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Review

Effect of surgical, medical, and behavioral weight loss on hormonal and sexual function in men: a contemporary narrative review

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***Abstract*:** This review explores the mechanisms and ramifications of weight loss achieved through lifestyle modifications, medical treatments, and bariatric surgery on testosterone levels and sexual health. Obesity significantly affects the hypothalamic–pituitary–gonadal axis in men, leading to diminished libido and erectile dysfunction. Here, we delve into the physiological disruptions caused by this imbalance and the intricate interplay of hormonal factors contributing to the dysregulation associated with obesity to comprehensively grasp the consequences of weight loss via diverse mechanisms. Lifestyle modifications involving dietary adjustments and regular exercise represent a widely employed and efficacious means of weight loss. While adherence demands discipline, our review scrutinizes various studies specifically investigating the impact of weight loss, attained through lifestyle modifications, on serum hormone levels and sexual function. Notably, several randomized controlled trials within the existing body of literature corroborate the enhancement of testosterone levels and sexual function consequent to weight loss through lifestyle modifications. The realm of medical management in addressing obesity is growing, notably propelled by the popularity of pharmacotherapy. Despite its prevalence, the current literature exploring the effects of weight loss medications on men remains insufficient. Nonetheless, we examine available studies on the medical management of obesity and its implications for sexual health, emphasizing pivotal avenues requiring further investigation. Bariatric surgery stands as an effective approach for individuals seeking substantial weight loss. Our review assesses existing literature that evaluates the impact of various surgical techniques on serum hormone levels, sexual function, and semen parameters. Despite certain limitations, the available body of evidence suggests enhancements in hormone levels and sexual function post-surgery, with semen parameters generally exhibiting minimal changes. This review critically evaluates the landscape of weight loss and its correlation with sexual function, while highlighting crucial areas necessitating future research endeavors.

Keywords: erectile dysfunction, glucagon-like peptide 1 receptor agonist, hypogonadism, obesity, testosterone

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Introduction

Obesity is a prevalent condition that is associated with multiple comorbidities and has also been shown to have a detrimental impact on health-related quality of life. For the last four decades the prevalence of obesity body mass index (BMI $\geq 30\,kg/m^2$) has increased worldwide. Between 1980 and 2014, the worldwide prevalence of obesity doubled to 13% in adults.[1] In the United States, the prevalence has steadily risen and according to Centers of Disease Control and Prevention (CDC) 2018 data, 42% of adults age

20 and older were obese.[2] While obesity was formerly regarded as primarily afflicting developed nations, this condition has transcended geopolitical boundaries, affecting developing nations as well, owing to the forces of globalization and the widespread adoption of Western dietary patterns. As the global prevalence of obesity escalates, so too do the widely acknowledged deleterious health consequences associated with it.

Obesity is intricately associated with a myriad of detrimental health outcomes that include metabolic syndrome, cardiovascular disease, various malignancies, as well as sexual and hormonal dysfunction.[3] Consequently, experts in the realms of nutrition, public health, pharmacology, and medicine have coalesced their efforts to formulate recommendations, guidelines, and therapeutic interventions aimed at ameliorating this pervasive health crisis, which some have characterized as a pandemic. In investigating obesity, its associated health outcomes, and treatments, it is important to note how obesity status is determined. Historically, BMI, calculated as weight divided by height in meters squared, has served as a prevalent means of stratifying individuals into categories that range from underweight to obese.[4] This metric has garnered widespread adoption and has been employed as a surrogate measure for prognosticating the morbidity and mortality risks attributable to heightened adiposity in individuals.[5] In addition to BMI, waist circumference has also been shown to be strongly associated with poor health outcomes, and some find it to be a superior measure of poor outcomes.[5] Waist circumference is thought to be more closely linked with visceral adipose tissue, which correlates more closely with cardiovascular outcomes.[6]

In this review, we take a deep dive into the effects lifestyle modifications, pharmacologic treatment, and surgical interventions have on weight loss, testosterone levels, and on male sexual health. In reviewing these methods for weight loss, we speculate on the potential acute and long-term effects of newer weight loss medications such as the glucagon-like peptide 1 (GLP-1) receptor agonists and their effect on sexual health.

