Quantifying esophageal peristalsis with high-resolution manometry: a study of 75 asymptomatic volunteers

Sudip K. Ghosh, John E. Pandolfino, Qing Zhang, Andrew Jarosz, Nimeesh Shah, and Peter J. Kahrilas

Department of Medicine, The Feinberg School of Medicine, Northwestern University, Chicago, Illinois

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A MAJOR OBJECTIVE in the clinical evaluation of dysphagia is to ascertain the integrity and adequacy of esophageal peristalsis. Of particular significance is that the peristaltic contraction maintains luminal closure behind the bolus as it traverses the esophagus, effecting clearance against downstream resistance. Peristalsis is considered “successful” when all bolus material is cleared into the stomach and dysfunctional when all or some of the bolus is not cleared (8).

Esophageal peristalsis can be studied quantitatively using manometry in which spatial variations of intraluminal pressure are recorded over time. Conventionally, this is done with devices incorporating three to eight pressure sensors spaced at 3- to 5-cm intervals within the esophagus, each characterizing the contraction in the region in which it resides; luminal contractile activity between sensors can only be inferred. However, a major evolution in manometric methodology has been the introduction of high-resolution manometry (HRM); the basic concept being that by vastly increasing the number of recording sites and decreasing the spacing between them, one can more completely define the intraluminal pressure environment, minimizing the impact of spatial gaps between recording sites. Of course, the vastly increased quantity of data associated with HRM studies creates 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 that can be displayed as isobaric contour plots (2–4). The advantages of isobaric contour plots are multiple, but the most evident is that it provides a seamless, dynamic representation of peristalsis at every axial position within and across the esophagus, as shown in Fig. 1. When so imaged, it becomes apparent that peristalsis is comprised of several distinct yet integrated elements: 1) a proximal propagated contraction, corresponding to the striated muscle portion of the esophagus; 2) a distal propagated contraction, corresponding to the smooth muscle esophagus; and 3) a zone of transition between the two (5, 7, 13). Not only does each of these elements occur in a reasonably stereotyped pattern but each is also timed in a stereotyped fashion for a given individual, in essence defining the functional limits of peristalsis.

Although the analysis of peristalsis made possible by HRM described above is unarguably elegant and evolutionary, its widespread clinical application has been hindered by the lack of availability of practical recording instrumentation and by a limited understanding of what constitutes “normal” in this new paradigm. Furthermore, the technical complexity of setup, utilization, and maintenance of high-resolution 21-channel and 32-channel water-perfused manometry systems used in highly specialized centers has limited their widespread application in a clinical setting (6, 7). However, a 36-channel solid-state HRM system has recently become available that circumvents two of these limitations (1). The aim of this study was to apply this novel device to a detailed analysis of esophageal peristalsis in normal individuals, leveraging the strengths of the HRM technique in conjunction with computational algorithms devised to measure the most fundamental, functionally relevant attributes of peristalsis. In so doing, new paradigms for the quantification of peristalsis were devised that will hopefully optimize the utility of HRM in clinical and investigative manometry studies.

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Address for reprint requests and other correspondence: S. K. Ghosh, Div. of Gastroenterology, Dept. of Medicine, Feinberg School of Medicine, Northwestern Univ., 676 N. St. Clair St., Suite 1400, Chicago, IL 60611 (e-mail: s-ghosh@northwestern.edu).
METHODS

Patients

Manometric studies were done on 75 asymptomatic subjects (40 men and 35 women, age: 19–48 yr). Subjects consisted of volunteers recruited by advertisement or word of mouth with no history of gastrointestinal symptoms, upper gastrointestinal tract surgery, or 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 circumferentially dispersed sectors. The sector pressures are then averaged to obtain a mean pressure measurement, 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). The data-acquisition frequency was 35 Hz for each sensor.

