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Relationship to Bariatric Surgery and their Gastrointestinal Hormones: how we Weight Loss?

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ABSTRACT

Obesity is a disease related to severe metabolic comorbidities due to the high accumulation of body fat. In the context of this pandemic, bariatric surgery is the most effective treatment for the long-term resolution of the disease, having both structural and anatomic and hormonal effects on the gastrointestinal tract. The hormones analyzed in this review are cholecystokinin, secrete, gastrin, glucagon-like peptide 1 (GLP-1), peptide YY, pancreatic polypeptide, leptin, adiponectin, ghrelin, glucose, cholesterol, gastric inhibitory peptide, insulin, and glucagon. After bariatric procedures, changes in vitamins and micronutrients are also observed, which can lead to anemia, changes in coagulation, bone metabolism, neurological, and immunological deficiencies.

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Introduction

Obesity has become a severe global pandemic, bringing relevant impacts to the patient's health, as it is related to the development of multiple serious metabolic comorbidities. It can also be attributed to multiple factors, including genetic inheritance, bad eating habits, lack of physical training, a disorder in the activity of the hypothalamic-gastrointestinal axis disorder, neuropsychic factors, and advanced age, proving to be a heterogeneous and complex disease [1].

Obesity is characterized by a high energy intake, resulting in excessive accumulation of body fat. It is usually evaluated by the body mass index (BMI), which is calculated by dividing the weight (W), in kilograms (Kg), by the height in square meters (m2), assuming classifications as overweight (BMI ≥ 25 kg/m2) and obesity (BMI ≥ 30 kg/m2), which stand out as globally relevant health conditions in modern society [2].

Excess body adiposity is one of the main risk factors for several metabolic diseases as arterial hypertension, chronic inflammation, type 2 diabetes mellitus (T2DM) and insulin resistance. Thus, obesity can trigger cardiovascular complications, obstructive sleep apnea, idiopathic intracranial hypertension, non-alcoholic fatty liver disease and steatohepatitis, gastroesophageal reflux, kidney dysfunction, in addition to mental disorders [3].

Aiming to solve these adverse health conditions, several weight loss treatments have emerged, including lifestyle modification, medication, and surgery [4]. As much as all these treatments can offer good long-term results, drug therapies can bring some adverse effects, such as hypoglycemia, liver functional impairment, and gastrointestinal symptoms. Considering the available therapies, bariatric surgery is the most effective long-term treatment for morbid obesity and T2DM, and insulin resistance. Thus, the techniques of removing part of the stomach or volumetric restriction, applied to gastroplasty, can maintain long-term weight loss, eliminating 50% or more of excess body weight [5].

Gastric Bypass or Roux-en-Y Intestinal Bypass Gastroplasty (Capella-RYGB) is a surgical treatment technique for obesity and metabolic diseases that combines gastric restriction (restriction in the ability to receive food through the stomach) and caloric malabsorption, altering the flow of nutrients and bile through the small intestine. Sleeve Gastrectomy or Vertical Gastrectomy (SG) is a restrictive operation that involves a longitudinal resection of the stomach, creating a narrow gastric pouch along the lesser curvature [6].

The weight loss achieved after bariatric surgery is due to the reduction in general food consumption, however, it is potentiated by changes in eating behavior, early satiety, and less preference for fatty and high-sugar foods, in addition to gastrointestinal motility adjustments (GI) [1]. It is important to highlight the impact on gastrointestinal and pancreatic hormonal changes as the GI tract is

the largest endocrine organ in the body and produces a variety of hormones, including incretins that regulate insulin release. Thus, these changes in incretin secretions after bariatric surgery play a role in promoting long-term weight reduction and improving glucose metabolism [3]. Several GI hormones have been shown to be involved in the regulation of energy balance and glucose homeostasis, including cholecystokinin (CCK), intestinal peptide hormone (PYY) secreted by endocrine L cells of the distal small intestine and large intestine, peptide-1 (GLP-1), glucagon-like peptide-2 (GLP-2), glucose-dependent insulinotropic hormone or gastric inhibitory polypeptide (GIP), oxyntomodulin (OXM), ghrelin, glicentin, and neurotensin [2].

