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Hybrid Duodenal Transit Bipartition: An Endoscopic and Laparoscopic Metabolic Procedure

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Abstract

Obesity has been increasing significantly in Brazil and worldwide, becoming a major public health issue. Traditional prevention and treatment strategies, including behavioral interventions, nutritional modifications, physical activity, pharmacotherapy, and metabolic/bariatric procedures, have proven insufficient to reverse this trend. Bariatric surgery is recognized as the most effective treatment for obesity and its comorbidities, but it carries potential long-term risks. Hybrid Duodenal Transit Bipartition is proposed as a minimally invasive "endobariatric" procedure combining endoscopic sleeve gastroplasty (ESG) with laparoscopic duodenoileal or distal duodenojejunal anastomosis. The main objective of this study is to demonstrate the importance of the intestinal metabolic component of hybrid duodenal transit bipartition. This intestinal component is responsible for optimizing and attempting to maintain weight loss and control comorbidities from an ESG through the incretin stimulus generated by the early arrival of food in the ileum or distal jejunum

(duodenoileal or distal duodenojejunal anastomosis). Additionally, it is a minimally invasive procedure that preserves the entire digestive system and does not involve gastrointestinal exclusion, allowing for endoscopic and nutritional access. To date, only one patient has undergone the hybrid duodenal bipartition procedure, with satisfactory early postoperative results at 60 days and weight loss exceeding the scientific literature on patients who underwent isolated endoscopic sleeve gastroplasty. Further studies are needed to validate these results and assess the long-term metabolic benefits of this new approach.

Keywords

Duodenal Switch, Duodenal Transit Bipartition, Bariatric Surgery, Metabolic Surgery, Endoscopic Gastroplasty, Endobariatric, Hybrid Duodenal Transit Bipartition, Duodenal Bipartition, Hybrid Surgery

1. Introduction

Obesity has shown significant growth both in Brazil and worldwide. In Brazil, the prevalence of obesity among adults increased from 3% to 22% among men and from 9% to 30% among women from 1975 to 2019 [1]. This increase is observed across all regions of the country, with the highest growth rates in the capitals of the North, Northeast, and Midwest [2]. Furthermore, the prevalence of overweight among Brazilian adults rose from 33.5% in the period from 1974-1990 to 52.5% in the period from 2011-2020 [3].

Globally, obesity has also been increasing at an alarming rate. In 2010, approximately 57% of the Brazilian male population was overweight or obese, with projections suggesting that this rate could reach 95% by 2050 [4]. This phenomenon is not exclusive to Brazil, as the prevalence of obesity is rising across all sub-regions of the Americas, including the United States, where there is a significant correlation between the obesity trends of the two countries [5].

These data indicate that obesity is a growing public health issue and that current prevention and treatment policies have been insufficient to curb this trend both in Brazil and globally.

Traditional weight loss approaches, including dietary and pharmacological interventions, often fail to provide sustainable long-term results, particularly in individuals with severe obesity. In this context, bariatric surgeries have emerged as the most effective intervention for substantial and lasting weight loss, in addition to offering additional metabolic benefits, such as the remission of type 2 diabetes. However, despite the success of bariatric and metabolic procedures, there is a growing need to adapt surgical procedures to optimize metabolic outcomes and minimize potential long-term complications in a minimally invasive manner. The Hybrid Duodenal Transit Bipartition proposed in this study aims to fill this gap by combining the effects of endoscopic sleeve gastroplasty (ESG) with an intestinal metabolic component, promoting a more robust incretin response and improving metabolic outcomes compared to traditional endoscopic methods. Nonetheless,

we will review some of the current approaches: behavioral interventions, nutritional modifications, physical activity, pharmacotherapy, and metabolic/bariatric procedures.

Behavioral interventions are the cornerstone of treatment and involve lifestyle modification programs that include at least 14 sessions over 6 months, focusing on self-monitoring of weight, dietary and physical activity counseling, and problem-solving. These interventions can result in a weight loss of 5% to 10% [6] [7].