Study Protocol

After a brief interview and examination to ensure the absence of gastrointestinal symptoms and to make anthropometric measurements, subjects underwent transnasal placement of the manometric assembly. Studies were done in a 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 set this pressure as zero and calculated the magnitude of the pressure correction required for each sensing element. Those sensor-specific thermal correction factors were 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

Fig. 1. Scheme for the regional analysis of esophageal peristalsis. A spatial pressure variation plot of the resting state (A) was used to localize the spatial limits of the upper esophageal sphincter (UES) and esophagogastric junction (EGJ). The isocontour plot (B) illustrates four isobaric contour pressure levels: −10 (blue), 10 (green), 30 (red), and 50 mmHg (brown). These isobaric contours clearly demonstrate the proximal and distal esophageal contractions separated by a transition zone (TZ). The transition zone is more precisely localized in C, which is a spatial pressure variation plot depicting the greatest contractile pressure at each axial position along the esophagus; the center of the TZ is localized as the minimum along this plot (xyz).
correction factors applied to reestablish the zero reference also correct error attributable to thermal drift in the entire data set.

**Manometry data analysis.** Further characterization of esophageal peristalsis 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 double-precision 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 in both the time dimension (between sampling times) and spatial dimension (between pressure-recording sites). This interpolation was done using a cubic hermite interpolating polynomial in MATLAB 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 per centimeter and doubling the temporal sampling rate from 35 to 70 Hz (3, 9).

After thermal correction, peristaltic characteristics were analyzed according to the scheme defined in Fig. 1. The peristaltic contraction

Fig. 1. Methodology for defining the maximal pressure and duration of the distal esophageal contraction. Maximal pressure was identified within the distal contraction (white circle) and the contraction parameters at that locus were quantified. A similar analysis was done for the proximal esophageal segment (not illustrated).

**Proximal esophageal peristalsis.** As evident in Figs. 1 and 2, the proximal esophageal contraction is tightly integrated with that of the upper esophageal sphincter (UES), making them somewhat difficult to differentiate. Thus we used the resting state of the esophagus (Fig. 1A) to define the lower margin of the upper sphincter. Conversely, the
spatial pressure variation plot depicting the greatest contractile pressure during peristalsis at each axial position along the esophagus (Fig. 1C) was used to localize another key landmark, the center of the transition zone. To enable comparison of peristaltic variables across subjects, the length of the proximal esophagus was then normalized, assigning a value of 0 to the lower margin of the upper esophageal sphincter and a value of 1 to the center of the transition zone. A grid was then applied that identified 50 equally spaced loci along the segment, and proximal esophageal peristaltic amplitude (PEPA) was measured at each locus. PEPA was then plotted as median focal amplitude on the y-axis and normalized length of the proximal esophageal segment (spanning from the lower margin of the UES to the transition zone) on the x-axis.

The propagation rate of the contractile front through the proximal esophageal segment was also derived from the isobaric contour plots and characterized as the proximal contractile propagation velocity (PCPV). Because contraction wave velocity varies along the length of the esophagus (5), PCPV was also calculated at many locations along a normalized grid, although in this case only at 10 equally spaced loci to reduce artifacts. At isobaric contour levels of 20, 30, and 40 mmHg, propagation velocity was calculated (in cm/s) between each adjacent pair of proximal segment loci. The PCPV plot was then constructed with propagation velocity on the y-axis and normalized length of the proximal esophageal segment on the x-axis.

In addition to the parameters defined above, three measures summarizing the magnitude of the proximal peristaltic contraction were derived. The maximal contractile pressure was the greatest pressure within the proximal peristaltic segment. The maximal contractile duration was the duration of contraction at the same locus as the maximal contractile pressure. Finally, the proximal contractile integral was calculated as follows. If the isobaric contour map is envisioned as a solid, the footprint of the solid would be time (in s) multiplied by axial domain (in cm) and the height of the solid would be pressure (in mmHg). The proximal contractile integral was the volume of that solid spanning from 10 mmHg at the base to the maximal contractile pressure (expressed as mmHg cm s).

**Distal esophageal peristalsis.** The analysis of distal esophageal peristalsis largely mirrored that of proximal peristalsis with a few requisite refinements. In this case, we used the resting state of the esophagus (Fig. 1A) to define the lower margin of the esophageogastric junction (EGJ) and defined the span of the distal esophagus as from that point to the center of the transition zone. Again, a normalized grid of 50 equally spaced loci was created along the segment, and distal esophageal peristaltic amplitude (DEPA) was measured at each locus. Similarly, the distal contraction propagation velocity (DCPV) was analogous to the PCPV, representing an expression of the propagation velocity of the contractile front as a function of isobaric contour pressure.

