Am J Physiol Gastrointest Liver Physiol 282: G1052–G1058, 2002;
10.1152/ajpgi.00279.2001.

Esophagogastric junction distensibility: a factor contributing to sphincter incompetence

JOHN E. PANDOLFINO, GUOXIANG SHI, JENNIFER CURRY, RAYMOND J. JOEHL, JAMES G. BRASSEUR, AND PETER J. KAHRILAS
Department of Medicine, Northwestern University Medical School, Chicago, Illinois 60611-3008

Received 3 July 2001; accepted in final form 15 January 2002

Pandolfino, John E., Guoxiang Shi, Jennifer Curry, Raymond J. Joehl, James G. Brasseur, and Peter J. Kahrilas. Esophagogastric junction distensibility: a factor contributing to sphincter incompetence. *Am J Physiol Gastrointest Liver Physiol* 282: G1052–G1058, 2002; 10.1152/ajpgi.00279.2001.—To quantify the effect of hiatus hernia (HH) on esophagogastric junction (EGJ) distensibility, eight normal subjects and nine gastroesophageal reflux disease (GERD) patients with HH were studied with concurrent manometry, fluoroscopy, and stepwise controlled barostatic distention of the EGJ. The minimal barostatic pressure required to open the EGJ during the interswallow period was determined. Thereafter, barium swallows were imaged in 5-mmHg increments of intrabag pressure. EGJ diameter and length were measured at each pressure during deglutitive relaxation. The EGJ opening diameter was greater in hernia patients compared with normal subjects during deglutitive relaxation at all pressures, and EGJ length was 23% shorter. EGJ opening pressure among hernia patients was lower than normal subjects during the interswallow period. In conclusion, the EGJ of GERD patients with HH was more distensible and shorter than normal subjects. These findings partially explain why HH patients are predisposed to reflux by mechanisms other than transient lower esophageal sphincter relaxations, sustain greater volumes of refluxate, and have a reduced ability to discriminate gas from liquid reflux.

hiatus hernia; gastroesophageal reflux disease

THE CARDINAL ABNORMALITY of gastroesophageal reflux disease (GERD) is incompetence of the esophagogastric junction (EGJ) to reflux of gastric secretions. This functional compromise can be attributable to perturbation of a number of anatomical or physiological components of the EGJ, including the intrinsic lower esophageal sphincter (LES), the extrinsic compression of the distal esophagus at the diaphragmatic hiatus, the intra-abdominal location of the LES, or the physiology of transient LES relaxations (tLESRs). Physiological investigations suggest that the net result of these perturbations is an increased number of acid reflux events by three mechanisms: *1*) tLESR, *2*) strain-induced reflux in the setting of a hypotensive LES, or *3*) free reflux during periods of low LES pressure or deglutitive relaxation (1, 12, 19).

Gaining acceptance as a cofactor in the pathogenesis of GERD is anatomical distortion of the EGJ inclusive of, but not limited to, hiatus hernia (7, 9, 13, 14). When examining GERD in the context of hiatus hernia, certain distinctions become evident. Patients with more severe forms of GERD, such as erosive esophagitis and Barrett's metaplasia, almost invariably have a hiatus hernia (2, 18), and GERD patients with hiatus hernia have increased esophageal acid exposure compared with patients without hiatus hernia (8, 18). The mechanistic profile for reflux in hiatus hernia patients is also distinct. Whereas tLESRs can account for up to 90% of reflux events in normal subjects or in patients without hiatus hernia, patients with hiatus hernia have a more heterogeneous mechanistic profile with reflux episodes frequently occurring in the context of low LES pressure, straining, and swallow-associated LES relaxation (19).

In contemplating the occurrence of reflux in the setting of a relaxed or hypotensive sphincter, it is necessary to explore other mechanical attributes of the system that may account for a relaxed sphincter remaining closed in one case and physically open in another; one such attribute is compliance. Acquired anatomic defects associated with hiatus hernia may increase compliance at the EGJ during relaxation, thereby decreasing resistance to gastroesophageal flow. Increased compliance may exacerbate reflux in two ways: *1*) incremental increase in intra-abdominal pressure required to open the relaxed or hypotensive EGJ may be lower, and *2*) relaxed EGJ may open wider than normal under a given physiological circumstance, resulting in a reduced discriminative resistance for liquid as opposed to gas reflux.

The aim of this study was to compare the distensibility of the EGJ both at rest and during relaxation of hiatus hernia patients with GERD with normal subjects using a combined barostatic/fluoroscopy technique that allowed for direct measurement of intraluminal EGJ diameter at predetermined intraluminal distention pressures.

