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GERD AND OBESITY

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The introduction of minimally invasive surgical techniques in the management of both obesity and gastroesophageal reflux disease (GERD) has made surgical intervention itself as well as earlier intervention more palatable. Gastroesophageal reflux is extremely common in Western society. Fifteen to twenty percent of adults in the United States experience episodes of GERD. GERD can be a lifelong problem with multiple sequelae including erosive esophagitis, Barrett's changes of the esophagus, stricture formation, and ultimately adenocarcinoma of the esophagus. Quality of life is also negatively impacted by the presence of GERD.[1] Obesity, defined as a body mass index (BMI) greater than 30 kg/m^2,[2] is a significant problem today. The incidence of this disease is rapidly increasing, with an estimated 22 million now considered to be morbidly obese (BMI $>$ 40 kg/m^2).[3] There are many comorbid conditions that are associated with being morbidly obese. These include diabetes, hypertension, and sleep apnea. It is common to find gastroesophageal reflux associated with morbid obesity. The incidence of GERD in the obese has been reported as high as 72%.[4] In a series of 826 patients with a BMI of 48 kg/m^2 presenting for gastric bypass surgery the presence of GERD was 18%.[5] Though there are persons affected with GERD who are not overweight, the actual causal relationship of these two diseases is unknown in the setting of normal acid clearance mechanisms. This is a particularly important question to answer because the management of these diseases separately can be quite different. Though initially both of these diseases are managed by lifestyle modification and medication, severe and refractory cases do come to surgical intervention. This chapter will address the following questions: (1) Is there an association between obesity and GERD? (2) What is the effect of obesity on traditional antireflux surgical therapies? (3) What are the surgical options available for patients with morbid obesity and how do they affect GERD?

RELATIONSHIP OF OBESITY AND GERD

The relationship of GERD symptoms and BMI is unclear. A relationship between GERD increasing BMI has been suggested in females. There appears to be an augmentation of this relationship with the addition of postmenopausal hormones. Recently a publication reviewing the Helseundersolkelsen I Nord-Trondelag (HUNT 2) survey[1] examined the relationship between obesity and estrogen as risk factors for gastroesophageal reflux symptoms. In males, a dose-dependent observation between an increase in BMI and reflux symptoms was observed. In males with a BMI greater than 35 kg/m^2 there was a threefold increase in symptoms compared to normal-weight men. In women the trend was even stronger, with a sixfold increase in GERD symptoms compared to a normal-weight patient. The association of BMI and GERD symptoms was statistically stronger in severely obese premenopausal women compared to postmenopausal women. There was increase in GERD symptoms in the highest BMI category of women who had received hormone therapy, suggesting an effect modification.

Obesity may also increase the severity of GERD. El-Serag et al. reviewed risk factors for the severity of erosive esophagitis. Patients were identified during screening esophagogastroduodenoscopy (EGD) for a study of *Helicobacter pylori*–negative patients being treated with esomeprazole or omeprazole to treat erosive esophagitis. There were 6,709 patients identified. Patients were stratified into mild or severe esophagitis based on the Los Angeles classification of esophagitis: Grade A, one or more mucosal breaks less than 5 mm in maximal length; Grade B, one or more mucosal breaks greater than 5 mm without continuity across mucosal folds; Grade C, continuous mucosal breaks that involve less than 75% of the circumference of the esophagus; Grade D, more than 75% of the mucosal surface contains continuous mucosal breaks. In comparing mild esophagitis (LA grades A and B) to severe esophagitis (LA grades C and D), having a BMI greater than 35 kg/m^2 was a significantly greater risk factor for the development of EE than having a BMI less than 35 kg/m^2. The relationship of BMI and esophagitis did not exist as a continuous but rather as a dichotomous variable.[6]

