Restoration of Normal Distensive Characteristics of the Esophagogastric Junction After Fundoplication

John E. Pandolfino, MD, Jennifer Curry, MD, Guoxiang Shi, MD, Raymond J. Joehl, MD, James G. Brasseur, PhD, and Peter J. Kahrilas, MD

Objective: To study the mechanical characteristics of the esophagogastric junction (EGJ) of postfundoplication patients and compare them with previously reported data on normal subjects and GERD patients.

Methods: Eight normal subjects, 9 GERD patients, and 8 fundoplication patients were studied with concurrent manometry, fluoroscopy, and stepwise controlled barostat distention of the EGJ. The minimal barostat pressure required to open the EGJ during the interswallow period was determined. Thereafter, barium swallows were imaged in 5-mm Hg increments of intrabag pressure. EGJ diameter and length were measured at each pressure during deglutitive relaxation.

Results: EGJ opening diameter during deglutitive relaxation was on average 0.5 cm greater in GERD patients compared with normal subjects and fundoplication patients ($P < 0.05$). EGJ opening pressure and opening diameter were comparable between normal subjects and fundoplication patients; however, the EGJ length was 32% longer in fundoplication patients.

Conclusions: Fundoplication restores distensibility of the EGJ to a level similar to normal subjects. Since trans-EGJ flow is related to EGJ length and EGJ diameter, these findings suggest that retrograde flow through the EGJ would be decreased by both a reduction in diameter and an increase in length of the EGJ.

(*Ann Surg* 2005;242: 43–48)

Under normal conditions, reflux of caustic gastric juice is prevented by an intact esophagogastric junction (EGJ). The EGJ is a complex anatomic zone whose functional integrity is attributed to the intrinsic lower esophageal sphincter (LES), extrinsic crural diaphragm, the intra-abdominal segment of the LES, integrity of the phrenoesophageal ligament, and maintenance of the gastroesophageal flap valve or acute angle of His. Each of these components is operant under specific conditions and, as each of these mechanisms are disrupted, the worse the severity of gastroesophageal reflux disease (GERD).

To explore the mechanisms of EGJ incompetence in GERD, we previously studied the mechanical properties of the EGJ of normal subjects and GERD patients with hiatal hernia using a method combining barostat technique with fluoroscopy.[1] The major finding of that study was that distensibility of the EGJ was significantly increased in GERD patients with hiatal hernia compared with normal subjects and that EGJ opening occurred at a significantly lower distention pressure in GERD patients. In addition, it also appeared that the main contributor to EGJ compliance was the hiatal canal. This increase in distensibility or compliance at the EGJ could potentially exacerbate GERD by lowering the opening pressure of the EGJ and permitting wider opening diameters, which in turn could lead to greater amounts of retrograde flow of gastric juice.

Unlike medical therapy, which seeks to reduce the causticity of gastric juice, fundoplication attempts to cure reflux by restoring the anatomic components of the antireflux barrier.[2] This is accomplished by reducing and repairing hiatal hernia, lengthening the LES, and repositioning the sphincter back into the intra-abdominal cavity so that the LES is in proximity of the extrinsic crural diaphragm. In addition, a new anatomic component is created, the fundic wrap. Together, these modifications will result in an improved EGJ pressure profile that is a function of the extrinsic effect of the hiatal canal and the fundic wrap while it is independent of the intrinsic LES.[3] Whether these surgical modifications will improve other mechanical parameters of the EGJ, such as compliance, is unclear. We hypothesize that repair of the hernia and lengthening the EGJ high-pressure zone via the wrap will decrease compliance at the EGJ. Thus, the aim

From the Department of Medicine, Northwestern University Medical School, Chicago, IL.

Supported by grant RO1 DC00646 (to P.J.K.) and K23 DK062170-01 (to J.E.P.) from the Public Health Service.

Reprints: John Pandolfino, MD, Northwestern University Feinberg School of Medicine, Division of Gastroenterology, Department of Medicine, 676 N. St. Clair St., Suite 1400, Chicago, IL 60611. E-mail: j-pandolfino@northwestern.edu.

ISSN: 0003-4932/05/24201-0043
DOI: 10.1097/01.sla.0000167868.44211.f0

of the current study was to compare EGJ distensibility in fundoplication patients to both normal subjects and GERD patients using a modified barostat technique.

