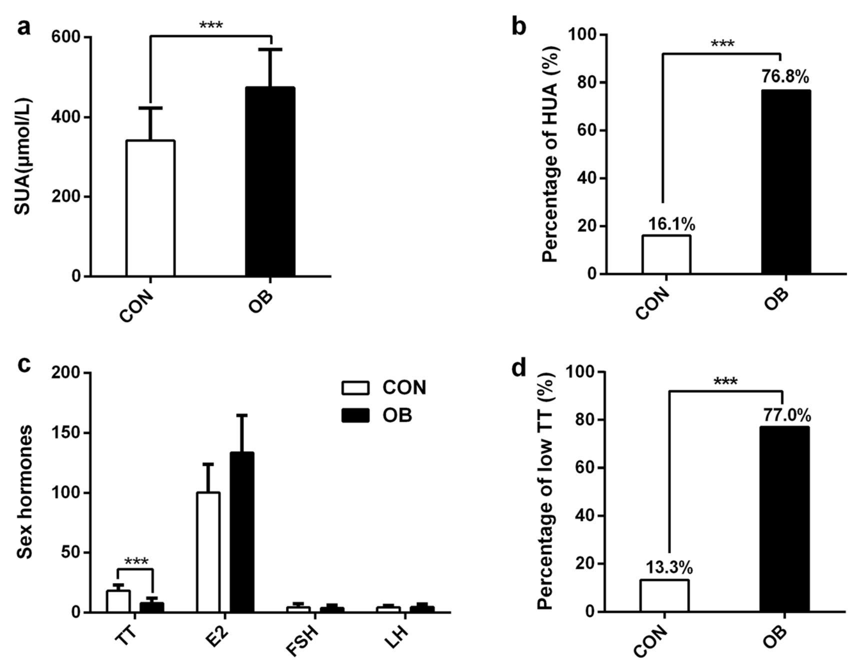

Fig. 1 Comparison of SUA levels, percentage of HUA, and sex hormones between OB and CON groups. **a**, **b** The OB group had significantly higher SUA levels and percentage of HUA compared to the CON group. **c**, **d** The OB group had significantly lower TT levels and higher percentage of low TT compared to the CON group, while no significant differences were observed in E2, FSH, and LH between the two groups. *OB* obesity group, *CON* healthy control group, *SUA* serum uric acid, *HUA* hyperuricemia, *TT* total testosterone, *E2* estradiol, *FSH* follicle-stimulating hormone, *LH* luteinizing hormone. OB group vs CON group: three asterisks, $P < 0.001$

Table 1 Anthropometric measurements and metabolism variables at baseline and 12 months after LSG

Parameters	Baseline	12 months after LSG	*P* value
Age (years)	30.8 ± 7.8	/	/
Weight loss			
Weight (kg)	129.4 ± 18.2	89.5 ± 15.6	< 0.001
BMI (kg/m^2)	41.9 ± 5.8	26.1 ± 4.3	< 0.001
WC (cm)	127.8 ± 9.9	97.7 ± 10.2	< 0.001
HC (cm)	125.9 ± 10.0	103.6 ± 8.5	< 0.001
WHR	1.0 ± 0.1	0.9 ± 0.0	< 0.001
%TWL	–	30.9 ± 6.1	–
SBP (mmHg)	137 ± 16	124 ± 12	< 0.001
DBP (mmHg)	85 ± 10	76 ± 11	0.004
Glucose metabolism			
FPG (mmol/L)	6.5 ± 2.7	4.6 ± 0.7	0.003
Ln FINS (mU/L)	3.7 ± 0.6	2.0 ± 0.7	< 0.001
Ln HOMA-IR	2.4 ± 0.8	0.9 ± 0.8	< 0.001
Lipid metabolism			
TC (mmol/L)	4.7 ± 1.4	4.2 ± 1.0	0.034
TG (mmol/L)	1.7 ± 0.7	0.9 ± 0.3	< 0.001
HDL-C (mmol/L)	0.9 ± 0.2	1.3 ± 0.4	< 0.001
LDL-C (mmol/L)	3.1 ± 1.1	2.6 ± 0.8	0.008