Address for reprint requests and other correspondence: P. J. Kahrilas, Northwestern University Medical School, Division of Gastroenterology & Hepatology, Dept. of Medicine, Searle Bldg., 10th Floor, Suite 541, 303 East Chicago Ave., Chicago, IL 60611-3008 (E-mail: p-kahrilas@northwestern.edu).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

MATERIALS AND METHODS

Subjects

Eight normal subjects (4 males, 4 females; 24–59 yr old) without reflux symptoms and nine patients with GERD and hiatus hernia (3 males, 6 females; 22–57 yr old) were studied. Patients were enrolled from the endoscopy lab at Northwestern Memorial Hospital. GERD patients were defined by presence of esophagitis ($n = 8$) or chronic heartburn responsive to proton pump inhibitor therapy ($n = 9$). 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 were taking any medication known to affect esophageal contractility. None of the subjects had a history of surgical manipulation of the EGJ. The protocol was approved by the Northwestern University Institutional Review Board, and informed consent was obtained from all participants.

Endoscopy

All potential hiatus hernia/GERD patients underwent endoscopy to ascertain the presence and size of hiatus hernia and to localize the squamocolumnar junction (SCJ). Normal subjects were not required to undergo endoscopy. During endoscopy, which was done under conscious sedation with 1–4 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). After appropriate postendoscopy recovery time (at least 1 h), the patient was moved to the fluoroscopy suite for the remainder of the study. The presence of hiatus hernia was determined with fluoroscopy using the clip as a reference point for the SCJ and the indentation in the barium column during a barium swallow as the location of the diaphragmatic hiatus. Patients were included in the hiatus hernia group if the position of the SCJ between swallows was ≥1 cm above the center of the hiatal impression as determined during deglutitive emptying.

Manometric and Barostat Instrumentation

A custom-made, 21-lumen silicon rubber extrusion was used for both the manometric recordings and barostatic distention (Dentsleeve, 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). 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, Warriedwood, NSW, Australia) and processed using Gastromac software (Neomedix). Before the recording, the transducers were calibrated at 0 and 70 mmHg with the use of externally applied pressure. Response characteristics of each side-hole manometric channel exceeded 200 mmHg/s.

Barostat bags were designed so that, when fully distended, they had a cylindrical shape 2.75 cm in diameter and 20 cm in length. The length of the bag ensured that position could be maintained across the EGJ during distention without need for repositioning (pilot experiments with 6-cm bags failed because of bag migration). 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. Before use, the catheter and bag were checked for leaks ex vivo by inflation to 40 mmHg under water. The large-bore 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. With the use of this apparatus, the maximal barostat bag inflation rate was 57 ml/s.

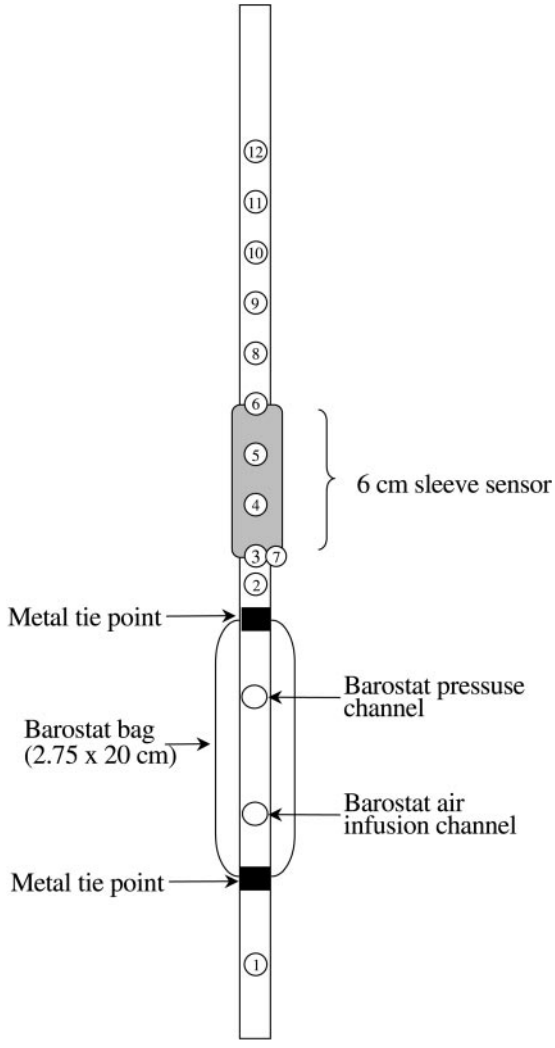

Fig. 1. The barostat catheter was constructed from a 21-lumen silicon rubber. This assembly incorporated a 6-cm sleeve sensor, 12 side-hole recording sites, 2 cylindrical metal tie points for the barostat bag, a large-bore infusion port for the barostat bag, and pressure monitoring ports between the tie points for monitoring barostat bag pressure. Barostat bags were designed so that when fully distended, they had a cylindrical shape 2.75 cm in diameter and 20 cm in length. *Channels 1–12* are pressure channels. *Channel 7* perfused the 6-cm sleeve.