The hypothalamic–pituitary–gonadal axis and obesity

Obesity is a chronic medical illness that significantly impacts the hypothalamic–pituitary–gonadal (HPG) axis leading to hypogonadism in males and ovulatory disorders in females.[7,8] Ovulatory dysfunction in females may be more apparent due to disruption in their menstrual cycle, whereas hypogonadism in the male is more likely to be unrecognized due to less overt and disease-specific symptomatology. Hypogonadism in men is characterized biochemically by androgen deficiency and clinically with symptoms of decreased libido, erectile dysfunction, adverse cardiovascular events, and increased fat accumulation along with decreased muscle mass.[7,9] Hypogonadism can be classified as primary or secondary. In primary hypogonadism, there is testicular dysfunction in producing an adequate testosterone level while in secondary hypogonadism, there is disruption of the HPG axis with impairment of gonadotropin release.[10] Obesity is a commonly recognized precipitant of secondary hypogonadism.

Normal physiology

Kisspeptin is a neuropeptide that is housed in the arcuate nucleus and anteroventral periventricular nuclei of the hypothalamus and is responsible for the release of gonadotropin-releasing hormone (GnRH). GnRH activates the release of gonadotropins, namely luteinizing hormone (LH) and follicle-stimulating hormone (FSH), from the anterior pituitary gland into systemic circulation. LH stimulates testicular Leydig cells to produce testosterone while the FSH along with intratesticular testosterone targets Sertoli cells for support of spermatogenesis. The majority of testosterone is bound to serum albumin or sex hormone binding globulin (SHBG) as it travels through blood circulation. Only about 1%–2% of testosterone is freely circulating in the bloodstream which is measured as free testosterone (fT). The action of testosterone can be direct via binding to an androgen receptor or indirect by conversion to active metabolites including estradiol via aromatase or dihydrotestosterone via 5-α reductase. Estradiol-binding estrogen receptors in the kisspeptin-producing KNDy neurons inhibits GnRH production which subsequently suppresses gonadotropins.[10]

Obesity impact on hormone levels

An often disregarded, but critical factor in testosterone physiology and circulating total testosterone (TT) levels is SHBG. Cooper et al.[11] reported that SHBG is significantly lower in men with obesity, which decreases TT levels more significantly

than is seen with aging. The exact mechanism of lower SHBG that is seen in obesity has not been fully elucidated. Previously, it has been speculated that lower SHBG in obesity is secondary to insulin resistance because insulin is an inhibitor of SHBG production in the liver.[12] However, recent studies report that the fat content in the liver is a strong determinant of circulating SHBG; it was recently published that as liver fat content decreases, SHBG levels increase.[13] Estradiol in men is necessary for maintaining libido, erectile function, and spermatogenesis. However, excess estradiol can decrease circulating testosterone due to negative feedback on GnRH signaling as described above.[14] Since aromatase is found in adipocytes, men with obesity have higher estradiol levels secondary to conversion of testosterone to estradiol via the aromatase enzyme found in peripheral tissue. Therefore, with lower levels of circulating SHBG and greater aromatization of testosterone to estradiol, obese men have decreased TT and fT levels compared to men with a normal BMI.[15] Paradoxically, some have reported that the relationship between obesity and hypogonadism is "bidirectional" such that men with hypogonadism have increased adiposity that in turn can contribute to exacerbation of hypogonadism.[10,16] Several studies have published that testosterone and visceral fat have an inverse relationship.[17,18] Owen et al. compared 70 men on androgen deprivation therapy for prostate cancer to a healthy controls. In this study, the authors reported that men who were on androgen deprivation therapy had a greater fat mass compared to the control group.[19] Corona et al. conducted a meta-analysis on testosterone supplementation and its impact on body composition. They reviewed 59 trials and reported that testosterone supplementation led to a reduction in fat mass as well as increase in lean body mass.[20]

