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Obesity & GERD

Paul Chang, MD and **Frank Friedenberg, MD, MS (Epi)**
Gastroenterology Section, Temple University School of Medicine, Philadelphia, PA

Abstract

Epidemiological data have demonstrated that obesity is an important risk factor for the development of gastroesophageal reflux disease. There is also accumulating data that obesity is associated with complications related to longstanding reflux such as erosive esophagitis, Barrett's Esophagus, and esophageal adenocarcinoma. Central obesity, rather than BMI, appears to be more closely associated with these complications. Pathophysiological disturbances in obesity include esophageal motor disorders, lower esophageal sphincter abnormalities, a trend toward the development of hiatal hernia, increased intragastric pressure and increased gastric capacity. Additionally, alterations in the secretion of adiponectin and leptin from adipocytes is a proposed link between obesity and Barrett's esophagus and esophageal adenocarcinoma. Evidence to date suggest that bariatric surgery, specifically Roux-en-Y gastric bypass, can ameliorate reflux disease through loss of excess weight. Surgical data is confounded by the concomitant repair of prevalent hiatal hernias in many patients. The data for medical weight loss as a treatment for GERD is less robust, but there does appear to be an association with successful weight loss and fewer GERD symptoms.

Keywords

obesity; gastroesophageal reflux disease; Barrett's esophagus; waist-to-hip ratio; adiponectin; leptin

Introduction

Disease description

The typical manifestations of GERD are heartburn and/or regurgitation. GERD can be further classified into erosive GERD and non-erosive GERD based on endoscopic appearance of esophageal mucosa. The term “Atypical GERD” is used in situations where the predominant symptoms are extra-esophageal such as cough, laryngitis, and asthma.[1] GERD is a common disorder with a prevalence of ~20% in the US.[2] The recognized sequelae of GERD include Barrett's esophagus and esophageal adenocarcinoma. Obesity, defined as a BMI $\geqslant$30, is common in the Western world and is increasing in other parts of the world, particularly Asia. Epidemiologic data demonstrates that overall obesity (typically measured as body mass index kg/m^2, BMI) is a risk factor for both GERD and esophageal

Frank Friedenberg (corresponding author) friedfk@tuhs.temple.edu Temple University Hospital Parkinson Pavilion, 8th Floor 3401 North Broad Street Philadelphia, PA 19140.

adenocarcinoma.[3] There is evidence that central abdominal obesity, as opposed to an elevated BMI, is the most important factor associated with Barrett's.[4] (Table 1)

Prevalence/Incidence

A systematic review estimated the prevalence of GERD in the United States at 18.1% – 27.8%.[2] El Serag and others in their systematic review divided studies on the prevalence of GERD into four temporal categories. Relative to pre-1995, the rate ratio for GERD prevalence was 1.45 for 1995–1999, 1.46 for 2000–2004, and 1.51 for 2005–2009. Obesity is an even more common health issue in the United States. Data from the 2009–2010 National Health and Examination Survey (NHANES) estimates a prevalence of 35.5% for men and 35.8% for women, which is not significantly changed compared to the period 2003–2008.[5] Previous trends showed that the prevalence of obesity was increasing in America but the trend may beginning to level.

Cross-sectional epidemiological studies have demonstrated a higher prevalence of GERD in obese individuals compared to the non-obese. Jacobsen et al used a supplemental GERD questionnaire added to the Nurses' Health Study to show that subjects that reported at least weekly symptoms had a near linear increase in the adjusted OR for reflux symptoms for each BMI strata.[6] A similar link was seen in the results from the 80,110 insurance members from the Kaiser Permanente MultiPhasic Health Check-Up cohort.[7] The association between BMI and GERD was stronger among whites compared to black members, with odds ratios of 1.58 and 1.33 respectively. When controlling for abdominal diameter the odds ratios were 1.39 and 1.15 respectively.

Smaller studies have confirmed the link between obesity and GERD. El-Serag and others interviewed 453 hospital employees, and found that 26% had weekly heartburn or regurgitation symptoms. [8] Subjects were offered endoscopy and 196 agreed, and they found that increasing levels of obesity were associated with a greater likelihood of GERD and esophagitis. The proportion of subjects with GERD symptoms were 23.3%, 26.7%, and 50% for BMI groups <25, 25–30, and >30 respectively. Prevalence rates for erosive esophagitis were 12.5%, 29.8%, and 26.9%. Two small cohort studies from Olmstead County, MN have also evaluated the relationship between obesity and GERD. The first study identified obesity as a risk factor for the initial development of GERD as well as the persistence of symptoms.[9] The second study found that BMI was associated with GERD (OR=1.9) independent of diet and energy expenditure.[10]

The effect of weight change on GERD symptoms has been studied. Jacobson et al studied select individuals from the Nurses' Health Study, and found that an increase of BMI by > 3.5 kg/m^2 when compared to no weight change was associated with an increase risk of frequent symptoms of reflux.[11]

