Published in final edited form as:

J Gastrointest Surg. 2010 February ; 14(2): 268–276. doi:10.1007/s11605-009-1086-1.

Esophagogastric Junction Distensibility After Fundoplication Assessed with a Novel Functional Luminal Imaging Probe

Monika A. Kwiatek,

Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA.
Division of Gastroenterology, Department of Medicine, Feinberg School of Medicine, Northwestern University, 676 N. St. Clair Street, Suite 1400, Chicago, IL 60611-2951, USA

Peter J. Kahrilas,

Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

Nathaniel J. Soper,

Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

William J. Bulsiewicz,

Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

Barry P. McMahon,

Medical Physics & Clinical Engineering, Department of Clinical Medicine, Trinity College, Dublin, Ireland

Hans Gregersen, and

Mech-Sense, Aalborg Hospital, Århus University Hospital, Århus, Denmark

John E. Pandolfino

Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

Monika A. Kwiatek: monika.kwiatek@gmail.com

Abstract

Objective—The aim of the study was to compare the esophagogastric junction (EGJ) compliance in response to controlled distension in fundoplication (FP) patients and controls using the functional luminal imaging probe (FLIP).

Background—FP aims to replicate normal EGJ distensibility. FLIP is a new technology that uses impedance planimetry to measure intraluminal cross-sectional area (CSA) during controlled distension.

Methods—Ten controls and ten FP patients were studied with high-resolution esophageal pressure topography (HREPT) and then the FLIP placed across the EGJ. Deglutitive and interdeglutitive EGJ distensibility was assessed with volume-controlled distension. The FLIP measured eight CSAs spaced 4 mm apart within a cylindrical saline-filled bag along with the corresponding intrabag pressure.

Results—The EGJ formed an hourglass shape during distensions with the central constriction at the diaphragmatic hiatus. The distensibility of the hiatus was significantly greater during deglutitive relaxation in both subject groups, but FP patients exhibited reduced EGJ distensibility and

Correspondence to: Monika A. Kwiatek, monika.kwiatek@gmail.com.

This paper was presented at the Digestive Disease Week and the 109th Annual Meeting of the American Gastroenterological Association Institute, May 17–22, 2008, San Diego, CA, USA.

compliance compared to controls. During the interglutitive period, the corresponding increase in intrabag pressures at larger volumes were also greater in FP patients implying a longer segment of EGJ constriction. The EGJ distensibility characteristics did not correlate with HREPT measures.

Conclusions—FLIP technology was used to compare EGJ distensibility in FP patients and control subjects. The least distensible locus within the EGJ was always at the hiatus. EGJ distensibility was significantly reduced, and the length of constriction increased in FP patients. Future FLIP studies will compare patients with and without post-FP dysphagia and gas bloat, symptoms suggestive of an overly restrictive FP.

Keywords

Esophagogastric junction; Fundoplication; Functional luminal imaging probe; Manometry

Patients with gastroesophageal reflux disease have an abnormally compliant esophagogastric junction (EGJ)^{1–4} that inadequately impedes reflux of gastric contents and thus contributes to a greater likelihood of esophageal mucosa injury and reflux-related symptoms. Increased EGJ compliance is likely multifactorial with potential contributing defects of lower esophageal sphincter pressure, extrinsic compression by the crural diaphragm, and misalignment between the two manifest as a sliding hiatal hernia.^{3,5,6} Potential deleterious mechanical consequences of increased EGJ compliance include increased volumes of liquid reflux,⁷ a reduced threshold for eliciting transient LES relaxations,⁸ and allowing gastric juice to track within the closed sphincter.^{9–11} Surgical antireflux procedures aim to correct the defective EGJ by fashioning a mechanical antireflux barrier that allows adequate EGJ opening for passage of swallowed ingesta into the stomach as well as gastric venting when required.^{12,13} Ideally, a normal healthy EGJ would be replicated.