MATERIALS AND METHODS

Subjects

Eight normal subjects (4 males, 24–59 years of age) without reflux symptoms, 9 patients with GERD and hiatal hernia (3 males, 22–57 years of age), and 8 postfundoplication patients (5 males, 30–68 years of age) were studied. The patients were enrolled from the endoscopy laboratory at Northwestern Memorial Hospital. Eight of the 9 hiatal hernia patients had a history of endoscopic esophagitis ($n = 8$) while the ninth had heartburn responsive to proton pump inhibitor therapy. Although these patients did not undergo fundoplication, they are representative of patients likely to undergo the procedure and had similar clinical profiles to the fundoplication group prior to surgery. At the time of the study, all patients were in endoscopic and symptomatic remission as a result of maintenance treatment with a proton pump inhibitor ($n = 7$) or nonprescription therapy ($n = 2$), and none was taking any medication known to affect esophageal contractility. None of the normal subjects or GERD patients with HH had a history of upper gastrointestinal surgery. Fundoplication patients had a good response to surgery with improvement in GERD symptoms and were not taking medication to control reflux at the time of the study. At the time of the study, patients were at a postoperative period of 3 to 52 months (median, 16 months). All patients were eating an unrestricted diet.

Fundoplication

All fundoplications were performed laparoscopically by the same surgeon (R.J.J.). At least 10 cm of the proximal stomach was mobilized by coagulating and dividing the gastrocolic and gastrosplenic omentum, including the short gastric vessels, with ultrasonic shears. In each case, the hiatal opening was found to be dilated and was narrowed by placing a single 2-0 silk suture that approximated the right and left halves of the crux behind the esophagus, buttressed with polytetrafluoroethylene pledgets. The criterion for complete fundic mobilization was that, when drawn posterior to the esophagus in preparation for the fundoplication, the gastric fundus would remain in place without continuous traction. The fundoplication was constructed after a 50-F Maloney dilator was inserted through the mouth and across the EGJ. The wrap was secured with 2 interrupted sutures of 2-0 silk placed 1 cm apart and each buttressed with polytetrafluoroethylene pledgets; the proximal 2 sutures were anchored to esophageal musculature and were placed above the anatomic EGJ. Thus, the wrap was approximately 3 cm in length and surrounded by distal esophagus, the EGJ, and proximal stomach. All patients reported a period of postoperative dysphagia that required cautious eating for a mean period of 6 weeks.

Endoscopy

All potential hiatal hernia/GERD patients underwent endoscopy to ascertain the presence and size of hiatal hernia and to localize the squamocolumnar junction (SCJ). Normal subjects and fundoplication (FP) patients were not required to undergo endoscopy. During endoscopy, which was done under conscious sedation with 1 to 4 mg of midazolam, the SCJ was marked by placement of an 11-mm stainless steel clip using a clipping device passed through the working channel of the endoscope (Olympus HX-SLR-1 clip fixing device, Japan). After appropriate postendoscopy recovery time (at least 1 hour) the patient was moved to the fluoroscopy suite for the remainder of the study. The presence of hiatal hernia was determined with fluoroscopy using the clip as a reference point for the SCJ and the indention in the barium column during a barium swallow as the location of the diaphragmatic hiatus. Patients were included in the hiatal hernia group if the position of the SCJ between swallows was $\geq$1.0 cm above the center of the hiatal impression as determined during fluoroscopy.

Manometric and Barostat Instrumentation

A custom-made 21-lumen silicon rubber extrusion was used for both the manometric recordings and barostat distention (Dentsleeve Pty. Ltd, Parkside, South Australia). This assembly incorporated a 6-cm sleeve sensor, 12 side-hole recording sites, 2 cylindrical metal tie points for the barostat bag, a large bore infusion port for the barostat bag, and pressure monitoring ports between the tie points to monitor barostat bag pressure (Fig. 1).[1] During the manometric study, each side-hole channel was connected to an extracorporeal pressure transducer and perfused with sterile water at a rate of 0.15 mL/min using a low compliance perfusion pump (Dentsleeve Mark II, 16 channel model); the sleeve channel was perfused at 0.6 mL/min. Output of the pressure transducers was connected to a computer polygraph set at a sampling frequency of 40 Hz (Neomedix systems Pty Ltd, Warriedwood, NSW, Australia) and processed using Gastromac software (Neomedix). Prior to the recording, the transducers were calibrated at 0 and 70 mm Hg using externally applied pressure. Response characteristics of each side-hole manometric channel exceeded 200 mm Hg/s.