Based on the increasement of obesity's global prevalence, it is imperative to look for the improvement of bariatric procedures and more effective treatments to a better quality and lifestyle. Therefore, it is important to identify the underlying mechanisms responsible for the weight loss process after bariatric surgery to provide safer, more effective, and less invasive treatments [1].

In this regard, some mechanisms that interfere in the process of adiposity reduction after bariatric surgery will be addressed in this review, including neuromodulation and hormonal regulation, thus proposing a critical and thoughtful analysis of the influence of metabolic changes in patients undergoing for surgical interventions: Gastric Bypass and Vertical Gastrectomy.

Objective

To determine the metabolic changes in patients after bariatric surgery (Gastric Bypass and Gastric Sleeve) and the impact of the surgery on them.

Discussion

Obesity is characterized by the excessive accumulation of body fat in the individual, which can be measured by the body mass index (BMI). According to the World Health Organization, patients with a BMI greater than 35 kg/m2 are classified as morbidly obese and, in this case, bariatric surgery is proposed as a conspicuous and effective therapeutic option [2].

Nowadays, considering the various surgical techniques applied to control excess weight, Gastric Bypass (RYGB) and Vertical Gastrectomy (SG) deserves to be highlighted, as they demonstrate more expressive results in the weight loss process and relevant impacts on the control of comorbidities associated, as in DMT2. Morbid obesity can be defined as a body mass index (BMI; measured as weight in kilograms divided by height in meters squared) of 35 kg/m2, being considered a global epidemic in all age groups [6]. Bariatric surgery is the most effective treatment for morbid obesity when lifestyle changes and drugs results are no longer satisfactory.5 Obesity predisposes to other comorbidities, such as cardiovascular disease, type 2 diabetes, obstructive sleep apnea, non-alcoholic fatty liver disease, steatohepatitis, orthopedic diseases, and psychiatric disorders [6].

Gastric Bypass or Roux-en-Y Intestinal Bypass Gastroplasty (Capella-RYGB) is a mixed technique (restrictive and malabsorptive) that has been considered the standard of bariatric surgery since it has high levels of satisfaction, excellent control of associated diseases, excellent long-term weight loss maintenance. RYGB creates a small gastric pouch and attaches it to the middle jejunum, bypassing most of the stomach and proximal jejunum [7]. Malabsorption of nutrients is one of the explanations for the weight loss achieved such as biliopancreatic diversion/duodenal switch (DBP), with about 25% of protein and 72% of fat not being absorbed [8].

The Sleeve Gastrectomy (SG) procedure is a restrictive operation that involves resection of 2/3 of the stomach, including the bottom of the stomach, which is the ghrelin-producing region. Thus, during the SG, in addition to the decrease in stomach volume, hormonal and neuromodulation changes occur involving the feeling of satiety, which will lead on the reduction of the volume of food consumption. This bariatric procedure has become the most applied [7].

According to Lautenbach et al., after SG or RYGB, an improvement in glucose metabolism was observed at the beginning of the postoperative period before any significant weight loss. Early changes in postoperative gastrointestinal hormones, as well as beneficial changes in pancreatic peptide hormones, such as insulin and glucagon, demonstrate a relevant impact on the long-term weight reduction process and improvement of glucose metabolism [9].

