Bariatric Procedures: Anatomical and Physiological Changes

4

Almino Cardoso Ramos, Hugo V. Coca Jimenez Carraso, and Eduardo Lemos De Souza Bastos

In understanding the basics of digestion, you'll discover who's in charge. Here's a hint. It's not you.

– Nancy Mure

4.1 Introduction

Obesity is a chronic, multifactorial, disease with increasing incidence and prevalence, especially in countries with western lifestyles [1, 2]. Although dietary control, regular physical activity and/or drug therapy have been considered as the first line of therapeutic approach, bariatric surgery seems to be the most effective

A. C. Ramos (✉)
International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO), Naples, Italy

Gastro-Obeso-Center, Advanced Institute for Metabolic Optimization, Sao Paulo, Brazil

Hugo V. Coca Jimenez Carraso
Intensive Care Unit, Santa Casa de Misericordia de Marilia Hospital, Marilia, Brazil

Nutrition Department, Santa Casa de Misericordia de Marilia Hospital, Marilia, Brazil

Federal University of Sao Paulo, Sao Paulo, Brazil

Eduardo Lemos De Souza Bastos
International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO), Naples, Italy

Gastro-Obeso-Center, Advanced Institute for Metabolic Optimization, Sao Paulo, Brazil

Division of Gastrointestinal Surgery, Marilia Medical School (FAMEMA), Marilia, Brazil

Brazilian Society of Bariatric and Metabolic Surgery (SBCBM), Sao Paulo, Brazil

A. G. Bhasker et al. (eds.), *Management of Nutritional and Metabolic Complications of Bariatric Surgery*,
https://doi.org/10.1007/978-981-33-4702-1_4

approach for patients with higher body mass index (BMI) and/or with associated comorbidities. Studies comparing medical and surgical treatment in individuals with clinically severe obesity have shown better results in short, medium, and long term in favor of the surgical approach in terms of sustained weight loss, control of comorbidities, reduction in major macrovascular events and mortality [3–7].

Since the 1950s, several surgical procedures have been proposed to achieve the desired weight loss and control of comorbidities [8]. Roughly, they are categorized as predominantly restrictive, predominantly malabsorptive, and mixed procedures (combination of both). However, this classification is merely didactic, since only gastric restriction and/or nutrient malabsorption appear to be inaccurate to provide a full explanation of all successful outcomes attributed to most bariatric procedures currently in use. It has now been recognized that anatomical alterations directed at restricting the amount of food or reducing the absorptive intestinal surface are less relevant than substantial changes in neural and endocrine signaling pathways commonly seen after bariatric surgery [9–16].

Therefore, it is more appropriate to anatomically classify the bariatric procedures into two groups, according to the absence or presence of small bowel diversion. In the first group (without intestinal bypass), Laparoscopic Adjustable Gastric Band (LAGB), Vertical Banded Gastroplasty (VBG), and Laparoscopic Sleeve Gastrectomy (LSG) are well-fitted. Examples of the second (with intestinal bypass) are Roux-en-Y Gastric Bypass (RYGB), One-Anastomosis Gastric Bypass (OAGB), Biliopancreatic Diversion (BPD—Scopinaro's Surgery), Biliopancreatic Diversion with Duodenal Switch (BPD-DS), Single-Anastomosis Duodenoileal Bypass with Sleeve Gastrectomy (SADI-S), Ileal Interposition, Transit Bipartition and Jejunoileal Bypass (JIB). Currently, some of these techniques are no longer being used, for example, VBG and JIB. Still, there is a wide range of operative techniques, each procedure with its peculiarity in relation to the technical design and mechanism of action. Some procedures are time-honored, such as RYGB, while some new procedures are emerging and gaining acceptance among patients and surgeons, such as LSG and OAGB.

With or without small bowel diversion, surgical bariatric procedures modify the anatomy of the digestive system and have an impact on entire gastrointestinal (GI) physiology, by restricting the food intake, altering the digestive and absorptive process, changing the GI hormones, motility, microbiota balance, neural signaling among other lesser-known mechanism. In addition, bariatric surgeries can strongly alter the regulation of hunger/satiety in the central nervous system, change food preferences and taste, and modify energy expenditure [9, 17–19]. All these postoperative changes can be summarized in the so-called BRAVE effect, i.e., Bile flow alteration, Reduction of gastric size, Anatomical gut rearrangement and Altered flow of nutrients, Vagal manipulation, and Enteric and adipose hormones modulation [20].

Although most of these physiological changes are part of the therapeutic purpose and therefore expected, they can also cause adverse effects such as food intolerance, nutritional deficiencies, chronic abdominal pain, diarrhea, flatulence, dumping syndrome, gastroesophageal reflux disease, small intestinal bacterial overgrowth,

among others [21–32]. Occasionally, adverse events can be clinically severe and impair the quality of life. In these situations, the attempt to restore normal anatomy may sometimes be the only viable therapeutic option. The changes caused by the adjustable gastric band (AGB) are completely reversible by simply withdrawing the device. LSG and BPD-DS are not subject to reversal, as both include partial gastrectomy. While it is technically feasible to restore the original food transit after RYGB and OAGB, since nothing is removed, the restoration includes new GI anastomoses. The anatomical configuration of the gastrointestinal tract is not completely normal and therefore, neither is the physiology.

Therefore, it is essential to know the anatomical and physiological changes caused in the digestive system by the different bariatric procedures. For understanding the expected outcomes and for the immediate recognition of their possible adverse events. In this chapter, only the anatomical changes associated with the most common bariatric procedures performed around the world will be addressed-LSG (45.9%), RYGB (39.6%), LAGB (7.4%), OAGB (OAGB) (1.8%), and BPD-DS (1.1%) [33], here sorted according to absence or presence of small bowel diversion.

4.2 Anatomical Changes of Procedures Without Small Bowel Diversion

4.2.1 Laparoscopic Adjustable Gastric Band

The LAGB is a restrictive procedure that consists of placing a silicone band around the upper stomach, very close to the cardia (Fig. 4.1). When left in place, the device provides a significant reduction in gastric capacity by creating a superior pouch of reduced size (10–20 mL) and a luminal narrowing that slows the emptying of ingested food to the lower portions of the stomach. Through a connection tube and a subcutaneous access port, it is possible to perform adjustments to the internal diameter of the device in order to manage the level of restriction and the emptying speed of the upper gastric pouch. LAGB is a completely reversible procedure, and the simple removal of the device totally restores the original anatomy and physiology of the GI tract.

4.2.2 Laparoscopic Sleeve Gastrectomy

The LSG is the fastest growing bariatric procedure in recent years, preferred by both surgeons and patients mainly due to excellent results in terms of weight loss, control of obesity-related comorbidities, and quality of life, which is achieved through a faster, technically less demanding surgical procedure [33, 34]. In addition, the absence of intestinal bypass preserves the original absorptive surface, significantly reducing adverse events related to nutrient malabsorption, which is a common concern associated with bypass procedures.

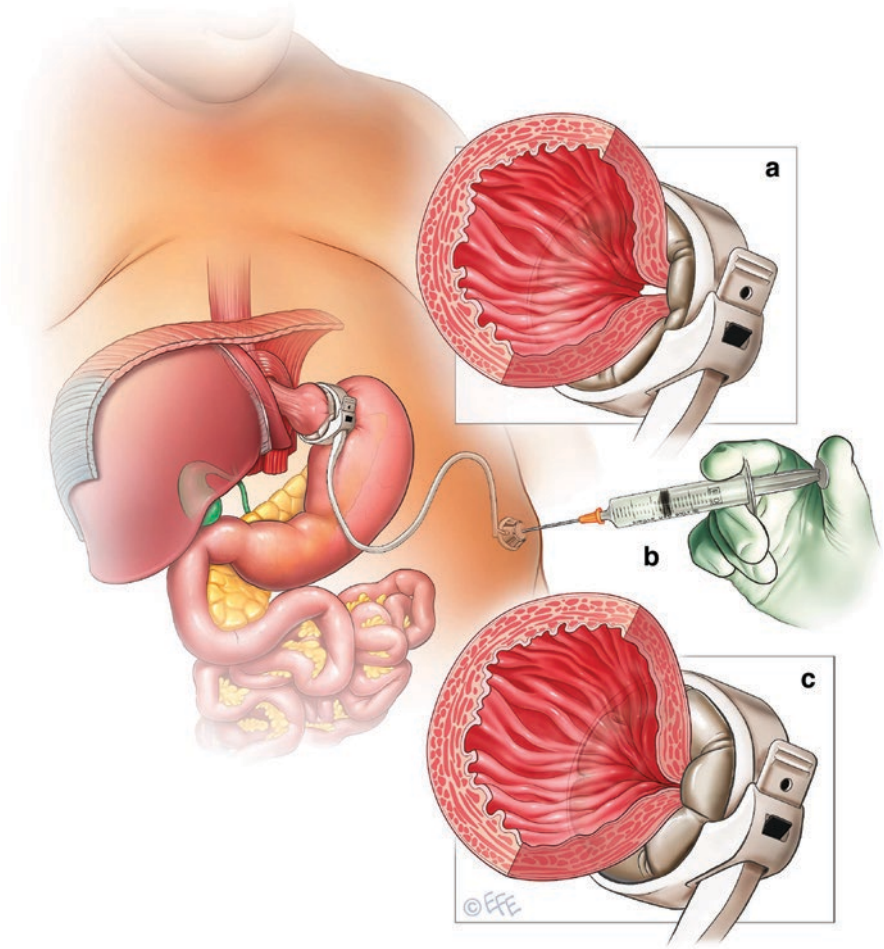

Fig. 4.1 Schematic drawing showing AGB in place. (**a**) Deflated band ("open"); (**b**) subcutaneous access port; (**c**) inflated band ("closed")

The operative technique can be summarized in the removal of about 70–80% of the stomach by means of stapled vertical gastrectomy, which includes a small part of the antrum, a large part of the body, and the entire gastric fundus (Fig. 4.2). The pylorus is preserved, and therefore, the gastric emptying mechanism is kept intact. The only anatomical change is a reduction in the size of the gastric reservoir, which is approximately 100–150 mL capacity. This single, "simple" anatomical alteration (partial gastrectomy), however, can cause deep modifications in the functioning of the entire digestive system. Because of a partial gastrectomy, LSG is an irreversible bariatric procedure.

