Effect of Roux-en-Y Gastric Bypass Surgery on the Sex Steroids and Quality of Life in Obese Men

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Context: The effect of bariatric surgery on the reproductive function of obese men is not entirely elucidated.

Objective: The aim of the study was to define the effect of Roux-En-Y gastric bypass surgery on the reproductive hormones and sexual function in obese men.

Design and Setting: The cohort was followed for 2 yr at a clinical research center.

Patients: Sixty-four severely obese men (22 who had gastric bypass surgery and 42 controls) participated in the study.

Intervention(s): Anthropometrics [weight, body mass index (BMI), and percentage body fat] and reproductive hormones were measured. The sexual quality of life was assessed using the Impact of Weight on the Quality Of Life-Lite questionnaire.

Main Outcome Measure(s): Reproductive hormones and sexual quality of life were measured.

Results: The mean age was 48.9 $\pm$ 1.2 yr. At baseline, mean weight was 333.0 $\pm$ 7.1 lb, BMI was 46.2 $\pm$ 0.9 kg/m^2, and total testosterone was 339.9 $\pm$ 21.32 ng/dl. BMI correlated positively with estradiol and negatively with total and free testosterone. Indices of dissatisfaction with sexual quality of life correlated positively with measures of obesity. Difficult sexual performance and low sexual desire correlated negatively with free and total testosterone ($r = -0.273$, $P = 0.038$; and $r = -0.267$, $P = 0.042$, respectively). After 2 yr, the gastric bypass surgery group had a significant decrease in BMI (-16.6 ± 1.2 *vs.* -0.46 ± 0.51 kg/m^2) and estradiol (-8.1 ± 2.4 *vs.* 1.6 ± 1.4 pg/ml) and had an increase in total testosterone (310.8 ± 47.6 *vs.* 14.2 ± 15.3 ng/dl) and free testosterone (45.2 ± 5.1 *vs.* -0.4 ± 3.0 pg/ml). Sexual quality of life was improved after gastric bypass surgery.

Conclusion: Hormonal alterations and diminished sexual quality of life among obese men are related to degree of obesity, and both are improved after gastric bypass surgery. (***J Clin Endocrinol Metab* 94: 1329–1332, 2009**)

Recent reports have found that male obesity is associated with decreased sexual quality of life, alterations in sperm parameters, and reduced fertility (1–4). Moreover, male obesity has been associated with increased estrogen and reduced total testosterone (5–10), but the relation between obesity and free testosterone levels is less well understood (11). There are few studies describing the effect of weight loss on the reproductive potential in obese males. Obese men showed increases in SHBG

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Abbreviation: BMI, Body mass index.

and total testosterone levels after weight loss through low-energy diet or bariatric surgery (12, 13). Existing data do not agree regarding the effects of weight loss on free testosterone levels (14) or erectile dysfunction (13, 15).

The purpose of this study was to describe sex hormones and sexual function in a population of severely obese men and evaluate changes in these measures after Roux-en-Y gastric bypass surgery.

Subjects and Methods

This study is part of the Utah Obesity Study that aimed at studying the 2-yr morbidity of severely obese men undergoing Roux-en-Y gastric bypass surgery compared with controls (16). For the purpose of this analysis, we included 64 men. Of those, 22 men had gastric bypass surgery, 30 were controls from the community who did not seek surgery, and 12 were controls who sought surgery but either were denied insurance coverage or ultimately refused the surgery. The analysis for this study considered both groups of controls together as a single group (42 controls). The remaining 142 men of the Utah Obesity Study (45 surgical subjects and 97 controls) were not included in the analysis because they did not follow up after 2 yr (6 men) or because stored blood samples were insufficient from the first or second visits (136 men). Anthropometrics and percentage body fat were not different between the study population and the group of men not included in the analysis (supplemental Table 1, published as supplemental data on The Endocrine Society's Journals Online web site at http://jcem.endojournals.org).

