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Reconstructive

Oxidative Stress in Postbariatric Patients: A Systematic Literature Review Exploring the Long-term Effects of Bariatric Surgery

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Background: The present study investigates the impact of oxidative stress after bariatric surgery in patients with obesity. This field of study has gained great interest in recent years due to the role that oxidative stress plays in metabolic diseases. Obesity, by itself, can generate an increase in reactive oxygen and nitrogen species, intensifying cellular damage and promoting the progression of adverse metabolic conditions. In this context, bariatric surgery emerges as a candidate capable of modifying oxidative stress biomarkers, facilitating the patient's metabolic recovery.
Methods: A systematic review was carried out, identifying 30 studies found in databases such as PubMed, Scopus, Web of Science, and Google Scholar. It looked at the link between oxidative stress and recovery after bariatric surgery in patients. The selection of studies was based on the measurement of oxidative stress biomarkers before and after surgical intervention.
Results: The results reveal a significant decrease in oxidative stress biomarkers after bariatric surgery. However, a notable variability in antioxidant activity is observed between different patients, as well as a significant influence of comorbidities.
Conclusions: Bariatric surgery is postulated as an effective intervention in reducing oxidative stress in patients with obesity, enhancing antioxidant activity and improving patient recovery. This finding highlights the importance of considering oxidative stress management as an integral part of postoperative care, suggesting the need to implement complementary treatment strategies to optimize health outcomes. *(Plast Reconstr Surg Glob Open 2024; 12:e5646; doi: 10.1097/GOX.0000000000005646; Published online 21 March 2024.)*

INTRODUCTION

Bariatric surgery has emerged as an alternative treatment option for obesity. Obesity is defined as the excessive accumulation of lipids, operationally established by a body mass index (BMI) ≥ 30kg/m^2, resulting from an imbalance between high caloric intake and reduced energy expenditure.[1] The goal of bariatric surgery is to achieve a reduction in body weight, mainly in abdominal obesity, which also requires lifestyle changes and possibly pharmacological treatment, thus becoming part of a multidisciplinary approach.[2]

Under this framework, surgical interventions that focus on reversing obesity have evolved since their inception. Currently, Roux-en-Y gastric bypass, sleeve gastrectomy, and gastric bands are the most commonly selected bariatric procedures for obesity treatment.[3,4] However, it is important to note that the success of these interventions is dependent on several factors, among which oxidative stress has scarcely been explored, although at the molecular level, a considerable influence on tissue repair processes has been suggested.[5–7]

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Oxidative stress, characterized by an excessive increase in reactive species such as reactive oxygen species (ROS) or reactive nitrogen species (RNS), is recognized as a determining factor in the development and progression of various metabolic diseases such as obesity, insulin resistance, type 2 diabetes mellitus, and cardiovascular diseases.[8–10] Under physiological conditions, ROS and RNS play a critical role in cellular homeostasis and intracellular signal transduction pathways, acting as second messengers.[11,12] However, dysregulation of oxidative-antioxidant systems leads to the development of oxidative stress, which is associated with metabolic dysregulation and oxidative damage due to the increased generation of end products of lipid, DNA, and protein oxidation.[11,13–15]

The relationship between oxidative stress and metabolic diseases such as obesity could be an indicator of disease progression; thus, it is relevant to study the link between the two in detail.[10–18] Oxidative stress has been observed to be elevated in people with metabolic diseases, especially in adipose tissue and immune cells.[17] A higher concentration of ROS has been found in obese patients, which is related to alterations in mitochondrial function due to excess nutrient intake.[17]

Researching the impact of oxidative stress in this context is crucial for achieving comprehensive care and improving long-term outcomes in patients undergoing bariatric surgery. This study aimed to determine the role of oxidative stress in the postsurgical period in patients undergoing bariatric surgery.

Takeaways

Question: What is the status of oxidative stress in patients undergoing bariatric surgery?

Findings: There are changes in the different biomarkers of oxidative stress in the period after bariatric surgery. These changes are reflected in the success of the therapeutic alternative and the recovery of the body that has undergone the stress of the surgical procedure.

Meaning: The integration of the assessment and consideration of oxidative stress biomarkers will determine important guidelines for achieving optimal recovery and addressing obesity effectively.