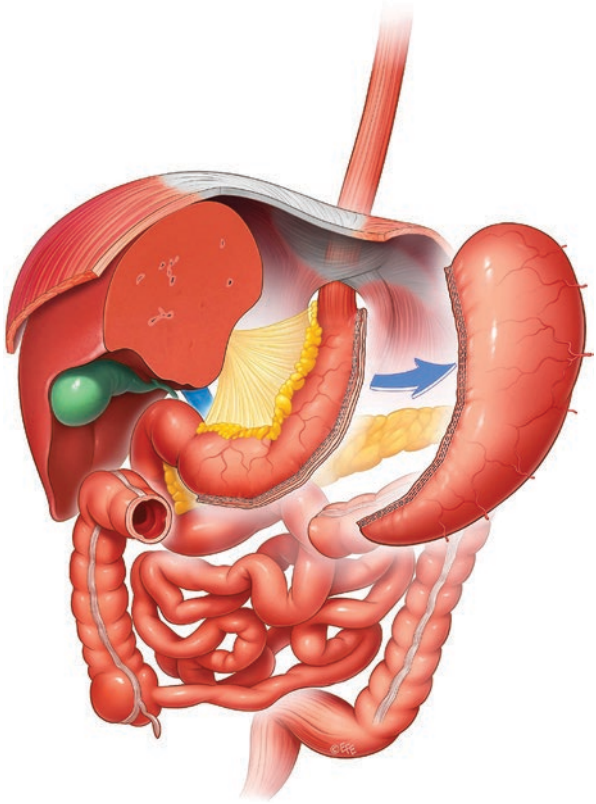

Fig. 4.2 Schematic drawing representative of the final surgical aspect of LSG highlighting the removed stomach, remaining only a long gastric tube (the Sleeve itself). The entire gut is kept untouched

4.3 Anatomical Changes in Procedures with Small Bowel Diversion

4.3.1 Roux-en-Y Gastric Bypass

A small pouch based on lesser gastric curvature is constructed in the upper stomach through linear staplers, excluding about 95% of the stomach. The alimentary pathway is reconstructed in Roux-en-Y fashion, using alimentary and biliopancreatic limbs, connected to each other by distal enteroenterostomy (Fig. 4.3). The alimentary limb usually is about 100–120 cm long, through which only food mixed with saliva and minimal gastric juices flow down. On the other hand, within the biliopancreatic limb (50–150 cm in length) only gastric and biliopancreatic secretions flow without food. Thus, the ingested food only meets gastric and biliopancreatic secretions after enteroenterostomy, in the common channel. The length of the common channel varies according to the total length of the small bowel since the surgeons usually work with fixed lengths of only the alimentary and biliopancreatic limbs.

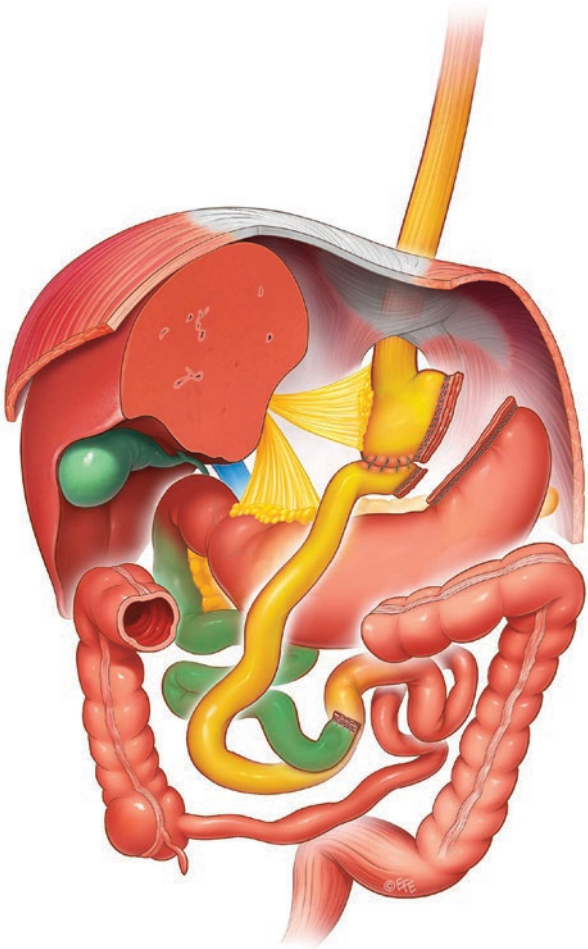

Fig. 4.3 Schematic drawing representative of the final surgical aspect of RYGB with small, vertical gastric pouch, Roux-en-Y reconstruction, and longer common channel

Therefore, the anatomic configuration of RYGB provides a reduced gastric capacity (20–30 mL), along with an exclusion of the stomach (95%), duodenum and a variable length of the jejunum (usually 50–150 cm). This causes a restriction, in addition to substantially altering the neurohormonal signaling of the GI tract and modifying the well-tuned processes of digestion and absorption. Although RYGB is prone to induce some nutrient deficiencies (mainly due to duodenal bypass), the malabsorptive component itself is generally mild.

4.3.2 One-Anastomosis Gastric Bypass

The OAGB was originally described in the early 2000s and is a procedure with principles similar to RYGB, but technically simpler and faster. The procedure involves the creation of a long and narrow pouch ("Sleeve-like") based on the lesser

curvature of the stomach, followed by end-to-side anastomosis between the gastric pouch and the small bowel approximately 150–200 cm distal to the duodenojejunal flexure (angle of Treitz). Unlike the RYGB, there is not an alimentary limb, but rather afferent and efferent loops, since the reconstruction of the food transit occurs following the Billroth II design (Fig. 4.4). The capacity of the gastric reservoir is diminished (more than LSG, but less than RYGB), and the entire duodenum and the first 150 to 200 cm of the small bowel (jejunum) are bypassed.

The OAGB has been usually reported as a hypo absorptive procedure with a higher incidence of diarrhea, steatorrhea, deteriorated liver parameters, and nutritional adverse events [35, 36], although the amount of small bowel diversion is very similar to RYGB with long limbs. Thus, the pivotal anatomical and perhaps also physiological difference with RYGB is the absence of an alimentary limb (Roux-limb).

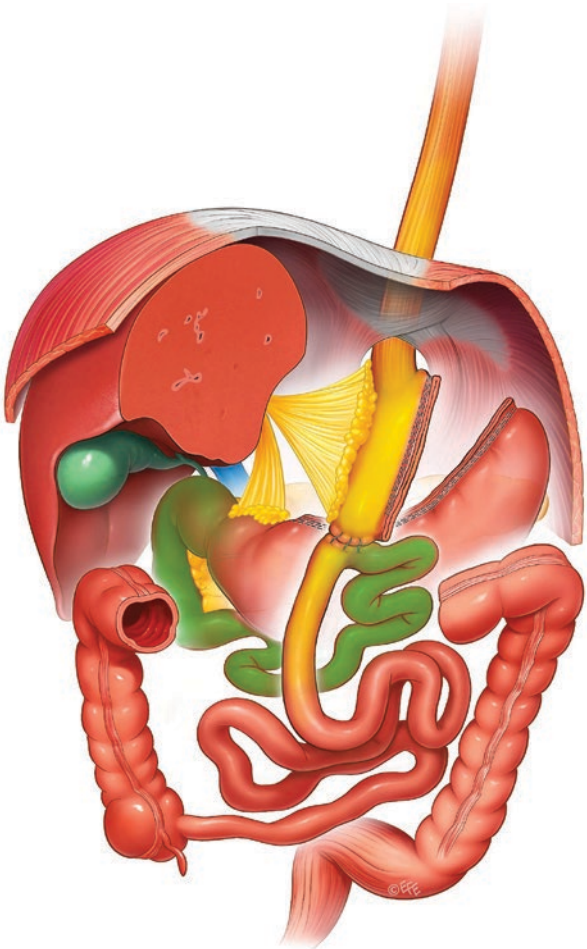

Fig. 4.4 Schematic drawing representative of the final surgical aspect of OAGB with long gastric pouch and Billroth II type reconstruction

4.3.3 Biliopancreatic Diversion with Duodenal Switch

Rarely performed today, BPD-DS is a chiefly malabsorptive procedure. Recently, a new single-anastomosis-based BPD-DS design (Single-Anastomosis Duodenoileal bypass with Sleeve Gastrectomy—SADI-S) represents a current attempt to reduce side effects and provide a technical simplification [37, 38].

Usually described as a "malabsorptive" procedure, BPD-DS includes both restrictive and malabsorptive components. The restriction is due to a Sleeve gastrectomy. A linear stapled transection of the duodenum immediately after the pylorus is performed and the food transit is reconstructed by means of an end-to-side, hand-sewn Roux-en-Y duodenoileostomy. Enteroenterostomy is then performed at a distance of 50–120 cm from the ileocecal valve. The final configuration of the small bowel diversion in the BPD-DS (as well as the classic BPD and SADI-S) is longer alimentary and biliopancreatic limbs and shorter common channels (Figs. 4.5, 4.6

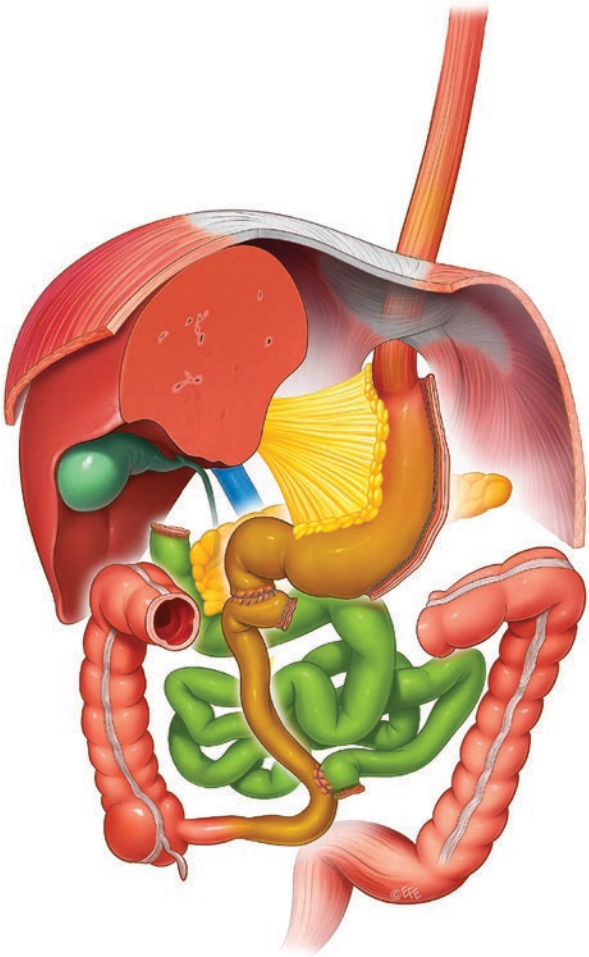

Fig. 4.5 Schematic drawing representative of the final surgical aspect of BPD-DS with sleeve gastric pouch, post-pyloric Roux-en-Y reconstruction, and short common channel