Postoperative integrity of the EGJ junction is usually assessed by manometry. Such functional assessments are often provoked by persistent or recurrent gastroesophageal reflux symptoms suggestive of a defective fundoplication (FP) or because of postoperative dysphagia. Although manometric technology has evolved recently to high-resolution esophageal pressure topography (HREPT),^{14–16} it still fundamentally measures intraluminal pressure. However, the surgical modification of the EGJ during fundoplication may not be best gauged by measurement of intraluminal pressure. Fundoplication entails tightening of the diaphragmatic hiatus and construction of a loose floppy fundic wrap around the distal esophagus, neither of which necessarily affects the intraluminal pressures. Alternatively, FP integrity may be better assessed when challenged with intraluminal distension.¹⁷

Measurement of intraluminal distensibility at the EGJ is complex. The distending pressure must be localized within the EGJ and dimensional measurements restricted to the area of interest. Although this can be achieved with a barostat (or hydrostat), this is somewhat cumbersome and requires concurrent fluoroscopic imaging.^{2–4} Nonetheless, barostat assessment of compliance at the narrowest locus within the EGJ after FP suggested it to be similar in asymptomatic FP patients compared to control subjects.² A potentially more robust method for measuring EGJ distensibility, capable of making measurements at multiple adjacent segments without need for fluoroscopy, is by adaptation of the principle of impedance planimetry^{18,19} into a functional luminal imaging probe (FLIP). FLIP recordings allow dynamic imaging of EGJ distention as a three-dimensional structure based on instantaneous measurement of multiple intraluminal cross-sectional areas with concurrent pressure measurements, thereby facilitating measurement of EGJ distensibility.^{20,21} Hence, the aim of the current study was to compare the EGJ distensibility in FP patients during the interdeglutitive period and during deglutitive EGJ relaxation to that of asymptomatic control subjects using the FLIP.

Materials and Methods

Subjects

Ten asymptomatic control subjects (2M, 23–50 years) and ten patients who have had laparoscopic Nissen FP surgery (2M, 42–68 years) were studied. The control subjects were recruited from a pool of volunteers who had neither gastrointestinal symptoms, any prior gastrointestinal surgery, nor were taking medications known to affect gastrointestinal function. FP patients were recruited successively from referrals to the Gastroenterology Outpatient Clinic and Gastrointestinal Diagnostic Laboratory for follow-up assessment of mild to moderate postoperative symptoms. All subjects gave written informed consent. The study protocol was approved by the Northwestern University Institutional Review Board.

Functional Luminal Imaging Probe

Esophagogastric junction distensibility was measured using a custom-made FLIP designed to measure intraluminal cross-sectional areas (CSAs) as a function of distention pressure as previously described.²¹ In brief, the probe assembly was 80 cm long, with the proximal 68 cm constructed from a 4.5-mm outer diameter nine-lumen polyurethane tube and the distal 12 cm constructed of a 1.6-mm outer diameter double-lumen polyethylene tube (Fig. 1; GMC Medical, Hornslet, Denmark). A noncompliant 35- μ m-thick polyesterurethane bag was mounted on the distal end. Within the bag was a 3.2-cm segment comprised of nine-ring electrodes spaced 4 mm apart for impedance planimetry measurement. Excitation electrodes at either end emitted a constant low current of 100 μ A at a frequency of 5 kHz making the voltage measured across each of the eight adjacent pairs of ring electrodes proportional to the impedance between them. As the bag was filled with 0.2% saline, the impedance across each segment was thus inversely proportional to the CSA of the bag at that locus. Maximal bag diameter was 3.2 cm. The probe also contained two low compliance saline perfused channels (1 mm ID), connected to external pressure transducers (Edwards TruWave, Edwards Lifesciences, Irvine, CA, USA), providing pressure measurements within and 2.5 cm proximal to the bag.

Measurements from the eight electrode pairs and pressure transducers were sampled at 10 Hz with the data acquisition system, transmitted serially to a personal computer, and displayed in real-time using custom-made software programmed in Labview[®] version 6.1 (National Instruments, Austin, TX, USA). The probe was calibrated at body temperature prior to each study by filling the bag with 0.2% saline within a calibration block containing a set of cylindrical cutouts with CSAs ranging from 50 to 616 mm². The pressure transducers were calibrated at 0 and 75 mmHg.