Recognizing that bolus transport is effected by a combination of esophageal closure pressure and intraluminal pressure gradients (10), we plotted the manometric data as spatial variations of intraluminal pressure over time (Fig. 3). Spatial pressure variation plots have the advantage of clearly illustrating the relationship among closure pressure (peristaltic amplitude), intrabolus pressure, and EGJ outflow resistance. The instantaneous relationship among these pressures defines whether flow is likely to occur and, if so, in which direction. While DEPA defined the magnitude of distal esophageal peristaltic force, the efficacy of that force in achieving esophageal emptying depends on its coordination with EGJ relaxation. The outflow permissive pressure gradient (OPPG) was derived as an assessment of the balance between distal peristalsis and swallow-induced EGJ relaxation. OPPG parameters were derived from a plot with time on the x-axis (time 0 being the onset of maximal UES relaxation) and three pressure tracings on the y-axis: 1) instantaneous E-sleeve relaxation pressure, 2) instantaneous intrabolus pressure at a location 2 cm above the upper margin of the resting state EGJ, and 3) instantaneous distal peristaltic amplitude (Fig. 3C). Thus conditions are permissive of esophageal emptying (antegrade flow permissive) during periods when the peristaltic amplitude exceeded intrabolus pressure (measured 2 cm proximal to the EGJ), which in turn exceeded E-sleeve pressure. On the other hand, periods during which the peristaltic amplitude was less than intrabolus pressure, which was in turn less than E-sleeve pressure, were considered consistent with retrograde flow and permissive for retrograde “escape” of the bolus. Summary statistics of the OPPG were 1) the duration of time that pressure conditions are optimal for esophageal emptying (antegrade flow permissive), 2) the mean emptying pressure during the potential emptying period (intrabolus pressure 2 cm proximal to the EGJ minus E-sleeve pressure), and 3) the duration of time that conditions are right for retrograde escape to occur (retrograde flow permissive time).

In addition to the parameters defined above, three measures were derived, summarizing the magnitude of the distal peristaltic contraction wave. The maximal contractile pressure, maximal contractile duration, and contractile integral were analogous to the corresponding indexes described in *Proximal esophageal peristalsis* (Fig. 2). However, the calculation of the distal esophageal contraction integral began at the 20 mmHg isobaric contour rather than 10-mmHg isobaric contour in view of the greater intrabolus pressure associated with the bolus being compartmentalized within the lesser volume of the distal esophagus compared with the total esophagus during the proximal contraction wave.

**Transition zone.** The proximal and distal esophageal contractions sometimes smoothly blended with one another and at other times exhibited a spatial gap and/or temporal delay between the termination of the proximal contraction and the initiation of the distal contraction. Even in instances in that they smoothly blended, there was characteristically a pressure trough between them. The duration of this delay (or the persistence of the trough) increased when analyzed at increased isobaric contour pressures. Parameters of the transition zone were calculated based on the scheme shown in Fig. 2. At each isobaric contour pressure, beginning at 10 mmHg and increasing in increments of 5 mmHg, the transition delay was \( t_d = t_e - t_p \) in duration spanning a length of \( x_d = x_e - x_p \) cm (Fig. 2). Each of these variables, defining the length and duration of the transition zone, was then plotted as a function of contractile pressure.

**Statistical Analysis**

Means, SD, SE, and median and interquartile range were calculated for all the paradigms developed above and are summarized in the ensuing figures and tables. In addition, coefficient of variation (CV) analysis was used to assess the intrasubject variability for each paradigm. The CV was calculated as the SD divided by the mean for each subject and expressed as a percentage. The mean CV from all 75 subjects is presented.

**RESULTS**

Manometry was well tolerated by all 75 subjects, and the studies were completed without technical problems. The MATLAB program was used to delineate the transition zone, proximal esophagus, distal esophagus, and EGJ for each swallow (Fig. 1). The automated program accurately delineated these measurements in 712 swallows. Morphology parameters for the remaining 38 swallows were adjusted manually. The primary reason for failure of the program in these 38 swallows was absent or delayed peristalsis in the distal esophagus or an excessively strong pressure signal from heart beat in the aortic arch region, both of which resulted in an inaccurate localization of the transition zone. In either case, after manual identification of the transition zone, the automated program determined the remaining morphometric parameters accurately. Summary statistics on these parameters for all 750 swallows
are presented in Table 1. A total of 18 swallows (from all 75 subjects) exhibited failed peristalsis in the distal esophagus, defined as the absence of any contractile activity. Two subjects exhibited failed distal peristalsis in five or more swallows. In these cases, distal esophageal parameters could not be calculated, and therefore the corresponding swallows were not included in the summary calculations.