Barostat bag compliance was measured ex vivo to ensure operation in the low-elastance portion of the pressure-volume curve (Fig. 2) according to the recommendations of Whitehead and Delvaux (21). This confirmed that at operating

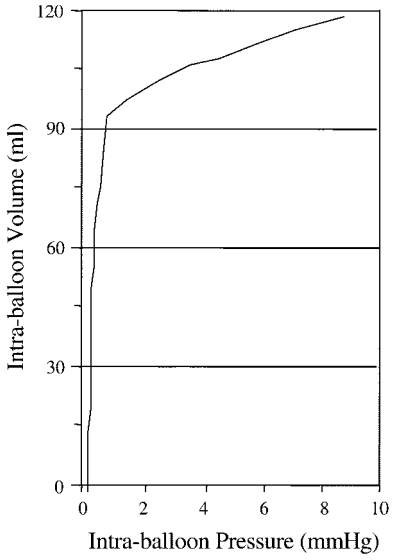

Fig. 2. Barostat bag compliance was measured ex vivo to ensure operation in the low-elastance portion of the pressure-volume curve. At operating volumes of <100 ml and bag diameters of <2.75 cm, the bag was essentially infinitely compliant. Ex vivo, a bag diameter of 2.75 cm was obtained at barostatic pressures <3 mmHg.

volumes of <100 ml and bag diameters of <2.75 cm, the bag itself did not significantly contribute to resistance to inflation; a bag diameter of 2.75 cm was obtained at barostatic pressures of <3 mmHg. Thus the barostatic pressure and volume required in vivo to obtain luminal distension up to a 2.75-cm diameter depended on the mechanical properties of the surrounding structures (in particular, the EGJ) and not of the bag, catheter, or barostat.

Experimental Protocol

Manometry. All subjects were studied after an overnight fast. The barostat catheter was placed orally while the patient was in a sitting position. Once the catheter was passed such that the midpoint of the sleeve sensor was at least 40 cm distal to the incisors, the patient was placed in a supine position. The position of the manometric assembly was then optimized for a sleeve recording of the high-pressure zone, was taped in place, and a baseline recording was obtained for a 5-min period during which the subject was instructed to minimize swallowing. Ten 5-ml water swallows were then obtained at 30- to 60-s 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. Distensibility was defined as relationship between EGJ diameter and intraluminal pressure as regulated by the barostat. Despite the fact that this measurement was one 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 distension (10). Compliance of the EGJ is otherwise difficult to measure, because it is a relatively short anatomical segment and the barostat bag volume mainly localizes either distally in the stomach or proximally in the esophageal lumen.

Opening pressure of the EGJ was determined after the subject refrained from swallowing for at least 30 s. The barostat was set at a distension pressure of 5 mmHg and then increased in 2-mmHg increments 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, Westbury, NY). Barostatic distension pressure was set at increments of 5 mmHg, and a swallow was recorded for each pressure ≤30 mmHg. One barium swallow was obtained at each pressure with the potential for a repeat swallow, if the first was technically inadequate. Fluoroscopic images were recorded using a videotape recorder (model VO 9800; Panasonic). 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 1-V, 10-ms pulse to an instrumentation channel of the polygraph at whole second intervals.

Mathematical Modeling of Flow Through the EGJ

The underlying hypothesis for measuring the compliance of the EGJ during LES relaxation was that the increased diameters observed in hernia patients would have qualitative and quantitative effects on retrograde gastroesophageal flow. To estimate these effects, we applied a simplified mathematical model on the basis of Newton's law of motion to flow through the narrowed segment of the EGJ with the catheter in place. The model estimated the flow resulting from a balance between the pressure difference across the narrow segment and the frictional forces within the segment during flow; inertial effects are neglected. We approximated the narrowed segment as circular in cross section around the 0.7-cm diameter catheter at EGJ diameters measured across a 10-mmHg range of barostatic pressures. The pressure driving flow through the narrowed EGJ segment at each lumenal diameter was estimated as the barostatic pressure, and we approximated the esophageal pressure on the proximal margin of the narrowed segment as atmospheric.