Data are expressed as means ± SD. Non-normally distributed data were log-transformed before analysis. Compared with baseline values using paired 聂 test. $P < 0.05$ was considered to be statistically significant

/ There was no significant change in patients' age before and 12 months after LSG

Abbreviations: *LSG* laparoscopic sleeve gastrectomy, *BMI* body mass index, *WC* waist circumference, *HC* hip circumference, *WHR* waist/hip ratio, *%TWL* percentage of total weight loss, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *FPG* fasting plasma glucose, *FINS* fasting insulin, *HOMA-IR* homeostasis model assessment of insulin resistance, *TC* total cholesterol, *TG* triglyceride, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol

Changes in SUA and Sex Hormone Levels After LSG

Twelve months after surgery, we observed remarkable improvement in SUA and hormonal imbalance. As shown in Fig. 2, SUA levels declined significantly from 474.9 ± 94.6 μmol/L to 338.8 ± 81.9 μmol/L and the percentage of HUA decreased significantly from 76.8% to 54.1% at 12 months postsurgery from baseline ($P < 0.001$, $P < 0.001$, respectively) (Fig. 2a, b). As presented in Fig. 3, there was a significant increase in TT, SHBG, and cFT levels after LSG, changing from 7.9 ± 4.2 nmol/L to 17.4 ± 4.6 nmol/L ($P < 0.001$), from 13.2 ± 3.9 nmol/L to 28.8 ± 8.3 nmol/L ($P < 0.01$), and from 145.6 ± 42.0 nmol/L to 216.8 ± 65.9 nmol/L ($P < 0.05$) at 12 months after surgery from baseline values, while E2, FSH, and LH failed to reach a statistical significance (Fig. 3a). The percentage of low TT significantly decreased after LSG, changing from 77.0% at baseline to 8.7% at 12 months after surgery (Fig. 3b). In addition, the TT levels increased by 401% after surgery, which was more than 148% in SHBG, 116% in cFT, 14% in E2, 13% in FSH, and 11% in LH (Fig. 3c).

Relationship Between SUA Reduction and Sex Hormone Changes After LSG

As shown in Fig. 4, changes (Δ) in SUA at 12 months after surgery were found to be positively correlated with ΔBMI ($r = 0.457$, $P < 0.05$), FINS ($r = 0.625$, $P < 0.05$), and HOMA-IR ($r = 0.589$, $P < 0.05$), as well as negatively correlated with ΔTT ($r = -0.578$, $P < 0.05$), ΔSHBG ($r = -0.823$, $P < 0.001$), and ΔcFT ($P = -0.870$, $P < 0.001$), whereas no significant association was observed between ΔSUA and ΔE2, ΔFSH, and ΔLH (all $P > 0.05$). In order to examine the major contributing factors in the reduction of SUA after