One of the concerns of prolonged reflux disease is the progression to malignancy. The incidence of esophageal adenocarcinoma has increased rapidly in the United States over the past several years. Engle et al. evaluated the population adjustable risk (PAR) for patients being studied with

esophageal and gastric malignancy. PAR is the proportion of a disease that is attributable to a particular risk factor. The PAR gives an idea of the societal health sequelae of the particular risk. Patients with gastric adenocarcinoma, esophageal squamous carcinoma, and gastric cardia adenocarcinoma were evaluated. In patients with esophageal adenocarcinoma and gastric cardia adenocarcinoma the PAR of obesity (BMI greater than the lowest quartile) was 41% and 19.2% respectively. A history of smoking, in comparison, had a PAR of 39.7% for esophageal adenocarcinoma.[7]

Data linking the actual presence of GERD symptoms to obesity is not concrete. There are several population-based surveys that have mixed results. A German study composed of 5,000 respondents to a calling center identified 1,296 patients with heartburn and regurgitation. Subjects were grouped according to BMI: less than 25 kg/m^2, 25 to 30 kg/m^2, and greater than 30 kg/m^2. Neither the frequency nor the duration of the reflux symptoms differed significantly in any group. Notably, the range of BMIs in this study does not reflect the extreme range of BMIs of patients who come to the surgeon for consideration of bariatric surgery.[8] Locke et al.[9] from the Mayo Clinic reported an association between symptoms of GERD and BMI. Drawing on the Rochester Epidemiologic Project they were able to identify 2,118 patients between the ages of 25 and 74 years of age. The population represented a random sample of patients cared for in Olmstead County, Minnesota, between 1988 and 1991. Age groups were stratified at 5-year intervals until 110 patients were identified in each age and gender strata. Seventy-two percent of the subjects responded to the questionnaire. Heartburn or regurgitation was reported in 57% of these participants. Symptoms were categorized into frequent (weekly) or infrequent. In the final analysis, symptoms of GERD were more common in respondents with the highest BMI (>30 kg/m^2). When broken down, the percentage of patients with frequent GERD increased from 15% in those patients with a BMI less than or equal to 24 kg/m^2 to 30% in those patients with a BMI greater than 30 kg/m^2. In this study there was a significant linear trend to an increase in symptoms in relation to an increase in BMI units. Another prospective study of 1,228 patients demonstrated the BMI to be higher in patients with endoscopic evidence of GERD than in those patients with an otherwise normal endoscopy.[10,11]

Not all studies have consistent findings. A nationwide case control study in Sweden failed to show a relation between gastroesophageal reflux symptoms and body mass. In this study the primary aim was to identify risk factors for adenocarcinoma of the esophagus and gastric cardia. Participants in the study were randomly selected middle-aged or elderly patients. The average age of patients experiencing reflux symptoms of at least once per week was 66. There was no relationship between the maximal BMI and the risk of GERD either as a dichotomous or continuous variable.[12]

It is important to note that the upper limit BMI in the population-based studies was 30 kg/m^2 or greater. The average BMI of patients who present for bariatric procedures is at least 45 kg/m^2 in most studies. Fisher et al.[13] studied 30 morbidly obese patients who were being evaluated for bariatric surgery. Twenty-eight of these patients were also evaluated for evidence of GERD, both by subjectively and objectively using 24-hour pH probe monitoring. All 30 patients underwent manometry. The mean BMI of the group was 51.5 kg/m^2, with a range of 40.3 to 76.4 kg/m^2. The authors found a significant correlation between an increase in the BMI and an increase in esophageal acid exposure and episodes of acid reflux ($P < .05$). The average BMI of those patients with an upright esophageal pH less than 4 for less than 5% of the time was 48.1, whereas the average BMI for patients with a pH less than 4 for more than 5% of the time was 57 when upright ($P < .05$). Statistical significance was also found for those patients who were supine. BMI was significantly different in terms of normal versus abnormal reflux scores: the average BMI of patients with a total reflux score less than 14.5 was 47.5 kg/m^2 whereas the average BMI was 52.15 for those patients with a reflux score greater than 14.5. Manometric data did not show any correlation between BMI, lower esophageal sphincter pressure, or esophageal body peristalsis.