Barostat bags were designed so that when fully distended they had a cylindrical shape (diameter, 2.75 cm; length, 20 cm). Barostat bags were constructed from polyethylene sandwich bags using a heating iron (Impulse Heat Sealer, Midwest Pacific, St. Louis, MO) and were tied at each end with nylon surgical suture over the metal tie points on the assembly. Prior to use, the catheter and bag were checked for leaks by inflation to 40 mm Hg under water. The large-bore

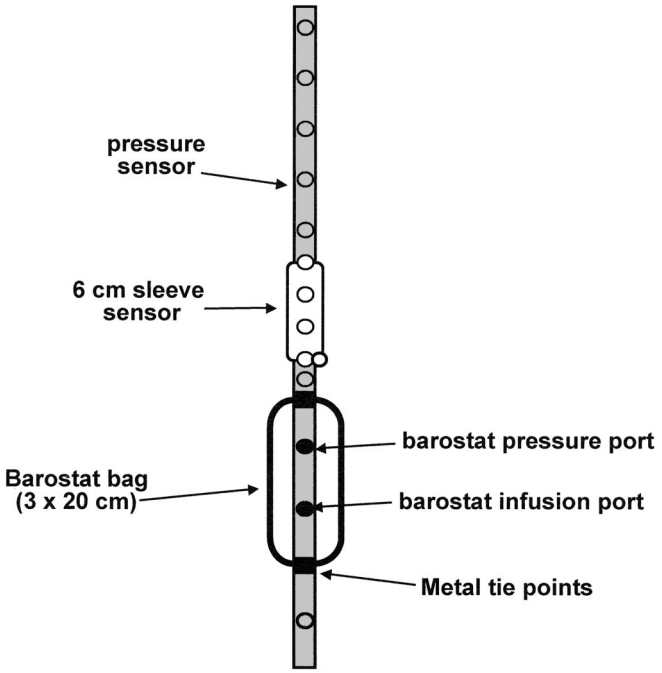

FIGURE 1. The combined manometry/barostat catheter. The sleeve sensor was used for baseline recordings of the EGJ high-pressure zone. The barostat bag was cylindrical in shape and infinitely compliant in vivo. The barostat pressure required to obtain a bag diameter of 2.75 cm ex vivo was <3 mm Hg. Thus, the barostat pressure and volume required to obtain luminal distention were dependent on the mechanical properties of the surrounding structures (EGJ) and not the elastic properties of the barostat bag.

catheter channel used to fill the bag with air was connected to the electronic barostat (Distender Series II, Dual Drive Barostat, G and J Electronics), and pressure was monitored inside the barostat bag via the enclosed unperfused side-hole recording sites. Using this apparatus, the maximal barostat bag inflation rate was 57 mL/s. Barostat bag compliance was measured ex vivo to ensure operation in the low elastance portion of the pressure-volume curve according to the recommendations of Whitehead and Delvaux.[4]

Experimental Protocol

Manometry

All subjects were studied after an overnight fast. The barostat catheter was placed orally with the patient in a sitting position and positioned such that the midpoint of the sleeve sensor was at least 40 cm distal to the incisors. The patient was then placed in a supine position and the position of the manometric assemble was then optimized for a sleeve recording of the high-pressure zone. The catheter was taped to the nose and baseline recordings were obtained for a 5-minute period during which the subject was instructed to minimize swallowing. Ten 5-mL water swallows were then obtained at 30- to 60-second intervals to assess peristaltic function and deglutitive relaxation. The subject was then shielded below the umbilicus with a lead apron and the catheter was repositioned under fluoroscopy (Easy Diagnostics, Phillips Medical Systems, Shelton, CT) such that the proximal tie point of the barostat bag was at least 7 cm proximal to the hiatal canal. The assembly was again taped in position.

