Hypothesis: Obesity impairs the antireflux function of a structurally intact barrier.

Design: Retrospective analysis of body mass index in patients with normal esophageal manometric findings but with symptomatic and objectively confirmed gastroesophageal reflux.

Setting: Specialist esophageal center.

Patients: Patients symptomatic and diagnostic for gastroesophageal reflux, referred between October 1, 1998, and June 30, 2000. Exclusion criteria were a defective barrier, motility disorders, or previous surgery.

Main Outcome Measures: Reflux was defined and quantified using the DeMeester score, and body mass index was calculated.

Results: There was a strong correlation between body mass index and severity of gastroesophageal reflux. Patients who were overweight had significantly higher distal esophageal acid exposure. No significant difference in manometric findings was demonstrated between patients with normal weight and those who were overweight.

Conclusion: The barrier to gastroesophageal reflux is rendered insufficient in patients who are overweight.

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EXPOSURE of the distal esophagus to pathologic levels of refluxed gastric juices causes the clinical phenomenon of gastroesophageal reflux disease (GERD) and its sequelae. Reflux is prevented by a mechanically competent lower esophageal sphincter (LES), which provides a barrier between the gastric and esophageal compartments, and a proper clearance activity of the esophageal body by appropriate LES relaxation and peristaltic contractions on swallowing.1,2

Despite the presence of a structurally normal LES and effective esophageal clearance, excessive gastroesophageal reflux and consequent esophageal damage may still occur. In these patients, other factors must therefore exist that override the standard barrier to reflux.

A possible simple explanation for the existence of GERD in this subgroup of patients might be a local impairment of the normal barrier mechanism. This may be caused by an external alteration in the anatomical and physiological characteristics of the LES or esophageal body. Excessive fat deposition could interfere directly with the LES esophageal body complex, preventing it from functioning effectively, or it could change the intra-abdominal pressure dynamics and render the barrier incompetent. We investigated the effect of body mass index (BMI), a standard marker for obesity and body fat content, as a possible factor in the generation of GERD in these individuals.

RESULTS

Patient demographics, esophageal characteristics, and disease variables are summarized in the Table. The mean age of the entire cohort was 48.6 years (range, 19-85 years), with 41 men and 29 women. The primary presenting complaint was heartburn in 37 patients, with dysphagia and regurgitation representing another 15, totaling 52 with typical symptoms. The remainder presented with atypical symptoms still attributable to GERD. Body mass index was abnormally high in 55 patients, and no patient within this cohort qualified as being underweight. Of the 55 patients who were overweight, 37 were...
PATIENTS AND METHODS

PATIENTS

A retrospective analysis of data obtained between October 1, 1998, and June 30, 2000, was made of patients referred to the esophageal laboratory, Department of Surgery, University of Southern California, Los Angeles, for assessment of clinically suspected GERD. Patients with symptoms or a history strongly suggestive of GERD and with objective evidence of increased distal esophageal acid exposure on 24-hour ambulatory pH monitoring were excluded. Those with any structural abnormality of the LES, incomplete LES relaxation, or any abnormality of esophageal body function were excluded. Patients with a history of esophageagastrectomy were also excluded. Patients were requested to discontinue any antacid medication 2 weeks before esophageal investigations. The remaining patients formed the study cohort and consisted of those with an apparently structurally normal LES and functional esophageal body, but with objective evidence of increased acid exposure to the esophagus.

ESOPHAGEAL STUDIES

Esophageal Manometry

Manometry was performed using a single-catheter assembly consisting of 8 fluid-filled, perfused polyvinyl tubes bonded together with five 0.8-mm lateral openings placed 5 cm apart and radially oriented 120° from each other. The recording catheter was continuously perfused with distilled water using a low-compliance, pneumohydraulic capillary infusion pump (Arndorfer Medical Specialties, Green- dale, Wis) at a rate of 0.5 mL/min. Each tube was connected to an external pressure transducer positioned at the midaxillary level. Before each test, the pressure transducers were calibrated using a mercury-filled manometer, so that a change in pressure of 1 mm Hg corresponded to 0.5 mm on the recording paper. A belt pneumograph was positioned around the chest to record respiratory excursions. A piezoelectric transducer was taped on the neck at the level of the cricoid cartilage to record pharyngeal swallows. Manometry was performed in the fasted state, and all medications were discontinued 24 hours before the test. The subject was placed in the supine position and encouraged to relax. The recording catheter was passed through an anesthesiologist’s nostril into the stomach and withdrawn at 1-cm increments every 20 seconds back into the esophagus.

