Abstract

Increases in the prevalence of obesity and gastroesophageal reflux disease (GERD) have paralleled one another over the past decade, which suggests the possibility of a linkage between these two processes. In both instances, surgical therapy is recognized as the most effective treatment for severe, refractory disease. Current surgical therapies for severe obesity include Roux-en-Y gastric bypass, adjustable gastric banding, sleeve gastrectomy, and biliopancreatic diversion with duodenal switch, while fundoplication remains the mainstay for the treatment of severe GERD. In several large series, however, the outcomes and durability of fundoplication in the setting of severe obesity are not as good as those in patients who are not severely obese. As such, bariatric surgery has been suggested as a potential alternative treatment for these patients. This article reviews current concepts in the putative pathophysiological mechanisms by which obesity contributes to gastroesophageal reflux and their implications with regards to surgical therapy for GERD in the setting of severe obesity.

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as these longitudinal population-based studies rely primarily upon subjective GERD symptoms rather than physiological measures of GERD. Nonetheless, there has been a significant increase in the prevalence of serious sequelae related to GERD\textsuperscript{[9,11]}, including Barrett’s esophagus and adenocarcinoma of the distal esophagus, which strongly suggests that the severity, if not the prevalence, of GERD is in fact increasing.

Furthermore, because the prevalence of GERD is markedly higher in overweight and obese individuals as compared to those with normal BMI\textsuperscript{[12,13]}, GERD itself is now recognized as obesity-related comorbidity. Indeed, the importance of the relationship between excess visceral adiposity and GERD is demonstrated by the greater correlation between GERD and waist circumference and waist-to-hip ratio (markers of central obesity) than that between GERD and BMI\textsuperscript{[14,15]}. However, the prevalence of GERD, even in the setting of severe obesity, is $< 50\%$\textsuperscript{[16]}, which suggests that severe obesity itself is not sufficient to cause GERD, and that in the majority of severely obese individuals, at least some of the physiological mechanisms that prevent GERD remain reasonably intact. As such, when managing GERD in a severely obese patient and considering surgical therapy, it is useful to review the proposed mechanisms by which obesity contributes to GERD pathophysiology.

**ROLE OF SEVERE OBESITY IN GERD PATHOPHYSIOLOGY**

Fundamental to the development of GERD is a failure of the anti-reflux barrier that comprises the lower esophageal sphincter (LES) and the crural portion of the hiatus. LES function is directly dependent on intrinsic LES pressure (LESP, normal, 10-24 mmHg), total LES length, intraabdominal LES length, and the frequency and duration of transient LES relaxation (TLESR). Indirectly, LES function is affected by the pressure gradient between the intragastric and intrathoracic environment.

When compared to healthy asymptomatic control subjects, 43 consecutive severely obese patients were found to have a lower LESP (11.9 ± 5.3 mmHg vs 15.9 ± 2.7 mmHg), and 51% were noted to have abnormal acid exposure\textsuperscript{[17,18]}. Similarly, in a large cohort of patients with foregut symptoms, the prevalence of a mechanically defective LES (based on hypotensive LES, total length, or abdominal length) increased as BMI increased, with 55% of obese patients demonstrating a defective LES\textsuperscript{[19]}. While nearly 30% of the 1659 subjects in this study were noted to be obese, specific data regarding severely obese individuals were not described. In contrast, in another large cohort of patients with GERD, mean LESP was in fact significantly greater in subjects with severe obesity (17 ± 9.2 mmHg vs 14 ± 7.6 mmHg), and 62% of severely obese subjects with GERD had a normal (39%) or hypertensive (23%) LES compared to only 46% of individuals with BMI ≤ 35 kg/m²; 10% of whom were noted to have a hypertensive LES\textsuperscript{[20]}. The authors of this study hypothesized that the mechanisms responsible for GERD might be different in the setting of severe obesity, and that the observed increased LESP could represent a compensatory mechanism against the increased pressure gradient between the stomach and esophagus, which ultimately remains inadequate to prevent GERD. This finding also has important implications with regards to surgical therapy, as conventional anti-reflux procedures (i.e. fundoplication) seek to correct the defective LES.

