Do we understand the pathophysiology of GERD after sleeve gastrectomy?

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Gastroesophageal reflux disease (GERD), a prevalent problem among obese individuals, is strongly associated with obesity and weight loss. Hence, bariatric surgery effectively improves GERD for many patients. Depending on the type of bariatric procedure, however, surgery can also worsen or even cause a new onset of GERD. As a consequence, GERD remains a relevant problem for many bariatric patients, and especially those who have undergone sleeve gastrectomy (SG). Affected patients report not only a decrease in physical functioning but also suffer from mental and emotional problems, resulting in poorer social functioning. The pathomechanism of GERD after SG is most likely multifactorial and triggered by the interaction of anatomical, physiological, and physical factors. Contributing factors include the shape of the sleeve, the extent of injury to the lower esophageal sphincter, and the presence of hiatal hernia. In order to successfully treat post-sleeve gastrectomy GERD, the cause of the problem must first be identified. Therapeutic approaches include lifestyle changes, medication, interventional treatment, and/or revisional surgery.

Keywords: gastroesophageal reflux; sleeve gastrectomy; bariatric surgery; morbid obesity

Introduction

Gastroesophageal reflux disease (GERD), defined as >2 episodes of GERD symptoms per week that adversely affect an individual’s well-being, affects 15% of the general population worldwide and is present in up to 22% of obese individuals.1,2 GERD can present with symptoms, such as heartburn, regurgitation, or dysphagia, leading to a relevant impairment of quality of life.3 Furthermore, long-term GERD significantly increases the risk of reflux complications, such as Barrett’s esophagus, stenosis, and/or esophageal cancer.4,5 GERD is strongly associated with obesity. Weight loss, especially following bariatric surgery, effectively improves GERD as well as gastrointestinal and general quality of life in many patients.6–8 However, depending on the type of bariatric procedure, GERD can worsen following surgery and, in some cases, even new onset GERD can occur.9 As a consequence, GERD remains a relevant problem for many bariatric patients, and especially for those who have undergone sleeve gastrectomy (SG), although de novo GERD also occurs in about 10% of patients following Roux-Y gastric bypass (RYGB).10 In our narrative review,
possible pathomechanisms of GERD after SG are discussed, and available strategies for preventing and treating GERD after SG are elucidated.

How frequent is GERD after SG?

SG, as well as RYGB, can improve or resolve GERD. However, the respective rates of GERD improvement are 40–60% for SG patients and more than 80% for RYGB patients. According to a meta-analysis of randomized clinical trials comparing the outcomes of SG versus RYGB, the odds ratio (OR) for GERD after SG is four times higher (OR = 4.08, \( P < 0.001 \)). Furthermore, SG is a significant risk factor for the development of de novo reflux, the occurrence of which correlates with the length of follow-up, varying between 8% and 30 percent.\(^\text{17,18}\)

GERD is the major cause of impaired quality of life after bariatric surgery and may be associated with a decrease in physical functioning as well as an increase in mental and emotional problems, resulting in poorer social functioning.\(^\text{19,20}\) Owing to these potentially severe consequences, GERD still remains the most common reason for revisional surgery after SG.\(^\text{10}\)

However, assessing the impact of GERD in general and after SG in particular is challenging owing to the lack of standardized reporting and varying definitions. Some studies had a vigorous assessment with all patients undergoing pre- and postoperative upper endoscopy (UGD), manometry, 24-h pH-metry, and collection of proton pump inhibitor (PPIs) use.\(^\text{10}\) Other studies used questionnaires or did not specify the definition and assessment mode of GERD at all.\(^\text{14}\) These kinds of assessment are problematic since gastrointestinal symptoms do not often correlate with endoscopic and functional findings. By contrast, the majority of patients with endoscopic lesions are asymptomatic, making an objective assessment of real GERD rates before and after surgery difficult to determine.\(^\text{21}\) Thus, reliable rates of GERD after SG in large cohorts are rarely available despite the large body of literature and the undisputed relevance of the problem.

Which changes in the lower esophageal sphincter lead to GERD after SG?

Since the lower esophageal sphincter (LES) likely has a crucial role in the pathomechanism of GERD after SG, a deeper understanding of the related anatomical functions is necessary. Several anatomical structures of the gastroesophageal junction comprise the antireflux barrier. The most important of these are the LES and the sling fibers at the cardia, along with the diaphragmatic crura. Alterations in the anatomy of either of these are thought to be associated with the occurrence of reflux symptoms.\(^\text{22}\)

