Quantifying EGJ morphology and relaxation with high-resolution manometry: a study of 75 asymptomatic volunteers

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Pandolfino, John E., Sudip K. Ghosh, Qing Zhang, Andrew Jarosz, Nimeesh Shah, and Peter J. Kahrilas. Quantifying EGJ morphology and relaxation with high-resolution manometry: a study of 75 asymptomatic volunteers. Am J Physiol Gastrointest Liver Physiol 290: G1033–G1040, 2006. First published February 2, 2006; doi:10.1152/ajpgi.00444.2005.—Our aim was to define normal esophagogastric junction (EGJ) morphology and relaxation characteristics using high-resolution manometry (HRM). To this end, 75 asymptomatic controls underwent HRM with a solid-state manometric assembly incorporating 36 circumferential sensors spaced at 1-cm intervals positioned to record from the hypopharynx to the stomach. Ten 5-ml water swallows were obtained. EGJ relaxation was quantified by 1) nadir pressure, 2) the lowest 3-s mean residual pressure after swallow (E-sleeve), and 3) the transsphincteric gradient 2–6 s after swallowing measured from 2 cm above to 2 cm below the EGJ. A new parameter, integrated relaxation resistance (IRR), was also calculated. The IRR calculation accounted for both the duration of EGJ relaxation and instantaneous E-sleeve-type relaxation pressures during the entire interval of relaxation. The means and ranges (5–95th percentile) for nadir lower esophageal sphincter relaxation pressure (mean: 3.9 mmHg, range: 0–10.1 mmHg) and E-sleeve relaxation pressure (mean: 8.1 mmHg, range: 4.1–15.1 mmHg) were consistent with previously reported values. The mean relaxation interval was 7.95 ± 0.2 s (mean ± SE), whereas the median relaxation pressure during that interval was 10.7 ± 0.5 mmHg (mean ± SE). Mean IRR was 1.3 mmHg/s (95th percentile: 3.0 mmHg/s). Mean EGJ length was 3.7 cm. In conclusion, HRM provides a seamless dynamic representation of pressure within and across the EGJ. In addition to providing conventional EGJ relaxation parameters, this technology also creates opportunities to quantify more precise measures of EGJ relaxation and morphology.

THE ANALYSIS of esophagogastric junction (EGJ) pressure dynamics, particularly deglutitive relaxation, is arguably the most important measurement made during clinical esophageal manometry. The diagnosis of achalasia hinges on defining and detecting impaired lower esophageal sphincter (LES) relaxation. Furthermore, EGJ incompetence is a primary determinant of gastroesophageal reflux disease (GERD) severity, and pressure gradients across the EGJ during LES relaxation have important implications in GERD pathogenesis and in the evaluation of functional outlet obstruction in dysphagic individuals. Despite these observations, there is a notable lack of quantitative normative data regarding swallow-induced LES relaxation and trans-EGJ pressure gradients. This deficiency is largely attributable to the lack of standardized recording methodology for esophageal manometry and to various technical limitations of existing manometric systems.

A major evolution in manometric methodology has been the introduction of high-resolution manometry (HRM), with the basic concept being that by vastly increasing the number of recording sites and decreasing the spacing between them, one can completely define the intraluminal pressure environment without spatial gaps between recording sites and, consequently, with minimal movement-related artifacts. However, the vastly increased quantity of data associated with HRM studies introduces new challenges with respect to data display and data analysis. Hence, algorithms have been devised to smoothly interpolate HRM data, making it appear as a space-time continuum (5), usually displayed in the format of isobaric contour plots (1). The advantages of analyzing EGJ pressure dynamics with isobaric contour plots are multiple, but the most evident is that it provides a seamless, dynamic representation of pressure at every axial position within and across the EGJ. An example of this is found in the work of Staiano and Clouse (5), which aimed at defining the optimal criteria for incomplete EGJ relaxation with HRM. They reported that using isobaric contour analysis, a transsphincteric pressure gradient exceeding 5 mmHg had high sensitivity (94%) and specificity (89%) for achalasia regardless of the presence or absence of peristalsis.

