Changes in Gut Hormones After Roux en Y Gastric bypass, Sleeve Gastrectomy, and Adjustable Gastric Banding

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Key words: bariatric surgery, gut hormones, weight loss

Abstract
The obesity epidemic has burdened healthcare systems worldwide. Bariatric surgery is currently the most effective method for long-term weight loss in obese adults, but the exact mechanism of weight loss is poorly understood. Bariatric procedures were initially classified by their presumed mechanism of action into restrictive, malabsorptive, or mixed procedures; however, due to recent advancements in the field of neuroendocrinology, hormones are increasingly recognized as important regulators of satiation, hunger, and energy expenditure. Studies examining changes in gut hormones following bariatric surgery have yielded conflicting results and the relationship between these hormones and weight loss is not yet clear. This review will summarize the effect of Roux en Y gastric bypass, sleeve gastrectomy and adjustable gastric banding on various gut hormones including ghrelin, cholecystokinin, glucagon-like polypeptide-1, peptide YY3, and pancreatic polypeptide. Furthermore, the relationship between these hormones and weight loss will be examined.
1. Introduction
The global prevalence of obesity has continued to increase placing an enormous burden on healthcare systems worldwide [1]. Obesity is the result of complex interactions between genetic, hormonal and environmental factors [2]. Bariatric surgery has proved to be the most effective method for long-term weight loss in obese adults. Surgical candidates include patients with a body mass index (BMI) >40 kg/m² or those with a BMI>35 kg/m² after conventional treatment for obesity has failed and obesity-related comorbidities are present [3]. Patients lose approximately 12-39% of their initial weight, or 40-70% excess weight loss (EWL) [4-6]. In addition, improvements in obesity-related complications are observed [7]. Despite these promising results, individual patient differences exist and 15-20% of patients have insignificant weight loss following bariatric surgery [4]. The reasons behind these individual differences are unclear [8].

The dramatic weight loss that follows bariatric surgery cannot only be explained by the “restrictive” or “malabsorptive” properties of these procedures. Following bariatric procedures patients are in a constant state of negative energy balance, yet they report feeling less hungry [9]. Mounting evidence suggests that gut hormones are important regulators of satiation, hunger, and energy expenditure following bariatric procedures [10]. Studies that have investigated hormone changes following bariatric procedures have yielded conflicting results and the relationship between these hormones and weight loss is nothing but clear. This review will summarize the effect of bariatric surgery on various gut hormones.

2. Energy homeostasis
A complex physiological system maintains energy homeostasis and this system resists weight loss more than weight gain. Energy intake depends on both short-term and long-term afferent signals that are released from the periphery and integrated within the hypothalamus. Short-term, meal-related signals are released from the gastrointestinal system and classified as orexigenic if they stimulate hunger (ghrelin), or anorexigenic if they stimulate satiety and subsequent meal cessation. Anorexigenic hormones include glucagon-like peptide-1 (GLP-1), peptide YY3-36 (PYY3-36), cholecystokinin (CCK), and pancreatic polypeptide (PP). Gut hormone physiology is summarized in Table 1. Leptin and insulin are examples of long-term signals that sense total body energy

Table 1. Characteristics of various gut hormones that regulate energy homeostasis

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Hormone type</th>
<th>Site released</th>
<th>Signal for release</th>
<th>Other effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghrelin</td>
<td>Orexigenic</td>
<td>Oxynic glands in the fundus and body of the stomach.</td>
<td>Increases with fasting:</td>
<td>Increases gastric emptying</td>
</tr>
<tr>
<td>GLP-1</td>
<td>Anorexigenic</td>
<td>Distal enteroendocrine L cells</td>
<td>Presence of nutrients in the small intestine</td>
<td>Stimulates insulin secretion Decreases gastric emptying Increases β-cell mass</td>
</tr>
<tr>
<td>PYY3-36</td>
<td>Anorexigenic</td>
<td>Endocrine L-cells of the distal gut</td>
<td>Food ingestion, proportional to calories</td>
<td>Reduces appetites Slows gastric emptying</td>
</tr>
<tr>
<td>CCK</td>
<td>Anorexigenic</td>
<td>Proximal intestinal I cells</td>
<td>Presence of fats and proteins in the duodenum</td>
<td>Gallbladder contraction Slows gastric emptying Promotes pancreatic enzyme secretion</td>
</tr>
<tr>
<td>PP</td>
<td>Anorexigenic</td>
<td>Pancreatic F cells</td>
<td>Presence of food, high protein content</td>
<td>Regulates pancreatic exocrine secretion Modulates gastric acid and GI motility</td>
</tr>
</tbody>
</table>

