Impact of Weight Loss Surgery on Esophageal Physiology

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Abstract: Bariatric surgery has come to the forefront of weight loss treatment due to its complex interactions via anatomic, physiologic, and neurohormonal changes leading to sustained weight loss. Unlike lifestyle and pharmacologic options, which fail to show long-term sustained weight loss, bariatric surgery has been shown to decrease overall mortality and morbidity. Bariatric surgery can be purely restrictive, such as laparoscopic adjustable gastric band (LAGB) or laparoscopic sleeve gastrectomy (LSG), or restrictive-malabsorptive, such as Roux-en-Y gastric bypass (RYGB). These surgeries cause specific anatomic changes that promote weight loss; however, they also have unintended effects on the esophagus, particularly in terms of gastroesophageal reflux disease (GERD) and esophageal motility. Via restrictive surgery, LAGB has been widely reported to cause significant weight loss, although studies have also shown an increase and worsening of GERD as well as elevated rates of esophageal dilation, aperistalsis, and alterations in lower esophageal sphincter pressure. Along with LAGB, LSG has shown not only a worsening of GERD, but also the formation of de novo GERD in patients who were asymptomatic before the operation. In a restrictive-malabsorptive approach, RYGB has been reported to improve GERD and preserve esophageal motility. Bariatric surgery is a burgeoning field with immense implications on overall mortality. Future randomized, controlled trials are needed to better understand which patients should undergo particular surgeries, with greater emphasis on esophageal health and prevention of GERD and esophageal dysmotility.

Rising rates of obesity, a condition defined as having a body mass index (BMI) greater than 30, have led to an increase in the incidence of metabolic syndrome, type 2 diabetes mellitus, hypertension, nonalcoholic fatty liver disease, and hyperlipidemia.[1-3] The increase in obesity is complex and involves genetic predisposition, hormonal changes, and dysbiosis.[4] Moreover, there is a considerable economic burden associated with obesity, with an average of 5% of the total global health care cost going toward treating obese patients.[5] Weight reduction is vital to alter the course of obesity and its related medical conditions, as well as to decrease the medical and economic burdens.

Lifestyle modifications have been utilized for weight loss, but the results have been disappointing. Despite an initial weight loss of typically 5% to 10% in the first 6 months, most weight is regained. Most lifestyle changes encompass a low-calorie diet and increased physical exercise but lack consistent weight loss, which is needed to decrease metabolic syndrome.[6-9]

An alternative to diet and exercise is medication, such as orlistat, lorcaserin, and phentermine/topiramate extended-release. Similar to lifestyle changes, there have been limited data on prolonged weight loss and long-term improvements in risk for metabolic syndrome due to a lack of substantial weight loss. Additionally, these medications are not without harm; prior weight loss medications have been implicated in pulmonary disorders (eg, pulmonary hypertension) and cardiac disorders (eg, valvulopathies).[10-12]

The third and most viable option for weight loss is bariatric surgery, which is the only modality that has shown long-term sustained weight loss, reduction in comorbidities, and improvement in all-cause mortality.[8,13] Bariatric surgery is reserved for patients with a BMI greater than 40 or a BMI greater than 35 with comorbidities. For instance, one study examining the effect of Roux-en-Y gastric bypass (RYGB) reported a mean loss of 50% to 70% of excess body weight and a decrease in the rate of metabolic syndrome.[14] However, bariatric surgery does have complications, including stenosis at anastomotic sites, stomal ulcers, band erosion, and fistulae, all of which have implications on the esophagus.[15-17]

This article summarizes the relationship of obesity with esophageal health and the physiologic changes that occur after bariatric surgery. The focus will be on gastroesophageal reflux disease (GERD) and esophageal motility as well as the most common forms of bariatric surgery: laparoscopic adjustable gastric band (LAGB), laparoscopic sleeve gastrectomy (LSG), and RYGB.

The Relationship Between Obesity and Esophageal Health

Obesity is associated with an increase in esophageal disorders, which range from GERD to conditions of the lower esophageal sphincter (LES) and motility dysfunction. GERD, as defined by the Montreal Classification, is the reflux of stomach contents that leads to symptoms of heartburn and regurgitation.[18-21] The natural antireflux mechanism is composed of the LES, esophageal hiatus of the diaphragm, phrenoesophageal ligaments, and angle of His. Combined, these parts serve as a unit to prevent reflux of stomach contents.[22] Breakdown of this barrier leads to reflux of low pH stomach contents and GERD, which damages the esophageal mucosa.

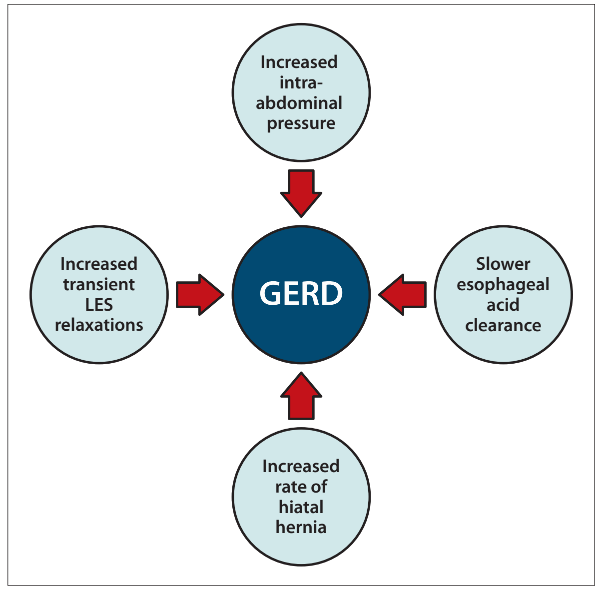
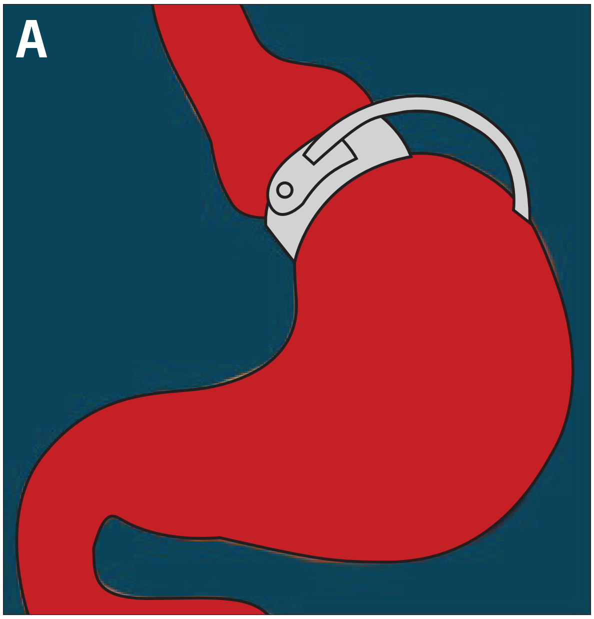