**Proximal Esophagus**

As evident in Table 1, the proximal esophageal contractile zone averaged 6.1 cm in length. This is consistent with observations made by Clouse and Staiano (3) and Meyer et al. (13), who quantified the location of the pressure trough as ~6 cm from the lower margin of the UES. The characteristics of the
proximal esophageal contraction are depicted in Fig. 4. The 50th percentile value for the PEPA at the midpoint of the proximal segment was 70.1 mmHg. PCPV was remarkably uniform at an average of about 2.4 cm/s across the 20- to 40-mmHg range of pressures analyzed. Note that there were no instances of a failed contraction through this region in any subject. Table 2 summarizes the characteristics of the contraction through the proximal segment in terms of maximal pressure, duration, and contractile integral.

Distal Esophagus

As evident in Table 1, the distal esophageal contractile zone, spanning from the transition zone to the lower margin of the EGJ, encompassed most of the length of the esophagus, averaging 19.9 cm in length. The characteristics of the distal esophageal contraction are depicted in Fig. 5. When the DEPA plot (Fig. 5) was compared with the PEPA plot (Fig. 4), distal esophageal peristalsis was less uniform than proximal peristalsis but similar in the sense that both gradually diminished with proximity to the transition zone. Peristaltic amplitude also diminished approaching and within the EGJ. DCPV, on average, similar to that through the proximal segment with the caveat that it was markedly slower emerging from the transition zone and approaching the EGJ. Table 3 summarizes the characteristics of the contraction through the distal segment in terms of maximal pressure, duration, and contractile integral.

The results of the OPPG analysis, characterizing the balance between peristaltic closure force in the distal esophagus, intraluminal pressure and EGJ relaxation, are summarized in Table 4. During an average swallow, intraluminal pressure conditions were favorable for antegrade flow from the distal esophagus to the stomach for 2.3 s with a mean pressure gradient of 2.3 mmHg. Although conditions favorable for retrograde flow were occasionally observed, this was an uncommon occurrence in this normal population. However, an example of a possible retrograde flow event is illustrated in Fig. 6. Note that the occurrence of retrograde flow is also suggested by the paradoxical increase in intraesophageal pressure proximal to the contractile front during inspiration when intraesophageal pressure would normally decrease.

Transition Zone

The transition zone is represented in Fig. 1 as the region of the isocontour plot bridging the proximal and distal esophageal segments centered at the nadir pressure along the spatial pressure variation plot of Fig. 1C. The spatial and temporal characteristics of the transition zone varied with isococontracture pressure, as evident in Fig. 2. In Fig. 2, the length of the

Table 1. Summary of morphometric measurements of the esophageal contractile regions depicted in Fig. 1

<table>
<thead>
<tr>
<th>Region</th>
<th>Mean ± SE (SD)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UESL → EGJL, cm</td>
<td>22.9 ± 0.2 (2.1)</td>
<td>22.7 (21.6–24.6)</td>
</tr>
<tr>
<td>UESL → TZ, cm</td>
<td>6.1 ± 0.2 (1.3)</td>
<td>6.2 (5.0–7.2)</td>
</tr>
<tr>
<td>TZ → EGJL, cm</td>
<td>16.8 ± 0.2 (2.1)</td>
<td>16.6 (15.4–17.8)</td>
</tr>
<tr>
<td>EGJL → EGJU, cm</td>
<td>16 ± 0.1 (0.4)</td>
<td>15 (1.3–1.7)</td>
</tr>
<tr>
<td>EGJU → EGJL, cm</td>
<td>3.1 ± 0.1 (0.7)</td>
<td>3.1 (2.6–3.5)</td>
</tr>
</tbody>
</table>

Values are means ± SE (SD) and medians (intraquartile ranges (IQR)); n = 75 subjects. UESL, lower margin of the upper esophageal sphincter (UES); EGJL, lower margin of the EGJ; EGJU, upper margin of the esophagogastric junction (EGJ); TZ, transition zone; EGJL, peak pressure within the EGJ; EGJU, lower margin of the EGJ.