Although the HRM studies briefly described above are unarguably elegant and evolutionary, the following limitations remain: 1) HRM systems using water-perfused catheters are not widely available, 2) they are still extremely demanding methodologically, and 3) they are ultimately limited by hydrostatic artifacts. However, a 36-channel solid-state HRM system has recently become available that circumvents these limitations. The aim of this study was to apply this novel device to a detailed analysis of EGJ pressure dynamics during swallowing in normal individuals, leveraging the strengths of the HRM technique in conjunction with computational algorithms devised to reduce sphincter performance to its most fundamental attributes. In so doing, a new paradigm for the quantification of EGJ pressure dynamics during swallowing was devised that will hopefully optimize the utility of HRM in clinical and investigative manometry studies.

METHODS

Patients

Manometric studies were done on 75 asymptomatic volunteers (40 men and 35 women, age: 19–48 yr). Subjects consisted of volunteers recruited by advertisement or word of mouth. Subjects had no history of gastrointestinal symptoms or upper gastrointestinal tract surgery.
and all were without any significant medical conditions. The study protocol was approved by the Northwestern University Institutional Review Board, and informed consent was obtained from each subject.

High-Resolution Manometry

A solid-state manometric assembly with 36 circumferential sensors spaced at 1-cm intervals (4.2 mm outer diameter) was used (Sierra Scientific Instruments; Los Angeles, CA). This device uses proprietary pressure transduction technology (TactArray) that allows each of the 36 pressure-sensing elements to detect pressure over a length of 2.5 mm in each of 12 radially dispersed sectors (Fig. 1). The sector pressures are then averaged, making each of the 36 sensors a circumferential pressure detector with the extended frequency response characteristic of solid-state manometric systems. Before the recording, transducers were calibrated at 0 and 100 mmHg using externally applied pressure. The response characteristics of each sensing element were such that they could record pressure transients in excess of 6,000 mmHg/s and were accurate to within 1 mmHg of atmospheric pressure for measurements obtained for at least the final 5 min of the study, immediately before thermal recalibration (see Study Protocol).

Study Protocol

After a brief interview and exam to assure the absence of gastrointestinal symptoms and to make anthropometric measurements, subjects underwent transnasal placement of the manometric assembly. Studies were done in the supine position after at least a 6-h fast, and the manometric assembly was positioned to record from the hypopharynx to the stomach with about five intragastric sensors. The catheter was fixed in place by taping it to the nose. The manometric protocol included a 5-min period to assess basal sphincter pressure, 10 water swallows of 5 ml, and 1 water swallow each of 1 (dry), 10, and 20 ml.

HRM. Manometric data were initially analyzed using ManoView analysis software (Sierra Scientific Instruments). First, data were corrected for the thermal sensitivity of the pressure-sensing elements using the thermal compensation function of ManoView. This was done by visually identifying the instant when the assembly was pulled from the nose at the end of the recording. Immediately after that instant, the catheter was still at body temperature, but all pressure sensors were exposed to atmospheric pressure. The software routine then sets this pressure as zero and calculates the magnitude of the pressure correction required for each sensing element. Those sensor-specific thermal correction factors are then applied to the entire manometric data set, in essence correcting it for temperature-dependent calibration drift. Note that although this sensor technology is subject to thermal drift, that effect is almost linear so that the correction factors applied to reestablish the zero reference will also correct errors attributable to thermal drift in the entire data set.

Further characterization of EGJ pressure morphology was performed with a computer program (MATLAB, The MathWorks; Natick, MA) customized for processing binary manometric data into isocontour pressure plots and spatial pressure variation plots. This was done by first exporting the binary manometry data from ManoView in ASCII text format for processing and storage. These ASCII files were then reconverted into a known binary format for use in MATLAB, and isocontour or spatial pressure variation plots were generated. In order for these plots to appear smooth (as opposed to notched), the data set was enhanced both in the time dimension (between sampling times) and spatial dimension (between pressure recording sites). This interpolation was done using a cubic spline algorithm implemented on a finely resolved rectilinear space-time grid to generate intermediate data points, resulting in a virtual increase in the spatial data from 1 to 10 recording sites/cm and doubling the temporal sampling from 35 to 70 Hz (2).