All study participants underwent an initial evaluation that included standardized medical history and physical endpoints questionnaires. In addition to other questionnaires, the Impact of Weight on Quality of Life-Lite questionnaire (IWQOL-Lite) was administered. The IWQOL-Lite is a validated 31-item self-report questionnaire designed to assess the impact of weight on quality of life in obese individuals (3, 17). The IWQOL-Lite assesses five domains, including a sexual life domain that evaluates four items pertaining to: 1) lack of enjoyment of sexual activity; 2) lack of sexual desire; 3) difficulty with sexual performance; and 4) avoidance of sexual encounters. Each item has five possible response options: always true, usually true, sometimes true, rarely true, and never true. Each of the items was analyzed separately, and an overall score of dissatisfaction with sexual quality of life was calculated using the sum of scores from each question. Higher overall scores indicate higher sexual quality of life dissatisfaction.

All men had detailed anthropometric analysis. Height was measured using a Harpenden anthropometer (Holtain, Ltd., Crymych, UK) to the nearest centimeter. Weight was measured in a hospital gown with a Scaletronix scale (model 5100; Scaletronix Corporation, Wheaton, IL). Body mass index (BMI) was calculated as body weight (kilograms) divided by height (meters) squared. Circumferences (Lufkin metal tape) were measured at the waist (at the top of the iliac crest) and hip (at the largest circumference over the buttocks). The percentage body fat was measured using whole-body bioelectrical impedance (RJL Systems Analyzer; Quantum II, Clinton, MI).

Study participants underwent a morning venous blood draw after 12-h overnight fasting. The following were measured: homeostasis model of assessment for insulin resistance (glucose and insulin); total testosterone, using electrochemiluminescent immunoassay (Elecsys Testosterone kit; Roche Diagnostics, Indianapolis, IN); SHBG, using electrochemiluminescent immunoassay (Elecsys SHBG kit; Roche Diagnostics), estradiol, using liquid chromatography/tandem mass spectrometry; LH, using electrochemiluminescent immunoassay (Elecsys LH kit; Roche Diagnostics), FSH, using electrochemiluminescent immunoassay (Elecsys FSH kit; Roche Diagnostics), and C-reactive protein, using immunoturbidimetric (CRPLX Tina-Quant kit; Roche Diagnostics) as a marker of inflammation. Free testosterone (FT) was calculated using the following formula: $FT = [T] - (N \times [FT])/Kt\,(SHBG - [T] + N \times [FT])$ (18). All hormonal analyses were performed at the ARUP Institute for Clinical and Experimental Pathology. ARUP is a national reference laboratory located in Salt Lake City, Utah. When the men presented for the follow-up appointment 2 yr after the initial visit, they answered the same questionnaires and had the same anthropometrics and blood testing done.

The data analysis at baseline consisted of Pearson correlations among the anthropometric measures and the hormonal and sexual dysfunction parameters. Means are reported as mean ± SE. When used as a categorical variable, BMI was divided into three categories: 30–39, 40–49, and at least 50 kg/m^2. ANOVA with linear trend analysis and logistic regression were used, respectively, when mean free testosterone levels at baseline and frequency of low free testosterone (free testosterone ≤ 47 pg/ml) were compared between the BMI categories after correcting for age.

The "mean 2-yr change" of hormonal and sexual quality of life parameters was compared between the Roux-En-Y gastric bypass and control groups using the unpaired Student's *t* test. Paired Student's *t* test was used separately in both the Roux-En-Y gastric bypass and control groups to compare the initial values to the values after 2 yr of hormonal and sexual quality of life parameters.

All statistical operations were performed using SPSS (version 16.0; SPSS, Inc., Chicago, IL).

Results

The mean age of our subjects was 48.9 ± 1.2 yr. The mean weight was 333.0 ± 7.1 lb, and mean BMI was 46.2 ± 0.9 kg/m^2. Baseline anthropometrics and percentage body fat were not different in the Roux-En-Y gastric bypass group when compared with the control group (supplemental Table 1).

