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Original Article

The Role of Hypogonadism in the Body Composition of Obese Men in the Preoperative Period of Bariatric Surgery

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ABSTRACT

Objective: To describe clinical characteristics, hormonal profile and body composition of obese men in preoperative of bariatric surgery.
Methods: Cross-sectional, population-based study. Patients evaluated from June 2019 to December 2021 in 2 obesity referral centers. Patients underwent clinical evaluation, androgen deficiency screening using Androgen Deficiency in the Aging Male questionnaire, hormonal profile and body composition assessment through body mass index (BMI), body fat percentage (FM-%) and mass (FM-kg) measured by electrical bioimpedance and dual energy x-ray absorptiometry. To characterize hypogonadism, 2 cut-off points were considered: TT <264 ng/dL and TT <164 ng/dL.
Results: Thirty patients were included, mean age 35.6 ± 8.8 years, mean weight 129.4 ± 14.0 kg and mean BMI 42.3 ± 4.7 kg/m^2. Dyslipidemia was the most prevalent comorbidity. Considering TT <264 ng/dL, 22 patients (73%) had hypogonadism. The mean TT in hypogonadal men was 198.9 + 68.7 ng/dL and in eugonadal men 357.0 + 59.5 ng/dl (P < .001). Using TT <164 ng/dL, 7 patients (23%) had hypogonadism. The mean TT in hypogonadal patients was 116.6 + 28.9 ng/dL and in eugonadal patients 279.0 + 75.0 ng/dL (P < .001). In Androgen Deficiency in the Aging Male questionnaire, 93.3% had positive screening, with no significant difference between groups. There was no statistically significant difference in body composition between groups when using TT <264 ng/dL as the hypogonadism cutoff. Considering hypogonadism TT <164 ng/dL, hypogonadal patients had significantly higher values of weight (139.0 × 126.5 kg P = .036), BMI (46.1 × 41.2 kg/m^2 P = .014), FM-% (48.0 × 42.8% P = .010) and FM-kg (66.3 × 53.9 kg P = .007) than eugonadal patients.
Conclusion: Hypogonadism was identified in at least 23% of patients. Considering TT below the lower limit of normality for characterization of hypogonadism, we identified a significant worsening in body composition parameters.

Introduction

Obesity, defined as abnormal or excessive fat accumulation, is a chronic and progressive disease that, when not controlled, can develop more serious comorbidities.[1] Its prevalence is increasing, with harmful effects on health. In a 2017 systematic review, a worldwide prevalence of obesity was found in 603.7 million adults (12% of the population).[2] Data published by the Brazilian Institute of Geography and Statistics (IBGE) show that the percentage of brazilian's populations with obesity in adulthood more than

Abbreviations: ADAM, Androgen Deficiency in the Aging Male questionnaire; BIA, bioelectrical impedance; BMI, body mass index; DLP, dyslipidemia; E2, estradiol; EEW, estimated excess weight; FM-%, fat mass percentage; FM-kg, fat mass; FSH, follicle stimulating hormone; FT, free testosterone; LH, luteinizing hormone; MOSH, Male Obesity-related Secondary Hypogonadism; PA, physical activity; SAH, systemic arterial hypertension; SHBG, sex hormone-binding globulin; T2DM, type 2 diabetes mellitus; TT, total testosterone; WC, waist circumference.

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doubled in 17 years, from 12.2% (2002-2003) to 25.9% (2019), corresponding to 41.2 million people with obesity.[3]

Male hypogonadism is a clinical syndrome that results from the inability to produce physiological concentrations of testosterone, normal amounts of sperm, or both.[4] Male Obesity-related Secondary Hypogonadism (MOSH), has an estimated prevalence between 45.0 and 57.5%,[4] is a subtype of functional hypogonadism, so to reach the diagnosis other causes must be excluded, such as testicular and pituitary pathologies.[4] The most frequently associated changes in sex hormones are low levels of total testosterone (TT) and free testosterone (FT), in the presence of reduced or inappropriately normal gonadotropins, which may be associated with high serum estrogen levels.[5] The most suggestive signs and symptoms are decreased libido, reduced spontaneous erections, erectile dysfunction, decreased muscle mass and increased body fat.[6] There are questionnaires to identify patients most likely to have reduced testosterone levels, such as the Androgen Deficiency in the Aging Male (ADAM) Questionnarie and Aging Males' Symptoms scale.[7] The laboratory diagnosis of hypogonadism is primarily based on the measurement of TT, with substantial variation in reference intervals.[6] The main treatment for obesity-related hypogonadism is weight loss. However, it is known that testosterone replacement therapy can not only contribute to weight loss, but also to the improvement of metabolic parameters, renal function, and comorbidities such as type 2 diabetes mellitus, steatosis and cardiovascular diseases.[8]

There are no studies that correlate clinical, symptomatologic (ADAM), laboratory and body composition (bioelectrical impedance [BIA] and DXA) assessment with hypogonadism in patients with obesity who will undergo bariatric surgery. These evaluations will help to better understand these pathologies, as well as to optimize their management.

This study aims to evaluate clinical characteristics, hormonal profile and body composition of men with obesity with indication for bariatric surgery. To compare clinical data, hormonal profile, and body composition between hypogonadal and eugonadal patients, using TT <264 ng/dL, according to the Endocrine Society[6] and TT <164 ng/dL, below the local laboratory's normal limit.[9] The present study is a cross-sectional study carried out from June 2019 to December 2021 in 2 obesity treatment referral centers and conducted in accordance with the Declaration of Helsinki.

Highlights

- Hypogonadism is an important and prevalent condition related to male obesity.
- Symptoms of hypogonadism in obese are strongly associated with being overweight.
- The lower the testosterone levels, the worse body composition parameters tend to be.

