Chapter 38

Upper Gastrointestinal Diseases Before and After Bariatric Surgery

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LIST OF ABBREVIATIONS

BMI	body mass Index
GERD	gastroesophageal reflux disease
GI	gastrointestinal
H. pylori	*Helicobacter pylori*
HH	hiatal hernia
LES	lower esophageal sphincter
LGB	laparoscopic gastric banding
LSG	laparoscopic sleeve gastrectomy
NW	normal weight
PPI	proton pump inhibitor
RYGB	Roux-en-Y gastric bypass
TLESRs	transient lower esophageal sphincter relaxations

Obesity represents an important risk factor for the development of gastrointestinal (GI) disorders, most notably gastroesophageal reflux disease (GERD), but also dyspepsia, as well as other symptoms such as nausea, vomiting, and upper abdominal pain. However, the prevalence of proximal abdominal diseases and their relative complications are difficult to assess just on clinical evaluation; the presence of motor and endoscopic alterations are often asymptomatic, probably due to a dysfunction of the autonomic nervous system, which determines an impaired visceral sensation [1,2]. The preoperative GI setting is dramatically changed after bariatric surgery, affecting both gut anatomy and physiology, and influencing the outcomes of GI diseases.

GASTROESOPHAGEAL REFLUX DISEASE

GERD is a common condition, clinically characterized by heartburn and/or regurgitation, determined by the occurrence of several pathophysiological mechanisms, all hampered by obesity, that lead to an increased esophageal exposure to gastric contents (Fig. 38.1). The prevalence of GERD is higher in obese patients compared with normal weight (NW) controls, with 2.5 times the risk of developing the disease, mainly as erosive esophagitis [3]. Obesity influences the following factors:

- *Transient lower esophageal sphincter relaxations (TLESRs)*: In overweight and obese patients a substantial increase of TLESRs in the postprandial phase has been reported [4]. TLESRs are a vagal nerve–mediated phenomenon that represent the most important mechanism concurring with GERD pathogenesis in NW patients.
- *Hiatal hernia (HH)*: Obese subjects are more likely to have esophagogastric junction disruption that leads to hernia development [5]; it can be identified with high-resolution manometry [6]. HH is diagnosed in 26–52.6% of obese

Metabolism and Pathophysiology of Bariatric Surgery.

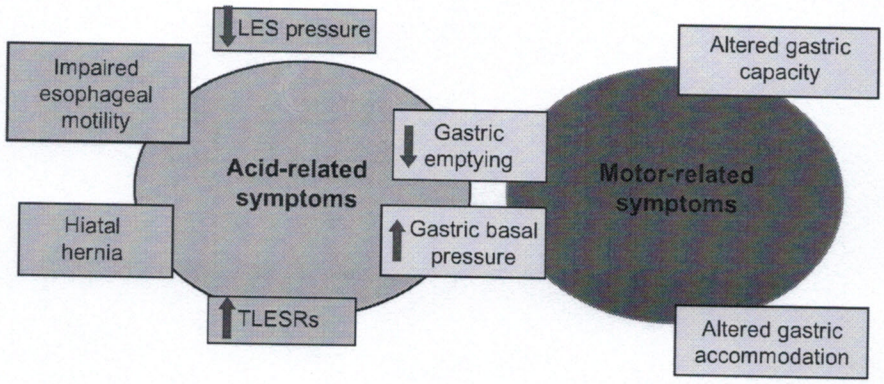

FIGURE 38.1 Pathophysiological mechanisms involved in the development of upper gastrointestinal (GI) symptoms in obese patients. The main mechanisms involved in the pathogenesis of acid-related symptoms (GERD) and motor-related diseases (dyspepsia, nausea, and vomiting) are summarized. *LES*: Lower Esophageal Sphincter; *TLESRs*: Transient Lower Esophageal Sphincter Relaxations.

candidates for bariatric surgery [7,8], and is frequently associated with more severe forms of GERD. Its prevalence is significantly higher in patients with esophagitis (68.2%) with respect to patients without (11.4%) [9].

- *Esophageal motility*: An impaired esophageal clearance can also contribute to GERD. Abnormal esophageal manometric findings have been reported in 25–51% of obese patients candidate to bariatric surgery, hypomotility of the esophageal body being the most common alteration. It has been noted, however, that esophageal dysmotility might occur in the absence of GI symptoms [1,8].
- *Basal lower esophageal sphincter (LES) pressure*: This factor likely covers a less relevant importance in the pathogenesis of GERD. Similar to NW, the contribution of LES pressure in the development of GERD in obese patients still needs to be established. Conflicting results are available, with some studies showing a decreased pressure [10], and others a normal one [11].
- *Gastric basal pressure*: The increased intraabdominal pressure, resulting from the mechanical burden of fat, promotes retrograde flow of gastric juice into the esophagus. A significant correlation between body mass index (BMI) and waist circumference with intragastric pressure and gastroesophageal pressure gradient has been observed [5]. Furthermore, an increased gastric basal pressure, associated with overeating, may contribute to the increase in TLESRs.
- *Gastric emptying*: Delayed gastric emptying could be another factor contributing to GERD. However, data show conflicting results both in NW and obese patients [12].