After thermal correction, the EGJ pressure profile was analyzed. Components of the EGJ were readily identified on the isocontour plots as abrupt pressure transitions. The proximal border of the EGJ was defined by a pressure increase of ≥2 mmHg/cm pressure relative to intraesophageal pressure. The distal border of the EGJ was defined by a pressure increase of ≥2 mmHg/cm relative to intragastric pressure. The axial position of maximal EGJ pressure (EGJmax) was defined as the greatest pressure peak encountered progressing into the EGJ from the esophagus. Inspiratory EGJ pressure was defined as the maximal, or peak, pressure occurring during the normal respiratory cycle. To minimize sampling errors, a mean of five consecutive values was derived. Expiratory sphincter pressure was defined as the pressure at the midpoint between adjacent inspiratory sphincter pressures during the normal respiratory cycle. Again, to minimize sampling errors, a mean of five consecutive values was derived. All EGJ pressures and EGJ relaxation parameters were referenced to intragastric pressure; analyses focused on concurrent esophageal and gastric pressure gradients were referenced to atmospheric pressure.

EGJ relaxation parameters. EGJ basal and relaxation pressures were measured using the isobaric contour tool in ManoView. The isobaric contour tool allows delineation of the anatomic/temporal boundaries of a pressure domain of user-designated magnitude (Fig. 2). EGJ relaxation parameters were initially quantified by three methods (Fig. 3): 1) nadir pressure during the relaxation interval ascertained using the isobaric contour tool, 2) an automated measurement of the lowest mean residual pressure over a 3-s interval within the postdeglutitive period (Manoscan E-sleeve), and 3) the trans sphincteric gradient. The trans sphincteric gradient was computed using an algorithm that first isolated the 4-s period beginning 2 s after the swallow. The observer then identified the midpoint of the EGJ, and the algorithm computed the mean pressure differential between the distal esophagus (2 cm above the upper aspect of the EGJ) and the proximal stomach (2 cm below the distal aspect of the EGJ) during that 4-s period. The three relaxation parameters were also measured for the swallows of 1 (dry), 10, and 20 ml.

In addition to the above analyses, a program was written in MATLAB to quantify the integrated relaxation resistance (IRR) during EGJ relaxation. IRR was expressed as mmHg/s relative to intragastric pressure. IRR curves were derived from a computational algorithm that examined the EGJ region from the onset of deglutition at the upper esophageal sphincter (UES) until the closure event (or 10 s if no peristalsis occurred) within the region spanning from 2 cm above the proximal aspect of the EGJ to its distal aspect. The computational routine examined each time sample (35 Hz) within the interval of interest and ascertained the instantaneous EGJmax. Thus

![Fig. 1. Solid-state manometric assembly with 36 sensors spaced at 1-cm intervals. Each pressure sensor consists of 12 radially dispersed sensing elements that are 2.5 mm in length. Sector pressures are averaged within each sensor, making it circumferentially sensitive.](image-url)
Fig. 2. Isobaric contour plot of transesophageal contractile activity during normal respiration displaying an overview of regional differences in intraluminal pressure integrated over time. High-pressure zones, such as the upper esophageal sphincter (UES; top) and esophagogastric junction (EGJ; bottom) are easily recognized by sharp transitions in pressure. This contour plot illustrates the use of the isobaric contour tool of ManoView software, set here at 14 mmHg. The time of peak inspiration is identified by the maximal augmentation (and descent) of EGJ pressure. Expiratory pressures were measured midway between adjacent peak inspirations. The isobaric contour tool allows delineation of anatomic/temporal boundaries of a pressure domain of user-designated magnitude. LES, lower esophageal sphincter.