Clinical Relevance

Considering that hypogonadism is an important and prevalent condition related to male obesity, we presented this original study that aimed to evaluate clinical characteristics, hormonal profile and body composition of obese men with indication for bariatric surgery.

Materials and Methods

Patients

We conducted a cross-sectional study carried out from June 2019 to December 2021 in 2 obesity treatment referral centers in accordance with the Declaration of Helsinki. All patients were informed about the objectives of the study and signed an informed consent form.

After evaluation by a multidisciplinary team, men with obesity aged 18 to 60 years with an indication for bariatric surgery were included in the study. Patients with incomplete data, with conditions that could justify secondary causes of hypogonadism (such as prolactin above the normal range and previous use of anabolic steroids) or previous diagnosis of hypogonadism for causes other than obesity were excluded.

Procedures

The study complies with the standards contained in resolution 466/2012 of the Brazilian's National Health Committee. The study was approved by an Institutional Review Board, the Research Ethics Committee of the Federal University of Health Sciences of Porto Alegre and Santa Casa of Porto Alegre Hospital.

For clinical evaluation, patients were interviewed by the researcher to assess comorbidities and life habits (physical activity [PA], smoking and alcohol consumption). To characterize PA a frequency greater than 3 times a week was considered. To characterize alcohol consumption, a frequency greater than 3 times a week was considered. Heavy alcohol consumption, was defined as consumption of more than 15 drinks per week (with a drink defined as 330 mL of beer, 140 mL of wine, or 40 mL of other distilled spirits ou liquor), and alcohol dependence as a period of heavy alcohol consumption greater than 12 months.

For the clinical screening of androgen deficiency, the ADAM questionnaire was used, consisting of 10 questions. A positive ADAM result is defined as a "yes" answer to questions 1 or 7 (3 points each, referring to low libido and less vigorous erections), or to 3 of the other questions (1 point each), with a score of >3 points, suggesting symptoms that could be consistent with hypogonadism.[7]

For hormonal evaluation, the following were measured: luteinizing hormone (LH), follicle stimulating hormone (FSH), sex hormone-binding globulin (SHBG), TT, FT, estradiol (E2) and prolactin. Hormonal measurements were performed in the morning (between 7 and 9 AM). All the laboratory tests were performed at Santa Casa of Porto Alegre Hospital central laboratory, which is CDC-certified by chemiluminescence immunoassay (TS TII Siemens).[9] During the entire study period, the laboratory dosage methodology was not modified. To characterize hypogonadism, 2 cut-off points were considered for TT: <264 ng/dL, according to the Endocrine Society[6] and <164 ng/dL, below the local laboratory's normal limit, according to age group.[9] The reference range used in the study for TT of the TS TII Siemens chemiluminescence immunoassay is: 164 to 753 ng/dL.

To assess anthropometric data, height (m), weight (kg), waist circumference (WC) (cm) and body mass index (BMI) (kg/m^2) were measured. Through the BMI, we calculated the estimated excess weight (EEW) (kg), defined by the amount of weight that would need to be reduced (in kg) to reach a BMI <25 kg/m^2 (for example, a patient weighing 120 kg, with a BMI of 37 kg/m^2 needs to reduce 39 kg to reach a BMI of 25 kg/m^2, therefore his EEW is 39 kg). To assess body composition, we used 2 of the main methods validated in the obese population, with dual energy x-ray absorptiometry (DXA) being considered the gold standard. Body fat percentage (FM-%) and fat mass (FM-kg) were measured using BIA, InBody 120

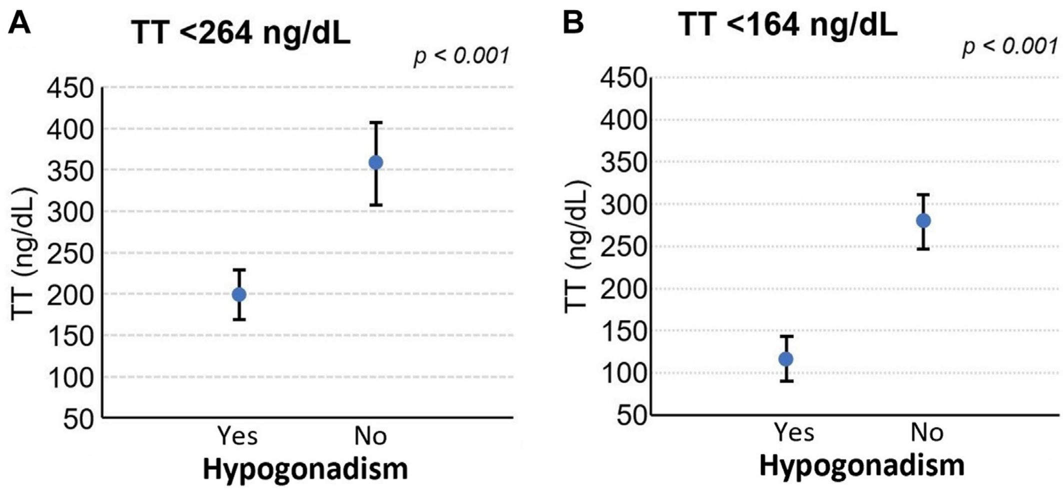

Fig. 1. *A* and *B*, Comparison between TT levels: hypogonadal patients with TT <264 ng/dL × eugonadal and hypogonadal patients with TT <164 ng/dL × eugonadal patients. *TT* = total testosterone.

model (InBody Co, Ltd) and DXA, Lunar iDXA model (GE Healthcare).