Determining EGJ Distensibility

Compliance of the EGJ is otherwise difficult to measure because it is a relatively short anatomic segment and the barostat bag volume mainly localizes either distally in the stomach or proximally in the esophageal lumen. Thus, we studied distensibility of the EGJ by plotting the relationship between EGJ diameter and intraluminal distensive pressure as regulated by the barostat. Despite the fact that this measurement was 2-dimensional, it was proportional to the EGJ cross-sectional area and, hence, reflective of the compliance of the EGJ. Studies evaluating EGJ anatomy using endoscopic ultrasound reveal that the EGJ takes on a nearly circular or elliptical shape during balloon distention.[5]

Opening pressure of the EGJ was determined after the subject refrained from swallowing for at least 30 seconds. The barostat was set at a distention pressure of 5 mm Hg and incrementally increased by 2 mm Hg until opening of the EGJ was noted fluoroscopically. Throughout the barostat protocol, all pressures were referenced to atmospheric pressure. After the opening pressure was determined, the patient performed a series of 5 mL dilute barium swallows (Liquid E-Z, E-Z-EM Inc., Westbury, NY). Barostat distention pressure was set at increments of 5 mm Hg and a swallow was recorded for each pressure up to 30 mm Hg. One barium swallow was obtained at each pressure and a repeat swallow was performed if the first was technically inadequate. Fluoroscopic images were recorded using a videotape recorder (Panasonic VO 9800). Manometric data and fluoroscopic images were synchronized using a video timer (model VC 436, Thalner Electronics Laboratories, Ann Arbor, MI) that encoded time in hundredths of a second on each video frame and sent a 1V-10 milliseconds pulse to an instrumentation channel of the polygraph at whole second intervals.

Data Analysis

Manometric data were analyzed using Gastromac software. Basal high-pressure zone measurement was reported as a mean value during the initial 5-minute recording. All pressure values were referenced to end-expiratory intraesophageal pressure (approximately atmospheric pressure) so that they would be directly comparable to barostat bag pressures. Opening pressures of the EGJ during the interswallow period were determined from digitized fluoroscopic images obtained

during each barostat pressure increment. Digitized fluoroscopic images were analyzed with Macintosh video and NIH image software using the 10-mm length of the proximal tie ring on the manometric assembly to correct for magnification and a vertebral body for spatial reference. Each measurement was performed by 2 investigators. An EGJ diameter of 1 cm was considered a confident indicator of opening given that the assembly diameter was about 7 mm when the bag was deflated. Distention of the EGJ at each barostat pressure was similarly measured from digitized videofluorographic images obtained during the dilute barium swallows. The maximal deglutitive diameter was measured at the narrowest point of the EGJ in all study groups (Fig. 2). In addition, the length of the EGJ was measured at the distention pressure corresponding to a 1-cm opening diameter. Since the width of the zone of narrowing was not uniform, the length was taken as the zone across which width measurements were within 1.5 cm.

Data were summarized as mean ± SEM unless specified otherwise. Averaged data were compared using one-way ANOVA. Least square regression analysis was used to determine the correlation between the opening pressure of the EGJ and the basal LES pressure. A $P < 0.05$ was considered significant.

RESULTS

Endoscopic, Manometric, and Barostat Measures of the EGJ

Among the 9 patients screened for inclusion in the hiatal hernia group, all met the entry criterion such that the mean axial separation between the SCJ and the center of the hiatal canal was 1.5 ± 0.3 cm. The mean measurement of the high-pressure zone of the hiatal hernia patients was significantly lower than both normal subjects and fundoplication patients (Fig. 3). There was no significant difference in the mean measurement of the high-pressure zone between the normal subjects and fundoplication patients. Intragastric pressure was similar between groups (hiatal hernia, 6.8 ± 0.9 mm Hg; normal subjects, 6.4 ± 0.9 mm Hg; fundoplication patients, 6.9 ± 0.9 mm Hg). Normal subjects and GERD patients with hiatal hernia had normal peristalsis and LES relaxation. All fundoplication subjects had normal LES relaxation; however, peristaltic dysfunction was significantly increased compared with normal subjects (normals, 0%; fundoplication patients, 23% ± 10%, P value <0.05).