The 3 manometric characteristics of the distal esophageal sphincter measured were sphincter pressure, abdominal length, and overall length. The end respiratory gastric baseline pressure was used as a zero reference for pressure measurement. A persistent rise in pressure exceeding 2 mm Hg above the gastric baseline marked the distal border of the sphincter. The proximal border was marked by the point at which sphincter pressure dropped to end-inspiratory esophageal baseline pressure. Five measurements of the distance between these 2 points were averaged and represented the overall length of the sphincter. The point at which the end-inspiratory pressure changed from a positive to a negative deflection represented the respiratory inversion point. Five measurements of the distance between the respiratory inversion point and the distal border of the sphincter, that is, the length of the pressure wave that reflected positive excursions with respiration, were averaged and represented the abdominal length of the sphincter. The amplitude of the sphincter was measured as the difference (in millimeters of mercury) between the gastric baseline and the pressure at the respiratory inversion point during the middle of the respiratory

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classified as grade 1 overweight, 16 were grade 2 overweight, and 2 were grade 3 overweight.

Manometric evidence of a hiatal hernia was present in 35 patients. No significant differences in patient characteristics, however, were noted between those with and without evidence of a hiatal hernia, including BMI and the esophageal and reflux severity variables presented in the Table. Similarly, subgrouping patients on the basis of sex or presenting symptoms (typical vs atypical) did not reveal any significant differences among any variables.

A strong and significant correlation between BMI and DeMeester score was observed. Using Spearman ρ analysis, a coefficient of 0.38, with P < .001, was derived (Figure 1). A similar relationship was also noted between BMI and the total percentage duration the pH was less than 4 (coefficient 0.26, P = .03).

Dichotomizing the cohort into normal and overweight subgroups based on BMI confirmed the major difference in the objective severity of esophageal acid exposure. For patients with a normal BMI, the mean DeMeester score was 21.5, and the total percentage duration the pH was less than 4 was 6.2%. This compared with a mean score of 34.7 and a percentage duration of 9.2% for the patients who were overweight. Using a Mann-Whitney analysis, this difference was significant, with P < .001 for the DeMeester score (Figure 2) and P < .01 for the total percentage duration the pH was less than 4. Nearly half the patients with a normal BMI had abnormal acid exposure during the postprandial period, while only a small number of the overweight group had the same problem, with 22 (40%) of these having upright reflux disease.

Further subdivision of the overweight patients into their respective WHO classification groups reflected the trend of increasing distal esophageal acid exposure with increasing BMI, although these did not distinguish themselves from each other statistically. Of note, it appeared that weight alone, as opposed to weight and height, was the major discriminating factor between the 2 groups. Both groups had a similar mean height but contrasted markedly in weight.

No significant differences with regard to patient details or manometric features were noted between the normal and overweight groups. Lower esophageal sphincter lengths and pressures were almost identical. However, the difference in manometric esophageal lengths, with a mean shorter value of 1.2 cm in patients who were overweight, approached significance in this study (P = .06).
cycle. Five measurements of resting sphincter pressure were obtained and averaged to obviate the variation of pressures at each orifice due to the radial asymmetry of the sphincter.

Normal values for the overall length of the sphincter, abdominal length of the sphincter, and resting sphincter pressure were defined as greater than 2 cm, greater than 1 cm, and 6 to 26 mm Hg, respectively, with values outside these limits representing the 2.5th percentile of a normal population distribution.3

The presence of a “double hump” profile of the lower esophageal high pressure zone signifies manometric evidence of a hiatal hernia, and measurements of the LES were made at the start of the most proximal hump, in these cases.

Relaxation of the LES was determined by positioning 4 radially placed channels at the level of the respiratory inversion point, and the activity at this level and the channel 5 cm proximal to it (within the distal esophagus) was recorded in response to 5 separate swallows of 5-mL water boluses. Normal relaxation was recorded if the pressure in the LES fell to gastric baseline during the swallows.

Esophageal body motility was investigated by placing the 3 recording channels along the length of the esophagus. The most proximal channel was located at a point 1 cm distal to the lower border of the upper esophageal sphincter, and pressure activity was assessed in response to 10 separate swallows each of a 5-mL water bolus. Normal esophageal motility was recorded only if normal peristalsis in the total absence of simultaneous or interrupted waves occurred, and if the pressure at each level was within normal 95th percentile limits for that level.

Distal Esophageal Acid Exposure

This was determined by 24-hour ambulatory pH monitoring. A 1-channel bipolar pH probe (Ingold; MUI Scientific, Mississauga, Ontario) was positioned to lie 5 cm proximal to the manometric upper border of the LES. Using a digital data recording device (MK III; Medtronic, Shoreview, Minn), pH in the distal esophagus was monitored for 24 hours, during which a test refluxogenic meal was given to induce postprandial reflux. To assess positional reflux, the patients were asked to maintain a diary to record activity. Calculation of a composite (DeMeester) score was used to assess severity of the reflux disease,3,4 and the total duration that the esophageal pH was less than 4 was recorded and expressed as a percentage of total ambulatory duration.

