Neurogastroenterology & Motility

Neurogastroenterol Motil (2012) **24** (Suppl. 1), 48–56

REVIEW ARTICLE

Future directions in esophageal motility and function – new technology and methodology

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Abstract

Background *Symptom based diagnosis is not reliable in patients with swallowing problems, heartburn, and other dyspeptic complaints. The aim of investigation is to provide clinically relevant measurements of gastrointestinal structure and function that explain the cause of symptoms, identify pathology, and guide effective management. Current practice rarely meets these ideals.*

Purpose *This review considers recent advances in technology such as high-resolution manometry (HRM) with esophageal pressure topography (EPT), HRM with impedance, high frequency ultrasound, and endoscopic functional luminal impedance planimetry (Endo-FLIP) that provide new opportunities to identify the pathophysiologic basis of esophageal symptoms and disease. As experience with these new devices increases researchers are developing new methodologies that maximize their utility in clinical practice. For example, application of HRM to assess motility and function during and after a test meal can identify the causes of swallowing problems, reflux and other postprandial symptoms and intra-operative application of Endo-FLIP may help surgeons perform antireflux surgery. These examples illustrate the potential of physiologic measurement to direct rational and effective clinical management for individual patients.*

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Received: 30 August 2011
Accepted for publication: 5 September 2011

Keywords *3D high-resolution manometry, esophageal impedance planimetry, high frequency esophageal endoscopic ultrasound, high-resolution impedance manometry, high-resolution manometry.*

INTRODUCTION

Symptom based diagnosis is not reliable in patients with swallowing problems, heartburn and other dyspeptic complaints.[1,2] The aim of investigation is to provide clinically relevant measurements of gastrointestinal (GI) structure and function that explain the cause of symptoms, identify pathology, and guide effective management.[3,4] Current practice rarely meets these ideals. Once 'organic disease' has been ruled out by laboratory tests, endoscopy and imaging, guidelines recommend assessment of upper GI physiology.[5,6] Unfortunately, in many patients, manometry with 5–8 pressure sensors and reflux studies also fail to establish a definitive diagnosis.[3,7] In such cases diagnoses such as 'functional dysphagia' or 'functional heartburn' are applied. This is not helpful to the patient or doctor because these labels are nonspecific and simply reflect the presence of symptoms and the absence of objective findings on investigation. No insight into the pathophysiologic basis of disease is given. Furthermore, such labels may imply psychological disease and provide little direction for therapeutic decisions.

ADVANCES IN MANOMETRY: FROM MOTILITY TO FUNCTION

Recent advances in physiologic measurement such as high-resolution manometry (HRM) with esophageal pressure topography (EPT) provide a new opportunity to move beyond symptom based diagnosis in functional

GI disease. A key insight from studies that combined conventional manometry with impedance is that esophageal symptoms are rarely caused by dysmotility unless this is accompanied by bolus retention or reflux.[8,9] This approach changed the terminology of 'non-specific esophageal dysmotility' to 'ineffective esophageal motility' and allowed these disorders to be stratified in terms of their impact on bolus transport;[8,9] however, this method still did not explain the causes of dysfunction. In contrast, HRM/EPT with closely spaced sensors provides sufficient spatial resolution to assess not only contractile force (motility) but also the forces that drive the movement of fluid and food (function).[10] The presence of well coordinated peristaltic contraction without wide breaks in the contractile front from the pharynx to the stomach defines whether or not esophageal motility is normal. The presence of a positive intra-bolus pressure (IBP) gradient across the esophagogastric junction (EGJ) defines whether or not this motility is consistent with effective function.[3]

The Chicago Classification presented in this supplement[11] represents an important advance because it is built on these physiomechanical principles. The system is hierarchical with EGJ dysfunction considered first because failure of the EGJ to relax and/or open in achalasia and outflow obstruction has a greater impact on bolus transport than abnormal peristalsis.[12] In addition, it makes a clear distinction between dysmotility and dysfunction that is 'never seen in normal individuals' from that which is merely 'outside the normal range'. In the former there is a clear rationale for treatment directed at correcting the pathology. In the latter symptoms are likely to be associated with both esophageal motor dysfunction and visceral hyperalgesia or hypervigilance.[13,14]