Leptin and hypogonadism

Obesity is characterized by accumulation of adipose tissue, which in turn increases the release of many adipokines such as leptin. Leptin is one of the principal hormones that regulates energy expenditure and plays a role in food satiety. Leptin receptors are found in many different sites such as the hypothalamus, pituitary gland, gastrointestinal system, and reproductive organs. In obesity, there is an excess release of leptin, coined hyperleptinemia, which can lead to leptin resistance at the hypothalamic-pituitary level. Elevated leptin has been shown to reduce secretion of GnRH, which causes downstream reductions in gonadotropins and circulating levels of testosterone.[21]

Lifestyle modification induced weight loss and its effect on testosterone and sexual health

The management of obesity is multifaceted and demands effective and sustainable approaches for long-term success. Among the array of interventions available, lifestyle modifications, particularly through dietary changes and regular exercise, stand as foundational pillars in combating and controlling obesity. This section delves into the profound impact that strategic alterations in diet and the incorporation of tailored exercise regimens can have on lowering weight and indirectly on testosterone and sexual health. By exploring the intricate interplay between nutrition, physical activity, and weight management, we aim to elucidate the pivotal role that lifestyle modifications leading to weight loss have on testosterone and sexual health.

The effect of weight loss on testosterone and sexual health is generally regarded as having a neutral to positive effect. Given mixed data, Kaukua et al.[22] designed and executed a randomized controlled trial to investigate the impact of a weight loss program on sex hormones and sexual function. In this study, 38 men with a BMI $\geq 35\,kg/m^2$ were evenly randomized into two groups. The treatment group was enrolled in a 4-month weight loss program that included 10 weeks of a "very-low-energy" diet, which limited caloric intake to 525 calories/day. Over the course of 17 weeks, these individuals also attended weekly behavior modification sessions led by a clinical nutritionist and a nurse that promoted a healthy lifestyle that included exercise. The control group did not have an assigned diet or attend behavior modification sessions. Participants were followed for a total of 8 months, meaning that those in the treatment group were followed for 22 weeks after having undergone the period dedicated to the strict diet. At the end of the 8 month follow-up, the maintained weight loss was 17 kg from baseline weight in the intervention group versus 0.2 kg weight gain in the control group. The intervention group experienced a sustained and significant increase in the levels of fT and TT ($p < 0.01$, $p < 0.05$) and SHBG ($p < 0.001$), while levels of insulin and leptin were decreased ($p < 0.001$). The decrease in insulin, indicating an improvement in insulin

resistance, was notably correlated with the rise in testosterone level, with an r of −0.2. This study did not reveal any changes in sexual function in either the intervention or control group as documented using the International Index of Erectile Function (IIEF). Importantly, at the end of this study the mean BMI in the treatment group was 33.8 kg/m^2 from 39.3 kg/m^2 at baseline. It remains to be seen whether further weight reduction aiming to achieve an average BMI below 30 kg/m^2 would yield a substantial enhancement in sexual function as evaluated by the IIEF.

In another study from Finland, Niskanen et al.[23] sought to investigate the effect of rapid weight loss and sustained weight maintenance on testosterone and other sex hormones in obese men with known metabolic syndrome. Fifty-eight men with an average BMI of 36.1 kg/m^2 were placed on a low-calorie diet of 800 calories/day for 9 weeks and were then followed for at least 1 year. Patients who lost $>5\%$ of their original weight were further randomized into groups who received orlistat, an inhibitor of gastric and pancreatic lipases that prevents absorption of free fatty acids, or a placebo during the weight maintenance period. In this study, SHBG levels significantly increased during the low-calorie diet phase, decreased during the maintenance phase, but remained significantly elevated at the 12 month follow-up when compared to baseline ($p<0.001$). Free testosterone levels increased during the low-calorie diet phase and remained elevated after the 1-year maintenance period ($p<0.001$). This study shows that significant improvements in fT are possible with meaningful weight loss in obese men with metabolic syndrome. However, no conclusions can be made about how this translates into clinically meaningful changes in sexual function as this was not assessed.