EVALUATION OF OBESITY

Body mass index was calculated as weight in kilograms divided by the square of height in meters. Using the World Health Organization (WHO) classification,5 a normal BMI was defined as a value between 18.5 and 24.9. Values of 25.0 to 29.9 were defined as grade 1 overweight, 30.0 to 39.9 as grade 2 overweight (obese), and 40.0 or higher as grade 3 overweight (morbidly obese).

STATISTICAL ANALYSIS

Data were reported as mean±SEM. Correlation between variables was assessed using Spearman ρ analysis. Nonparametric testing between 2 groups of variables was carried out using a Mann-Whitney analysis, and a Fisher exact test was used for comparison between 2 sets of distinct subgroups. All tests were 2-tailed, with significance defined as P<.05. Analysis was performed using standard commercially available biomedical software (SPSS, version 10.0; SPSS Inc, Chicago, Ill).

The key question in understanding the pathophysiology of GERD is what causes an overriding of the normal valve mechanism. Structural defects in the LES or esophageal body dysfunction predispose to disease evolution in most cases.6,7 In this study, we identified a cohort of patients who shared the same manometric LES and esophageal body characteristics as 97.5% of the normal, asymptomatic general population, but whose distal esophagus was not protected from excessive gastric juice exposure. Fifty-five (79%) of these patients had an elevated BMI, and the increasing level of their obesity strongly correlated with the severity of the gastroesophageal reflux. This overweight subgroup of patients had a greater degree of reflux, as measured by pH probe, than the small number with a normal BMI. Patients with a normal BMI in this study had a mild level of increased distal esophageal acid exposure, predominantly during the postprandial period.

Obesity is now regarded as a worldwide disease of epidemic proportions, which may induce ill health through several means. It is strongly associated with a wide spectrum of medical diseases, including diabetes mellitus, cardiovascular and respiratory disorders, cho-
sure, may interfere with and delay gastric emptying.15 This nal viscera, in addition to elevating intra-abdominal press-
ting. Similarly, the potentiation effect on sphincter com-
distension to more readily induce transient sphincter op-
come blunted, thus enabling moderate levels of gastric
tric wall tension from pulling the LES apart,11,12 may be-
tained pressure, and this relates to the sagittal abdominal
space within the peritoneal cavity is likely to result in re-
sum to 100 because of rounding.

The finding of similar values for the LES character-
istics in both groups suggests that the barrier intrinsi-
cally is not at fault in causing reflux in the patients who
were overweight. It has been argued that a neural phe-
nomenon is primarily responsible for generating gastro-
esophageal reflux, through so-called transient LES re-
laxations.17 Therefore, by some unexplained mechanism,
obesity invokes an increased frequency or duration of
these events. There is no obvious evidence for this and
no clear reason why progressive increases in BMI should
potentiate this effect. A direct, multifactorial mechan-
ical process, interfering with the ability of the LES to pre-
shortening or to offer adequate resistance to gastric
pressure, is a more obvious explanation for the observa-
tions in this study.

Obese individuals have a higher intra-abdominal rest-
ing pressure, and this relates to the sagittal abdominal
diameter.14 Excess fat deposition in and around abdomi-
ral viscera, in addition to elevating intra-abdominal press-
ure, may interfere with and delay gastric emptying.15 This
promotes fundic distension, with corresponding sphinc-
ter unfolding and length shortening, reducing its ability
to function as an effective barrier.16 The restriction of free
space within the peritoneal cavity is likely to result in re-
duced pressure compliance within the abdominal com-
partmen. Fluctuations in the intra-abdominal press-
ure, such as occurs with positional or postural change,
coughing, or straining, are therefore exaggerated, with
sudden sharp rises in gastric pressure overcoming LES
resistance.

The finding of similar values for the LES character-
istics in both groups suggests that the barrier intrinsi-
dently associated with GERD. Studies of the massively obese and investigations of the effect of weight loss therapy in symptomatic improvement have been contradictory in their conclusions.

This study investigated patients with definitive symptoms and proven disease and then specifically examined those in whom reflux would not normally be expected to occur. This population will thus differ from more generalized studies. Among these patients, those who have a normal BMI have a mild form of disease and might benefit therapeutically from simple conservative measures, including lifestyle changes. Patients who are overweight, however, have a more severe form of disease. There may be some benefit achieved from simple weight reduction, although compliance with this form of treatment is likely to vary considerably, depending on the individual patient. There is also a potential role of surgical intervention. Because the barrier to reflux in these patients is rendered ineffective, augmentation of LES resting pressure and length could provide sufficient reserve to prevent the mechanistic overriding from taking place. Simple endoscopic procedures or laparoscopic Nissen fundoplication will prevent loss of length with gastric distension and thus restore barrier competency.

