Review Article

BJMP 2011;4(2):a417

Oesophageal dysfunction and disease in obesity

Zakir K Mohamed and Stephen E Attwood

Abstract

Patients with morbid obesity suffer a wide range of symptoms that relate to their oesophagus and stomach. It is rather paradoxical that patients who are overweight suffer the symptoms of difficulty in swallowing, pain during eating or pain after eating, because the symptoms of difficulty eating do not translate into weight reduction. There are a range of underlying causes that include gastro-oesophageal reflux disease, dysmotility in the oesophagus, peptic ulceration and the nature and pattern of dietary intake. In addition the surgical treatments used for morbid obesity cause similar symptoms from gastric bands leading to dysphagia or reflux from being too tight or from erosion into the stomach, from balloons being displaced and bypass complications. Serious oesophageal conditions occur more frequently in patients with obesity such as Barrett's oesophagus and Adenocarcinoma of the oesophagus. This article reviews the literature to highlight the range of potential problems from oesophageal symptoms and disease and how they can be managed in the context of morbid obesity.

Keywords

Obesity, Reflux, GORD, Bariatric, Balloon, Gastric band, Gastric Bypass, Dysphagia, Sleeve gastrectomy, Vertical gastric banding

Introduction

Patients with morbid obesity suffer a wide range of symptoms that relate to their oesophagus and stomach. It is rather paradoxical that patients who are overweight suffer the symptoms of difficulty in swallowing, pain during eating or pain after eating because the symptoms of eating difficulty do not translate into weight reduction. There are a range of underlying causes that include gastro-oesophageal reflux disease, dysmotility in the oesophagus, peptic ulceration and the nature and pattern of dietary intake. The pathophysiology of gastro-oesophageal reflux disease and of dysphagia will be considered. The detrimental effects of the treatments of balloons, gastric bands and gastric bypass will be described and options for management discussed. The serious complications of adenocarcinoma and its premalignant precursor, Barrett's oesophagus will be reviewed.

Gastro-oesophageal reflux disease (GORD)

GORD is highly prevalent in obese people with increasing BMI a risk factor for developing the disease. The relation between GORD and obesity has been studied for decades and there have been conflicting results. A person with BMI of ≥30 kg/m^2 is 3 times more likely to suffer from heartburn and acid regurgitation [1].

Though the mechanism of this is poorly understood, a number of epidemiological studies have proven this association. Since recently, more evidence has emerged in favour of a positive association [2]. In 2000, Lagergren et al, based on a population based interview study on 820 Swedish, concluded that GOR symptoms occurred independent of BMI [3]. His claim was supported by two previous studies, one of which used oesophageal pH measure and other assessed the impact of weight loss on symptom relief [4, 5]. A contrary view has emerged since this, with large number of western studies showing a positive association [1, 2, 6-12]. This, however, has not been the case with Asian and Afro-Caribbean population. In a large population study with various ethnicities, a strongly positive association was found between BMI and GOR symptoms in white population. This was not the case in Asian and black population [13], a view re-iterated by another study from Iran [14]. The overall incidence of GORD is high in western world between 10% and 20%, compared to 5% in Asia [6].

The mechanism of GORD in obesity is very poorly understood. Various theories have been postulated and the evidence for each is discussed below, including the theory that the patho-physiology of reflux in the morbidly obesity could differ from others and might require a different therapeutic approach [9]

Increased intra-abdominal pressure as a cause of reflux

Increasing intra-abdominal pressure has been hypothesised to be the cause for reflux symptoms. Increasing BMI has been shown to increase intra-gastric pressure and pressure study in a prospective cohort has shown 10% increase in intra-gastric pressure with rise in each unit of BMI [15]. A pH and manometry study in general population with GORD showed a higher pressure gradients across the Oesophago-gastric junction than that in controls both before and during transient lower oesophageal sphincter relaxation. This phenomenon is thought to be caused by increased intra-gastric pressure, supporting the above theory [16].

Lower oesophageal sphincter dysfunction as a cause

Kuper et al showed a dysfunction of LOS and altered oesophageal motility even in asymptomatic patients with morbid obesity using pH and manometry study (BMI >40 kg/m^2) [17] and Wu et al showed an abnormal post-prandial LOS with prolonged transient lower oesophageal relaxation [18, 19].These findings were re-iterated by ayazi et al, showing obese patients to be more than twice as likely to have a mechanically defective LOS [20]. However, another study back in 1987 had shown a similar LOS pressure in normal weight and obese patients, though the gastro-oesophageal pressure gradient to LOS pressure ratio was high in obese [21].