High-Resolution Manometry

HREPT data were obtained using a solid-state manometric assembly (4.2 mm outer diameter) with 36 circumferential sensors spaced at 1-cm intervals (Sierra Scientific Instruments, Los Angeles, CA, USA), the recording characteristics of which have been previously described.^{22,23} Pressure transducers were calibrated at 0 and 100 mmHg using externally applied pressure prior to the study.

Experimental Protocol

Studies were performed in a supine position after at least a 6-h fast. Patients underwent transnasal placement of the manometry assembly, which was positioned to record from the hypopharynx to the stomach with about five intragastric sensors. The assembly was fixed in place by taping it to the nose. The manometric protocol included at least a 30-s period of baseline recording in a supine position followed by a series of ten 5-ml and two 10-ml test

water swallows. Once the manometric assembly was removed, the FLIP was placed transnasally into the stomach and withdrawn until the bag was centered at the EGJ based on HREPT measurements.^{23,24} Bag position was also confirmed fluoroscopically by partially filling the FLIP bag (20–30 ml) and observing transit of swallowed barium into the stomach (Fig. 2). The probe was then fixed in place by taping it to the nose. Interdeglutitive (30 s) and deglutitive (dry swallow) FLIP measures of CSA and distention pressure were made with the bag filled to 30, 40, 50, and 60 ml. Each volume was tested in triplicate and repeated if the subject inadvertently swallowed. Swallows were evident by a peristaltic contraction at the perfused channel 2.5 cm proximal to the bag. EGJ geometry was monitored in real time to assure proper bag placement, and instances of suspected migration were confirmed fluoroscopically before repositioning and repeating the measurement.²⁰

Data Analysis

High-Resolution Manometry—The HREPT plots were analyzed to characterize EGJ morphology and deglutitive function in terms of end-expiratory EGJ pressure, inspiratory augmentation of EGJ pressure, length of the EGJ high-pressure zone (HPZ), abdominal length of the EGJ HPZ, and integrated relaxation pressure (IRP) during deglutitive relaxation as previously described.^{22–27} Distal esophageal peristalsis was considered normal when the peristaltic amplitude and velocity were ≥ 30 mmHg and < 10 cm/s. Failed or hypotensive peristalsis with 50–60% of test swallows constituted intermittent hypotensive peristalsis, 70–90% frequent hypotensive peristalsis, and 100% absent peristalsis. Distal esophageal contractile vigor was measured by the distal contractile integral (DCI). Peristalsis-related intrabolus pressure (IBP) was measured 1 cm proximal to the EGJ and summarized as an average pressure during the 3 s of maximal IBP during esophageal emptying (IBP_{esoph}).²⁸

Functional Luminal Imaging Probe—Interdeglutitive EGJ CSAs and intrabag pressure were assessed at each FLIP bag volume by quantifying the 50th percentile of each measure during each test 30-s recording. The corresponding deglutitive EGJ measures were assessed during the period between a dry swallow and the distal esophageal peristaltic or postdeglutitive EGJ contraction. The deglutitive EGJ response was quantified by the 1-s nadir in the intrabag pressure and the corresponding CSAs. Measurements of CSA were made at each of the eight electrode pairs covering a span of 3.2 cm.

EGJ compliance (volume vs. pressure) was calculated based on the intrabag pressure and an approximation of EGJ volume across the range of FLIP bag volumes associated with measureable distention. EGJ volume was estimated by identifying the narrowest CSA (invariably at the diaphragmatic hiatus), extending distally for three additional CSAs and applying the formula $(CSA_x + CSA_{x+4 \text{ mm}} + CSA_{x+8 \text{ mm}} + CSA_{x+12 \text{ mm}}) \times 0.004$ to convert the 4-mm segment CSAs (square millimeters) to milliliters. A linear regression analysis was then applied with the slope of the line representing EGJ compliance (milliliters per millimeters of mercury).

Statistical Analysis

The data from triplicate trials were averaged to describe the EGJ response at each FLIP bag volume for each subject. Data from all the subjects was then expressed as median (5th–95th percentile). Statistical comparisons were performed using Wilcoxon matched pairs test and Kruskal–Wallis test. The relationships between measures provided by the FLIP and HREPT were assessed with Spearman's rank correlation coefficient (r_s). A p value < 0.05 was considered significant.