CCK-Cholecystokinin, PYY3-36-Peptide YY3-36, PP-Pancreatic polypeptide, GLP-1-Glucagon-like polypeptide-1, GI-gastrointestinal
### Table 2. A comparison of ghrelin concentrations following Roux en Y gastric bypass, adjustable gastric banding, and sleeve gastrectomy procedures

<table>
<thead>
<tr>
<th>Bariatric method</th>
<th>Author</th>
<th>Study design</th>
<th>Patient n.</th>
<th>Postop. month</th>
<th>% WL</th>
<th>Ghrelin postop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>RYGB</td>
<td>Cummings et al.</td>
<td>Prospective</td>
<td>5</td>
<td>9-31</td>
<td>36</td>
<td>↓</td>
</tr>
<tr>
<td>RYGB</td>
<td>Holdstock et al.</td>
<td>Prospective</td>
<td>66</td>
<td>6</td>
<td>22</td>
<td>↑</td>
</tr>
<tr>
<td>RYGB</td>
<td>Leonetti et al.</td>
<td>Cross-sectional Comparative</td>
<td>11 10</td>
<td>NK</td>
<td>NK</td>
<td>↓↓↓↓↓</td>
</tr>
<tr>
<td>RYGB</td>
<td>Korner et al.</td>
<td>Prospective</td>
<td>28 15</td>
<td>1</td>
<td>30</td>
<td>↓</td>
</tr>
<tr>
<td>RYGB</td>
<td>Couce et al.</td>
<td>Prospective</td>
<td>49</td>
<td>6</td>
<td>NK</td>
<td>↔</td>
</tr>
<tr>
<td>RYGB</td>
<td>Borg et al.</td>
<td>Prospective</td>
<td>6</td>
<td>1,3,6</td>
<td>NK</td>
<td>↔</td>
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<td>RYGB</td>
<td>Fruhbek et al.</td>
<td>Prospective</td>
<td>8</td>
<td>6</td>
<td>NK</td>
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<td>RYGB</td>
<td>Roth et al.</td>
<td>Prospective</td>
<td>18</td>
<td>24</td>
<td>63</td>
<td>↓</td>
</tr>
<tr>
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<td>Stoeckli et al.</td>
<td>Prospective</td>
<td>NK</td>
<td>3, 6, 12, 24</td>
<td>30</td>
<td>↔</td>
</tr>
<tr>
<td>AGB</td>
<td>Krieger et al.</td>
<td>Prospective</td>
<td>30</td>
<td>12</td>
<td>23</td>
<td>↔</td>
</tr>
<tr>
<td>RYGB</td>
<td>Karamanakos et al.</td>
<td>Prospective</td>
<td>16 16</td>
<td>NK</td>
<td></td>
<td>↔</td>
</tr>
<tr>
<td>SG</td>
<td>Peterli et al.</td>
<td>Prospective</td>
<td>12 11</td>
<td>12</td>
<td>35</td>
<td>↔</td>
</tr>
</tbody>
</table>

WL-weight loss, RYGB- Roux-en-Y gastric bypass, AGB-adjustable gastric banding, SG-Sleeve gastrectomy, NK-not known, NI-not investigated, ↑increased, ↓decreased, ↔ no change
stores. They modulate the short-term signals within the hypothalamus and efferent responses are subsequently determined. Efferent responses then regulate food intake and energy expenditure [10-14].