Nutritional modifications aim to reduce total caloric intake, with dietary strategies tailored to the patient's preferences. Diets that create a caloric deficit of at least 500 kcal/day are effective for weight loss [7].

Physical activity is crucial for maintaining weight loss, although the initial weight loss is modest (2 - 3 kg) without caloric reduction [6] [7].

Pharmacotherapy is recommended for patients with obesity or overweight with weight-related comorbidities, in conjunction with lifestyle modifications. In the U.S., six medications are approved by the FDA for long-term use: GLP-1 receptor agonists (semaglutide and liraglutide), tirzepatide, phentermine-topiramate, naltrexone-bupropion, and orlistat. Tirzepatide has the greatest effect, with an average weight loss of 21% over 72 weeks [6] [7].

Metabolic/bariatric procedures are indicated for patients with obesity who do not respond to other interventions and are candidates for bariatric surgery. Surgeries such as laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass show satisfactory results in weight loss. Endoscopic procedures, such as the intragastric balloon and endoscopic sleeve gastroplasty, are also showing promising results in weight loss [6] [7].

The American Society for Gastrointestinal Endoscopy and the European Society of Gastrointestinal Endoscopy recommend a multimodal and long-term approach for the management of obesity, combining behavioral, pharmacological, and surgical interventions as appropriate for each patient [8].

Bariatric surgery is widely recognized as the most effective treatment for obesity and its associated comorbidities, such as hypertension and dyslipidemia. Studies show that bariatric procedures result in significant and lasting weight loss, as well as substantial improvements in glycemic control and remission of type 2 diabetes [9] [10].

The safety of bariatric surgery is also well-documented. Perioperative mortality is low, ranging from 0.03% to 0.2%, and the rates of major complications are comparable to other common abdominal surgeries, such as cholecystectomy and hysterectomy [9] [11] [12]. The American Gastroenterological Association, along with other societies, states that bariatric surgery is safe and effective for the treatment of obesity and its comorbidities [13].

However, it is important to consider the long-term risks, which include nutritional deficiencies, anemia, osteoporosis, and gastrointestinal complications. These risks can be mitigated with continuous follow-up and appropriate nutritional supplementation [10] [11].

Therefore, bariatric surgery should be considered a viable and safe option for

patients with obesity, especially those with significant comorbidities, following a careful evaluation and a shared decision-making process [9] [11] [13].

Endoscopic gastroplasty is a minimally invasive technique for reducing gastric volume performed via endoscopy. One of the most common methods is Endoscopic Sleeve Gastroplasty (ESG), which involves placing full-thickness endoluminal sutures in the gastric wall, creating a tubular configuration similar to laparoscopic vertical sleeve gastrectomy, but without the need for external incisions [13] [14].

ESG is performed using endoscopic suturing devices, such as the Overstitch (Apollo Endosurgery), which allows for the placement of sutures along the greater curvature of the stomach, from the pre-pyloric antrum to near the gastroesophageal junction [14]. This procedure reduces gastric capacity and consequently food intake, promoting weight loss. Multicenter studies have shown that ESG can result in a total weight loss of 16.8% to 19.8% over 6 to 18 months, with a serious adverse event rate of approximately 2% [13] [14].

The American Gastroenterological Association (AGA) and the American Society for Gastrointestinal Endoscopy (ASGE) recognize ESG as a safe and effective option for managing obesity, particularly in patients who are not ideal candidates for traditional bariatric surgery [8] [14]. ESG has proven to be a viable and safe alternative in the treatment of obesity [15].

Incretins, such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), play a crucial role in the metabolic effects of bariatric surgery. After bariatric surgery, there is a significant increase in postprandial GLP-1 secretion, which is associated with improved β-cell function and glycemic control, independent of weight loss [16] [17]. GLP-1 is particularly important after Roux-en-Y gastric bypass (RYGB), where its plasma concentration can increase up to tenfold, contributing to increased insulin secretion and improved glucose tolerance [18] [19]. The increased secretion of GLP-1 and GIP after surgery is related to the accelerated delivery of nutrients to the distal intestine, which stimulates the release of these hormones [20].