Fig. 3. Measurement of EGJ relaxation parameters using isocontour plots. Nadir EGJ relaxation pressure was measured by scaling down the isobaric contour tool to the pressure level at which the minimal pressure domain is imaged. In this example, the nadir LES pressure is 4 mmHg. The E-sleeve measurement tool is illustrated by the solid black box, which provides the 3-s interval in which the mean residual pressure is measured. In this example, the E-sleeve measurement is 8.2 mmHg. The dashed white box represents the spatial and temporal domain used for the integrated relaxation resistance (IRR) measurement. The interval analyzed begins with swallowing and ends when peristalsis of the distal esophagus intersects with the EGJ.
Fig. 4. Methodology for the calculation of IRR. 

A: Isobaric contour plot of a swallow highlighting the interval of potential EGJ relaxation extending from UES relaxation to the arrival of the peristaltic contraction (white dashed box). The inset in A magnifies the EGJ relaxation in time, spatial resolution, and pressure resolution; note the clear definition of crural diaphragm contractions 1 and 2. B–E each focus on the same dataset as the inset in A but illustrate the calculation of the period of flow-permissive time at 20 (B), 22 (C), 24 (D), and 26 mmHg (E). In B–E, the thick solid isobaric contour line indicates the flow-permissive pressure. Note that as the flow-permissive pressure increases, added periods of flow-permissive time are identified. F: Spatial pressure variation plot of the same dataset as in A, with the inset in F again showing the period of EGJ relaxation. Note how the EGJ is obstructive to flow until the 4.2-s point, at which time a favorable flow-permissive gradient occurs, persisting until 6.2 s (flow-permissive period is highlighted).
mean EGJ pressure (E-sleeve), and the transsphincteric gradient were 0.5-mmHg increment of esophageal clearance pressure (up to 50 mmHg) throughout deglutitive relaxation (Fig. 4). To summarize the plot, two numbers were derived: 1) the relaxation interval, defined as the period of time until the cumulative IRR curve attained 95% of its plateau value; and 2) median flow permissive pressure, defined as the pressure magnitude at which half the relaxation interval is greater and half less. These two measures have opposite implications with respect to sphincter performance: a low median flow-permissive pressure and a high-relaxation interval facilitate transsphincteric flow as each is indicative of low sphincter resistance. Hence, the summary term for the IRR is median flow-permissive pressure divided by the relaxation interval, expressed as mmHg/s, with lower values indicative of good relaxation performance.

Morphology of the EGJ pressure profile. The analyses of EGJ pressure morphology and transsphincteric gradients during normal respiration were performed by converting the manometric data into spatial pressure variation plots with a sampling frequency of 5 Hz (Fig. 5). For each line of the spatial pressure variation plot, position along the y-axis indicates spatial position of the pressure sensor and deflection along the x-axis indicates pressure magnitude. As with isobaric contour plots, spatial data resolution is enhanced by interpolation between adjacent sensor positions with a smoothing function. Transsphincteric gradients were characterized by measuring esophageal pressure and gastric pressure at inspiration and expiration (Fig. 5). EGJ pressure morphology was summarized by the axial positions of EGJtop, EGJmax and EGJbottom relative to the UES, again, in both inspiration and expiration (Fig. 5). Note that measurements of EGJ spatial limits were made at actual (whole cm) rather than interpolated (each mm) data points, making the overall accuracy of any spatial measurement ±5 mm and EGJ length, because it entailed two axial measurements, ±1 cm. Thus a compensation correction of 5 mm was added to each measurement that assessed either EGJtop or EGJbottom.

Statistical Analysis

Basal EGJ pressure, nadir EGJ relaxation pressure, 3-s residual mean EGJ pressure (E-sleeve), and the transsphincteric gradient were summarized using means ± SE. ANOVA was used to compare the mean values of EGJ relaxation parameters across volume swallows. Pearson’s correlation coefficient was calculated to assess the relationship among the three EGJ relaxation parameters. Similarly, the relaxation interval, median flow-permissive pressure, and IRR were also summarized using means ± SE.