Postoperative Gastroesophageal Reflux Disease Outcomes

The outcomes of GERD depend on the type of surgical procedure. Nevertheless, available data are conflicting, which is probably related to the different methods used for GERD detection (questionnaire, pH-metry, manometry, endoscopy, proton pump inhibitor (PPI) treatment) and the different times of follow-up. As of now, Roux-en-Y gastric bypass (RYGB) is considered the best surgical treatment option for GERD in the morbidly obese patient, since both the small size of the gastric pouch and the diversion of bile lead to a remarkable reduction of the gastric content that can reflux into the esophagus. Several studies reported an improvement of reflux symptoms, reduction of esophageal acid exposure, erosive esophagitis, and PPI prescription after RYGB [13]. On the other hand, impact of laparoscopic sleeve gastrectomy (LSG) on GERD symptoms is controversial. The Second International Consensus Summit for Sleeve Gastrectomy reported a prevalence of postoperative GERD ranging from 0% to 83% [14]. Again, the discrepancy might arise from the different definitions and methodologies used for GERD diagnosis, but also from the different LSG surgical procedures used. In particular the different positions of the stapler at the angle of His, bougie size, and the presence of HH might influence GERD outcomes [15]. LSG-related anatomical modifications lead to a new balance between exacerbating and protective factors for GERD, the latter being mainly represented by the supposed reduced acid load and possible faster gastric emptying. Finally, the most recent data has shown notable evidence of worsening of GERD after laparoscopic gastric banding, above all regurgitation, in both previously symptomatic and asymptomatic patients [13].

DYSPEPSIA AND OTHER UPPER GASTROINTESTINAL DISORDERS

Visceral adiposity is associated with an increased risk of functional dyspepsia [16] and globus [17]. By means of a validated GI symptoms questionnaire based on the Rome Criteria, it has been reported, in a cohort of 120 consecutive patients candidate to bariatric surgery, that 89% complained of functional symptoms (31% esophageal and 38% gastroduodenal) [18]. An association has been found between increased BMI and abdominal pain associated with nausea or vomiting (OR 2.0, 95% CI 1.0–2.9; $p = 0.04$) [19]. Similarly, increased BMI categories are associated with bloating (OR = 1.3, 95% CI 1.1–1.6) [20]. The higher prevalence of upper GI symptoms has also been found in a population-based study: nausea, vomiting, early satiety, upper abdominal pain, and bloating were respectively present in 10.6%, 4.0%, 9.0%, 19.8%, and 23.4% of obese patients compared to 7.9%, 1.2%, 6.5%, 3.5%, 11.4% in the NW control subjects [21].

In contrast to GERD, whose pathophysiological mechanisms are well-known, the underlying reasons for upper functional GI disorders are poorly understood, with scarce data availability (Fig. 38.1). Different mechanisms have been proposed, such as an alteration in gastric emptying, gastric capacity, and accommodation [12,22]. Available evidence has suggested that obese patients have a higher gastric capacity or enlarged antrum, even if it remains to be established whether these are a cause or a consequence of obesity [23]. It is also possible that altered psychological behaviors and eating disorders, often present in obese patients, influence the development of GI symptoms.

Postoperative Outcomes

The prevalence of functional upper GI symptoms after bariatric surgery has been poorly analyzed, likely because upper GI symptoms (mainly dyspepsia) represent an expected outcome related to the marked anatomical manipulation intrinsic to bariatric procedures. After RYGB, the increase in gastric symptoms, such as postprandial fullness, early satiation, pain, or epigastric burning, is not observed, likely due to the exclusion of the stomach from the continuity of the digestive tract. Comparing RYGB and LSG 1 year after surgery, nausea ($p < 0.01$) and vomiting ($p < 0.001$) were significantly more frequent among LSG subjects [24]. Nevertheless, after RYGB, dysphagia can occur, probably not GERD-related, but ascribable to the impaired emptying of the gastric pouch [25,26]. When dysphagia is associated with pain, nausea, and vomiting, likely a marginal ulcer of the gastro-jejunal anastomosis occurred [27,28]. Esophageal dysmotility, with decrease in esophageal body amplitude and ineffective esophageal peristalsis, are reported in a quarter of patients after RYGB, despite absence of dysphagia or chest pain [29].