3. Classification of bariatric procedures
There are three types of bariatric procedures: malabsorptive, restrictive, and mixed procedures. Purely malabsorptive procedures including the jejunoileal bypass are rarely used today. Restrictive procedures include the sleeve gastrectomy (SG) and adjustable gastric banding (AGB). During the SG procedure, the majority of the greater curvature of the stomach is vertically resected [3]. SG is associated with a 60–70% EWL after 2 years [15]. In AGB procedures, an inflatable silicone ring is placed around the upper part of the stomach and inflated to various degrees, which restricts the size of the lumen [3]. This procedure results in approximately 50% EWL loss at 2 years [16]. Mixed procedures have both restrictive and malabsorptive components. Examples of mixed procedures include the biliopancreatic diversion and duodenal switch (BPD/DS) and Roux-en Y gastric bypass (RYGB). RYGB is the most commonly performed bariatric procedure. The restrictive component of this procedure is achieved by creating a 15 to 30 mL gastric pouch, which is separated from the remainder of the stomach. A Roux-Y limb then connects the gastric pouch to the jejunum, bypassing the duodenum and jejunum [3]. In comparison to other procedures, RYGB is associated with significantly more weight loss and improvements in diabetes. In addition, 70% EWL is observed [17]. These findings indicate that the specific anatomic variations of this procedure may result in different physiologic adaptations that aid in weight loss [18, 19].

4. Changes in gut hormones after bariatric surgery

4.1 Ghrelin
Ghrelin is a 28-amino acid peptide that is primarily released from the oxyntic glands in the fundus and body of the stomach. It is an orexigenic hormone that stimulates feeding. Ghrelin levels rise before meals and decrease following food intake [9, 10]. Studies have shown that obese patients have lower fasting ghrelin concentrations, a possible compensatory mechanism that results from long-term positive energy balance [20]. In addition, obese patients have reduced postprandial ghrelin suppression as compared with normal-weight controls. Following diet-induced or exercise-induced weight loss, compensatory increases in ghrelin secretion are observed, a finding that can explain weight loss resistance [9, 10].

4.12 Ghrelin changes after Roux en Y gastric bypass
Studies examining ghrelin concentrations following RYGB have yielded conflicting results (Table 2). While some studies have shown that baseline ghrelin levels decrease after RYGB [21-27], others have reported increases [28] or no change [29-31]. Cummings et al. found that patients had significantly lower 24-hour ghrelin profiles compared with normal weight and obese controls [21]. In addition, the physiologic meal-related changes were less pronounced in patients treated with gastric-bypass. The authors explained that the long-term absence of stomach contents might produce a continuous stimulatory signal that eventually suppresses ghrelin by “override inhibition”. In comparison, the prospective follow-up of 66 patients undergoing RYBG showed that ghrelin levels on the sixth and 12th postoperative month were increased and correlated with BMI reduction [28]. An explanation for these discrepancies, although controversial, is the degree of vagal dysfunction that follows these procedures [10]. Previous studies have implied that a functioning vagus nerve is required for the appetite-stimulating effect of ghrelin [32]. In addition, hyperinsulinemia has been shown to suppress ghrelin levels, and the variable degree of insulin resistance among the studied subjects may explain these inconsistencies. Additionally, timing of measurement, operative technique, and remnant pouch size can explain the variability [33,34].

4.13 Ghrelin changes after adjustable gastric banding
Most studies investigating ghrelin changes after AGB procedures have shown that ghrelin levels increase postoperatively [23, 24, 35, 36]. One study included 17 AGB patients that had blind crossover breakfast tests after having their gastric bands optimally or minimally restricted [35]. After having their gastric bands optimally restricted, patients reported significantly greater fasting and postprandial satiety; however, ghrelin levels were similar in both groups. Stoeckli et al. found no change in ghrelin dynamics following RYGB and increased ghrelin secretion following adjustable silicone gastric banding [36]. The authors explained, “the smaller long-term weight loss after ASGB compared with RYGB may be due, at least in part, to an absent increase in plasma ghrelin after RYGB”. In contrast, Lonetti et al. compared plasma ghrelin concentrations in patients undergoing RYGB and AGB, showing that although overall ghrelin concentrations decreased in both groups, ghrelin concentrations were significantly lower in patients treated with RYGB [22].
To make matters more confusing, 30 patients that underwent AGB procedures were prospectively followed for 12 months and were not found to have significant changes in ghrelin secretion [37]. This conflicting evidence suggests that further prospective randomized studies with long-term follow up and greater study samples are required in order to better understand this relationship.