Statistical Analysis

Clinical data were described as mean ± SD (Standard Deviation) for continuous variables and as prevalence in categorical variables. The association of categorical variables with hypogonadism was verified using the chi-square test or Fisher's exact test, when appropriate. For continuous variables, Student's t test and Mann-Whitney test were applied, according to the distribution of the variable. The significance level adopted was 0.05. Analyzes were performed using SPSS statistical software (IBM SPSS Statistics for Windows, Version 25.0.).

Results

Sample Characterization

Thirty male patients met the inclusion criteria. The mean age was 35.6 + 8.8 years, weight was 129.4 + 14.0 kg and BMI was 42.3 + 4.7 kg/m^2, with 37% having class II obesity and 63% class III obesity. The mean of EEW was 52.6 + 13.6 kg.

Regarding comorbidities, 60% of patients have some previous comorbidity. The most prevalent was dyslipidemia (DLP) (33.3%), systemic arterial hypertension (SAH) (30%) and type 2 diabetes mellitus (T2DM) (16.7%). Regarding the degree of obesity, 100% of patients with class ≥ II and 42% of patients with class III obesity had some comorbidity. With regard to habits, more than half of the patients (56.7%) reported drinking alcohol at least 3 times a week, but none of them had alcohol dependence or heavy alcohol consumption. Only 6.7% of patients were smokers and 40% were physically active.

Regarding the symptomatology related to hypogonadism, 28 of the 30 patients (93.3%) had positive screening, with an average score of 4.9 + 1.4 on the ADAM. Of the 28 patients with positive screening, 23 (82%) answered “yes” to question 1 (decreased libido), question 7 (less vigorous erections), or both.

About the assessment of body composition, 15 patients underwent assessment by BIA and 14 by DXA. The mean FM-% was 44.1 + 4.8% and FM-kg 56.6 + 11.1 kg. The mean WC was 131.3 + 7.6 cm.

Regarding the hormonal profile, the mean LH was 4.4 + 2.4 mUl/mL, FSH 5.3 + 5.3 mUl/mL, SHBG 19.1 + 9.5 nmol/L and E2 30.3 + 10.3 pg/dL. About testosterone levels, the means of TT and FT were 241.1 + 96.6 and 6.2 + 2.3 ng/dL, respectively.

Comparison Between Hypogonadal Patients with TT <264 ng/dL × Eugonadal Patients

Using TT <264 ng/dL, 22 patients (73%) had hypogonadism. The mean TT in hypogonadal patients was 198.9 + 68.7 ng/dL and in eugonadal was 357.0 + 59.5 ng/dl ($P < .001$). Regarding FT, the mean in hypogonadal group was 5.4 + 2.0 ng/dL and in eugonadal was 8.3 + 1.6 ng/dL ($P < .001$) (Fig. 1*A* and *B*) Hypogonadal patients showed significantly lower values of SHBG than eugonadal, 16.5 × 26.2 nmol/L ($P = .02$), E2 showed no significant difference between the groups.

Hypogonadal TT <264 ng/dL and eugonadal patients did not show a statistically significant difference in the assessment of comorbidities, lifestyle habits and body composition. There was no significant difference in the assessment of symptoms related to hypogonadism, either in the ADAM score or in the assessment of answered “yes” to question 1 (decreased libido), question 7 (less vigorous erections), or both, of the questionnaire (Table 1).

Comparison Between Hypogonadal Patients with TT <164 ng/dL × Eugonadal Patients

Using TT <164 ng/dL, 7 patients (23%) had hypogonadism. The mean TT in hypogonadal patients was 116.6 + 28.9 ng/dL and in eugonadal was 279.0 + 75.0 ng/dL ($P < .001$). In relation to FT, the mean in hypogonadal group was 3.2 + 1.0 ng/dL and in eugonadal 7.1 + 1.7 ng/dL ($P < .001$) (Fig. 1*A* and *B*).

Regarding body composition, hypogonadal patients had significantly higher values of weight (139.0 + 13.1 × 126.5 + 13.1 kg; $P = .036$), BMI (46.1 + 4.6 × 41.2 + 4.2 kg/m2; $P = .014$), EEW (63.4 + 13.3 × 49.3 + 12.1 kg; $P = .013$), FM-% (48.0 + 5.0 × 42.8 + 4.1%; $P = .010$) and FM-kg (66.3 + 9.9 × 53.9 + 9.9 kg; $P = .007$) than the eugonadal. The other parameters were very similar, with no statistically significant difference between the groups. There was also no significant difference in the assessment of symptoms related to hypogonadism, either in the ADAM score or in the assessment of “yes” to question 1

Table 1
Comparison between hypogonadal patients with TT <264 ng/dL × eugonadal patients

Variables	Hypogonadal TT < 264 ng/dL $n = 22$	Eugonadal $n = 8$	P value
Age (y) − mean ± SD	35.9 (9.7)	34.9 (5.8)	.781
Comorbidities − n (%)			
DLP	9 (40.9)	1 (12.5)	.210
SAH	6 (27.3)	3 (37.5)	.666
T2DM	5 (22.7)	0 (0)	.287
CVD	1 (4.5)	0 (0)	1.000
Habits − n (%)			
PA	8 (36.4)	4 (50)	.678
Alcohol consumption	12 (54.5)	5 (62.6)	>.999
Smoking	1 (4.5)	1 (12.5)	.469
Laboratory − mean ± SD			
LH (mUI/mL)	4.2 ± 2.7	4.9 ± 0.7	.057
FSH (mUI/mL)	5.3 ± 5.9	5.1 ± 2.7	.606
SHBG (nmol/L)	16.5 ± 7.4	20.6 ± 11.7	.020[a]
TT (ng/dL)	198.9 ± 68.7	357.0 ± 59.5	<.001[a]
FT (ng/dL)	3.0 ± 0.8	6.9 ± 1.7	<.001[a]
E_2 (pg/mL)	28.3 ± 10.6	35.3 ± 8.6	.268
Anthropometric data − mean ± SD			
Weight (kg)	129.3 ± 15.7	129.7 ± 8.3	.944
BMI (km/m^2)	42.6 ± 4.8	41.7 ± 4.6	.666
EEW (kg)	53.0 ± 14.6	51.6 ± 11.2	.810
WC (cm)	132.8 ± 7.7	127.0 ± 5.9	.199
Body composition − mean ± SD			
FM-% (%)	44.3 ± 11.8	43.4 ± 4.8	.612
FM-kg (kg)	57.3 ± 11.8	55.8 ± 9.4	.748
ADAM			
Positive (%)	20 (90.9)	8 (100)	>.999
Mean ± SD	4.7 ± 1.5	5.5 ± 0.9	.152
"Yes" for questions 1 and/or 7 (%)	18 (90)	5 (62)	.123

