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TOPIC HIGHLIGHT

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Gastroesophageal reflux disease and severe obesity: Fundoplication or bariatric surgery?

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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 (in descending frequency) 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.

PARALLEL TRENDS IN GASTROESOPHAGEAL REFLUX DISEASE AND SEVERE OBESITY: CAUSALITY OR COINCIDENCE

Obesity has dramatically increased over the past few decades, with the prevalence of obesity among adults in the United States, defined as body mass index (BMI) $\geqslant$ 30 kg/m^2, increased from 13% in 1960-1962[1] to 32% in 2003-2004, with 3% of men and 7% of women classified as being severely obese (BMI $\geqslant$ 40 kg/m^2) in a recent estimate[2]. BMI itself is a strong predictor of overall mortality, with a progressive excess in mortality noted above the optimum BMI of 22.5-25 kg/m^2, due mainly to metabolic and vascular disease[3]. Indeed, the prevalence of the metabolic comorbidities that contribute to atherosclerosis appears to increase significantly with increasing BMI[4,5].

In parallel with this trend in obesity is the perception that the prevalence of gastroesophageal reflux disease (GERD) has increased as well, currently affecting between 8% and 26% of the population in the western world[6-8]. These data, however, are somewhat difficult to interpret,

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[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[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[14]. However, the prevalence of GERD, even in the setting of severe obesity, is < 50%[15], 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, intra-abdominal 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 intraesophageal 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[16]. 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[17]. 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/m^2; 10% of whom were noted to have a hypertensive LES[18]. 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[19]. 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[20]. 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[21]. Similar findings have been noted in the setting of severe obesity[22].

Several factors might contribute to the increased gastroesophageal gradient seen with obesity[23], including increased intra-abdominal pressure[24], increased intragastric pressure[25], increased negative inspiratory intrathoracic pressure[26], and a mechanical separation between the LES and the extrinsic compression provided by the diaphragmatic crura[23]. 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[27,28]. 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*[17].

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[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, 53.8% BM-Ⅳ), compared to 4.5% in normal-weight individuals[31]. 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[32]. This study was limited by the small number of severely obese patients (only seven out of 166) 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[33]; 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[34-37]. 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[38,39]. 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[40]. 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[41]. Instead, discussion today is centered around the differential effects of currently performed bariatric operations [Roux-en-Y gastric bypass (RYGB), adjustable gastric banding (LAGB), biliopancreatic 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[42-45]. Its recognized effectiveness has even led to its use in non-severely obese patients with GERD[46], particularly in the setting of failed fundoplication[33]. 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[47], reduction of esophageal biliopancreatic refluxate by use of a roux limb measuring at least 100 cm in length[48,49], 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 $\geqslant$ 50 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[15].

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[16], while others show improvement on GERD questionnaires and/or through the discontinuation of GERD medications[50,51]. In contrast, several studies have demonstrated measured exacerbation of esophageal acid exposure, GERD symptoms, and the development or worsening of esophageal dysmotility following LAGB[52-54]. The mechanism by which LAGB may improve GERD is not well characterized, but is thought to include weight loss, increase in LESP, 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[55], 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[56]. 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[57], 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[15]. 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 life-long 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 treatment of GERD.