With the model described above, the relationship between the rate of volume flow through the EGJ, Q (ml/s), and the pressure differences across the narrowed segment of the EGJ (dP; in Pa), with the catheter in place is given by

$$Q = \frac{(dP \times D^4)}{(CVL)} \times \left[(1 - R^4) + \frac{(1 - R^2)^2}{(ln\ R)}\right]$$

In this equation, $R = d/D$, the ratio of the diameter of the catheter (d) to the diameter of the narrowed segment (D) in cm, V is the viscosity of air or water flowing across the EGJ (Pascal seconds), and L is the length of the narrowed segment within the EGJ (cm) (20). C is a unitless constant equal to 40.74. Note that the viscosity of water (0.001 Pascal s) is 55.6 times the viscosity of air. Although it is not possible to consistently obtain measurements of EGJ length, values were obtained for a 1-cm opening diameter, and these were assumed to be constant among opening diameters. Because most physiologically relevant values of increased intra-abdominal pressure are low, the D vs. dP from our data evaluating EGJ opening diameter during deglutitive relaxation is linearly extrapolated below dP = 10 mmHg and for lumen diameter larger than the catheter diameter. Using these measurements along with the assumptions and approximations above, esophagogastric flow across the EGJ for water and air were estimated as shown in Fig. 7 for the two

subject groups with increments of intra-abdominal pressure ranging from 0 to 10 mmHg.

Data Analysis

Manometric data were analyzed using Gastromac software. Basal high-pressure zone measurement was reported as a mean value during the initial 5-min recording, and deglutitive relaxation pressure was reported as the mean of the minimum values obtained during the water swallows. All pressure values were referenced to end-expiratory intraesophageal pressure (approximately atmospheric pressure) so they would be directly comparable with barostat bag pressures.

Opening pressures of the EGJ during the interswallow period were determined from digitized fluoroscopic images obtained during each barostatic pressure increment. Digitized fluoroscopic images were analyzed with Macintosh video and National Institutes of Health image software using a vertebrae as a spatial reference and the 10-mm length of the proximal tie ring on the manometric assembly to correct for magnification. Each measurement was performed by two investigators. An EGJ diameter of 1 cm was considered a confident indicator of opening, given that when the bag was deflated, the assembly diameter was ~7 mm. Distension of the EGJ at each barostatic pressure was similarly measured from digitized video fluorographic images obtained during the dilute barium swallows. In normal subjects, the maximal deglutitive diameter was measured at the narrowest point of the EGJ. In hernia patients, the diameter was measured at the SCJ and at the narrowest point of the EGJ (Fig. 3). In addition, the length of the EGJ was measured at the distension pressure corresponding to a 1-cm opening diameter. Because 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 are summarized as means ± SE unless specified otherwise. Averaged data were compared using Student's *t*-test. Least square regression analysis was used to determine the correlation between the opening pressure of the EGJ and the basal LES pressure. $P < 0.05$ was considered significant.

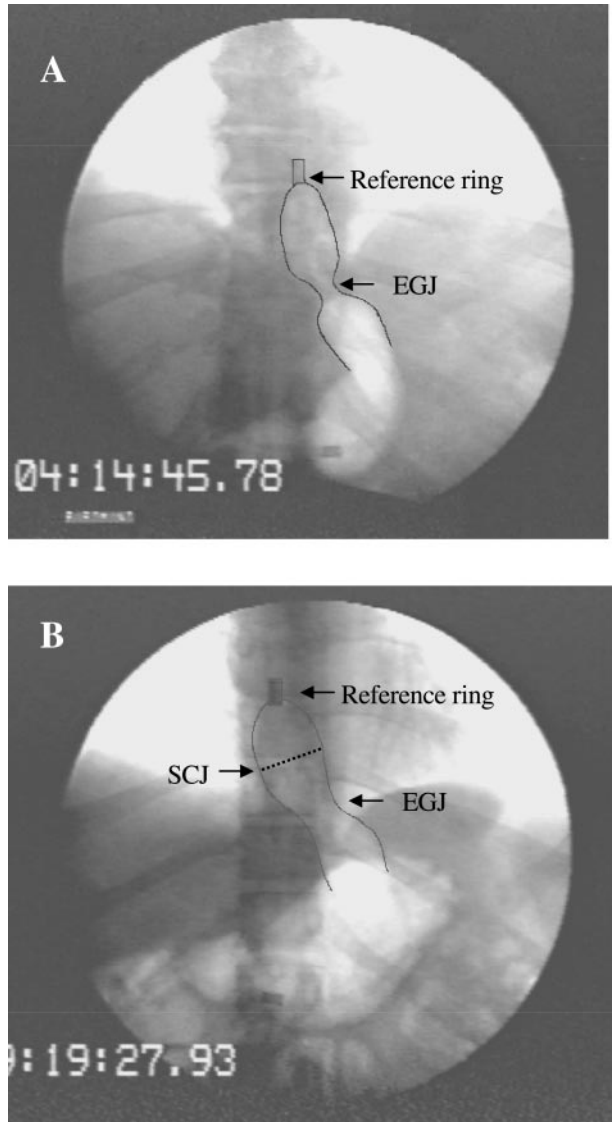

Fig. 3. Representative images of barostatic distention during deglutitive relaxation in a normal subject (*A*) and a hiatus hernia patient (*B*). The diameter of the esophagogastric junction (EGJ) at each barostatic distention pressure was measured from digitized video fluorographic images obtained during the dilute barium swallows. *A*: in normal subjects, the maximal deglutitive diameter was measured at the narrowest point of the EGJ. *B*: in hiatal hernia (HH) patients, the diameter was measured at both the squamocolumnar junction(SCJ) and at the narrowest point of the EGJ.