After LSG, in a prospective clinical study evaluating upper GI symptoms before and after surgery through validated questionnaires, the main postsurgical complaint was dyspepsia; this was true in almost 60% of patients, LSG being associated with de novo dyspepsia, with an OR of 7.00 (95% CI 2.9–18.3, $p < 0.0001$) [30].

HELICOBACTER PYLORI INFECTION

Helicobacter pylori infection represents one of the most common human infections, present in more than half of the world's population, with a disparity between developed and developing countries. An inverse correlation between *H. pylori* infection and BMI has been proposed based on the significant weight gain observed after *H. pylori* eradication [31]. Especially in developed areas, the reduced prevalence of infection has been proposed as a contributing factor for the increased prevalence of overweight and obese individuals [32].

The significant weight gain observed after *H. pylori* eradication might be related to different mechanisms. First, the improvement of *H. pylori*–related GI symptoms may favor dietary excess and promote weight gain. Second, the reversal of mucosal gastritis after *H. pylori* eradication can cause an increase in ghrelin, the orexigenic hormone produced by gastric mucosa relevant in the regulation of appetite and weight gain. Data on the relationship between *H. pylori* and ghrelin are however discordant. Some studies showed that *H. pylori* infection has a negative impact on density of gastric ghrelin-positive cells in obese patients [33], whereas others showed an increase in the number of immunoreactive ghrelin cells in obese patients compared to NW subjects, independent of *H. pylori* status [34]. Other studies aimed at analyzing this topic are needed.

Helicobacter pylori Infection Outcome After Bariatric Surgery

The advantages of preoperative *H. pylori* screening and eradication in reducing postsurgical complications are still controversial, mainly due to a lack of randomized controlled trials. An effective *H. pylori* eradication prior to RYGB brings

a reduced incidence of viscus perforations [35] and marginal ulcers [36], whose prevalence after RYGB is about 1–16% [37]. In a retrospective study including 560 patients, the incidence of ulcers was 2.4% in patients tested and treated for *H. pylori* infection prior to surgery, compared to 6.8% in those who did not undergo such screening [36]. Nevertheless, this positive effect is not confirmed by recent data that reported a significantly lower incidence of postoperative anastomotic ulcer complications in *H. pylori*–positive versus negative patients at the time of RYGB, which does not support a routine identification and eradication of infection prior to RYGB [38].

After LSG, different authors have not reported an increase in postsurgical complications in patients with *H. pylori* who are undergoing surgery [39–41]. The gastric environment for *H. pylori* colonization may dramatically change after LSG, with possible spontaneous clearance of infection [42]. However, these data need to be confirmed in a long-term follow-up. Guidelines on the necessity of preoperative *H. pylori* screening and management are discordant. The American Association of Clinical Endocrinologists, The Obesity Society, and the American Society for Metabolic and Bariatric Surgery guidelines [43] do not provide a clear indication. *H. pylori* screening is recommended only in patients in high-prevalence areas, and upper endoscopy in selected cases. European guidelines [44] in turn recommend performing an upper GI endoscopy before bariatric surgery in all patients in order to diagnose and treat any lesions (including *H. pylori* infection) that may cause postoperative complications.

Even if controversial, there are plausible reasons to attempt eradication in *H. pylori*–positive patients (Table 38.1). First of all, a large part of the stomach is endoscopically inaccessible after RYGB. Second, it has to be taken into account that *H. pylori* is a class I carcinogen in the development of gastric cancer, with an odds ratio of 2.0–5.9 [45]. Third, its eradication might lead to a moderate benefit on symptomatic dyspepsia [46]. Nevertheless, it remains to define the correct eradication strategy, since there is a need to test new regimens. The methods available in clinical practice for *H. pylori* infection diagnosis, and the key facts of the its eradication treatment, are listed in Table 38.2 [47].

BMI represents an independent risk factor for eradication failure, with a 6% increase of risk of eradication failure for each unit of BMI [48]. With a 7-day regimen, a successful eradication was obtained in 55.0% of the overweight/obese group compared with 85.4% of the NW group [48]. The advantage of a longer treatment has been reported, with an eradication rate achieved with a 14-day triple therapy significantly higher than with a 7-day triple therapy (OR = 1.96; 95% CI 1.16–3.30; $p = 0.016$) [49]. Although the mechanisms underlying the low rates of eradication remained unclear, two hypotheses emerged: (1) the physiological changes occurring in obesity (i.e., altered gastric emptying) may lead to a

TABLE 38.1 Reasons to Attempt or Not Attempt *H. pylori* Eradication

Why Eradicate	Why Not Eradicate
H. pylori-infected persons present a higher risk for gastric cancer.	Eradication therapy is less effective in obese than NW patients.
H. pylori eradication might improve dyspepsia.	Doubts about the real benefits in terms of reduction of postsurgical complications.
Stomach may be difficult to explore after RYGB.	Spontaneous eradication has been described after LGS.