The two aforementioned studies primarily enforced a strict low-calorie diet as a means of inducing weight loss. Khoo et al.[24] conducted a randomized controlled trial that combined a calorie deficit diet with varying levels of moderate intensity exercise to assess their effects on testosterone and sexual function, among other outcomes measured. A total of 90 Asian men with a BMI >27.5 kg/m^2 were randomized to perform either moderate-intensity exercise of under 150 min/week, or moderate intensity exercise of 200–300 min/week, with both groups on a calorie deficit diet of under 400 kcal below their calculated daily requirement.[24] Moderate intensity exercise of longer weekly duration resulted in significantly more notable reductions in weight (-5.9 ± 0.7 kg, -6.2%) and waist circumference (-4.9 ± 0.8 cm, -4.9%) than was seen in the group that performed less than 150 min of exercise per week. The group performing longer weekly exercise also saw significantly greater increases in testosterone levels (2.06 ± 0.46 nmol/L) and improved IIEF scores (2.6 ± 0.5 points). A subanalysis of the IIEF scores in the high-volume exercise group revealed that those who had scores that classified them in the moderate-to-severe erectile dysfunction group saw the highest mean improvement in IIEF scores, 5.3 ± 0.6 ($p<0.05$), which meets the threshold of clinical relevance.[24,25]

Similar to Khoo's 2013 study, Kumagai et al. investigated how increased physical activity and a calorie restricted diet affected serum testosterone levels in overweight and obese men. This study aimed to compare the impact of physical activity with the changes induced by a calorie-restricted diet, seeking to discern which approach yielded superior outcomes.[26] Forty-one overweight and obese men with a mean BMI of 29 ± 1 kg/m^2 completed a 12-week lifestyle modification program that included aerobic exercise training and dietary modification. Aerobic exercise training entailed participating in three 90-min weekly exercise classes and participants were encouraged to exercise by themselves at least 1 additional day per week. Participants were limited to a dietary consumption of 1680 kcal/day. At the end of the study participant's median change in number of steps per day, median change in caloric intake, and testosterone levels before and after the end of the study were analyzed. Results showed that increasing physical activity levels led to greater improvements in serum testosterone levels than more stringent caloric restriction.

A follow-up study by the same group investigated the effect of aerobic exercise on circulating testosterone levels in normal weight versus overweight/obese men.[27] Normal weight men (mean BMI of 22.5 ± 0.5 kg/m^2) and overweight/obese men (mean BMI of 27.4 ± 0.4 kg/m^2) were instructed to participate in a 12 week aerobic exercise program. At the end of the study, their physical activity was categorized as light, moderate, and vigorous based on their level of activity. At 12 weeks, only the overweight group showed a significant increase in TT and fT ($p<0.01$) and multivariate linear regression analysis showed

that vigorous physical activity was independently associated with increased serum testosterone levels in the overweight group.

Collectively, these studies shed light on the complex relationship between weight loss, physical activity, and testosterone levels, showcasing the potential of lifestyle modifications and exercise in influencing testosterone levels in overweight and obese men. While some of these studies show a positive effect in improving testosterone levels, it is difficult to ascertain how clinically relevant this increase in testosterone is, as not all studies evaluated changes in sexual function. Furthermore, additional research is warranted to determine the specific thresholds of physical activity or weight loss required to assist testosterone-deficient obese men in restoring their hormone levels and achieving clinically meaningful improvements in sexual health scores for individuals experiencing sexual dysfunction.

Medical weight management and its effect on testosterone and sexual health

As previously described, the initial modality utilized for obesity management is conservative management with lifestyle modifications that include diet and exercise. When conservative management does not result in significant changes, there are multiple pharmacological options available. Most anti-obesity medications have not been reported to impact androgen levels or improve sexual function; however, there are some specific classes of medications which may impact sex hormones such as orlistat and GLP-1 agonists.