Table 2. Summary statistics of the characteristics of the proximal esophageal contraction

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SE (SD)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal pressure, mmHg</td>
<td>119.5 ± 3.8 (32.9)</td>
<td>114.0 (90.9–133.3)</td>
</tr>
<tr>
<td>Maximal duration, s</td>
<td>3.0 ± 0.1 (0.9)</td>
<td>2.9 (2.2–3.6)</td>
</tr>
<tr>
<td>Contractile integral, mmHg cm · s</td>
<td>779.2 ± 87.8 (760.8)</td>
<td>621.6 (414.0–918.4)</td>
</tr>
</tbody>
</table>

Values are means ± SE (SD) and medians (IQR); n = 75 subjects. Maximal contractile duration was measured at the same locus as maximal contractile pressure within the proximal segment. The contractile integral was the “volume” of the proximal contraction when depicted as a three-dimensional solid with the x, y, and z-axes being time, spatial domain, and pressure magnitude, respectively.
transition zone is \( x_{\text{d}(20)} - x_{\text{f}(20)} \) cm for the 20-mmHg isobaric contour and \( x_{\text{d}(40)} - x_{\text{f}(40)} \) cm for the 40-mmHg isobaric contour. Similarly, the duration of the transition zone was \( t_{\text{d}(20)} - t_{\text{f}(20)} \) s for the 20-mmHg isobaric contour and \( t_{\text{d}(40)} - t_{\text{f}(40)} \) s for the 40-mmHg isobaric contour. Summary data for the length and duration of the transition zone as a function of isocontour pressure are shown in Fig. 7. Following the 50th percentile values of Fig. 7, the transition zone was first definable at an isocontour pressure of 30 mmHg and gradually increased to a magnitude of 2.5 cm and 1.5 s as the isocontour pressure increased to 50 mmHg. On the other hand, by examining the 5th percentile values of Fig. 7, the transition zone was already evident at the 10-mmHg isocontour and expanded to 3.5 cm and 7 s as the isocontour pressure increased to 50 mmHg. Note that none of the subjects had a transition zone pressure lower than 10 mmHg and the duration was 0 at pressures \( \leq 20 \) mmHg.

**Intrasubject Variability**

The CV analysis, presented as the mean CV from 75 subjects, is summarized in Table 5. The CV ranged between 5% and 20% with the contractile integral showing the greatest intrasubject variability in both esophageal segments, probably because of its sensitivity to variations in all three components of peristalsis: space, time, and pressure. The length of the contractile segment exhibited the lowest variability among all parameters, most likely because of the concordance of the esophageal segments with the neuromuscular anatomy of the esophagus. On average, the distal esophagus exhibited higher intrasubject variability compared with the proximal esophagus in all paradigms.

**DISCUSSION**

Although few would argue with the relevance of esophageal manometry as an analytic tool in the assessment of esophageal peristalsis, achieving a consensus on what constitutes a clinically relevant abnormality is a difficult task. This is partly attributable to the lack of standardization of manometry apparatus or clinical testing protocol and partly to conflicting notions of how to best analyze manometric data. Direct evidence of the latter can be found in a recent publication (14) highlighting the poor interobserver agreement in the analysis of clinical manometry even among expert practitioners. The cited reasons for interobserver variability were poor adherence of the observers to published diagnostic criteria, misinterpretation of intrabolus pressure, and technical inadequacy.

Table 3. Summary statistics of the characteristics of the distal esophageal contraction

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SE (SD)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal pressure, mmHg</td>
<td>132.0 ± 4.9</td>
<td>125.7 (105.1–154.8)</td>
</tr>
<tr>
<td>Maximal duration, s</td>
<td>3.6 ± 0.2</td>
<td>3.2 (2.7–3.8)</td>
</tr>
<tr>
<td>Contractile integral, mmHg · cm · s</td>
<td>2,797.8 ± 108.1 (936.0)</td>
<td>2,416.6 (1,966.8–2,963.2)</td>
</tr>
</tbody>
</table>

Values are means ± SE (SD) and medians (IQR); \( n = 75 \) subjects. Maximal contractile duration was measured at the same locus as maximal contractile pressure within the distal segment. As with the proximal segment, the contractile integral was the “volume” of the proximal contraction when depicted as a three-dimensional solid with the \( x, y, \) and \( z \)-axes being time, spatial domain, and pressure magnitude, respectively.