The GI tract influences directly in glucose homeostasis, modulating gastric emptying, carbohydrate digestion, and glucose absorption during and between meals [10]. Besides unbalanced diets, high stress, excessive consumption of medications, smoking habits can also interfere with gastrointestinal barrier function, triggering metabolic endotoxemia. Considering a large number of bacteria present in the intestinal lumen, it is possible to detect more than one gram of LPS (lipopolysaccharide of the outer membrane of gram-negative bacteria). The process of metabolic endotoxemia stems from a change in intestinal permeability allowing LPS to reach the bloodstream. LPS in the blood is able to induce immune responses and activate pathways that lead to inflammation (by coming into contact with macrophages), inhibiting insulin signaling and promoting weight gain. Endotoxemia is a causal factor of subclinical inflammation related to the development of chronic metabolic diseases since it promotes insulin resistance and a greater chance of macrophage infiltration [5]. Thus, physiological changes driven by RYGB gastroplasty may improve intestinal permeability and consequently decrease endotoxemia and glucose intolerance [8].

Regarding neuromodulators aspects, the feeling of satiety is a relevant factor to be considered in the process of reducing food intake and weight loss [10]. Gastrointestinal hormonal changes are closely related to complex gut-brain signaling [8]. Hunger and appetite are mediated by an interaction of nervous and endocrine signals [9]. Neural signaling is mediated by the hypothalamus, which plays a role in controlling food intake according to caloric needs. Many brain neurotransmitters, including dopamine and serotonin, and various neuropeptides [neuropeptide Y (NPY), leptin, orexin A, ghrelin, growth hormone releasing factor, leptin, and peptide-1 (GLP-1) can also affect appetite [8]. Some neurotransmitters and neuropeptides may suffer alterations after performing Roux-en-Y bariatric surgery, impacting satiety and thus, food intake. The arcuate (infundibular) nucleus has orexigenic (AgRP/NPY) and anorexigenic (POMC/CART) neurons that associates several neuroendocrine processes, regulating energy metabolism by integrating satiety signals [7]. In this sense, bariatric surgeries interfere with neurons. NPY and POMC, impacting a reduction in leptin and ghrelin levels and an increase in peptides YY (PYY) and GLP-1, thereby affecting appetite and food intake [4].

Although suppression of food intake has a strong effect on metabolism, particularly carbohydrates and lipid turnover, the

hormonal system has a relevant impact on weight loss, since anatomical rearrangements resulting from gastroplasty promote changes in GI hormone secretion.14 Thus, hormonal changes are associated with the metabolic effects of bariatric surgery, contributing to the regulation of homeostasis, weight loss, and resolution of comorbidities [7].

Gastrointestinal Hormones
They have a recognized role in food intake, satiety, insulin secretion, systemic metabolism, and appetite regulation [3].

Cholecystokinin (CCK)
CCK is a polypeptide that acts in the presence of fatty acids, vague nerve stimulation, and amino acids, and is synthesized and secreted by L cells in the duodenojejunal extension. Its function is related to satiety (gastric emptying time is slowed), digestion and absorption of lipids, generation of bile acids, and release of pancreatic enzymes [2].

Postprandial CCK levels after bariatric surgery are increased by the stimulation of the parasympathetic nerves. Possibly, CCK at high levels contributes to greater satiety and improved glucose homeostasis after RYBG [1]. These findings are surprising, considering that there is a diversion of the duodenum in access to nutrients after this surgery and, therefore, would indicate an indirect regulation of this population of cells [3].

Ghrelin
Described in 1999, ghrelin is a peptide hormone composed of 28 amino acids and is part of a range of gastrointestinal hormones involved in appetite control. Its secretion occurs mainly by oxyntic cells located in the gastric fundus mucosa; however, it can also be expressed in hypothalamic arcuate nucleus neurons, pancreas, ovary, testis, small intestine, pituitary, skeletal muscle, lung, and, to a lesser extent, in the duodenum and colon [8].

Known as the "hunger hormone", ghrelin has the role of regulating food intake, body weight, adiposity, and glucose homeostasis through its action in the brain. It acts via neuropeptide Y and aguti-related peptide in the hypothalamic arcuate nucleus, to amplify appetite, food intake and, consequently, weight [8].