Therefore, in hybrid duodenal transit bipartition, we propose combining ESG with a metabolic intestinal component, represented by duodenoileal or distal duodenojejunal anastomosis.

Furthermore, the recovery of the incretin effect after bariatric and metabolic surgery is associated with the remission of type 2 diabetes, highlighting the importance of these hormones in the metabolic improvement observed after bariatric procedures [21]. Therefore, incretins are fundamental to the metabolic benefits of bariatric surgery, contributing to improved glycemic control and β-cell function.

2. Justification

The classic duodenal switch is a well-established model of bariatric surgery; however, due to its malabsorptive component, some patients may experience nutritional

complications and postoperative diarrhea. Therefore, over the years, some researchers have proposed adaptations to this procedure to minimize the adverse effects caused by malabsorption while maintaining its satisfactory results in weight loss and comorbidities. Among these proposals are intestinal transit bipartition, SADIS (Single Anastomosis Duodenal Ileal Bypass with Sleeve Gastrectomy), ileal interposition, and SADJB-SG (Single Anastomosis Duodenal Jejunal Bypass with Sleeve Gastrectomy), which is a modification of the duodenal switch with duodenojejunal anastomosis [22]-[24].

Metabolic concepts, unlike classic bariatric procedures that were developed before this knowledge was available and therefore relied on mechanical restriction, intestinal malabsorption, or a combination of both, are obviously non-physiological. A physiological metabolic procedure should not include these characteristics, nor use prostheses or create excluded segments. An ideal surgical procedure should maintain gastric, duodenal, jejunal, and ileal functions. Additionally, it would be beneficial to create a smaller functional stomach that signals earlier with distension, given that modern diets are more caloric. Furthermore, in cases of obesity, it is advantageous to reduce fasting ghrelin levels and increase the secretion of GLP-1 and PYY [22] [25].

Duodenal Transit Bipartition (DTB) is an adaptation of the classic Duodenal Switch that has been proposed and studied. This adaptation involves performing a sleeve gastrectomy with a duodenoileal or distal duodenojejunal anastomosis without septation of the duodenum, meaning without the duodenal exclusion characteristic of the classic technique [20]-[23].

Considering minimally invasive concepts, we propose the integration of endoscopic procedures for obesity treatment with laparoscopic bariatric surgery concepts, which we refer to as "endobariatric" hybrid procedures. An example of this is publications showing satisfactory results of duodenoileal anastomosis performed magnetically in patients who have previously undergone laparoscopic sleeve gastrectomy or are undergoing it simultaneously in the same operative session. Magnetic anastomosis represents a significant advancement in the concept of minimally invasive procedures and is gradually gaining traction [26]-[29].

Based on the aforementioned concepts, we propose a hybrid Duodenal Transit Bipartition, combining endoscopic gastroplasty with laparoscopic duodenoileal or distal duodenojejunal anastomosis. This aims to optimize and sustain satisfactory weight loss through a minimally invasive "endobariatric" hybrid procedure. Additionally, the duodenal transit bipartition may enhance the incretin effect in endoscopic gastroplasty by bringing the ileum and distal jejunum closer (**Figure 1**).

Hybrid Duodenal Transit Bipartition possesses characteristics of a physiological metabolic procedure as it preserves gastric functions through Endoscopic Sleeve Gastroplasty (ESG) and maintains duodenal, jejunal, and ileal functions. Furthermore, hybrid duodenal bipartition does not involve duodenal exclusion and theoretically allows for revision, conversion to any other metabolic technique, and even complete reversal.