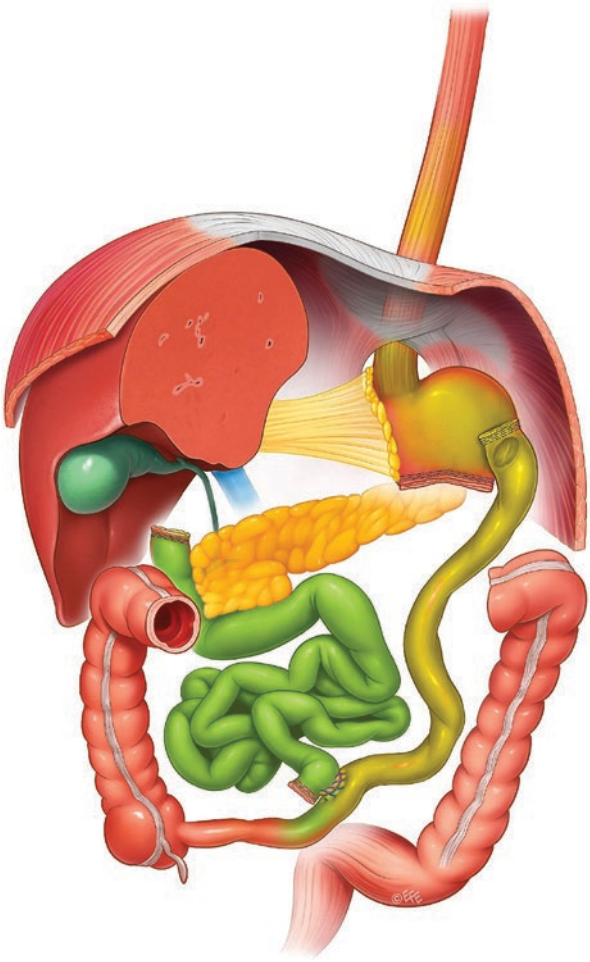

Fig. 4.6 Schematic drawing representative of the final surgical aspect of classic BPD (Scopinaro's Surgery) with partial gastrectomy, large horizontal gastric pouch, and short common channel

and 4.7). The length of the common channel (how short it is left) predominantly defines the degree of malabsorption and can be a factor for the severe and sometimes uncontrollable adverse effects.

4.4 Physiological Changes on GI Tract After Bariatric Procedures

The anatomical changes brought about by the various procedures also induce changes in the physiology of the digestive system in different ways and to different degrees. Bariatric surgery targets various organs and systems beyond the GIT, including the central nervous system, liver, pancreas, adipose tissue, and muscle, among others, impacting the whole metabolism of the human body. Profound

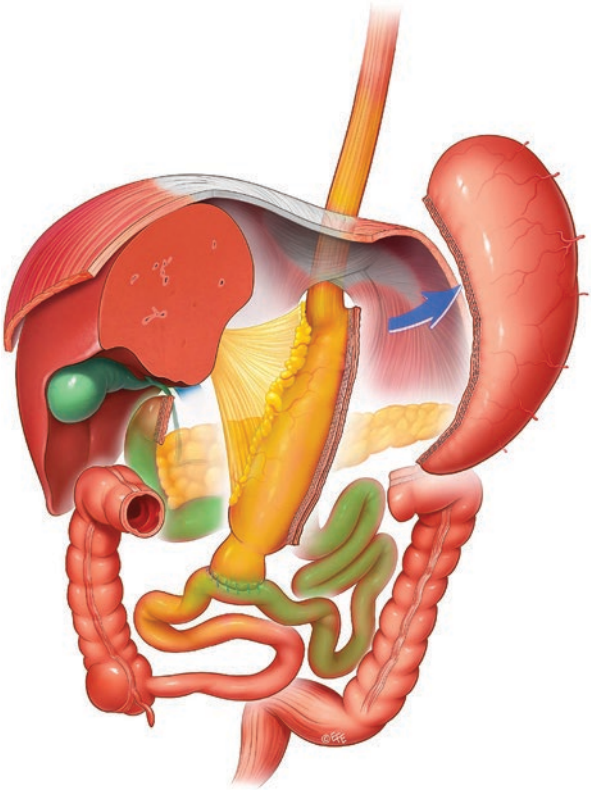

Fig. 4.7 Schematic drawing representative of the final surgical aspect of SADI-S with sleeve gastric pouch, post-pyloric (duodenoileal) end-to-side single anastomosis, and short common channel

metabolic alterations occur that go beyond physical restriction and involve food preferences, taste perception, and changes in hunger/satiety control signaling. In addition, digestion and absorption of nutrients is also affected. Apart from the restriction and malabsorption factors, these changes are mediated through neural pathways and substances like leptin, ghrelin, insulin, cytokines, and several gut-derived hormones, among others. Even in procedures considered purely restrictive, such as LAGB, the efficacy of weight loss may be associated with neurohormonal mechanisms [18, 19, 39–41].

In spite of the available literature, the actual impact of bariatric procedures on the physiology of the digestive system is far from completely understood and needs to be studied further.

4.5 Food Intake

In general, food intake is reduced following bariatric surgery. The impact on food intake starts from the cephalic phase itself. Hormones like ghrelin, insulin, and gastrin are released in response to the thought, sight and/or smell of food [19, 42]. Soon

after bariatric procedure, patients usually show a significant reduction in fasting and postprandial ghrelin levels. However, these low levels appear not to be sustained in the long term. Therefore, although the significant drop in serum ghrelin may be contributory in the weight loss immediately after bariatric surgery, this may not have the same relevance in weight loss maintenance.

Return to baseline levels may also be implicated in recidivism in the long term. In this sense, the surgical impact of LSG on ghrelin levels seems to be more consistent and durable than RYGB, since most ghrelin secreting cells are irreversibly removed by the operation (gastric fundus) [12, 43–45]. However, it remains open to debate as the incidence of weight regain after LSG has been shown to be significant.

Changes in appetite, food preferences, and taste perception may also diminish food intake postoperatively, impacting on weight loss. An increased preference for low-sugar and low-fat diets have been frequently observed after bariatric procedures [46]. The exact underlying mechanism of this remarkable modification in food preferences and palatability is poorly understood since self-reporting is the most common method used to record food preferences after bariatric surgery, which gives inconsistent and less than reliable findings [47–50]. Interestingly these changes do not appear to be strongly related to the type of bariatric procedure. In addition, modification in chewing time should be also considered as a contributing factor in reducing food intake. Although dependent on the dental state and the type of food ingested, bariatric patients tend to increase chewing, especially for solid foods [51].

Given the reduced gastric capacity resulting from bariatric procedures, meal sizes are proportionally reduced after bariatric procedures [52]. However, in addition to the restriction, postoperative food intake reduction is also known to be related to an expressive shift in the signaling of the hunger/satiety neuronal center due to increased levels of GI satiety hormones, such as pancreatic polypeptide (PP), peptide YY (PYY), glucagon-like peptide 1 (GLP-1) and 2 (GLP-2), gastrin, secretin, obestatin, vasoactive intestinal polypeptide (VIP), gustducin, oxyntomodulin (OXM) and glucose-dependent insulinotropic polypeptide (GIP) [53]. Although it is a common effect of almost all procedures, changes on hunger/satiety center mediated by digestive substances seem to be more profound after diversionary procedures.

4.6 Gastric Emptying: Digestive Motility

Upper GI motility may also play a role in the pathophysiology of obesity, since accelerated gastric emptying may decrease the satiety time and consequently promote greater food intake. Therefore, it is interesting to evaluate the behavior of gastric emptying and upper GI motility after bariatric procedures. Esophageal motor dysfunction and dilation by emptying scintigraphy, esophageal dysmotility by manometry, and signals of esophagitis by upper endoscopy are the most common methods employed to clinically evaluate gastric emptying. Although GI motility can also be investigated by methods such as the migrating motor complex and

postprandial motor pattern, the relationship between abnormalities usually found and clinical symptoms remains uncertain [54, 55].

Gastric emptying seems to be normal or accelerated after LSG (and probably also after BPD-DS). Although this acceleration in emptying of gastric sleeve may compromise the perception of postprandial satiety to some extent, a rapid delivery of the ingested food may also promote greater release of satiety gut hormones, such as GLP-1, contributing to the efficacy of the procedure [56]. Notwithstanding, it remains controversial whether the amount of antrectomy and Sleeve calibration influence weight loss. Another source of concern regarding the emptying of gastric sleeve is the occurrence of the dumping syndrome. Although believed to be less prevalent, mainly due to preservation of the pyloric sphincter, symptoms perceived as dumping may occur after LSG, depending on the type of food ingested [57]. The pathophysiology of this late dumping is probably linked to increased release of several enteric hormones such as neurotensin, VIP, GIP, and GLP-1, inducing disordered GI motility and hypoglycemia.

As for RYGB (and probably also OAGB), the major concern about gastric pouch emptying is indisputably the dumping syndrome. The pathophysiology of the early dumping observed after RYGB appears to be related to the absence of pylorus as a valve regulating gastric pouch emptying rather than increased motility [58]. At the same time, the rapid delivery of food ingested in the small bowel (alimentary limb and common channel) can co-produce symptoms of late dumping [32]. In this sense, calibrated gastroenteroanastomosis can mimic the barrier normally caused by the pylorus, providing greater stasis of the food ingested within the gastric pouch, increasing the feeling of satiety, possibly decreasing the occurrence of early dumping, and ultimately contributing to the postoperative weight loss after RYGB [59].

In AGB, as expected, several esophageal abnormalities associated with impaired gastric emptying are observed, depending on the amount of insufflation/deflation of the device. This dysmotility may be related to the mechanical barrier caused by the narrow lumen that separates the upper and lower gastric chambers when the device is in place. In some situations, the severity of disorders and symptoms of the upper digestive system may need withdrawal of the band, and some sequelae can persist in the long term [54].