MECHANISMS OF REFLUX IN OBESITY

As difficult as it is to establish a clear causal link of obesity and GERD, it is clear that these two entities do exist in common. There have been many proposed mechanisms that may be unique to the obese patient. Clearly, patients with a defective lower esophageal sphincter, impaired acid clearance, or a hiatal hernia are more likely to develop significant reflux. It is possible to have symptoms of GERD, either typical or atypical, and have an intact physiologic barrier by manometry. There are several explanations, which include: (1) Pathologic reflux is increased in the obese because of inadequate resistance of the lower esophageal sphincter. (2) Obesity may result in a decrease in gastric emptying because of increased intra-abdominal pressure. (3) Fat at the gastroesophageal junction may alter some of the critical anatomic relationships to the crura designed to prevent reflux.

Wajed et al.[14] performed a retrospective study comparing the BMI to objective evidence of GERD using a 24-hour pH probe analysis in patients with normal manometry. They identified 70 patients and divided them into normal-weight and obese categories. BMI conversion of their presented data established two groups: thin, with a BMI of 23 kg/m^2, and obese, with a BMI of 30.7 kg/m^2. Though there was no difference in manometry, a trend toward a 1.2 cm shorter esophageal length approached significance ($P = .06$). In those patients with a normal BMI, the mean DeMeester score was 21.5, with the total time of pH less than 4 being 6.2%. In contrast, the obese cohort had a DeMeester score of 34.7 and a pH less than 4 9.2% of the time ($P < .05$).

Several years earlier, Mercer et al.[15] had examined the relationship between lower esophageal sphincter pressure and gastroesophageal pressure gradients (GEPG) in order to determine if obesity alone contributes to GERD. The authors defined GEPG as the difference between the supra-atmospheric pressure in the abdomen (baseline intragastric pressure) and subatmospheric intrathoracic pressure (baseline intraesophageal pressure). Acid sensitivity was also tested. Eight lean volunteers were selected (BMI 23 calculated from data in the paper) and eight obese patients (calculated BMI 46) without clinical evidence of GERD. Incidentally, six of the eight obese patients were noted to have a small hiatus hernia. No significant differences in the lower esophageal sphincter pressures were noted between the groups. There was a significant difference in the GEPG in the obese patients. Six of the seven obese patients experienced heartburn during acid testing, suggesting an indirect presence of abnormal reflux. One of the concerns in the interpretations of this study was the significant presence of hiatus hernias in the obese patients. Wilson et al.[10] retrospectively reviewed 1,389 patients undergoing upper endoscopy between 1974 and 1995. There was a significant relationship between increase in BMI and the presence of hiatus hernia. This was also true for the presence of esophagitis. When controlling for the effect of hiatus hernia the relationship of BMI and esophagitis was diminished but still remained significant. Another postulated mechanism for the increase in reflux in the obese patient is an increase in transient lower esophageal sphincter relaxations. By placing intragastric balloons in morbidly obese patients, Hirsch et al.[16] were able to demonstrate that the resultant chronic gastric distension increased reflux up to 10 weeks. There was a concomitant rise in the lower esophageal sphincter pressure. The mechanism of reflux was an increase in the transient lower esophageal sphincter relaxations. This effect diminished after 20 weeks, suggesting some adaptation.

Differences in gastrointestinal secretory function have been postulated as possible contributions to GERD in obese patients. Wisen et al., however, were unable to demonstrate difference in gastric acid output in obese compared to thin patients following a fat-rich meal.[16a,16b] On the other hand, obese patients were found to have higher resting-state bile and pancreatic secretion outputs than normal patients, although response to cholecystokinin of these secretions was half that of controls. Barak et al. have suggested that this may change the composition of the refluxed material by enhancing GERD symptoms.[17]

MANAGEMENT STRATEGIES FOR GERD IN OBESE PATIENTS

Traditionally, approaches to GERD have been disease-specific rather than etiology-specific. Patients are first managed medically with bed elevation, avoidance of caffeine, and avoidance of chocolate. Traditionally, patients have been asked to lose some weight. Proton pump inhibitors are generally added. Efforts to date have been on treatment of the peptic reflux rather than its cause. These patients may have associated dyslipidemias, insulin resistance, hypertension or other comorbid conditions that may stem from the same etiology as the reflux. Surgical management of GERD is considered for intractability or for quality of life issues. Another subgroup of patients are "failures" of primary antireflux procedures who are also morbidly obese.