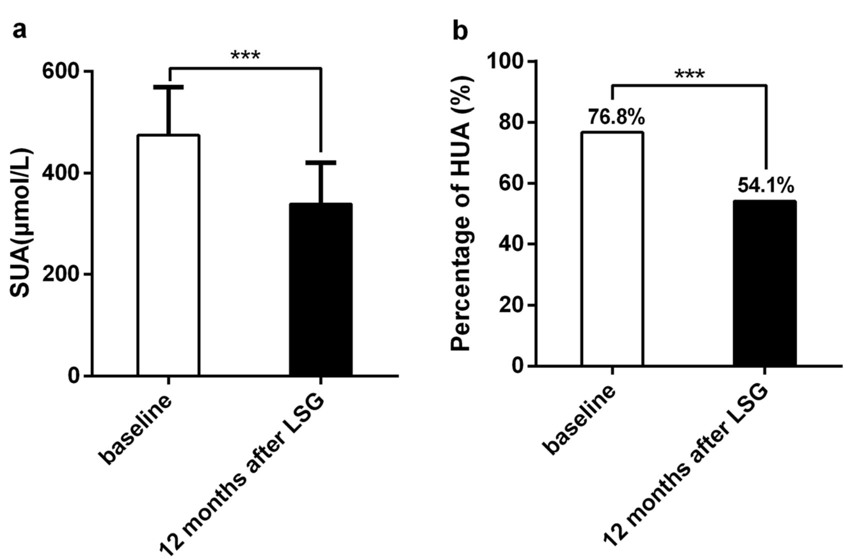

Fig. 2 Changes in SUA levels and percentage of HUA at 12 months after LSG from baseline. **a** SUA levels were remarkably declined at 12 months after surgery compared to baseline values. **b** Percentage of HUA was not noticeably decreased at 12 months after surgery from baseline. *SUA* serum uric acid, *HUA* hyperuricemia. Three asterisks, $P < 0.001$

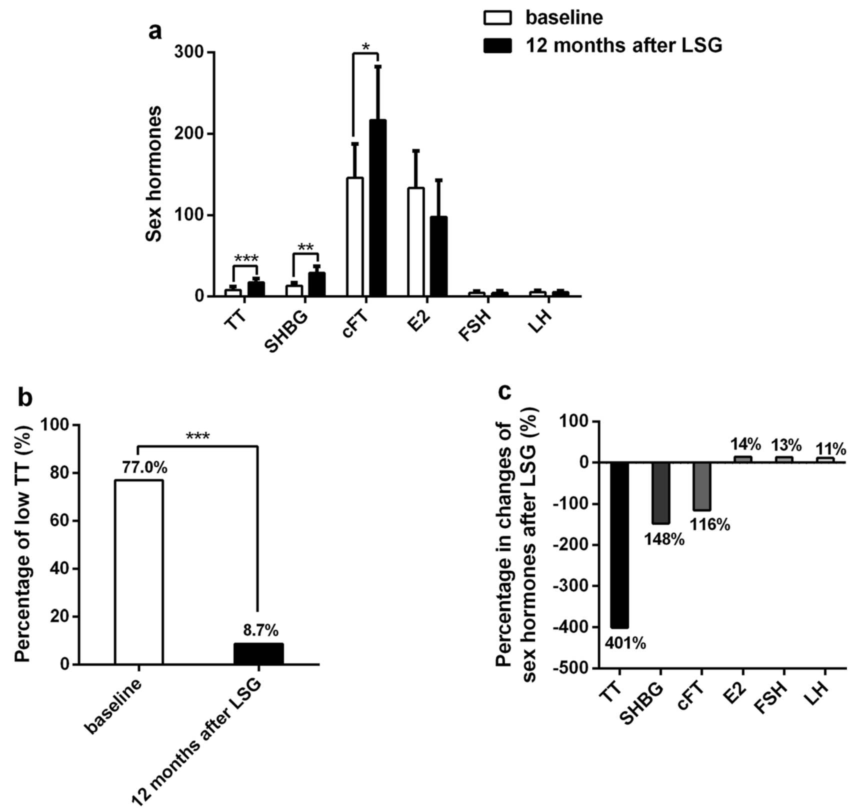

Fig. 3 Changes in sex hormone levels and percentage of low TT at 12 months after LSG from baseline. **a** TT, SHBG, and cFT levels were increased significantly at 12 months after surgery from baseline. **b** The percentage of low TT was remarkably decreased at 12 months after surgery. **c** After LSG, the TT levels were changed more than SHBG, cFT, E2, FSH, and LH. One asterisk, $P < 0.05$; two asterisks, $P < 0.01$; three asterisks, $P < 0.001$

LSG, multivariate linear regression analysis was performed (Table 2). After adjusting age and BMI, the reduction in SUA correlated significantly with increased TT ($\beta = -1.077$, $P < 0.05$) and SHBG ($\beta = -0.258$, $P < 0.05$) and decreased FINS ($\beta = 1.381$ $P < 0.05$). In contrast, there were no significant associations of changes in SUA with changes in BMI, TC, TG, HDL-C, LDL-C, FPG, E2, FSH, LH, or cFT at 12 months after LSG.