The overall length of the LES in healthy subjects varies between 2.5 and 4.5 centimeters.\(^\text{23}\) The most common LES injuries consist of three components: a decrease in the overall and/or abdominal LES length (anatomical failure) as well as hypotensive LES disorders (dynamic failure).\(^\text{24}\) Swallowing relaxes the LES, which then allows food to pass in an aboral direction.\(^\text{25}\) Transient LES relaxations (TLESRs) occur independently of swallowing and are strongly associated with a dynamic failure of the LES. These are defined as periods (lasting 10–60 s) of spontaneous (not preceded by swallowing), simultaneous relaxations of the LES and crural diaphragm.\(^\text{26}\) Since LES pressure is still normal in most GERD patients,\(^\text{27}\) the TLESRs likely contribute significantly to GERD, especially in patients with obesity. When compared with normal weight control groups, obese individuals had an increased number of total TLESRs and significantly higher numbers of postprandial TLESRs with acid reflux.\(^\text{28}\)

There are two hypotheses for the occurrence of TLESRs. The first hypothesis indicates a neuromedi ated reflex initiated by postprandial gastric distension as the cause of TLESRs, while the other proposes a shortening of the LES itself.\(^\text{29,30}\) LES injury defines not only the reflux pattern (postprandial, upright, and supine) but also determines the amount of acid exposure.\(^\text{31}\) Patients with a dynamic LES failure (due to TLESRs) present with a mean DeMeester score of around 30 (normal is <14), whereas a permanent LES failure (due to a hiatal hernia (HH)) can increase the mean DeMeester score to as high as 60, depending on the number of defective sphincter components.\(^\text{24}\)

Some authors believe that the increased number of TLESRs after SG is responsible for the severity of GERD symptoms.\(^\text{32}\) However, anatomical LES defects alone do not translate into symptoms in patients with obesity. The length of the LES is altered in 70% of patients after SG, but this does not correlate with the development of postoperative GERD symptoms.\(^\text{33,34}\) The frequency of a structurally defective LES was not significantly different.
in symptomatic versus asymptomatic patients with obesity (12% versus 10%, respectively). Rather, esophageal motility dysfunction in general seems to play a pivotal role in the development of GERD. Patients with esophageal motility disorders revealed by high-resolution esophageal manometry had GERD in 43% compared with 24% without motility disorder. In addition, the simultaneous occurrence of an HH seems to contribute to GERD development. Manometric data have also shown that LES pressure significantly decreases from 13 to 8 mmHg in the presence of an HH. Importantly, this observation has only been made in obese individuals. However, routine repair of HH <4 cm does not influence GERD. In a randomized controlled trial with 100 patients, Snyder et al. showed that routine repair of HH <4 cm does not affect GERD symptoms over a 12-month follow-up. If a large HH (>4 cm) is present, a concomitant repair to restore the acute Angle of His seems to be appropriate. Soricelli et al. reported that about 73% of patients with preoperative GERD experienced symptom remission after SG plus repair of a large HH, and that no patients in their sample developed de novo reflux. Furthermore, the recognition of HH by the surgeon seems also to impact the rate of repair and postoperative GERD. Conversely, surgeon experience seems not to influence the occurrence of GERD.

Another aspect of the antireflux barrier at the gastroesophageal junction seems to be an acute Angle of His. To preserve this natural barrier during surgery, a careful dissection at the Angle of His must be maintained in order to spare the sling fibers and avoid blunting the Angle of His. Petersen et al. showed that the positioning of the stapler line close to the Angle and without injuring the sling fibers or LES results in higher pressure at the Angle of His and, as a consequence, higher LES pressure. Consequently, the reflux barrier is increased and GERD symptoms less frequent. By contrast, a too-narrow sleeve at the Angle of His, with injury to the LES and sling fibers, can cause GERD symptoms.

Sleeve shape and functional changes of the stomach that may contribute to GERD

By creating a gastric sleeve, the diameter of the new gastric lumen is decreased and intraluminal gastric pressure rises. Additionally, after resecting the fundus, the vagovagal reflex is reduced and the physiological postprandial relaxation of the stomach is abolished. This results in even higher intraluminal pressure, pushing the gastric content in a retrograde direction. Furthermore, a sleeve stenosis or an overly narrow SG can easily aggravate postoperative GERD symptoms. GERD is present in over 80% of patients with sleeve stenosis and is often accompanied by further symptoms, such as nausea, vomiting, and food intolerance. Sleeve stenosis is mostly due to postoperative edema, kinking, angulation, and/or cicatrization of the sleeve. Most stenoses are located in the middle portion of the sleeve, although other locations are possible. Additionally, a narrow sleeve or stenosis increases intragastric pressure, which may also contribute to more severe complications, such as fistulas, especially in the upper third of the sleeve. However, sleeve stenoses are an infrequent complication occurring in only 0.5–4% of cases. Thus, sleeve stenosis alone can also not explain the occurrence of GERD after SG. Nonetheless, sleeve stenosis is responsible for about 30% of conversions from SG to RYGB.