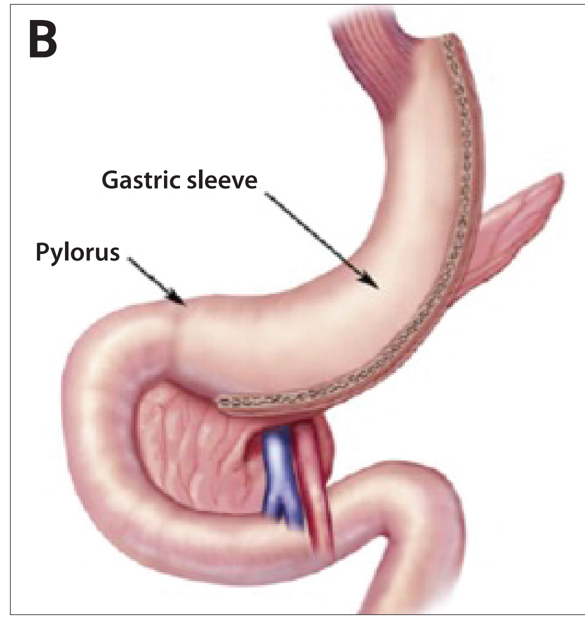
Figure 1. Mechanisms by which obesity leads to gastroesophageal reflux disease (GERD).

LES, lower esophageal sphincter.

Obesity has been shown to increase the risk of GERD symptoms by 50% as well as cause a 2-fold increase in esophageal adenocarcinoma.[23] Furthermore, obese patients have a 2.5-fold increased risk of developing a hiatal hernia, which is a known risk factor for GERD.[24] The physiology of increased GERD with obesity is believed to be multifactorial, including increased abdominal girth leading to high intra-abdominal pressure, increased rate of hiatal hernia, high rate of transient LES relaxations, and slower esophageal acid clearance, all of which favor the development of GERD (Figure 1).[24-28] Obesity also leads to an increase in fatty tissue, which produces estrogen; in turn, elevated transient LES relaxations cause increased GERD.[29,30]

Morbid obesity has been associated with an increase in esophageal dysmotility, ranging in prevalence from 20% to 61%.[31,32] Studies have shown that morbidly obese patients have higher rates of hypotensive LES, although a lack of subjective symptoms was attributed to decreased sensation via altered sympathetic and parasympathetic innervation.[31,33-36] In one prospective study evaluating obese patients selected for bariatric surgery, the presurgical manometric data showed that patients had varied changes to the esophagus, including defective LES (16%), hypertensive LES (18%), diffuse esophageal spasm (3%), nutcracker esophagus (5%), ineffective esophageal disorder (2%), and nonspecific motility disorder (23%).[37] Understanding the pretest probability of esophageal motility disorders is





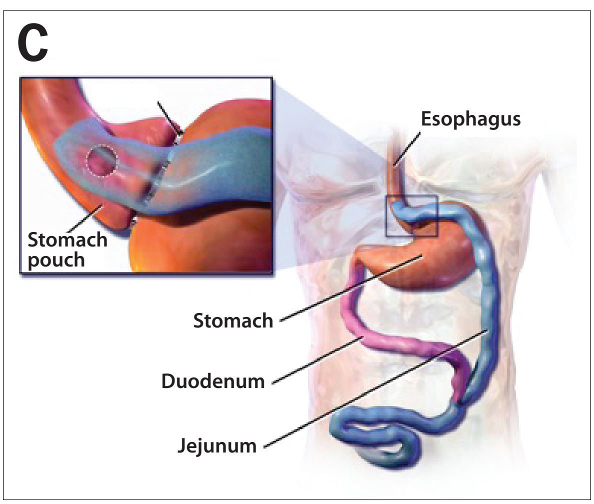


Figure 2. There are 2 main types of bariatric surgery: restrictive procedures, such as **(A)** laparoscopic adjustable gastric band and **(B)** laparoscopic sleeve gastrectomy, and restrictive-malabsorptive procedures, such as **(C)** Roux-en-Y gastric bypass. Figure 2B is adapted from Mechanick et al.[125] Figure 2C is adapted from Blaus.[126]

important, as underlying motility disorders have been shown to be predictors of the need for LAGB reoperation.[38]

Overview of Bariatric Surgery

The 2 main types of bariatric surgery, restrictive and restrictive-malabsorptive, are divided by anatomic and functional differences (Figure 2). Restrictive surgeries, which include LAGB and LSG, decrease the functional capacity of the stomach without a notable change in absorption. Restrictive-malabsorptive surgeries, of which RYGB is the most common, both restrict the carrying capacity of the stomach and lead to anatomic resections that serve to limit calorie and, as a byproduct, nutrient absorption.

Despite anatomic differences, the bariatric surgeries have in common modifications to the digestive tract and anatomic rearrangement. These modifications are known as the BRAVE effects: bile flow alteration, reduction of gastric size, anatomic gut rearrangement and altered flow of nutrients, vagal manipulation, and enteric gut hormone modulation.[39-47] Weight loss due to bariatric surgery has been shown to decrease all-cause mortality at 10 years with significant morbidity improvements. Growing attention has been placed on neurohormonal changes (such as the alteration of peptide-1 and ghrelin) and their positive effects in sustained weight loss.[48]

The following sections will discuss LAGB, LSG, and RYGB, along with associated changes in GERD and motility. When determining the appropriate surgical approach, clinicians should consider patient history (eg, preexisting esophageal motility) and understand the physiologic changes that result from the surgery.

Laparoscopic Adjustable Gastric Band

Surgical Approach

LAGB is a restrictive surgery that involves placing an adjustable gastric band around the proximal stomach to divide it into a small pouch and a larger pouch, the latter of which connects to the remainder of the small bowel (Figure 2A).[43,49] The inflatable band, and thus the size of the pouches, can be adjusted via a subcutaneous access point as needed. A smaller proximal pouch limits food intake due to decreased stomach size and increased food transit time.