World Wide Incidence Rates

The prevalence of obesity is somewhat lower outside of the United States. The European Prospective Investigation into Cancer and Nutrition (EPIC) study estimated the prevalence of obesity was 17% in 2005, increased from 13% in 1998.[12] Based on a systematic review, the prevalence rate of GERD in Europe was estimated to be 15% for the period 2005–2009. Similar to the trend seen in the United States, this prevalence rate is significantly higher than prior to 1995.[2] The epidemiologic relationship between obesity and GERD has been observed in Europe as well. The German National Health Interview and Examination Survey found the OR for GERD to be 1.8 for overweight and 2.6 for obese individuals.[13] In England, the Bristol Helicobacter Project found that obese individuals had an OR= 2.91 for heartburn, and an OR= 2.23 for regurgitation.[14] A telephone survey

in Spain of 2,500 subjects revealed that obese individuals had an OR of 1.74 for GERD symptoms. It was also noted that patients with GERD symptoms for >10 years were more likely to be obese (OR 1.92).[15] This group also found that a weight gain of >5 kg in the past year demonstrated a 2.7 fold higher risk of new GERD symptoms.[16] In Norway, Nilson and others conducted nationwide surveys during 1984–1986 (N=74,599) and 1995–1997 (N=65,363). They found that for severely obese men (BMI>35 kg/m^2) the OR for GERD was 3.3, while the OR for severely obese women was 6.3. A link showing an association between estrogen levels and GERD was observed. Pre-menopausal women and those who were post-menopausal but taking hormone replacement therapy were at an increased risk for GERD relative to untreated post-menopausal women.[17]

A relationship between obesity and GERD has been seen in Asia. Kang and others studied 2,457 subjects who underwent upper endoscopy in Korea. They found a relationship between higher strata of BMI and the presence of erosive esophagitis.[18] In Shanghai, a nested case-control study found an association between obesity and dwelling in an urban environment with GERD.[19]

Studies that have failed to identify a relationship between GERD and obesity have also been reported. A study from Sweden of 820 subjects showed that those who had been overweight or obese had an adjusted OR of 0.99 for GERD. They also found no association between obesity and severity of reflux symptoms.[20] Similarly, a prospective cohort study in Olmsted, MN of 607 individuals surveyed over 10.5 years did not find an association with GERD symptoms and weight loss of >10 pounds.[9]

In summary, the preponderance of population-based studies support the association between obesity and GERD reflux. The association has been demonstrated in the US where obesity rates are the highest, and has also been seen in Europe and Eastern Asia. (Figure 1) Shortcomings of these studies are that they primarily relied on self-reported height and weight to calculate BMI, and did not look specifically at abdominal obesity. There appears to be a dose response as well with increasing levels of obesity associated with higher prevalence rates. Weight loss has not been consistently associated with amelioration of symptoms at a population level.

Clinical Correlation

Complications of GERD

Long term complications of GERD such as erosive esophagitis (EE), Barrett's esophagus (BE), and esophageal adenocarcinoma have been associated with obesity. In a large endoscopic study El-Serag reported that relative to those with no erosions, those with EE were more likely to be overweight or obese.[8] A similar association has was seen in Korea where Lee et al. did an endoscopy study in Korea studying 3,000 participants.[30] They found that obese individuals compared to normal weight subjects had an OR=3.3 for EE. A meta analysis by Hampel et al. confirmed the association with increasing levels of obesity and esophageal mucosal injury.[31]

Associations of BE and obesity have been demonstrated by Stein and others who established that for each 5-unit increase in BMI, the risk of BE increased by 35%.[32] Abdominal obesity (“central obesity”) has been shown to be a more specific risk factor for BE. Corley and others utilizing data from the Kaiser Permanente database found that a larger abdominal circumference (measured at the iliac crest with the abdomen relaxed), independent of BMI, was associated with BE.[33] Edelstein et al, found that for individuals in the highest category of waist-to-hip ratio the adjusted OR for BE was 1.9, and 4.1 for long-segment BE. [34] Rubenstein et al. found that abdominal obesity as measured by waist circumference

increased the risk of erosive esophagitis and Barrett's, whereas gluteo-femoral obesity was protective.[35] Finally, El-Serag utilized abdominal CT imaging to demonstrate that greater amounts of visceral adipose tissue but not subcutaneous adipose tissue conferred a significantly increased risk for BE.[4]

Not all studies have demonstrated an association between obesity and BE. An Australian study found that BMI was not an independent risk factor for BE.[36] A study in Canada by Veugelers and others also did not show an association between obesity and BE. They did, however, find an association of BMI with esophageal adenocarcinoma.[37]

The incidence of esophageal adenocarcinoma has been rising in the United States.[38] From 1975 to 2001 the incidence of esophageal adenocarcinoma rose approximately six-fold. There are a number of studies which have examined the relationship between obesity and esophageal adenocarcinoma. In 1998, a National Cancer Institute study by Chow and others found an association between increasing strata of BMI and esophageal cancer, specifically among younger non-smoking individuals.[39] A Swedish study identified obesity with an OR of 16.2 for the development of adenocarcinoma compared with the leanest individuals (BMI<22 kg/m^2). A recently pooled analysis from 12 world-wide epidemiological studies showed that patients with a BMI of ≥40 compared to non-overweight patients had an OR of 4.76 for esophageal adenocarcinoma.[40] Engel and others found that the population attributable risk (proportion of occurrences in the population that may be preventable if a factor were totally eliminated) for increase weight (using BMI <23.1 as the control group) rose steadily from 5.4% (BMI = 23.2–25.1) to 21.3% (BMI 27.3–40.1).[41]

Pathophysiology

Several physiologic abnormalities which could lead to prolonged esophageal acid exposure have been found to occur more frequently in obese compared to normal weight individuals. Many of these disturbances have been identified in the severely obese (BMI > 35) prior to bariatric surgery and may not apply to those with lesser degrees of obesity. For example, esophageal manometry prior to bariatric surgery has revealed that many patients have a motility disorder. In a study of 345 patients 25.6% of patients had abnormal manometry. The most common abnormal findings were nutcracker esophagus and non-specific motility disorder.[42] Other studies in severely obese subjects revealed similar findings, with non-specific motility disorder, nutcracker esophagus, and hypotensive LES as the most common manometric abnormalities.[43, 44] Interestingly, most of these patients were asymptomatic.