Orlistat

Orlistat is an inhibitor of gastric and pancreatic lipase, which leads to a decrease in absorption of free fatty acids from the gastrointestinal tract. Orlistat confers an average of 6% of weight loss; however, this medication is not well tolerated due to gastrointestinal disturbances, which often leads to medication cessation.[28] There have been several publications reporting that orlistat decreased androgen levels in women with polycystic ovarian syndrome.[29] Suleiman et al.[30] evaluated the impact of orlistat in rodent models. Male mice that received orlistat were noted to have decreased leptin levels, improved sperm parameters, and decreased sperm DNA fragmentation. In this study, investigators hypothesized that incorporating orlistat in overweight/obese men may improve fertility potential. However, there is limited literature published on the impact of orlistat on androgen levels in men; therefore, additional studies are needed to draw robust conclusions.

GLP-1 receptor agonist

GLP-1 is an incretin hormone released from the gastrointestinal tract that acts on receptors found in the hypothalamus and the gastrointestinal system. This hormone functions to suppress appetite, delay gastric emptying, and decrease glucagon secretion.[31] It has a glucose lowering effect that has proved effective for glycemic control. However, in recent years, it has gained popularity for obesity management. The SCALE Diabetes Randomized Clinical Trial was a randomized double blinded study conducted between 2011 and 2013 at 126 sites in nine countries that assessed weight loss with liraglutide in patients with type 2 diabetes. Participants received either liraglutide 3.0 mg, liraglutide 1.8 mg, or a placebo for 12 weeks. The liraglutide 3.0 mg group saw a 6.0% (6.4 kg) weight loss, liraglutide 1.8 mg group had 4.7% (5.0 kg) weight loss, while the placebo group had 2% (2.2 kg) weight loss.[32] Liraglutide subsequently became the first GLP-1 receptor agonist that was FDA approved in 2014. Newer GLP-1 receptor agonists have since been approved after clinical trials showed greater weight loss with semaglutide 2.4 mg versus liraglutide 3.0 mg, 15.8% versus 6.4% weight loss, respectively.[33]

There is limited data on the impact of GLP-1 receptor agonists on the HPG axis in men. Caltabiano et al. reported that the GLP-1 receptor is found in the testes of humans and rodents as was seen with immunohistochemistry specific staining for GLP-1 receptors.[34] It has been previously published that the Ras homolog gene family (RhoA)/Rho-associated protein kinase 2 (ROCK2) signaling pathway (RhoA/ROCK2) increases oxidative stress, which reduces the contractility of cavernosum smooth muscle.[35,36] Yuan et al. showed that liraglutide improved erectile function in a rodent model with type 1 diabetes by downregulating the RhoA/ROCK2 signaling pathway, which leads to relaxation of corpus cavernosum smooth muscle cells.[37] Zhang et al. published that exenatide, another GLP-1 receptor agonist, attenuated impaired sperm quality that was present in mice with high fat diet induced

obesity.[38] Interestingly, liraglutide has been shown to ameliorate hypogonadism symptoms in mice who underwent orchiectomies.[39]

There are few studies that report an improvement in erectile dysfunction in obese diabetic men when combining GLP-1 receptor agonists and metformin. Shao et al. reported an observational prospective study of men with type 2 diabetes and obesity with hypogonadism who were on exenatide plus metformin (EXE + MET) versus glimepiride plus metformin (GLI + MET). In the group that were on EXE + MET, subjects had a significant increase in serum TT levels when compared to GLI + MET group. They further stratified the groups based on percentage of weight loss; those who had greater than 5% weight loss had a significant greater increase in serum testosterone compared to their counterparts in both groups.[39,40] A retrospective observational study was conducted on 43 men with obesity, diabetes, and hypogonadism who were receiving testosterone undecanoate and MET for a year. In those who continued to have poor glycemic control, liraglutide 1.2 mg was added during the second year; participants were asked to fill out the International Index of Erectile Function (IIEF-15) questionnaires and levels of sex hormones were analyzed. Participants who were poor responders had an increase in SHBG, TT and improvement of IIEF score compared to the group that remained on testosterone and MET alone.[40] In a 16-week prospective study, 30 men with obesity-associated functional hypogonadism were randomized to liraglutide 3.0 mg (LIRA) or 50 mg of 1% transdermal gel and sexual function and anthropometric measures were obtained. Serum testosterone levels were increased in both arms with significant improvement in sexual function. However, participants who were in LIRA group had a significant increase in LH and FSH with greater weight loss of 7.9 ± 3.8 kg compared with a 0.9 ± 4.5 kg in the transdermal gel group. The investigators concluded that liraglutide was superior to testosterone supplementation in men with obesity associated functional hypogonadism.[41] La Vignera et al. published initial results from a study of 110 men with hypogonadism, who were divided into three groups: Group A were seeking fatherhood, Group B did not seek fatherhood and Group C had already fathered children. Group A received gonadotropins (urofollitropin and human chorionic gonadotropin), Group B received liraglutide 3.0 mg and Group C received testosterone. Participants in the liraglutide groups had improvement in sperm parameters such as sperm concentration and motility compared to their baseline and Group A participants. Interestingly, participants in Group B had higher levels of TT and SHBG compared to the other groups.[42] Most of the literature on GLP-1 agonists and hypogonadism is centered on men who have diabetes. There is limited publication on men with hypogonadism who do not have diabetes—this is an area ripe for prospective research.