Table 1. The Relationship Between Laparoscopic Adjustable Gastric Banding and Esophageal Disease

Study	Pathology	Evaluation	Findings
de Jong et al[50]	GERD	Endoscopy, manometry, ambulatory pH monitoring	Reduced GERD
Woodman et al[51]	GERD	Symptom reporting	Reduced GERD
Iovino et al[56]	LES pressure	Manometry, questionnaire, 24-hour ambulatory pH-metry	Increase in LES pressure
Weiss et al[59]	LES pressure	Endoscopy, barium swallow, manometry, 24-hour esophageal monitoring	Impaired LES relaxation, increased esophageal dilation
Milone et al[65]	Esophageal dilation	Barium swallow	Increased esophageal dilation
Dargent[68]	Esophageal dilation	Barium swallow, band removal	Increased esophageal dilation

GERD, gastroesophageal reflux disease; LES, lower esophageal sphincter.

Table 2. Consequences of Esophageal Disorders After Bariatric Surgery

Bariatric Surgery	Mechanistic Changes to the Esophagus	Esophageal Complications
Laparoscopic adjustable gastric band	Weak esophageal motility, pouch dilation, preexisting reduced esophageal motility, increased lower esophageal sphincter pressure, increased high-pressure zone length	Worsened gastroesophageal reflux disease, esophageal dilation, esophageal stasis, achalasia-type symptoms
Laparoscopic sleeve gastrectomy	Weak lower esophageal sphincter pressure, decreased gastric compliance leading to high intragastric pressure, breaking of sling fibers disrupting competency of the esophagogastric junction, increased rate of hiatal hernia, surgical damage to phrenoesophageal ligament, sleeve migration	Worsened gastroesophageal reflux disease (recurrent and de novo), increased gastric emptying
Roux-en-Y gastric bypass	Malabsorption	Improved gastroesophageal reflux disease, minimal effect on motility

Implications With Gastroesophageal Reflux Disease

The relationship between LAGB and GERD changes over time. Many studies show an initial improvement in GERD symptoms in short-term follow-up (<6 months); however, longer follow-up periods show a return of GERD symptoms.[50-52] Symptoms are typically heartburn in the preoperative period, as a result of direct reflux, and regurgitation in the postoperative period, in which surgical placement of the band is associated with pouchstasis. Few studies have shown improvement in GERD with this technique and consider LAGB a physical barrier to GERD; however, the burden of evidence supports an increase in GERD, predominantly exhibited via regurgitation.[53]

Changes in Esophageal Motility

LAGB has been associated with multiple esophageal motility changes primarily related to proximal migration of the inflatable band. The pathology of this migration was elucidated in animal models, in which a nonobstructive band was placed around the esophagogastric junction in a fashion similar to a LAGB and was found to cause esophageal dilation and elevated LES pressure.[54,55] Many studies have shown similar esophageal dilations (with rare cases of megaesophagus) and increased LES pressures (Table 1).[52,56-61] The etiology of these changes is associated with increases in LES high-pressure zone length, defective propagations, and increased rate of esophageal dilations (Table 2).[62-70] There is a lack of randomized, controlled trials for LAGB; one of the largest studies, which evaluated 1232 patients with LAGB over a 9-year period, found anterior and posterior slippage with esophageal dilations in concordance with prior studies' findings of increased rates of esophageal dilation, achalasia, and pouch dilation.[58,68,71] However, due to recent changes in surgical approach and band design, the rates of both anterior and posterior prolapses have decreased significantly. When the band is placed suprabursally, the rate of posterior prolapse approaches 0, while the rate of anterior prolapse is also drastically reduced.[72,73]

Laparoscopic Sleeve Gastrectomy

Surgical Approach

Sleeve gastrectomy is a restrictive surgery that involves removing a large portion of the body and all of the fundus of the stomach to create a smaller gastric pouch (Figure 2B). The remaining portion of the stomach is formed into a narrow sleeve and is stapled closed, with the remainder of the stomach connected to the small bowel. The reduced gastric pouch leads to a decrease in acid production.

Table 3. The Relationship Between Laparoscopic Sleeve Gastrectomy and Esophageal Disease

Study	Pathology	Evaluation	Findings
Arias et al[69]	GERD	Symptom reporting	Increased GERD
Lakdawala et al[78]	GERD	Symptom reporting	Increased GERD
Melissas et al[81]	GERD, gastric emptying	Symptom reporting	Increased GERD, increased gastric emptying
Melissas et al[82]	GERD, gastric emptying	Symptom reporting	Reduced GERD, increased gastric emptying
Howard et al[91]	GERD	Symptom reporting	Reduced GERD
Del Genio et al[92]	Peristalsis	High-resolution impedance manometry	Increased ineffective peristalsis

GERD, gastroesophageal reflux disease.

Implications With Gastroesophageal Reflux Disease

There have been mixed results in determining the relationship of GERD with LSG, likely owing to decreased literature on this surgical approach (Table 3). Studies show both improvement and worsening of GERD symptoms when using symptom reporting and medication.[74-89] Many authors think that reducing the gastric pouch with surgical resection should improve GERD. However, other authors propose that de novo formations of hiatal hernias, sleeve migration, and disruption of the esophagogastric junction lead to worsening, and sometimes de novo formation, of GERD symptoms (Table 3).[81,90,91] Hence, despite the surgical resection of a proacidic environment, there are many proregurgitant factors that lead to increased GERD.

Changes in Esophageal Motility

LSG has been shown to cause increased rates of global gastrointestinal motility. There is evidence of ineffective peristalsis after LSG with an increase in LES pressures (Table 3).[92,93] Moreover, there are global findings of increased rates of gastric and small bowel transit, which contribute to the excision of the gastric fundus, leading to altered intestinal motility.[81,82,94] Two studies by the same group evaluating patients after LSG reported increased gastric emptying, which has been postulated to be due to lack of peristalsis in the sleeve portion.[81,82,95] This acceleration of gastric emptying has been utilized by combining LSG and fundoplication for patients with GERD and delayed gastric emptying, with improvement in both areas.[96] However, a few studies have shown that there is, conversely, a delay in esophageal and gastric emptying, likely owing to the location of the gastrectomy from the gastroesophageal junction.[92] Thus, there is a lack of substantial studies evaluating the effects of LSG, although current studies show a trend toward alteration in gastrointestinal motility with increased ineffective peristalsis. This leads to downstream small bowel motility changes, although the effect on the esophagus has not been fully ascertained.