Abbreviations: ADAM = Androgen Deficiency in the Aging Male questionnaire; BMI = body mass index; CVD = cardiovascular disease; DLP = dyslipidemia; E2 = estradiol; EEW = estimated excess weight; FM-% = fat mass percentage; FM-kg = fat mass; FSH = follicle stimulating hormone; FT = free testosterone; LH = luteinizing hormone; PA = physical activity; SAH = systemic arterial hypertension; SHBG = sex hormone-binding globulin; T2DM = type 2 diabetes mellitus; TT = total testosterone; WC = waist circumference.
[a] $P < .05$.

(decreased libido), question 7 (less vigorous erections), or both of ADAM (Table 2).

Discussion

Obesity and hypogonadism are linked in a vicious cycle, in which low levels of testosterone favor weight gain and, in turn, adiposity induces hypogonadism.[10]

The population studied included men with obesity, with a mean age of 35.6 years. According to international data described in a systematic review, the mean age at which patients undergo bariatric surgery is 38.9 years.[11] In our study, the mean weight was 129.4 kg and BMI was 42.3 kg/m^2, and most patients had class III obesity (63%).

Regarding comorbidities, most patients (60%) had at least one comorbidity; DLP (33%) and SAH (30%) were the most common. Our data agree with the international literature, according to Residori et al,[12] the prevalence of DLP and SAH in patients undergoing bariatric surgery was 35% and 38%. In relation to T2DM, the prevalence of 16.6% was also similar to that described in the literature, in a systematic review, the prevalence of DLP, SAH and T2DM was 36%, 35% and 15%, respectively.[11]

In our study, more than half of the patients (56.7%) reported drinking alcohol at least 3 times a week, which is similar to the data described by King et al,[13] in which 62% of the patients also had this habit preoperatively. There was no significant difference in alcohol intake between hypogonadal and eugonadal patients, suggesting that alcohol consumption was not the cause of hypogonadism.

Preoperative smoking rates for bariatric surgery vary widely between studies, with the country of origin of the population playing an important role.[14] Our study showed a prevalence of only 6.7%. Chow et al,[14] in a systematic review, showed that the prevalence of smoking among patients undergoing bariatric surgery has been decreasing over the years, with studies describing rates of up to 40% in 2011, compared to current rates of 10% to 17%, in 2019.

Regarding PA, 40% of patients reported performing PA at least 3 times a week. This data is above that reported in the literature, as described by Samir et al,[15] that only 27% of patients with obesity are physically active.

Studies have shown that ADAM, when compared to other questionnaires, has high sensitivity to identify androgen deficiency (97%), but low specificity (30%).[16] Until this moment, we still do not have a validated questionnaire for screening for hypogonadism, specifically for the obese population. Therefore, several other studies with obese men in the context of bariatric surgery use ADAM questionnaire, even though it is widely validated for men over 50 years of age, regardless of weight.[16,17] In our study, 93.3% of patients had positive screening, with a mean score of 4.9. In the study carried out by Machado et al,[16] with men with obesity in the preoperative period of bariatric surgery, 75% had a positive screening for hypogonadism, through the evaluation of 2 questionnaires, ADAM and Aging Males' Symptoms.[18] Boonchaya-Anant et al[17] found a mean of 4.6 points on the ADAM prior to bariatric surgery. Several authors establish that the most specific symptoms for hypogonadism are low libido and less vigorous erections.[19] In a sub analysis of our study, we found that 83% of patients who screened positive for hypogonadism had at least one of these

Table 2
Comparison between hypogonadal patients with TT <164 ng/dL × eugonadal patients

Variables	Hypogonadal TT < 164 ng/dL $n = 7$	Eugonadal $n = 23$	P value
Age (y) − mean ± SD	32.0 ± 10.4	36.7 ± 8.2	.271
Comorbidities − n (%)			
DLP	2 (28.6)	8 (34.8)	>.999
SAH	0 (0)	9 (39.1)	.071
T2DM	1 (14.3)	4 (17.4)	>.999
CVD	0 (0)	1 (4.3)	>.999
Habits − n (%)			
PA	2 (28.6)	10 (43.5)	.669
Alcohol consumption	3 (42.9)	14 (60.9)	.666
Smoking	1 (14.3)	1 (4.3)	.418
Laboratory − mean ± SD			
LH (mUI/mL)	6.1 ± 3.9	3.9 ± 1.5	.193
FSH (mUI/mL)	7.8 ± 9.8	4.5 ± 2.7	.462
SHBG (nmol/L)	15.6 ± 7.8	20.1 ± 9.9	.230
TT (ng/dL)	116.6 ± 28.9	279.0 ± 75.0	<.001[a]
FT (ng/dL)	3.2 ± 1.0	7.1 ± 1.7	<.001[a]
E_2 (pg/mL)	44.8 ± 16.1	27.9 ± 7.6	.370
Body composition − mean ± SD			
Weight (kg)	139.0 ± 13.1	126.5 ± 13.1	.036[a]
BMI (km/m^2)	46.1 ± 4.6	41.2 ± 4.2	.014[a]
EEW (kg)	63.4 ± 13.3	49.3 ± 12.1	.013[a]
WC (cm)	131.8 ± 6.2	131.0 ± 8.5	.855
Body composition − mean ± SD			
FM-% (%)	48.0 ± 5.0	42.8 ± 4.1	.010[a]
FM-kg (kg)	66.3 ± 9.9	53.9 ± 9.9	.007[a]
ADAM			
Positive (%)	7 (100)	21 (91.3)	>.999
Mean ± SD	4.7 ± 1.0	5.0 ± 1.5	.690
"Yes" for questions 1 and/or 7 (%)	6 (85)	10 (47)	.184