Results

Demographic and HREPT Data

The FP patients were assessed with FLIP at 4 months to 7 years postoperative with eight of the ten having had their surgery at Northwestern Memorial Hospital (NMH). Those eight operative reports uniformly described a laparoscopic “short floppy” Nissen fundoplication, 2.0–2.5 cm in length, constructed with a 51–60-Fr Maloney dilator placed within the esophagus and mobilization of the fundus by dividing the short gastric vessels. Operative reports were not available for the two patients who had their surgery elsewhere but who were certain that they had complete 360° fundoplication on the basis of preoperative consultation with their surgeons.

The symptoms prior to and following the surgery were recorded in seven of the eight FP patients who had their surgery at NMH. Symptoms of heartburn and regurgitation were consistently present in six of the seven patients prior to the surgery. The three other patients reported having severe heartburn and regurgitation before the surgery. At the time of the study, four of the ten patients reported mild dysphagia, three of the ten patients reported bloating, three of the ten patients reported chest pain, one of the ten patients reported nausea, one of the ten patients reported abdominal pain, two of the ten patients reported heartburn, and one of the ten patients reported heartburn and regurgitation. None of these problems were sufficiently severe for any of these patients to undergo revision surgery.

HREPT data on EGJ parameters showing similar contractile function between control subjects and FP patients are summarized in Table 1. One significant difference between groups was that the length of the EGJ HPZ, both total and intra-abdominal, was slightly shorter in FP patients ($p<0.02$). None of the subjects had a HREPT signature of hiatal hernia defined as a separation greater than 2 cm between the components of the EGJ HPZ (LES and crural diaphragm).²⁴ The barium swallow used to confirm the position of the FLIP bag across the EGJ, verified the absence of hiatal hernia. With respect to peristaltic function, one of the normal controls had frequent hypotensive peristalsis while the remainder were normal. Among the FP patients, two had frequent and one had intermittent hypotensive peristalsis. However, the distal esophageal contractile vigor, summarized as the DCI of the normal and hypotensive peristaltic contractions, was comparable between groups (control, 2,640 (1,297–3,429); FP, 2,193 (418–6,578) mmHg s cm, $p=0.55$). An abnormally high deglutitive IRP (>15 mmHg) was detected in one control and two FP patients.

EGJ Distensibility

When straddling the EGJ, the FLIP bag assumed an hourglass shape with the central constriction at the diaphragmatic hiatus in both control subjects and FP patients. The hourglass shape was present during both the interdeglutitive period and deglutitive relaxation at all FLIP bag volumes (Fig. 3). In fact, evident in Table 2, many subjects in both groups had CSA measurements at the hiatus that were the minimum detectable (50 mm^2) implying that all of the saline within the FLIP bag displaced proximal or distal to it. This suggested that the hiatus was uniformly the least distensible locus within the EGJ. Only with the FLIP bag volume of 60 ml was there nearly consistent hiatal distention above the minimum, at which point the hourglass opened and closed with respiration confirming this to be the diaphragmatic hiatus. Of note, the 60-ml bag volume resulted in pronounced hiatal opening in controls during deglutitive relaxation to a CSA significantly greater than that observed in FP patients (Table 2; $p<0.001$).

In the EGJ dynamic described above, distensile pressure within the FLIP bag increased with increasing bag volume in both subject groups and in both test conditions (Table 3; $p<0.0001$).

Furthermore, the distending pressure within the FLIP bag was consistently greater in FP patients than in control subjects particularly with FLIP bag volumes of 40, 50, and 60 ml ($p < 0.05$; Table 3). Conceptually, pressure within the FLIP bag increased when the increased volume of saline within it could no longer disperse to highly compliant regions proximal or distal to the EGJ presumably because the bag was filled to capacity in those regions. Hence, the observed difference in pressure between the control subjects and FP patients implies that there was a longer zone of measured constriction in the FP patients. This difference was further brought out by the estimated EGJ volume, a measure that utilized the CSA of the hiatus and three distal adjacent FLIP segments. Examining Fig. 4, both during the interdeglutitive period and during deglutitive relaxation, the EGJ of control subjects was widely distended at distensile pressures insufficient to achieve any measureable opening during the same conditions in the FP patients.