Diet

The amount or composition of dietary intake and its relation to GORD has been studied. There is some evidence that volume, fat content and a high-caloric diet increases the oesophageal acid exposure time, giving rise to symptoms [22-24]. This would suggest an improvement of symptoms with reduction of these in the diet. More studies have shown an improvement in reflux symptoms with improved diet [25-29]. But, there is no convincing evidence to implicate the role of diet in reflux symptoms of obese patients.

Hiatus hernia

The incidence of hiatus hernia is over 50% in morbid obesity [30]. Hiatus has been shown to be predicted by intra-gastric pressure, gastro-oesophageal presssure gradient and BMI. BMI has in turn been shown to predict the former two. This confirms a positive association between BMI and presence of hiatus hernia [31]. High BMI is more likely to have oesophago-gastric junction disruption, leading to hiatal hernia and an augmented gastro-oesophageal pressure gradient, providing a perfect scenario for reflux to occur [32]. The incidence of defective LES was twice as much in obese patients with hiatus hernia, compared to obese without it [20]. Hiatus hernia thus plays a role in the obese patients and the subsequent development of GORD [33].

Poor mobility and mental state

There is no evidence to support the theory of reflux symptoms secondary to poor mobility and depression in the morbidly obese patients.

Treatment of GORD in obesity

Medical therapy

Medical therapy with a PPI remains the first line of treatment of GORD symptoms in obesity as in patients with a normal BMI. No guidelines are available for dose adjustments in the obese patients [34]. They continue to receive the standard therapy, adjusted to the severity of disease and symptoms.

Endoluminal therapy

Endoluminal therapy was introduced recently as treatment alternative for GORD and has shown promising results. This looked a safe option for use in obese patients. However, published results have shown high rate of post-operative PPI requirement in the obese patients [35]. Further evidence has to emerge before this option can be recommended for use in the obese patients.

Balloon

Intra-gastric balloon therapy has been an established temporary procedure for weight loss. GORD symptoms in obese tends to improve with weight loss, but as studies have shown, a balloon insertion tended to worsen symptoms [36, 37]. Balloon is hence not considered an option for treatment of obesity with patients with reflux symptoms.

Gastric band

Gastric banding provides a sufficient anti-reflux barrier in most of the obese patients with GORD. Abnormal manometric findings like increased LES (lower oesophageal sphincter) residual pressure and peristaltic wave duration are frequently encountered after banding. The clinical significances of these manometric abnormalities are not clear [38]. The oesophageal stasis caused by the band could explain the reflux in patients during longer follow up. Though, the reflux from the distal stomach is prevented by the gastric band, formation of a proximal pouch predisposes to stasis and reflux. This is more common in patients with preoperatively defective oesophageal motility. The studies suggesting a good GORD symptom control following banding had shorter follow up, explaining the results [39, 40]. Hence it could be concluded that gastric banding may aggravate GORD symptoms and cause oesophageal dilatation, especially in patients with pre-operative motility defects. Routine pre-operative testing should be done and alternative bariatric surgical procedures such as Roux-en-Y gastric bypass considered in these patients [41-43].

Sleeve Gastrectomy (Vertical gastric banding)

Gastrectomy reduces weight, but not gastro-oesophageal acid reflux. Although this procedure has been shown to have anti-reflux properties [44], it has fallen to disrepute in terms of relieving the reflux symptoms, especially with the superior results of RYGB [45-48]. A number of these cases requiring revision, due to reflux symptoms, have been reported [49-51].

Gastric Bypass Vs Anti-reflux surgery

Though laparoscopic fundoplication is the standard operation for GORD, gastric bypass has been shown to improve the reflux symptoms in the morbidly obese, apart from reducing their weight and obesity related co-morbid conditions such as diabetes mellitus, hypertension etc. Patterson et al. showed an equivalent symptomatic improvement and objective DeMeester score improvement with Laparoscopic Nissen fundoplication

and laparoscopic gastric bypass. The LES (lower oesophageal sphincter) pressure was also noted to improve, following bypass [52]. This was in light of an earlier report of 31% recurrence rate of reflux symptoms following laparoscopic Nissen's in obese patients [53]. Hence, morbidly obese patients with GORD should be offered laparoscopic gastric bypass as a surgical option [27, 30, 54-59].