From its precursor, proghrelin, is released in two forms: acylated ghrelin (AG) and deacylated ghrelin (DAG). Two ghrelin receptors have been described: GHS-R1a and GHS-R1b. Only AG can bind to GHS-R1a under physiological conditions, acting as a growth hormone (GH) stimulant; under abnormal conditions, DAG can also become a ligand for this receptor. GHS-R1b is considered an inactive receptor, as none of the forms of ghrelin can bind to it. Ghrelin-O-acetyltransferase (GOAT) is an enzyme that allows the binding between AG and GHS-R1a, being expressed mainly in the stomach, brain, and pancreas, and its concentration is related to energy balance [8].

Concerning the proghrelin secretion, it increases in the pre-prandial period and, in the first hour after the beginning of the meal, its levels decrease in response to macronutrients and caloric intake in a situation of positive energy balance (obesity), ghrelin-secreting cells become if desensitized and secretion and plasma levels become reduced compared to an individual of normal weight. In its release, the adrenergic and cholinergic pathways of the autonomic nervous system are involved; both adrenergic and cholinergic agonists act to increase ghrelin release. On the other hand, its antagonists reduce circulating levels of the hormone. Gastrointestinal hormones (somatostatin, cholecystokinin, gastric inhibitory peptide, GLP-1, and peptide YY), triglycerides, and total parenteral nutrition cause blunting of their release. About glucose metabolism, ghrelin increases its plasma levels and glucagon secretion and reduces insulin release [8].

This hormone is present in cardiomyocytes and confers cardioprotective effects. It has an important role in cardiovascular disorders and hypertension, becoming a treatment option for the condition. Benefits are also seen in reducing cardiac sympathetic nerve activity, inflammation, and oxidative stress in the heart, as well as inducing angiogenesis [8].

There is an increase in ghrelin levels with prolonged fasting and a decrease after a meal. However, ghrelin levels increase in patients who lose weight by caloric restriction, which may contribute to the lower efficiency of this hormone in the long term of dietary manipulation to control obesity [1]. There is still no consensus on the effects of long-term ghrelin, according to the evaluated references.

Secretin and Gastrin
When the intraluminal pH becomes acidic, S cells in the duodenum synthesize secretin. This hormone is responsible for glycemic control, amplifies the synthesis of pancreatic bicarbonate, reduces duodenal and gastric motility, and decreases the production of hydrochloric acid in gastric juice and gastrin. Gastrin, in turn, elevates acid secretion and gastric enzymes, pancreatic enzymes, and suppresses appetite. Its synthesis and release are carried out by the G cells of the stomach and duodenum when direct contact occurs from food ingestion and stomach stretching [2].

Postprandial plasma secretin levels after bariatric surgery were lower than the initial ones, because gastrointestinal anastomosis. In addition to determining the release of secretin, contains several secretin cells, which can help to avoid pancreatic dysfunction, given that, its function is to increase the production of pancreatic bicarbonate and promotes the release of insulin. Secretin reduces gastric acid synthesis and gastrin release and decreases gastric and duodenal motility [2].

After RYGB, there may be a decrease in G cells, leading to a decrease in gastric secretion. It can be assumed that the high levels of secretin and somatostatin after some bariatric procedures (gastric sleeve) also inhibit gastric secretion. It can be concluded that gastrin is decreased after RYGB and increased after VSG for reasons still unclear [3].

Incretins
They are associated with carbohydrate metabolism, both by stimulating the release of insulin by pancreatic ÿ cells (responsible for half of the insulin synthesis) and by controlling leptin and ghrelin [11].

Glucose-Dependent Insulinotropic Peptide (GIP)
It is an incretin synthesized by K cells in the small intestine (especially in the duodenum and proximal jejunum), and its receptors are found in adipose tissue, central nervous system, heart, pancreas, and adrenal gland cortex. After glucose ingestion, GIP stimulates insulin secretion and amplifies GLUT-1 expression, promoting intestinal glucose absorption [3].