The integration of endoscopic and laparoscopic techniques in the hybrid duodenal transit bipartition procedure reinforces the concept of minimally invasive interventions, preserving the patient's entire anatomy since it does not involve resections or gastrointestinal exclusions. Endoscopic sleeve gastroplasty (ESG) keeps the stomach and its blood supply intact, reducing surgical trauma, complications, and improving postoperative recovery. When combined with laparoscopic duodenoileal or distal duodenojejunal anastomosis in a single anastomosis, the procedure adds an intestinal incretin component, enhancing its effectiveness while maintaining minimally invasive principles. This procedure is conservative, as it preserves the stomach and its blood supply, and the metabolic component is represented by the laparoscopic duodenoileal and distal duodenojejunal anastomosis, which are absent in isolated endoscopic sleeve gastroplasty. Furthermore, there is no gastrointestinal exclusion, and it allows endoscopic access to the duodenum, features that may offer greater safety to patients. During the procedure, endoscopic sleeve gastroplasty is monitored by laparoscopy. Based on these characteristics, the hybrid duodenal transit bipartition may yield superior metabolic outcomes compared to isolated endoscopic sleeve gastroplasty, utilizing concepts from modern bariatric surgery.

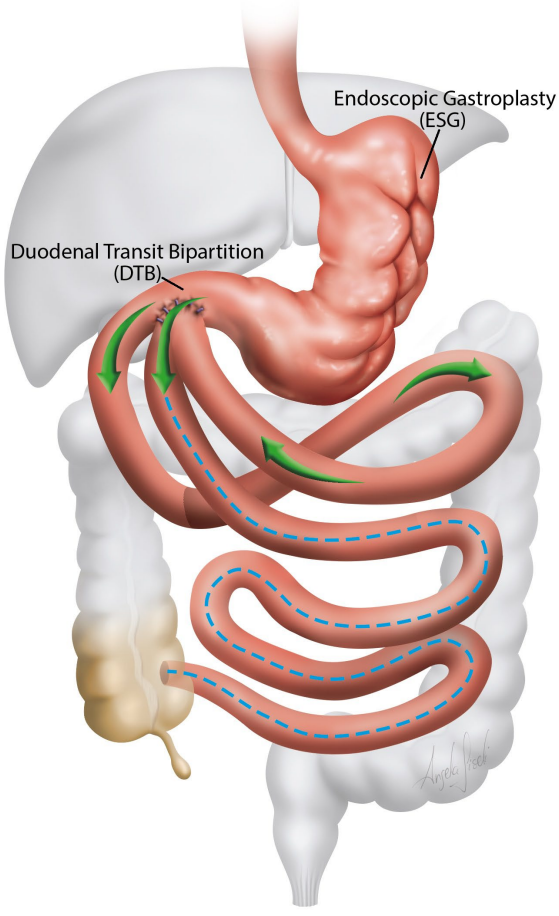

Figure 1. Hybrid duodenal transit bipartition.

3. Methods

This is a prospective pilot clinical trial involving four cases, with intentional sample selection, and a duration of 18 months. The study consists of two arms. In the first arm, we will include patients with a BMI greater than or equal to 40, and in the second arm, patients with a BMI between 30 and 39.9. For patients with a BMI of 40 or more, we will perform endoscopic sleeve gastroplasty and duodenoileal anastomosis. For patients with a BMI between 30 and 39.9, we will perform endoscopic sleeve gastroplasty and distal duodenojejunal anastomosis. This study has been approved by an ethics committee, with Professor Paulo Reis Rizzo Esselin de Melo as the principal investigator.

Patients will be followed up postoperatively with check-ups at 7 days, 30 days, 90 days, 6 months, 12 months, and 18 months. The set of clinical outcomes will be published in the future.

4. Discussion

Laparoscopic duodenal transit bipartition is a surgical procedure with a metabolic framework supported by several key components. These include an intact sleeve, the approximation of the ileum and distal jejunum through duodenoileal or distal duodenojejunal anastomosis, which enhances the incretin effect, and pyloric protection, as the anastomosis is performed post-pylorically in the first duodenal portion. Thus, in laparoscopic duodenal transit bipartition, there is a combination of metabolic components characterized by the association of the sleeve with duodenoileal or distal duodenojejunal anastomosis [22] [23].