METHODOLOGY

Search methodology (see Fig. 1):

1. Keywords and related terms: “oxidative stress,” “obesity,” “bariatric surgery,” and “reactive oxidative species.”
2. Combinations of keywords AND, OR, NOT related terms: Boolean operators (AND, OR, and NOT) were used to combine keywords and related terms in more specific search queries.
3. Searches were conducted in relevant scientific and bibliographic databases, such as PubMed, Web of Science, Scopus, and Google Scholar. Filters and advanced search options, such as date ranges (from 2017 to 2023), document types (research articles, reviews, meta-analyses), and specific research fields

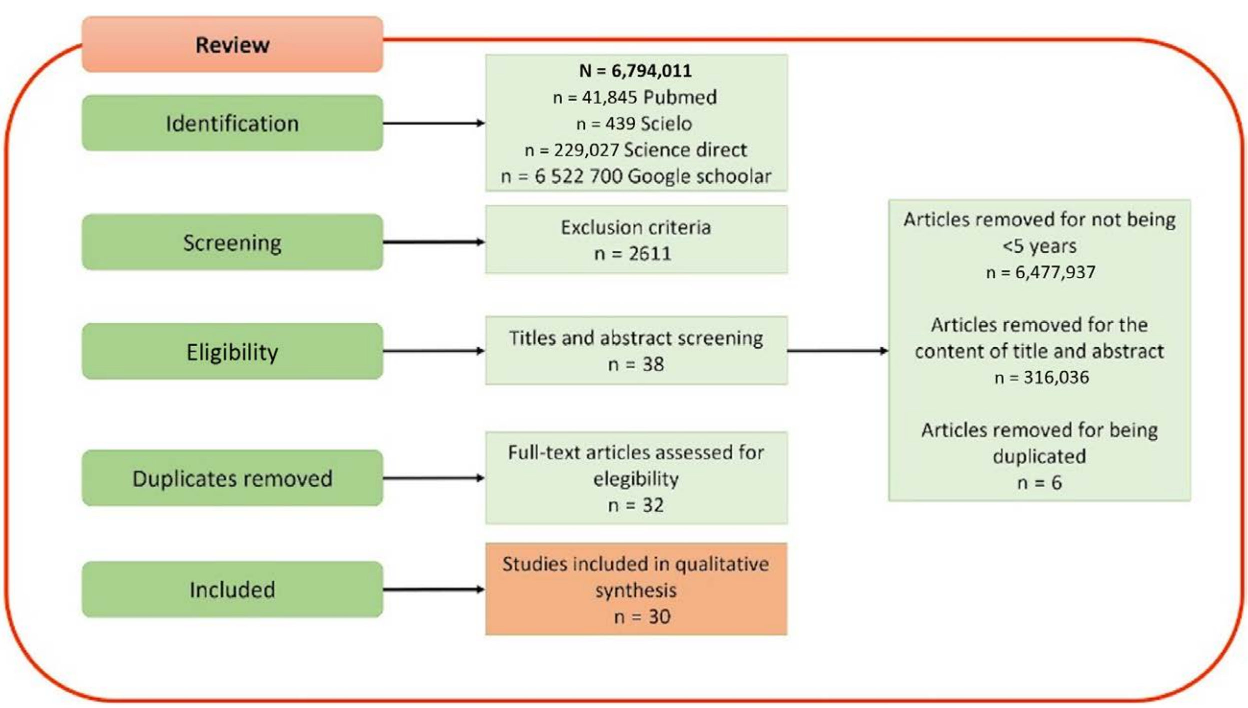

Fig. 1. Flow chart of the literature search according to PRISMA guidelines, showing the four search engines used together with the inclusion and exclusion criteria in the order they were applied and the total number of resulting articles.

(medicine, biology, biochemistry), were applied to refine the results and obtain more relevant studies.

4. Evaluation and selection of studies: The inclusion criteria were studies evaluating oxidative stress in the context of obesity; bariatric surgery described in clinical trials, meta-analyses or systematic reviews; or experiments in human and animal patients. Exclusion criteria included studies unrelated to the research questions, studies with nonrigorous methodologies, or duplicate studies.

The results of this search and subsequent analysis of the selected studies provide a solid basis for the discussion and conclusions presented in the systematic review. (**See table, Supplemental Digital Content 1,** which displays the Boolean operators used in this search. **http://links.lww.com/PRSGO/D89**).