REFERENCES

1 **Flegal KM**, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA* 2002; **288**: 1723-1727
2 **Ogden CL**, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006; **295**: 1549-1555
3 **Whitlock G**, Lewington S, Sherliker P, Clarke R, Emberson J, Halsey J, Qizilbash N, Collins R, Peto R. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009; **373**: 1083-1096
4 **Bays HE**, Chapman RH, Grandy S. The relationship of body mass index to diabetes mellitus, hypertension and dyslipidaemia: comparison of data from two national surveys. *Int J Clin Pract* 2007; **61**: 737-747
5 **Nguyen NT**, Magno CP, Lane KT, Hinojosa MW, Lane JS. Association of hypertension, diabetes, dyslipidemia, and metabolic syndrome with obesity: findings from the National Health and Nutrition Examination Survey, 1999 to 2004. *J Am Coll Surg* 2008; **207**: 928-934
6 **Nandurkar S**, Locke GR 3rd, Fett S, Zinsmeister AR, Cameron AJ, Talley NJ. Relationship between body mass index, diet, exercise and gastro-oesophageal reflux symptoms in a community. *Aliment Pharmacol Ther* 2004; **20**: 497-505
7 **Shaheen N**, Provenzale D. The epidemiology of gastroesophageal reflux disease. *Am J Med Sci* 2003; **326**: 264-273
8 **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**: 1243-1250
9 **Cook MB**, Greenwood DC, Hardie LJ, Wild CP, Forman D. A systematic review and meta-analysis of the risk of increasing adiposity on Barrett's esophagus. *Am J Gastroenterol* 2008; **103**: 292-300
10 **Thukkani N**, Sonnenberg A. The influence of environmental risk factors in hospitalization for gastro-oesophageal reflux disease-related diagnoses in the United States. *Aliment Pharmacol Ther* 2010; **31**: 852-861
11 **Devesa SS**, Blot WJ, Fraumeni JF Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer* 1998; **83**: 2049-2053
12 **El-Serag HB**, Ergun GA, Pandolfino J, Fitzgerald S, Tran T, Kramer JR. Obesity increases oesophageal acid exposure. *Gut* 2007; **56**: 749-755
13 **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**: 199-211
14 **Corley DA**, Kubo A, Zhao W. Abdominal obesity, ethnicity and gastro-oesophageal reflux symptoms. *Gut* 2007; **56**: 756-762
15 **Prachand VN**, Ward M, Alverdy JC. Duodenal switch provides superior resolution of metabolic comorbidities independent of weight loss in the super-obese (BMI > or = 50 kg/m2) compared with gastric bypass. *J Gastrointest Surg* 2010; **14**: 211-220
16 **Iovino P**, Angrisani L, Tremolaterra F, Nirchio E, Ciannella M, Borrelli V, Sabbatini F, Mazzacca G, Ciacci C. Abnormal esophageal acid exposure is common in morbidly obese patients and improves after a successful Lap-band system implantation. *Surg Endosc* 2002; **16**: 1631-1635
17 **Ayazi S**, Hagen JA, Chan LS, DeMeester SR, Lin MW, Ayazi A, Leers JM, Oezcelik A, Banki F, Lipham JC, DeMeester TR, Crookes PF. Obesity and gastroesophageal reflux: quantifying the association between body mass index, esophageal acid exposure, and lower esophageal sphincter status in a large series of patients with reflux symptoms. *J Gastrointest Surg* 2009; **13**: 1440-1447
18 **Herbella FA**, Sweet MP, Tedesco P, Nipomnick I, Patti MG. Gastroesophageal reflux disease and obesity. Pathophysiology and implications for treatment. *J Gastrointest Surg* 2007; **11**: 286-290
19 **Bahmeriz F**, Dutta S, Allen CJ, Pottruff CG, Anvari M. Does laparoscopic antireflux surgery prevent the occurrence of transient lower esophageal sphincter relaxation? *Surg Endosc* 2003; **17**: 1050-1054
20 **Pandolfino JE**, Zhang QG, Ghosh SK, Han A, Boniquit C, Kahrilas PJ. Transient lower esophageal sphincter relaxations and reflux: mechanistic analysis using concurrent fluoroscopy and high-resolution manometry. *Gastroenterology* 2006; **131**: 1725-1733
21 **Wu JC**, Mui LM, Cheung CM, Chan Y, Sung JJ. Obesity is associated with increased transient lower esophageal sphincter relaxation. *Gastroenterology* 2007; **132**: 883-889
22 **Schneider JH**, Küper M, Königsrainer A, Brücher B. Transient lower esophageal sphincter relaxation in morbid obesity. *Obes Surg* 2009; **19**: 595-600
23 **Pandolfino JE**, El-Serag HB, Zhang Q, Shah N, Ghosh SK, Kahrilas PJ. Obesity: a challenge to esophagogastric junction integrity. *Gastroenterology* 2006; **130**: 639-649
24 **Sugerman HJ**, DeMaria EJ, Felton WL 3rd, Nakatsuka M, Sismanis A. Increased intra-abdominal pressure and cardiac filling pressures in obesity-associated pseudotumor cerebri.