Abbreviations: ADAM = Androgen Deficiency in the Aging Male questionnaire; BMI = body mass index; CVD = cardiovascular disease; DLP = dyslipidemia; E2 = estradiol; EEW = estimated excess weight; FM-% = fat mass percentage; FM-kg = fat mass; FSH = follicle stimulating hormone; FT = free testosterone; LH = luteinizing hormone; PA = physical activity; SAH = systemic arterial hypertension; SHBG = sex hormone-binding globulin; T2DM = type 2 diabetes mellitus; TT = total testosterone; WC = waist circumference.
[a] $P < .05$.

symptoms. The absence of a significant difference in scores between hypogonadal (TT < 164 ng/dL and TT < 264 ng/dL) and eugonadal patients suggests that the symptoms presented by patients are more influenced by excess weight, common to all, than by hypogonadism.

Obesity is characterized by major changes in body compartments.[20] Currently, DXA and BIA have been widely used to assess the body composition of individuals with obesity.[20] BIA has been proposed as an alternative tool in the absence of confounding fluid balance abnormalities as it is portable, easy to use, relatively low cost, and free from radiation. The evaluation with BIA in people with obesity is reliable enough for the estimation of FM, with good correlation and low bias to DXA.[21] The normal values of FM-% and FM-kg vary according to the sex, age and level of physical conditioning of each individual.[21] In young adult men, FM-% levels range from 12% to 20%, while levels above 25% are considered obesity.[22] Our study found a mean FM-% of 44.1% and FM-kg of 56.6 kg. Ippersiel et al[23] evaluated the body composition, using BIA, of men with a BMI between 35 and 47 kg/m^2 prior to bariatric surgery and identified a mean FM-% of 36%. De Lorenzo et al,[24] in their assessment of men in the preoperative period of bariatric surgery with a mean BMI of 36 kg/m^2, the FM-% and FM-kg assessed by DXA were 39% and 42 kg, respectively. De Freitas Junior et al[20] evaluated the body composition through BIA of individuals with obesity with a BMI ≥40 kg/m^2 prior to bariatric surgery and found a mean FM-% of 50.6% and FM-kg of 71 kg.

The WC measurement aims to assess abdominal adiposity, which, unlike the concentration of fat in other regions of the body, has a direct correlation with the increased risk of developing T2DM and cardiovascular disease.[25] Katchunga et al[25] showed a high correlation between WC and visceral fat assessed by BIA, in 143 men with high cardiovascular risk. Currently, a cutoff point of 94 cm of WC for men has been recommended.[26] Our study identified a mean of 131.3 cm. Mokhtari et al evaluated 1.909 patients with a BMI >35 kg/m^2 in the preoperative period of bariatric surgery with a mean WC of 132.9 cm,[27] whereas Samavat et al,[28] in their assessment of patients with a BMI >40 kg/m^2, the mean was of 140.1 cm.

It is already known that increasing testosterone levels can improve not only body composition parameters, but also metabolic ones. Maseroli et al[29] identified that testosterone treatment in people with severely obesity, hypogonadal individuals induces metabolically healthier preadipocytes, improving insulin sensitivity, mitochondrial functioning, and lipid handling.

Men with obesity, when compared to eutrophic, tend to have lower levels of testosterone.[11,18] In our study, the mean TT and FT were 241.1 and 6.2 ng/dL. Samavat et al,[28] in their evaluation of 55 men in the preoperative period of bariatric surgery, identified a mean of TT 259.9 and FT 6.0 ng/dL. De Lorenzo et al[24] evaluated TT in 12 men prior to bariatric surgery with a mean TT 300.2 ng/dL.

The alterations in sex hormones most frequently associated with hypogonadism in men with obesity are low levels of TT and FT, in the presence of reduced or inappropriately normal gonadotropins.[4,30] In our study, the hormonal profiles of LH and FSH indicate a central origin for the dysfunction observed in hypogonadal patients. In both characterizations of hypogonadism, TT <264 ng/dL according to the Endocrine Society[6] and <164 ng/dL, below the laboratory limit of normality,[9] gonadotropins were inadequately