Operations to treat reflux are generally of two types: those that augment or bolster physiologic or anatomic defenses against reflux or those that divert acid or bile or diminish parietal cell mass in order to diminish reflux. Examples of bolstering procedures include the Nissen fundoplication, the anterior Dor fundoplication (180°), the posterior Toupet fundoplication (270°). Additional procedures include the Hill posterior gastropexy and the transthoracic Belsy wrap.[18,19] Different approaches are based on surgeon experience and anatomic considerations (i.e., obesity, reoperative surgery). Further differences in wrap technique are based on findings at manometry. For severely disordered peristalsis, Toupet fundoplication would be considered over a Nissen (360°) wrap to prevent dysphagia.

When gastroesophageal physiology is not necessarily a problem, a number of different approaches exist. In patients with severe diabetes or history of vagal injury, pyloroplasty is a viable option. In fact in persons with seemingly normal lower esophageal sphincter pressure and intact clearance mechanisms, it may be reasonable to consider a gastric emptying study.

Some authors have found a significant association between reflux and duodenal reflux. DeMeester described the duodenal switch (DS) to minimize duodenogastric reflux. In this operation the stomach is left intact and there is no vagotomy.[20] The pylorus and proximal duodenum are left intact. Later this operation was modified by Hess et al.[21] to include gastric sleeve resection to promote weight loss and diminish parietal cell mass. The presence of duodenum markedly decreases the incidence of marginal ulceration and decreases the frequency of dumping syndrome.

In patients with severe reflux esophagitis and Barrett's changes of the esophagus, Csendes et al.[22] have devised a similar strategy to the DeMeester group. In this procedure a fundoplication is added to a vagotomy, antrectomy, and Roux-en-Y gastrojejunostomy.

OUTCOMES OF GERD PROCEDURES IN OBESE PATIENTS

The procedures designed to increase cardioesophageal competence have been a successful treatment of GERD symptoms in patients of normal weight. As patterns of failure are recognized, more emphasis is placed on the role of obesity as a risk factor for recurrence in traditional fundoplication-type procedures. Perez et al.[23] reviewed the records of 224

consecutive patients undergoing antireflux procedures. Patients were classified into groups based on the operation performed (laparoscopic Nissen fundoplication or Belsy Mark IV procedures) or their BMIs (<25, 25–30, or >30). The mean follow-up was 37 months; 21.4% of patients were obese (BMI > 30 kg/m^2). They observed a total of 26 recurrences; 31% of these recurrences were in the obese group compared with 4.5% in the normal weight group ($P < .05$). Looking at difference of procedures, there was no difference in the obese subgroup.

Conversely, other authors have not observed this clear pattern of failure in obese patients undergoing fundoplication type procedures. McNatt et al. identified 37 patients with a BMI greater than 35 from a prospectively collected database of 1,000 patients undergoing laparoscopic antireflux surgery between October 1991 and October 1999. There was no improvement in symptoms scores between preoperative and postoperative in both groups. Curiously, there was a difference in regurgitation scores at final follow-up (<1 year) in the morbidly obese group compared with the normal group.[24] Fraser et al. did not observe a correlation between BMI and outcome 1 year following laparoscopic antireflux surgery.[25]

Though the data is somewhat mixed regarding the efficacy of cardioesophageal bolstering, it is clear that these procedures alone will do little to treat the underlying disorder and associated comorbid conditions.