These findings taken together strongly suggest that the shape of the sleeve likely plays a major role in the pathophysiology of post-sleeve gastrectomy GERD. A contrast swallow study by Lazoura et al. identified three radiological patterns of gastric sleeves and correlated them with GERD symptoms. These radiological patterns were first described by Werquin et al. and refer to the shape of the gastric sleeve after ingestion of a contrast medium. The tubular pattern was characterized by an almost homogenous tube-like shape, the superior pouch pattern showed a wider proximal portion of the sleeve, and the inferior pouch pattern described a wider antral portion of the sleeve. Although a homogenous tubular shape may seem desirable, the patients in this group had higher levels of postoperative regurgitation and vomiting. Only patients with the inferior pouch pattern had a lower rate of gastrointestinal symptoms. The incidence of heartburn symptoms was the same in all groups. This study’s authors hypothesized that the main factor leading to these findings was an increase in intragastric pressure and the antrum’s decreased capacity to distend and accommodate gastric contents.

Accordingly, Kandeel et al. compared gastric emptying rate and gastric retention of liquids and solids in patients with obesity before and after SG
surgery via a series of scintigraphy studies. For both liquids and solids, emptying rate was significantly increased and gastric retention decreased following SG. Garay et al. found similar results as late as 1 year after surgery. In addition, their study made an interesting distinction between two surgical techniques, the antrum-preserving and resecting SG. In the antrum-preserving group, the first stapler firing took place 5 cm from the pylorus, compared with 2 cm from the pylorus in the antrum-resecting group. Even if there was a tendency for accelerated gastric emptying in both groups, the antrum-preserving SG showed a significant additional increase over time (2 and 12 months after surgery).

What is the “perfect” SG to prevent GERD?

Since the above outlined evidence is based on small, retrospective studies, the relative impact of all these observations is impossible to define. However, the available evidence fits together nicely, and the findings point in the same direction. Hence, some important technical considerations can be discussed to reduce the risk of post-sleeve GERD. Daes et al. reported that if close attention was paid to technical details, GERD could be successfully avoided in 64 out of 66 patients with SG. Numerous studies attempted to disentangle which technical factors contributed to a successful, GERD-free SG. Keidar et al. observed that a narrowing of the mid-portion of the sleeve, at the angular notch, and with upstream dilation was associated with higher rates of GERD following SG. Therefore, the sleeve should be the widest at the antrum and the narrowest at the cardia. Some controversy concerning the ideal bougie size used for sleeve calibration exists. However, a retrospective study on 120 SG patients showed that using a 42-Fr bougie has a positive impact on the prevalence of GERD after surgery when compared with a 32-Fr bougie. For the group with a 42-Fr bougie, around 80% of patients reported postoperative improvement of GERD symptoms, compared with 60% of patients in the 32-Fr group. Further, GERD symptoms decreased postoperatively in 3% and 10% of the patients, respectively. This observation is in keeping with the law of Laplace, which predicts the narrower the sleeve, the higher the intragastric pressure, which could obviously lead to gastroesophageal reflux. A similar phenomenon might be related to the preservation of the antrum. As already mentioned above, Garay et al. were able to show that the preservation of the antrum accelerates gastric emptying, which might also reduce intragastric pressure and, consequently, GERD. While clinical data did not show any differences in this regard, we would suggest placing the first firing of the staple line at least 5 cm from the pylorus to preserve the antrum, in keeping with Garay et al.

Furthermore, special attention should be paid to ensure that the sleeve is wide enough at the angular notch, because most sleeve stenoses are produced when the stapler is positioned too close to it. Moving upward with the stapler, the sleeve should become progressively narrower, with the tightest portion at the level of the LES (trapezoid shape of the sleeve), without narrowing the esophagogastric junction itself. Therefore, it is paramount that the last staple line be placed far enough away from the LES in order to prevent injury to the LES and the sling fibers. A trapezoid sleeve shape also results in less stenosis and decreased intragastric pressure, which also reduces the risk for fistula. A summary of the criteria for optimal SG creation, with a risk for postoperative GERD as low as possible, is shown in Table 1 and Figure 1.

What are the treatment options for GERD following SG?

While up to 30% of patients may experience some GERD symptoms after SG, most do not require operative therapy and can be treated successfully with medication. According to two large randomized controlled trials (RCTs) with 5-year follow-up periods, the conversion rate of SG to RYGB due to severe GERD was 6–8 percent. In order to successfully treat post-sleeve gastrectomy GERD, the cause of the problem must first be identified using a stepwise diagnostic approach (Fig. 2). Therapeutic options, including lifestyle changes, medication, interventional treatment, and/or surgery, can be applied in increasing levels of invasiveness until symptoms and, if present, ulcerations are relieved (Fig. 2).