In adipose tissue, GIP increases glucose uptake, activates lipase (breaks down fat molecules to facilitate intestinal absorption), and promotes lipogenesis (synthesis of triglycerides and fatty acids to later be stored in the adipose tissue and liver). There is

an inconsistency in gastric inhibitory peptide levels after bariatric surgery, although an increase has been reported after RYGB [2].

Glucagon-Like Peptide-1 (GLP-1)
It is secreted by intestinal enteroendocrine L cells, ileum, colon, and some neuronal cells of the central nervous system.4 Like GIP, GLP-1 is an incretin; therefore, it is related to the regulation of carbohydrates, normalizing their metabolism, and promoting a reduction in the body mass index (BMI) [11].

It has a role in promoting satiety (decreased rate of gastric emptying), producing anorectics, stimulating insulin release from pancreatic ÿ-cells (thus improving glucose tolerance), and preventing glucagon secretion. After bariatric surgery, the release of anorectic intestinal hormones such as GLP-1, PYY3-36 and oxyntomodulin was shown to be increased [2].

After RYGB, with oral glucose stimulation or meal, GLP-1 levels were persistently elevated, even without sufficient literature to understand the roles of peptides in this regulation. There is an extreme elevation of postprandial GLP-1 levels after RYGB and VSG. This increase has been consistent across preclinical and clinical studies after 2 days of surgery and is maintained for at least 2 years, making this substance a possible marker rather than an indicator of successful bariatric surgery [3].

GLP-1 increased both fasting and postprandial after 2 days of RYGB and remains so for up to 10 years. After VSG, postprandial GLP-1 levels also show an increase within 6 weeks post-op by up to 1.7-fold. However, fasting levels show no changes. By increasing glucose-dependent insulin secretion, it appears to be a potential hormonal mediator of the positive metabolic effects of bariatric surgery. However, it is still unclear how much this peptide is responsible for these results [4].

RYGB and SG create an increase in postprandial levels of GLP-1 and PYY. This is mainly due to the early delivery of nutrients to the distal intestine that ends up stimulating enteroendocrine L cells. Furthermore, ghrelin was proved to have an inhibitory effect on the secretion of GLP-1 and PYY. Thus, when ghrelin ceases after bariatric surgery, an increase in GLP-1 and PYY levels is generated [12].

Therefore, we found that both LRYGB and LSG cause a considerable increase in fasting GLP-1 levels. The literature shows that when ingesting a mixed meal after these mentioned procedures, a significant increase in GLP-1 is generated.

Peptide YY (PYY)
It is an anorectic secreted by L cells on the small and large intestine, whose circulating levels increase in the postprandial period, inhibit gastric, intestinal, and pancreatic secretions [1]. In the human body, PYY3-36 decreases insulin after a meal, increases gastric emptying time and, despite being described as controversial data, this peptide has also been attributed to the altering and reducing gastrointestinal motility and regulating appetite [5].

Both incretins, PYY3-36, and postprandial OXM are elevated in the first two months after RYGB. However, there is still not enough literature to understand the role of intestinal peptides in the regulation of energy balance after RYGB [2].

Most clinical studies have shown that postprandial PYY secretion levels after RYGB and VSG are elevated. Immediately following RYGB, there is a modest increase (~20%) in fasting plasma PYY levels and another increase in the postprandial period. Similarly, postprandial PYY levels are found to be increased for one year after GSV. Therefore, the increase in PYY secretion may be related to weight loss after RYGB [4].

Adipose Tissue and Adipokines
Known for acting as an active endocrine organ, adipose tissue (AT) has a role in the pathophysiology of obesity and comorbidities, modulating body metabolism, homeostasis, immune and inflammatory responses in conditions of positive energy balance and aiming to facilitate the storage of excess energy, alteration occurs morphology of the AT, with hyperplasia or hypertrophy of adipocytes. Hypertrophy is related to low-grade chronic inflammation and modification of its secretion, with increased release of tumor necrosis factor-alpha (TNF-a), interleukins (IL) 1, 6 and 8, resistin, visfatin and chemerin [13].