OBESITY PROCEDURES AND GERD

Criteria for bariatric surgery are more rigid perhaps than for traditional antireflux procedures. Patients must meet National Institutes of Health (NIH) criteria for surgery: having a BMI greater than 40 kg/m^2 or with significant comorbid conditions plus a BMI greater than 35 kg/m^2. There must be a documented series of weight loss attempts and no untreated psychopathology.[26]

Bariatric procedures work through two mechanisms. Both mechanisms ideally result in significant weight loss that will alter intra-abdominal pressure and possibly diminish the gradient across the lower esophageal sphincter. One mechanism of producing weight loss is by purely increasing gastric or esophageal restriction to produce a sense of fullness or possibly satiety. Examples of these procedures include the vertical banded gastroplasty (VBG) and the esophagogastric band. Procedures such as gastric partitioning (removing staples from the middle of a gastric stapler with reinforcement of the stoma) and adjustable gastric banding are of historical interest and will not be further discussed. These other types of bariatric procedures include malabsorptive operations such as the DS as described previously and the biliopancreatic diversion (BPD). A combination of the restrictive and malabsorptive procedures is the gastric bypass. Here gastric restriction with a small pouch is combined with a variable length intestinal bypass to enjoy the benefits of both procedures. All of these procedures, including a number of revisional procedures, can be performed laparoscopically.

In theory, both of the gastric restrictive procedures should reduce weight loss, and this in turn may diminish GERD symptoms. At the time of surgery an identifiable hiatus hernia greater than 2 cm can be identified and repaired. Beyond that the two procedures differ. The esophagogastric band is placed just below the gastroesophageal junction anteriorly, possibly creating a band to reflux with gastric distension. The concept is similar to the now abandoned Anglechick prosthesis (an antireflux device); which was placed around the gastroesophageal junction.[27]

The mechanism of the malabsorptive procedures is primarily to direct bile, as in the case of the BPD or DS. There is reduction of parietal cell mass, but the gastric conduit still remains about 200 to 500 cc. The gastric bypass involves an extremely small pouch and in some cases a micropouch. Theoretically this should markedly diminish acid production and leave a much smaller reservoir to be a nidus for reflux.

Outcomes relating to restrictive bariatric procedures and their response to GERD are mixed. The VBG involves a gastric band with a narrow outlet. In comparison to esophagogastric banding the ring is placed 3 to 4 cm from the gastroesophageal junction. The VBG procedure does not appear to be effective in the treatment of GERD. In fact the VBG may accentuate reflux, possibly by increasing intragastric pressure and providing a reservoir for refluxate. Vercet et al. found that the gastroplasty increased the prevalence of esophagitis even in the presence of weight loss.[28]

Results of the esophagogastric banding are better but also mixed. Slippage, one of the key complications, known to occur up to 1.5%[29] of the time, may predispose to reflux. Forsell et al. reported GERD to be one of the most frequent complications of the esophagogastric band.[30] Conversely, Dixon et al. reported an increased improvement in symptoms of GERD in patients who carried this diagnosis preoperatively.[31]

There have been many reports of symptomatic improvement of GERD following the gastric bypass. This has been observed in both laparoscopic and open cases. Improvement in GERD symptoms has also been observed in conversions of the VBG to the gastric bypass. The Roux-en-Y bypass (RYGBP) is not directly designed to augment lower esophageal sphincter pressure or change the length of the intra-abdominal esophagus. One mechanism is potential decrease in acid production in the gastric pouch. Anatomic studies have shown that the cardia of the stomach is absent of parietal cells.[32] Rather they can be seen to traverse down the lesser curvature of the stomach. In theory a small gastric cardia–based pouch would produce little in the way of acid to reflux. Markedly diminished basal and stimulated acid secretion has also been demonstrated following a gastric by-

pass. Distal bypass of bile diminishes the likelihood of alkaline reflux.