Table 4. Summary statistics of the coordination between distal esophageal peristalsis and EGJ relaxation as quantified by the outflow permissive pressure gradient

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SE (SD)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antegrade flow permissive, s</td>
<td>1.7 ± 0.1 (0.9)</td>
<td>1.5 (0.8–2.3)</td>
</tr>
<tr>
<td>Antegrade pressure gradient, mmHg</td>
<td>2.3 ± 0.03 (0.3)</td>
<td>2.3 (2.2–2.4)</td>
</tr>
<tr>
<td>Retrograde flow permissive, s</td>
<td>0.1 ± 0.01 (0.1)</td>
<td>0.0 (0.0–0.1)</td>
</tr>
</tbody>
</table>

Values are means ± SE (SD) and medians (IQR); \( n = 75 \) subjects (732 swallows). The window of EGJ relaxation was analyzed to ascertain the balance among instantaneous distal peristaltic amplitude, intrabolus pressure (measured 2 cm proximal to the EGJ), and E-sleeve pressure. Periods during which the amplitude value exceeded intrabolus pressure, which in turn exceeded E-sleeve pressure, were considered permissive of antegrade flow, whereas periods during which the amplitude value was less than intrabolus pressure, which was in turn less than E-sleeve pressure, were considered consistent with retrograde flow and incomplete bolus clearance. The antegrade pressure gradient was the average difference between intrabolus pressure (measured 2 cm proximal to the EGJ) and the E-sleeve pressure during periods permissive of antegrade flow (see also Fig. 5).
Fig. 6. Example of the OPPG analysis in which there was manometric evidence of retrograde flow and bolus retention in the esophagus. A: isobaric contour representation of the swallow. B: series of spatial pressure variation plots of the swallow at 0.4-s intervals. Pressure scaling is shown by the shaded plots at 2.4 s in B and 16.8 s in the inset. C: OPPG calculation during the period of esophageal emptying when the intrabolus pressure in the distal esophagus increased to a point that it either exceeded E-sleeve pressure, thereby being permissive of esophageal emptying, or exceeded the distal peristaltic amplitude, thereby being permissive of bolus escape and retrograde flow. In this example, two periods permissive of bolus escape occur, as evident in C by the shaded areas during which E-sleeve pressure exceeds the distal peristaltic amplitude. Further evidence that retrograde escape did indeed occur is shown in the inset, in which intraesophageal pressure proximal to the contractile front paradoxically increased from 5 to 8 mmHg, despite being timed with inspiration, a time when intraeosophageal pressure otherwise decreases. The absence of any period of time during which peristaltic amplitude was greater than intrabolus pressure, which was in turn greater than E-sleeve pressure, suggests that no bolus clearance occurred with this swallow.
of HRM offers us an opportunity to improve upon this by standardizing the testing protocol and facilitating an automated quantitative analysis. Such was the central objective of this paper. With the use of a state-of-the-art HRM probe, we sought to combine manometric data from 75 normal subjects with extensive computational power to quantify the essential, functionally relevant attributes of esophageal peristalsis to serve as a foundation from which to analyze dysfunction. A substantial outcome of this analysis was the development of an automated system to generate summary quantitative measures of esophageal function, removing most of the subjectivity associated with interobserver variability, and thereby enhancing the reproducibility of the analysis.

The key physiological function of peristalsis is bolus transport, effected by a sequenced contraction propagated through the esophagus. Abnormal peristalsis can be characterized by abnormal propagation, inadequate contractility, or excessive contractility. Examining first the concept of adequacy, effective bolus clearance is contingent on the presence of a seamless contractile front of appropriate amplitude and velocity propagating over a length of the esophagus. Furthermore, although relatively tightly integrated, we know from a wide array of investigations that the proximal and distal esophagus have distinct characteristics with respect to neural control, muscle type, and manometric attributes (Fig. 1) (5, 7, 12, 13); hence, the concept of PEPA and DEPA, HRM paradigms for quantifying spatial variation in peristaltic amplitude. Summary data on PEPA and DEPA, shown in Figs. 4A and 5A, respectively, are presented in a format such that the range of normal values are readily evident, thus serving as a yardstick against which to measure patient data.