Studies looking specifically at pre-bariatric surgical patients with symptoms of GERD, excluding asymptomatic patients have also been reported. Hong and others studied 61 patients and 32.8% had abnormal manometry, most commonly non-specific esophageal motor disorder. Another study using manometry, 24-hour pH measurement and impedance grouped patients into 3 groups. Group 1 (control group) had 10 normal weight asymptomatic subjects, group 2 had 22 non-obese GERD patients, and group 3 consisted of 22 obese GERD patients. All group 1 patients had normal esophageal acid exposure, motility, and bolus transit. From group 2 there were five patients with abnormal manometry, 2 with ineffective esophageal motility, two with nutcracker esophagus, and one with hypertensive LES (>50 mmHg). Group 3 also had five patients with abnormal manometry including two with ineffective esophageal motility, two with nutcracker esophagus, and one with diffuse esophageal spasm. The only difference between the obese and non-obese GERD subjects, was that obese patients had fewer episodes of complete bolus transit (as measured by impedance) compared to the non-obese, 66% vs. 88% p=0.01[45]

A hypotensive LES, defined as basal pressure <10 mmHg, is clearly a predisposing factor for GERD. Studies examining the relationship between LES pressure and BMI have been

performed, although the results are inconsistent. One study examined 64 consecutive patients and divided subjects into 3 groups. Group A had 23 subjects with BMI <25, group B had 25 subjects with a BMI between 25 and 30, and group C had 16 subjects with a BMI >30. The authors observed a strong inverse relationship between BMI and LES pressure ($p<0.001$).[46]

Transient relaxations of the lower esophageal sphincter (TRLES) have been observed to be more common in patients with obesity. The main stimulus for TRLES is gastric distension, particularly in the fundus.[47, 48] A study by Wu et al. divided subjects into 3 groups, 28 obese, 28 overweight, and 28 normal subjects. These individuals were studied with upper endoscopy, manometry, and pH recordings. The overweight and obese groups were found to have significantly higher rates of TRLES during the 2 hour postprandial period (obese group 17.3, overweight 3.8, normal 2.1 episodes per hour; $p<0.001$).. Total distal esophageal acid exposure as well as the proportion of TRLES accompanied by acid reflux was also greater in the obese and overweight groups.[49]

The presence of a hiatal hernia has also been associated with obesity. Suter et al, studied morbidly obese patients with history of reflux symptoms with upper endoscopy, 24-H pH monitoring, and manometry. [42] They observed that of 345 subjects approximately half had a hiatal hernia. Furthermore patients with a hiatal hernia were more likely to have esophagitis compared to those without a hiatal hernia. Pandolfino et al. subsequently reported that obese patients have a pressure gradient along the esophagogastric junction that supported the development of a hiatal hernia.[50]

Abdominal obesity likely increases intra-abdominal pressure due to transmission of gravitational force of the adipose tissue to the abdominal cavity. Lambert et al. studied morbidly obese patients with a urinary catheter as a surrogate for intra-abdominal pressure, and found that obese patients compared to non-obese patients had higher intra-abdominal pressures.[51] This relationship between obesity and elevated intra-abdominal/intra-gastric pressures has been confirmed by others with use of intra-gastric manometry.[52, 53]

Gastric volume and motor abnormalities have been proposed as other mechanisms for GERD in obese individuals. Multiple studies have found that the capacitance of gastric contents in obese subjects is larger compared to lean individuals.[54, 55] Whether the greater volume of contents leads to increased GERD is not known. It has also been theorized that obese individuals may have delayed gastric emptying due to neuronal or humoral mechanisms. [56–58] Buchholz et al. using standardized scintigraphic gastric emptying studies, showed no difference in gastric emptying in obese versus non-obese patients. Retention percentages at one hour were 48% and 47% respectively, and at 4 hours, 1.7% and 1.1%. [59]

The link between obesity and esophageal neoplasia may be via altered secretion of adipokines such as adiponectin and leptin. Adiponectin is a protein which has anti-inflammatory and immunomodulatory functions and stimulates apoptosis.[60] Secretion of adiponectin decreases with obesity. Rubenstein et al. found an inverse association between plasma adiponectin levels and the presence of BE in a case-control study. [61] In a separate study this group found that levels of the low molecular weight subtype of adiponectin was inversely associated with the risk of Barrett's.[62] In contrast to the inverse relationship seen between obesity and adiponectin, leptin levels correlate directly with obesity. [63]Leptin is secreted by adipocytes and gastric chief cells and has been shown to have mitogenic properties and to induce proliferation in a number of human cell lines including esophageal cancer cells.[64] Dendall and others found that male subjects with BE had higher levels of plasma leptin relative to healthy controls. Those with a leptin level in the highest quartile

had an OR of 3.3 for the presence of BE.[65] The link between BE and central obesity (rather than BMI) may be partially explained by the fact that leptin reaches very high values in central obesity. (Figures 2 and 3)

Weight Loss and GERD

In Norway the HUNT 3 study surveyed 44,997 from 2006–2009 and found that weight loss was dose-dependently associated with a reduction of symptoms.[66] A prospective cohort study of 332 obese adults enrolled in a structured weight loss program was performed by Singh and others. Mean weight loss was 13 kg and the prevalence of GERD decreased from 37% to 15% with 81% of subjects experiencing a reduction in symptom scores.[67] Fraser-Moodie et al followed 34 patients who had GERD and a BMI >23.[68] Patients were given dietary advice (not a structured weight loss protocol) and lost an average of 4 kg. For the 27 patients (79.4%) who lost weight, they experienced a decrease in symptoms by 75% compared to baseline using a modified DeMeester questionnaire.