RELATIONSHIP BETWEEN OBESITY AND OXIDATIVE STRESS

Obesity is a chronic endocrine disease of multifactorial origin (social, behavioral, psychological, metabolic, cellular, and molecular factors), where there is an increase in lipid reserves in adipose tissue. It is clinically manifested as a disproportionate increase in body weight in relation to height, a characteristic used by the World Health Organization to establish that a BMI greater than 30 is considered obesity.[19–24]

In the context of obesity, a close association between inflammation and oxidative stress has been observed. However, the mechanisms and their importance are not completely clear.[20–25] In white adipose tissue, mitochondrial oxidative stress and ROS accumulation affect the endocrine and metabolic functions of adipose cells. Biochemical mechanisms have been identified through which obesity can induce oxidative stress, such as NADPH Oxidase activation, oxidative phosphorylation, glyceraldehyde autooxidation, protein kinase C activation, polyol and hexosamine pathways, hyperleptinemia, decreased antioxidant defense, chronic inflammation, and postprandial ROS generation.[23–25] Therefore, obesity is associated with increased oxidative stress due to increased formation of ROS and decreased serum concentrations of antioxidant micronutrients despite high dietary intake.[17]

BARIATRIC PROCEDURE AND ITS RELATIONSHIP WITH OXIDATIVE STRESS

Types of Bariatric Surgery

The constant improvement of surgical intervention techniques in the field of obesity has expanded its scope beyond the reduction of BMI, allowing for the impact on various metabolic alterations related to obesity. Therefore, two main categories of bariatric surgery can be currently considered, whereby the group of restrictive techniques includes, for example, sleeve gastrectomy and the gastric band, whereas the group of poorly absorbent restrictive techniques includes the Roux-en-Y gastric bypass[3,26,27] (Fig. 2).

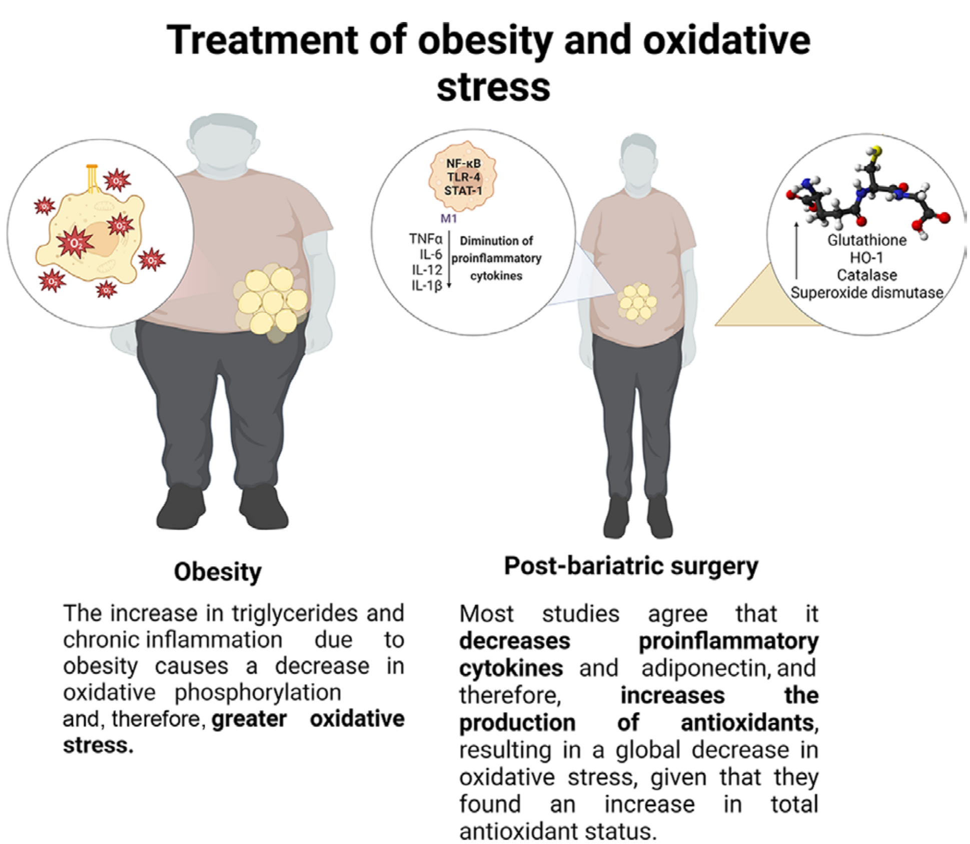

Fig. 2. Oxidative stress during obesity, postbariatric surgery.[10,45]