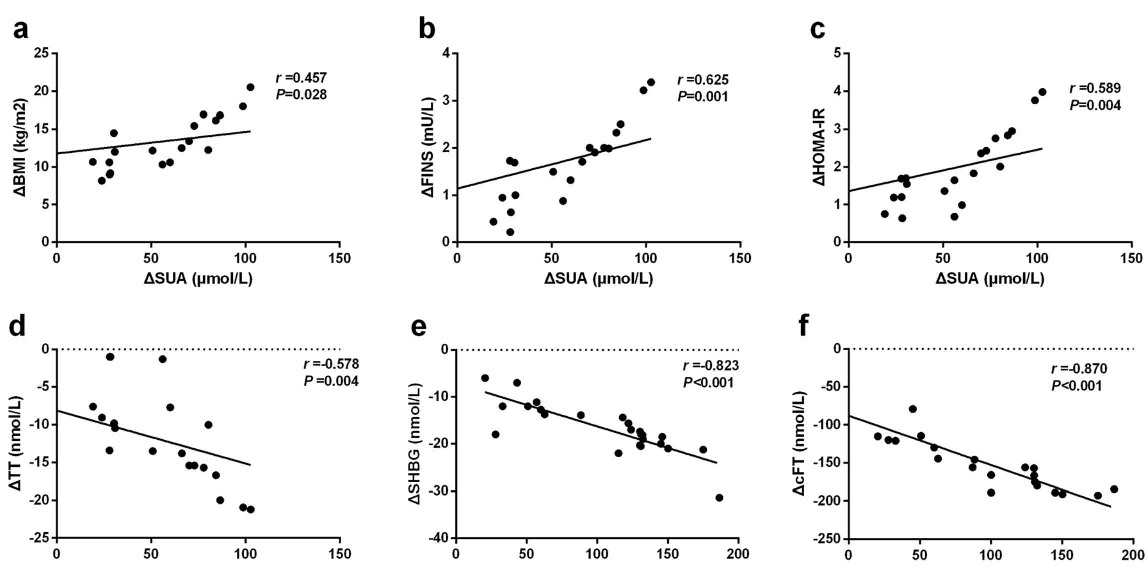

Fig. 4 Correlation of SUA reduction with changes in sex hormones after surgery. **a**–**f** Changes (Δ) in SUA levels were positively correlated with ΔBMI, ΔFINS, and ΔHOMA-IR, as well as negatively correlated with ΔTT, ΔSHBG, and ΔcFT after surgery. $P < 0.05$ was considered to be statistically significant

Table 2 Multiple regression analysis of variation in SUA with changes in sex hormones and related metabolic parameters after LSG

Independent variables	ΔSUA		
	β	*t*	*P* value
ΔBMI (kg/m^2)	− 0.960	− 2.010	0.079
ΔTC (mmol/L)	0.482	1.319	0.235
ΔTG (mmol/L)	− 0.121	− 0.484	0.645
ΔHDL-C (mmol/L)	− 0.233	− 1.594	0.150
ΔLDL-C (mmol/L)	− 1.144	− 2.454	0.050
ΔFPG (mmol/L)	0.024	0.098	0.925
ΔFINS (mU/L)	1.381	3.351	0.010
ΔHOMA-IR	− 0.151	− 0.367	0.723
ΔTT (nmol/L)	− 1.077	− 2.390	0.044
ΔE2 (pmol/L)	0.652	2.033	0.077
ΔFSH (IU/L)	− 0.205	− 1.178	0.273
ΔLH (IU/L)	− 0.292	− 1.403	0.198
ΔSHBG (nmol/L)	− 0.258	− 2.726	0.041
ΔcFT (nmol/L)	− 0.177	− 2.266	0.073