Roux-en-Y Gastric Bypass

Surgical Approach

RYGB is a restrictive-malabsorptive procedure in which the stomach is transected to form a proximal stomach pouch that is connected to a divided jejunal loop called the Roux limb (Figure 2C). The proximal stomach transection leads to the restrictive component of this surgery; the bypassed small bowel with direct connection to the jejunal loop leads to the malabsorption component. Decreased acid production, as seen in the LSG, leads to faster transit times in the stomach.[97] Restrictive-malabsorptive surgery leads to larger weight loss than purely restrictive surgeries, likely due to neurohormonal changes; however, there are associated micronutrient deficiencies in vitamin B_{12}, vitamin D, folate, iron, and calcium, which require lifelong supplementation. Moreover, there are associated complications such as anastomotic leakage and marginal ulcers.[98-102]

Implications With Gastroesophageal Reflux Disease

In patient questionnaires and manometry that evaluates symptoms, RYGB has been shown to decrease symptoms of GERD, the need for proton pump inhibitor therapy, and time with a pH less than 4 (Table 4).[86,88,103-108] The decrease in symptoms is due to the combination of altered stomach anatomy via primary resection and a change in the downstream small bowel loop causing both a decrease in acid production and a lack of formation of a proregurgitant environment. There are several studies that show an increase in GERD after RYGB, but in general, RYGB is thought to be a superior surgery in regard to GERD when compared with LAGB and LSG.[61,109,110]

Changes in Esophageal Motility

There has been little evidence of esophageal dysmotility after RYGB (Table 4). There are a few retrospective studies with relatively low numbers of patients that have shown a trend toward increased frequency of hypotonic LES, hypertonic upper esophageal sphincter, and esophageal

Table 4. The Relationship Between Roux-en-Y Gastric Bypass and Esophageal Disease

Study	Pathology	Evaluation	Findings
Merrouche et al[61]	Esophageal dyskinesia	Symptom scoring, endoscopy, manometry, 24-hour pH monitoring	No esophageal dyskinesia
Peterli et al[88]	GERD	Symptom reporting	Reduced GERD
Madalosso et al[107]	GERD	Symptom reporting, pH monitoring	Reduced GERD
Cassao et al[111]	Esophageal sphincter pressure	High-resolution manometry	Increased LES hypotonia
Valezi et al[112]	LES pressure	High-resolution manometry	Increased LES hypotonia
Clements et al[113]	Dysphagia	Symptom scoring	Reduced GERD, worsening of dysphagia
Foster et al[114]	Dysphagia	Symptom scoring	Reduced GERD, no change in dysphagia

GERD, gastroesophageal reflux disease; LES, lower esophageal sphincter.

wave duration and wave amplitude after RYGB.[62,106,111,112] There is also mixed evidence on dysphagia and esophageal contractility; multiple studies report conflicting results.[61,104,106,113,114] One study reported an improvement in esophageal dysmotility after RYGB.[106] Thus, the lack of evidence supporting overt esophageal dysmotility after RYGB is a large reason why it is the preferred surgery for patients with known esophageal disorders prior to bariatric surgery.[61,115]

Hernia Repair

In addition to the primary goal of weight loss, the timing of hernia closure in morbidly obese patients is an increasingly important topic. Many studies have shown repair of hernias during bariatric surgery, and some studies have shown no recurrence of hernia.[116-118] However, there are side effects of hernia repair, including seroma (as high as 18%) and mesh infections (4.4%).[116,119] The ultimate decision of hernia repair becomes a risk-benefit calculation of the risk of recurrence and perioperative complications and the risk of hernia-associated complications. With improving techniques, recent studies have moved toward concomitant hernia repair, but the literature is still in its infancy, and additional, high-quality studies are needed.[120]

Conclusion

Given the limited effectiveness of lifestyle modifications and medications, bariatric surgery has come to the forefront for sustained weight loss therapies. Due to the anatomic, neurohormonal, and microbiota changes associated with these surgeries, weight loss is profound and sustainable, and leads to a reduction in morbidity as a result of a decrease in type 2 diabetes mellitus, hypertension, hyperlipidemia, and mortality.[121] One study comparing all 3 bariatric procedures found LAGB to be inferior to LSG and RYGB in terms of weight reduction, number of long-term complications, and need for revisional surgery; LSG and RYGB reported similar complication rates, although 9% of LSG patients had to be converted to RYGB due to insufficient weight loss.[122]

RYGB has been shown to improve GERD, whereas restrictive surgeries generally lead to new or worsening GERD through hypotensive LES, decreased gastric compliance and volume, esophageal dilation (via proximal migration in LAGB), or aperistalsis (via surgical resection in LSG).[113,114] The largest limitation of these findings is that most studies are retrospective reviews or analyses of prospective cohorts; even randomized, controlled trials typically feature a small number of patients and make general statements. Hence, high-quality studies are needed to better elucidate these findings.

In regard to esophageal motility, LAGB is also associated with worsening motility via surrogates such as esophageal stasis, dilation, and esophagitis.[56,65,68] Although preoperative manometry is not generally performed, it could be helpful, as preexisting dysmotility would favor RYGB over LAGB.[71,112,123,124] There are limited trials on the effect of LSG, and current studies are focused on the global motility changes of LSG without focusing on the esophagus.[82,92] Current data show that RYGB is the safest surgery for patients with known esophageal dysmotility, as it has been shown not only to prevent, but also improve, esophageal disorders.[88,114] LAGB should be avoided in patients with known preoperative esophageal concerns because it can lead to proximal migration of the band, causing esophageal dilation mimicking achalasia.[56]

Therefore, bariatric surgery is an important surgical tool for the treatment of obesity. Each bariatric surgery has key esophageal changes in regard to GERD and esophageal motility; these are important characteristics to understand prior to recommending particular bariatric surgeries and when taking care of these patients postoperatively. LAGB leads to pronounced increases in GERD and esophageal motility issues, whereas RYGB shows continued improvement in GERD symptoms without overt effects on the esophagus.[113,114] LSG is discussed less frequently in the literature, so any conclusions on its effects on GERD and motility are premature. This field needs large-volume, randomized, controlled studies to better characterize the limitations of each surgery; elucidate mechanisms of improvement for the surgical technique; and help understand the neurohormonal changes, which have been vastly underappreciated in the current body of evidence. Such studies can offer better evidence on the role of preoperative manometry, indications and restrictions on each bariatric surgery, and maintenance of the health of the esophagus while still promoting improvements in morbidity and mortality.