In the context of obesity, there is leptin resistance (which promotes increased energy expenditure and decreased food intake) and, consequently, a decrease in its secretion [13].

Anti-inflammatory and insulin-sensitizing factors, adiponectin, omentin, and IL-10 are reduced, which demonstrates dysregulation in the secretion of pro-inflammatory and anti-inflammatory factors, implying a role in insulin resistance [13].

Adipokines are Responsible for the Following Functions
Glucose and lipid metabolism, hemostasis, blood pressure and inflammatory processes [2].

Leptin is an anorectic hormone secreted by TA, responsible for increasing energy expenditure and limiting food intake to regulate body weight. In addition to its central function, leptin is also recognized in the context of inflammatory processes, regulation of the neuroendocrine axis and in the inverse modulation of insulin and glucagon secretion, leading to a reduction in the second hormone. It is known that adiposity and leptin levels are positively related, so obesity is characterized by high levels of leptin, with resistance to its response; however, energy expenditure and food intake are not properly regulated [2].

The literature shows that in long term, there is a significant increase (about 12%) in circulating levels of adiponectin and an exacerbated reduction (about 45%) in leptin levels. Apparently, this effect is dependent on weight loss, which was more pronounced in combined surgeries than in those patients who had restrictive approaches. It was also found that as a reflection of the reduction in fat mass, reduces leptin levels after bariatric surgery, and studies suggest that the sensitivity of this hormone may be increasing. The findings indicate that leptin resistance (which has been associated with obesity) is reduced by the procedure [13].

It was shown that resistin induces insulin resistance, and its expression increases during adipocyte differentiation and in the context of diet-induced obesity. Increased levels of resistin are related to insulin resistance and glucose intolerance, while its reduction is associated with decreased hepatic glycogenesis. In addition to the effects already mentioned, it is known that, in smooth muscle cells, resistin promotes a pro-inflammatory effect [2].

When analyzing adiponectin and its functions, there is the oxidation of fatty acids, increased insulin sensitivity, and modulation of

inflammation by decreasing the synthesis and activity of IL-6 and TNF-ÿ. It acts through two receptors located on its cell surface: AdipoR2 in the liver and AdipoR1 in skeletal muscle. Unlike leptin, adiponectin levels are elevated in the context of negative energy balance and reduced in the context of DM2 and positive energy balance. It has been seen that adiponectin, omentin, and IL-10 are considerably reduced after bariatric surgery. Furthermore, adipokine modulation likely is one of the potential mechanisms underlying the metabolic improvements associated with bariatric surgery – not immediately after the procedure, but in the long-term maintenance of the metabolic effects caused, including increased peripheral sensitivity to insulin [13].

The literature shows that visfatin is synthesized by visceral TA, and it is known as a pre-B cell colony-enhancing factor (PBEF). From its known effects (lowering plasma glucose by insulin mimicry, energy metabolism homeostasis, pro-inflammatory anti-apoptotic effects), this protein is studied as a possible target for glycemic regulation [2].

Vaspina was also studied, and it is an adipokine that, when associated with a healthy ED, promotes cardioprotective, anti-inflammatory, and insulin sensitizing effects. In the context of positive energy balance (high BMI) and DM2, it promotes glucose tolerance and insulin resistance, suggesting a pro-inflammatory and atherogenic environment. The main tissues involved in vaspin synthesis are the visceral TA, stomach, liver, pancreas, and hypothalamus [2].

Muscle and Myokines

Obesity and its comorbidities implicate a role in skeletal muscle and myocardium. At the beginning of T2DM, the muscle develops insulin resistance, generating changes in the secretion of myokines (myostatin, osteonectin [SPARC], fibroblast growth factor [FGF] 21, brain-derived neurotrophic factor [BDNF]), it also accumulates intracellular lipid. FGF21, BDNF improve insulin sensitivity and metabolic functions, while myostatin and SPARC are increased and associated with inhibition of fiber self-renewal and myocyte differentiation, dual regulation of adipogenesis, insulin resistance, and fibrosis in the liver, adipose tissue, and muscle [13].