4.7 Digestion and Absorption

The major alterations in the digestive and absorptive processes are related to the gastric volume reduction and length of bypass. The digestion begins in the mouth during chewing by mixing the food with the saliva. The salivary flow behavior following bariatric surgery is somewhat controversial, but there is some evidence to suggest that it remains unchanged after RYGB [60]. Gastrin and cholecystokinin (CCK) are homologous hormone systems that act synergistically in gastric acid secretion and in gastric and gallbladder emptying. Gastrin is released by G-cells located primarily in the gastric antrum and duodenum to stimulate the secretion of gastric acid by the parietal cells of the stomach and enhance gastric motility. Gastrin

may impact on insulin secretion via gastrin receptors in the islet of the pancreas [61]. As one would expect, serum levels of gastrin are generally suppressed after techniques that provide wide gastric and duodenal exclusion, such as RYGB. The impact of LSG with preserved antrum on gastrin secretion appears to be lower, or even absent [62]. In turn, CCK behaves controversially. It is synthesized and secreted by I-cells localized in the duodenal mucosa, helps in satiety, and inhibits gastric motility and emptying. After LSG, given the non-exclusion of the food bolus from the lumen of the duodenum, CCK levels appear to be normally increased [63]. Paradoxically, similar observations have been noted after RYGB. Other factors for CCK release like parasympathetic signaling may be implicated in the increased levels of CCK following bariatric procedures with duodenal exclusion, like RYGB, OAGB, and BPD-DS [53, 61]. Pancreatic juice containing several enzymes is released into the duodenum in response to chime along with bile and helps in the digestion of proteins, carbohydrates, and lipids. The major enzymes are lipase (lipid decompositions in fatty acids and glycerol), trypsin (break proteins in minor fragments), and pancreatic amylase (starch decomposition). The secretion of these enzymes and their actions are usually impaired in procedures with small bowel (duodenum) diversion, such as RYGB, OAGB, and BPD-DS, impairing the absorption of these macronutrients.

The overall absorptive capacity of the digestive system is mainly due to the integrity of the small bowel, including the duodenum. In procedures without small bowel diversion, such as AGB and LSG, the absorptive surface remains intact, and therefore, limited change in the absorption is expected postoperatively. Nutritional deficiencies observed after exclusive gastric procedures such as LSG can be due to reduced food intake (mechanical restriction and/or early satiety), food intolerance (vomiting), and/or changes in the regulation and release of digestive enzymes. Surgical procedures with intestinal diversion can additionally lead to impaired absorption of macro and micronutrients, depending on the extent of the intestinal bypass. The larger the bypassed area, the greater is the impairment in the absorptive process. In this regard, malabsorptive procedures, such as BPD-DS and distal RYGB (longer alimentary and/or biliopancreatic limbs and shorter common channels) are more commonly associated with postoperative nutritional disorders. Severe, and sometimes clinically uncontrollable, nutritional disorders represent the high biological cost associated with this group of procedures for a greater efficacy in weight loss and control of comorbidities [64–67]. According to the recent literature, OAGB has also been associated with a higher rate of hypoalbuminemia and anemia [36, 68, 69]. However, regardless of small bowel diversion, all types of bariatric procedures can virtually cause nutritional deficiencies, each due to specific reasons [70].

Although specific deficiencies are expected according to the gut segments bypassed, due to disruption of the digestive sequence, additional deficiencies of macro- and micronutrients can manifest.

Micronutrients are essential dietary factors that are needed in minimal amounts to support various biochemical pathways and metabolic processes in the human body and include trace elements (chromium, copper, manganese, selenium, and

zinc), essential minerals (calcium, iodine, iron, and magnesium), fat-soluble vitamins (vitamins A, D, E, and K) and water-soluble vitamins such as thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), pantothenic acid (vitamin B5), pyridoxine (vitamin B6), biotin (vitamin B7), folic acid (vitamin B9), cobalamin (vitamin B12), and ascorbic acid (vitamin C). In turn, macronutrients are nutrients that provide daily energy and make up the structure of the human body and are therefore required in large quantities. Major components are proteins, fats, carbohydrates, and also water. The most common micronutrients deficiencies with clinical significance after bariatric procedures, especially after small bowel diversion, are related to iron (iron-deficiency anemia), vitamin B12 (pernicious anemia), folates (macrocytic anemia), thiamine (neurological commitment), and calcium and vitamin D (osteoporosis/fractures). In turn, protein malnutrition is the most common macronutrient deficiency associated with patients undergoing bariatric surgery [28, 71–74].

4.8 Micronutrient Deficiencies

Bariatric techniques that include either gastric resection or gastric exclusion, such as LSG and RYGB, respectively, may lead to hypochlorhydria and reduction in the intrinsic factor. Reduction of gastric acid decreases the bioavailability of vitamin B12 from food, while the quantitative reduction of gastric intrinsic factor may significantly compromise the absorption of B12 in the distal ileum. The result of these two mechanisms can be a low rate of serum vitamin B12. In addition, impairment in the pancreatic proteases action caused by duodenal exclusion may contribute to poor vitamin B12 absorption. Other secondary causes of B12 deficiency may include food intolerance (and therefore even more drastic reduction of food intake) and small intestinal bacterial overgrowth. Fortunately, body storage of vitamin B12 is substantial and clinical deficiencies usually only emerge in the late postoperative period (after 1 year) [28, 71, 72, 75].

A low-iron diet and chronic disease features associated with obesity predispose for iron deficiency and anemia in morbidly obese patients in the preoperative period. Post bariatric surgery, this situation may be worsened by hypochlorhydria, reduction in iron intake, and duodenojejunal bypass. The hypochlorhydria resulting from almost all bariatric procedures hinders the reduction of ferric iron into the absorbable ferrous form, reducing iron uptake. In addition, food intolerances, especially for red meat, maybe a relevant factor for low oral iron intake. Finally, poor adherence to dietary guidelines and recommended supplementation may also reduce the luminal amount of iron available to be absorbed. Thus, even in procedures without small bowel diversion, such as LSG, there may be deficiencies in serum iron availability, albeit to a lesser extent [76]. However, techniques that bypass the primary site of iron absorption (duodenum), such as RYGB, OAGB, and BPD-DS, significantly increase the incidence of clinical or laboratory deficiency of iron, especially in menstruating women [77].

Folic acid is a micronutrient primarily absorbed in the duodenum and proximal jejunum. Although widely present in several types of foods, folate storage in the liver is generally not sufficient for more than 2–3 months of consumption. Folate deficiency has been associated with macrocytic anemia in patients following bariatric surgery, mainly after procedures with small bowel diversion (RYGB, OAGB, and BPD-DS). Poor intake can also be blamed as a source of deficiency after AGB and LSG. On the other hand, high serum levels of folic acid in the postoperative period may also occur and have been considered as a marker of small intestinal bacterial overgrowth following bariatric surgery [71, 74].

Thiamine deficiency is a worrisome nutritional complication after bariatric surgery, since this co-enzyme is essential for the metabolism of carbohydrates and amino acids, and in the reactions that produce energy (Krebs cycle). In addition, cerebral metabolism is highly dependent on thiamine. The major consequence of thiamine deficiency is beriberi, a clinical syndrome featured by psychiatric, neurologic, cardiac and/or gastrointestinal manifestations. The hallmark of neurological commitment associated with low levels of thiamine is the paresthesia of the hands or feet, motor impairment, or loss of balance soon after 1–3 months after bariatric surgery ("bariatric beriberi"). The presence of small intestinal bacterial overgrowth should always be considered when oral thiamine supplementation is not resolutive [78]. In addition, symptoms of Wernicke's encephalopathy or acute psychosis should be considered medical emergencies. Although thiamine can be absorbed throughout the small bowel (jejunum and ileum), an efficient absorptive process is also dependent on the duodenal mucosal enzymes [28, 71]. Thus, techniques with duodenal bypass may be more prone to the development of thiamine deficiency, such as RYGB [79]. However, reduced food intake, supplementation non-adherence, and especially recurrent vomiting also appear to be important factors, since thiamine deficiency has been reported after LSG as well [80].

Vitamin D is a prohormone steroid that has two main sources: skin (in response to ultraviolet radiation) and dietary. Intestinal absorption occurs primarily in the small bowel with an efficiency of approximately 50% in the normal digestive system and is facilitated by bile salts. After its synthesis or absorption, vitamin D is metabolically activated in the liver to form 25-hydroxyvitamin D (25OHD), and then into the kidney to generate the active circulating metabolite, 1,25-dihydroxy vitamin D (1,25(OH)2D), or calcitriol. Vitamin D is an essential modulator of calcium metabolism, maintaining adequate calcium and phosphate levels required for bone formation by promoting absorption in the intestines [81]. Based on this, low sunlight exposure, reduced food intake, and decrease in the gut absorptive surface are considered pivotal causes of post-bariatric vitamin D deficiency. The major impact of vitamin D deficiency is the decrease in calcium absorption, secondary hyperparathyroidism, hypophosphatemia, and increased bone turnover. Altogether, these alterations usually result in lower bone mineral density and can lead to the development of skeletal disorders, notably osteopenia, osteomalacia, and osteoporosis. Therefore, bariatric patients undergoing techniques that combine restriction in food intake with a significant decrease in the small bowel absorptive area (distal RYGB, OAGB, and BPD-DS) are more likely to exhibit impairment in the

metabolic availability of vitamin D and, hence, the development of clinical features. In turn, calcium plays a crucial role in numerous biological processes, ranging from muscle contraction and blood clotting. Adequate intestinal absorption is essential for calcium acquisition and bone is the major calcium reservoir. Resorption is a physiological pathway in maintaining calcium homeostasis, closely regulated by the parathyroid hormone. When calcium absorption is declined and serum levels drop (due to low intestinal absorption related to hypochlorhydria, poor consumption of calcium-containing foods, and/or vitamin D deficiency), excessive resorption is triggered, generally at the expense of decreasing bone density mineralization and acceleration of bone remodeling, probably increasing the risk of osteoporosis and bone fractures mainly in unsupplemented situations [28, 71, 72, 74, 82, 83]. After LSG, where anatomical small bowel absorption area is not compromised, preoperative suboptimal levels (both calcium and vitamin D) plus postoperative restricted dietary intake may probably be the reasons for clinical deficiencies.