If a patient presents with any sort of symptom following SG, be it GERD, dysphagia, or unspecific abdominal pain, a UGD should be performed. As a matter of course, we recommend a planned UGD approximately 3 years after SG, to rule out any asymptomatic GERD with esophagitis and/or
Table 1. Criteria for a “perfect” sleeve gastrectomy to prevent GERD

| Criterion                                                                 | Goal                                           |
|--------------------------------------------------------------------------|------------------------------------------------|
| Use a large (e.g., 42 Fr) bougie to reduce the risk of narrowing          | Minimizing intragastric pressure                |
| Shape the sleeve in such a manner that it is the widest at the antrum and | Preventing (functional) stenosis                |
| the narrowest at the cardia (trapezoid shape)                             |                                                |
| Prevent narrowing of the mid-portion of the sleeve, especially at the    | Preventing (functional) stenosis                |
| angular notch, by appropriate angulation of the stapler and preventing   |                                                |
| twisting or kinking of the sleeve                                         |                                                |
| Preserve the antrum (by placing the first staple line >5 cm from the     | Minimizing intragastric pressure                |
| pylorus) to preserve antral motility                                     |                                                |
| Place the last staple line close, but not too close, to the esophagus to  | Preserving an acute Angle of His and            |
| not injure the sling fibers of the LES                                    | maintaining high pressure at the LES            |
| Repair large hiatal hernias (>4 cm)                                      | Restoring the Angle of His                     |

LES, lower esophageal sphincter.

Barrett’s esophagus. Matar et al. showed that nearly 4 out of 10 patients had erosive esophagitis at a median of 4 years after SG and that 10.7% of patients had severe postoperative esophagitis (Los Angeles classification C and D). Additionally, erosive esophagitis was even more prevalent in the presence of HH, affecting around half of patients after SG, and also irrespective of PPI treatment. These findings are partially in line with aforementioned data. Furthermore, while stenosis, ulcers, or pylorospasms can be identified by UGD, twisting, kinking, functional stenosis, and cicatrization may remain undetected. Intrathoracic slippage of the sleeve is easily detected by contrast studies, which can also show esophageal function and reveal esophageal motility disorders as a possible cause of reflux symptoms. A dynamic contrast study is, therefore, necessary. Since UGD and contrast studies are easy to do and pose a low risk, we recommend conducting both examinations liberally in patients with problems following SG.

In patients with GERD symptoms without dysphagia and no signs of stenosis, the first-line therapy consists of PPIs. Over 50% of patients who undergo SG need PPIs during the first year after surgery. Even 4 years after SG, the number of patients needing PPIs can be as high as 26%, as shown in a large (n > 11,000) retrospective nationwide study in France. Interestingly, this study also showed that higher body mass index and preoperative antidepressant treatment were, in addition to SG, major risk factors for persistent PPI treatment. We suggest an initial dose of 40–80 mg of PPI twice daily for 2 weeks, followed by a dose reduction. If symptoms resolve, this therapy can be continued. However, if esophagitis is present, a follow-up UGD with biopsies should be performed 4–8 weeks later to confirm that the esophagitis has fully resolved and that no Barrett’s mucosa with dysplasia is present.
In patients with good results, the dosing of the PPI should be reduced as much as possible, to limit the potential side effects of PPIs, such as dementia, gynecomastia, severe iron and vitamin deficiencies, osteoporosis, and/or enteric infections. However, patients should also be made aware that none of these supposed side effects of PPIs have been proven.

If GERD symptoms persist despite high doses of PPIs, further examinations, including 24-h pHmetry and manometry, should be performed. For patients with proven acid reflux and unresponsiveness to PPI therapy, conversion to RYGB can also be considered. Conversion to RYGB effectively reduces GERD and has been shown to improve symptoms in up to 100% of patients. Other reports show that 75% of patients experienced complete resolution of GERD and its associated symptoms 1 year after surgery. The complication rate after conversion to RYGB is only slightly higher than that of primary surgery. Hence, the indication for conversion surgery can be treated somewhat generously. More experimental techniques, such as electric stimulation or magnetic augmentation of the LES, have also been described, but on a case-report level.

If the cause of GERD is more of a technical nature, for example, sleeve stenosis, twisting, kinking, or cicatrization, an endoscopic or surgical intervention should be considered. Sleeve stenosis is first treated endoscopically by balloon dilation or endoluminal stents. According to a meta-analysis by Chang
et al., the overall success rate for balloon dilation in sleeve stenosis was 76%, and the number of dilations needed per patient was approximately 1.8. If this approach fails, a stent treatment or conversion to RYGB should be considered. Importantly, for patients who also complain of insufficient weight loss after SG, it should be noted that conversion to RYGB does not usually lead to a relevant additional weight loss. These patients with both insufficient weight loss and severe GERD constitute a difficult problem and a careful assessment of the causes of the GERD should be performed.

Conclusions

GERD is a common problem in patients with obesity and has multifactorial causes. While bariatric surgery reliably improves GERD, de novo GERD or worsening may also occur, especially after SG. Unfortunately, the occurrence of GERD after SG cannot be predicted preoperatively. Building an SG that is technically as perfect as possible is pivotal for preventing de novo GERD and improving existing GERD symptoms. In patients with postoperative GERD, a careful examination is necessary to identify its cause. UGD and contrast studies should be applied liberally and may even be routinely performed 3 years postoperatively to detect asymptomatic GERD. Nevertheless, most evidence originates from retrospective studies with a small number of cases or is based on experts’ opinions. The presented data are limited, very heterogeneous, and reveal the great need for RCTs.