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References

1. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care*. 2005;28(7):1769-1778.
2. Resnick HE, Jones K, Ruotolo G, et al; Strong Heart Study. Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease in nondiabetic American Indians: the Strong Heart Study. *Diabetes Care*. 2003;26(3):861-867.
3. Hamaguchi M, Kojima T, Takeda N, et al. The metabolic syndrome as a predictor of nonalcoholic fatty liver disease. *Ann Intern Med*. 2005;143(10):722-728.
4. Aron-Wisnewsky J, Doré J, Clement K. The importance of the gut microbiota after bariatric surgery. *Nat Rev Gastroenterol Hepatol*. 2012;9(10):590-598.
5. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser*. 2000;894:i-xii, 1-253.
6. Dyson PA. The therapeutics of lifestyle management on obesity. *Diabetes Obes Metab*. 2010;12(11):941-946.
7. Wing RR, Phelan S. Long-term weight loss maintenance. *Am J Clin Nutr*. 2005;82(1 suppl):222S-225S.
8. Sjöström L, Lindroos AK, Peltonen M, et al; Swedish Obese Subjects Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med*. 2004;351(26):2683-2693.
9. Astrup A, Dyerberg J, Selleck M, Stender S. Nutrition transition and its relationship to the development of obesity and related chronic diseases. *Obes Rev*. 2008;9(suppl 1):48-52.
10. Rich S, Rubin L, Walker AM, Schneeweiss S, Abenhaim L. Anorexigens and pulmonary hypertension in the United States: results from the surveillance of North American pulmonary hypertension. *Chest*. 2000;117(3):870-874.
11. Frachon I, Etienne Y, Jobic Y, Le Gal G, Humbert M, Leroyer C. Benfluorex and unexplained valvular heart disease: a case-control study. *PLoS One*. 2010;5(4):e10128.
12. Sachdev M, Miller WC, Ryan T, Jollis JG. Effect of fenfluramine-derivative diet pills on cardiac valves: a meta-analysis of observational studies. *Am Heart J*. 2002;144(6):1065-1073.
13. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA*. 2004;292(14):1724-1737.
14. Balsiger BM, Murr MM, Poggio JL, Sarr MG. Bariatric surgery. Surgery for weight control in patients with morbid obesity. *Med Clin North Am*. 2000;84(2):477-489.
15. Westling A, Bjurling K, Ohrvall M, Gustavsson S. Silicone-adjustable gastric banding: disappointing results. *Obes Surg*. 1998;8(4):467-474.
16. Filho AJ, Kondo W, Nassif LS, Garcia MJ, Tirapelle Rde A, Dotti CM. Gastrogastric fistula: a possible complication of Roux-en-Y gastric bypass. *JSLS*. 2006;10(3):326-331.
17. Gumbs AA, Duffy AJ, Bell RL. Incidence and management of marginal ulceration after laparoscopic Roux-Y gastric bypass. *Surg Obes Relat Dis*. 2006;2(4):460-463.
18. Vakil N, van Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol*. 2006;101(8):1900-1920; quiz 1943.
19. Spechler SJ. Epidemiology and natural history of gastro-oesophageal reflux disease. *Digestion*. 1992;51(suppl 1):24-29.
20. Vaezi MF. Therapy insight: gastroesophageal reflux disease and laryngopharyngeal reflux. *Nat Clin Pract Gastroenterol Hepatol*. 2005;2(12):595-603.
21. Poelmans J, Tack J. Extraoesophageal manifestations of gastro-oesophageal reflux. *Gut*. 2005;54(10):1492-1499.
22. Trus TL, Hunter JG. Minimally invasive surgery of the esophagus and stomach. *Am J Surg*. 1997;173(3):242-255.
23. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med*. 2005;143(3):199-211.
24. Wilson LJ, Ma W, Hirschowitz BI. Association of obesity with hiatal hernia and esophagitis. *Am J Gastroenterol*. 1999;94(10):2840-2844.
25. Zacchi P, Mearin F, Humbert P, Formiguera X, Malagelada JR. Effect of obesity on gastroesophageal resistance to flow in man. *Dig Dis Sci*. 1991;36(10):1473-1480.
26. El-Serag HB, Graham DY, Satia JA, Rabeneck L. Obesity is an independent risk factor for GERD symptoms and erosive esophagitis. *Am J Gastroenterol*. 2005;100(6):1243-1250.
27. Kitchin LI, Castell DO. Rationale and efficacy of conservative therapy for gastroesophageal reflux disease. *Arch Intern Med*. 1991;151(3):448-454.
28. Mercer CD, Rue C, Hanelin L, Hill LD. Effect of obesity on esophageal transit. *Am J Surg*. 1985;149(1):177-181.
29. Yang SS, Cheng KS, Lai YC, et al. Decreasing serum alpha-fetoprotein levels in predicting poor prognosis of acute hepatic failure in patients with chronic hepatitis B. *J Gastroenterol*. 2002;37(8):626-632.
30. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Obesity and estrogen as risk factors for gastroesophageal reflux symptoms. *JAMA*. 2003;290(1):66-72.
31. Jaffin BW, Knoepflmacher P, Greenstein R. High prevalence of asymptomatic esophageal motility disorders among morbidly obese patients. *Obes Surg*. 1999;9(4):390-395.
32. Almogy G, Anthone GJ, Crookes PF. Achalasia in the context of morbid obesity: a rare but important association. *Obes Surg*. 2003;13(6):896-900.
33. Granström L, Backman L. Stomach distension in extremely obese and in normal subjects. *Acta Chir Scand*. 1985;151(4):367-370.
34. Geliebter A, Westreich S, Gage D. Gastric distention by balloon and test-meal intake in obese and lean subjects. *Am J Clin Nutr*. 1988;48(3):592-594.
35. Backman L, Granström L, Lindahl J, Melcher A. Manometric studies of lower esophageal sphincter in extreme obesity. *Acta Chir Scand*. 1983;149(2):193-197.
36. O'Brien TF Jr. Lower esophageal sphincter pressure (LESP) and esophageal function in obese humans. *J Clin Gastroenterol*. 1980;2(2):145-148.
37. Hong D, Khajanchee YS, Pereira N, Lockhart B, Patterson EJ, Swanstrom LL. Manometric abnormalities and gastroesophageal reflux disease in the morbidly obese. *Obes Surg*. 2004;14(6):744-749.
38. Greenstein RJ, Nissan A, Jaffin B. Esophageal anatomy and function in laparoscopic gastric restrictive bariatric surgery: implications for patient selection. *Obes Surg*. 1998;8(2):199-206.
39. Ashrafian H, Ahmed K, Rowland SP, et al. Metabolic surgery and cancer: protective effects of bariatric procedures. *Cancer*. 2011;117(9):1788-1799.
40. Ashrafian H, Athanasiou T, Li JV, et al. Diabetes resolution and hyperinsulinaemia after metabolic Roux-en-Y gastric bypass. *Obes Rev*. 2011;12(5):e257-e272.
41. Beckman LM, Beckman TR, Earthman CP. Changes in gastrointestinal hormones and leptin after Roux-en-Y gastric bypass procedure: a review. *J Am Diet Assoc*. 2010;110(4):571-584.
42. Ryan KK, Tremaroli V, Clemmensen C, et al. FXR is a molecular target for the effects of vertical sleeve gastrectomy. *Nature*. 2014;509(7499):183-188.
43. Lo Menzo E, Szomstein S, Rosenthal RJ. Changing trends in bariatric surgery. *Scand J Surg*. 2015;104(1):18-23.
44. Korner J, Inabnet W, Febres G, et al. Prospective study of gut hormone and metabolic changes after adjustable gastric banding and Roux-en-Y gastric bypass. *Int J Obes (Lond)*. 2009;33(7):786-795.
45. le Roux CW, Welbourn R, Werling M, et al. Gut hormones as mediators of appetite and weight loss after Roux-en-Y gastric bypass. *Ann Surg*. 2007;246(5):780-785.
46. Cummings DE, Weigle DS, Frayo RS, et al. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. *N Engl J Med*. 2002;346(21):1623-1630.
47. Geloneze B, Tambascia MA, Pilla VF, Geloneze SR, Repetto EM, Pareja JC. Ghrelin: a gut-brain hormone: effect of gastric bypass surgery. *Obes Surg*. 2003;13(1):17-22.
48. Ochner CN, Gibson C, Carnell S, Dambkowski C, Geliebter A. The neurohormonal regulation of energy intake in relation to bariatric surgery for obesity. *Physiol Behav*. 2010;100(5):549-559.