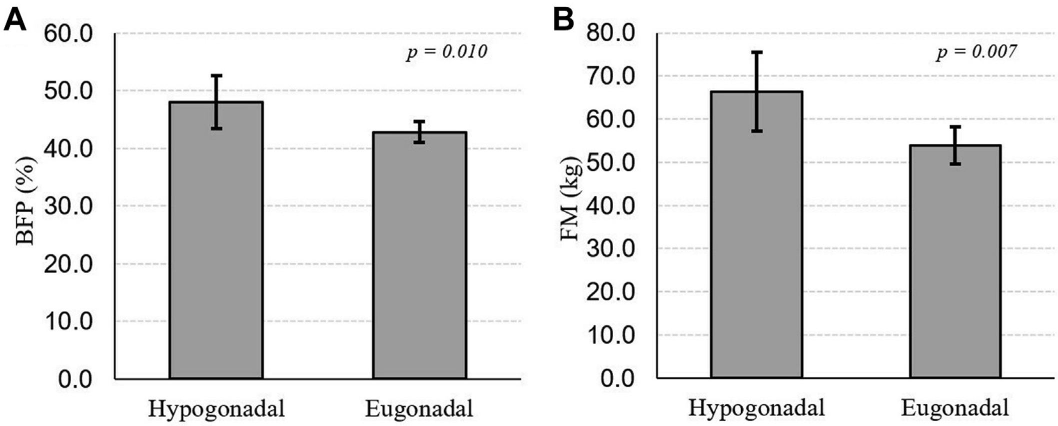

Fig. 2. *A* and *B*, Comparison of FM-% (%) and FM-kg (kg) between hypogonadal patients with TT <164 ng/dL x eugonadal patients. *FM-%* = fat mass percentage; *FM-kg* = fat mass;TT: total testosterone.

normal, with LH averages between 4.4 and 5.3 mIU/mL and FSH between 6.1 and 7.8 mIU/mL.

As with testosterone, obese individuals commonly have lower levels of SHBG.[31] This finding can be explained by the increase in insulin resistance, which results in compensatory hyperinsulinemia and consequent suppression of hepatic production of SHBG.[17] In our study, the mean SHBG was 19.1 nmol/L, with reference values ranging from 13.2 to 89.5 nmol/L. De Lorenzo et al identified a mean of 21.7 nmol/L and Samavat et al of 21.5 nmol/L.[24,28]

In relation to E2, levels are commonly high in men with obesity.[27] The main mechanism to explain this change is based on the conversion of testosterone to E2 by the aromatase enzyme P450, highly expressed in adipose tissue.[32] The mean E2 in our study was 30.3 pg/mL, with a reference value <39.8 pg/mL. De Lorenzo et al identified a mean of 48 pg/mL and Samavat et al found 38 pg/mL.[24,28]

TT reference values for defining hypogonadism vary greatly depending on laboratory and assay methods. These variations are due to the absence of standardized tests, different calibrations, and evaluation of different populations to generate normality intervals.[29] There is no consensus in the literature on the most appropriate cutoff point for hypogonadism in obese patients.[30,33]

Rigon et al[30] used 3 TT cut-off points to define hypogonadism, TT <264 ng/dL, according to the Endocrine Society,[6] < 241 ng/dL, according to laboratory reference[30] and < 150 ng/dL, according to Anawalt et al[34] De Lorenzo et al[24] used a TT value <349 ng/dL, associated with signs and symptoms of hypogonadism to define MOSH. In the study by Samavat et al,[28] who evaluated men with obesity in the preoperative period of bariatric surgery, the TT cut-off point to define hypogonadism was 230 ng/dL.

Regarding the definition of hypogonadism through FT, there is also no consensus in the literature. Bhasin et al[6] recommend that FT should be quantified in the presence of TT modestly above or below the lower limit of normality, for example, between 200 and 400 ng/dL. In men whose TT concentrations are far below the lower limit of normal, for example <150 ng/dL, the likelihood that the FT concentration is within the normal range is low. Therefore, the measurement of FT is generally not necessary.[33]

Rigon et al,[30] identified a prevalence of 65% with TT <264 ng/dL, 55% with TT <241 ng/dL, and 21% with TT <150 ng/dL. Calderón et al,[4] identified MOSH in 45% of patients, using levels of TT <300 ng/dL and/or FT <6.4 ng/dL, with a mean TT in hypogonadal patients of 230.5 ng/dL and in eugonadal patients of 440.9 ng/dL ($P < .001$). In relation to FT, the average in hypogonadal patients was 5.7 ng/dL and in eugonadal patients was 10.5 ng/dL ($P < .001$).

Hofstra et al[35] identified a prevalence of hypogonadism of 58% using TT <317 ng/dL as a criterion and 35.6% with FT <6.4 ng/dL, with TT and FT levels being inversely proportional to the degree of obesity. Pellitero et al[5] evaluated men with a mean BMI of 50 kg/m^2 and identified a prevalence of 79% of hypogonadism with TT < 300 ng/dL, 30% with TT < 200 ng/dL and 51% with FT < 6.5 ng/dL.

In our study, using as a criterion value below the laboratory's limit of normality,[9] TT <164 ng/dL, hypogonadal men had significant higher values of weight, BMI, EEW, FM-%, and FM-kg than eugonadal men. Calderón et al[4] evaluated the hormonal profile of 95 men with obesity with a mean age of 40 years and a BMI of 47 kg/m^2. The hypogonadal individuals were older (44 × 37 years; $P < .01$), but the other parameters analyzed (weight, BMI, EEW, SHBG) were very similar, with no statistically significant difference between the groups. Ippersiel et al[23] evaluated the body composition and hormonal profile of 75 men with obesity, with a mean age of 43 years, BMI of 41 kg/m^2 and TT of 314 ng/dL and found that the greater the degree of obesity, more specifically the abdominal adiposity, lower are the levels of testosterone.

Bariatric surgery has been shown to be more effective than dietary interventions in increasing testosterone, due to the greater weight loss obtained with surgery (32%) compared to diet alone (9.8%).[10] In addition, Crisóstomo et al[36] demonstrated that TT has a positive correlation with the percentage of weight lost, having a greater impact on younger men, without diabetes and with more severe degrees of obesity. Regarding testosterone levels and body composition, we identified an inverse correlation between TT levels and excess body fat (FM-% and FM-kg). Therefore, the lower the TT levels, the worse body composition parameters were identified. This analysis only showed statistical significance in the hypogonadal patients with TT < 164 ng/dL group (Fig. 2*A* and *B*).