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Competing interests

The authors declare no competing interests.

References

1. Eusebi, L.H., R. Ratnakumaran, Y. Yuan, et al. 2018. Global prevalence of, and risk factors for, gastro-oesophageal reflux symptoms: a meta-analysis. Gut 67: 430–440.
2. Vakil, N., S.V. van Zanten, P. Kahrilas, et al. 2006. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am. J. Gastroenterol. 101: 1900–1920; quiz 1943. 
3. Lenderking, W.R., E. Hillson, J.A. Crawley, et al. 2003. The clinical characteristics and impact of laryngopharyngeal reflux disease on health-related quality of life. Value Health 6: 560–565.
4. Qumseya, B.J., A. Bukanann, S. Gendy, et al. 2019. Systematic review and meta-analysis of prevalence and risk factors for Barrett’s esophagus. Gastrointest. Endosc. 90: 707–717.e701.
5. Findlay, J.M., M.R. Middleton & I. Tomlinson. 2016. Genetic biomarkers of Barrett’s esophagus susceptibility and progression to dysplasia and cancer: a systematic review and meta-analysis. Dig. Dis. Sci. 61: 25–38.
6. Kindel, T.L. & D. Oleynikov. 2016. The improvement of gastroesophageal reflux disease and Barrett’s after bariatric surgery. Obes. Surg. 26: 718–720.
7. Nickel, F., L. Schmidt, T. Bruckner, et al. 2017. Influence of bariatric surgery on quality of life, body image, and general self-efficacy within 6 and 24 months—a prospective cohort study. Surg. Obes. Relat. Dis. 13: 313–319.
8. Nickel, F., L. Schmidt, T. Bruckner, et al. 2017. Gastrointestinal quality of life improves significantly after sleeve gastrectomy and Roux-en-Y gastric bypass—a prospective cross-sectional study within a 2-year follow-up. Obes. Surg. 27: 1292–1297.
9. Gu, L., B. Chen, N. Du, et al. 2019. Relationship between bariatric surgery and gastroesophageal reflux disease: a systematic review and meta-analysis. Obes. Surg. 29: 4105–4113.
10. Peterli, R., B.K. Wolnerhanssen, T. Peters, et al. 2018. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss in patients with morbid obesity; the SM-BOSS randomized clinical trial. JAMA 319: 255–265. 
11. Peterli, R., B.K. Wolnerhanssen, D. Vetter, et al. 2017. Laparoscopic sleeve gastrectomy versus Roux-Y-gastric bypass for morbid obesity—3-year outcomes of the prospective randomized Swiss Multicenter Bypass Or Sleeve Study (SM-BOSS). Ann. Surg. 265: 466–473.
12. Ignat, M., M. Vix, I. Imad, et al. 2017. Randomized trial of Roux-en-Y gastric bypass versus sleeve gastrectomy in achieving excess weight loss. Br. J. Surg. 104: 248–256.
13. Kehagias, I., S.N. Karamanakos, M. Argentou, et al. 2011. 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. 21: 1650–1656.
14. Salminen, P., M. Helmio, J. Ovaska, et al. 2018. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss at 5 years among patients with morbid obesity: the SLEEVEPASS randomized clinical trial. JAMA 319: 241–254.
15. Schauer, P.R., D.I. Bhatt, J.P. Kirwan, et al. 2017. Bariatric surgery versus intensive medical therapy for diabetes — 5-year outcomes. N. Engl. J. Med. 376: 641–651.
16. Schauer, P.R., D.I. Bhatt, J.P. Kirwan, et al. 2014. Bariatric surgery versus intensive medical therapy for diabetes—3-year outcomes. N. Engl. J. Med. 370: 2002–2013.
17. Boza, C., D. Daroch, D. Barros, et al. 2014. Long-term outcomes of laparoscopic sleeve gastrectomy as a primary bariatric procedure. Surg. Obes. Relat. Dis. 10: 1129–1133.
34. Kuper, M.A., K.M. Kramer, A. Kirschniak, et al. 2009. Dysfunction of the lower esophageal sphincter and dysmotility of the tubular esophagus in morbidly obese patients. Obes. Surg. 19: 1143–1149.

35. Kristo, L. M. Paireder, G. Jomrich, et al. 2019. Modern esophageal function testing and gastroesophageal reflux disease in morbidly obese patients. Obes. Surg. 29: 3536–3541.

36. Snyder, B., E. Wilson, T. Wilson, et al. 2016. A randomized trial comparing reflux symptoms in sleeve gastrectomy patients with or without hiatal hernia repair. Surg. Obes. Relat. Dis. 12: 1681–1688.