Conversely, Kjellin and others randomized 20 obese patients with GERD to a very low-caloric diet (VLCD, approximately 800 Kcal/d) or no change in diet. Patients in the VLCD group lost an average of 10.8 kg, and the control group gained 0.6 kg. Those on the VLCD did not have significant changes in reflux symptoms. The control group was then given the VLCD and lost weight but again no change in symptoms were observed.[69] Frederiksen and others studied 34 morbidly obese patients prescribed liquid VLCD pre- and post-vertical banded gastroplasy and found no change in acid exposure time from baseline compared with 10–14 days after the start of VLCD or three weeks after surgery.

Bariatric Surgery and GERD

The use of bariatric surgery has increased over the past two decades as it has proved to be an effective treatment for obesity. In 2006 the number of bariatric operations in the U.S. was reported as 112,999.[70] Bariatric surgeries can be classified as restrictive, malabsorptive, or both. In restrictive surgeries the gastric anatomy is altered to reduce gastric volume to induce early satiety which in turn leads to weight loss. Examples of restrictive surgeries include vertical banded gastroplasty, intra-gastric balloon, sleeve gastrectomy (SG) and laparoscopic adjustable gastric banding (LAGB). Malabsorptive surgeries induce malabsorption by shortening the gut and/or altering the time food is subjected to digestive juices. Examples of malabsorptive surgeries include biliopancreatic diversion with and without duodenal switch, and jejunal ileal bypass. Combined techniques include Roux-en-Y gastric bypass (RYGB).

There have been several studies published that have examined changes in GERD symptoms after bariatric surgery. These studies have generally been prospective cohort and retrospective studies and not randomized controlled studies. Analysis of results is confounded by the common practice of repairing hiatal hernias during surgery, and the heterogeneity in post bariatric diet, lifestyle modification and PPI use.

The most common bariatric surgeries performed are the RYGB, LAGB,[70] and more recently the SG.[71] RYGB involves stapling of the stomach to create a small (≤30 ml) upper gastric pouch.[72] A roux limb of jejunum is then anastomosed to the gastric pouch bypassing absorptive surface area. Potential mechanism for RYGB reducing GERD symptoms include diverting bile away from the esophagus[73], eliminating acid production in the gastric pouch, [74] or reducing volume of acid refluxate.[75] De Groot et. al performed a systematic review on bariatric surgery and the effects on GERD. They identified eight studies that evaluated GERD symptoms after RYGB, and three studies that compared RYGB to other weight loss techniques with respect to GERD symptoms. [76] All

studies showed an improvement in GERD symptoms after RYGB except one by Korenkov et. al.[77] Most of the studies included in the systematic review used questionnaires (QUEST) and only four of the eleven studies used objective measurements (i.e. endoscopy, 24-hour pH monitoring) to define GERD.

In LAGB a band device is placed around the fundus of the stomach immediately below the esophagogastic junction and a subcutaneous reservoir is used to adjust the band size.[76] In the same systematic review by De Groot et. al the effects of LAGB on GERD were analyzed. Of twelve studies identified, four reported a positive effect on GERD, two studies found a positive effect so long as there was no pouch dilatation and/or a prior esophageal motility disorder was not present, two studies showed an increase in symptoms based on pH metry, manometry, and/or endoscopic findings, and four studies showed conflicting data in different domains of the diagnostic tests.[76] Due to the conflicting data it is difficult to come to a conclusion on the effects of LAGB on GERD symptoms.

In sleeve gastrectomy the stomach is vertically divided reducing the volume to about 25% of the original size. In a recent systematic review by Chiu et. al which included 15 studies of SG, four found a post-operative increase in GERD prevalence, seven showed reduced prevalence, and in four studies the prevalence before and after surgery could not be determined.[71] As with most studies examining the effects of bariatric surgery on GERD there was significant heterogeneity between studies including differences in follow up time ranging from 6 months to 5 years, differences in the case definition of GERD, and lack of control groups. Therefore, similar to LAGB, it is difficult to come to conclusively determine the effects of SG on GERD.

In summary, surgical management is an effective approach to weight loss, and the data has generally shown that this weight loss can have positive effects on GERD. RYGB studies have provided the most consistent evidence for reducing GERD after surgery. Thus, in patients with severe GERD preoperatively, preferential consideration should be given to performing RYGB as the bariatric procedure of choice.