4.14 Ghrelin changes after sleeve gastrectomy

Following SG, the ghrelin-producing cells in the fundus of the stomach are removed, and 40-50% decreases in fasting and meal-related ghrelin have been reported. These changes have been shown to persist for up to 5 years [38]. In comparison to RYGB, studies have reported larger decreases in post-prandial or fasting ghrelin after SG [38, 39]. The pattern of ghrelin secretion must be observed over longer follow-up periods, as ghrelin dynamics change with time. One prospective randomized study pointed out marked differences in fasting and meal-stimulated ghrelin secretion after RYGB and SG over a one-year period [40]. Although ghrelin levels initially decreased in the RYGB group, they increased after 12 months, exceeding preoperative values. Interestingly, although the physiologic meal-related oscillations were absent preoperatively, they returned after 12 months in the RYGB group. In comparison, ghrelin levels remained extremely low after 1 year in the SG group, but postprandial oscillations remained absent. Once again, larger reductions in ghrelin secretion were observed in the SG group. The authors explained that decreased ghrelin secretion might be responsible for the significant decrease in weight loss, appetite, and food intake in both groups. In addition, the improvements in glycaemia can also be attributed to ghrelin decrease, as ghrelin stimulates insulin-sensitizing adipokines and inhibits insulin secretion. Although the authors attributed the weight loss to attenuated ghrelin secretion, the SG group had a more significant decrease in ghrelin, yet RYGB patients lost slightly more weight. Therefore, ghrelin dynamics alone cannot explain these differences. Similarly, another study found consistently attenuated ghrelin concentrations following SG but variable levels after RYGB [41]. Although fasting ghrelin

<table>
<thead>
<tr>
<th>Bariatric method</th>
<th>Author</th>
<th>Study design</th>
<th>Patient n.</th>
<th>Fasting GLP-1</th>
<th>Fasting PYY3-36</th>
<th>Postprandial GLP-1</th>
<th>Post prandial PYY3-36</th>
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<tr>
<td>RYGB GB</td>
<td>Rodieux et al.</td>
<td>Cross-sectional comparison</td>
<td>8</td>
<td>NK</td>
<td>NK</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>RYGB</td>
<td>Le Roux et al.</td>
<td>Prospective</td>
<td></td>
<td>NK</td>
<td>NK</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>RYGB</td>
<td>Borg et al.</td>
<td>Prospective</td>
<td>6</td>
<td>NK</td>
<td>NK</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>RYGB SG</td>
<td>Peterli et al.</td>
<td>Prospective Randomized</td>
<td>12</td>
<td>NK</td>
<td>NK</td>
<td>↑↑↑</td>
<td>↑</td>
</tr>
<tr>
<td>RYGB SG</td>
<td>Yousseif et al.</td>
<td>Prospective comparative</td>
<td>10</td>
<td>←→</td>
<td>←→</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>RYGB ABG</td>
<td>Korner et al.</td>
<td>Prospective</td>
<td>28</td>
<td>←→</td>
<td>←→</td>
<td>↑↑↑↑↑</td>
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</tr>
</tbody>
</table>

RYGB- Roux-en-Y gastric bypass, AGB-adjustable gastric banding, SG-Sleeve gastrectomy, NK-not known, NI-not investigated, CCK-Cholecystokinin, PYY3-36-Peptide YY3-36, PP-Pancreatic polypeptide, NK-not known, NI-not investigated, ↑increased, ←→ no change
concentrations decreased six weeks after RYGB, they rose to basal levels after 12 weeks, while post-meal ghrelin concentrations remained suppressed. The altered ghrelin dynamics at different time points highlights the importance of timing when measuring ghrelin levels.