Surgical treatment induced weight loss

Bariatric surgery has emerged as a safe and effective, albeit invasive, approach to assist individuals in attaining substantial weight loss. Its rise in popularity stems from its effectiveness in addressing obesity and associated health conditions. Although primarily aimed at weight reduction, these surgical interventions often exert extensive impacts on diverse facets of health, such as hormonal equilibrium and sexual well-being.

Bariatric surgery has been utilized as a weight loss method for several decades, but its widespread adoption gained traction in the 1980s. A pivotal moment came in 1991 with the National Institute of Health consensus panel releasing definitive criteria for this surgical intervention.[43] These criteria established that individuals with a BMI exceeding 40 kg/m² are eligible candidates for bariatric surgery. Additionally, patients with a BMI ranging from 35 to 40, who have accompanying comorbidities exacerbated by obesity, also meet the criteria for surgical consideration.[43] These comorbidities encompass various conditions either triggered or exacerbated by obesity, including hypertension, cardiovascular disease, congestive heart failure, cardiac arrhythmias, and type 2 diabetes, among others.[43]

The selection of the appropriate surgical approach hinges upon multiple factors, including the patient's weight, overall health condition, desired weight loss goals, and any history of prior abdominal surgeries. Among the most prevalent procedures are gastric bypass, gastric banding, sleeve gastrectomy, biliopancreatic diversion, and duodenal switch, each tailored to suit individual patient needs and health circumstances.[44] These procedures are known to result in sustained long-term weight loss, albeit with varying effectiveness.

For instance, in a retrospective cohort study of Veterans Affairs bariatric surgery patients, Roux-en-Y gastric bypass (RYGB) resulted in 21% weight loss at the 10-year mark. Other studies have reported consistent long-term weight loss ranging from 10% to 30% of baseline weight.[43,45] Overall, numerous studies consistently affirm that bariatric surgery serves as a highly effective intervention for weight loss among severely obese individuals.

Bariatric surgery and testosterone

Testosterone deficiency is often seen in obese men without any other identifiable causes for dysfunction in their HPG axis. In men with obesity, HPG axis changes can occur causing hypogonadotropic hypogonadism, or secondary hypogonadism.[44,46] Testosterone deficiency in the setting of obesity can lead to a self-propagating cycle of worsening TT and fT levels that then favor reduced muscle mass and weight gain. Bariatric surgery is thought to be one of the most effective methods of weight loss, with a recent meta-analysis showing that patients achieved 71%, 60%, and 49% loss of excessive weight with a biliopancreatic diversion with duodenal switch, laparoscopic RYGB, and laparoscopic adjustable gastric band procedures, respectively.[47]