In the case of Hybrid Duodenal Bipartition, which includes an endoscopic sleeve gastroplasty, the metabolic component is primarily associated with the duodenoileal anastomosis at 300 cm from the ileocecal valve and the duodenojejunal anastomosis at 200 cm from the angle of Treitz, post-pyloric (in the first portion of the duodenum). These anastomosis likely enhance the incretin effect by allowing food to reach more distal portions of the small intestine earlier, thereby optimizing weight loss and maintaining this loss compared to the results of isolated endoscopic sleeve gastroplasty [22] [23] [30].

Post-pyloric anastomosis follows physiological concepts, reducing the chances of dumping, reactive hypoglycemia, diarrhea, bile reflux, malnutrition and allowing them to be performed in a loop (one anastomosis) [22]. Furthermore, another benefit of the anastomosis being post-pyloric, in the hybrid duodenal transit bipartition, is that, as in the laparoscopic duodenal transit bipartition, they have a size of approximately 4 cm located in the first duodenal portion. This strategy hinders or prevents the occurrence of stenosis, ensuring the intestinal incretin mechanism remains effective even if the endoscopic gastroplasty loses the support of the plications. As a result, patients are more likely to maintain weight loss and control comorbidities until they need to consider other options, such as adding a laparoscopic sleeve or repeating the endoscopic gastric plication. Adolescents, individuals with severe obesity, and older patients may benefit from this hybrid

treatment option.

As the intestinal component represents the metabolic structure of this hybrid procedure and is considered extremely important for the outcomes, we will now delve into the neuroendocrine mechanisms involved in this part of the procedure. One of the main mechanisms in metabolic procedures is the early arrival of food in the distal portions of the intestine, as this is associated with improved stimulation and action of incretin hormones [22] [25] [30].

These hormonal mechanisms in metabolic procedures involve a complex interaction of gut hormones that regulate appetite, satiety, and glucose homeostasis. Glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) are two of the main hormones involved. After bariatric and metabolic procedures, there is a significant increase in the postprandial secretion of these hormones, which contributes to improved glucose tolerance and weight loss [31]-[33].

GLP-1, in particular, plays a crucial role in improving glucose homeostasis by increasing insulin secretion and reducing glucagon secretion, which enhances insulin sensitivity [31] [34]. Additionally, the increased secretion of PYY following surgery contributes to reduced appetite and caloric intake, facilitating weight loss [31] [33].

Another important mechanism is the alteration in the secretion of ghrelin, an orexigenic hormone. Metabolic surgery, especially sleeve gastrectomy, reduces ghrelin levels, which contributes to decreased appetite [34] [35].

In addition to intestinal hormones, changes in bile acid metabolism and gut microbiota also play significant roles. Bile acids can influence metabolic signaling through FXR and TGR5 receptors, while alterations in gut microbiota can affect nutrient absorption and inflammation [32] [36].

These hormonal mechanisms are fundamental to the metabolic effects of surgery, which include the remission of type 2 diabetes and sustained weight loss [31] [33] [34].

Next, we will discuss in more detail the incretin hormones and other mechanisms involved in metabolic procedures:

GLP-1

Glucagon-like peptide-1 (GLP-1) exerts multiple effects on glycemic control. Firstly, GLP-1 is secreted by enteroendocrine L cells in the intestine in response to nutrient intake. It primarily acts through the activation of GLP-1 receptors (GLP-1R) on pancreatic β-cells, promoting glucose-dependent insulin secretion [37] [38].

Additionally, GLP-1 inhibits glucagon secretion by pancreatic α-cells, contributing to the reduction of hepatic glucose production [37] [39]. This inhibitory effect can occur both directly, through the expression of GLP-1R on α-cells, and indirectly, mediated by products of β or δ cells [37].