**4.15 Future direction**
The variable follow-up period and timing of ghrelin measurement (i.e. fasting, postprandial, 24-ghrelin profile) among these studies makes it difficult to compare results. Future studies should take this into consideration. Twenty-four hour ghrelin profiles are more reliable than single basal measurements. Furthermore, future studies should be designed in way to minimize age, sex, BMI and insulin resistance as potential confounding factors for ghrelin secretion. Randomized trials can address this issue. Ghrelin secretion depends on meal content and quantity; therefore, standardized meals with similar concentrations of proteins, carbohydrates and fats should be used to assess postprandial ghrelin suppression.

**4.2 Glucagon-like peptide-1**
GLP-1 is a 30 amino acid peptide that is primarily released from the distal enteroendocrine L cells of duodenum and large intestine. Its release is stimulated by the presence of nutrients in the gut lumen [42, 43]. It is an anorexigenic hormone that inhibits food intake and belongs to the family of incretins. GLP-1 increases insulin secretion in a glucose-dependent manner and decreases glucagon secretion. In addition, it slows gastric emptying and increases β-cell mass [9]. Human studies have shown that peripherally infused, or orally administered GLP-1 reduces appetite and food intake in normal weight, obese, and diabetic adults [44, 45].

Diet-induced or exercise-induced weight loss improves insulin sensitivity and fasting glucose kinetics in patients with type 2 diabetes [46, 47]. Similarly, diabetic patients undergoing bariatric procedures experience significant improvements in glucose tolerance following post-surgical weight loss. However, patients treated with SG and RYGB experience improved glucose sensitivity immediately following surgery, before substantial weight loss has occurred [48-50]. In fact, improved post-prandial beta-cell responses occur during the first postoperative week following RYGB [49]. Incretins including GLP-1 and glucose-dependent insulinoatropic polypeptide (GIP) could be responsible for the weight-loss independent improvements in glucose homeostasis [51].

Exaggerated postprandial GLP-1 levels following RYGB and SG have been reported [23, 32, 33, 40, 52]. Comparative studies have shown that RYGB enhances GLP-1 secretion to a greater extent than SG [41, 50]. Changes in GLP-1 concentrations following bariatric procedures are summarized in Table 3. The exact mechanism behind exaggerated GLP-1 release, and improved glucose tolerance after these procedures is not fully understood. Currently, two proposed hypotheses, “the foregut” and “hindgut” hypotheses have been used to describe this phenomenon [40]. The “foregut hypothesis” describes the anti-diabetic effect that results from bypassing the proximal small intestine, hence decreasing intraluminal calorie exposure. The “hindgut” hypothesis describes the increased delivery of calories and nutrients to the distal small intestine and subsequent increase in enteroendocrine secretion. These hypotheses can also explain why only postprandial, and not fasting GLP-1 concentrations significantly change following bariatric surgery. Consistent with the hindgut hypothesis, a one-year follow-up trial including 23 patients randomized to either RYGB or SG showed early, exaggerated postprandial GLP-1 secretion in both groups, with more prominent changes in the RYGB group [40]. The preoperative GLP-1 and PPY levels were low in both cohorts suggesting that obese patients have attenuated endogenous levels of these hormones. The authors explained that the direct nutrient contact with distal intestinal L cells lead to an increased incretion response following RYGB. An explanation for the increased GLP-1 secretion observed after SG could be that proximal CCK secretion stimulates GLP-1 release, which is supported by the exaggerated CCK secretion seen in the SG group. Alternatively, the GLP-1 rise after SG could result from increased gastric emptying, resulting in earlier contact of chyme with the distal enteroendocrine L cells.