4.9 Macronutrient Deficiencies

Protein malnutrition is the principal macronutrient deficiency after bariatric surgery and is a major source of concern in the postoperative period since, unlike carbohydrates and fat, protein is not stored in the human body. Protein deficiencies may have a very broad clinical presentation ranging from mild laboratory hypoalbuminemia to generalized edema and death. Thus, protein malnutrition following bariatric surgery should be inspected periodically by serum albumin levels, which can accuse difficulties in protein uptake long before the arising of more serious clinical features. The incidence of postoperative hypoproteinemia depends on the type of bariatric surgery, being relatively smaller after restrictive procedures without intestinal bypass (AGB and LSG) and greater after procedures with a malabsorptive component. Notoriously, the greater the small bowel bypass the greater the risk of protein malnutrition [72, 84–86]. Pathogenesis is most commonly related to malabsorption due to bypassing segments of the small bowel where the protein is absorbed primarily (duodenum and proximal jejunum). To a lesser extent, limitation in food intake, substantial decrease in pepsinogen levels, and reduction of pancreatic secretion of proteolytic enzymes may also be unfavorable factors for digestion and protein absorption [18]. Dietetic counseling with increased protein intake in the daily diet and oral supplementation are the most effective management to prevent postbariatric hypoproteinemia. If this fails consistently, reversion of the malabsorptive component of the surgery may be lifesaving in selected cases.

Fat uptake mainly depends on biliary and lipolytic enzymes released by the gallbladder and pancreas, which are primarily regulated by CCK. In bariatric procedures with small bowel diversion (RYGB, OAGB, and BPD-DS), dietary fats (triglycerides, phospholipids, cholesterol) remain almost intact until reaching the common channel (or distal segments of efferent limb, in case of OAGB). Later lipids breakdown with delayed formation of micelles strongly limiting the amount of fat available for absorption in the small bowel. Hence, undigested fat goes to the

large intestine and produces fat malabsorption and steatorrhea. Although uncommon, this pathophysiology can be present even after procedures that comprise a weaker malabsorptive component, such as RYGB [87].

Although bariatric procedures can alter carbohydrate digestion and absorption, mainly due to the limited action of the pancreatic amylase to convert polysaccharides into oligosaccharides present in small bowel diversion techniques, deficiencies are virtually nonexistent, as this essential macronutrient is absorbed in the entire gut. Absorbed carbohydrates are stored in the liver and skeletal muscle as quickly available glycogen to serve as a major source of energy for body metabolism and, most importantly, for the brain and red blood cells. In addition, in the face of inadequate carbohydrate substrate (low food intake and/or some degree of malabsorption), fat and protein are broken down through gluconeogenesis to provide nutritional substrate for the brain and red blood cells. Thus, carbohydrate deficiency is always preceded by a marked loss of fat mass and severe protein deficiency [18].

Based on these expected adverse effects common to almost all types of bariatric procedures, periodic clinical and laboratory screening for nutritional deficiencies and, if needed, targeted and standardized supplementation both for macro and micronutrients, are recommended. A more intensive surveillance is recommended after malabsorptive procedures. In the long term, it is even admissible that small bowel adaptive mechanisms would attenuate mainly macronutrients deficiencies in post-bariatric patients.

4.10 Enterohormones

Undoubtedly, the growing understanding of the postoperative behavior of enterohormones may be considered as one of the major advances in bariatric surgery in recent years. These sets of knowledge gave rise to the principles of so-called metabolic surgery and anchored new pharmacological drugs for the clinical treatment of obesity and T2DM. Liraglutide, a glucagon-like peptide 1 agonist (GLP-1), is a prime example.

Fasting and postprandial levels of several enterohormones are significantly altered after bariatric surgery, with a well-documented impact on the hunger/satiety regulation and metabolic control in bariatric patients. Although all obesity-associated metabolic diseases may be positively affected, the incretin-mediated T2DM outcomes have been the most addressed to date.

The incretin effect is a very old concept in which the oral glucose administration promotes greater insulin secretion compared to a similar parenteral infusion [88, 89]. The insulinotropic gut-derived factors that could be responsible for this enhancement in insulin secretion after oral/enteral glucose intake were then denominated as incretins. Thus, the incretin effect is an amplification of insulin secretion driven by incretins and is recognized as the major mechanism for normal glucose tolerance. As expected, this effect is greatly reduced or totally missing in obese diabetic patients and the restoration of this physiological effect is one of the goals sought by bariatric procedures. To date, only glucose-dependent insulinotropic

polypeptide (GIP) and GLP-1 fulfill the definition of an incretin hormone in humans. GIP and GLP-1 are produced by specialized enteroendocrine K- and L-cells, respectively. K- and L-cells are sensitive to mainly macronutrients (carbohydrates, fats, and proteins). By responding more to the nutrient uptake than to the presence in the gut lumen, increased enterohormones levels may accurately indicate the arrival of such nutrients into the bloodstream [90].

GIP was the first incretin identified and was initially nominated as a gastric inhibitory polypeptide, given its ability to delay gastric emptying (satiety hormone). Later, GIP was renamed to glucose-dependent insulinotropic polypeptide after recognition of its action as an enhancer of insulin secretion by the pancreas. GIP is secreted mainly by enteroendocrine K-cells, found at higher density in the duodenum. It was recognized that GIP alone could not fully explain the incretin effect commonly observed after bariatric surgery, since impairment of endogenous GIP activity attenuates but does not abolish the incretin effect. Given its controversial profile after bariatric procedures, with scarce data after procedures like LSG, the relevance of GIP in mediating weight loss and incretin effect remains to be better determined and therefore has currently been undervalued [53, 91, 92].

GLP-1 is undoubtedly the most powerful incretin associated with bariatric surgery [93]. This gut hormone is primarily secreted by enteroendocrine L-cells, which increase in number toward the distal small bowel, being also numerous in the large intestine [91, 92]. GLP-1 is a satiety hormone that delays gastric emptying, increases insulin release, and decreases glucagon production. Although fasting GLP-1 levels do not markedly change after bariatric surgery, postprandial levels of GLP-1 increase significantly after most bariatric procedures [93]. RYGB (and other procedures with small bowel bypass and hence, functional gut shortening such as OAGB and BPD-DS) have exhibited high postprandial levels of GLP-1, coinciding with high rates of glycemic control in diabetic patients. Indeed, bariatric surgery provides an expressive increase in GLP-1 release, normalizing the attenuated incretin effect generally presented in diabetic patients. The higher and earlier the stimulation of ileal L-cells by luminal content (secretions, bile salts, and foods), the greater the release of GLP-1. Thus, dramatically elevated postprandial levels of GLP-1 were measured after RYGB (10–20 times higher than normally observed in healthy people with original digestive tube) [11, 58], a phenomenon also observed after BPD-DS [94] but not after LAGB [95]. These high levels substantially contribute to both weight loss (suppression of appetite) and glucose homeostasis (incretin effect) [11]. After LSG, GLP-1 also rises, but at slightly lower levels [45, 58, 96]. Faster gastric emptying and lower small bowel transit time have been indicated as the key mechanism for sustained post-Sleeve stimulation of ileal L-cells, rising the GLP-1 levels and subsequently activating the ileal brake [56, 97, 98].

In addition to the well-documented effects of incretins (GIP and GLP-1), a plethora of enterohormones have also their fasting and postprandial profile significantly changed after bariatric surgery. Glucagon-like peptide 2 (GLP-2) is produced by enteroendocrine cells and also by neurons in the central nervous system. Intestinal GLP-2 is derived from proglucagon and co-secreted by L-cells along with GLP-1 upon nutrient uptake [11]. The main recognized action of GLP-2 in the digestive

system is to promote intestinal villi hypertrophy and to downregulate apoptosis. In general, the post-bariatric GLP-2 profile has sparked little interest to date and therefore has been rarely addressed. After RYGB, high postprandial levels of GLP-2 have already been observed and interestingly correlated with aspects of satiety regulation [53, 99]. Oxyntomodulin (OXM) is an anorexigenic peptide also derived from proglucagon and co-secreted with GLP-1 by enteroendocrine L-cells. OXM appears to reduce hunger, food intake, and ghrelin levels, as well as decrease gastric acid secretion and GI motility (satiety hormone). Although high levels of OXM have been observed shortly after RYGB [100] no OXM-specific receptor has yet been well identified, and its relevance in bariatric outcomes remains to be better determined [19, 53]. Peptide YY (PYY) is also released by enteroendocrine L-cells in the distal small bowel and colon in response to feeding. In the bloodstream, PYY is converted to PYY(3-36), its active form. PYY(3-36) appears to be a satiety hormone, since circulating levels usually increase in the postprandial period, leading to a delayed gastric emptying, reduced insulin production, and altered GI motility. However, the major target of PYY(3-36) is the central regulation of appetite, reducing food intake. Serum levels of PYY(3–36) appear to be enhanced postprandially following bariatric surgery, regardless of procedure (RYGB, LSG, and BPD-DS). However, a better understanding of the PYY(3-36) physiology is still needed to establish the real impact of this enterohormone on weight loss and metabolic control after bariatric surgery [19, 53, 94, 101, 102].

In summary, the release of enterohormones and the interaction between them is profoundly altered after bariatric surgery, assuming a pivotal place in weight loss and improvement/remission of obesity-related comorbidities, and even surpassing in relevance the role of classic restrictive and malabsorptive mechanisms.

4.11 Gut Microbiota

As gut microbiota disarray has often been associated with obesity and its metabolic comorbidities [103, 104], there also has been a rising interest in gut microbiota behavior following bariatric surgery since some studies have suggested that gut microbial communities play a key role in mediating beneficial effects attributed to bariatric procedures, whether in relation to weight loss or to metabolic control [105–107]. The list of the gut microbiota modifications after bariatric surgery is already very long, but it is still far from complete or fully understood, since few studies have specifically addressed this relevant topic in humans at present. The increased relative abundance of the phylum Proteobacteria (class Gammaproteobacteria; genera Escherichia, Klebsiella, and Enterobacter), as well as an increase in members of the phylum Bacteroidetes and a general decrease in members of the phylum Firmicutes, are the major changes commonly observed [105, 108], regardless of the procedure.

The relevance in assessing the species Escherichia coli in studies involving gut microbial changes after bariatric surgery comes from the fact that it constitutes part of the “core microbiome,” that is, bacterial species that can be found in most gut

microbiota profiles of healthy individuals. Also, Escherichia coli is recognized by its high translocation ability which may impact chronic systemic inflammatory response. In turn, the assessment of the Bacteroidetes/Firmicutes ratio takes a leading role in the studies of gut microbiota after bariatric surgeries because these phyla correspond to about 90% of the gut microbial community [104, 109–111]. Although the profile of higher levels of several species in the Gammaproteobacteria class and lower levels in species belonging to Firmicutes phylum seem to be sustainable in the long term [112], the investigations that address the stability of microbial profile after bariatric surgery are still sturdy.