Neurology 1997; **49**: 507-511
25 **de Vries DR**, van Herwaarden MA, Smout AJ, Samsom M. Gastroesophageal pressure gradients in gastroesophageal reflux disease: relations with hiatal hernia, body mass index, and esophageal acid exposure. *Am J Gastroenterol* 2008; **103**: 1349-1354
26 **Salome CM**, King GG, Berend N. Physiology of obesity and effects on lung function. *J Appl Physiol* 2010; **108**: 206-211
27 **Stene-Larsen G**, Weberg R, Frøyshov Larsen I, Bjørtuft O, Hoel B, Berstad A. Relationship of overweight to hiatus hernia and reflux oesophagitis. *Scand J Gastroenterol* 1988; **23**: 427-432
28 **Wilson LJ**, Ma W, Hirschowitz BI. Association of obesity with hiatal hernia and esophagitis. *Am J Gastroenterol* 1999; **94**: 2840-2844
29 **Hesselink VJ**, Luijendijk RW, de Wilt JH, Heide R, Jeekel J. An evaluation of risk factors in incisional hernia recurrence. *Surg Gynecol Obstet* 1993; **176**: 228-234
30 **Sauerland S**, Korenkov M, Kleinen T, Arndt M, Paul A. Obesity is a risk factor for recurrence after incisional hernia repair. *Hernia* 2004; **8**: 42-46
31 **Perez AR**, Moncure AC, Rattner DW. Obesity adversely affects the outcome of antireflux operations. *Surg Endosc* 2001; **15**: 986-989
32 **Morgenthal CB**, Lin E, Shane MD, Hunter JG, Smith CD. Who will fail laparoscopic Nissen fundoplication? Preoperative prediction of long-term outcomes. *Surg Endosc* 2007; **21**: 1978-1984
33 **Kellogg TA**, Andrade R, Maddaus M, Slusarek B, Buchwald H, Ikramuddin S. Anatomic findings and outcomes after antireflux procedures in morbidly obese patients undergoing laparoscopic conversion to Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2007; **3**: 52-57; discussion 58-59
34 **Anvari M**, Bamehriz F. Outcome of laparoscopic Nissen fundoplication in patients with body mass index >or=35. *Surg Endosc* 2006; **20**: 230-234
35 **Winslow ER**, Frisella MM, Soper NJ, Klingensmith ME. Obesity does not adversely affect the outcome of laparoscopic antireflux surgery (LARS). *Surg Endosc* 2003; **17**: 2003-2011
36 **Chisholm JA**, Jamieson GG, Lally CJ, Devitt PG, Game PA, Watson DI. The effect of obesity on the outcome of laparoscopic antireflux surgery. *J Gastrointest Surg* 2009; **13**: 1064-1070
37 **D'Alessio MJ**, Arnaoutakis D, Giarelli N, Villadolid DV, Rosemurgy AS. Obesity is not a contraindication to laparoscopic Nissen fundoplication. *J Gastrointest Surg* 2005; **9**: 949-954
38 **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**: 515-529
39 **Buchwald H**, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, Schoelles K. Bariatric surgery: a systematic review and meta-analysis. *JAMA* 2004; **292**: 1724-1737
40 **Patterson EJ**, Davis DG, Khajanchee Y, Swanström LL. Comparison of objective outcomes following laparoscopic Nissen fundoplication versus laparoscopic gastric bypass in the morbidly obese with heartburn. *Surg Endosc* 2003; **17**: 1561-1565
41 **Varela JE**, Hinojosa MW, Nguyen NT. Laparoscopic fundoplication compared with laparoscopic gastric bypass in morbidly obese patients with gastroesophageal reflux disease. *Surg Obes Relat Dis* 2009; **5**: 139-143
42 **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**: 244-248
43 **Smith SC**, Edwards CB, Goodman GN. Symptomatic and clinical improvement in morbidly obese patients with gastroesophageal reflux disease following Roux-en-Y gastric bypass. *Obes Surg* 1997; **7**: 479-484
44 **Frezza EE**, Ikramuddin S, Gourash W, Rakitt T, Kingston A, Luketich J, Schauer P. Symptomatic improvement in gastroesophageal reflux disease (GERD) following laparoscopic Roux-en-Y gastric bypass. *Surg Endosc* 2002; **16**: 1027-1031
45 **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**: 950-953; discussion 953-954
46 **Jones KB Jr**. Roux-en-Y gastric bypass: an effective antireflux procedure in the less than morbidly obese. *Obes Surg* 1998; **8**: 35-38
47 **Smith CD**, Herkes SB, Behrns KE, Fairbanks VF, Kelly KA, Sarr MG. Gastric acid secretion and vitamin B12 absorption after vertical Roux-en-Y gastric bypass for morbid obesity. *Ann Surg* 1993; **218**: 91-96
48 **Ritchie WP Jr**. Alkaline reflux gastritis. Late results on a controlled trial of diagnosis and treatment. *Ann Surg* 1986; **203**: 537-544
49 **Collard JM**, Romagnoli R. Roux-en-Y jejunal loop and bile reflux. *Am J Surg* 2000; **179**: 298-303
50 **Dixon JB**, O'Brien PE. Gastroesophageal reflux in obesity: the effect of lap-band placement. *Obes Surg* 1999; **9**: 527-531
51 **Angrisani L**, Iovino P, Lorenzo M, Santoro T, Sabbatini F, Claar E, Nicodemi O, Persico G, Tesauro B. Treatment of morbid obesity and gastroesophageal reflux with hiatal hernia by Lap-Band. *Obes Surg* 1999; **9**: 396-398
52 **Suter M**, Dorta G, Giusti V, Calmes JM. Gastric banding interferes with esophageal motility and gastroesophageal reflux. *Arch Surg* 2005; **140**: 639-643
53 **Klaus A**, Gruber I, Wetscher G, Nehoda H, Aigner F, Peer R, Margreiter R, Weiss H. Prevalent esophageal body motility disorders underlie aggravation of GERD symptoms in morbidly obese patients following adjustable gastric banding. *Arch Surg* 2006; **141**: 247-251
54 **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**: 941-948
55 **Greenstein RJ**, Nissan A, Jaffin B. Esophageal anatomy and function in laparoscopic gastric restrictive bariatric surgery: implications for patient selection. *Obes Surg* 1998; **8**: 199-206
56 **Gulkarov I**, Wetterau M, Ren CJ, Fielding GA. Hiatal hernia repair at the initial laparoscopic adjustable gastric band operation reduces the need for reoperation. *Surg Endosc* 2008; **22**: 1035-1041
57 **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**: 1450-1456

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