Summary/Discussion

Epidemiologic studies strongly suggest that the prevalence of GERD is increasing and the major contributing factor to this trend is the rising prevalence of obesity. This trend has been observed in the United States as well as in Europe and Eastern Asia. Central obesity as opposed to BMI appears to be a better marker for the risks of metaplastic and neoplastic complications of GERD. Visceral adipose tissue secretes hormonal mediators which may increase the risk or Barrett's and esophageal adenocarcinoma. Studies have preliminarily shown that leptin levels have a direct relationship with the development of Barrett's and adiponectin levels are inversely related. Other factors which may play a role in the pathophysiology of GERD due to obesity include the increased prevalence of esophageal motor disorders, higher number of transient relaxations of the lower esophageal sphincter, and increased intra-abdominal pressure. The benefit of weight loss through diet as a means to decrease GERD symptoms is not yet established. However, gastric bypass surgery leads to substantial weight loss and the data has consistently shown a decrease in GERD symptoms. Unfortunately, only a few studies have included pH data to confirm improvement after surgery.

References

1. Hom C, Vaezi MF. Extraesophageal manifestations of gastroesophageal reflux disease. Gastroenterol Clin North Am. 2013; 42(1):71–91. [PubMed: 23452632]

2. El-Serag HB, Sweet S, Winchester CC, et al. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2013
3. El-Serag H. The association between obesity and GERD: a review of the epidemiological evidence. Dig Dis Sci. 2008; 53(9):2307–12. [PubMed: 18651221]
4. El-Serag HB, Hashmi A, Garcia J, et al. Visceral abdominal obesity measured by CT scan is associated with an increased risk of Barrett's oesophagus: a case-control study. Gut. 2013
5. Flegal KM, Carroll MD, Kit BK, et al. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. JAMA. 2012; 307(5):491–7. [PubMed: 22253363]
6. Jacobson BC, Somers SC, Fuchs CS, et al. Body-mass index and symptoms of gastroesophageal reflux in women. N Engl J Med. 2006; 354(22):2340–8. [PubMed: 16738270]
7. Corley DA, Kubo A, Zhao W. Abdominal obesity, ethnicity and gastro-oesophageal reflux symptoms. Gut. 2007; 56(6):756–62. [PubMed: 17047097]
8. El-Serag HB, Graham DY, Satia JA, et al. Obesity is an independent risk factor for GERD symptoms and erosive esophagitis. Am J Gastroenterol. 2005; 100(6):1243–50. [PubMed: 15929752]
9. Cremonini F, Locke GR 3rd, Schleck CD, et al. Relationship between upper gastrointestinal symptoms and changes in body weight in a population-based cohort. Neurogastroenterol Motil. 2006; 18(11):987–94. [PubMed: 17040409]
10. Nandurkar S, Locke GR 3rd, Fett S, et al. Relationship between body mass index, diet, exercise and gastro-oesophageal reflux symptoms in a community. Aliment Pharmacol Ther. 2004; 20(5): 497–505. [PubMed: 15339321]
11. Jacobson BC, Somers SC, Fuchs CS, et al. Body-mass index and symptoms of gastroesophageal reflux in women. N Engl J Med. 2006; 354(22):2340–8. [PubMed: 16738270]
12. von Ruesten A, Steffen A, Floegel A, et al. Trend in obesity prevalence in European adult cohort populations during follow-up since 1996 and their predictions to 2015. PLoS One. 2011; 6(11):e27455. [PubMed: 22102897]
13. Nocon M, Labenz J, Willich SN. Lifestyle factors and symptoms of gastro-oesophageal reflux -- a population-based study. Aliment Pharmacol Ther. 2006; 23(1):169–74. [PubMed: 16393294]
14. Murray L, Johnston B, Lane A, et al. Relationship between body mass and gastro-oesophageal reflux symptoms: The Bristol Helicobacter Project. Int J Epidemiol. 2003; 32(4):645–50. [PubMed: 12913045]
15. Diaz-Rubio M, Moreno-Elola-Olaso C, Rey E, et al. Symptoms of gastro-oesophageal reflux: prevalence, severity, duration and associated factors in a Spanish population. Aliment Pharmacol Ther. 2004; 19(1):95–105. [PubMed: 14687171]
16. Rey E, Moreno-Elola-Olaso C, Artalejo FR, et al. Association between weight gain and symptoms of gastroesophageal reflux in the general population. Am J Gastroenterol. 2006; 101(2):229–33. [PubMed: 16454823]
17. Nilsson M, Johnsen R, Ye W, et al. Obesity and estrogen as risk factors for gastroesophageal reflux symptoms. JAMA. 2003; 290(1):66–72. [PubMed: 12837713]
18. Kang MS, Park DI, Oh SY, et al. Abdominal obesity is an independent risk factor for erosive esophagitis in a Korean population. J Gastroenterol Hepatol. 2007; 22(10):1656–61. [PubMed: 17845694]
19. Ma XQ, Cao Y, Wang R, et al. Prevalence of, and factors associated with, gastroesophageal reflux disease: a population-based study in Shanghai, China. Dis Esophagus. 2009; 22(4):317–22. [PubMed: 19207545]
20. 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. [PubMed: 10861260]
21. Martinez JA, Moreno B, Martinez-Gonzalez MA. Prevalence of obesity in Spain. Obes Rev. 2004; 5(3):171–2. [PubMed: 15245386]
22. Ponce J, Vegazo O, Beltran B, et al. Prevalence of gastro-oesophageal reflux disease in Spain and associated factors. Aliment Pharmacol Ther. 2006; 23(1):175–84. [PubMed: 16393295]
23. Thorburn AW. Prevalence of obesity in Australia. Obes Rev. 2005; 6(3):187–9. [PubMed: 16045631]