Systematic analysis of HRM/EPT data increases diagnostic accuracy in large case series.[15,16] In particular, attention to breaks in the contractile front detects functionally relevant segmental dysmotility not

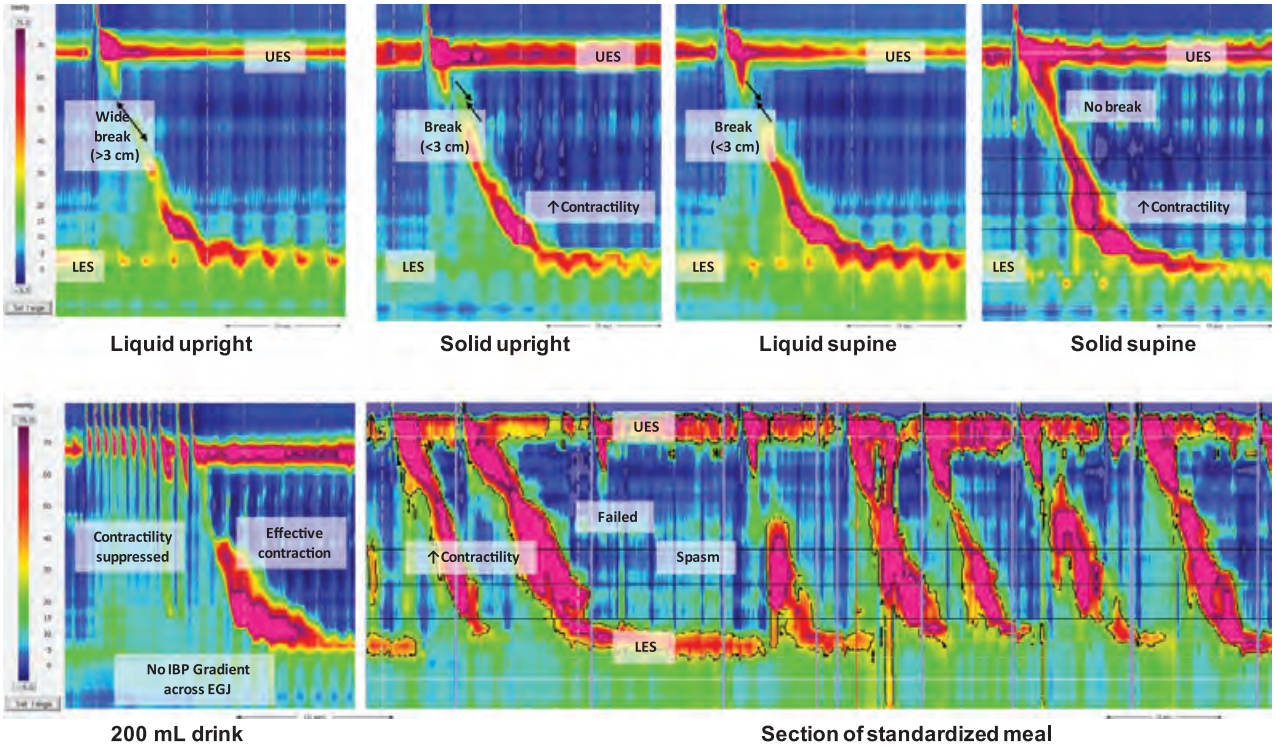

Figure 1 Examples of HRM studies of swallowing function from healthy subjects. Note how the esophagus responds to increasing esophageal workload by improving coordination and increasing the power of contraction (upper panel of figures, moving from liquid swallows in the upright position to solid swallows lying down). On drinking 200 ml water, esophageal contractility is suppressed during repeated swallowing and there is no sign of outlet obstruction (i.e. no intra-bolus pressure gradient across the EGJ) and this is followed by a powerful contraction that clears the esophagus (lower left figure). Powerful contractions are observed also during a solid test meal (lower right figure); however, these are interspersed with occasional failed swallows and spasm. These 'abnormalities' do not cause symptoms unless several ineffective swallows occur one after another.