Roux-en-Y gastric bypass is a reversible procedure that involves the creation of a pouch in the stomach combined with a gastroenterostomy to the intestine. This enterostomy avoids the duodenum and a variable length of the jejunum, which causes a reduction in the functional size of the stomach and a restriction of nutrient absorption in the small intestine; likewise, the gastric band is a reversible procedure consisting of the surgical insertion of an eccentric constriction ring at the gastric *fundus* level. For sleeve gastrectomy, this is a nonreversible process, consisting of the longitudinal section of the stomach, with preservation of the lower esophageal sphincter and pylorus, which leads to volume reduction of the gastric cavity.[26]

Preoperative Evaluation

Given the patients' obesity condition involved in the preoperative state, their preoperative evaluation results in a determining challenge of the expected success, especially regarding high-risk patients who, in turn, tend to benefit the most after undergoing this surgical intervention.[28]

Preoperative evaluation limits or decreases the operative risk by correcting the optimizable risk factors before surgery, guiding the patient through a less risky surgical procedure, and/or referring the patient to a center with a more adequate technical capacity and even advise against the operation if the risks are greater than the expected benefits. Determining factors included advanced age, male sex, smoking habit, nutritional factors such as weight loss before the intervention, hypoalbuminemia, and the presence of comorbidities such as obstructive sleep apnea syndrome, diabetes, insulin resistance, nonalcoholic fatty liver disease, steatohepatitis, gastroesophageal reflux disease, and cardiovascular diseases.[28,29]

With regard to obesity, particularly as a risk factor in the preoperative evaluation, the evidence suggests that the maximum weight observed during the obesity period is of greater influence than the weight at the time of the consultation, and some formulas that allow estimates to be made considering the obesity parameter are the Framingham equation 2008-body mass index; the PROCAM model (Münster Heart Study), which includes lipid parameters that are not in the Framingham equation; and the European Coronary Systematic Risk (SCORE) evaluation model that evaluates the risk of cardiovascular mortality at 10 years in individuals between 40 and 65 years of age, taking into account total cholesterol, smoking, and systolic blood pressure.[28] Additionally, preoperative evaluation through gastroscopy is suggested mainly in candidates for sleeve gastrectomy and partially in those for Roux-en-Y gastric bypass.[30]

In terms of postoperative risk assessment, the Obesity Surgery Mortality Risk Score (OS-MRS) is considered a useful tool based on the conditions of BMI greater than 50 kg per m^2, male sex, systemic arterial hypertension, thromboembolic disease, and age greater than 45 years. In relation to this evaluation, classification of postoperative complications is equally useful; however, only thromboembolic and gastrointestinal fistula risks have been studied more thoroughly, leaving a wide information gap that requires further study in terms of complications and factors that affect the course and recovery during the perioperative period.[28]

POSTBARIATRIC PATIENTS AND OXIDATIVE STRESS

In postbariatric patients, a significant deficiency of carotenoids, retinol, and tocopherols in the serum or plasma has been reported; therefore, adequate supplementation of these micronutrients has been proposed as a strategy to reduce this deficiency caused by malabsorption after bariatric surgery; however, adherence to treatment is less than 30% at 6 months after intervention.[17]

It has been reported that in the 4-year period after bariatric surgery, the overall plasma indicator of oxidative stress [total antioxidant status] increased by 19%, whereas the other thiobarbituric acid reactive substances indicators showed no significant changes compared with the preoperative status.[10] In particular, the postoperative course in patients with obesity and metabolic syndrome is more challenging because, unlike in those with obesity, a reduction in antioxidant status is observed in a period of up to 1-year postintervention.[31] In this context, peroxynitrite and S-nitrosothiols have been proposed as differential markers for the presence of metabolic syndrome associated with oxidative stress with high specificity and sensitivity.[9] Another study suggested that total antioxidant capacity, total oxidant status, oxidative damage to proteins, advanced glycation end products (AGEs), advanced oxidation protein products (AOPP), and lipids such as F2-isoprostanes and hydroxyalkenals, such as 4-hydroxynonenal, are elevated in obese patients regardless of the presence of metabolic syndrome and gradually decrease after bariatric surgery.[32]