The improvement in GORD symptoms after gastric bypass is related to the way that the operation staples off the distal 90% or more of the stomach body and antrum, removing any possibility that acid generated in this part of the stomach can reach the oesophagus. The parietal cell mass within the small gastric pouch that is left attached to the oesophagus, the complete elimination of duodeno-gastric reflux owing to a long Roux limb, and decrease in intra-abdominal pressure with weight loss all contribute to an almost total reflux control in all patients. The overall complications secondary to this procedure were lower than in laparoscopic fundoplication [54]. It is also the procedure of choice for previous other weight-loss surgery, when reflux symptoms develop [49-51]. Thus, a bariatric team prior to surgical intervention should review obese patients with GORD symptoms.

Dysphagia in obesity

Dysphagia in obesity is often related to the interventions used to treat obesity, though it can be primary in nature.

Various modalities of interventions available in obesity have been discussed above. Intra-gastric balloon therapy can be complicated by its displacement into the distal stomach, precipitating dysphagia and outlet obstruction. Gastric bands can be overfilled, causing this problem, and a slipped band or a band eroding through the stomach wall can also lead to dysphagia [60-64]. There has been no report of gastric bypass resulting in dysphagia, in the literature.

It is our understanding that patients with obesity may present with primary oesophageal dysmotility. Although there is little published literature on this issue, it is our hypothesis that fatty infiltration of the oesophageal wall and myenteric plexus may result in a poor amplitude peristaltic contraction.

Other oesophageal conditions associated with obesity

Barrett's Oesophagus

This is characterised by the replacement of the normal squamous epithelium of the lower oesophagus by a specialised metaplastic columnar epithelium. Barrett's oesophagus is a known risk factor for oesophageal adenocarcinoma, with a 30 to 125 times increased risk compared to general population [65]. Risk factors leading to Barrett's have been poorly understood, though GORD is widely believed to be the main risk factor [66-68]. Since several studies have found an association between obesity and GORD [1, 2, 6-12], and obesity as a risk factor for Barrett's have gained momentum in the recent year. Abdominal obesity or waist circumference has been shown to be more associated with Barrett's than BMI [69].

A recent systematic review showed a statistically significant relation between increasing BMI and Barrett's [70]. However, two older systematic reviews had found a rather week relation between these two, showing a need for further well designed studies [71, 72]. To mention a few studies, Jacobson et al showed a positive relation between BMI and Barrett's in women, independent of GORD, though the waist circumference was not found to have any association [73] and Stein at al., found a positive relation between BMI and Barrett's in war veterans [74]. Abdominal obesity or circumference appears to be more influential in the incidence of Barrett's oesophagus in another study [75]. There is however, little evidence to suggest an increased progression of Barrett's to neoplasia in obesity [69]

Obesity is a modifiable risk factor and if proven to be a risk for Barrett's and subsequent neoplasia, resources can be directed at modifying this, as there is evidence to suggest the regression Barrett's with weight loss [69]. Barrett's have been shown to regress with weight loss following gastric bypass and hence this has been recommended as bariatric procedure of choice in the morbidly obese with Barrett's [76-79]. A precise endoscopic evaluation before bariatric surgery with continuing postsurgical surveillance in patients with known Barrett's oesophagitis, and early evaluation in patients who develop new symptoms of GERD after bariatric surgery is suggested [80, 81]

Adenocarcinoma of oesophagus

The incidence of oesophageal adenocarcinoma has increased about 400% during the past three decades, the most rapid rate of increase of any cancer in the United States [82-84]. The association between high BMI and oesophageal adenocarcinoma is strong and well established, though the mechanism of this is still unclear. The risk is higher with increasing BMI, especially in men [85-94]. Obesity has also been shown to play a role in adenocarcinomas with a family history [95]. The incidence of adenocarcinoma of the cardia of stomach has not been so strongly related to BMI [96, 97]. Squamous cell carcinoma of oesophagus has not shown any association to obesity either [85, 93, 94, 98, 99]. Few studies have negated the association of obesity with oesophageal adenocarcinoma, but many were due to the fact that they included oesophageal and proximal stomach together [96]. The majority of these cancers arise from a background of premalignant Barrett's oesophagus, though less than 10% of the patients with oesophageal adenocarcinoma were known to have Barrett's oesophagus previously. Presently there is no evidence that strongly supports any specific strategy to screen a subgroup of the population at risk for Barrett's oesophagus and adenocarcinoma of the oesophagus [100].