visualized by other methods[4,17] and the IBP gradient detects functional EGJ outlet obstruction.[15,16,18,19] This approach has implications for the design of outcome studies. In achalasia three distinct patterns of aperistalsis are discernable with HRM/EPT that predict responsiveness to therapy.[20] Studies have also defined specific 'clinical phenotypes' of hypotensive[21] and hypertensive esophageal dysmotility[22] that may respond to specific interventions.[23,24]

FUTURE DIRECTIONS IN MANOMETRY: FROM FUNCTION TO SYMPTOMS

Despite the technical advances set out above, standard methodologies using HRM/EPT still fail to establish a definitive diagnosis that explains the cause of symptoms in many patients with swallowing problems or reflux.[4,25] This may be because it does not provide a direct assessment of esophageal shortening, sensitivity or certain other biomechanical properties (see below). Alternatively it may be because tests based on small volume water swallows in the supine position are not representative of normal behavior and/or do not 'challenge' esophageal function. High-resolution manometry/ Esophageal pressure topography can facilitate the assessment of complex pressure activity that occurs during normal drinking and eating in the physiologic upright, seated position (Fig. 1). Specifically, in healthy volunteers, the esophagus responds to solids by increasing coordination and vigor of peristaltic contraction.[26] Similar results are found in patients with mild-moderate reflux disease but not in more severe disease (Fig. 2). Interestingly, although hypotensive dysmotility is common with water swallows in both groups, only failure to respond to the 'challenge' of bread swallows is associated with poor clearance and increased acid exposure on ambulatory pH-studies, and the presence of erosive esophagitis on endoscopy.[27]