Mean opening pressure of the EGJ during the interswallow period was significantly lower among the hiatal hernia

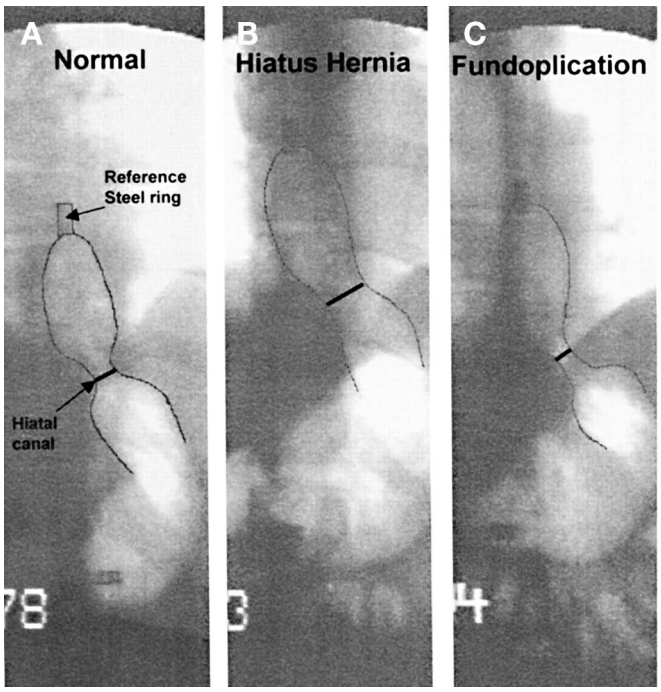

FIGURE 2. Representative images of barostat distention during deglutitive relaxation in a normal subject (A), GERD patient with hiatal hernia (B), and fundoplication (C). The diameter of the EGJ at each distensive pressure was measured from digitized images during dilute barium swallows. The narrowest point was measured as this would be the limiting diameter for flow.

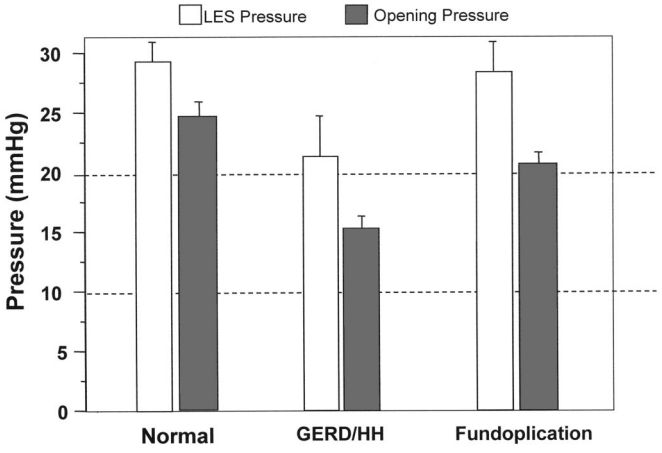

FIGURE 3. Mean basal LES pressure and opening pressure during the interswallow period. Mean basal LES pressure was significantly increased in normal subjects and fundoplication patients compared with GERD patients with hiatal hernia ($P < 0.05$). There was no significant difference in basal LES pressure between normal subjects and GERD patients. Opening pressure during the interswallow period was significantly increased in normal subjects and fundoplication patients compared with GERD patients with hiatal hernia ($P < 0.05$). There was no significant difference in EGJ opening pressure between normal subjects and GERD patients. An interesting phenomenon was that EGJ opening pressure during the interswallow period was lower than basal LES pressure. This is likely due to LES relaxation secondary to barostat bag distention in the distal esophagus.

patients compared with both normal subjects and fundoplication patients (Fig. 3). There was no significant difference in the opening pressure of the EGJ during the interswallow period when normal subjects were compared with fundoplication patients. In addition, there was a significant correlation between EGJ opening pressure during the interswallow period and basal LES pressure ($R = 0.51$, $P < 0.05$).

EGJ Distention During Deglutitive Relaxation

Figure 4 illustrates the EGJ opening diameter during deglutitive relaxation as the barostat distention pressure was incrementally increased. The EGJ diameter as it traversed the diaphragmatic hiatus was significantly wider among the hernia patients compared with the normal subjects and fundoplication patients at every distention pressure ($P < 0.05$, at each distention pressure, ANOVA). There was no significant difference in EGJ opening diameter during deglutitive relaxation between the normal subjects and fundoplication patients. Figure 4 also illustrates the mean threshold distention pressure required to achieve a 1-cm EGJ opening diameter in each subject group. This "threshold opening pressure" was substantially lower among the hernia patients compared with normal subjects and fundoplication patients (GERD/hiatal hernia, 6.0 ± 0.9 mm Hg; normals, 13.0 ± 2.8 mm Hg; fundoplication, 12.0 ± 2.4, $P < 0.005$).