Δ was calculated as changes of metabolic variables (12-month baseline). *P* values < 0.05 were accepted as statistically significant. All data were adjusted for age and BMI

SUA serum uric acid, *BMI* body mass index, *TC* total cholesterol, *TG* triglyceride, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *FPG* fasting plasma glucose, *FINS* fasting insulin, *HOMA-IR* homeostasis model assessment of insulin resistance, *TT* total testosterone, *E2* estradiol, *FSH* follicle-stimulating hormone, *LH* luteinizing hormone, *SHBG* sex hormone binding-globulin, *cFT* calculated free testosterone

Table 3 Multiple regression analysis of variation in TT levels with changes in related metabolic parameters and after LSG

Independent variables	ΔTT		
	β	*t*	*P* value
ΔBMI (kg/m^2)	− 0.712	− 6.184	< 0.001
ΔTC (mmol/L)	− 0.960	1.716	0.105
ΔTG (mmol/L)	− 0.422	− 1.736	0.102
ΔHDL-C (mmol/L)	− 0.525	− 1.937	0.071
ΔLDL-C (mmol/L)	− 0.648	− 1.232	0.237
ΔFPG (mmol/L)	− 0.356	− 1.660	0.113
ΔFINS (mU/L)	0.381	1.692	0.114
ΔHOMA-IR	− 0.652	− 2.915	0.012
ΔE2 (pmol/L)	0.219	0.902	0.380
ΔFSH (IU/L)	− 0.056	− 0.209	0.837
ΔLH (IU/L)	− 0.196	− 0.778	0.447
ΔSHBG (nmol/L)	0.759	4.626	< 0.001
ΔcFT (nmol/L)	0.173	1.057	0.310

Δ was calculated as changes of metabolic variables (12-month baseline). *P* values < 0.05 were accepted as statistically significant. All data were adjusted for age and BMI

BMI body mass index, *TC* total cholesterol, *TG* triglyceride, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *FPG* fasting plasma glucose, *FINS* fasting insulin, *HOMA-IR* homeostasis model assessment of insulin resistance, *TT* total testosterone, *E2* estradiol, *FSH* follicle-stimulating hormone, *LH* luteinizing hormone, *SHBG* sex hormone-binding globulin, *cFT* calculated free testosterone

Relationship Between Changes in Other Metabolic Parameters and Sex Hormone Changes After LSG

As shown in Table 3, we further evaluated the association of changes in related metabolic parameters with sex hormone changes after surgery. In the multivariate regression analysis, change in TT was included as the dependent variable, while changes in BMI, TC, TG, HDL-C, LDL-C, FPG, FINS, HOMA-IR, E2, FSH, LH, cFT, and SHBG were included as independent variables. The results showed significant correlation between increased TT and decreased BMI ($\beta = -0.712$, $P < 0.001$) and HOMA-IR ($\beta = -0.652$, $P < 0.05$), as well as increased SHBG ($\beta = 0.759$, $P < 0.001$), respectively. No significant correlation was observed between changes in TT and changes in TC, TG, HDL-C, LDL-C, FPG, FINS, E2, FSH, LH, and cFT (all $P > 0.05$).

Discussion

Many observational studies have reported that obesity is often accompanied by a variety of metabolic diseases including HUA and male hypogonadism [2, 8, 30]. Marked weight loss induced by bariatric surgery has been recently proved to decrease SUA levels and improve testosterone levels in male obese patients [20, 21, 31]. However, the association between changes in sex hormones and changes in related metabolic parameters especially SUA following bariatric surgery in Chinese obese men is lacking. In the present study, we provided the first evidence that increased TT levels at 12 months after LSG in male obese patients were significantly correlated with SUA reduction, marked weight loss, and improved IR.