24. Moraes-Filho JP, Chinzon D, Eisig JN, et al. Prevalence of heartburn and gastroesophageal reflux disease in the urban Brazilian population. Arq Gastroenterol. 2005; 42(2):122–7. [PubMed: 16127569]
25. Rtveladze K, Marsh T, Webber L, et al. Health and economic burden of obesity in Brazil. PLoS One. 2013; 8(7):e68785. [PubMed: 23874763]
26. He J, Ma X, Zhao Y, et al. A population-based survey of the epidemiology of symptom-defined gastroesophageal reflux disease: the Systematic Investigation of Gastrointestinal Diseases in China. BMC Gastroenterol. 2010; 10 94,230X-10-94.
27. Wang Y, Mi J, Shan XY, et al. Is China facing an obesity epidemic and the consequences? The trends in obesity and chronic disease in China. Int J Obes (Lond). 2007; 31(1):177–88. [PubMed: 16652128]
28. Bhatia SJ, Reddy DN, Ghoshal UC, et al. Epidemiology and symptom profile of gastroesophageal reflux in the Indian population: report of the Indian Society of Gastroenterology Task Force. Indian J Gastroenterol. 2011; 30(3):118–27. [PubMed: 21792655]
29. Griffiths PL, Bentley ME. The nutrition transition is underway in India. J Nutr. 2001; 131(10): 2692–700. [PubMed: 11584092]
30. Lee HL, Eun CS, Lee OY, et al. Association between GERD-related erosive esophagitis and obesity. J Clin Gastroenterol. 2008; 42(6):672–5. [PubMed: 18360294]
31. 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. [PubMed: 16061918]
32. Stein DJ, El-Serag HB, Kuczynski J, et al. The association of body mass index with Barrett's oesophagus. Aliment Pharmacol Ther. 2005; 22(10):1005–10. [PubMed: 16268976]
33. Corley DA, Kubo A, Levin TR, et al. Abdominal obesity and body mass index as risk factors for Barrett's esophagus. Gastroenterology. 2007; 133(1):34,41. quiz 311. [PubMed: 17631128]
34. Edelstein ZR, Bronner MP, Rosen SN, et al. Risk factors for Barrett's esophagus among patients with gastroesophageal reflux disease: a community clinic-based case-control study. Am J Gastroenterol. 2009; 104(4):834–42. [PubMed: 19319131]
35. Rubenstein JH, Morgenstern H, Chey WD, et al. Protective role of gluteofemoral obesity in erosive oesophagitis and Barrett's oesophagus. Gut. 2013
36. Smith KJ, O'Brien SM, Smithers BM, et al. Interactions among smoking, obesity, and symptoms of acid reflux in Barrett's esophagus. Cancer Epidemiol Biomarkers Prev. 2005; 14(11 Pt 1):2481–6. [PubMed: 16284367]
37. Veugelers PJ, Porter GA, Guernsey DL, et al. Obesity and lifestyle risk factors for gastroesophageal reflux disease, Barrett esophagus and esophageal adenocarcinoma. Dis Esophagus. 2006; 19(5):321–8. [PubMed: 16984526]
38. Pohl H, Welch HG. The role of overdiagnosis and reclassification in the marked increase of esophageal adenocarcinoma incidence. J Natl Cancer Inst. 2005; 97(2):142–6. [PubMed: 15657344]
39. Chow WH, Blot WJ, Vaughan TL, et al. Body mass index and risk of adenocarcinomas of the esophagus and gastric cardia. J Natl Cancer Inst. 1998; 90(2):150–5. [PubMed: 9450576]
40. Hoyo C, Cook MB, Kamangar F, et al. Body mass index in relation to oesophageal and oesophagogastric junction adenocarcinomas: a pooled analysis from the International BEACON Consortium. Int J Epidemiol. 2012; 41(6):1706–18. [PubMed: 23148106]
41. Engel LS, Chow WH, Vaughan TL, et al. Population attributable risks of esophageal and gastric cancers. J Natl Cancer Inst. 2003; 95(18):1404–13. [PubMed: 13130116]
42. Suter M, Dorta G, Giusti V, et al. Gastro-esophageal reflux and esophageal motility disorders in morbidly obese patients. Obes Surg. 2004; 14(7):959–66. [PubMed: 15329186]
43. Koppman JS, Poggi L, Szomstein S, et al. Esophageal motility disorders in the morbidly obese population. Surg Endosc. 2007; 21(5):761–4. [PubMed: 17285388]
44. Jaffin BW, Knoepflmacher P, Greenstein R. High prevalence of asymptomatic esophageal motility disorders among morbidly obese patients. Obes Surg. 1999; 9(4):390–5. [PubMed: 10484299]