GLP-1 also slows gastric emptying, which helps control postprandial glucose spikes, and enhances satiety, reducing food intake [38] [39]. These combined effects contribute to the improvement of glycemic homeostasis.

Additionally, GLP-1 has beneficial effects on β-cell function, promoting the proliferation and neogenesis of these cells while reducing apoptosis [38] [40]. These mechanisms are essential for maintaining pancreatic function in patients with type 2 diabetes.

In summary, GLP-1 controls blood glucose levels by stimulating insulin secretion, inhibiting glucagon secretion, delaying gastric emptying, and increasing satiety, in addition to restoring pancreatic β-cell functions.

GLP-1 AND THE CENTRAL NERVOUS SYSTEM

Glucagon-like peptide-1 (GLP-1) exerts its satiety effects on the central nervous system (CNS) through various mechanisms. Firstly, neurons that express GLP-1 in the brainstem, particularly in the nucleus of the solitary tract (NTS), project to several brain regions, including the hypothalamus, which is crucial in regulating food intake [41]. Activation of GLP-1 receptors (GLP-1R) in the NTS reduces food reward behavior and modulates the mesolimbic system, thereby decreasing the motivation to obtain food [42].

Furthermore, the activation of GLP-1 receptors (GLP-1R) in the paraventricular nucleus of the hypothalamus (PVN) enhances excitatory synaptic strength in neurons that release corticotropin-releasing hormone (CRH). This promotes a protein kinase A (PKA)-dependent signaling cascade that leads to the phosphorylation of AMPA receptors and their trafficking to the plasma membrane, resulting in the suppression of food intake [43].

Another mechanism involves GLP-1R neurons in the dorsomedial hypothalamus (DMH), which encode pre-ingestive satiety. Optogenetic manipulation of these neurons has shown that their activation induces satiety, and the administration of GLP-1R agonists selectively increases the activity of these neurons during feeding behavior [44].

Additionally, the activation of GLP-1 receptors (GLP-1R) in the dorsal raphe nucleus modulates central serotonin levels, which also contributes to the reduction of appetite and body weight [45].

These mechanisms demonstrate that GLP-1 acts in multiple brain regions and through various molecular pathways to regulate satiety and food intake.

GIP

The glucose-dependent insulinotropic polypeptide (GIP) is an incretin hormone secreted by the K cells of the small intestine in response to nutrient intake, particularly glucose and lipids. GIP exerts several important incretin effects:

1) Potentiation of Insulin Secretion: GIP enhances insulin secretion by pancreatic beta cells in a glucose-dependent manner, contributing to the regulation of postprandial blood glucose levels [46] [47] [48].

2) Effects on Pancreatic Alpha and Beta Cells: In addition to stimulating insulin secretion, GIP also promotes glucagon secretion by pancreatic alpha cells, particularly under hypoglycemic conditions, helping to stabilize blood glucose levels [47] [49].

3) Extrapancreatic Effects: GIP acts on adipocytes by stimulating fat storage and

influencing lipid metabolism. It may also have anorexigenic effects through actions in the hypothalamus [46] [50].

4) Effects in Patients with Type 2 Diabetes: In patients with type 2 diabetes, the response of beta cells to GIP is often diminished, limiting its effectiveness as a standalone therapeutic agent. However, long-acting GIP agonists and dual GIP/GLP-1 agonists have demonstrated significant therapeutic potential [46] [48] [51].

These effects make GIP a crucial component in the regulation of glucose homeostasis, although its standalone therapeutic utility is limited in some cases of type 2 diabetes due to beta cell resistance to GIP.

SYNERGY BETWEEN GLP-1 AND GIP

The synergy between glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP) is a topic of increasing interest in endocrinology, particularly in the context of treating type 2 diabetes and obesity. Both incretin hormones are secreted following food intake and play complementary roles in the regulation of postprandial glucose.