A number of studies have also looked at the mechanism or pathway of this metaplasia-dysplasia-adenocarcinoma sequence. Visceral adiposity rather than BMI is thought to have a greater role in chronic inflammation and subsequent neoplasia. It has a clear association with Barrett's as above. Increasing abdominal girth increases the risk of adenocarcinoma and it has been shown for Barrett's [98]. Visceral fat is hypothesised as a major producer of interleukin-6, adinopectin, leptin and other adipokines that may be associated with the development of various gastro-intestinal cancers [101-103]. More specifically, insulin-like growth factor has been implicated in the pathogenesis of adenocarcinoma in the obese [104]. Oesophago-gastric tumours after bariatric surgery, has been reported, though rare. This condition, when occurs, requires the close collaboration of the bariatric team to achieve a successful oncological result, due to the altered anatomy like the blood supply to the gastric pouch and excluded stomach [105].

Conclusion

Obesity is associated with oesophageal disease, benign and malignant, and both the effects of obesity and the effects of it's treatment can aggravate oesophageal symptoms. The management of reflux and of dysphagia in obese patients requires a broad understanding of these issues.

Competing Interests
None declared
Author Details
Z K MOHAMED, MRCSEd, Specialist Registrar, North Tyneside Hospital, Rake Lane, North Shields NE29 8NH
S E ATTWOOD, FRCS. Consultant Upper GI Surgeon, North Tyneside Hospital Rake Lane North Shields NE29 8NH
CORRESSPONDENCE: S E ATTWOOD, FRCS, Consultant Upper GI Surgeon, North Tyneside Hospital Rake Lane North Shields NE29 8NH
Email: Stephen.Attwood@northumbria-healthcare.nhs.uk