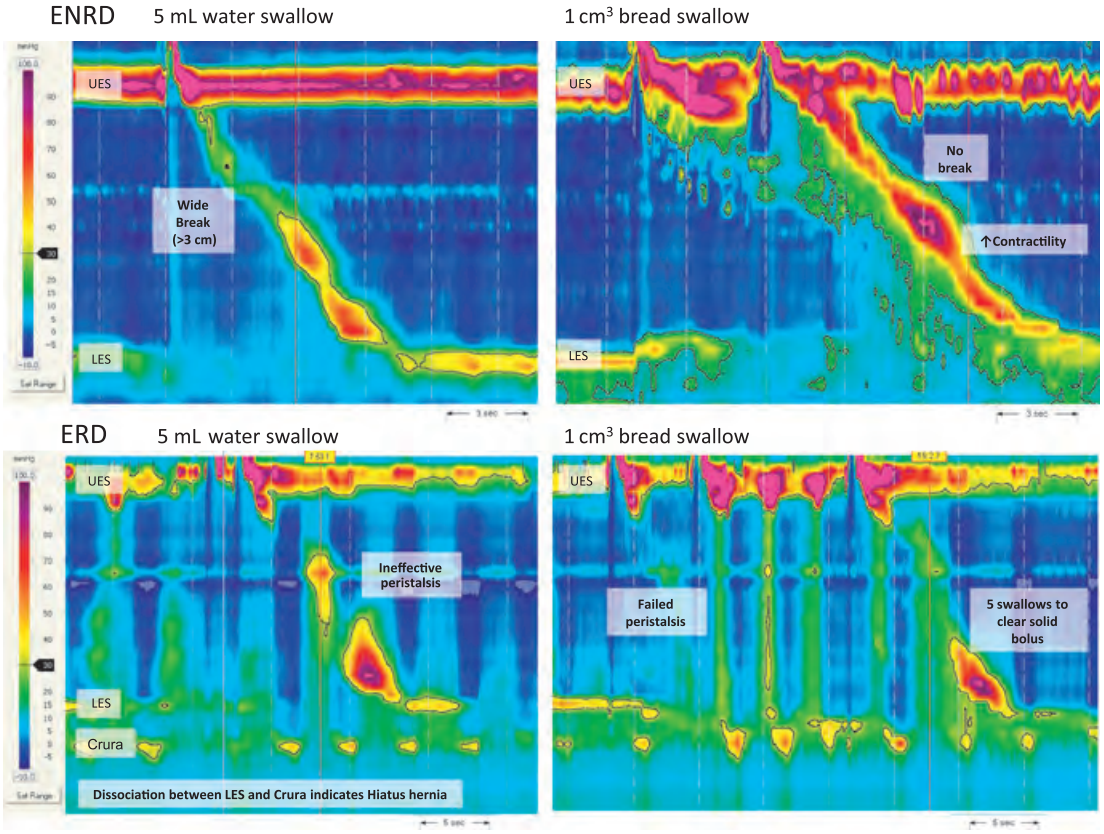

Figure 2 Representative HRM/EPT from water and solid swallows in patients with non-erosive (above) and erosive reflux disease (below). Peristaltic function following water swallows is ineffective with wide (>3 cm) separation of proximal and mid-distal esophageal contractions in both patients. In contrast, there is an 'effective peristaltic response' to solid swallows only in the patient with non-erosive disease. Failure to respond to physiologic challenge characterizes esophageal motility in erosive gastro-esophageal reflux disease. ENRD = Endoscopy negative reflux disease; ERD = Erosive reflux disease. Note also the presence of a small hiatus hernia in the patient with erosive disease. Reproduced with permission from Daum *et al.* Neurogastroenterol Motil 2011.[27]

This is a novel observation; however, the major impact of including free drinking [multiple water swallows (MWS)] and solids in clinical studies may be to provoke esophageal dysfunction and symptoms (Fig. 3).[28,29] The introduction of high-resolution impedance manometry (HRIM) is valuable in this context because impedance provides a direct assessment of bolus transport that confirms the functional effects of the complex pressure data that is observed during normal drinking and eating behavior (Fig. 4).[30] Demonstration of a close temporal association between 'abnormal pressure events', bolus retention and typical patient symptoms on multiple occasions during a test meal provides strong support for the clinical relevance of these 'events'. Symptom association analysis in ambulatory reflux studies provides a direct explanation for patient symptoms[31] that can guide effective management.[32,33] Ambulatory HRM is not, as yet, available; however, this may not be essential because swallowing problems take place almost exclusively during meals. Certainly, case reports and initial findings from case series in patients with functional dysphagia suggest that this approach increases diagnostic sensitivity to symptomatic esophageal dysfunction.[3,4,28]

The Chicago Classification is focused on peristaltic dysfunction and EGJ outlet obstruction; however, the majority of patients referred for physiologic studies complain of reflux symptoms. Stationary HRM/EPT studies detail the structure and function of the reflux barrier;[34,35] however, standard parameters such as LES pressure and length have not been included in the current system because their association with acid exposure on ambulatory studies is weak (Fig. 2).[35] New '3D HRM' technology provides even more detail than standard HRM, revealing the functional anatomy of the EGJ anatomy, especially the contribution of the crural diaphragm (Fig. 5).[36] Notwithstanding these insights, in the absence of gross disruption (i.e. hiatus