RESULTS

Among the nine patients screened for inclusion in the hiatus hernia group, all met the entry criterion, which was the mean axial separation between the SCJ and the center of the hiatal canal (1.5 ± 0.3 cm).

Manometric and Barostat Measures of EGJ Function

The mean measurement of the high-pressure zone of the hiatus hernia patients was lower than that of normal subjects (22.2 ± 2.5 vs. 29.5 ± 2.1 mmHg, $P < 0.05$). Intragastric pressure, however, was similar between groups (hiatus hernia group 6.8 ± 0.9 mmHg; normal subjects 6.4 ± 0.9 mmHg). Mean relaxation pressure of the high-pressure zone during water swallow was also similar for the hiatus hernia patients (10.3 ± 0.8 mmHg) and normal subjects (9.1 ± 0.8 mmHg); 3.5 ± 0.8 and 2.7 ± 0.8 mmHg, respectively, when referenced to intragastric pressure. All subjects had normal peristalsis and LES relaxation.

Mean opening pressure of the EGJ during the interswallow period was lower among the hiatus hernia patients compared with normal subjects (16.0 ± 1.2 vs. 24.8 ± 1.3 mmHg, $P < 0.001$). However, a significant correlation between opening pressure and mean basal high-pressure zone measurement did not exist, as illustrated in Fig. 4 ($r = 0.42$, $P = 0.09$).

EGJ Distension During Deglutitive Relaxation

Figure 5 illustrates the EGJ opening diameter during deglutitive relaxation as the barostatic distension pressure was incrementally increased. Among the hernia patients, the narrowest point within the EGJ invariably occurred at the diaphragmatic hiatus rather than at the SCJ, which, on average, opened 0.6 cm

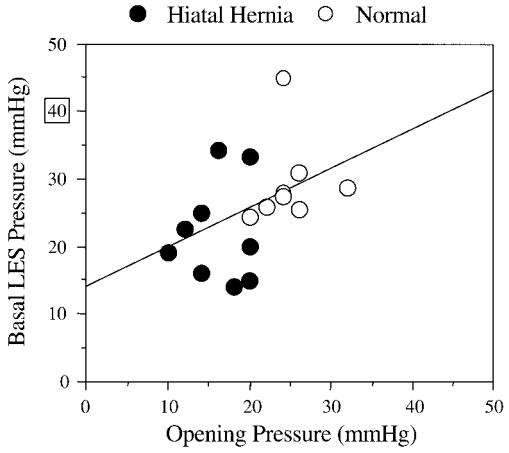

Fig. 4. Correlation between opening pressure of the EGJ during the interswallow period and basal lower esophageal sphincter (LES) pressure. Opening pressure of the EGJ during the interswallow period was lower among the HH patients compared with controls. A significant correlation did not exist between opening pressure and mean basal LES pressure ($P = 0.09$).

wider than the diaphragmatic hiatus. Note that the EGJ diameter as it traversed the diaphragmatic hiatus was typically 0.5 cm wider among the hernia patients compared with normal subjects at every distention pressure. Along with the increased diameter, the mean length of the EGJ at a 1-cm distension diameter was significantly shorter in the GERD patients with hiatus hernia compared with normal subjects (1.0 ± 0.1 vs. 1.3 cm ± 0.1, $P < 0.05$).

Figure 5 also illustrates the mean threshold distension 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 (6.0 ± 0.9 vs. 13.0 ± 2.8 mmHg, $P < 0.005$). Note that when referenced to the group mean intragastric pressures, these threshold opening pressure values become −0.4 and 6.2 mmHg, respectively. This relationship was further explored by plotting the pressure increment between resting intragastric pressure and threshold opening pressure on a case-by-case basis as illustrated in Fig. 6. Note that, not only is there minimal overlap among the groups, but essentially all of the hernia patients required a pressure increment of <5 mmHg that might easily be experienced during respiration. In addition, some of the hernia patients had an opening diameter of 1 cm during LES relaxation with the distension pressure set at zero.