Interestingly, some studies involving morbidly obese individuals submitted to bariatric surgery have shown changes in gut microbiota profile soon after 3 months of surgery, therefore, long before the final weight loss [113, 114]. This finding is in agreement with prompt metabolic improvement usually observed after bariatric surgery, since gut microbial balance has been recognized as a hallmark of the host's health status [115–117]. In general, technical designs of bariatric surgeries appear to be a favoring factor to commonly observed changes in the gut microbial communities. These functional changes may be influenced by drastic changes in food intake, either in quantity or in quality/preferences [118, 119]. Thus, the intestinal microbiota would be forced to conform to this new pattern of food consumption. In addition, changes in luminal pH, nutrient supply, motility, and increased oxygen concentration in the small bowel can be implicated in the arising of a new microbiota profile, which would ultimately represent no more than an adaptation to the new anatomic and physiological configuration of GI tract.

Not surprisingly, most studies on changes in gut microbiota following bariatric surgery involve RYGB, the most traditional bariatric procedure worldwide and also the most commonly performed until very recently. This procedure may increase the richness of gut microbiota, especially the bacteria belonging to Proteobacteria [113]. Although the exact mechanism is still unclear, factors such as the luminal pH and modifications in the nutrient supply can be pivotal. On the other hand, few studies have addressed the postoperative gut microbial behavior after LSG to date. Notwithstanding, some data available have shown that LSG also affects both the microbiota profile and gut permeability [106, 120, 121]. The exact underlying mechanism also remains poorly understood, but, as expected, the LSG appears to provide a different and less pronounced impact on microbiota balance than procedures with small bowel diversion, such as RYGB and duodenojejunal bypass [106, 121, 122]. Even so, the alterations in gut microbiota after LSG appear to go beyond dietary restriction and consequent fat mass loss [123, 124]. Food preferences, decrease in energy intake, and alterations in GI motility may be underlying factors.

4.12 Conclusion

The anatomy and physiology of the digestive system are markedly altered after bariatric surgery. Most of these changes are expected and are the therapeutic target of surgical interventions, having a positive impact on obesity and related

comorbidities. The same anatomical and physiological changes may also be the source of severe adverse effects following bariatric surgery. Therefore, all professionals involved in the surgical treatment of morbid obesity should be thoroughly familiar with the anatomical and physiological changes caused by a variety of procedures, to help them recognize the therapeutic targets as well as deal with the possible adverse outcomes.

Key Points

- *Bariatric surgery brings about changes in the GI system by means of Bile flow alteration, Reduction of gastric size, Anatomical gut rearrangement and Altered flow of nutrients, Vagal manipulation, and Enteric and adipose hormones modulation.*
- *Changes in appetite, food preferences, taste perception and chewing time may diminish food intake postoperatively, impacting weight loss. An increased preference for low-sugar and low-fat diet have been frequently observed after bariatric procedures.*
- *Gastric emptying time is reduced after sleeve gastrectomy and BPD-DS.*
- *Late dumping, commonly seen after the diversionary procedures, is also reported after Sleeve gastrectomy, probably secondary to accelerated gastric emptying. It is related to the increased release of several enterohormones such as neurotensin, VIP, GIP, and GLP-1, inducing disordered GI motility and hypoglycemia.*
- *A decrease in absorption is due to hypochlorhydria, decreased Intrinsic Factor, reduction in absorptive surface due to division, billow alteration, and reduced intestinal transit time.*
- *Increased delivery of nutrients to the distal intestine leads to increased levels of enterohormones like GLP1, GIP, PYY, and oxyntomodulin leading to an incretin effect.*
- *An increase in members of the phylum Bacteroidetes and a general decrease in members of the phylum Firmicutes are the commonly observed major changes in the gut microbiome. The changes precede the weight loss and are seen as soon as 3 months after the surgery. These changes have been observed in some studies after LSG as well.*

References

1. NCD Risk Factor Collaboration. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. Lancet. 2016;387(10026):1377–96.
2. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9945):766–81.
3. Courcoulas AP, Yanovski SZ, Bonds D, Eggerman TL, Horlick M, Staten MA, et al. Long-term outcomes of bariatric surgery: a National Institutes of Health symposium. JAMA Surg. 2014;149(12):1323–9.

4. Fisher DP, Johnson E, Haneuse S, Arterburn D, Coleman KJ, O'Connor PJ, et al. Association between bariatric surgery and macrovascular disease outcomes in patients with type-2 diabetes and severe obesity. JAMA. 2018;320(15):1570–82.
5. Maciejewski ML, Arterburn DE, Van Scoyoc L, Smith VA, Yancy WS Jr, Weidenbacher HJ, et al. Bariatric surgery and long-term durability of weight loss. JAMA Surg. 2016;151(11):1046–55.
6. Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Aminian A, Brethauer SA, et al. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. N Engl J Med. 2017;376(7):641–51.
7. Sjöström L, Peltonen M, Jacobson P, Sjöström CD, Karason K, Wedel H, et al. Bariatric surgery and long-term cardiovascular events. JAMA. 2012;307(1):56–65.
8. Phillips BT, Shikora SA. The history of metabolic and bariatric surgery: development of standards for patient safety and efficacy. Metabolism. 2018;79:97–107.
9. Abdeen G, le Roux CW. Mechanism underlying the weight loss and complications of Roux-en-Y gastric bypass. Obes Surg. 2016;26(2):410–21.
10. Chakravartty S, Tassinari D, Salerno A, Giorgakis E, Rubino F. What is the mechanism behind weight loss maintenance with gastric bypass? Curr Obes Rep. 2015;4(2):262–8.
11. Holst JJ, Madsbad S, Bojsen-Møller KN, Svane MS, Jørgensen NB, Dirksen C, et al. Mechanisms in bariatric surgery: gut hormones, diabetes resolution, and weight loss. Surg Obes Relat Dis. 2018;14(5):708–14.
12. Kim KS, Sandoval DA. Endocrine function after bariatric surgery. Compr Physiol. 2017;7(3):783–98.
13. Miras AD, le Roux CW. Mechanisms underlying weight loss after bariatric surgery. Nat Rev Gastroenterol Hepatol. 2013;10(10):575–84.
14. Mulla CM, Middelbeek RJW, Patti ME. Mechanisms of weight loss and improved metabolism following bariatric surgery. Ann N Y Acad Sci. 2018;1411(1):53–64.
15. Pucci A, Batterham RL. Mechanisms underlying the weight loss effects of RYGB and SG: similar, yet different. J Endocrinol Invest. 2019;42(2):117–28.
16. Schlottmann F, Galvarini MM, Dreifuss NH, Laxague F, Buxhoeveden R, Gorodner V. Metabolic effects of bariatric surgery. J Laparoendosc Adv Surg Tech A. 2018;28(8):944–8.
17. Herron DM, Roohipour R. Bariatric surgical anatomy and mechanisms of action. Gastrointest Endosc Clin N Am. 2011;21(2):213–28.
18. Ponsky TA, Brody F, Pucci E. Alterations in gastrointestinal physiology after Roux-en-Y gastric bypass. J Am Coll Surg. 2005;201(1):125–31.
19. Quercia I, Dutia R, Kotler DP, Belsley S, Laferrère B. Gastrointestinal changes after bariatric surgery. Diabetes Metab. 2014;40(2):87–94.
20. Wabitsch M. Gastrointestinal endocrinology in bariatric surgery. Endocr Dev. 2017;32:124–38.
21. Boerlage TC, van de Laar AW, Westerlaken S, Gerdes VE, Brandjes DP. Gastrointestinal symptoms and food intolerance 2 years after laparoscopic Roux-en-Y gastric bypass for morbid obesity. Br J Surg. 2017;104(4):393–400.
22. Borbély YM, Osterwalder A, Kröll D, Nett PC, Inglin RA. Diarrhea after bariatric procedures: diagnosis and therapy. World J Gastroenterol. 2017;23(26):4689–700.
23. Borbély Y, Schaffner E, Zimmermann L, Huguenin M, Plitzko G, Nett P, et al. De novo gastroesophageal reflux disease after sleeve gastrectomy: role of preoperative silent reflux. Surg Endosc. 2019;33(3):789–93.
24. Bordalo LA, Mourão DM, Bressan J. Nutritional deficiencies after bariatric surgery: why they happen? Acta Med Port. 2011;4 (Suppl):1021–8.
25. Høgestøl IK, Chahal-Kummen M, Eribe I, Brunborg C, Stubhaug A, Hewitt S, et al. Chronic abdominal pain and symptoms 5-years after gastric bypass for morbid obesity. Obes Surg. 2017;27(6):1438–45.
26. Liakopoulos V, Franzén S, Svensson AM, Miftaraj M, Ottosson J, Näslund I, et al. Pros and cons of gastric bypass surgery in individuals with obesity and type 2 diabetes: nationwide, matched, observational cohort study. BMJ Open. 2019;9(1):e023882.