As for GLP-1 response following AGB procedures, because this procedure does not alter the delivery of nutrients to the small intestine, it is unlikely that this procedure has marked effects on satiety hormones released from the intestine. A comparative, longitudinal study of 15 patients undergoing AGB procedures and 28 undergoing RYGB found that postprandial GLP-1 levels were threefold greater after RYGB [23]. Furthermore, the area under the curve (AUC) for PYY in the RYGB was greater.

A small number of patients experience postprandial hyperinsulinemia after gastric bypass [10, 53-55]. The enhanced
GLP-1 secretion and improved insulin sensitivity that follows these procedures has been implicated in the development of this syndrome. This syndrome has rarely been reported after restrictive procedures, further supporting the role of incretins in its development [51]. Perhaps patients with adequate preoperative postprandial GLP-1 levels can be treated with bariatric methods that do not alter these hormones in order to decrease postprandial hyperglycemia.

4.3 Peptide YY3
Peptide YY is a 36-amino acid peptide that belongs to the neuropeptide Y (NPY) and PP family. Two forms have been identified: PYY1-36 and PYY 3-36. The dipeptidyl amino-peptidase IV (DPP IV) enzyme cleaves PYY1-36 to PYY 3-36 [56, 57]. Therefore, the accurate measurement of PYY3-36 requires rapid addition of DPP4-inhibitor to studied samples [58]. PYY3-36 is released from the endocrine L-cells of the distal gut following food ingestion, in proportion to the calorie intake [59]. PPY3-36 is an endogenous agonist to Y2-receptors (Y2R) in the arcuate nucleus. Obese individuals have attenuated circulating PPY3-36 levels, but whether or not this is a cause or a consequence is unknown [60]. Furthermore, the role of PPY3-36 in energy homeostasis remains elusive. Batterham et al. were one of the first groups to report reduced food intake and weight gain in rodents peripherally infused with PYY3-36, a finding that was not seen in Y2R-null mice [61]. These findings were reproduced in later studies [62-64]. On the other hand, human studies have not clearly shown that systemically administered PYY1-36 alters appetite [56]. Exaggerated postprandial PYY3-36 levels following RYGB and SG have been reported [23, 31, 40, 52], while fasting levels have remained unchanged [41, 22]. Comparative SG and RYGB studies have shown enhanced PYY3-36 secretion after RYGB (Table 3). Future studies are warranted in order to better understand how bariatric surgery enhances circulating endogenous PYY3–36 levels. This knowledge is a key for developing novel non-invasive bariatric procedures or other potential therapies for obesity.

4.4 Cholecystokinin
Cholecystokinin is secreted from I cells in the duodenum and jejunum after meal consumption [65, 66]. Postprandial plasma CCK concentrations peak approximately 15 min after meal ingestion [66]. CCK stimulates gallbladder contraction, slows gastric emptying, and promotes pancreatic enzyme secretion. CCK is also an anorexigenic hormone that reduces appetite and promotes satiety by activating CCK1 receptors in the afferent vagal nerves [67]. Obese individuals have decreased basal, as well as postprandial CCK levels [68].

Although initial studies showed no change in CCK following RYGB [69, 70], this relationship was reevaluated in a latter study that found increased CCK secretion following mixed meal tests in eight obese non-diabetic patients within 2 weeks after RYGB [71]. CCK is regarded as an anorexigenic hormone; however, in a cross-sectional study of RYGB patients with successful body mass index loss (ESL), defined as ESL >60%, and patients with poor weight loss, poor responders had increased postprandial CCK release [72]. Therefore, the role of CCK after bariatric surgery is unclear. In a prospective, comparative (RYBG vs. SG) randomized 1-year trial, CCK concentrations were increased in both groups postoperatively, but more so in the SG group [40]. CCK dynamics after AGB are unknown. One study examined CCK concentrations after the administration of an acidified meal in patients after AGB and in normal-weight controls [73]. Although there was no difference in terms of basal CCK levels between the groups, the postprandial peak of CCK was higher in the AGB group as compared to the controls. The authors attributed the satiety effects of AGB procedures to these changes.