Prospective and retrospective studies have demonstrated that bariatric surgery can lead to reversal of testosterone deficiency in obese men.[46] A retrospective study published in 2014 by Samavat et al. followed a cohort of morbidly obese Italian men (BMI $>$ 40 kg/m^2) undergoing bariatric surgery. The authors sought to assess the effect of bariatric surgery on waist circumference, BMI, and testosterone levels in morbidly obese men stratified according to gonadal state. Participants with a TT $<$ 8 nmol/L were classified as hypogonadal. At 12 months postoperatively, TT and fT were sufficiently increased in 93% of the hypogonadal men to reclassify them as eugonadal, illustrating the significant impact weight loss surgery can have toward improving hormonal function.[44]

Several other studies have shown that men undergoing bariatric surgery experience improvements in their serum testosterone levels. A group in Spain followed 12 patients and found a 10 nmol/L increase in TT 18 months after surgery.[48] Abouelgreed et al.[49] followed 54 men after sleeve gastrectomy and found an approximately 10 nmol/L increase in TT with an associated increased in SHBG. Of note, both studies also showed an increase in fT, which is an important facet in comprehensively assessing hormonal parameters.

Finally, a recent meta-analysis of 28 studies examined the effects of bariatric surgery on sex hormone production. The authors found that there was a 7.5 nmol/L (216 ng/dL) increase in TT and 22.6 pmol/mL decrease in estradiol after bariatric surgery, both significant changes.[46] LH, FSH, and SHBG were all increased, with calculated fT also being increased in the meta-analysis after surgery. These results suggest that the considerable weight loss associated with bariatric surgery leads to a global normalization of the sex hormone milieu in men with preoperative hormonal dysfunction.

Bariatric surgery and sexual health

With an observed increase in testosterone identified as an effect of bariatric surgery, several studies have examined the effects these procedures on erectile function and sexual health. A decrease in the inflammatory milieu as a result of the loss of adiposity combined with increased testosterone levels is hypothesized to improve sexual function in men.

In a retrospective analysis of twelve men, Minambres et al. found that the erectile function domain of the IIEF improved by four points at 6 months after their surgery, which was statistically significant.[48] A separate study limited to sleeve gastrectomy patients found statistically significant increases in sexual function, erectile function, sexual satisfaction, and overall satisfaction domains of the IIEF.[49] In a meta-analysis of five studies that utilized the erectile function domain of the IIEF, the authors found a statistically significant improvement in the patient self-reported outcome, although the magnitude was small with an average improvement of only 0.5 points.[46] It stands to reason that the profound impact of bariatric surgery on weight loss, decreased adiposity and sex hormone function does confer some improvement to male sexual function. While the mechanism has not been manifested in the literature, the finding is clinically important and may provide further compelling rationale for men considering bariatric surgery.

Semen quality after bariatric surgery

The effects of bariatric surgery related weight loss on semen parameters have also been examined. Large population data have revealed a global decline in semen quality over the past 50 years, coinciding with the drastic acceleration of the obesity epidemic.[50] It is unclear if the aforementioned hormonal axis changes promoted by obesity are partially mediating the decline in semen quality. Conversely, it has been shown that weight loss from lifestyle modifications improves semen quality.[51] Whether the lifestyle modifications themselves, or rather the weight loss is driving this observation is not fully elucidated.

This concept has driven research into understanding whether correcting obesity with bariatric surgery can result in improved semen parameters. A meta-analysis produced by a Canadian group specifically investigated the change in semen parameters after bariatric surgery.[46] In their analysis of 28 studies of patients undergoing bariatric study, three had suitable data on sperm parameters for analysis, and together there was no significant effect on sperm volume, concentration, motility, morphology, or progressive motility.[46] Importantly, the authors also raise the concern that there have been important reports of worse sperm parameters after bariatric surgery, which may be in part to the nutritional deficiencies seen as a result of the digestive effects of the surgery.[52–54]

A recent meta-analysis solely evaluating semen parameters after bariatric surgery also found inconclusive evidence of an effect, either positive or negative, on sperm parameters in the six studies that met their inclusion criteria.[55] The authors in this article found significant heterogeneity in the literature, and specifically, very small samples sizes ranging from 3 to 46. Therefore, the authors concluded it would be premature and not statistically sound to draw definitive conclusions from the available literature.