Simultaneous baseline EGJ pressure, intraesophageal pressure, intragastric pressure, and the gastroesophageal pressure gradient were analyzed during both inspiration and expiration and referenced to atmospheric pressure to assess the effect of respiration on these parameters. These measurements were summarized using means (SD) and compared using a paired t-test. Measurements made from the spatial pressure variation plots to assess EGJ pressure morphology were also expressed as means (SD).

RESULTS

All 75 subjects completed the manometry protocol. The study population was evenly divided in terms of gender (40 men and 35 women) with a mean age of 27.3 yr (5.7 SD). Mean height and weight were 172.5 cm (10.0 SD) and 77.9 kg (22.0 SD), respectively. Mean body mass index and waist circumference were 22.5 kg/m² (2.7 SD) and 80.1 cm (10.6 SD) respectively.

EGJ Relaxation Parameters

Means and normal ranges for basal EGJ pressure and EGJ relaxation parameters for 5-ml water swallows are shown in Table 1. The correlations between the transsphincteric gradient and both the E-sleeve and nadir EGJ pressure measurements were moderate (Fig. 6). Furthermore, the three subjects with E-sleeve measurements greater than the 95th percentile of the

![Diagram of EGJ pressure profile](http://ajpgi.physiology.org/)

**Table 1. EGJ relaxation parameters during swallowing**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
<th>Normal Range (5–95th percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal EGJ pressure, mmHg</td>
<td>15.8 (8.4)</td>
<td>5.0–31.6</td>
</tr>
<tr>
<td>Nadir EGJ relaxation pressure, mmHg</td>
<td>3.9 (3.2)</td>
<td>0.0–10.1</td>
</tr>
<tr>
<td>E-sleeve, mmHg</td>
<td>8.1 (3.3)</td>
<td>4.1–15.1</td>
</tr>
<tr>
<td>Transsphincteric gradient, mmHg</td>
<td>2.2 (3.6)</td>
<td>−3.4 to 6.9</td>
</tr>
</tbody>
</table>

EGJ, esophagogastric junction.
group (15.1 mmHg) also had nadir pressure values greater than the 95th percentile value (10.1 mmHg). EGJ relaxation pressure (E-sleeve) also varied with bolus volume such that dry swallows (1 ml) were associated with greater relaxation pressures compared with 5-, 10-, and 20-ml swallows (Fig. 7). Five-milliliter swallow E-sleeve relaxation pressures were significantly greater than 20-ml swallow values \( P < 0.05 \), whereas 10-ml swallows revealed a trend toward greater values compared with 20-ml swallow values \( P = 0.07 \). Similarly, the mean nadir EGJ relaxation pressures during dry swallow (1 ml) measurements were significantly greater than the three larger volume swallows. However, no statistical difference existed in nadir EGJ relaxation among the three larger volume swallows.

The mean transsphincteric gradient for 5-ml swallows was 2.2 mmHg with a 95th percentile value of 6.9 (Table 1). As expected, the transsphincteric gradient was also altered by increasing the bolus volume (Fig. 7). Dry swallows were associated with negative transsphincteric gradients, significantly less than with 5-, 10-, or 20-ml swallows. There was also a significant increase in the transsphincteric gradient between 5- and 20-ml water swallows. Two of the three subjects with outlier values for the transsphincteric gradient also had greater than normal E-sleeve and nadir LES relaxation measurements. One subject had a grossly abnormal transsphincteric gradient (18.4 mmHg) without abnormal LES relaxation. Further analysis revealed that this subject had a short esophagus with elevated intrabolus pressure values but normal emptying through the EGJ as determined from spatial pressure variation plots.