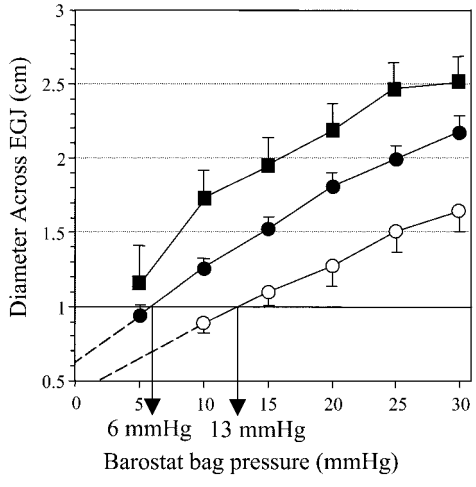

Fig. 5. EGJ opening diameter during deglutitive relaxation. The EGJ diameter was typically 0.5 cm wider among the HH patients compared with the controls at every distension pressure. The SCJ diameter in HH patients (■) was typically 0.6 cm wider at each distension pressure. Threshold distension pressure required to achieve a 1-cm EGJ opening diameter in each subject group was substantially lower among the HH patients (●) compared with controls (○; 6.0 vs. 13.0 mmHg, $P < 0.005$).

Estimated Effect of Increased EGJ Compliance on Retrograde Flow

By the use of data from Fig. 5 and the mathematical model described in MATERIALS AND METHODS for modeled flow across the EGJ, flow rates were calculated for a 0–10 mmHg range of ΔP values (Fig. 7). Note that flow for either air or water is two to three orders of magnitude greater for the hernia group compared with normal subjects at each value of gastroesophageal pressure gradient. Within each group, flow of air is about two orders of magnitude greater than the flow of water.

DISCUSSION

Recent data (19) suggest that a physiological consequence of hiatus hernia is increasing the proportion of reflux events occurring by mechanisms dependent on LES hypotension as opposed to tLESR. Other data (6, 15), although not specifically addressing the role of hiatus hernia, suggest that a distinction between reflux patients and normal controls is not of an increased frequency of tLESR but of an increased proportion of tLESRs associated with acid as opposed to gas reflux. The current study explored the hypothesis that altered compliance of the EGJ may partly explain these obser-

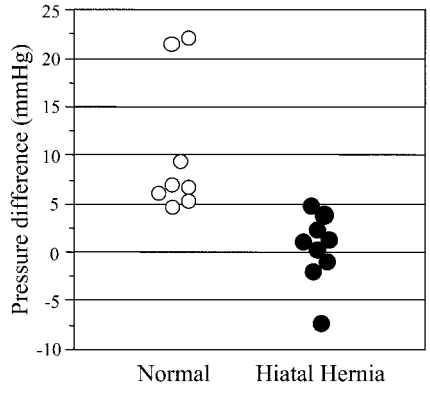

Fig. 6. Relationship between resting intragastric pressure and the threshold distension pressure required to achieve an 1-cm opening diameter. The pressure on the *y*-axis is expressed as the difference between intragastric pressure and the 1-cm distension pressure. On a case-by-case basis, it appears that some of the HH patients are able to achieve opening diameters of 1 cm at distensive pressure equal to or lower than the measured intragastric pressure. Note there is minimal overlap among the groups.

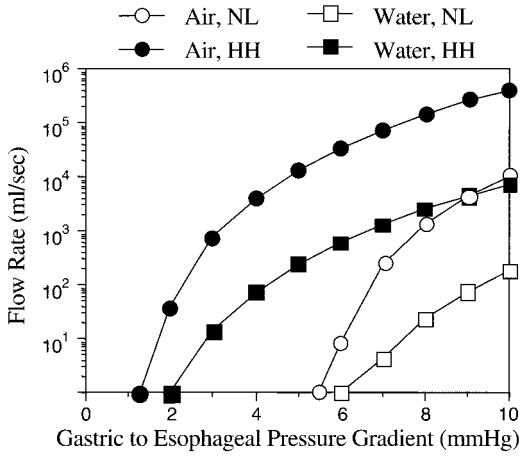

Fig. 7. The modeled effect of increased EGJ compliance on retrograde flow. Volume flow (Q; ml/s) is estimated using a simplified mathematical model on the basis of Newton's law of motion as detailed in the text. From the equation, it is evident that flow is highly dependent on diameter, given that it is factored to the 4th power. Note that for a given value of the gastric-to-esophageal pressure gradient, flow is 2 to 3 orders of magnitude greater for the HH group compared with normal subjects (NL) for either air or water and that within each group, flow rate of air is about 2 orders of magnitude greater than for water.

vations. The major finding was that distensibility of the EGJ was significantly increased in GERD patients with hiatus hernia such that opening occurred at a significantly lower distension pressure, and that for a given distention pressure, the resultant opening diameter was ~0.5 cm wider. These observations may partially explain two aspects of GERD pathophysiology: *1*) the occurrence of reflux associated with low LES pressure, swallow-associated LES relaxation, and straining and *2*) increased refluxate volume along with reduced discrimination between gas and liquid reflux.