To our best knowledge, HUA and male hypogonadism were common in obese men. In the present study, we observed that 76.8% of them were considered to have HUA prior to surgery, which was higher than 50% in Indian obese males reported by Remedios et al. [32]. In addition, 77.0% of obese men were regarded to have low TT in our study, which was in line with previous studies showing that approximately 75% of men with obesity grade III awaiting bariatric surgery had low TT [33]. Thus, it is reasonable to consider that effective treatment of obesity may improve the HUA and male hypogonadism.

To date, bariatric surgical intervention is a safe and effective means of achieving substantial weight reduction and significant metabolic control of obesity-related metabolic abnormalities [34, 35]. Consistently, our results showed significant weight loss and metabolic improvement in glucose, insulin, HOMA-IR, and lipid profiles at 12 months after LSG. Moreover, we demonstrated significant reduction in SUA levels and percentage of HUA at 12 months after surgery in Chinese severely obese men, which was accompanied by an average 39.8 kg weight loss. In accordance with our results, a prospective longitudinal study including 60 obese patients (BMI > 35 kg/m^2) reported a significant reduction in SUA concentrations after bariatric surgery, which led to an average of 34.3 kg weight reduction [22]. Another prospective longitudinal study of 154 obese patients demonstrated an 18% reduction of SUA levels in patients with HUA [21]. In the present study, we observed a 7.1% reduction in SUA levels at 12 months after LSG in obese men. This discrepancy might be due to different study populations and surgical procedures. In addition, the close association between glucolipid metabolism and uric acid level has been recognized [36]. To confirm whether these changes are correlated with SUA reduction, Serpa et al. investigated the changes in SUA levels and prevalence of HUA in morbidly obese patients after Roux-en-Y gastric bypass (RYGB) and examined their correlation with metabolic syndrome (MetS) components. The results showed significantly greater SUA reduction in patients with improvement of MetS after surgery than those without improvement of MetS (− 1.52 ± 1.10 vs. 1.23 ± 1.23, respectively; $P = 0.031$) [37]. Also, we observed a significant association between IR alleviation and SUA reduction, which is in line with a previous study [38].

Multiple observational studies have shown that male hypogonadism is closely related to obesity, and weight loss induced by bariatric surgery has produced significant improvement in sex hormone profiles [39, 40]. Consistently, our findings indicated a marked increase in TT, SHBG, and cFT levels as well as a decrease in percentage of low TT at 12 months after LSG. In line with our study, Gao et al. [18] and Mihalca et al. [40] found a significant increase in TT and SHBG levels after LSG. Botella-Carretero et al. [41] also reported that TT, SHBG, and cFT significantly increased after bariatric surgery. However, another study by Bastounis et al. [42] found a controversial result, in which there was an improvement in SHBG and TT after vertical gastroplasty without any change in cFT levels. In view of this fact, it is important to underline that the inconsistent results among these studies may result from different available formulas for calculating free testosterone. Moreover, our findings observed a significant reduction in waist circumference, which is noted to be a reliable predictor of visceral fat in obese men postoperation. Low testosterone has been reported to be associated with visceral obesity. However, whether an increased testosterone was due to a decrease in visceral adipose tissue is still unclear. Our previous study has examined the changes in body fat distribution after LSG and revealed that changes in visceral fat were correlated with increased testosterone [18]. Visceral fat is the one that most easily contributes to hypogonadism because its action at peripheral levels increases leptin. Therefore, the reduction in visceral fat induced by LSG would decrease leptin levels and contribute to an increase in gonadotropin release, finally leading to increased testosterone [43].