In a series involving morbidly obese patients with GERD, Smith et al. showed a significant reduction in GERD symptoms after RYGBP with or without distal gastrectomy and gastropexy, with a follow-up of 4 to 48 months.[33] GERD medication requirement was significantly decreased from 100% to 7%. Similarly, Jones et al. showed RYGBP to be an effective antireflux procedure when compared with Nissen fundoplication.[34] The same group demonstrated the efficacy of RYGBP in patients with endoscopically proven GERD and only modest obesity (mean BMI of 33 kg/m^2).[35] At 56 months follow-up only 2% were symptomatic for GERD. Balsiger et al. showed that conversion of VBG to RYGBP for management of GERD resulted in significant improvement or resolution of GERD symptoms in 96% of patients.[36] Wittgrove et al. have demonstrated substantial improvement in GERD following the laparoscopic gastric bypass in consecutive publications.

Frezza et al. recently evaluated the effect of laparoscopic RYGBP on GERD symptoms, quality of life, and patient satisfaction in 152 morbidly obese patients with chronic GERD.[37] The authors found a significant reduction in both typical and atypical GERD symptoms. The immediate improvement in symptoms suggests that GERD improvement results primarily from anatomic rearrangement and secondarily from weight loss. In addition, chronic medication use for GERD decreased from 100% to 3% after laparoscopic RYGBP. The GERD-HQRL (health-related quality of life) analysis showed very effective reflux control in all parameters studied, similar to the Nissen fundoplication. Patient satisfaction scores for improvement in GERD-related symptoms were very favorable. Quality of life changes were also favorable, suggesting benefit from weight loss and improvement in GERD.

In an attempt to define the change in gastric pouch parietal cell function, Schauer et al. evaluated 19 patients after gastric bypass for morbid obesity with a mean follow-up of 13 months. All patients had documented GERD preoperatively with a DeMeester score greater than 14.7. In 59% of patients, pH studies were still noted to be abnormal. The majority of patients had documented parietal cells by biopsy. The majority of patients had acid production in the pouch as identified by Congo red staining. Curiously, there was no relationship to the size of the gastric pouch.[5] Patterson et al. compared the changes in esophageal function and pH probe data in obese patients undergoing laparoscopic Nissen fundoplication to patients undergoing gastric bypass. Data was collected preoperatively and postoperatively for both groups. Both the laparoscopic Nissen fundoplication and gastric bypass effectively treated heartburn with no significant difference in heartburn scores. Also, there were no statistical differences in the pH probe data, either preoperatively or postoperatively, between the two groups. Interestingly, in three of the six gastric bypass patients there was a doubling on the lower esophageal sphincter pressure.[4]

Less data for the malabsorptive procedures exists. Sugerman reported a 76% resolution of GERD in patients undergoing the biliopancreatic diversion.[38] However, the likelihood of stomal ulceration following the BPD is significant.[39,40] Baltasar reported a 100% resolution of GERD symptoms following the BPD-DS at 5 years of follow-up.[41] Certainly bile reflux in the DS will be markedly diminished.

OUR APPROACH

All patients are sent a lengthy questionnaire in anticipation of their first visit to the office. Symptoms of GERD are elicited at the first visit. For patients with a significant history of GERD we primarily offer the gastric bypass. All patients with a significant history are sent for a preoperative upper endoscopy. Information from this study is used to determine the presence of a large hiatal hernia and, more important, the presence of Barrett's changes in the esophagus. The presence of ulcer disease is excluded in these patients. For those patients who are still interested in laparoscopic banding we obtain an upper GI study pH probe and manometry. If there is evidence of impaired clearance in these patients or disordered motility then we do not offer the adjustable band. A small hiatal hernia is not a deterrent to placement of an adjustable band. In patients with a large hiatal hernia, in particular in patients with a paraesophageal hernia, we perform the gastric bypass. We will not perform banding in the presence of a shortened esophagus. In those patients with concomitant ulcer disease, considerations for a biliopancreatic bypass or BPD-DS are made.

CONCLUSION

Obesity and GERD are extremely common in Western society. Evidence of linkage of the two diseases exists. GERD can exist in the presence of anatomically and physiologically intact sphincter mechanisms. Primarily antireflux surgery in patients who have a BMI greater than 35 should be deferred to obesity surgery. The gastric bypass appears to be an effective modality in the treatment of GERD in patients who are overweight.

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