At baseline

Analysis of all study subjects (Roux-En-Y gastric bypass and control groups) showed that the mean estradiol level was 39.0 ± 3.34 pg/ml, mean free testosterone was 64.6 ± 2.86 pg/ml, and mean total testosterone was 339.9 ± 21.32 ng/dl. BMI levels correlated positively with serum estradiol levels and negatively with total testosterone levels. The correlation between anthropometric parameters and percentage body fat with various hormonal levels is given in Table 1. In our sample, BMI correlated negatively with free testosterone levels. Low free testosterone levels (≤47 pg/ml) were most prevalent among severely obese men with BMI of at least 50 kg/m^2 (29.4%), when compared with men with BMI of 40–50 kg/m^2 (15.2%) and 30–40 kg/m^2 (0%) ($P = 0.016$). A weight increase of 10 lb (≈4.5 kg) was associated with a reduction in free testosterone of 1.35 pg/ml and a reduction in total testosterone of 11.79 ng/dl. Indices of dissatisfaction of sexual quality of life also correlated positively with anthropometric measures among all subjects at baseline (Table 1). In particular, increased weight was associated with increased avoidance of sexual encounters and increased difficulty with sexual performance. Increased difficulty with sexual performance and reduced desire for sex were negatively correlated with free testosterone levels ($r = -0.273$, $P = 0.038$; and $r = -0.267$, $P = 0.042$, respectively). A linear regression model to predict dissatisfaction with sexual quality of life (total score) was constructed that included terms for free testosterone, BMI, C-reactive protein, smoking, alcohol intake, presence of coronary artery disease, presence of hypertension, presence of diabetes, and

TABLE 1. Relation between anthropometric, hormonal, and sexual quality of life measures at baseline

At baseline (Pearson's coefficient of correlation)	Weight (lb)	BMI (kg/m²)	Waist/hip ratio	Body fat (%)
Hormonal parameters				
Estradiol (pg/ml)	0.354[b]	0.322[a]	0.160	0.100
Total testosterone (ng/dl)	−0.399[b]	−0.360[b]	−0.042	0.015
SHBG (nmol/liter)	−0.204	−0.124	−0.009	−0.059
Free testosterone (pg/ml)	−0.344[b]	−0.341[b]	−0.020	0.058
C-reactive protein (mg/dl)	0.554[b]	0.503[b]	0.069	0.105
LH (IU/liter)	0.039	0.067	0.296[a]	0.102
FSH (IU/liter)	0.136	0.151	0.215	0.139
Sexual quality of life				
Avoid sexual encounters	0.326[a]	0.277[a]	−0.163	0.191
Difficulty with sexual performance	0.376[b]	0.344[b]	−0.105	0.187
Have little sexual desire	0.186	0.133	−0.080	0.187
Do not enjoy sex	0.137	0.079	−0.132	0.167
Total score of dissatisfaction	0.289[a]	0.226	−0.134	0.204

[a] Correlation is significant at the 0.05 level.

[b] Correlation is significant at the 0.01 level.

age. In this model, free testosterone levels (standardized coefficient, −0.299; $P = 0.048$) and alcohol intake (standardized coefficient, 0.478; $P = 0.008$) had an independent effect on sexual quality of life. At baseline, there were negative, but not statistically significant, correlations between homeostasis model of assessment for insulin resistance, free testosterone ($r = -0.24$; $P = 0.059$), and total testosterone ($r = -0.22$; $P = 0.082$).

Two-year follow-up

Mean 2-yr change of anthropomorphic measures, hormone levels, and sexual quality of life scores for surgery and control are shown in Table 2. Weight loss through gastric bypass surgery was effective in reducing serum estradiol levels (37.7 ± 10.1 to 29.6 ± 7.0 pg/ml; $P = 0.003$) and increasing both total testosterone (314.9 ± 201.0 to 625.8 ± 185.6 ng/dl; $P < 0.001$) and free testosterone (57.6 ± 20.3 to 102.8 ± 20.0 pg/ml; $P < 0.001$) levels. Weight loss after surgery was also associated with an improvement in all four aspects of sexual quality of life. Non-surgical control subjects did not exhibit significant changes in anthropomorphic, hormonal, or sexual quality of life measures.