REFERENCES

1. Murray L, Johnston B, Lane A, Harvey I, Donovan J, Nair P, et al. Relationship between body mass and gastro-oesophageal reflux symptoms: The Bristol Helicobacter Project. *Int J Epidemiol* 2003;32(4):645-50.
2. Fisichella PM, Patti MG. Gastroesophageal reflux disease and morbid obesity: is there a relation? *World J Surg* 2009;33(10):2034-8.
3. Lagergren J, Bergstrom R, Nyren O. No relation between body mass and gastro-oesophageal reflux symptoms in a Swedish population based study. *Gut* 2000;47(1):26-9.
4. Kjellin A, Ramel S, Rossner S, Thor K. Gastroesophageal reflux in obese patients is not reduced by weight reduction. *Scand J Gastroenterol* 1996;31(11):1047-51.
5. Lundell L, Ruth M, Sandberg N, Bove-Nielsen M. Does massive obesity promote abnormal gastroesophageal reflux? *Dig Dis Sci* 1995;40(8):1632-5.
6. Dent J, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2005;54(5):710-7.
7. Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CA, Jr. Body-mass index and symptoms of gastroesophageal reflux in women. *N Engl J Med* 2006;354(22):2340-8.
8. Nocon M, Labenz J, Jaspersen D, Meyer-Sabellek W, Stolte M, Lind T, et al. Association of body mass index with heartburn, regurgitation and esophagitis: results of the Progression of Gastroesophageal Reflux Disease study. *J Gastroenterol Hepatol* 2007;22(11):1728-31.
9. 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(3):286-90.
10. El-Serag H. The association between obesity and GERD: a review of the epidemiological evidence. *Dig Dis Sci* 2008;53(9):2307-12.
11. Breckan RK, Paulssen EJ, Asfeldt AM, Mortensen L, Straume B, Florholmen J. The impact of body mass index and Helicobacter pylori infection on gastro-oesophageal reflux symptoms: a population-based study in Northern Norway. *Scand J Gastroenterol* 2009;44(9):1060-6.
12. Schneider JM, Brucher BL, Kuper M, Saemann K, Konigsrainer A, Schneider JH. Multichannel intraluminal impedance measurement of gastroesophageal reflux in patients with different stages of morbid obesity. *Obes Surg* 2009;19(11):1522-9.
13. Corley DA, Kubo A, Zhao W. Abdominal obesity, ethnicity and gastro-oesophageal reflux symptoms. *Gut* 2007;56(6):756-62.
14. Solhpour A, Pourhoseingholi MA, Soltani F, Zarghi A, Habibi M, Ghafarnejad F, et al. Gastro-esophageal reflux symptoms and body mass index: no relation among the Iranian population. *Indian J Gastroenterol* 2008;27(4):153-5.
15. El-Serag HB, Tran T, Richardson P, Ergun G. Anthropometric correlates of intragastric pressure. *Scand J Gastroenterol* 2006;41(8):887-91.
16. Frankhuisen R, Van Herwaarden MA, Scheffer R, Hebbard GS, Gooszen HG, Samsom M. Increased intragastric pressure gradients are involved in the occurrence of acid reflux in gastroesophageal reflux disease. *Scand J Gastroenterol* 2009;44(5):545-50.
17. Kuper MA, Kramer KM, Kischniak A, Zdichavsky M, Schneider JH, Stuker D, et al. Dysfunction of the lower esophageal sphincter and dysmotility of the tubular esophagus in morbidly obese patients. *Obes Surg* 2009;19(8):1143-9.
18. Wu JC, Mui LM, Cheung CM, Chan Y, Sung JJ. Obesity is associated with increased transient lower esophageal sphincter relaxation. *Gastroenterology* 2007;132(3):883-9.
19. Schneider JH, Kuper M, Konigsrainer A, Brucher B. Transient lower esophageal sphincter relaxation in morbid obesity. *Obes Surg* 2009;19(5):595-600.
20. Ayazi S, Hagen JA, Chan LS, DeMeester SR, Lin MW, Ayazi A, et al. 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(8):1440-7.
21. Mercer CD, Wren SF, DaCosta LR, Beck IT. Lower esophageal sphincter pressure and gastroesophageal pressure gradients in excessively obese patients. *J Med* 1987;18(3-4):135-46.
22. Colombo P, Mangano M, Bianchi PA, Penagini R. Effect of calories and fat on postprandial gastro-oesophageal reflux. *Scand J Gastroenterol* 2002;37(1):3-5.
23. Fox M, Barr C, Nolan S, Lomer M, Anggiansah A, Wong T. The effects of dietary fat and calorie density on esophageal acid exposure and reflux symptoms. *Clin Gastroenterol Hepatol* 2007;5(4):439-44.
24. Iwakiri K, Kobayashi M, Kotoyori M, Yamada H, Sugiura T, Nakagawa Y. Relationship between postprandial esophageal acid exposure and meal volume and fat content. *Dig Dis Sci* 1996;41(5):926-30.
25. 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):1243-50.
26. Austin GL, Thiny MT, Westman EC, Yancy WS, Jr., Shaheen NJ. A very low-carbohydrate diet improves gastroesophageal reflux and its symptoms. *Dig Dis Sci* 2006;51(8):1307-12.
27. De Groot NL, Burgerhart JS, Van De Meeberg PC, de Vries DR, Smout AJ, Siersema PD. Systematic review: the effects of conservative and surgical treatment for obesity on gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2009;30(11-12):1091-102.
28. Fass R. The pathophysiological mechanisms of GERD in the obese patient. *Dig Dis Sci* 2008;53(9):2300-6.
29. Weiss H, Labeck B, Klocker J, Nehoda H, Mittermair R, Aigner F, et al. Effects of adjustable gastric banding on altered gut neuropeptide levels in morbidly obese patients. *Obes Surg* 2001;11(6):735-9.
30. Suter M, Dorta G, Giusti V, Calmes JM. Gastro-esophageal reflux and esophageal motility disorders in morbidly obese patients. *Obes Surg* 2004;14(7):959-66.
31. 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(6):1349-54.
32. Pandolfino JE, El-Serag HB, Zhang Q, Shah N, Ghosh SK, Kahrilas PJ. Obesity: a challenge to esophagogastric junction integrity. *Gastroenterology* 2006;130(3):639-49.