37. Soricelli, E., A. Iossa, G. Casella, et al. 2013. Sleeve gastrectomy and crural repair in obese patients with gastroesophageal reflux disease and/or hiatal hernia. Surg. Obes. Relat. Dis. 9: 356–361.

38. Ehlers, A.P., K. Chhabra, J.R. Thumma, et al. 2020. In the eye of the beholder: surgeon variation in intra-operative perceptions of hiatal hernia and reflux outcomes after sleeve gastrectomy. Surg. Endosc. https://doi.org/10.1007/s00464-020-07668-4.

39. Varban, O.A., J.R. Thumma, D.A. Telem, et al. 2020. Surgeon variation in severity of reflux symptoms after sleeve gastrectomy. Surg. Endosc. 34: 1769–1775.

40. Petersen, W.V., T. Meile, M.A. Kuper, et al. 2012. Functional importance of laparoscopic sleeve gastrectomy for the lower esophageal sphincter in patients with morbid obesity. Obes. Surg. 22: 360–366.

41. Mion, F., S. Tolone, A. Garros, et al. 2016. High-resolution impedance manometry after sleeve gastrectomy: increased intragastric pressure and reflux are frequent events. Obes. Surg. 26: 2449–2456.

42. Del Genio, G., S. Tolone, P. Limongelli, et al. 2014. Sleeve gastrectomy and development of “de novo” gastroesophageal reflux. Obes. Surg. 24: 71–77.

43. Yehoshua, R.T., L.A. Eldelman, M. Stein, et al. 2008. Laparoscopic sleeve gastrectomy—volume and pressure assessment. Obes. Surg. 18: 1083–1088.

44. Csendes, A. & I. Braghetto. 2016. Changes in the anatomy and physiology of the distal esophagus and stomach after sleeve gastrectomy. J. Obes. Weight Loss Ther. 6, https://doi.org/10.4172/2165-7904.1000297.

45. Dhorepatil, A.S., D. Cottam, A. Surve, et al. 2018. Is pneumatic balloon dilation safe and effective primary modality of treatment for post-sleeve gastrectomy strictures? A retrospective study. BMC Surg. 18: 52.

46. Levy, J.L., M.S. Levine, S.E. Rubesin, et al. 2018. Stenosis of gastric sleeve after laparoscopic sleeve gastrectomy: clinical, radiographic and endoscopic findings. Br. J. Radiol. 91: 20170702.

47. Burgos, A.M., A. Csendes & I. Braghetto. 2013. Gastric stenosis after laparoscopic sleeve gastrectomy in morbidly obese patients. Obes. Surg. 23: 1481–1486.

48. Dapri, G., G.B. Cadiere & J. Hlimpens. 2009. Laparoscopic seromyotomy for long stenosis after sleeve gastrectomy with or without duodenal switch. Obes. Surg. 19: 495–499.

18. DuPree, C.E., K. Blair, S.R. Steele, et al. 2014. Laparoscopic sleeve gastrectomy in patients with preexisting gastroesophageal reflux disease: a national analysis. JAMA Surg. 149: 328–334.

19. Felsenreich, D.M., G. Prager, R. Kefurt, et al. 2019. Quality of life 10 years after sleeve gastrectomy: a multicenter study. Obes. Facts 12: 157–166.

20. Biter, L.U., M.M.A. van Buuren, G.H.H. Mannets, et al. 2017. Quality of life 1 year after laparoscopic sleeve gastrectomy versus laparoscopic Roux-en-Y gastric bypass: a randomized controlled trial focusing on gastroesophageal reflux disease. Obes. Surg. 27: 2557–2565.

21. Carabotti, M., M. Avallone, F. Cereatti, et al. 2016. Usefulness of upper gastrointestinal symptoms as a driver to prescribe gastroscopy in obese patients candidate to bariatric surgery. A prospective study. Obes. Surg. 26: 1075–1080.

22. Lipan, M.J., I.S. Reidenberg & J.T. Laitman. 2006. Anatomy of reflux: a growing health problem affecting structures of the head and neck. Anat. Rec. B New Anat. 289: 261–270.

23. Zaninotto, G., T.R. DeMeester, W. Schwizer, et al. 1988. The lower esophageal sphincter in health and disease. Am. J. Surg. 155: 104–111.

24. Worrell, S.G. & T.R. DeMeester. 2016. Role of LES augmentation for early progressive disease in GERD and fundoplication for end-stage disease in GERD. In Diagnosis and Treatment of Gastroesophageal Reflux Disease. M.F. Vaezi, Ed.: 145–160. Cham: Springer International Publishing.

25. Hershcovici, T., H. Mashimo & R. Fass. 2011. The lower esophageal sphincter. Neurogastroenterol. Motil. 23: 819–830.

26. Roman, S., R. Holloway, J. Keller, et al. 2017. Validation of criteria for the definition of transient lower esophageal sphincter relaxations using high-resolution manometry. Neurogastroenterol. Motil. 29:e12920.