PP

Postprandial PP was elevated after GSV but not after RYGB. This may suggest an increase in the parasympathetic impulse in the GSV [2].

Glucose and Cholesterol

The results confirm the existence of favorable metabolic alterations after bariatric procedure. There is a positive impact on blood glucose and triglycerides, trending into towards normalization of HDL cholesterol. In that study, at 12 months postoperatively, participants achieved lower glucose concentrations like the behavior of total cholesterol, LDL, and TG concentrations, while lower HDL was achieved a little over 12 months after surgery [14].

Insulin

It has been extensively reported that fasting blood insulin levels are reduced in patients after RYGB and ESV, a consequence that is correlated with the degree of weight loss after surgery. This fact is not so surprising, given that weight loss, by itself, already increases insulin sensitivity, therefore, it already decreases fasting insulin levels [3].

There is also a reduction of a non-physiological peptide fragment generated in insulin processing, the C-peptide, after RYGB and VSG. Thus, changes in insulin levels reflect reduced secretion rather than an increase in fasting clearance [3].

Glucagon

After caloric restriction, fasting and postprandial glucagon levels decrease, while there is a significant increase in postprandial glucagon levels after RYGB. Patients without DM2 do not show relevant changes in fasting glucagon levels, while T2DM carriers show a significant decrease in fasting [3].

Table 1: Hormones Analysis in Obese Patients after the Bariatric Procedures Studied (VSG and RYGB)

	Function	Obese	After VSG	After RYGB
CCK	Satiety, Digestion and Absorption of Lipids, Generations of Bile Proteins and Release Pancreatic Enzymes	Decreased	Increased	Decreased
Secretin	Glycemic Control and Amplification of Pancreatic Bicarbonate Synthesis	Increased	Decreased	Decreased
Gastrin	Elevates Gastric and Pancreatic acid Secretion and Enzymes, in Addition to Decreasing Appetite	Increased	Increased	Decreased
GLP-1	Promotes Satiety, Produces Anorectics, and Stimulates the Release of Insulin by Pancreatic ÿ Cells	Decreased	Increased	Increased
PYY	Decreases Insulin after a meal	Decreased	Increased	Increased
PP	Decreases Appetite	Decreased	Increased	Kept initial values
Leptin	Increases Energy Expenditure and Limit Food Intake	Increased	Decreased	Decreased
Adiponectin	AG Oxidation, Increased Insulin Sensitivity; in Addition to Modulating Inflammation	Decreased	Decreased	Decreased
Ghrelin	Regulation of Food Intake, Adiposity and Glucose Homeostasis by Brain Action	Decreased	Fasting Increase and Post-Prandial Decrease	Fasting Increase and Post-Prandial Decrease
Glucose	Main Source of Energy for Cellular Metabolism	Increased	Tendency to Normalize	Tendency to Normalize
Cholesterol	Formation of Bile Acids that Acts in Digestion and Compose some Hormones and Vitamins	Increased	Tendency to Normalize	Tendency to Normalize
GIP	After Glucose Ingestion, It Stimulates Insulin Secretion and Amplifies Glut1 Expression, Promoting Intestinal Glucose Absorption	Decreased	Literature Inconsistency	Literature Inconsistency

Insulin	Regulates Glucose Homeostasis, Stimulating its Peripheral Storage, Uptake and Stimulating Glycogen Synthesis	Increased	Decreased	Decreased
Glucagon	Stimulates the Production Of Glucose in The Liver, Preventing Hypoglycemia	Decreased/ Dysfunction	Decreased in Fasting	Postprandial Increase and Fastind Decrease

There is great concern about micronutrients and vitamin deficiency after bariatric procedures, even with oral supplementation. It is believed that these deficiencies may persist due to some factors such as restricted intake, food intolerance, poor eating habits, and decreased absorption capacity. Despite having evidence incosistency, most were reported as high as: a 65% drop in B12; 38% folate; 51% vitamin D; 34% vitamin C; 11% for vitamin A; 18% pair B1; 14% for B2 18% for vitamin C. As a consequence of these high drops, the clinical manifestations include osteoporosis, neuropathy, xerophthalmia, nyctalopia and, Wernicke's encephalopathy [15].