33. Stene-Larsen G, Weberg R, Froyshov Larsen I, Bjortuft O, Hoel B, Berstad A. Relationship of overweight to hiatus hernia and reflux oesophagitis. *Scand J Gastroenterol* 1988;23(4):427-32.
34. Anand G, Katz PO. Gastroesophageal reflux disease and obesity. *Rev Gastroenterol Disord* 2008;8(4):233-9.
35. White B, Jeansonne LO, Cook M, Chavarriaga LF, Goldenberg EA, Davis SS, et al. Use of endoluminal antireflux therapies for obese patients with GERD. *Obes Surg* 2009;19(6):783-7.
36. Mathus-Vliegen EM, van Weeren M, van Eerten PV. Los function and obesity: the impact of untreated obesity, weight loss, and chronic gastric balloon distension. *Digestion* 2003;68(2-3):161-8.
37. Rossi A, Bersani G, Ricci G, Petrini C, DeFabritiis G, Alvisi V. Intragastric balloon insertion increases the frequency of erosive esophagitis in obese patients. *Obes Surg* 2007;17(10):1346-9.
38. Gamagaris Z, Patterson C, Schaye V, Francois F, Traube M, Fielding CJ, et al. Lap-band impact on the function of the esophagus. *Obes Surg* 2008;18(10):1268-72.
39. Korenkov M, Kohler L, Yucel N, Grass G, Sauerland S, Lempa M, et al. Esophageal motility and reflux symptoms before and after bariatric surgery. *Obes Surg* 2002;12(1):72-6.
40. Ovrebo KK, Hatlebakk JG, Viste A, Bassoe HH, Svanes K. Gastroesophageal reflux in morbidly obese patients treated with gastric banding or vertical banded gastroplasty. *Ann Surg* 1998;228(1):51-8.
41. Tolonen P, Victorzon M, Niemi R, Makela J. Does gastric banding for morbid obesity reduce or increase gastroesophageal reflux? *Obes Surg* 2006;16(11):1469-74.
42. Klaus A, Gruber I, Wetscher G, Nehoda H, Aigner F, Peer R, 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):247-51.
43. Suter M, Dorta G, Giusti V, Calmes JM. Gastric banding interferes with esophageal motility and gastroesophageal reflux. *Arch Surg* 2005;140(7):639-43.
44. Deitel M, Khanna RK, Hagen J, Ilves R. Vertical banded gastroplasty as an antireflux procedure. *Am J Surg* 1988;155(3):512-6.
45. Di Francesco V, Baggio E, Mastromauro M, Zoico E, Stefenelli N, Zamboni M, et al. Obesity and gastro-esophageal acid reflux: physiopathological mechanisms and role of gastric bariatric surgery. *Obes Surg* 2004;14(8):1095-102.
46. Naslund E, Granstrom L, Melcher A, Stockeld D, Backman L. Gastro-oesophageal reflux before and after vertical banded gastroplasty in the treatment of obesity. *Eur J Surg* 1996;162(4):303-6.
47. Ortega J, Escudero MD, Mora F, Sala C, Flor B, Martinez-Valls J, 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):1086-94.
48. Braghetto I, Lanzarini E, Korn O, Valladares H, Molina JC, Henriquez A. Manometric changes of the lower esophageal sphincter after sleeve gastrectomy in obese patients. *Obes Surg*;20(3):357-62.
49. Balsiger BM, Murr MM, Mai J, Sarr MG. Gastroesophageal reflux after intact vertical banded gastroplasty: correction by conversion to Roux-en-Y gastric bypass. *J Gastrointest Surg* 2000;4(3):276-81.
50. Sugerman HJ, Kellum JM, Jr., DeMaria EJ, Reines HD. Conversion of failed or complicated vertical banded gastroplasty to gastric bypass in morbid obesity. *Am J Surg* 1996;171(2):263-9.
51. Iannelli A, Addeo P, Dahman M, Buratti MS, Ben Amor I, Piche T, et al. Laparoscopic conversion of vertical banded gastroplasty with an antireflux wrap into Roux-en-Y gastric bypass. *Obes Surg* 2007;17(7):901-4.
52. Patterson EJ, Davis DG, Khajanchee Y, Swanstrom LL. Comparison of objective outcomes following laparoscopic Nissen fundoplication versus laparoscopic gastric bypass in the morbidly obese with heartburn. *Surg Endosc* 2003;17(10):1561-5.
53. Perez AR, Moncure AC, Rattner DW. Obesity adversely affects the outcome of antireflux operations. *Surg Endosc* 2001;15(9):986-9.
54. 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(2):139-43.
55. Mejia-Rivas MA, Herrera-Lopez A, Hernandez-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):1217-24.
56. Tai CM, Lee YC, Wu MS, Chang CY, Lee CT, Huang CK, et al. The effect of Roux-en-Y gastric bypass on gastroesophageal reflux disease in morbidly obese Chinese patients. *Obes Surg* 2009;19(5):565-70.
57. Merrouche M, Sabate JM, Jouet P, Harnois F, Scaringi S, Coffin B, 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.