Unlike normal subjects or GERD patients without hiatus hernia, GERD patients with hiatus hernia are vulnerable to reflux in the context of a low LES pressure (17) and such events accounted for the majority of reflux events during ambulatory manometry (19). The difference in the mechanistic profile of reflux events among hiatus hernia patients suggests that gastroesophageal reflux requires a "two hit" phenomenon to the EGJ; both the intrinsic LES and the diaphragmatic hiatus need to be overcome. During transient LES relaxation, this is accomplished by reflex inhibition of both the intrinsic LES and the crural diaphragm (12). In this setting, gastroesophageal reflux occurs with a modest increment of ~3 mmHg intragastric pressure (5). On the other hand, reflux does not occur during normal swallowing, because only the intrinsic LES, not the crural diaphragm, is neurally inhibited (11). Thus the relaxed sphincter remains closed until adequate pressure develops within the swallowed bolus to overcome the mechanical resistance attributable to the diaphragmatic hiatus (16). However, in the setting of hiatus hernia, the first "hit" to the competence of the EGJ is the inherent anatomical disruption of the hiatus. Thus the only prerequisite for reflux becomes LES relaxation, be that in the setting of swallow-induced relaxation, tLESR or a period of prolonged LES hypotension. Data presented from the current experiment suggest that among hernia patients, the increment in intragastric pressure required to open the EGJ during deglutitive relaxation (which was assumed to be similar to what would occur during tLESR) was not only substantially lower than that observed in the normal subjects, but was uniformly <5 mmHg, an incremental increase of intra-abdominal pressure likely to be achieved during normal activities or even respiration. Even during interswallow periods without the benefit of LES relaxation, the mean distention pressure required to open the EGJ of the hernia patients was significantly lower than that observed in controls, partly explaining their increased susceptibility to strain-induced reflux (17, 19).

An interesting observation during our evaluation of distensibility during the interswallow period was that opening pressure was lower than LES pressure. This was likely secondary to stimulation of a descending inhibitory pathway secondary to distal esophageal distension. However, this limitation only pertains to our opening pressure study during the interswallow period and should not significantly alter the measurement of EGJ distensibility during swallowing.

Transient LES relaxation is a frequent mechanism of reflux in both healthy individuals and GERD patients (3, 4). However, tLESR is also the physiological mechanism of belching (22), and an important distinction among GERD patients seems to be in the proportion of tLESRs associated with liquid as opposed to gas reflux. In an experiment that sought to quantify this difference, normal subjects exhibited acid reflux with 40–50% of tLESRs compared with 60–70% in patients with GERD (15). Figure 7 models show this discrimination can result from the observed difference in EGJ compliance plotted in Fig. 4. Conceptually, air/water discrimination occurs, because trans-EGJ flow is directly proportional to EGJ diameter to the fourth power and inversely proportional to viscosity. Thus the 55-fold difference in viscosity between water and air coupled with the lower opening pressure and 0.5-cm increase in EGJ diameter observed in hernia patients makes a normal individual capable of venting large volumes of gas from the stomach at low pressure with minimal potential for liquid reflux, whereas hernia patients will vent large volumes of air or water at similar pressures. A correlate of this is that the volume of refluxate is also uniformly higher among the hernia patients, a phenomenon exacerbated by the observed 23% decrement in EGJ length in this group.

Although our data reveal a significant increase in distensibility of the EGJ in GERD patients with hiatus hernia compared with normal subjects, further studies are needed to determine which component of the EGJ is most important. The increased distensibility in hiatus hernia patients could be related to axial displacement of the SCJ, crural diaphragm disruption, or an altered smooth muscle LES. Studies involving GERD patients without hiatus hernia and asymptomatic hia-

tus hernia patients may be helpful in determining the role of each of these variables in distensibility of the EGJ.

In summary, this experiment utilized a combination of barostat-controlled distention, manometry, and fluoroscopy to directly measure the compliance of the EGJ. Several parameters of EGJ compliance were shown to be increased in hiatus hernia patients with GERD: *1*) the EGJ opened at lower distension pressure; *2*) the relaxed EGJ opened at distension pressures at or near resting intragastric pressure; and *3*) for a given distension pressure, the EGJ opened about 0.5 cm wider. It is hypothesized that these alterations of EGJ mechanics are secondary to a disrupted, distensible, crural diaphragm and contribute to the physiological aberrations associated with hiatus hernia and GERD. Such patients have a more heterogeneous mechanistic profile of reflux events. Specifically, reflux events may occur in the context of low LES pressure, straining, and deglutitive relaxation. Furthermore, the wider EGJ opening diameters in the hernia patients may predispose to increased retrograde flow of gastric juice during tLESRs because of reduced air/water discrimination.

This work was supported by National Institute of Diabetes and Digestive and Kidney Diseases Grant RO1-DK-56033 (to P. J. Kahrilas).