27. Meining, A., A. Fackler, K. Tzavella, et al. 2004. Lower esophageal sphincter pressure in patients with gastroesophageal reflux diseases and posture and time patterns. Dis. Esophagus 17: 155–158.

28. Wu, J.C., L.M. Mui, C.M. Cheung, et al. 2007. Obesity is associated with increased transient lower esophageal sphincter relaxation. Gastroenterology 132: 883–889.

29. Pauwels, A., E. Altan & J. Tack. 2014. The gastric accommodation response to meal intake determines the occurrence of transient lower esophageal sphincter relaxations and reflux events in patients with gastro-esophageal reflux disease. Neurogastroenterol. Motil. 26: 581–588.

30. Kuo, P., I. Bravi, U. Marreddy, et al. 2013. Postprandial cardiac vagal tone and transient lower esophageal sphincter relaxation (TLESR). Neurogastroenterol. Motil. 25: 841–869.

31. Campos, G.M., J.H. Peters, T.R. DeMeester, et al. 1999. The pattern of esophageal acid exposure in gastroesophageal reflux disease influences the severity of the disease. Arch. Surg. 134: 882–887.

32. Bou Daher, H. & A.I. Sharara. 2019. Gastroesophageal reflux disease, obesity and laparoscopic sleeve gastrectomy: the burning questions. World J. Gastroenterol. 25: 4805–4813.

33. Braghetto, I., E. Lanzarini, O. Korn, et al. 2010. Manometric changes of the lower esophageal sphincter after sleeve gastrectomy in obese patients. Obes. Surg. 20: 357–362.
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49. Parikh, A., J.B. Alley, R.M. Peterson, et al. 2012. Management options for symptomatic stenosis after laparoscopic vertical sleeve gastrectomy in the morbidly obese. Surg. Endosc. 26: 738–746.

50. Rebibo, L., S. Hakim, A. Dhahri, et al. 2016. Gastric stenosis after laparoscopic sleeve gastrectomy: diagnosis and management. Obes. Surg. 26: 995–1001.

51. Cottam, D., F.G. Qureshi, S.G. Mattar, et al. 2006. Laparoscopic sleeve gastrectomy as an initial weight-loss procedure for high-risk patients with morbid obesity. Surg. Endosc. 20: 859–863.

52. Zundel, N., J.D. Hernandez, M. Galvao Neto, et al. 2010. Strictures after laparoscopic sleeve gastrectomy. Surg. Laparosc. Endosc. Percutan. Tech. 20: 154–158.

53. Brethauer, S.A., V. Niësma, V. Sherman, et al. 2006. Endoscopy and upper gastrointestinal contrast studies are complementary in evaluation of weight regain after bariatric surgery. Surg. Obes. Relat. Dis. 2: 643–648; discussion 649–650.

54. Landreneau, J.P., A.T. Strong, J.H. Rodriguez, et al. 2018. Conversion of sleeve gastrectomy to Roux-en-Y gastric bypass. Obes. Surg. 28: 3843–3850.

55. Lazoura, O., D. Zacharoulis, G. Triantafyllidis, et al. 2011. Symptoms of gastroesophageal reflux following laparoscopic sleeve gastrectomy are related to the final shape of the sleeve as depicted by radiology. Obes. Surg. 21: 295–299.

56. Werquin, C., J. Caudron, J. Mezghani, et al. 2008. [Early imaging features after sleeve gastrectomy]. J. Radiol. 89: 1721–1728.

57. Kandeel, A.A., M.D. Sarhan, T. Hegazy, et al. 2015. Comparative assessment of gastric emptying in obese patients before and after laparoscopic sleeve gastrectomy using radionuclide scintigraphy. Nucl. Med. Commun. 36: 854–862.

58. Garay, M., C. Balague, C. Rodriguez-Otero, et al. 2018. Influence of antrum size on gastric emptying and weight-loss outcomes after laparoscopic sleeve gastrectomy (preliminary analysis of a randomized trial). Surg. Endosc. 32: 2739–2745.

59. Daes, J., M.E. Jimenez, N. Said, et al. 2012. Laparoscopic sleeve gastrectomy: symptoms of gastroesophageal reflux can be reduced by changes in surgical technique. Obes. Surg. 22: 1874–1879.

60. Keidar, A., L. Appelbaum, C. Schweiger, et al. 2010. Dilated upper sleeve can be associated with severe postoperative gastroesophageal dysmotility and reflux. Obes. Surg. 20: 140–147.

61. Spivak, H., M. Rubin, E. Sadot, et al. 2014. Laparoscopic sleeve gastrectomy using 42-French versus 32-French bougie: the first-year outcome. Obes. Surg. 24: 1090–1093.