TLESR could be the most important reflux mechanism in the setting of a functioning LES, and it has been observed that fundoplication reduces the frequency of TLESR\textsuperscript{[18,21]}. Based on high-resolution manometry and concurrent fluoroscopy in non-obese patients, the key events that lead to opening of the gastroesophageal junction during TLESR include LES relaxation, crural diaphragm inhibition, esophageal shortening, and a positive pressure gradient between the stomach and the gastroesophageal junction lumen\textsuperscript{[22]}. Obese individuals without GERD were noted to have an increased frequency of TLESR (7.3 ± 2.0 events/2 h vs 2.1 ± 1.2 events/2 h) compared to normal weight individuals, whereas LESP and LES length were similar between the two groups\textsuperscript{[23,24]}. Similar findings have been noted in the setting of severe obesity\textsuperscript{[25]}.

Several factors might contribute to the increased gastroesophageal gradient seen with obesity\textsuperscript{[26]}, including increased intra-abdominal pressure\textsuperscript{[27]}, increased intragastric pressure\textsuperscript{[28]}, increased negative inspiratory intrathoracic pressure\textsuperscript{[29]}, and a mechanical separation between the LES and the extrinsic compression provided by the diaphragmatic crura\textsuperscript{[30]}. The latter is a key step in the development of hiatal hernia, which, based on endoscopic evidence, is more prevalent in obese individuals than normal weight individuals\textsuperscript{[26,30,31]}. Indeed, the negative effects of the presence of hiatal hernia on LES function might in fact be greater than the effects of obesity per se\textsuperscript{[32]}.

**SURGICAL TREATMENT OF GERD**

There is substantial controversy regarding the long-term efficacy and durability of fundoplication in the setting of obesity, and fewer data still to inform clinicians as to its effectiveness in the setting of severe obesity. A major concern regarding the long-term durability of fundoplication in severe obesity is the presumed increased risk of hiatal hernia recurrence, projected from the well-recognized contribution of obesity to the risk of hernia recurrence following abdominal wall hernia repair\textsuperscript{[29,30]}. In a study of 224 consecutive patients with 3 years follow-up who underwent laparoscopic Nissen or transthoracic Belsey Mark IV (BM-IV) fundoplication, overall symptomatic recurrence was 31.3% in obese patients (22.9% Nissen, 33.8% BM-IV), compared to 4.5% in normal-weight individuals\textsuperscript{[33]}. In another cohort study, preoperative severe obesity was associated with a higher rate of fundoplication failure, defined as the need for reoperation, lack of satisfaction, or severe symptoms at follow-up\textsuperscript{[34]}. This study was limited by the small number of severely obese patients (only seven out of 160) and loss of patients to follow-up.
In another study of patients who were undergoing gastric bypass after failed fundoplication, the majority of failures were found to be due to wrap disruption rather than intrathoracic wrap migration; the latter being the most common anatomical failure in normal and overweight patients. In contrast, several studies have demonstrated short-term and medium-term outcomes in obese patients that are comparable to those in non-obese patients. These data are somewhat limited in their applicability to severely obese individuals, however, due to their lack of physiological outcomes measures, small numbers of severely obese patients, and relatively short follow-up period.

**BARIATRIC SURGERY AND GERD**

Bariatric surgery has become a widely accepted form of treatment for severe obesity, and several studies have demonstrated a significant reduction in GERD symptoms and medication utilization, as well as weight and metabolic comorbidity, including diabetes, hypertension and dyslipidemia. Indeed, given the frequent presence of these and other comorbidities in the setting of severe obesity, the importance of significant and sustained weight loss for the overall health of severely obese patients, and the conflicting data regarding the outcomes of fundoplication in severe obesity, bariatric surgery is increasingly being seen as a more appropriate surgical treatment for GERD in severe obesity, even though objective measures of GERD outcomes might be comparable between fundoplication and gastric bypass. Earlier concerns regarding the comparative safety of bariatric surgery (gastric bypass in particular) and Nissen fundoplication have been addressed by the recent finding that the morbidity and mortality rates of the two procedures were very comparable when using the University Health System Consortium database to identify morbidly obese patients who underwent laparoscopic gastric bypass \( (n = 21,156) \) or laparoscopic Nissen fundoplication \( (n = 6108) \) at American academic medical centers between 2004 and 2007. Instead, discussion today is centered around the differential effects of currently performed bariatric operations [Roux-en-Y gastric bypass (RYGB), adjustable gastric banding (LAGB), bilipancreatic diversion with duodenal switch (DS), and sleeve gastrectomy (SG)] on GERD, as well as other obesity-related comorbidity.