The results of the IRR analysis are illustrated in Fig. 8. The mean relaxation interval was \(~7.9 \pm 0.2\) s (means \( \pm \) SE) and the average flow-permissive pressure was \(10.7 \pm 0.6\) mmHg (means \( \pm \) SE). Thus the mean IRR value for all 75 subjects was \(1.3 \pm 0.2\) mmHg/s (means \( \pm \) SE). Plotting the 95th percentile value for each flow-permissive pressure gradient at 0.5-mmHg increments generated a second curve representing the 95th percentile cutoff for normal values and a 95th percentile IRR value of 3.0 mmHg/s. In addition, IRR was plotted against the three standard LES relaxation parameters (Fig. 9), demonstrating a significant, although relatively weak, correlation with each. Of note, however, only one normal subject exceeded the normal range of IRR, as opposed to three subjects with each of the other measures. This suggests that, by taking into account both relaxation pressure and the time available for bolus transit, IRR may prove to be a better clinical discriminator.

**Morphology of the EGJ Pressure Profile**

All measures of EGJ pressure exhibited significant variation with respiration such that the EGJ pressure itself and the emptying through the EGJ as determined from spatial pressure variation plots.

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pressure gradient across it almost doubled (Table 2). However, the overall EGJ length did not change significantly during respiration. The EGJ also appeared to be relatively fixed in place relative to the diaphragm such that it descended 0.85 cm during inspiration while maintaining a fixed relationship between the top of the EGJ pressure profile and the locus of EGJ\textsubscript{max}, indicative of the locus of crural diaphragm impingement; this synchronous movement is also evident in Fig. 2.

**DISCUSSION**

To date, esophageal manometry has been a poorly standardized clinical test. Largely owing to methodological inconsistency, there has been little precision of measurement, few agreed-upon conventions for the calculation or interpretation of manometric variables, and great reluctance of one center to base therapeutic decisions on manometric findings emanating from another center. Even within a highly specialized center, interobserver agreement in the interpretation of manometric studies has been poor (4). Examining the roots of this morass, it largely stems from the need to select among competing recording technologies, each with inherent limitations. Hence, the dialogue among investigators essentially amounted to arguments over which compromises were more tolerable: the enhanced recording fidelity of solid-state transducers versus the flexibility in sensor placement and greater number of sensors possible with water-perfused assemblies, the spatial integration of a sleeve sensor versus the spatial resolution of point sensors, the simplicity of unidirectional sensors versus the elegance of multidirectional sensors, etc. Despite these dialogues, the elements of the ideal manometric system have always been clear: a virtually limitless number of sensors spaced so closely together that intermediate spatial data between sensors can be interpolated, each with circumferential sensitivity and each with perfect recording fidelity not subject to hydrostatic artifacts. Although such perfection may never be completely achieved, a device closely approximating these characteristics was used in this investigation. What we report here is a comprehensive analysis of the resultant data set obtained from 75 normal individuals aimed at improving the precision and standardization of manometric assessment of the EGJ.

From a conceptual viewpoint, the EGJ represents the locus of outflow obstruction from the esophagus. Although that obstruction can be further characterized by EGJ contraction and luminal distensile characteristics in the absence of contraction, manometry is inherently able to directly measure only intraluminal pressure, which exhibits some dependence on each of these variables. Nonetheless, the object of the manometric measurement is to quantify intraluminal EGJ pressure, regardless of its determinants. Thus, to fully define EGJ relaxation in response to swallowing, we analyzed the entire postdeglutitive period and developed the concept of IRR as a precise measure of both the degree and duration of postdeglutitive outflow resistance. As evident in Fig. 9, IRR compares favorably with more conventional measures of EGJ relaxation.