62. McGlone, E.R., A.K. Gupta, M. Reddy, et al. 2018. Antral resection versus antral preservation during laparoscopic sleeve gastrectomy for severe obesity: systematic review and meta-analysis. Surg. Obes. Relat. Dis. 14: 857–864.

63. Matar, R., D. Maselli, E. Vargas, et al. 2020. Esophagitis after bariatric surgery: large cross-sectional assessment of an endoscopic database. Obes. Surg. 30: 161–168.

64. Felsenreich, D.M., R. Kefurt, M. Schermann, et al. 2017. Reflux, sleeve dilation, and Barrett’s esophagus after laparoscopic sleeve gastrectomy: long-term follow-up. Obes. Surg. 27: 3092–3101.

65. Korenkov, M., L. Kohler, N. Yucel, et al. 2002. Esophageal motility and reflux symptoms before and after bariatric surgery. Obes. Surg. 12: 72–76.

66. Thereaux, J., T. Lesuffleur, S. Czernichow, et al. 2017. Do sleeve gastrectomy and gastric bypass influence treatment with proton pump inhibitors 4 years after surgery? A nationwide cohort. Surg. Obes. Relat. Dis. 13: 951–959.

67. Bavishi, C. & H.L. Dupont. 2011. Systematic review: the use of proton pump inhibitors and increased susceptibility to enteric infection. Aliment. Pharmacol. Ther. 34: 1269–1281.

68. Leonard, J., J.K. Marshall & P. Moayyedi. 2007. Systematic review of the risk of enteric infection in patients taking acid suppression. Am. J. Gastroenterol. 102: 2047–2056; quiz 2057.

69. He, B., B. Carleton & M. Etmann. 2019. Risk of gynecomastia with users of proton pump inhibitors. Pharmacotherapy 39: 614–618.

70. Tai, S.Y., C.Y. Chien, D.C. Wu, et al. 2017. Risk of dementia from proton pump inhibitor use in Asian population: a nationwide cohort study in Taiwan. PLoS One 12: e0171006.

71. Malfertheiner, P., A. Kandulski & M. Venerito. 2017. Proton-pump inhibitors: understanding the complications and risks. Nat. Rev. Gastroenterol. Hepatol. 14: 697–710.

72. Parmar, C.D., K.K. Mahawar, M. Boyle, et al. 2017. Conversion of sleeve gastrectomy to Roux-en-Y gastric bypass is effective for gastro-oesophageal reflux disease but not for further weight loss. Obes. Surg. 27: 1651–1658.

73. Dijkhorst, P.J., A.B. Boerboom, I.M.C. Janssen, et al. 2018. Failed sleeve gastrectomy: single anastomosis duodenoejejunostomy bypass or Roux-en-Y gastric bypass? A multicenter cohort study. Obes. Surg. 28: 3834–3842.

74. Aguilar-Espinosa, F., J. Montoya-Ramirez, J. Gutierrez-Salinas, et al. 2020. Conversion to Roux-en-Y gastric bypass surgery through a robotic-assisted hybrid technique after failed sleeve gastrectomy: short-term results. Rev. Gastroenterol. Mex. 85: 160–172.

75. Casillas, R.A., S.S. Um, J.L. Zelada Getty, et al. 2016. Revision of primary sleeve gastrectomy to Roux-en-Y gastric bypass: indications and outcomes from a high-volume center. Surg. Obes. Relat. Dis. 12: 1817–1825.

76. Yorke, E., C. Sheppard, N.J. Switzer, et al. 2017. Revision of sleeve gastrectomy to Roux-en-Y gastric bypass: a Canadian experience. Am. J. Surg. 213: 970–974.

77. Boru, C.E., F. Greco, P. Giustacchini, et al. 2018. Short-term outcomes of sleeve gastrectomy conversion to R-Y gastric bypass: multi-center retrospective study. Langenbecks Arch. Surg. 403: 473–479.

78. Musella, M., V. Bruni, F. Greco, et al. 2019. Conversion from laparoscopic adjustable gastric banding (LAGB) and laparoscopic sleeve gastrectomy (LSG) to one anastomosis gastric bypass (OAGB): preliminary data from a multicenter retrospective study. Surg. Obes. Relat. Dis. 15: 1332–1339.

79. Hawasli, A., M. Tarakji & M. Tarboush. 2017. Laparoscopic management of severe reflux after sleeve gastrectomy using the LINX®(R) system: technique and one year follow up case report. Int. J. Surg. Case Rep. 30: 148–151.
80. Borbely, Y., N. Bouvy, H.G. Schulz, et al. 2018. Electrical stimulation of the lower esophageal sphincter to address gastroesophageal reflux disease after sleeve gastrectomy. Surg. Obes. Relat. Dis. 14: 611–615.

81. Chang, S.H., V.B. Popov & C.C. Thompson. 2020. Endoscopic balloon dilation for treatment of sleeve gastrectomy stenosis: a systematic review and meta-analysis. Gastrointest. Endosc. 91: 989–1002.e1004.