The data in Fig. 4 can also be utilized to estimate EGJ compliance, defined as the slope of the EGJ volume vs. intrabag pressure relationship. Since the data points associated with the 40-ml FLIP bag volume did not achieve measureable EGJ distention, this could only be done with the 50- and 60-ml data points. As evident in Fig. 5a, interdeglutitive EGJ compliance was comparable between control subjects and FP patients ($p = 0.13$). As expected, deglutition tended to increase EGJ compliance in controls ($p = 0.08$); the same change in compliance was not seen in FP patients ($p = 0.92$; Fig. 5b).

HREPT vs. FLIP EGJ Measures

The data from controls and FP patients were pooled to test hypotheses on association between FLIP vs. HREPT measures of distal esophageal function. Hypothetically, a less compliant EGJ might exert greater closing pressure and distal resistance for the bolus traversing the esophagus resulting in greater intrabolus pressure. However, there were no significant correlations between FLIP measure of interdeglutitive EGJ compliance and HREPT measures of expiratory EGJ pressure ($r_s = -0.12$, $p = 0.63$) or inspiratory EGJ augmentation ($r_s = 0.25$, $p = 0.29$). Likewise, deglutitive EGJ compliance did not correlate with IBP_{esoph} ($r_s = 0.14$, $p = 0.56$). However, IBP_{esoph} was related to DCI ($r_s = 0.56$, $p = 0.01$) suggesting that the contractile vigor of the distal esophagus increased with outflow resistance. An interesting contrast between the two technologies was that while HREPT estimates of sphincter length found the FP patients to have a significantly shorter HPZ than control subjects, FLIP measures of EGJ volume, by inference length, found the FP patients to have a significantly longer zone of constriction.

Discussion

The EGJ has two distinct dimensions of function—that during nondeglutitive periods to prevent reflux by maintaining closure and that during periods of opening to facilitate trans-EGJ flow, be it esophagogastric or gastro-esophageal. Manometry, or more recently HREPT, directly measures closure forces. This investigation tested the ability of the FLIP, a novel device based on impedance planimetry technology, to quantify EGJ opening CSA in response to controlled intraluminal distension variables. Studies were done on control subjects and patients with satisfactory to good functional outcome from laparoscopic Nissen fundoplication. The major findings of the study were that (1) the FLIP isolated the hiatus as the least distensible locus within the EGJ in both subject groups, (2) the distensibility of the hiatus was significantly greater during deglutitive relaxation in both subject groups, (3) fundoplication patients exhibiting reduced EGJ distensibility and reduced EGJ compliance during deglutitive relaxation compared to control subjects, (4) fundoplication patients exhibited a longer segment of reduced distensibility than did controls, and (5) EGJ attributes demonstrated with FLIP measurements were not mirrored by HREPT findings.

The finding that the least distensible locus within the EGJ is at the hiatus supports similar findings made using barostat^{2,4} or hydrostat³ technology. This was found to be true irrespective of the presence of hiatus hernia or fundoplication. The significance of quantifying this measurement is that this variable dominates the equation for trans-EGJ flow ($\text{Flow rate} = dP \times D^4 / CVL$) in which dP is the trans-EGJ pressure gradient, D is the opening diameter, C is a constant, V is viscosity, and L is the length of constriction.²⁹ Although the length of constriction also figures into the equation, note that D , the diameter of maximal constriction, is raised to the fourth power causing it to be the dominant variable. It follows that this variable is a key determinant of both the efficacy of swallow-related esophageal emptying and the volume of refluxate during periods of sphincter relaxation.² In postfundoplication patients, distensibility within the hiatus is a direct consequence of the details of operative hiatal repair. Quite possibly, this variable, a generally underappreciated source of technical variability in fundoplication surgery, is a major determinant of postoperative outcome in terms of dysphagia and gas bloat.