49. Miller K. Obesity: surgical options. *Best Pract Res Clin Gastroenterol*. 2004;18(6):1147-1165.
50. de Jong JR, Besselink MG, van Ramshorst B, Gooszen HG, Smout AJ. Effects of adjustable gastric banding on gastroesophageal reflux and esophageal motility: a systematic review. *Obes Rev*. 2010;11(4):297-305.
51. Woodman G, Cywes R, Billy H, Montgomery K, Cornell C, Okerson T; APEX Study Group. Effect of adjustable gastric banding on changes in gastroesophageal reflux disease (GERD) and quality of life. *Curr Med Res Opin*. 2012;28(4):581-589.
52. Gamagaris Z, Patterson C, Schaye V, et al. Lap-band impact on the function of the esophagus. *Obes Surg*. 2008;18(10):1268-1272.
53. Dixon JB, O'Brien PE. Gastroesophageal reflux in obesity: the effect of lap-band placement. *Obes Surg*. 1999;9(6):527-531.
54. Tung HN, Schulze-Delrieu K, Shirazi S, Noel S, Xia Q, Cue K. Hypertrophic smooth muscle in the partially obstructed opossum esophagus. The model: histological and ultrastructural observations. *Gastroenterology*. 1991;100(4):853-864.
55. O'Rourke RW, Seltman AK, Chang EY, et al. A model for gastric banding in the treatment of morbid obesity: the effect of chronic partial gastric outlet obstruction on esophageal physiology. *Ann Surg*. 2006;244(5):723-733.
56. Iovino P, Angrisani L, Tremolaterra F, et al. Abnormal esophageal acid exposure is common in morbidly obese patients and improves after a successful Lap-band system implantation. *Surg Endosc*. 2002;16(11):1631-1635.
57. de Jong JR, van Ramshorst B, Timmer R, Gooszen HG, Smout AJ. Effect of laparoscopic gastric banding on esophageal motility. *Obes Surg*. 2006;16(1):52-58.
58. Klaus A, Gruber I, Wetscher G, et al. Prevalent esophageal body motility disorders underlie aggravation of GERD symptoms in morbidly obese patients following adjustable gastric banding. *Arch Surg*. 2006;141(3):247-251.
59. Weiss HG, Nehoda H, Labeck B, et al. Adjustable gastric and esophagogastric banding: a randomized clinical trial. *Obes Surg*. 2002;12(4):573-578.
60. Weiss HG, Nehoda H, Labeck B, et al. Treatment of morbid obesity with laparoscopic adjustable gastric banding affects esophageal motility. *Am J Surg*. 2000;180(6):479-482.
61. Merrouche M, Sabaté JM, Jouet P, et al. Gastro-esophageal reflux and esophageal motility disorders in morbidly obese patients before and after bariatric surgery. *Obes Surg*. 2007;17(7):894-900.
62. Tolonen P, Victorzon M, Niemi R, Mäkelä J. Does gastric banding for morbid obesity reduce or increase gastroesophageal reflux? *Obes Surg*. 2006;16(11):1469-1474.
63. Gutschow CA, Collet P, Prenzel K, Hölscher AH, Schneider PM. Long-term results and gastroesophageal reflux in a series of laparoscopic adjustable gastric banding. *J Gastrointest Surg*. 2005;9(7):941-948.
64. Suter M, Dorta G, Giusti V, Calmes JM. Gastric banding interferes with esophageal motility and gastroesophageal reflux. *Arch Surg*. 2005;140(7):639-643.
65. Milone L, Daud A, Durak E, et al. Esophageal dilation after laparoscopic adjustable gastric banding. *Surg Endosc*. 2008;22(6):1482-1486.
66. DeMaria EJ, Sugerman HJ, Meador JG, et al. High failure rate after laparoscopic adjustable silicone gastric banding for treatment of morbid obesity. *Ann Surg*. 2001;233(6):809-818.
67. Naef M, Mouton WG, Naef U, van der Weg B, Maddern GJ, Wagner HE. Esophageal dysmotility disorders after laparoscopic gastric banding—an underestimated complication. *Ann Surg*. 2011;253(2):285-290.
68. Dargent J. Esophageal dilatation after laparoscopic adjustable gastric banding: definition and strategy. *Obes Surg*. 2005;15(6):843-848.
69. Arias IE, Radulescu M, Stiegeler R, et al. Diagnosis and treatment of megaesophagus after adjustable gastric banding for morbid obesity. *Surg Obes Relat Dis*. 2009;5(2):156-159.
70. Khan A, Ren-Fielding C, Traube M. Potentially reversible pseudoachalasia after laparoscopic adjustable gastric banding. *J Clin Gastroenterol*. 2011;45(9):775-779.
71. Klaus A, Weiss H. Is preoperative manometry in restrictive bariatric procedures necessary? *Obes Surg*. 2008;18(8):1039-1042.
72. Wiesner W, Weber M, Hauser RS, Hauser M, Schoeb O. Anterior versus posterior slippage: two different types of eccentric pouch dilatation in patients with adjustable laparoscopic gastric banding. *Dig Surg*. 2001;18(3):182-186.
73. Lee WK, Kim SM. Three-year experience of pouch dilatation and slippage management after laparoscopic adjustable gastric banding. *Yonsei Med J*. 2014;55(1):149-156.
74. Arias E, Martínez PR, Ka Ming Li V, Szomstein S, Rosenthal RJ. Mid-term follow-up after sleeve gastrectomy as a final approach for morbid obesity. *Obes Surg*. 2009;19(5):544-548.
75. Braghetto I, Csendes A, Lanzarini E, Papapietro K, Cárcamo C, Molina JC. Is laparoscopic sleeve gastrectomy an acceptable primary bariatric procedure in obese patients? Early and 5-year postoperative results. *Surg Laparosc Endosc Percutan Tech*. 2012;22(6):479-486.