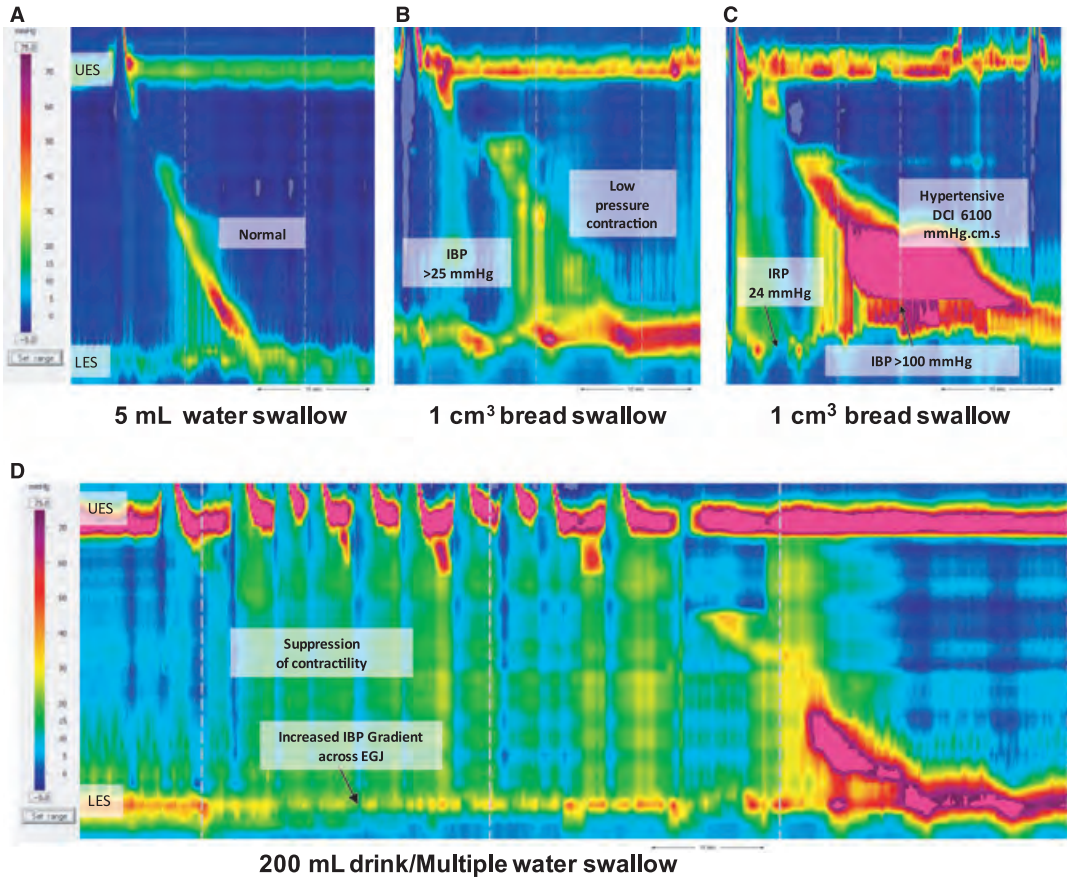

Figure 3 Representative swallows from a patient with dysphagia, regurgitation of food and weight loss with normal endoscopy. (A) Single water swallow is normal. (B, C) Single solid swallow shows variable peristaltic response but consistent evidence of outlet obstruction [raised intra-bolus pressure (IBP)]. Typical symptoms were reproduced. Endoscopic ultrasound identified a submucosal tumor at the EGJ. EGJ = Esophago-gastric junction; (D) MWS = Multiple water swallows.