45. Quiroga E, Cuenca-Abente F, Flum D, et al. Impaired esophageal function in morbidly obese patients with gastroesophageal reflux disease: evaluation with multichannel intraluminal impedance. Surg Endosc. 2006; 20(5):739–43. [PubMed: 16544079]
46. Kouklakis G, Moschos J, Kountouras J, et al. Relationship between obesity and gastroesophageal reflux disease as recorded by 3-hour esophageal pH monitoring. Rom J Gastroenterol. 2005; 14(2): 117–21. [PubMed: 15990929]
47. Kahrilas PJ, Shi G, Manka M, et al. Increased frequency of transient lower esophageal sphincter relaxation induced by gastric distention in reflux patients with hiatal hernia. Gastroenterology. 2000; 118(4):688–95. [PubMed: 10734020]
48. Fisher BL, Pennathur A, Mutnick JL, et al. Obesity correlates with gastroesophageal reflux. Dig Dis Sci. 1999; 44(11):2290–4. [PubMed: 10573376]
49. Wu JC, Mui LM, Cheung CM, et al. Obesity is associated with increased transient lower esophageal sphincter relaxation. Gastroenterology. 2007; 132(3):883–9. [PubMed: 17324403]
50. Pandolfino JE, El-Serag HB, Zhang Q, et al. Obesity: a challenge to esophagogastric junction integrity. Gastroenterology. 2006; 130(3):639–49. [PubMed: 16530504]
51. Lambert DM, Marceau S, Forse RA. Intra-abdominal pressure in the morbidly obese. Obes Surg. 2005; 15(9):1225–32. [PubMed: 16259876]
52. Varela JE, Hinojosa M, Nguyen N. Correlations between intra-abdominal pressure and obesity-related co-morbidities. Surg Obes Relat Dis. 2009; 5(5):524–8. [PubMed: 19560978]
53. El-Serag HB, Tran T, Richardson P, et al. Anthropometric correlates of intragastric pressure. Scand J Gastroenterol. 2006; 41(8):887–91. [PubMed: 16803686]
54. Geliebter A, Hashim SA. Gastric capacity in normal, obese, and bulimic women. Physiol Behav. 2001; 74(4–5):743–6. [PubMed: 11790438]
55. Granstrom L, Backman L. Stomach distension in extremely obese and in normal subjects. Acta Chir Scand. 1985; 151(4):367–70. [PubMed: 4036492]
56. Zahorska-Markiewicz B, Jonderko K, Lelek A, et al. Gastric emptying and obesity. Hum Nutr Clin Nutr. Jul; 1986 40(4):309–13. [PubMed: 3744891]
57. Wright RA, Krinksy S, Fleeman C, et al. Gastric emptying and obesity. Gastroenterology. 1983; 84(4):747–51. [PubMed: 6825986]
58. Tosetti C, Corinaldesi R, Stangellini V, et al. Gastric emptying of solids in morbid obesity. Int J Obes Relat Metab Diord. 1996; 20(3):200–5.
59. Buchholz V, Berkenstadt H, Goitein D, et al. Gastric emptying is not prolonged in obese patients. Surg Obes Relat Dis. 2012
60. Kelesidis I, Kelesidis T, Mantzoros CS. Adiponectin and cancer: a systematic review. Br J Cancer. 2006; 94(9):1221–5. [PubMed: 16570048]
61. Rubenstein JH, Dahlkemper A, Kao JY, et al. A pilot study of the association of low plasma adiponectin and Barrett's esophagus. Am J Gastroenterol. 2008; 103(6):1358–64. [PubMed: 18510610]
62. Rubenstein JH, Kao JY, Madanick RD, et al. Association of adiponectin multimers with Barrett's oesophagus. Gut. 2009; 58(12):1583–9. [PubMed: 19570765]
63. Weigle DS. Leptin and other secretory products of adipocytes modulate multiple physiological functions. Ann Endocrinol (Paris). 1997; 58(2):132–6. [PubMed: 9239232]
64. Ogunwobi O, Mutungi G, Beales IL. Leptin stimulates proliferation and inhibits apoptosis in Barrett's esophageal adenocarcinoma cells by cyclooxygenase-2-dependent, prostaglandin-E2-mediated transactivation of the epidermal growth factor receptor and c-Jun NH2-terminal kinase activation. Endocrinology. 2006; 147(9):4505–16. [PubMed: 16740977]
65. Kendall BJ, Macdonald GA, Hayward NK, et al. Leptin and the risk of Barrett's oesophagus. Gut. 2008; 57(4):448–54. [PubMed: 18178609]
66. Ness-Jensen E, Lindam A, Lagergren J, et al. Weight loss and reduction in gastroesophageal reflux. A prospective population-based cohort study: the HUNT study. Am J Gastroenterol. 2013; 108(3):376–82. [PubMed: 23358462]

67. Singh M, Lee J, Gupta N, et al. Weight loss can lead to resolution of gastroesophageal reflux disease symptoms: a prospective intervention trial. Obesity (Silver Spring). 2013; 21(2):284–90. [PubMed: 23532991]
68. Fraser-Moodie CA, Norton B, Gornall C, et al. Weight loss has an independent beneficial effect on symptoms of gastro-oesophageal reflux in patients who are overweight. Scand J Gastroenterol. 1999; 34(4):337–40. [PubMed: 10365891]
69. Kjellin A, Ramel S, Rossner S, et al. Gastroesophageal reflux in obese patients is not reduced by weight reduction. Scand J Gastroenterol. 1996; 31(11):1047–51. [PubMed: 8938895]
70. Livingston EH. The incidence of bariatric surgery has plateaued in the U.S. Am J Surg. 2010; 200(3):378–85. [PubMed: 20409518]
71. Chiu S, Birch DW, Shi X, et al. Effect of sleeve gastrectomy on gastroesophageal reflux disease: a systematic review. Surg Obes Relat Dis. 2011; 7(4):510–5. [PubMed: 21130052]
72. DeMaria EJ. Bariatric surgery for morbid obesity. N Engl J Med. 2007; 356(21):2176–83. [PubMed: 17522401]
73. Frezza EE, Ikramuddin S, Gourash W, et al. Symptomatic improvement in gastroesophageal reflux disease (GERD) following laparoscopic Roux-en-Y gastric bypass. Surg Endosc. 2002; 16(7): 1027–31. [PubMed: 11984683]
74. Cobey F, Oelschlager B. Complete regression of Barrett's esophagus after Roux-en-Y gastric bypass. Obes Surg. 2005; 15(5):710–2. [PubMed: 15946466]
75. 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(6):479–84. [PubMed: 9730504]
76. De Groot NL, Burgerhart JS, Van De Meeberg PC, et al. 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. [PubMed: 19758397]
77. Korenkov M, Kohler L, Yucel N, et al. Esophageal motility and reflux symptoms before and after bariatric surgery. Obes Surg. 2002; 12(1):72–6. [PubMed: 11868303]