The main positive point of the present study is the evaluation of a homogeneous population of men with obesity in the preoperative period of bariatric surgery and with assessment of body composition through the BIA and DXA methods. Another strong point of this study is the assessment of symptoms related to hypogonadism, through a standardized and validated questionnaire, ADAM.

Our study has some limitations. Due to the small sample size of our study, the significant differences detected should be interpreted with caution. Also, the evaluation of a specific population, located in southern Brazil, may make it difficult to validate the results in other populations and regions. We had one patient who did not undergo the DXA evaluation. Consequently, we worked with data from 29 patients (15 who underwent BIA and 14 DXA).

We performed a broad clinical, hormonal and symptomatologic assessment through the ADAM, however, the absence of significant differences between hypogonadal patients and eugonadal patients suggests that the symptoms presented are mainly due to excess weight. Additionally, in our study FT was measured by chemiluminescence immunoassay (TS TII Siemens), and current studies recommend that it is most accurately measured by tandem mass spectrometry and equilibrium dialysis.

As a positive side of this study, we consider the fact that we had a negligible data loss, only 1 patient was not submitted to body composition assessment.

Conclusion

Hypogonadism is an important and prevalent condition related to male obesity, in our sample, present in at least 23% of patients. The absence of a significant difference in ADAM between hypogonadal and eugonadal patients suggests that the symptoms presented are more influenced by excess weight than by hypogonadism. Considering TT below the normal limit of the laboratory for characterization of hypogonadism, we identified a significant worsening in the parameters of body composition.

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Cross-sectional study carried out from June 2019 to December 2021 at the Obesity Center of Irmandade Santa Casa da Misericórdia de Porto Alegre (ISCMPA), after approval by the Research Ethics Committee of the ISCMPA (Ethics Protocol number 4.686.897) and conducted in accordance with the Declaration of Helsinki. All patients were informed about the objectives of the study and signed an informed consent form.