Iron deficiency anemia after bariatric procedure involves several factors. First, when the surgical bypass technique is performed, the duodenum and jejunum (which are the sites of physiological iron absorption), are effectively excluded from the digestive tract. However, increasing the length of the dysfunctional jejunum from 75 cm to 150 cm using the RYGB technique does not change the high percentages of anemia in these patients. Furthermore, intolerance to red meat, which is a great source of iron, is found in more than 50% of bariatric patients after more than 4 years of procedure. And finally, when physiological demands for iron exceed its absorption (as example in menstruating women), continued depletion of the body's stores of iron will result in iron deficiency anemia [15].

Table 2: Changes in Micronutrients and Vitamins after Bariatric Procedures

Thiamine	Acute deficiency can occur after any bariatric surgery, more often after RYGB, in the presence of prolonged vomiting. Associated with potentially irreversible severe neurological symptoms (eg, Wernicke-Korsakoff syndrome)
B12	There is a decrease in its release and an increase in its degradation, mainly after malabsorptive or mixed surgical techniques (RYGB). Its deficiency can lead to anemia and nerve damage.
Proteins	Hypoalbuminemia (albumin < 3.5 g/dL), which interferes with oncotic pressure, triggering edema
Folinic acid	Deficiency due to decreased intake, especially after RYGB, leading to macrocytic anemia, leukopenia, thrombocytopenia, glossitis or megaloblastic marrow
Iron	Anemia can occur in up to two thirds of patients undergoing bariatric surgery, mainly RYGB. Ideal supplementation on an empty stomach, and accompanied by vitamin C
Calcium and vitamin D	Supplementation recommended for most weight loss therapies to prevent bone resorption as calcium absorption (influenced by vitamin D) is impaired
Osteocalcin	Osteocalcin and alkaline phosphatase increased more after RYGB, thus, this procedure induces greater deleterious effects on bone compared to SG. In addition, insulin and leptin (↓after RYGB) act on bone tissue by modulating osteocalcin secretion (↑after RYGB), forming a traditional feedback loop in which the skeleton becomes an endocrine organ.
Vitamin A and E	Annual monitoring of fat-soluble nutrients is important after malabsorptive procedures, also evaluating iron and copper deficiency, which impairs the resolution of retinol and carotenoid deficiency. The lack of these vitamins can lead to changes in the cornea, oxidative processes and immune deficiencies.

Conclusion

The significant physiological changes after the procedures studied pointed out by the literature were the reduction of secretin, gastrin, adiponectin, insulin, glucagon, and leptin. On the other hand, there is increased levels of CCK, GLP-1, PPY, and oxyntomodulin. The alteration of ghrelin is still too discussed since its concentration oscillations are different depending on the surgical method. These modifications are beneficial in the post-bariatric patient's body, since glucose levels are decreased, correlated with weight loss, concentrations of total cholesterol, LDL and triglycerides are significantly decreased [16,17].

More benefits were seen in Gastric Bypass when compared to Sleeve Gastrectomy for controlling obesity, metabolic syndrome, decreased insulin metabolism, maintenance of long-term weight loss, and improvement of comorbidities [18-30].

It is concluded, therefore, that the positive results of hormonal changes in the post-bariatric period are numerous and relevant, in the sense of treatment and prevention of diseases. Since there is a lot of divergence in the literature, the effects of some hormones according to the surgery method still need to be studied to discover the true relation between the technique and the real impact of hormonal changes and its benefits in weight loss and control in patients.

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