58. Clements RH, Gonzalez QH, Foster A, Richards WO, McDowell J, Bondora 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):610-4.
59. Frezza EE, Ikramuddin S, Gourash W, Rakitt T, Kingston A, Luketich J, et al. Symptomatic improvement in gastroesophageal reflux disease (GERD) following laparoscopic Roux-en-Y gastric bypass. *Surg Endosc* 2002;16(7):1027-31.
60. Bernante P, Francini Pesenti F, Toniato A, Zangrandi F, Pomerri F, Pelizzo MR. Obstructive symptoms associated with the 9.75-cm Lap-Band in the first 24 hours using the pars flaccida approach. *Obes Surg* 2005;15(3):357-60.
61. Lucchese M, Alessio F, Valeri A, Cantelli G, Venneri F, Borrelli D. Adjustable silicone gastric banding: complications in a personal series. *Obes Surg* 1998;8(2):207-9.
62. Patel SM, Shapiro K, Abdo Z, Ferzli GS. Obstructive symptoms associated with the Lap-Band in the first 24 hours. *Surg Endosc* 2004;18(1):51-5.
63. Pinsk I, Dukhno O, Levy I, Ovnat A. Gastric outlet obstruction caused by total band erosion. *Obes Surg* 2004;14(9):1277-9.
64. Srikanth MS, Oh KH, Keskey T, Rumbaut R, Fox SR, Fox ER, et al. Critical extreme anterior slippage (paragastric Richter's hernia) of the stomach after laparoscopic adjustable gastric banding: early recognition and prevention of gastric strangulation. *Obes Surg* 2005;15(2):207-15; discussion 215.
65. Wild CP, Hardie LJ. Reflux, Barrett's oesophagus and adenocarcinoma: burning questions. *Nat Rev Cancer* 2003;3(9):676-84.
66. Cameron AJ. Epidemiology of Barrett's esophagus and adenocarcinoma. *Dis Esophagus* 2002;15(2):106-8.
67. Conio M, Filiberti R, Blanchi S, Ferraris R, Marchi S, Ravelli P, et al. Risk factors for Barrett's esophagus: a case-control study. *Int J Cancer* 2002;97(2):225-9.
68. Eloubeidi MA, Provenzale D. Clinical and demographic predictors of Barrett's esophagus among patients with gastroesophageal reflux disease: a multivariable analysis in veterans. *J Clin Gastroenterol* 2001;33(4):306-9.
69. Murray L, Romero Y. Role of obesity in Barrett's esophagus and cancer. *Surg Oncol Clin N Am* 2009;18(3):439-52.
70. Kamat P, Wen S, Morris J, Anandasabapathy S. Exploring the association between elevated body mass index and Barrett's esophagus: a systematic review and meta-analysis. *Ann Thorac Surg* 2009;87(2):655-62.
71. Seidel D, Muangpaisan W, Hiro H, Mathew A, Lyratzopoulos G. The association between body mass index and Barrett's esophagus: a systematic review. *Dis Esophagus* 2009;22(7):564-70.
72. 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(2):292-300.
73. Jacobson BC, Chan AT, Giovannucci EL, Fuchs CS. Body mass index and Barrett's oesophagus in women. *Gut* 2009;58(11):1460-6.
74. Stein DJ, El-Serag HB, Kuczynski J, Kramer JR, Sampliner RE. The association of body mass index with Barrett's oesophagus. *Aliment Pharmacol Ther* 2005;22(10):1005-10.
75. Edelstein ZR, Farrow DC, Bronner MP, Rosen SN, Vaughan TL. Central adiposity and risk of Barrett's esophagus. *Gastroenterology* 2007;133(2):403-11.
76. Csendes A, Burgos AM, Smok G, Burdiles P, Henriquez A. Effect of gastric bypass on Barrett's esophagus and intestinal metaplasia of the cardia in patients with morbid obesity. *J Gastrointest Surg* 2006;10(2):259-64.
77. Houghton SG, Romero Y, Sarr MG. Effect of Roux-en-Y gastric bypass in obese patients with Barrett's esophagus: attempts to eliminate duodenogastric reflux. *Surg Obes Relat Dis* 2008;4(1):1-4; discussion 4-5.
78. Cobey F, Oelschlager B. Complete regression of Barrett's esophagus after Roux-en-Y gastric bypass. *Obes Surg* 2005;15(5):710-2.
79. Chang CG, Perez E. Case reports--resolution of Barrett's disease and esophageal epithelial atypia after gastric bypass and LAP-BAND. *Obes Surg* 2009;19(11):1597-8.
80. Melstrom LG, Bentrem DJ, Salvino MJ, Blum MG, Talamonti MS, Printen KJ. Adenocarcinoma of the gastroesophageal junction after bariatric surgery. *Am J Surg* 2008;196(1):135-8.
81. Varela JE. Barrett's esophagus: a late complication of laparoscopic adjustable gastric banding. *Obes Surg*;20(2):244-6.
82. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF, Jr. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991;265(10):1287-9.