Table 2. *EGJ pressure and morphology during normal respiration*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Expiration</th>
<th>Inspiration</th>
<th>Change From Expiration to Inspiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGJ pressure, mmHg</td>
<td>23.9 (9.3)*</td>
<td>40.9 (12.3)</td>
<td>16.9 (8.2)</td>
</tr>
<tr>
<td>Esophageal pressure, mmHg</td>
<td>0.3 (2.3)*</td>
<td>-4.7 (2.3)</td>
<td>5.0 (1.8)</td>
</tr>
<tr>
<td>Gastric pressure, mmHg</td>
<td>5.5 (2.1)*</td>
<td>8.6 (2.3)</td>
<td>-3.1 (1.0)</td>
</tr>
<tr>
<td>Gastroesophageal pressure</td>
<td>5.2 (2.3)*</td>
<td>13.3 (2.8)</td>
<td>-8.1 (2.1)</td>
</tr>
<tr>
<td>gradient, mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UES\textsubscript{b} - EGJ\textsubscript{T}, cm</td>
<td>22.4 (2.2)</td>
<td>23.3 (2.2)</td>
<td>-0.9 (0.7)</td>
</tr>
<tr>
<td>EGJ\textsubscript{T} - EGJ\textsubscript{max}, cm</td>
<td>1.7 (0.4)</td>
<td>1.7 (0.4)</td>
<td>0.0 (0.4)</td>
</tr>
<tr>
<td>EGJ\textsubscript{max} - EGJ\textsubscript{b}, cm</td>
<td>2.0 (0.6)</td>
<td>2.1 (0.8)</td>
<td>-0.1 (0.6)</td>
</tr>
<tr>
<td>EGJ\textsubscript{T} - EGJ\textsubscript{b}, cm</td>
<td>3.7 (0.7)</td>
<td>3.7 (0.9)</td>
<td>-0.1 (0.7)</td>
</tr>
</tbody>
</table>

*All values are expressed as (SD). UES\textsubscript{b}, bottom of the upper esophageal sphincter; EGJ\textsubscript{T}, top of the EGJ; EGJ\textsubscript{max}, maximal EGJ pressure; EGJ\textsubscript{b}, bottom of the EGJ. *P < 0.05 vs. inspiration.
Our control subjects had a mean IRR value of 1.3 and a 95th percentile value of 3.0. Furthermore, the most extreme outliers within our normal dataset, with E-sleeve relaxation pressures greater than the 95th percentile of normal and clearly within the achalasia range (16.5, 17.3, and 18.5 mmHg) (5) had normal IRR values (1.0, 2.4, and 2.9). This suggests that IRR may be a better discriminating variable in the clinical domain. Proof of that, however, awaits a more definitive analysis.

High-resolution manometry analysis also permits a more precise definition of EGJ pressure morphology (Fig. 5). In particular, the locus of the crural diaphragm within the EGJ is evident by its pressure signature during respiration. Furthermore, by referencing the position of pressure landmarks within the EGJ to the UES position, the degree of axial fixation of the EGJ to the diaphragm can be characterized (Table 2). That analysis revealed a respiratory excursion of the EGJ virtually superimposable on that of the diaphragm, suggesting that the two were relatively tightly attached to each other in these normal controls. This analytic technique may potentially stratify anatomic and physiological abnormalities of the EGJ such as phrenoesophageal ligament laxity, axial displacement of the LES relative to the diaphragm, and transphincteric pressure gradients that may all be important in GERD pathogenesis.

Although the precise quantification of EGJ relaxation after swallowing contributes greatly to the interpretation of clinical manometric evaluations, the functional outcome of a swallow with respect to esophageal emptying ultimately depends on the balance between peristaltic clearing forces and IRR. Thus further application of this analytic technique will require an equally precise analysis focused on the integrity and persistence of the peristaltic wavefront during the relaxation interval. Defects in EGJ bolus transit as occur in achalasia or after fundoplication are heterogenous in their EGJ relaxation characteristics and peristaltic performance, necessitating that the balance between the two be considered (3). Further evidence of this is the finding that >95% of patients with impaired EGJ relaxation have normal bolus transit when analyzed using intraluminal impedance (6).

In conclusion, this investigation demonstrated that HRM using a 36-channel solid-state catheter provides a seamless, dynamic representation of pressure within and across the EGJ both at rest and during deglutitive relaxation. Spatial resolution of the contributing elements of the EGJ and quantification of the degree to which they move and are augmented with respiration was achieved. Application of this technology permitted the development of new functional paradigms for assessing EGJ function and dysfunction. The clinical application of these new functional paradigms will require further analyses of well-defined patient groups using the normal values derived from this investigation along with clinical outcome studies.

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