LSG, Laparoscopic Sleeve Gastrectomy; NW, Normal Weight; RYGB, Roux-en-Y Gastric Bypass.

TABLE 38.2 Diagnosis of *H. pylori* Infection

Invasive Tests (during endoscopy)	Noninvasive Tests
Histology	^{13}C Urea breath test
Rapid urease test	Stool antigen
Culture	Immunoglobin G (IgG) serology

For the diagnosis of *H. pylori*, invasive and noninvasive tests are available. All tests, except serology, require discontinuation of proton pump inhibitors and antibiotics for at least 1 month before the test. Serology is not adequate to verify the eradication treatment.

decrease in the rate of drug absorption, regardless of the characteristics of the drug and (2) the volume of distribution of drugs may be altered because tissue mass can influence medications with lipophilic properties [50,51].

In conclusion, obese patients present several proximal GI diseases whose prevalence is probably underestimated due to the impairment of visceral sensation likely occurring in this setting. To attain optimal tailored management, it is important to understand with a multidisciplinary approach the different gut perturbations consequent to the anatomical and functional modifications inherent to each procedure.

MINI-DICTIONARY OF TERMS

- *Gastroesophageal reflux disease (GERD)*: A chronic digestive disease occurring when stomach contents, mainly acid, flow back into the esophagus. The refluxate damages esophageal mucosa, causing troublesome symptoms and/or complications.
- *Lower esophageal sphincter (LES)*: A specialized muscle segment of the distal esophagus characterized by a high-pressure zone that represents one of the mechanisms of the antireflux barrier.
- *Transient lower esophageal sphincter relaxations (TLESRs)*: LES opening not occurring after swallowing. They are mainly caused by gastric fundus relaxation.
- *Hiatal hernia (HH)*: Occurs when part of the stomach pushes upward through the diaphragm into the thorax. There are two main types: (1) sliding HH with upward shift of LES and (2) paraesophageal HH with upward shift of gastric fundus next to the esophagus without migration of LES. Only the more frequent "sliding hernia" will be discussed here.
- *Esophageal manometry*: Evaluates coordination of esophageal movements and pressures using a thin catheter with pressure sensors inserted through the esophagus. The high-resolution manometry with esophageal pressure topography plotting combines improvements in pressure-sensing technology with an increased number of pressure sensors.
- *Regurgitation*: A characteristic GERD symptom usually described as a sour taste in the mouth or a sense of fluid moving up and down in the chest.
- *Dysphagia*: Characterized by difficult swallowing that can occur both for solids and liquids. It can be a manifestation of stricture or, more commonly, of dysmotility of the esophagus.
- *Dyspepsia*: Defined by the presence of symptoms thought to originate in the gastroduodenal region. Following Roma III Criteria for functional disorders, it is further subdivided in *postprandial distress syndrome*, in the presence of postprandial fullness and/or early satiation, and *epigastric pain syndrome*, in the presence of pain or burning localized in the epigastrium and not associated with other abdominal- or chest-related symptoms.
- *Helicobacter pylori* (*H. pylori*): A gram-negative, microaerophilic and spiral-shaped bacteria that is the main etiological factor of chronic gastritis, benign peptic ulcer, and gastric cancer.
- *Ghrelin*: Ghrelin is a fast-acting hormone produced mainly in the gastric fundus by neuroendocrine cells (X/A-like cells in rodents and P/D1 cells in humans), and secreted into the circulation.

KEY FACTS

- The first-line therapy is represented by the triple treatment that includes a PPI, clarithromycin, and amoxicillin or metronidazole.
- Use of clarithromycin should be avoided if the resistance rate in the region is more than 15–20%.
- Bismuth-containing quadruple therapy represents an alternative.
- Use of PPI twice a day might increase the efficacy of therapy.
- Extending the duration of PPI–clarithromycin-containing triple therapies from 7 to 10–14 days might improve the eradication success.
- Use of probiotics and prebiotics might reduce side effects.
- After the first therapy, either a bismuth-containing quadruple therapy or levofloxacin-containing triple therapy are recommended.
- The repetition of the same eradication therapy must be avoided.
- After failure of the second therapy, an antimicrobial susceptibility test might be useful.
- After at least 4 weeks from the end of treatment, a urea breath test or stool test are recommended to determine the success of the treatment.

SUMMARY POINTS

- Obesity confers an increased risk of upper GI disorders, particularly GERD.
- Different surgical approaches are associated with variable GI outcomes, but RYGB is the most efficient option for the improvement of GERD.
- Other upper GI symptoms than GERD are associated with obesity, but the impact of bariatric surgery on these disturbances is less clear.
- The reduced prevalence of *H. pylori* infection in developed areas might relate to the augmentation of overweight and obese individuals.
- In patients candidate to bariatric surgery, the need for *H. pylori* screening and eradication is still debated.

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