The mean length of the EGJ at a 1-cm distention diameter was significantly longer in the fundoplication patients (1.9 cm) compared with both the normal subjects (1.3 cm) and GERD patients with hiatal hernia (1.0 cm) (P value < 0.05). The mean length was significantly shorter in the GERD patients with hiatal hernia compared with normal subjects (1.0 cm ± 0.05 versus 1.4 cm ± 0.1, $P < 0.05$).

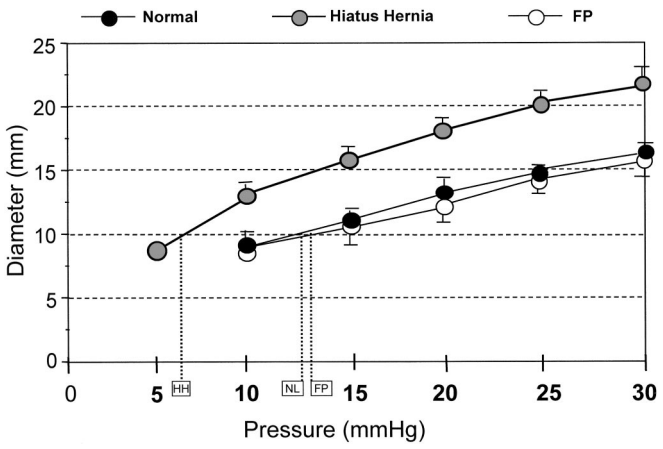

FIGURE 4. EGJ opening during deglutitive relaxation. The EGJ diameter in GERD patients with hiatal hernia was typically 0.5 cm wider at each distensive pressure compared with normal subjects and fundoplication patients. There was no significant difference in the EGJ diameter at each pressure when normal subjects were compared with fundoplication patients. The threshold pressure required to obtain an EGJ opening diameter of 1 cm was significantly increased in GERD patients (6 mm Hg) compared with normal subjects (12.5 mm Hg) and fundoplication (13.5 mm Hg) patients ($P < 0.05$).

DISCUSSION

The current study explored the hypothesis that EGJ competence is improved in fundoplication patients by reducing compliance or distensibility at the EGJ. The major findings were that distensibility of the EGJ was restored to a level similar to normal subjects while length of the EGJ was increased. These observations may help explain the therapeutic benefit of fundoplication in gastroesophageal reflux disease: 1) it may prevent opening of the EGJ sphincter during periods of LES relaxation, and 2) it may decrease retrograde trans-EGJ flow during transient lower esophageal sphincter relaxations (tLESRs).

The surgical goals of fundoplication are to correct the underlying abnormalities associated with GERD by anatomic modification of the EGJ.[2] This is accomplished by repairing the hiatal defect, lengthening the LES, and repositioning the sphincter back into the intra-abdominal cavity. Previous studies evaluating the mechanism of improved GERD in fundoplication patients reported an improvement in the EGJ high pressure zone.[6–8] This increased tone is likely the result of anatomic and mechanical factors related to the fundoplication procedure, and not an inherent recovery of the LES muscle itself. Indeed, a study modeling the pressure contribution of the fundic wrap and intrinsic LES to the overall pressure topography of the EGJ revealed that fundoplication can result in a completely adequate EGJ pressure without the LES.[3] Data from our study suggest that fundoplication restores distensibility of the EGJ to normal levels and that this may be an important component of its antireflux effect. By decreasing compliance and increasing the increment in pressure required to open the EGJ, fundoplication could prevent EGJ opening during physiologic LES relaxation. This would lead to a significant reduction in the number of acid reflux events during LES relaxation and LES hypotension. Strain-induced reflux may also be prevented as the increment of intragastric pressure required to open the EGJ is increased.