GLP-1 and GIP act synergistically to enhance insulin secretion in a glucose-dependent manner. GLP-1 also inhibits glucagon secretion when plasma glucose levels are above normal fasting values, while GIP has a glucagonotropic effect at low glucose levels [52] [53]. This combination of effects results in more effective glycemic control.

Recent studies have demonstrated that dual agonists of GLP-1 and GIP receptors can lead to significant improvements in glycemic control and weight loss. In a clinical trial, tirzepatide showed an average reduction in HbA1c of 1.94% and an average weight loss of 11.3 kg after 26 weeks of treatment [52]. These effects are attributed to the concomitant activation of GLP-1 and GIP receptors, which enhance insulin secretion and improve glucose homeostasis.

Additionally, the co-administration of GLP-1 and GIP may have additional effects, such as reducing food intake and modulating gastrointestinal motility, contributing to weight loss and metabolic control [54] [55].

In summary, the synergy between GLP-1 and GIP results in significant improvements in glycemic control and weight loss, making dual agonists of GLP-1 and GIP receptors a promising approach for the treatment of type 2 diabetes and obesity. However, their results are still inferior when compared to bariatric and metabolic procedures that produce this synergy in a physiological and continuous manner.

PYY

Peptide YY (PYY), particularly its truncated form PYY (3-36), is a hormone released by the endocrine cells of the intestine in response to food intake. The mechanism of action of PYY in promoting satiety involves interaction with Y2 receptors (Y2R) in both the central and peripheral nervous systems.

PYY (3-36) exerts its anorexigenic effects primarily through the inhibition of orexigenic neurons that express neuropeptide Y (NPY) in the arcuate nucleus of

the hypothalamus. Studies have shown that PYY (3-36) inhibits the activity of NPY neurons by reducing the frequency of action potentials and hyperpolarizing the cell membrane [56]. Additionally, PYY (3-36) also inhibits proopiomelanocortin (POMC) neurons, although the inhibition of NPY neurons is considered the main pathway for reducing food intake [56].

Another important mechanism involves peripheral signaling. PYY (3-36) acts on Y2 receptors located on the vagus nerve, which mediates the physiological effects of satiety induced by PYY. Vagal signaling is crucial for the anorexigenic effects of physiologically released PYY, but not for pharmacological doses administered peripherally [57].

Furthermore, the administration of Y2 receptor antagonists blocks the anorexigenic effects of PYY (3-36), confirming the importance of this receptor in mediating satiety [58].

Therefore, the mechanism of action of PYY in satiety involves the inhibition of NPY neurons in the hypothalamus and signaling through Y2 receptors on the vagus nerve, resulting in a reduction in food intake [56]-[58].

BILLARY ACIDS

Bile acids play a significant role in glucose control through various mechanisms. Firstly, they activate the farnesoid X nuclear receptor (FXR) and the G protein-coupled receptor TGR5, which are crucial in regulating glucose metabolism.

The activation of FXR by bile acids, such as taurochenodeoxycholate (TCDC), stimulates insulin secretion in pancreatic β-cells by inhibiting ATP-dependent potassium channels (KATP) and increasing cytosolic calcium concentration. This mechanism is mediated by non-genomic elements, suggesting a direct link between FXR activation and KATP channel inhibition [59].

Additionally, bile acids also activate the TGR5 receptor, which is primarily located on the basolateral membrane of intestinal L cells. Activation of TGR5 leads to the release of glucagon-like peptide-1 (GLP-1), which enhances insulin secretion and insulin sensitivity [60]. Studies have shown that the administration of bile acids can increase GLP-1 secretion and improve glucose homeostasis in animal models of diabetes [61] [62].

Therefore, bile acids control glucose by activating FXR and TGR5 receptors, resulting in increased secretion of insulin and GLP-1, as well as improved insulin sensitivity.