Discussion

In our study population, lower free testosterone levels and diminished ratings for sexual quality of life were correlated with increased BMI. Among subjects losing weight through bariatric surgery, there was a reduction in estradiol levels, an increase in total and free testosterone levels, and an increase in ratings for sexual quality of life. Studies in the literature had convergent findings on the relation between weight loss, testosterone levels, and sexual function. Leenen *et al.* (11) did not find a correlation between body fat distribution and free or total testosterone. Weight loss was not associated with change in free and total testosterone. Niskanen *et al.* (14) showed that abdominally obese men increased their free and testosterone levels after a very low-calorie diet; how-

TABLE 2. The 2-yr change in anthropometric, hormonal, and sexual quality of life measures in the gastric bypass surgery and control groups

Mean 2-year change (mean ± SE)	Roux-en-Y gastric bypass (n = 22)	Control group (n = 42)	*P* value for the unpaired *t* test
BMI	−16.6 ± 1.2[a]	−0.46 ± 0.51	<0.001
Body fat (%)	11.1 ± 1.65[a]	0.89 ± 1.04	<0.001
Hormonal parameters			
Estradiol (pg/ml)	−8.1 ± 2.4[a]	1.6 ± 1.4	0.006
Total testosterone (ng/dl)	310.8 ± 47.6[a]	14.2 ± 15.3	<0.001
SHBG (nmol/liter)	21.6 ± 2.8[a]	2.3 ± 0.8[a]	<0.001
Free testosterone (pg/ml)	45.2 ± 5.1[a]	−0.4 ± 3.0	0.047
C-reactive protein (mg/dl)	−0.5 ± 0.1[a]	−0.0 ± 0.05	<0.001
LH (IU/liter)	0.9 ± 0.36[a]	1.0 ± 0.31[a]	0.385
FSH (IU/liter)	1.0 ± 0.36[a]	0.7 ± 0.20[a]	0.759
Sexual quality of life			
Avoid sexual encounters	−1.8 ± 0.3[a]	−0.0 ± 0.2	<0.001
Difficulty with sexual performance	−2.3 ± 0.3[a]	−0.1 ± 0.2	<0.001
Have little sexual desire	−1.9 ± 0.2[a]	0.05 ± 0.2	<0.001
Do not enjoy sex	−1.7 ± 0.3[a]	−0.05 ± 0.2	<0.001
Total score of dissatisfaction	−7.5 ± 1.2[a]	−0.1 ± 0.6	<0.001

[a] Significant difference of the two year value when compared to baseline.

ever, there was no change in estrogen levels. Kaukua *et al.* (13) showed that weight loss increases free and total testosterone; however, it did not change sexual function scores. To the contrary, Esposito *et al.* (15) demonstrated that sexual function improves after a weight reduction program. Bastounis *et al.* (19) found an improvement in SHBG and total testosterone and a reduction in estradiol after gastric bypass surgery; however, the change in free testosterone was not significant. Globerman *et al.* (20) found an improvement in free and total testosterone in 16 obese men who underwent silastic ring gastroplasty. In summary, prior individual studies agree with some of our findings, although there is concurrence when these studies are considered in aggregate. This may be in part due to our larger sample size, which confers greater power to detect changes, and in part to differing effects of different types and degrees of weight loss.

Our study has several strengths, including a detailed anthropometric evaluation, long follow-up period (2 yr), a relatively large number of participants, and presence of a control group. Weaknesses of this study include the exclusion of a number of men because of lack of follow-up and unavailable blood samples. However, the excluded men had similar anthropometric characteristics in comparison to the study sample. We did not find an association between change in body fat and hormonal and sexual quality of life parameters, despite a correlation between these and change in weight; this may be due to the limitations of the bioelectric impedence when compared with other techniques such as dual-energy x-ray absorptiometry scans. The correlation between body weight, BMI, and SHBG is well established, yet it was not seen in our study population. It is likely that this is attributable to the narrow range for BMI, with associated very depressed SHBG levels in our study population. Inclusion of less obese and normal weight subjects would likely reveal this known correlation. Our results highlight an association between sexual quality of life and hormonal measures independent from weight. Because this relationship is confounded by biopsychosocial aspects of obesity, further studies are required to demonstrate a cause and effect relationship.

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