The effects on antioxidant activity depend on the type of surgery, with a drastic reduction in AOPP observed 6 months after the Roux-en-Y Gastric Bypass procedure compared with sleeve gastrectomy.[32] Despite this, it has also been observed that in the first 6 months after bariatric surgery, there are clinical and metabolic improvements that slowly go into remission, as some metabolic and nutritional alterations reappear within 1 year after surgery.[33,34] Oxidative stress regulation in the perioperative period, addressed by the methylation analysis of patients' genomes with obesity and normal weight, suggests the influence of methylation on *TPP2, PSMG6, ARL6IP1,* and *FAM49B* genes in the preintervention state and the differentially methylated *ZFP36L1* and *USP32* genes after bariatric surgery; gene ontology analysis showed that these genes were enriched in biological functions related to adipogenesis, orexigenesis, insulin metabolism pathways, and oxidative stress.[35]

ANIMAL STUDIES

Studies linking oxidative stress in humans and animals are diverse; however, most of the studies that have had an impact on the understanding of these alterations are based on animal models because, given their complexity and relative handling ease, studies on oxidative stress and physiological mechanisms in an obesity model are compatible and accessible for their study.[36]

Multiple animal models have been used to study oxidative stress and its effects on metabolic diseases, such as obesity, at different stages. For example, a study conducted in models of young sows with obesity found that maternal obesity induces placental dysfunction and intestinal microbial dysbiosis. In addition, the offspring had a decrease in birth weight, showing an increase in oxidative damage and inflammatory response in the placenta of obese sows, as evidenced by an increase in placental ROS, protein carboxyl, and interleukin-6 (IL-6), indicating that maternal obesity during late pregnancy increases oxidative damage in the placenta, induces mitochondrial dysfunction, and decreases the birth weight of newborns.[37–40]

In other schemes with animal models focused on the gender role in diet-induced obesity in an animal model, highlighting proteomic changes in skeletal muscle, showing that oxidative stress and metabolic alterations differ by gender, with male mice exhibiting more pronounced changes such as muscle stiffness and mitochondrial dysfunction, whereas women seem to be better able to use excess fatty acids as an energy source, exhibiting few metabolic changes. The early origins of metabolic syndrome have also been examined, identifying oxidative stress as an underlying early origin mechanism with nutritional imbalances, the main ones being adverse maternal conditions and exposure to chemicals. Finally, a third study examined intermittent fasting as a weight-loss strategy, presenting evidence from both animal models and clinical trials. Although the results vary, some animal models indicate that intermittent fasting may reduce oxidative stress, improve cognition, and delay aging; however, more research is needed to assess its effectiveness and long-term sustainability.[40–43]

The postbariatric patient and animal models of this intervention contribute to modifications in the course of oxidative stress processes, such as an increase in the release of antiinflammatory IL-10, superoxide dismutase, and GSH, associated with the improvement of adipocyte endocrine function and an increase in HDL cholesterol circulation. Additionally, there is an enhancement in insulin sensitivity and a reduction in triglycerides, along with a decrease in lipid release, such as malondialdehyde and oxidized low-density lipoprotein, which is associated with the decrease in lipid peroxidation markers, protein carbonylation, AOPP, and uric acid.[32,34] Other positive implications include an improvement in the M2/M1 ratio, with a tendency toward greater M2 polarization of macrophages and the activation of peroxisome proliferator-activated receptor gamma α (PPARα), with the latter being associated with an enhancement of renal function in obesity models.[32]

The changes mentioned in the postbariatric surgery process regarding the oxidative stress state are suggested to be related to alterations in gene expression, particularly in the genes ZFP36L1, whose methylation decreased while their expression increased, and USP32, whose methylation increased while their expression decreased in the leukocyte cell line. The role of ZFP36L1 in adipogenesis regulation through the control of PPARG2 expression is noteworthy.[35]