27. Mason ME, Jalagani H, Vinik AI. Metabolic complications of bariatric surgery: diagnosis and management issues. Gastroenterol Clin North Am. 2005;34(1):25–33.
28. Patel JJ, Mundi MS, Hurt RT, Wolfe B, Martindale RG. Micronutrient deficiencies after bariatric surgery: an emphasis on vitamins and trace minerals. Nutr Clin Pract. 2017;32(4):471–80.
29. Potoczna N, Harfmann S, Steffen R, Briggs R, Bieri N, Horber FF. Bowel habits after bariatric surgery. Obes Surg. 2008;18(10):1287–96.
30. Sabate JM, Coupaye M, Ledoux S, Castel B, Msika S, Coffin B, et al. Consequences of small intestinal bacterial overgrowth in obese patients before and after bariatric surgery. Obes Surg. 2017;27(3):599–605.
31. Souche R, de Jong A, Nomine-Criqui C, Nedelcu M, Brunaud L, Nocca D. Complications after bariatric surgery. Press Med. 2018;47(5):464–70.
32. van Beek AP, Emous M, Laville M, Tack J. Dumping syndrome after esophageal, gastric or bariatric surgery: pathophysiology, diagnosis, and management. Obes Rev. 2017;18(1):68–85.
33. Angrisani L, Santonicola A, Iovino P, Vitiello A, Higa K, Himpens J, et al. IFSO worldwide survey 2016: primary, endoluminal, and revisional procedures. Obes Surg. 2018;28(12):3783–94.
34. Bastos ELS. Why has laparoscopic sleeve gastrectomy become the most accomplished bariatric procedure? Interv Obes Diabetes. 2019;2(5). https://doi.org/10.31031/IOD.2019.02.000548.
35. Kruschitz R, Luger M, Kienbacher C, Trauner M, Klammer C, Schindler K, et al. The effect of Roux-en-Y vs. omega-loop gastric bypass on liver, metabolic parameters, and weight loss. Obes Surg. 2016;26(9):2204–12.
36. Robert M, Espalieu P, Pelascini E, Caiazzo R, Sterkers A, Khamphommala L, et al. Efficacy and safety of one anastomosis gastric bypass versus Roux-en-Y gastric bypass for obesity (YOMEGA): a multicentre, randomized, open-label, non-inferiority trial. Lancet. 2019;393(10178):1299–309.
37. Gebelli JP, Gordejuela AG, Ramos AC, Nora M, Pereira AM, Campos JM, et al. SADI-S with right gastric artery ligation: technical systematization and early results. Arq Bras Cir Dig. 2016;29(Suppl 1):85–90.
38. Topart P, Becouarn G. The single anastomosis duodenal switch modifications: a review of the current literature on outcomes. Surg Obes Relat Dis. 2017;13(8):1306–12.
39. Ellacott KL, Halatchev IG, Cone RD. Interactions between gut peptides ant the central melanocortin system in the regulation of energy homeostasis. Peptides. 2006;27:340–9.
40. Stefanidis A, Forrest N, Brown WA, Dixon JB, O'Brien PB, Kampe J, et al. An investigation of the neural mechanisms underlying the efficacy of the adjustable gastric band. Surg Obes Relat Dis. 2016;12(4):828–38.
41. Tewari N, Awad S, Lobo DN. Regulation of food intake after surgery and the gut brain axis. Curr Opin Clin Nutr Metab Care. 2013;16(5):569–75.
42. Power ML, Schulkin J. Anticipatory physiological regulation in feeding biology: cephalic phase responses. Appetite. 2008;50:194–206.
43. Kalinowski P, Paluszkiewicz R, Wróblewski T, Remiszewski P, Grodzicki M, Bartoszewicz Z, et al. Ghrelin, leptin, and glycemic control after sleeve gastrectomy versus Roux-en-Y gastric bypass: results of a randomized clinical trial. Surg Obes Relat Dis. 2017;13(2):1818.
44. Karamanakos SN, Vagenas K, Kalfarentzos F, Alexandrides TK. Weight loss, appetite suppression and changes in fasting and postprandial ghrelin and peptide-YY levels after Roux-en-Y gastric bypass and sleeve gastrectomy. A prospective, double blind study. Ann Surg. 2008;247:401–7.
45. Yousseif A, Emmanuel J, Karra E, Millet Q, Elkalaawy M, Jenkinson AD, et al. Differential effects of laparoscopic sleeve gastrectomy and laparoscopic gastric bypass on appetite, circulating acyl-ghrelin, peptide YY3-36 and active GLP-1 levels in non-diabetic humans. Obes Surg. 2014;24:241–52.
46. Miras AD, le Roux CW. Bariatric surgery and taste: novel mechanisms of weight loss. Curr Opin Gastroenterol. 2010;26(2):140–5.
47. Gero D, Steinert RE, le Roux CW, Bueter M. Do food preferences change after bariatric surgery? Curr Atheroscler Rep. 2017;19(9):38.

48. Kapoor N, Al-Najim W, le Roux CW, Docherty NG, Kapoor N. Shifts in food preferences after bariatric surgery: observational reports and proposed mechanisms. Curr Obes Rep. 2017;6(3):246–52.
49. Shoar S, Naderan M, Shoar N, Modukuru VR, Mahmoodzadeh H. Alteration pattern of taste perception after bariatric surgery: a systematic review of four taste domains. Obes Surg. 2019;29(5):1542–50.
50. Tichansky DS, Boughter JD Jr, Madan AK. Taste change after laparoscopic Roux-en-Y gastric bypass and laparoscopic adjustable gastric banding. Surg Obes Relat Dis. 2006;2:440–4.
51. Godlewski AE, Veyrune JL, Nicolas E, Ciangura CA, Chaussain CC, Czernichow S, et al. Effect of dental status on changes in mastication in patients with obesity following bariatric surgery. PLoS One. 2011;6:e22324.
52. Laurenius A, Larsson I, Bueter M, Melanson KJ, Bosaeus I, Forslund HB, et al. Changes in eating behavior and meal pattern following Roux-en-Y gastric bypass. Int J Obes. 2012;36:348–55.
53. Dimitriadis GK, Randeva MS, Miras AD. Potential hormone mechanisms of bariatric surgery. Curr Obes Rep. 2017;6(3):253–65.
54. Ardila-Hani A, Soffer EE. Review article: the impact of bariatric surgery on gastrointestinal motility. Aliment Pharmacol Ther. 2011;34(8):825–31.
55. Deloose E, Janssen P, Lannoo M, Van der Schueren B, Depoortere I, Tack J. Higher plasma motilin levels in obese patients decrease after Roux-en-Y gastric bypass surgery and regulate hunger. Gut. 2016;65(7):1110–8.
56. Sista F, Abruzzese V, Clementi M, Carandina S, Cecilia M, Amicucci G. The effect of sleeve gastrectomy on GLP-1 secretion and gastric emptying: a prospective study. Surg Obes Relat Dis. 2017;13(1):7–14.
57. Ahmad A, Kornrich DB, Krasner H, Eckardt S, Ahmad Z, Braslow A, et al. Prevalence of dumping syndrome after laparoscopic sleeve gastrectomy and comparison with laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2019;29(5):1506–13.
58. Svane MS, Bojsen-Møller KN, Martinussen C, Dirksen C, Madsen JL, Reitelseder S, et al. Postprandial nutrient handling and gastrointestinal hormone secretion after Roux-en-Y gastric bypass vs sleeve gastrectomy. Gastroenterology. 2019;156(6):1627–41.
59. Ramos AC, Marchesini JC, Bastos ELS, Ramos MG, de Souza MD, Campos JM, et al. The role of gastrojejunostomy size on gastric bypass weight loss. Obes Surg. 2017;27(9):2317–23.
60. Farias TMCP, Vasconcelos BCDE, Souto-Maior JR, Lemos CAA, de Moraes SLD, Pellizzer EP. Influence of bariatric surgery on salivary flow: a systematic review and meta-analysis. Obes Surg. 2019;29(5):1675–80.
61. Rehfeld JF. Incretin physiology beyond glucagon-like peptide 1 and glucose-dependent insulinotropic polypeptide: cholecystokinin and gastrin peptides. Acta Physiol. 2011;201:405–11.
62. Grong E, Græslie H, Munkvold B, Arbo IB, Kulseng BE, Waldum HL, et al. Gastrin secretion after bariatric surgery response to a protein-rich mixed meal following Roux-en-Y gastric bypass and sleeve gastrectomy: a pilot study in normoglycemic women. Obes Surg. 2016;26(7):1448–56.
63. Peterli R, Steinert RE, Woelnerhanssen B, Peters T, Christoffel-Courtin C, Gass M, et al. Metabolic and hormonal changes after laparoscopic Roux-en-Y gastric bypass and sleeve gastrectomy: a randomized, prospective trial. Obes Surg. 2012;22:740–8.
64. Billeter AT, Fischer L, Wekerle AL, Senft J, Müller-Stich B. Malabsorption as a therapeutic approach in bariatric surgery. Viszeralmedizin. 2014;30(3):198–204.
65. Müller MK, Räder S, Wildi S, Hauser R, Clavien PA, Weber M. Long-term follow-up of proximal versus distal laparoscopic gastric bypass for morbid obesity. Br J Surg. 2008;95(11):1375–9.
66. Ruiz-Tovar J, Vorwald P, Gonzalez-Ramirez G, Posada M, Salcedo G, Llavero C, et al. Impact of biliopancreatic limb length (70 cm vs 120 cm), with constant 150 cm alimentary limb, on long-term weight loss, remission of comorbidities and supplementation needs after Roux-En-Y gastric bypass: a prospective randomized clinical trial. Obes Surg. 2019;29(8):2367–72 [Epub ahead of print].

67. Via MA, Mechanick JI. Nutritional and micronutrient care of bariatric surgery patients: current evidence update. Curr Obes Rep. 2017;6(3):286–96.
68. Georgiadou D, Sergentanis TN, Nixon A, Diamantis T, Tsigris C, Psaltopoulou T. Efficacy and safety of laparoscopic mini gastric bypass. A systematic review. Surg Obes Relat Dis. 2014;10(5):984–91.
69. Magouliotis DE, Tasiopoulou VS, Tzovaras G. One anastomosis gastric bypass versus Roux-en-Y gastric bypass for morbid obesity: an updated meta-analysis. Obes Surg. 2019;29(9):2721–30 [Epub ahead of print].
70. Antoniewicz A, Kalinowski P, Kotulecka KJ, Kocoń P, Paluszkiewicz R, Remiszewski P, et al. Nutritional deficiencies in patients after Roux-en-Y gastric bypass and sleeve gastrectomy during 12-month follow-up. Obes Surg. 2019; https://doi.org/10.1007/s11695-019-03985-3. [Epub ahead of print]
71. Bal BS, Finelli FC, Shope TR, Koch TR. Nutritional deficiencies after bariatric surgery. Nat Rev Endocrinol. 2012;8(9):544–56.
72. Bloomberg RD, Fleishman A, Nalle JE, Herron DM, Kini S. Nutritional deficiencies following bariatric surgery: what have we learned? Obes Surg. 2005;15(2):145–54.
73. Toh SY, Zarshenas N, Jorgensen J. Prevalence of nutrient deficiencies in bariatric patients. Nutrition. 2009;25(11–12):1150–6.
74. Ziegler O, Sirveaux MA, Brunaud L, Reibel N, Quilliot D. Medical follow up after bariatric surgery: nutritional and drug issues. General recommendations for the prevention and treatment of nutritional deficiencies. Diabetes Metab. 2009;35(6):544–57.
75. Majumder S, Soriano J, Louie Cruz A, Dasanu CA. Vitamin B12 deficiency in patients undergoing bariatric surgery: preventive strategies and key recommendations. Surg Obes Relat Dis. 2013;9(6):1013–9.
76. Ruz M, Carrasco F, Rojas P, Codoceo J, Inostroza J, Basfi-Fer K, et al. Heme- and nonheme-iron absorption and iron status 12 mo after sleeve gastrectomy and Roux-en-Y gastric bypass in morbidly obese women. Am J Clin Nutr. 2012;96:810–7.
77. Steenackers N, Van der Schueren B, Mertens A, Lannoo M, Grauwet T, Augustijns P, et al. Iron deficiency after bariatric surgery: what is the real problem? Proc Nutr Soc. 2018;77(4):445–55.
78. Lakhani SV, Shah HN, Alexander K, Finelli FC, Kirkpatrick JR, Koch TR. Small intestinal bacterial overgrowth and thiamine deficiency after Roux- Y gastric bypass surgery in obese patients. Nutr Res. 2008;28:293–8.
79. Angstadt JD, Bodziner RA. Peripheral polyneuropathy from thiamine deficiency following laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2005;15:890–2.
80. Saab R, El Khoury M, Farhat S. Wernicke's encephalopathy three weeks after sleeve gastrectomy. Surg Obes Relat Dis. 2014;10(5):992–4.
81. Bell TD, Demay MB, Burnett-Bowie SA. The biology and pathology of vitamin D control in bone. J. Cell Biochem. 2010;111:7–11.
82. Liu C, Wu D, Zhang JF, Xu D, Xu WF, Chen Y, et al. Changes in bone metabolism in morbidly obese patients after bariatric surgery: a meta-analysis. Obes Surg. 2016;26(1):91–7.
83. Schafer AL. Vitamin D and intestinal calcium transport after bariatric surgery. J Steroid Biochem Mol Biol. 2017;173:202–10.
84. Ballesteros-Pomar MD, González de Francisco T, Urioste-Fondo A, González-Herraez L, Calleja-Fernández A, Vidal-Casariego A, et al. Biliopancreatic diversion for severe obesity: long-term effectiveness and nutritional complications. Obes Surg. 2016;26(1):38–44.
85. Shoar S, Poliakin L, Rubenstein R, Saber AAA. single anastomosis duodeno-ileal switch (SADIS): a systematic review of efficacy and safety. Obes Surg. 2018;28(1):104–13.
86. Verger EO, Aron-Wisnewsky J, Dao MC, Kayser BD, Oppert JM, Bouillot JL, et al. Micronutrient and protein deficiencies after gastric bypass and sleeve gastrectomy: a 1-year follow-up. Obes Surg. 2016;26(4):785–96.
87. Mahawar KK, Sharples AJ. Contribution of malabsorption to weight loss after Roux-en-Y gastric bypass: a systematic review. Obes Surg. 2017;27(8):2194–206.