83. Blot WJ, McLaughlin JK. The changing epidemiology of esophageal cancer. *Semin Oncol* 1999;26(5 Suppl 15):2-8.
84. Kubo A, Corley DA. Marked regional variation in adenocarcinomas of the esophagus and the gastric cardia in the United States. *Cancer* 2002;95(10):2096-102.
85. Lagergren J, Bergstrom R, Nyren O. Association between body mass and adenocarcinoma of the esophagus and gastric cardia. *Ann Intern Med* 1999;130(11):883-90.
86. Veugelers PJ, Porter GA, Guernsey DL, Casson AG. Obesity and lifestyle risk factors for gastroesophageal reflux disease, Barrett esophagus and esophageal adenocarcinoma. *Dis Esophagus* 2006;19(5):321-8.
87. 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.
88. Whiteman DC, Sadeghi S, Pandeya N, Smithers BM, Gotley DC, Bain CJ, et al. Combined effects of obesity, acid reflux and smoking on the risk of adenocarcinomas of the oesophagus. *Gut* 2008;57(2):173-80.
89. Abnet CC, Freedman ND, Hollenbeck AR, Fraumeni JF, Jr., Leitzmann M, Schatzkin A. A prospective study of BMI and risk of oesophageal and gastric adenocarcinoma. *Eur J Cancer* 2008;44(3):465-71.
90. Merry AH, Schouten LJ, Goldbohm RA, van den Brandt PA. Body mass index, height and risk of adenocarcinoma of the oesophagus and gastric cardia: a prospective cohort study. *Gut* 2007;56(11):1503-11.
91. Brown LM, Swanson CA, Gridley G, Swanson GM, Schoenberg JB, Greenberg RS, et al. Adenocarcinoma of the esophagus: role of obesity and diet. *J Natl Cancer Inst* 1995;87(2):104-9.
92. Lindblad M, Rodriguez LA, Lagergren J. Body mass, tobacco and alcohol and risk of esophageal, gastric cardia, and gastric non-cardia adenocarcinoma among men and women in a nested case-control study. *Cancer Causes Control* 2005;16(3):285-94.
93. Vaughan TL, Davis S, Kristal A, Thomas DB. Obesity, alcohol, and tobacco as risk factors for cancers of the esophagus and gastric cardia: adenocarcinoma versus squamous cell carcinoma. *Cancer Epidemiol Biomarkers Prev* 1995;4(2):85-92.
94. Ryan AM, Rowley SP, Fitzgerald AP, Ravi N, Reynolds JV. Adenocarcinoma of the oesophagus and gastric cardia: male preponderance in association with obesity. *Eur J Cancer* 2006;42(8):1151-8.
95. Chak A, Falk G, Grady WM, Kinnard M, Elston R, Mittal S, et al. Assessment of familiality, obesity, and other risk factors for early age of cancer diagnosis in adenocarcinomas of the esophagus and gastroesophageal junction. *Am J Gastroenterol* 2009;104(8):1913-21.
96. Kubo A, Corley DA. Body mass index and adenocarcinomas of the esophagus or gastric cardia: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2006;15(5):872-8.
97. Lagergren J, Bergstrom R, Lindgren A, Nyren O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *N Engl J Med* 1999;340(11):825-31.
98. Corley DA, Kubo A, Zhao W. Abdominal obesity and the risk of esophageal and gastric cardia carcinomas. *Cancer Epidemiol Biomarkers Prev* 2008;17(2):352-8.
99. Chow WH, Blot WJ, Vaughan TL, Risch HA, Gammon MD, Stanford JL, et al. Body mass index and risk of adenocarcinomas of the esophagus and gastric cardia. *J Natl Cancer Inst* 1998;90(2):150-5.
100. Pera M, Manterola C, Vidal O, Grande L. Epidemiology of esophageal adenocarcinoma. *J Surg Oncol* 2005;92(3):151-9.
101. Abrams JA. Obesity and Barrett's oesophagus: more than just reflux. *Gut* 2009;58(11):1437-8.
102. Rasouli N, Kern PA. Adipocytokines and the metabolic complications of obesity. *J Clin Endocrinol Metab* 2008;93(11 Suppl 1):S64-73.
103. Renehan AG, Roberts DL, Dive C. Obesity and cancer: pathophysiological and biological mechanisms. *Arch Physiol Biochem* 2008;114(1):71-83.
104. MacDonald K, Porter GA, Guernsey DL, Zhao R, Casson AG. A polymorphic variant of the insulin-like growth factor type I receptor gene modifies risk of obesity for esophageal adenocarcinoma. *Cancer Epidemiol* 2009;33(1):37-40.
105. Kuruba R, Jawad M, Karl RC, Murr MM. Technique of resection of esophageal adenocarcinoma after Roux-en-Y gastric bypass and literature review of esophagogastric tumors after bariatric procedures. *Surg Obes Relat Dis* 2009;5(5):576-81.