NEUROPODS

Neuropods are specialized cytoplasmic processes found in enteroendocrine cells of the intestine, playing a crucial role in sensory transduction between the gut and the brain. These cells, also known as neuropod cells, are capable of detecting nutrients in the intestinal lumen and transmitting signals directly to vagal afferent neurons through the release of neurotransmitters such as glutamate [63] [64].

The satiety mechanism mediated by neuropods involves the detection of nutrients, such as glucose, by neuropod cells, which utilize specific transporters like

SGLT1 (sodium-glucose co-transporter 1). Upon detection, these cells release glutamate, which activates vagal afferent neurons. These neurons, in turn, transmit signals to various brain regions, including the nucleus of the solitary tract, dopaminergic reward circuits in the basal ganglia, and homeostatic feeding circuits in the hypothalamus. This process modulates feeding behavior, influencing both immediate satiety and future food intake [64] [65].

Therefore, neuropods establish a direct and rapid connection between the gut and the central nervous system, allowing for an efficient response to ingested nutrients and contributing to the regulation of satiety.

GLP-2

Glucagon-like peptide 2 (GLP-2) plays several important roles in the context of bariatric surgery. GLP-2 is a gastrointestinal hormone secreted by enteroendocrine L cells in response to food intake. Its main functions include promoting nutrient absorption, increasing mesenteric blood flow, and activating pro-absorptive pathways in the intestine, thereby facilitating nutrient absorption [66].

After bariatric surgeries, GLP-2 levels increase significantly [67]. This increase is associated with several physiological adaptations, including the regulation of nutrient absorption, intestinal mucosal permeability, control of bone resorption, and regulation of satiety [67]. Additionally, GLP-2 has trophic effects on the intestinal mucosa, promoting crypt cell proliferation and inhibiting apoptosis, which increases the mucosal surface area and enhances the intestinal barrier function [68].

Studies also suggest that GLP-2 may play a role in modulating satiety after bariatric surgery. For instance, postprandial levels of GLP-2 have been correlated with the sensation of fullness and a reduced desire to eat in patients who have undergone modified biliopancreatic diversion [69].

In summary, GLP-2 plays crucial roles in intestinal adaptation post-bariatric surgery by promoting nutrient absorption, enhancing intestinal mucosal integrity, and contributing to the regulation of satiety.

The main objective of this study is to demonstrate the importance of the intestinal metabolic component of hybrid duodenal transit bipartition. This intestinal component is responsible for optimizing and attempting to maintain weight loss and control comorbidities from an ESG through the incretin stimulus generated by the early arrival of food in the ileum or distal jejunum (duodenoileal or distal duodenojejunal anastomosis). Additionally, it is a minimally invasive procedure that preserves the entire digestive system and does not involve gastrointestinal exclusion, allowing for endoscopic and nutritional access. To date, only one patient has undergone the hybrid duodenal bipartition procedure, with satisfactory early postoperative results at 60 days and weight loss exceeding the scientific literature on patients who underwent isolated endoscopic sleeve gastroplasty. Further studies are needed to validate these results and assess the long-term metabolic benefits of this new approach.

As described in the methods, this is a pilot study where 4 cases will be

conducted. In this article, we are focused on describing the conceptual aspects of hybrid duodenal transit bipartition, which is why we mention that so far only one case has been performed and we do not report the results of this patient. The results will be published in another article upon completion of the protocol.

5. Conclusion

The integration of endoscopic and surgical procedures represents the future of obesity treatment and its comorbidities by minimally invasive concepts. Duodenal transit bipartition is likely the first "endobariatric" hybrid metabolic procedure that is minimally invasive, proposing an ESG combined with laparoscopic duodenoileal or distal duodenojejunal anastomosis. This approach aims to optimize and sustain weight loss in patients undergoing endoscopic gastroplasty through intestinal incretin effects. This procedure has proven to be safe and effective so far, with no technical difficulties during its execution. The results of this pilot study will be published and will guide more in-depth future studies on this type of procedure.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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