REFERENCES

1. **Barham CP, Gotley DC, Mills A, and Alderson D.** Precipitating causes of acid reflux episodes in ambulant patients with gastro-oesophageal reflux disease. *Gut* 36: 505–510, 1995.
2. **Cameron AJ.** Barrett's esophagus: prevalence and size of hiatal hernia. *Am J Gastroenterol* 94: 2054–2059, 1999.
3. **Dent J, Dodds WJ, Friedman RH, Sekiguchi T, Hogan WJ, Arndorfer RC, and Petrie DJ.** Mechanism of gastroesophageal reflux in recumbent asymptomatic human subjects. *J Clin Invest* 65: 256–267, 1980.
4. **Dodds WJ, Dent J, Hogan WJ, Helm JF, Hauser R, Patel GK, and Egide MS.** Mechanisms of gastroesophageal reflux in patients with reflux esophagitis. *N Engl J Med* 307: 1547–1552, 1982.
5. **Holloway RH and Dent J.** Pathophysiology of gastroesophageal reflux. Lower esophageal sphincter dysfunction in gastroesophageal reflux disease. *Gastroenterol Clin North Am* 19: 517–535, 1990.
6. **Holloway RH, Kocyan P, and Dent J.** Provocation of transient lower esophageal sphincter relaxations by meals in patients with symptomatic gastroesophageal reflux. *Dig Dis Sci* 36: 1034–1039, 1991.
7. **Kahrilas PJ, Lin S, Chen J, and Manka M.** The effect of hiatus hernia on gastro-oesophageal junction pressure. *Gut* 44: 476–482, 1999.
8. **Kasapidis P, Vassilakis JS, Tzovaras G, Chrysos E, and Xynos E.** Effect of hiatal hernia on esophageal manometry and pH-metry in gastroesophageal reflux disease. *Dig Dis Sci* 40: 2724–2730, 1995.
9. **Klein WA, Parkman HP, Dempsey DT, and Fisher RS.** Sphincterlike thoracoabdominal high pressure zone after esophagogastrectomy. *Gastroenterology* 105: 1362–1369, 1993.
10. **Liu J, Parashar VK, and Mittal RK.** Asymmetry of lower esophageal sphincter pressure: is it related to the muscle thickness or its shape? *Am J Physiol Gastrointest Liver Physiol* 272: G1509–G1517, 1997.
11. **Mittal RK and Fisher MJ.** Electrical and mechanical inhibition of the crural diaphragm during transient relaxation of the lower esophageal sphincter. *Gastroenterology* 99: 1265–1268, 1990.
12. **Mittal RK, Holloway RH, Penagini R, Blackshaw LA, and Dent J.** Transient lower esophageal sphincter relaxation. *Gastroenterology* 109: 601–610, 1995.
13. **Mittal RK, Rochester DF, and McCallum RW.** Electrical and mechanical activity in the human lower esophageal sphincter during diaphragmatic contraction. *J Clin Invest* 81: 1182–1189, 1988.
14. **Mittal RK, Rochester DF, and McCallum RW.** Sphincteric action of the diaphragm during a relaxed lower esophageal sphincter in humans. *Am J Physiol Gastrointest Liver Physiol* 256: G139–G144, 1989.
15. **Sifrim D, Silny J, Holloway RH, and Janssens JJ.** Patterns of gas and liquid reflux during transient lower oesophageal sphincter relaxation: a study using intraluminal electrical impedance. *Gut* 44: 47–54, 1999.
16. **Sloan S and Kahrilas PJ.** Impairment of esophageal emptying with hiatal hernia. *Gastroenterology* 100: 596–605, 1991.
17. **Sloan S, Rademaker AW, and Kahrilas PJ.** Determinants of gastroesophageal junction incompetence: hiatal hernia, lower esophageal sphincter, or both? *Ann Intern Med* 117: 977–982, 1992.
18. **Sontag SJ, Schnell TG, Miller TQ, Nemchausky B, Serlovsky R, O'Connell S, Chejfec G, Seidel UJ, and Brand L.** The importance of hiatal hernia in reflux esophagitis compared with lower esophageal sphincter pressure or smoking. *J Clin Gastroenterol* 13: 628–643, 1991.
19. **Van Herwaarden MA, Samsom M, and Smout AJ.** Excess gastroesophageal reflux in patients with hiatus hernia is caused by mechanisms other than transient LES relaxations. *Gastroenterology* 119: 1439–1446, 2000.
20. **White FM.** *Fluid Mechanics*. New York: McGraw-Hill, 1999.
21. **Whitehead WE and 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* 42: 223–241, 1997.
22. **Wyman JB, Dent J, Heddle R, Dodds WJ, Toouli J, and Downton J.** Control of belching by the lower oesophageal sphincter. *Gut* 31: 639–646, 1990.