Indeed, further prospective cohort series and clinical trials should evaluate not only changes in semen parameters but also changes in other factors such as serum levels of known important vitamins, minerals, inflammatory markers, and reactive oxygen species (ROS). It is well known that chronically obese individual exhibit higher levels of ROS and that weight loss has the potential to improve levels of oxidative stress. However, it is not well known how bariatric surgery impacts the level of oxidative stress and its resultant impact on semen parameters.[56,57] It may be that patients seeking weight loss to see an improvement in sperm quality should be guided toward lifestyle changes or medical management rather than bariatric surgery based on the above literature.

Future directions

As the multifaceted relationship between obesity, testosterone levels, and sexual health continues to unfold, future research endeavors should aim to delve deeper into the nuanced interplay of these elements. Investigating the mechanisms underlying how weight loss, whether through lifestyle modifications, pharmacological interventions, or surgical procedures, influences the HPG axis is pivotal. Understanding the precise mechanisms by which weight loss impacts sex hormones like testosterone, and subsequently, sexual function, could pave the way for tailored interventions. Further exploration into specific thresholds of weight loss or physical activity needed to significantly improve testosterone levels and restore sexual health in individuals experiencing hypogonadism due to obesity remains an area ripe for investigation. Longitudinal studies with diverse cohorts could elucidate the sustained effects of weight loss interventions on hormone levels and sexual function over time, shedding light on the long-term implications for clinical practice.

Additionally, considering the potential bidirectional relationship between obesity and hypogonadism, research exploring the impact of hormonal therapies on weight management in individuals with testosterone deficiency might be promising. Investigating how treatments targeting testosterone deficiency affect adiposity and metabolic parameters could offer a comprehensive understanding of the interplay between hormone levels and obesity, thus guiding more holistic treatment approaches. Furthermore, given the inconclusive evidence regarding the effects of bariatric surgery on semen parameters, comprehensive studies evaluating nutritional factors post-surgery and their impact on reproductive health would be valuable. Understanding the potential trade-offs between weight loss procedures and reproductive health could inform clinical decision-making and patient counseling.

Clinical commentary

The research highlighted in this narrative review outlines the interplay between obesity and weight loss and its effects, or lack of thereof, on testosterone levels, sexual health, and sperm parameters. Weight loss via lifestyle modifications, such as implementing a calorie restricted diet with moderate intensity exercise, can lead to improvements in testosterone levels and sexual health. In men seeking to improve their overall health, including sexual function, working closely with a provider to set individualized goals and monitoring progress is essential. This is particularly important when utilizing weight loss medications or bariatric surgery as part of a personalized treatment plan. During the active weight loss phase, ordering a lab panel that includes gonadotropins and testosterone levels may be warranted based on patient reported symptoms and a clinical evaluation. There appear to be no current contraindications to attempting to conceive while on a GLP-1 agonist. However, if a couple were to be experiencing issues with infertility while on a GLP-1 agonist, we recommend they be evaluated according to guidelines set up by organizations such as the American Urologic Association and American Society for Reproductive Medicine.

Conclusion

In conclusion, obesity's intricate relationship with testosterone levels and sexual health necessitates ongoing research to delineate effective interventions. Lifestyle modifications, pharmacological treatments, and surgical interventions each present potential avenues for addressing obesity and its associated hormonal imbalances. However, while studies highlight the positive impact of weight loss on testosterone levels and sexual function, there remain nuances and uncertainties regarding the clinical significance of these changes. The potential of lifestyle modifications, including dietary changes and exercise, to improve hormonal imbalances underscores the importance of non-invasive approaches in managing obesity-related hypogonadism. Pharmacological interventions and surgical procedures also demonstrate promise, yet their long-term effects on reproductive health warrant further investigation. Specifically, new weight loss pharmaceuticals and interventions must each be individually studied to understand their impact on sexual health and function given the intricate relationship between different hormones, other circulating factors, and sexual function. Overall, continued research efforts exploring the interconnections among obesity, hormone levels, and sexual health are essential for developing tailored interventions and optimizing patient care in this complex domain.

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Author contributions

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