**RYGB AND GERD**

RYGB accounts for over half of the currently performed bariatric operation in the United States, and appears to have a very favorable impact on GERD. Its recognized effectiveness has even led to its use in non-severely obese patients with GERD, particularly in the setting of failed fundoplication. Its efficacy in treating GERD is thought to be related to the relatively low acid production of the small-volume (15-30 mL) gastric pouch, reduction of esophageal bilipancreatic reflux rate by use of a roux limb measuring at least 100 cm in length, and weight loss. The physiological effects of the anatomic configuration of RYGB, and specifically, the configuration of the gastric pouch, might in fact be a more important contributor to reflux improvement than reducing alkaline bile reflux or weight loss. When comparing GERD remission as measured by symptom resolution and medication discontinuation, super-obese patients \( (BMI \geq 50 \text{ kg/m}^2) \) who underwent RYGB had a higher rate of GERD resolution than those who underwent DS, despite the greater weight loss seen in the latter group.

**LAGB AND GERD**

Since its FDA approval in 2001, LAGB has rapidly become a popular bariatric surgical option for patients and surgeons due to its relative technical simplicity, perceived advantageous safety profile, and lack of gastrointestinal tract division or reconstruction (and consequent malabsorption). The effects of LAGB on GERD are conflicting; however, with some studies demonstrating improvement in physiological GERD metrics, while others show improvement on GERD questionnaires and/or through the discontinuation of GERD medications. In contrast, several studies have demonstrated measured exacerbation of esophageal acid exposure, GERD symptoms, and the development or worsening of esophageal dysmotility following LAGB. The mechanism by which LAGB may improve GERD is not well characterized, but is thought to include weight loss, increase in LES pressure, and reconstitution of the angle of His. It has been hypothesized that the poorer GERD outcomes following LAGB might be attributable to an unrecognized hiatal hernia at the time of initial band placement, which has led some to suggest that the presence of hiatal hernia is a contraindication to LAGB, whereas others have suggested that aggressive identification and concomitant repair of hiatal hernia improves outcomes and reduces the need for reoperation due to band slippage or pouch dilation. Given these conflicting data, most bariatric surgeons do not recommend LAGB to severely obese patients with significant GERD, particularly in the setting of hiatal hernia.

**SG, DS AND GERD**

SG is a restrictive procedure initially described as the first procedure of a two-staged duodenal switch operation in very-high-risk super-obese patients, and is rapidly gaining popularity as a stand-alone bariatric operation. As with LAGB, early data regarding the impact of SG on GERD are mixed, and very little long-term or comparative data regarding SG and GERD are available. While the resection of a substantial portion of the parietal cell mass, significant weight loss, and a possibly increased rate of gastric emptying might all contribute to improvement in GERD physiology, the relatively long and narrow anatomical configuration of the sleeve might increase resistance to esophageal emptying of physiological amounts of reflux, and the parietal cell mass remains significantly greater than that with RYGB. Furthermore, when bile reflux is
controlled as a factor (through biliopancreatic diversion in the setting of DS), symptomatic resolution of GERD is greater with RYGB. As such, SG in the setting of significant GERD should be recommended with caution.

**SEVERE OBESITY AND GERD: SURGICAL RECOMMENDATIONS**

When surgical treatment of GERD is indicated in a severely obese patient, bariatric surgery rather than fundoplication should be strongly considered. Not only does bariatric surgery, and RYGB in particular, better address the mechanisms that lead to GERD in obese patients with the potential for greater durability, but it also addresses concomitant obesity-related comorbidity by achieving significant and sustained weight loss. Therefore, in this case, the surgeon has the opportunity to substantially improve the patient’s quality of life, positively impact multiple chronic medical conditions, and possibly reduce the excess long-term mortality risk associated with severe obesity in an acceptably safe, minimally-invasive, and cost-effective manner. For many patients, this discussion might be the first in which bariatric surgery is introduced as a possible therapeutic option, and it is not uncommon for patients to express significant resistance to the idea. In other instances, patients might have been considering bariatric surgery but were hesitant to discuss the possibility with their primary care physician and are receptive to the opportunity to learn more about the procedures. Not uncommonly, this discussion might require several office visits with the surgeon, and it is important that, in addition to offering detailed information regarding the procedures, the severely obese patient with GERD undergoes multidisciplinary evaluation as do other potential bariatric surgery patients, given the need for long-term changes in eating and behavior, and the need for long-term medical follow-up and vitamin supplementation. In doing this, the surgeon can provide a therapy that goes significantly beyond the treatment of GERD.

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