Fundoplication may also decrease trans-EGJ flow once the EGJ is open by limiting the opening dimensions of the EGJ. This hypothesis is based on an equation modeling flow across the EGJ:

$$flow = \Delta P \times R^4/C \times L \times \eta$$

In the flow equation, flow is directly proportional to EGJ diameter to the 4th power and inversely proportional to the length of the narrowed segment and the viscosity of the gas or liquid traversing the segment. Fundoplication would therefore reduce trans-EGJ flow during tLESRs by reducing

TABLE 1. Relative Flow Rates Through the EGJ Using Measurements Made During 10 mmHg Distensive Protocol

	Tube Diameter (ID) (mm)	Tube Length (mm)	Relative Flow Based on Diameter/Length of EGJ
Normal	8	13	1
GERD	14	10	12
Fundoplication	9	19	1.1

opening diameter to levels similar to normal subjects. In addition, the observed doubling of EGJ length in fundoplication patients compared with GERD patients with hiatal hernia would also reduce trans-EGJ flow. This is illustrated in Table 1 where relative flow rates are calculated using the above equation and substituting the EGJ measurements made during a distensive pressure of 10 mm Hg (Table 1).

One limitation of this study was the fact that we did not have preoperative distensibility data to confirm that these values did indeed improve after surgery. However, given the fact that these subjects were symptomatic previously, and all had hiatal hernia, it is likely that our preoperative results would have mimicked the GERD patients with hiatal hernia and not the normals. Although the strategy of studying a well-defined GERD population with hiatal hernia likely improved the power of our statistical analysis, it also limits the generalizability of the study. Thus, our findings may not be applicable to GERD patients without hiatal hernia or esophagitis.

Another limitation of this study is the fact that we limited our analysis to fundoplication patients with an excellent functional result rather than including patients with recurrent efflux symptoms or dysphagia. If our hypothesis is correct, patients with recurrent symptoms should have disruption of the EGJ and wider opening diameters compared with normal. Using the same logic, fundoplication patients with dysphagia should have a narrower opening diameter or potentially a longer EGJ limiting antegrade flow. These issues will need to be addressed in future studies.

CONCLUSION

This experiment used a combined barostat fluoroscopic technique to evaluate the mechanical characteristics of the EGJ in fundoplication patients. The data presented suggest that the mechanical property of compliance is restored to levels similar to normal subjects while the length of the EGJ is significantly increased. These anatomic changes could potentially improve GERD in 2 ways: 1) decreasing the threshold for opening the relaxed EGJ, and 2) decreasing retrograde flow of gastric juice during tLESRs and deglutitive relaxation. Thus, current fundoplication technique appears to be on target in regards to restoring the mechanical properties of the EGJ.

REFERENCES

1. Pandolfino JE, Shi G, Manka M, et al. EGJ opening with hiatal hernia: lower pressure threshold, wider diameter. *Gastroenterology*. 2000;118: A860.
2. Hunter JG, Trus TL, Branum GD, et al. A physiologic approach to laparoscopic fundoplication for gastroesophageal reflux disease. *Ann Surg*. 1996;223:673–685; discussion 685–687.
3. Kahrilas PJ, Lin S, Manka M, et al. Esophagogastric junction pressure topography after fundoplication. *Surgery*. 2000;127:200–208.
4. Whitehead WE, Delvaux M. Standardization of barostat procedures for testing smooth muscle tone and sensory thresholds in the gastrointestinal tract: the Working Team of Glaxo-Wellcome Research, UK. *Dig Dis Sci*. 1997;42:223–241.
5. Liu J, Parashar VK, Mittal RK. Asymmetry of lower esophageal sphincter pressure: is it related to the muscle thickness or its shape? *Am J Physiol*. 1997;272:G1509–G1517.
6. Ludwig K, Bernhardt J, Amtsberg G, et al. Pathophysiological measurement and results after laparoscopic fundoplication for gastroesophageal reflux disease. *Surg Today*. 2003;33:89–94.
7. Lindeboom MA, Ringers J, Straathof JW, et al. Effect of laparoscopic partial fundoplication on reflux mechanisms. *Am J Gastroenterol*. 2003; 98:29–34.
8. Chrysos E, Athanasakis E, Pechlivanides G, et al. The effect of total and anterior partial fundoplication on antireflux mechanisms of the gastroesophageal junction. *Am J Surg*. 2004;188:39–44.