Recently, a significant inverse association between SUA levels and TT levels among male patients with T2DM has been reported [12, 13]. However, no previous study has been designed to investigate the association of changes in SUA and sex hormone changes after surgery. Thus, we further evaluated the changes of sex hormones after LSG and tried to investigate whether SUA reduction correlated with improved sex hormones in obese male patients. In our study, the correlation analysis results revealed that SUA reduction was significantly correlated with decreased BMI, FINS, and HOMA-IR as well as increased TT, SHBG, and cFT levels. There were no significant correlations between variations in LH, E2, FSH, and SUA levels, suggesting that the contribution of these hormones to the reduction of SUA levels is limited. To investigate the main contributing factors responsible for the reduction of SUA levels after LSG in Chinese obese men, multiple regression analysis was performed after adjusting age and BMI. Intriguingly, our data indicated that only the increased TT and SHBG, and decreased FINS, were significantly associated with SUA reduction independent of age and BMI. This indicates that reduction in SUA levels following LSG may benefit from the improvement of TT and SHBG in addition to reduced IR. Considering the significant improvement of sex hormones after surgery in males, we further evaluated the contribution of other metabolic parameters to the increase in TT after surgery. The results showed that increased TT were correlated significantly with decreased BMI and HOMA-IR as well as increased SHBG. There were no significant correlations between variations in E2, FSH, LH, and increased TT levels, suggesting that these hormones may have little impact on the increase of TT levels. Taken together, the increased TT after surgery may be mediated by marked weight loss, SUA reduction, improved IR, and increased SHBG.

To date, the underlying mechanism of the increase in TT concentration after LSG in obese men remains elusive. Some evidence has demonstrated that downregulated aromatase levels and activity after weight loss might lead to decreased estrogen and increased testosterone levels [44]. Aromatase is the enzyme that converts testosterone to estrogen irreversibly, and its expression is proportional to body fat mass. Increased aromatase activity as a result of body mass in obese men leads to more testosterone being converted into estrogens, thus causing increased estradiol and reduced testosterone levels [45]. This argues for the notion that weight loss should be the primary approach for improving male sex hormones. A second explanation may derive from a profound increase in SHBG levels in obese men. SHBG specifically binds to sex hormones and plays an important role in regulating the concentration of biologically active sex hormones in the blood [46]. Thus, the increase of SHBG in a previous study [16] and our study may partly explain the increase of TT levels after surgery. A third explanation may result from changes in leptin levels after weight loss. Considering that increased leptin levels in obese men can inhibit the effect of LH on testicular Leydig cells and result in decreased testosterone production [47], markedly decreased leptin levels after bariatric surgery may contribute to the improvement of testosterone levels. In the present study, we observed a significant association between reduced SUA and increased TT after surgery. Mukhin et al. [48] demonstrated that hyperuricemia can lower LH levels and reduce the synthesis of testosterone and estrogen. Therefore, we assumed that the reduction in SUA after weight loss induced by bariatric surgery may be associated with the increase of testosterone in addition to substantial weight loss and improved IR. Further mechanistic studies are needed to elucidate the precise mechanism.

The present study has several limitations. One limitation is the matter of a relatively small sample size for studying the levels of SUA, sex hormones, and their clinical outcomes after LSG in obese men, which could result in high variability. Larger studies are needed to confirm these results. Also, it is possible that unmeasured confounding variables may exist. Finally, we presented a relatively short follow-up (only 1 year) after LSG; therefore, our results shall not represent the long-term effects of LSG on SUA, sex hormones, and related metabolic markers in obese men. Future studies with longer follow-up on a large number of patients are warranted to examine the mechanisms underlying the metabolic and gonadal benefits of bariatric surgery.

Conclusion

LSG promotes significant improvement of sex hormone levels in Chinese obese men. The increased TT levels at 12 months post-LSG were significantly associated with reduced SUA, BMI, and HOMA-IR, as well as increased SHBG, indicating that the increased TT levels may be mediated by SUA reduction in addition to substantial weight reduction and improved IR. The long-term changes in SUA and sex hormone levels after LSG warrant further study.

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Authors' Contribution • Study design, data analysis, and draft of the work: *Cuiling Zhu and Yi Zhang*

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All the authors take responsibility for the content of this study.

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Compliance with Ethical Standards

Informed consent was obtained from all individual participants of the study. The study was approved by the ethics committee of the Shanghai Tenth People's Hospital of Tongji University.

Conflict of Interest The authors declare that they have no conflict of interest.

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