The FLIP findings of a less distensible hiatus and a longer length of constriction post-FP relative to control subjects, despite somewhat conflicting conclusions based on HREPT measures (Table 1), highlight the distinction between measuring resistance to physically opening the EGJ lumen (FLIP) and measuring contraction within a closed lumen (HREPT). To assume that these techniques are equivalent, assumes that a decrease in contractile pressure, mainly attributable to LES and crural diaphragm contraction, parallels luminal opening dimensions in the absence of that contractile activity. In fact, these two properties have no necessary relationship to each other as the latter is instead related to wall properties of the EGJ and the external constraint on the EGJ imposed by the diaphragmatic hiatus and fundoplication, if present. Fundoplication surgery is clearly designed to modify these latter variables and for that reason, the outcome is better measured with a technique such as FLIP. A “short floppy” fundoplication constructed with a larger caliber dilator within the esophageal lumen should have no obvious effect on the contractility of the LES or crural diaphragm but should limit EGJ distensibility. In fact, evident in Fig. 4, this is what was observed. EGJ distensibility during the interdeglutitive period (with both the LES and crural diaphragm contracting) was similar between subject groups but distensibility during deglutitive relaxation was significantly greater in the control subjects. Although beyond the scope of the current work, it would be of great interest to examine the profile of EGJ distensibility in postfundoplication patients with bothersome dysphagia or gas bloat to see if they are quantifiably different.

Although findings from the current study generally corroborate those obtained from a barostat distention study of a similar population of fundoplication patients,² there is an important difference. Both studies demonstrated increased length of the constricted segment after fundoplication but only the current FLIP study demonstrated reduced compliance during deglutitive relaxation; the barostat study suggested distensibility similar to that of control subjects.² The explanation for this discrepancy is likely methodological. In the barostat study, only a single two-dimensional plane was imaged leaving it vulnerable to error related to asymmetry of the EGJ. FLIP, on the other hand, calculates CSA bases on impedance characteristics irrespective of luminal shape and, thus, is inherently more accurate. FLIP also has the advantage of utilizing data from several adjacent segments within the EGJ, whereas the barostat study analyzed only the single locus of greatest constriction. Together, these advantages, as well as the rapid sampling of the FLIP device, argue that the FLIP is likely the more accurate method for ascertaining intraluminal CSA.

The key data related to EGJ distensibility and compliance gleaned from the FLIP measurements (summarized in Figs. 3 and 4) depend on measurement of the pressure within the FLIP bag rather than the volume within the bag. Although the design of the device does allow for measurement of intrabag pressure, the initial concept of its design was for volumetric distension, which is less relevant when assessing the EGJ. The problem with volumetric

distension is that a substantial portion of the measurement length of the FLIP resides outside of the zone of interest (the EGJ and hiatus), instead residing in the far more compliant distal esophagus or the nearly infinitely compliant proximal stomach. Hence, the initial saline volume instilled into the FLIP bag disperses to these more compliant ends before challenging the area of interest. EGJ distension occurs only when the more compliant ends are filled to capacity and intrabag pressure increases with added volume. In the current study, this occurred only with bag volumes of 50 and 60 ml (Fig. 3) making the data obtained with lesser distension volumes irrelevant to the EGJ. Given these considerations, improvements in FLIP design making it more applicable to the EGJ would reduce the overall bag capacity so that lesser volumes are required to achieve EGJ distension, make the pressure sensor more robust by incorporating solid state technology, and, hopefully, introduce an easier method to achieve pressure controlled distension, akin to hydrostat technology.³

Conclusion

This experiment evaluated the utility of FLIP technology in a comparison of EGJ distensibility in FP patients and control subjects. The FLIP found the least distensible locus to be at the hiatus in both subject groups. The other major finding was that EGJ distensibility was reduced and the length of constriction increased post-FP. These features were not paralleled by manometric findings emphasizing the difference between assessing contractility in a closed lumen and distensibility (opening dimensions) in the setting of EGJ relaxation. Further study will be needed to ascertain whether or not differences in FLIP measures of EGJ distensibility correlate with significant postoperative symptoms of dysphagia or gas bloat.

Acknowledgments

The authors would like to thank Mr. Patrick N. Smith-Ray (Department of Surgery, Feinberg School of Medicine, Northwestern University) for providing patient symptomatology reports and Dr. Sudip K. Ghosh (Department of Medicine, Feinberg School of Medicine, Northwestern University) for initial assistance with the study.