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REFERENCES


Carlos Pellegrini, MD, Seattle, Wash: As you know, primarily because of the work done by the World Health Organization, body mass index has emerged as the best proxy to measure the effects of overweight on health. It has been clearly shown that several diseases, like hypertension, degenerative joint diseases, diabetes, and even small increases in BMI, significantly change health. The authors of this study examined the relationship between the BMI and esophageal acid exposure in a group of 70 patients who had 24-hour pH monitoring demonstration of pathologic reflux and symptoms of abnormal gastroesophageal reflux. They found that in 55 of the 70 patients who had BMIs greater than 25, and would therefore be considered obese under the WHO classification, acid exposure was greater than in the 15 patients who had a BMI in the normal range. They also found a direct correlation between BMI and specific DeMeester score. Previous studies looking at obesity and the presence of abnormal gastroesophageal reflux have yielded conflicting information. Some studies have shown that, indeed, there is a positive correlation, and some large studies have failed to show that. What, then, is unique about the study you have heard today?

There are 2 aspects of this study that make it unique. First, the authors have an objective demonstration of gastroesophageal reflux. Many of the previous studies have been based simply on questionnaires. Secondly, the authors limited the study to a group of patients who have a structurally competent LES, that is, people who would normally not be expected to be refluxing. That is what I want to focus on. Limiting the study to a group of patients with the structurally competent LES eliminates a number of potential confounding factors and allows one to look at the effects of BMI on acid exposure. On the other hand, what concerns me is that if one is trying to determine the effects of obesity on reflux, limiting the study to just patients with a structurally normal sphincter eliminates essentially all patients with very severe reflux and eliminates, in fact, most patients with abnormal gastroesophageal reflux. Thus, the overall impact of obesity on acid exposure may be missed altogether. Is it possible, for example, that obesity, by increases in intragastric pressure as they suggested, leads to the develop-
opment of hiatal hernia or shortening of the sphincter? None of these patients would have been included in the study. Therefore, it would be important for the authors to tell us what the overall relationship is in their database between BMI and acid exposure in all patients, not just those with structurally incompetent sphincter.

The second question would be, since they postulated that increases in intra-abdominal pressure may be the result of an increase in BMI, was the intragastric pressure in these patients increased? Intragastric pressure is a good way to measure intra-abdominal pressure. Did they look at the transient LES relaxation in these patients? . . . increases in frequency or duration?

Lastly, from the point of view of a practical surgeon, is decreasing BMI and decreasing body weight really a cure for gastroesophageal reflux? Have they had any experience measuring acid exposure before and after losing significant amounts of weight? We have looked at symptoms and weight loss in a very small group of 6 patients who took the challenge of losing a significant amount of weight and were surprised to see that we did not see any decrease in symptoms or any decrease in acid exposure, despite the loss of weight, suggesting that, once a certain threshold is crossed in weight gain, in a certain individual, a certain damage occurs to the antireflux mechanism that cannot be repaired simply by losing weight.

Richard J. Finley, MD, Vancouver, British Columbia: There is a difference in distribution of fat between men and women. Males tend to have a greater percentage of fat in their peritoneal cavity than females, which may increase intra-abdominal pressure. Did the authors notice a difference in reflux between the sexes?

My other experience is that it is very difficult to get patients to lose weight when there is poor control of their reflux. What are your strategies for weight loss in patients with significant GERD?

Ronald W. Busuttil, MD, Los Angeles, Calif: Although the sphincter was hindered with obesity, was there a higher incidence of esophagitis, ulcers, or Barrett’s disease in these patients vs the nonobese? Secondly, did the proton-pump blockers have any kind of effect, or was it blunted in these obese patients compared with the normal patients?

Pellegrini, your first question was what is the relationship of BMI to acid exposure overall, and there was, in fact, no relationship in our study. You asked about relaxation of the LES, and relaxation was normal in both groups of patients. From a practical point of view, you asked is decreasing the BMI effective in improving the LES? Studies previously suggest not, and we haven’t, in fact, had the opportunity to do that ourselves. This would make an excellent study to assess whether obesity reduction restores barrier competency.

Dr Finley, there was no difference in the relation of sex to reflux in our series. You asked a practical question: how could we get these people to lose weight? Well, this is, as you know, a tremendous problem today, and perhaps there will one day be an alternative to bariatric surgery, which is the way we are all pushing at the moment.

There was a question about esophagitis: was esophagitis greater in the morbidly obese patients or the obese patients in our series? Our study was confined to manometric and pH studies alone, and we do not have the endoscopic details. All of these patients were off PPIs [proton-pump inhibitors] for the study.