The success or failure of the contractile front to effect clearance is further dependent on the downstream resistance that must be overcome. More specifically, owing to the timed nature of peristalsis, clearance is dependent on the instantaneous intraluminal relationship among clearance force (intrabolus pressure), closure force (peristaltic amplitude), and outflow resistance (E-sleeve pressure). An earlier study (8) combining manometry with fluoroscopy demonstrated that most instances of impaired bolus clearance occurred in the distal esophagus, suggesting that the downstream resistance from the proximal esophagus was minimal compared with that at the EGJ. Hence, the concept of OPPG, a HRM paradigm quantifying the window of opportunity for bolus flow across the EGJ, was developed. The data shown in Table 4 and Figs. 3 and 6 explain this concept and again provide a yardstick against which to gauge abnormality. Note that a much fuller description of EGJ relaxation characteristics defined in HRM paradigms is to be published in another study (15).

Other than clearance function, the analysis of abnormal esophageal motility has historically focused on states of abnormally propagated or excessive contractility: distal esophageal spasm, nutcracker esophagus, etc. Two parameters of the esophageal contraction define these states: propagation velocity and the magnitude of the contraction, as gauged by some combination of amplitude and duration. With respect to propagation, the issue is complicated by the nonuniform nature of propagation through the esophagus. Hence, the data shown in Figs. 4B and 5B completely describe the propagation velocity through the esophagus, leveraging the spatial resolution of the HRM method. Again, data are presented in a format such that the range of normal values are readily evident, thus serving as a yardstick against which to measure patient data. With respect to the magnitude of the peristaltic contraction, the enhanced spatial resolution of HRM allows localization of the maximal contraction within each esophageal region and thereby an establishment of normal limits (proximal esophagus, Table 2; distal esophagus, Table 3). Furthermore, a unique opportunity

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Table 5. Summary statistics of mean intrasubject variability

<table>
<thead>
<tr>
<th></th>
<th>Proximal Esophagus</th>
<th>Distal Esophagus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of esophageal segment</td>
<td>5.3</td>
<td>8.1</td>
</tr>
<tr>
<td>Maximal pressure</td>
<td>15.6</td>
<td>14.8</td>
</tr>
<tr>
<td>Maximal duration</td>
<td>14.7</td>
<td>18.4</td>
</tr>
<tr>
<td>Contractile integral</td>
<td>19.9</td>
<td>20.1</td>
</tr>
<tr>
<td>Midsegment peristaltic amplitude</td>
<td>12.2</td>
<td>14.0</td>
</tr>
<tr>
<td>Midsegment propagation velocity (30 mmHg)</td>
<td>7.9</td>
<td>12.7</td>
</tr>
</tbody>
</table>

Values are coefficients of variability for each proximal and distal esophageal variable (in %); n = 75 subjects. Peristaltic amplitude was analyzed at the midpoint of each esophageal segment, and the propagation velocity was evaluated at the center of the appropriate segment using the 30-mmHg value of the proximal/distal contraction propagation velocity analysis.
exists to quantify the integrated contractile activity of each esophageal segment and introduce a unique HRM paradigm, the contractile integral as a way of quantifying the overall vigor of the contraction. This paradigm is intended to be particularly sensitive in delineating focal or generalized abnormalities involving sustained and/or hypertensive esophageal contractions.

The final element of peristalsis to be characterized is the transition zone. The transition zone was in essence first defined using HRM techniques (5), although the existence of a pressure trough in the midesophagus was recognized before this (3, 11). However, the normal characteristics of this transition zone have not been previously defined. Again, leveraging the spatial and temporal resolution of HRM to analyze transition zone characteristics according to the paradigm illustrated in Fig. 2, we quantified the normal characteristics of the transition zone shown in Fig. 7. Once again, data are presented in a format such that the range of normal values is readily evident, thus serving as a yardstick against which to measure patient data.

In conclusion, HRM represents an evolution in manometric technology presenting the opportunity to redefine this clinical test in enhanced quantitative paradigms that may ultimately lead to more objective, consistent, and reproducible interpretation. With the use of a state-of-the-art manometric probe along with an extensive computational exercise, we performed a detailed analysis of esophageal peristalsis aimed at quantifying its essential features. In so doing, new paradigms for the quantification of peristaltic function during swallowing were devised that will hopefully optimize the utility of HRM in clinical and investigative studies. This, along with a companion study (15) on the HRM characteristics of the EGJ, are intended to set the stage for a reassessment of what constitutes normal and abnormal esophageal motor function.

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