76. Carter PR, LeBlanc KA, Hausmann MG, Kleinpeter KP, deBarros SN, Jones SM. Association between gastroesophageal reflux disease and laparoscopic sleeve gastrectomy. *Surg Obes Relat Dis*. 2011;7(5):569-572.
77. Himpens J, Dobbeleir J, Peeters G. Long-term results of laparoscopic sleeve gastrectomy for obesity. *Ann Surg*. 2010;252(2):319-324.
78. Lakdawala MA, Bhasker A, Mulchandani D, Goel S, Jain S. Comparison between the results of laparoscopic sleeve gastrectomy and laparoscopic Roux-en-Y gastric bypass in the Indian population: a retrospective 1 year study. *Obes Surg*. 2010;20(1):1-6.
79. Nocca D, Krawczykowsky D, Bomans B, et al. A prospective multicenter study of 163 sleeve gastrectomies: results at 1 and 2 years. *Obes Surg*. 2008;18(5):560-565.
80. Tai CM, Huang CK, Lee YC, Chang CY, Lee CT, Lin JT. Increase in gastroesophageal reflux disease symptoms and erosive esophagitis 1 year after laparoscopic sleeve gastrectomy among obese adults. *Surg Endosc*. 2013;27(4):1260-1266.
81. Melissas J, Koukouraki S, Askoxylakis J, et al. Sleeve gastrectomy: a restrictive procedure? *Obes Surg*. 2007;17(1):57-62.
82. Melissas J, Daskalakis M, Koukouraki S, et al. Sleeve gastrectomy—a "food limiting" operation. *Obes Surg*. 2008;18(10):1251-1256.
83. Chopra A, Chao E, Etkin Y, Merklinger L, Lieb J, Delany H. Laparoscopic sleeve gastrectomy for obesity: can it be considered a definitive procedure? *Surg Endosc*. 2012;26(3):831-837.
84. Rawlins L, Rawlins MP, Brown CC, Schumacher DL. Sleeve gastrectomy: 5-year outcomes of a single institution. *Surg Obes Relat Dis*. 2013;9(1):21-25.
85. Weiner RA, Weiner S, Pomhoff I, Jacobi C, Makarewicz W, Weigand G. Laparoscopic sleeve gastrectomy—influence of sleeve size and resected gastric volume. *Obes Surg*. 2007;17(10):1297-1305.
86. Kehagias I, Karamanakos SN, Argentou M, Kalfarentzos F. Randomized clinical trial of laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy for the management of patients with BMI<50 kg/m². *Obes Surg*. 2011;21(11):1650-1656.
87. Sieber P, Gass M, Kern B, Peters T, Slawik M, Peterli R. Five-year results of laparoscopic sleeve gastrectomy. *Surg Obes Relat Dis*. 2014;10(2):243-249.
88. Peterli R, Borbély Y, Kern B, et al. Early results of the Swiss Multicentre Bypass or Sleeve Study (SM-BOSS): a prospective randomized trial comparing laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass. *Ann Surg*. 2013;258(5):690-694.
89. DuPree CE, Blair K, Steele SR, Martin MJ. Laparoscopic sleeve gastrectomy in patients with preexisting gastroesophageal reflux disease: a national analysis. *JAMA Surg*. 2014;149(4):328-334.
90. Himpens J, Dapri G, Cadière GB. A prospective randomized study between laparoscopic gastric banding and laparoscopic isolated sleeve gastrectomy: results after 1 and 3 years. *Obes Surg*. 2006;16(11):1450-1456.
91. Howard DD, Caban AM, Cendan JC, Ben-David K. Gastroesophageal reflux after sleeve gastrectomy in morbidly obese patients. *Surg Obes Relat Dis*. 2011;7(6):709-713.
92. Del Genio G, Tolone S, Limongelli P, et al. Sleeve gastrectomy and development of "de novo" gastroesophageal reflux. *Obes Surg*. 2014;24(1):71-77.
93. Petersen WV, Meile T, Küper MA, Zdichavsky M, Königsrainer A, Schneider JH. Functional importance of laparoscopic sleeve gastrectomy for the lower esophageal sphincter in patients with morbid obesity. *Obes Surg*. 2012;22(3):360-366.
94. Bernstine H, Tzioni-Yehoshua R, Groshar D, et al. Gastric emptying is not affected by sleeve gastrectomy—scintigraphic evaluation of gastric emptying after sleeve gastrectomy without removal of the gastric antrum. *Obes Surg*. 2009;19(3):293-298.
95. Yehoshua RT, Eidelman LA, Stein M, et al. Laparoscopic sleeve gastrectomy—volume and pressure assessment. *Obes Surg*. 2008;18(9):1083-1088.
96. Le Page PA, Martin D. Laparoscopic partial sleeve gastrectomy with fundoplication for gastroesophageal reflux and delayed gastric emptying. *World J Surg*. 2015;39(6):1460-1464.
97. El Oufir L, Flourié B, Bruley des Varannes S, et al. Relations between transit time, fermentation products, and hydrogen consuming flora in healthy humans. *Gut*. 1996;38(6):870-877.
98. Hell E, Miller KA, Moorehead MK, Norman S. Evaluation of health status and quality of life after bariatric surgery: comparison of standard Roux-en-Y gastric bypass, vertical banded gastroplasty and laparoscopic adjustable silicone gastric banding. *Obes Surg*. 2000;10(3):214-219.
99. Wittgrove AC, Clark GW. Laparoscopic gastric bypass, Roux-en-Y- 500 patients: technique and results, with 3-60 month follow-up. *Obes Surg*. 2000;10(3):233-239.
100. Wittgrove AC, Clark GW, Schubert KR. Laparoscopic gastric bypass, Roux-en-Y: technique and results in 75 patients with 3-30 months follow-up. *Obes Surg*. 1996;6(6):500-504.
101. Pories WJ, MacDonald KG Jr, Morgan EJ, et al. Surgical treatment of obesity and its effect on diabetes: 10-y follow-up. *Am J Clin Nutr*. 1992;55(2 suppl):582S-585S.