88. Elrick H, Stimmler L, Hlad CJ, Arai Y. Plasma insulin response to oral and intravenous glucose administration. J Clin Endocrinol Metab. 1964;24(10):1076–82.
89. Perley MJ, Kipnis DM. Plasma insulin responses to oral and intravenous glucose: studies in normal and diabetic subjects. J Clin Invest. 1967;46(12):1954–62.
90. Holst JJ, Gribble F, Horowitz M, Rayner CK. Roles of the gut in glucose homeostasis. Diabetes Care. 2016;39:884–92.
91. Cavin JB, Bado A, Le Gall M. Intestinal adaptations after bariatric surgery: consequences on glucose homeostasis. Trends Endocrinol Metab. 2017;28(5):354–64.
92. Reimann F, Gribble FM. Mechanisms underlying glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 secretion. J Diabetes Investig. 2016;7(Suppl 1):13–9.
93. Holst JJ, Madsbad S. Mechanisms of surgical control of type 2 diabetes: GLP-1 is key factor. Surg Obes Relat Dis. 2016;12(6):1236–42.
94. Tsoli M, Chronaiou A, Kehagias I, Kalfarentzos F, Alexandrides TK. Hormone changes and diabetes resolution after biliopancreatic diversion and laparoscopic sleeve gastrectomy: a comparative prospective study. Surg Obes Relat Dis. 2013;9(5):667–77.
95. Korner J, Bessler M, Inabnet W, Taveras C, Holst JJ. Exaggerated glucagon-like peptide-1 and blunted glucose-dependent insulinotropic peptide secretion are associated with Roux-en-Y gastric bypass but not adjustable gastric banding. Surg Obes Relat Dis. 2007;3(6):597–601.
96. Nosso G, Griffo E, Cotugno M, Saldalamacchia G, Lupoli R, Pacini G, et al. Comparative effects of Roux-en-Y gastric bypass and sleeve gastrectomy on glucose homeostasis and incretin hormones in obese type 2 diabetic patients: a one-year prospective study. Horm Metab Res. 2016;48(5):312–7.
97. Maljaars PW, Peters HP, Mela DJ, Masclee AA. Ileal brake: a sensible food target for appetite control. A review. Physiol Behav. 2008;95:271–81.
98. Shah S, Shah P, Todkar J, Gagner M, Sonar S, Solav S. Prospective controlled study of effect of laparoscopic sleeve gastrectomy on small bowel transit time and gastric emptying half-time in morbidly obese patients with type 2 diabetes mellitus. Surg Obes Relat Dis. 2010;6(2):152–7.
99. Cazzo E, Pareja JC, Chaim EA, Geloneze B, Barreto MR, Magro DO. GLP-1 and GLP-2 levels are correlated with satiety regulation after Roux-en-Y gastric bypass: results of an exploratory prospective study. Obes Surg. 2017;27(3):703–8.
100. Laferrère B, Swerdlow N, Bawa B, Arias S, Bose M, Olivan B, et al. Rise of oxyntomodulin in response to oral glucose after gastric bypass surgery in patients with type 2 diabetes. J Clin Endocrinol Metab. 2010;95:4072–6.
101. Chandarana K, Gelegen C, Karra E, Choudhury AI, Drew ME, Fauveau V, et al. Diet and gastrointestinal bypass-induced weight loss: the roles of ghrelin and peptide YY. Diabetes. 2011;60(3):810–8.
102. Olivan B, Teixeira J, Bose M, Bawa B, Chang T, Summe H, et al. Effect of weight loss by diet or gastric bypass surgery on peptide YY3-36 levels. Ann Surg. 2009;249:948–53.
103. Karlsson F, Tremaroli V, Nielsen J, Bäckhed F. Assessing the human gut microbiota in metabolic diseases. Diabetes. 2013;62:3341–9.
104. Turnbaugh PJ, Hamady M, Yatsunenko T, Cantarel BL, Duncan A, Ley RE, et al. A core gut microbiome in obese and lean twins. Nature. 2009;457:480–4.
105. Anhê FF, Varin TV, Schertzer JD, Marette A. The gut microbiota as a mediator of metabolic benefits after bariatric surgery. Can J Diabetes. 2017;41(4):439–47.
106. Murphy R, Tsai P, Jüllig M, Liu A, Plank L, Booth M. Differential changes in gut microbiota after gastric bypass and sleeve gastrectomy bariatric surgery vary according to diabetes remission. Obes Surg. 2017;27(4):917–25.
107. Peat CM, Kleiman SC, Bulik CM, Carroll IM. The intestinal microbiome in bariatric surgery patients. Eur Eat Disord Rev. 2015;23(6):496–503.
108. Ulker İ, Yildiran H. The effects of bariatric surgery on gut microbiota in patients with obesity: a review of the literature. Biosci Microbiota Food Health. 2019;38(1):3–9.

109. Bastos ELS, Liberatore AMA, Tedesco RC, Koh IHJ. Gut microbiota imbalance can be associated with non-malabsorptive small bowel shortening regardless of blind loop. Obes Surg. 2019;29(2):369–75.
110. Eckburg PB, Bik EM, Bernstein CN, Purdom E, Dethlefsen L, Sargent M, et al. Diversity of the human intestinal microbial flora. Science. 2005;308:1635–8.
111. Lozupone CA, Stombaugh JI, Gordon JI, Jansson JK, Knight R. Diversity, stability and resilience of the human gut microbiota. Nature. 2012;489:220–30.
112. Tremaroli V, Karlsson F, Werling M, Stahlman M, Kovatcheva-Datchary P, Olbers T, et al. Roux-en-Y gastric bypass and vertical banded gastroplasty induce long-term changes on the human gut microbiome contributing to fat mass regulation. Cell Metab. 2015;22:228–38.
113. Kong LC, Tap J, Aron-Wisnewsky J, Pelloux V, Basdevant A, Bouillot JL, et al. Gut microbiota after gastric bypass in human obesity: Increased richness and associations of bacterial genera with adipose tissue genes. Am J Clin Nutr. 2013;98:16–24.
114. Palleja A, Kashani A, Allin KH, et al. Roux-en-Y gastric bypass surgery of morbidly obese patients induces swift and persistent changes of the individual gut microbiota. Genome Med 2016;8:67.
115. Cho I, Blaser MJ. The human microbiome: at the interface of health and disease. Nat Rev Genet. 2012;13(4):260–70.
116. Clemente JC, Ursell LK, Parfrey LW, Knight R. The impact of the gut microbiota on human health: An integrative view. Cell. 2012;148(6):1258–70.
117. Le Chatelier E, Nielsen T, Qin J, Prifti E, Hildebrand F, Falony G, et al. Richness of human gut microbiome correlates with metabolic markers. Nature. 2013;500:541–6.
118. De Filippo C, Cavalieri D, Di Paola M, Ramazzotti M, Poullet JB, Massart S, et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. Proc Natl Acad Sci USA. 2010;107:14691–6.
119. Furet JP, Kong LC, Tap J, Poitou C, Basdevant A, Bouillot JL, et al. Differential adaptation of human gut microbiota to bariatric surgery-induced weight loss: links with metabolic and low grade inflammation markers. Diabetes. 2010;59:3049–57.
120. Kellerer T, Brandl B, Büttner J, Lagkouvardos I, Hauner H, Skurk T. Impact of laparoscopic sleeve gastrectomy on gut permeability in morbidly obese subjects. Obes Surg. 2019;29(7):2132–43.
121. Kikuchi R, Irie J, Yamada-Goto N, Kikkawa E, Seki Y, Kasama K, et al. The impact of laparoscopic sleeve gastrectomy with duodenojejunal bypass on intestinal microbiota differs from that of laparoscopic sleeve gastrectomy in Japanese patients with obesity. Clin Drug Investig. 2018;38(6):545–52.
122. Ejtahed HS, Angoorani P, Hasani-Ranjbar S, Siadat SD, Ghasemi N, Larijani B, et al. Adaptation of human gut microbiota to bariatric surgeries in morbidly obese patients: A systematic review. Microb Pathog. 2018;116:13–21.
123. Damms-Machado A, Mitra S, Schollenberger AE, Kramer KM, Meile T, Königsrainer A, et al. Effects of surgical and dietary weight loss therapy for obesity on gut microbiota composition and nutrient absorption. Biomed Res Int. 2015;2015:1–11. Article ID 806248.
124. Tabasi M, Ashrafian F, Khezerloo JK, Eshghjoo S, Behrouzi A, Javadinia SA, et al. Changes in gut microbiota and hormones after bariatric surgery: a bench-to-bedside review. Obes Surg. 2019;29(5):1663–74.