4.5 Pancreatic polypeptide
Pancreatic polypeptide is a 36 amino acid peptide hormone that is released from pancreatic F cells following meal consumption, especially meals high in protein. It is structurally similar to PYY3 PP, and regulates pancreatic exocrine secretion and modulates gastric acid and GI motility [10, 65]. Vagal cholinergic reflex circuits regulate PP secretion [74]. Short-term vagal dysfunction following RYGB could explain why PP levels are decreased in the early postoperative period following RYGB, with subsequent return to preoperative values after one month [75]. In contrast, in obese, non-diabetic patients, postprandial PP responses were found to be unchanged 2 weeks after RYGB [72]. However, the importance of a PP in achieving weight loss after bariatric procedures is questionable because no changes in overall long-term weight loss were observed in patients with RYGB and vagal nerve preservation or vagal nerve dissection [76]. Although one prospective randomized study showed enhanced PP secretion after RYGB, as compared to SG, this finding did not reach statistical significance [39]. Thus, current evidence suggests that PP secretion is not substantially altered by bariatric procedures, but future studies are warranted to better understand this relationship.
5. Gut hormones as predictors of weight loss

The success of bariatric surgery varies between procedures, and not all patients have the same success rate after undergoing the same surgical procedure. Factors responsible for this substantial heterogeneity include psychosocial circumstances, dietary habits, psychological issues and presence of additional medical comorbidities [77]. Hormone adaptations may also account for these differences. Although experts have not reached a consensus regarding the exact definition of treatment failure, a WL of <50% has been used. Other definitions include failure to achieve BMI <40 kg/m² or <35 kg/m² [78, 79]. Patients at risk of bariatric treatment failure should be identified early as additional intervention may be necessary, and these patients necessitate more stringent follow-up. Therefore, identifying prognostic factors for successful long-term weight loss is of great clinical importance. Few studies have investigated the correlation between gut hormones and weight loss after bariatric surgery. Furthermore, these studies have reported weight loss using variable methods, which makes these results difficult to compare. While some studies have reported weight loss as absolute WL, others have reported EWL or BMI reduction. Future studies should use the same standardized method for reporting weight loss [80].

Postoperative PYY and GLP-1 levels might be able to predict the degree of weight loss after RYGB. One study found that RYGB patients with unsuccessful weight loss had early, attenuated, PYY and GLP-1 secretion within the first postoperative week compared to patients with significant weight loss [52]. Another study reported that the PYY response to a standard test meal 6 weeks after RYGB was significantly correlated with EWL at the 33rd postoperative month [81]. Similarly, GIP has also been associated with weight loss. A recent study followed 24 post-RYGB patients for 27-59 months and measured basal and postprandial (after 30, 60, 90, and 120 min) ghrelin, GIP, GLP-1, and leptin [82]. The authors found increased GIP and GLP-1 levels after 30 min in patients with sustained weight loss, as compared to patients with significant weight regain. Few studies found associations between weight loss and GI hormone profiles after SG and AGB. Furthermore, hormone profiles before bariatric procedures have rarely been studied, and their correlation with long-term weight loss is unknown. This is an interesting and potential area of future research. Once a clear correlation between gut hormones and bariatric weight loss is established, gut hormones could potentially be used prognostic factors for successful weight loss.

6. Future direction

Once results regarding changes in hormones after bariatric surgery become consistent, and this mechanism is fully understood, the impact on clinical decision will be immense. In addition to the potential use of gut hormones as prognostic factors for weight loss, the type of bariatric method could be tailored to the patient’s specific needs. Patients with certain pre-operative hormonal panels could be recruited to specific bariatric procedures that have been shown to ameliorate specific hormonal abnormalities. Furthermore, less invasive medical interventions that mimic the “beneficial” hormonal changes could be developed [83].

8. Conclusion

Although gut hormones have been implicated in the significant weight loss that follows bariatric procedures, studies have yielded conflicting results, and the relationship between these hormones and weight loss remains elusive. Future studies are needed to better understand this relationship.

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