References

1. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Obesity Society. *Circulation*. 2014;129(25 Suppl 2):S102–S138. https://doi.org/10.1161/01.cir.0000437739.71477.ee
2. GBD 20 Obesity Collaborators, Afshin A, Forouzanfar MH, Reitsma MB, et al. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med*. 2017;377:13–27. https://doi.org/10.1056/NEJMoa1614362
3. Stopa SR, Szwarcwald CL, Oliveira MM, et al. Pesquisa Nacional de Saúde 2019: histórico, métodos e perspectivas. *Epidemiol Serv Saúde*. 2020;29(5):e2020315. https://doi.org/10.1590/S1679-49742020000500004
4. Calderón B, Gómez-Martín JM, Vega-Piñero B, et al. Prevalence of male secondary hypogonadism in moderate to severe obesity and its relationship with insulin resistance and excess body weight. *Andrology*. 2016;4(1):62–67. https://doi.org/10.1111/andr.12135
5. Pellitero S, Olaizola I, Alastrue A, et al. Hypogonadotropic hypogonadism in morbidly obese males is reversed after bariatric surgery. *Obes Surg*. 2012;22(12):1835–1842. https://doi.org/10.1007/s11695-012-0734-9
6. Bhasin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2018;103(5):1715–1744. https://doi.org/10.1210/jc.2018-00229
7. Martínez-Jabaloyas JM, Queipo-Zaragozá A, Rodríguez-Navarro R, Queipo-Zaragozá JA, Gil-Salom M, Chuan-Nuez P. Relationship between the Saint Louis University ADAM questionnaire and sexual hormonal levels in a male outpatient population over 50 years of age. *Eur Urol*. 2007;52(6):1760–1767. https://doi.org/10.1016/j.eururo.2007.05.021
8. Al-Zoubi RM, Yassin AA, Alwani M, et al. A systematic review on the latest developments in testosterone therapy: innovations, advances, and paradigm shifts. *Arab J Urol*. 2021;19(3):370–375. https://doi.org/10.1080/2090598X.2021.1959260
9. Analyte C, Proprietary F. 510 (k) Substantial equivalence determination decision summary device only template [Internet]. FDA Web site. Accessed December 11, 2022. https://www.accessdata.fda.gov/cdrh_docs/reviews/k040445.pdf
10. Corona G, Rastrelli G, Monami M, et al. Body weight loss reverts obesity associated hypogonadotropic hypogonadism: a systematic review and meta-analysis. *Eur J Endocrinol*. 2013;168(6):829–843. https://doi.org/10.1530/EJE-12-0955
11. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA*. 2004;292(14):1724–1737. https://doi.org/10.1001/jama.292.14.1724
12. Residori L, García-Lorda P, Flancbaum L, Pi-Sunyer FX, Laferrère B. Prevalence of comorbidities in obese patients before bariatric surgery: effect of race. *Obes Surg*. 2003;13(3):333–340. https://doi.org/10.1381/096089203765887615
13. King WC, Chen JY, Mitchell JE, et al. Prevalence of alcohol use disorders before and after bariatric surgery. *JAMA*. 2012;307(23):2516–2525. https://doi.org/10.1001/jama.2012.6147
14. Chow A, Neville A, Kolozsvari N. Smoking in bariatric surgery: a systematic review. *Surg Endosc*. 2021;35(6):3047–3066. https://doi.org/10.1007/s00464-020-07669-3
15. Samir N, Mahmud S, Khuwaja AK. Prevalence of physical inactivity and barriers to physical activity among obese attendants at a community health-care center in Karachi, Pakistan. *BMC Res Notes*. 2011;4:174. https://doi.org/10.1186/1756-0500-4-174
16. Morley JE, Perry IIIHM, Kevorkian RT, Patrick P. Comparison of screening questionnaires for the diagnosis of hypogonadism. *Maturitas*. 2006;53(4):424–429. https://doi.org/10.1016/j.maturitas.2005.07.004
17. Boonchaya-Anant P, Laichuthai N, Suwannasrisuk P, Houngngam N, Udomsawaengsup S, Snabboon T. Changes in testosterone levels and sex hormone-binding globulin levels in extremely obese men after bariatric surgery. *Int J Endocrinol*. 2016;2016:1416503. https://doi.org/10.1155/2016/1416503
18. Machado FP, Rhoden EL, Pioner SR, et al. Weight loss through bariatric surgery in men presents beneficial effects on sexual function, symptoms of testosterone deficiency, and hormonal profile. *Sex Med*. 2021;9(4):100400. https://doi.org/10.1016/j.esxm.2021.100400
19. Morley JE, Charlton E, Patrick P, et al. Validation of a screening questionnaire for androgen deficiency in aging males. *Metabolism*. 2000;49(9):1239–1242. https://doi.org/10.1053/meta.2000.8625
20. de Freitas Junior WR, Ilias EJ, Kassab P, et al. Assessment of the body composition and the loss of fat-free mass through bioelectric impedance analysis in patients who underwent open gastric bypass. *Sci World J*. 2014;2014:843253. https://doi.org/10.1155/2014/843253
21. Ballesteros-Pomar MD, González-Arnáiz E, Maza BP-D, et al. Bioelectrical impedance analysis as an alternative to dual-energy X-ray absorptiometry in the assessment of fat mass and appendicular lean mass in patients with obesity. *Nutrition*. 2021;93:111442. https://doi.org/10.1016/j.nut.2021.111442
22. Bray GA, Heisel WE, Afshin A, et al. The Science of obesity management: an Endocrine Society Scientific Statement. *Endocr Rev*. 2018;39(2):79–132. https://doi.org/10.1210/er.2017-00253
23. Ippersiel V, Lepot A, Gruson D, et al. Hypogonadotropic hypogonadism among a population of obese men: prevalence, risk factors and reversibility after weight loss induced by bariatric surgery. *e SPEN J*. 2013;8(2):e37–e43. https://doi.org/10.1016/j.clnme.2012.12.003
24. De Lorenzo A, Noce A, Moriconi E, et al. MOSH syndrome (male obesity secondary hypogonadism): clinical assessment and possible therapeutic approaches. *Nutrients*. 2018;10(4):474. https://doi.org/10.3390/nu10040474
25. Katchunga PB, Hermans M, Bamuleke BA, Katoto PC, Kabinda JM. Relationship between waist circumference, visceral fat and metabolic syndrome in a Congolese Community: further research is still to be undertaken. *Pan Afr Med J*. 2013;14:20. https://doi.org/10.11604/pamj.2013.14.20.1258
26. Mokhtari T, Derby M, Mokhtari D, Morton J. Does waist circumference influence bariatric surgery Outcomes? *Surg Obes Relat Dis*. 2015;11(6):S126. https://doi.org/10.1016/j.soard.2015.08.191
27. Dallal RM, Chernoff A, O'Leary MP, Smith JA, Braverman JD, Quebbemann BB. Sexual dysfunction is common in the morbidly obese male and improves after gastric bypass surgery. *J Am Coll Surg*. 2008;207(6):859–864. https://doi.org/10.1016/j.jamcollsurg.2008.08.006
28. Samavat J, Facchiano E, Lucchese M, et al. Hypogonadism as an additional indication for bariatric surgery in male morbid obesity? *Eur J Endocrinol*. 2014;171(5):555–560. https://doi.org/10.1530/EJE-14-0596
29. Maseroli E, Comeglio P, Corno C, Cellai I, Filippi S, Mello T, et al. Testosterone treatment is associated with reduced adipose tissue dysfunction and nonalcoholic fatty liver disease in obese hypogonadal men. *J Endocrinol Invest*. 2021;44(4):819–842. https://doi.org/10.1007/s40618-020-01381-8
30. Rigon FA, Ronsoni MF, Hohl A, van de Sande-Lee S. Effects of bariatric surgery in male obesity-associated hypogonadism. *Obes Surg*. 2019;29(7):2115–2125. https://doi.org/10.1007/s11695-019-03829-0

31. Cooper LA, Page ST, Amory JK, Anawalt BD, Matsumoto AM. The association of obesity with sex hormone-binding globulin is stronger than the association with ageing–implications for the interpretation of total testosterone measurements. *Clin Endocrinol*. 2015;83(6):828–833. https://doi.org/10.1111/cen.12768
32. Rubinow KB. Estrogens and body weight regulation in men. *Adv Exp Med Biol*. 2017;1043:285–313. https://doi.org/10.1007/978-3-319-70178-3_14
33. Salter CA, Mulhall JP. Guideline of guidelines: testosterone therapy for testosterone deficiency. *BJU Int*. 2019;124(5):722–729. https://doi.org/10.1111/bju.14899
34. Anawalt BD, Hotaling JM, Walsh TJ, Matsumoto AM. Performance of total testosterone measurement to predict free testosterone for the biochemical evaluation of male hypogonadism. *J Urol*. 2012;187(4):1369–1373. https://doi.org/10.1016/j.juro.2011.11.095
35. Hofstra J, Loves S, van Wageningen B, Ruinemans-Koerts J, Jansen I, de Boer H. High prevalence of hypogonadotropic hypogonadism in men referred for obesity treatment. *Neth J Med*. 2008;66(3):103–109.
36. Crisóstomo L, Pereira SC, Monteiro MP, Raposo JF, Oliveira PF, Alves MG. Lifestyle, metabolic disorders and male hypogonadism - a one-way ticket? *Mol Cell Endocrinol*. 2020;516:110945. https://doi.org/10.1016/j.mce.2020.110945