Funding This work was supported by R01 DC00646 (P.J.K. and J. E.P.) from the Public Health Service and the AGA June and Donald O Castell Esophageal Clinical Research Award (J.E.P.).

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Figure 1.
Distal end of FLIP showing the electrode and pressure measurement loci within the bag (modified from McMahon et al.²⁰).

Figure 2.

A fluoroscopic image with a distended FLIP bag in situ straddling the EGJ following a 5-ml barium swallow.

Figure 3.

Esophagogastric junction geometry as depicted by the FLIP. The hourglass shape of the EGJ narrowed at the hiatus (y-axis=0 cm) in both control subjects (*black*) and fundoplication patients (*gray*). The *panels* show the EGJ measurements with a 60-ml FLIP bag volume during the interdeglutitive period (**a**) and deglutitive relaxation (**b**).

Figure 4.

Measured FLIP bag distensile pressure and estimated EGJ volume with the FLIP bag filled to 40 ml (*lower dots*), 50 ml (*middle dots*), and 60 ml (*upper dots*). Both control subjects (*black*) and fundoplication patients (*gray*) exhibited measureable EGJ distention during the interdeglutitive period (*solid lines*) and deglutitive relaxation (*dashed lines*) only with 50- and 60-ml FLIP bag volumes. Both groups exhibited increased EGJ volume during deglutitive relaxation. However, the distensile pressures associated with EGJ distention were consistently 8–10 mmHg greater in the FP patients compared to the control subjects (see also Table 3).

Figure 5. Esophagogastric junction compliance in controls and postfundoplication patients during the interdeglutitive period (**a**) and deglutitive relaxation (**b**). Median (5th–95th percentile); * $p < 0.05$ vs. controls.

Table 1

Esophagogastric Junction Pressure Morphology and Deglutitive Function Reported as Median (5th–95th Percentile)

	Controls	Fundoplication
Expiratory EGJ pressure (mmHg)	18 (10–36)	15 (6–22)
Inspiratory EGJ augmentation (mmHg)	17 (8–37)	13 (7–26)
Length of EGJ HPZ (mm)	45 (42–57)	37 (29–45) *
Abdominal length of EGJ HPZ (mm)	28 (24–44)	23 (19–30) *
Deglutitive IRP (mmHg)	12 (5–17)	13 (6–17)
IBP _{esoph}	17 (12–21)	18 (11–24)

Deglutitive IRP was abnormal (>15 mmHg) in one control and two patients. Median (5th–95th percentile)

HPZ high-pressure zone, IRP integrated relaxation pressure

*
 $p < 0.05$ vs. controls

Table 2

CSA (Square Millimeters) of the Diaphragmatic Hiatus (Narrowest EGJ CSA Measured by the FLIP) During Volume Distensions Reported as Median (5th–95th Percentile)

FLIP bag volume (ml)	Control subjects		Fundoplication patients	
	Interdeglutitive	Deglutitive	Interdeglutitive	Deglutitive
30	50 (50–68)	52 (50–166)	51 (50–60)	52 (50–70)
40	50 (50–50)	51 (50–55)	51 (50–56)	50 (50–54)
50	50 (50–52)	54 (50–106)	61 (52–88)	60 (50–109)
60	93 (50–182)	233 (55–429)**	159 (68–245)	102 (68–272)*

The minimal detectable CSA was 50 mm²

* $p < 0.001$ vs. controls;

** $p < 0.05$ vs. interdeglutitive period

Table 3

Pressure (Millimeters of Mercury) Within the FLIP Bag During Distension Reported as Median (5th–95th Percentile)

FLIP bag volume (ml)	Control subjects		Fundoplication patients	
	Interdeglutitive	Deglutitive	Interdeglutitive	Deglutitive
30	16 (13–19)	13 (10–16) **	19 (13–21)	13 (8–18) **
40	17 (11–21)	14 (8–18) **	22 (17–27) *	17 (12–20) **
50	20 (13–26)	15 (10–20) **	26 (19–31) *	21 (14–26) *, **
60	23 (15–30)	17 (11–25) **	30 (21–34) *	23 (16–28) *, **

* $p < 0.05$ vs. controls;

** $p < 0.05$ vs. interdeglutitive period