Despite the benefits that bariatric surgery offers in relation to oxidative stress, factors such as diet can have a positive or negative impact, sometimes even more significant than the surgery itself. Therefore, it is crucial to monitor this aspect after the intervention. For instance, the total antioxidant capacity decreases with higher consumption of ultra-processed foods, and diets rich in fats, red meat, salt, and sugar are associated with increased peroxidation. Conversely, balanced supplementation with antioxidants improves redox balance and alleviates the negative effects of obesity-induced oxidative stress, even in the postsurgical phase.[32]

DISCUSSION

Increased Oxidative Stress before Surgery in Patients with Obesity

The relationship between obesity and oxidative stress is determined by two main factors: is the production of ROS as a consequence of high levels of intracellular triglycerides, which are known to inhibit the movement of adenosine nucleotides, causing an increase in adenosine triphosphate and a decrease in adenosine diphosphate in the mitochondria, thereby decreasing the rate of oxidative phosphorylation and triggering the release of electrons and free radicals.[44–46]

Second, there is a chronic inflammation process triggered by the presence of ROS and the metabolism itself, which is present in adipose tissue. Tumor necrosis factor, macrophage inflammatory proteins 1α, 1β, and 2α (MIP-1α, MIP-1β, and MIP-2α), monocyte chemotactic protein 1, and antiinflammatory factors such as IL-1 receptor antagonist and interleukin 10 (IL-10) have been identified, whereby the above leads to macrophage infiltration in adipose tissue, and it is worth noting that the circulating levels of IL-1 receptor antagonist and IL-10 are elevated in obese individuals.[46–49]

The increase in ROS has been implicated in the development of chronic diseases. For example, in cardiovascular diseases, the rise in ROS levels leads to a decrease in nitric oxide availability and vasoconstriction, promoting arterial hypertension. ROS negatively influence the handling of myocardial calcium, causing arrhythmias, and contribute to cardiac remodeling by inducing hypertrophic signaling and apoptosis. Finally, it has also been demonstrated that ROS promote the formation of atherosclerotic plaques.[50]

REDUCTION OF OXIDATIVE STRESS AFTER BARIATRIC SURGERY IN PATIENTS WITH OBESITY

Postbariatric

Owing to the drastic increase in the obesity rate and the consequences on mental health, the demand for bariatric surgery has also increased. Under this framework, in 2020 Min et al measured the levels of adipokines (adiponectin, leptin), inflammatory cytokines (C-reactive protein, IL-6, and IL-10), and oxidative stress markers (thiobarbituric acid-reactive substances and total antioxidant status) before and 1 month, 6 months, and 4 years later. The study monitored 10 patients who underwent sleeve gastrectomy, two patients who underwent Roux-en-Y gastric bypass, and one patient who underwent laparoscopically adjustable gastric band. They found a linear decrease from 60.7 pg/mL at the preoperative stage to 40.4 pg/mL at one month. 33.7 pg/mL at 6 months and 32.1 pg/mL at 4 years of leptin ($P = 0.001$). Decrease in plasma cytochrome P450 reductase concentration from 11.4 ng/mL at the preoperative stage to 3.7 ng/mL at 1 month, 5.8 ng/mL at 6 months and 2.8 ng/mL at 4 years ($P = 0.003$) and IL-6 decreased significantly at 4 years compared with the preoperative value (73.8% decrease, $P = 0.009$).[48]

Finally, body contouring surgery is the final link in the comprehensive treatment of obese patients because it improves quality of life after bariatric surgery.[51–53] We consider that the increase in oxidative stress in this group of patients could be associated with the development of complications. Nevertheless, there are currently no studies in this regard.

CONCLUSIONS

The importance of oxidative stress biomarkers has been described in the postsurgical period for patients undergoing bariatric surgery. It is worth noting the variability in indicators of antioxidant activity and the influence of comorbidities. These indicators provide a valuable tool for monitoring patients with obesity, in whom the oxidative stress process undergoes changes after bariatric surgery. These changes are reflected in the success of the therapeutic alternative and the recovery of the body that has undergone the stress of the surgical procedure.

In conclusion, it cannot be categorically stated that ROS and RNS decrease health, but a relationship between oxidative stress and certain health issues is suggested, particularly in patients with obesity and metabolic syndrome. Therefore, it is suggested that in the future, the integration of the assessment and consideration of oxidative stress biomarkers will determine important guidelines for achieving optimal recovery and addressing obesity effectively.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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