Key Points

- The prevalence of obesity and GERD have increased substantially in the past 30 years.
- Central adiposity, measured as the waist to hip ratio, is more closely associated with GERD complications than measures of overall obesity such as BMI.
- Visceral adipose tissue is metabolically active and secretes adipokines along with inflammatory cytokines that may predispose to complications of GERD such as Barrett's esophagus and esophageal carcinoma

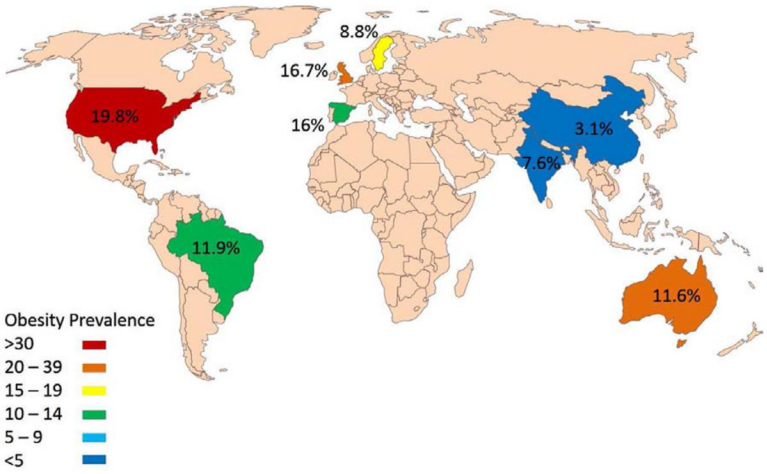

FIGURE 1.

World map of obesity and GERD prevalence in select countries. The obesity prevalence coded by the color key. The percentages indicate the GERD prevalence. Data from Refs 2, 5, 21–29.

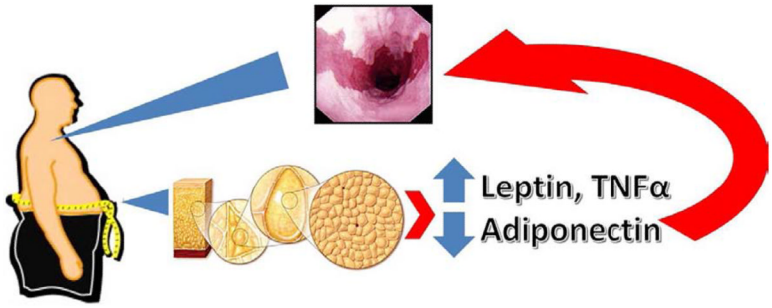

FIGURE 2.

Mechanism of increased abdominal obesity leading to Barrett's esophagus. The increased adipose tissue leads to increases in leptin and TNFα which have been linked to a higher risk of Barrett's. Increased adipose tissue has also been inversely linked with adiponectin levels which are protective for the development of Barrett's.

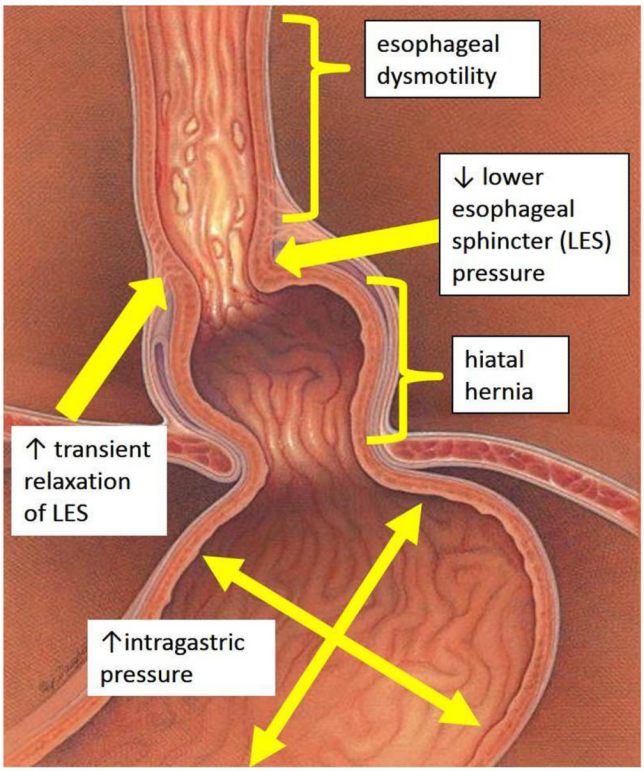

FIGURE 3.
Summary of potential pathogenic mechanisms in the obese leading to GERD.

Table 1

Risk Factors for GERD

Obesity	Pregnancy	Hiatal Hernia
Caffeine intake	Alcohol	Decreased LES tone
Spicy Foods	Recumbent position	Zollinger-Ellison syndrome
Tobacco	Connective tissue disorders	Post-prandial supination