102. Cleator IG, Litwin D, Phang P, Brosseuk D, Rae A. Laparoscopic ileogastrostomy for morbid obesity. *Obes Surg*. 1994;4(4):358-360.
103. Frezza EE, Ikramuddin S, Gourash W, et al. Symptomatic improvement in gastroesophageal reflux disease (GERD) following laparoscopic Roux-en-Y gastric bypass. *Surg Endosc*. 2002;16(7):1027-1031.
104. Ortega J, Escudero MD, Mora F, et al. Outcome of esophageal function and 24-hour esophageal pH monitoring after vertical banded gastroplasty and Roux-en-Y gastric bypass. *Obes Surg*. 2004;14(8):1086-1094.
105. Perry Y, Courcoulas AP, Fernando HC, Buenaventura PO, McCaughan JS, Luketich JD. Laparoscopic Roux-en-Y gastric bypass for recalcitrant gastroesophageal reflux disease in morbidly obese patients. *JSLS*. 2004;8(1):19-23.
106. Mejía-Rivas MA, Herrera-López A, Hernández-Calleros J, Herrera MF, Valdovinos MA. Gastroesophageal reflux disease in morbid obesity: the effect of Roux-en-Y gastric bypass. *Obes Surg*. 2008;18(10):1217-1224.
107. Madalosso CA, Gurski RR, Callegari-Jacques SM, Navarini D, Thiesen V, Fornari F. The impact of gastric bypass on gastroesophageal reflux disease in patients with morbid obesity: a prospective study based on the Montreal Consensus. *Ann Surg*. 2010;251(2):244-248.
108. Nelson LG, Gonzalez R, Haines K, Gallagher SF, Murr MM. Amelioration of gastroesophageal reflux symptoms following Roux-en-Y gastric bypass for clinically significant obesity. *Am Surg*. 2005;71(11):950-953.
109. Schauer PR, Ikramuddin S, Gourash W, Ramanathan R, Luketich J. Outcomes after laparoscopic Roux-en-Y gastric bypass for morbid obesity. *Ann Surg*. 2000;232(4):515-529.
110. Pallati PK, Shaligram A, Shostrom VK, Oleynikov D, McBride CL, Goede MR. Improvement in gastroesophageal reflux disease symptoms after various bariatric procedures: review of the Bariatric Outcomes Longitudinal Database. *Surg Obes Relat Dis*. 2014;10(3):502-507.
111. Cassão BD, Herbella FA, Silva LC, Vicentine FP. Esophageal motility after gastric bypass in Roux-en-Y for morbid obesity: high resolution manometry findings. *Arq Bras Cir Dig*. 2013;26(suppl 1):22-25.
112. Valezi AC, Herbella FA, Junior JM, de Almeida Menezes M. Esophageal motility after laparoscopic Roux-en-Y gastric bypass: the manometry should be preoperative examination routine? *Obes Surg*. 2012;22(7):1050-1054.
113. Clements RH, Gonzalez QH, Foster A, et al. Gastrointestinal symptoms are more intense in morbidly obese patients and are improved with laparoscopic Roux-en-Y gastric bypass. *Obes Surg*. 2003;13(4):610-614.
114. Foster A, Laws HL, Gonzalez QH, Clements RH. Gastrointestinal symptomatic outcome after laparoscopic Roux-en-Y gastric bypass. *J Gastrointest Surg*. 2003;7(6):750-753.
115. Weber M, Müller MK, Michel JM, et al. Laparoscopic Roux-en-Y gastric bypass, but not rebanding, should be proposed as rescue procedure for patients with failed laparoscopic gastric banding. *Ann Surg*. 2003;238(6):827-833.
116. Praveenraj P, Gomes RM, Kumar S, et al. Concomitant bariatric surgery with laparoscopic intra-peritoneal onlay mesh repair for recurrent ventral hernias in morbidly obese patients: an evolving standard of care [published online September 3, 2015]. *Obes Surg*. doi:10.1007/s11695-015-1875-4.
117. Long AJ, Burton PR, Laurie CP, et al. Concurrent large para-oesophageal hiatal hernia repair and laparoscopic adjustable gastric banding: results from 5-year follow up [published online October 10, 2015]. *Obes Surg*. doi:10.1007/s11695-015-1881-6.
118. Ardestani A, Tavakkoli A. Hiatal hernia repair and gastroesophageal reflux disease in gastric banding patients: analysis of a national database. *Surg Obes Relat Dis*. 2014;10(3):438-443.
119. Chan DL, Talbot ML, Chen Z, Kwon SC. Simultaneous ventral hernia repair in bariatric surgery. *ANZ J Surg*. 2014;84(7-8):581-583.
120. Bonatti H, Hoeller E, Kirchmayr W, et al. Ventral hernia repair in bariatric surgery. *Obes Surg*. 2004;14(5):655-658.
121. Puzziferri N, Roshek TB III, Mayo HG, Gallagher R, Belle SH, Livingston EH. Long-term follow-up after bariatric surgery: a systematic review. *JAMA*. 2014;312(9):934-942.
122. Dogan K, Gadiot RP, Aarts EO, et al. Effectiveness and safety of sleeve gastrectomy, gastric bypass, and adjustable gastric banding in morbidly obese patients: a multicenter, retrospective, matched cohort study. *Obes Surg*. 2015;25(7):1110-1118.
123. Suter M, Giusti V, Calmes JM, Paroz A. Preoperative upper gastrointestinal testing can help predicting long-term outcome after gastric banding for morbid obesity. *Obes Surg*. 2008;18(5):578-582.
124. Mion F, Roman S, Lindecker V. Esophageal dilation after gastric banding: to test or not to test before surgery? *Surg Endosc*. 2010;24(4):972-973.
125. Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient—2013 update: cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. *Obesity (Silver Spring)*. 2013;21(0 1):S1-27.
126. Blaus B. Blausen Medical Communications. Wikiversity Journal of Medicine. https://en.wikiversity.org/wiki/Wikiversity_Journal_of_Medicine/Blausen_gallery_2014. Published October 8, 2013. Accessed November 9, 2015.