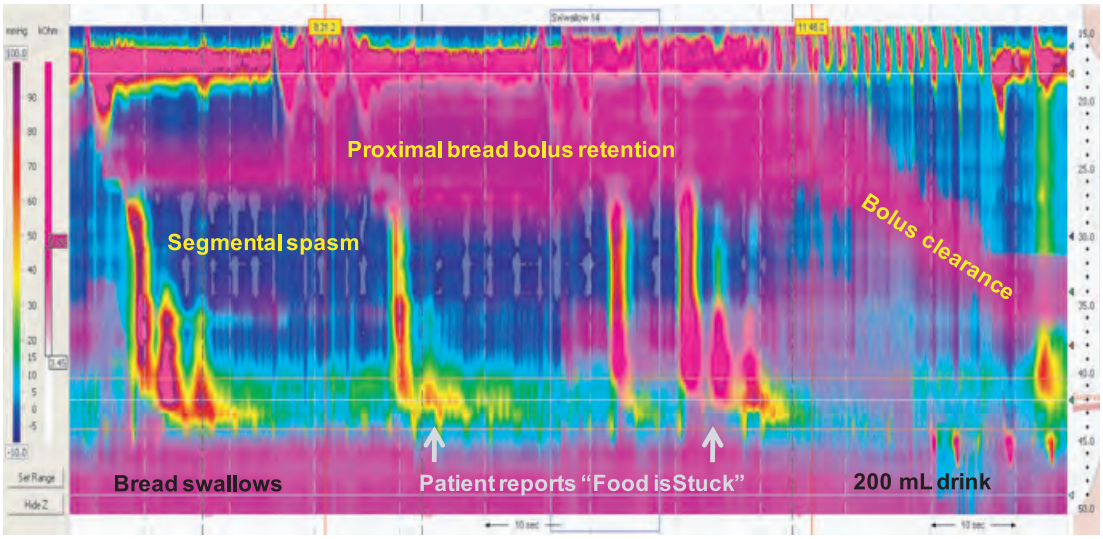

Figure 4 Representative swallows during a test meal from a patient with dysphagia and regurgitation. Water swallows showed normal motility. With solid swallows diffuse and segmental esophageal spasm was present. Impedance demonstrated that *in this case* these events caused proximal bolus retention and were not an effect of bolus obstruction [dysmotility can be the cause or the effect of such events[30]]. The patient reported dysphagia when this was present. Note how the solid bolus is cleared by free drinking. MWS = Multiple water swallows.

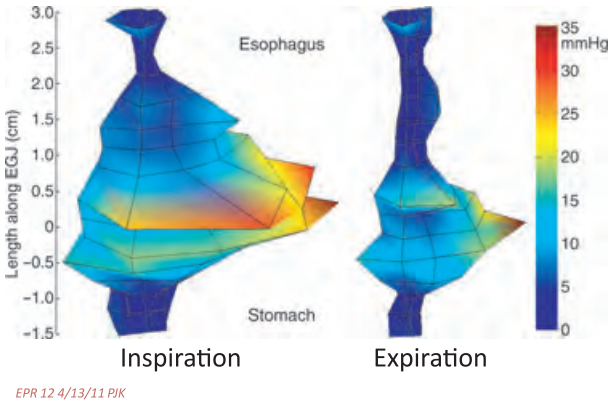

Figure 5 3D HRM acquires detailed pressure measurement across the EGJ with 96 independent solid-state pressure sensors (axial spacing 0.75 cm, radial spacing 45 degrees over 7.5 cm). The functional anatomy of the reflux barrier is revealed as shorter than that with conventional HRM and profoundly asymmetric with the vigorous crural component to EGJ pressure superimposed on the LES. EGJ = Esophagogastric junction. Reproduced with permission from Kwiatek *et al.* Neurogastroenterol Motil 2010.[36]

hernia) baseline measurements are not able to predict the presence of severe reflux or the likelihood of reflux related symptoms. GERD diagnosis requires ambulatory pH ± impedance studies; however, postprandial manometric studies can provide insights into the mechanism of disease. HRM accurately detects transient and swallow related lower esophageal sphincter relaxations (TLESR and SLESR), intermittent separation of the intrinsic and extrinsic components of the EGJ, straining, rumination and other events that can result in the return of gastric contents to the esophagus and mouth (Fig. 6).[16,37–39] High-resolution manometry /Esophageal pressure topography can predict and HRIM can document whether or not these events are associated with reflux of liquid or gas (belching). These observations explain the cause of symptoms and have the potential to direct specific medical, behavioral, and surgical treatment.

FUTURE DIRECTIONS: BEYOND HRM

Several important biomechanical properties of the esophagus and EGJ cannot be assessed by manometry. Contraction of the longitudinal muscle layer is required for effective peristaltic contraction and normal EGJ relaxation. This cannot usually be detected by pressure measurement but is visualized by high frequency endoscopic ultrasound. This technique detects impaired coordination between the longitudinal and circular muscle in some patients with esophageal dysfunction.[40] Moreover, esophageal shortening due to 'longitudinal spasm' has been associated with chest pain and other symptoms.[41,42] However, the clinical relevance of these events is not certain because dramatic esophageal shortening can often be seen by the movement of radio-opaque clips on videofluoroscopy during TLESRs without symptoms.[43]

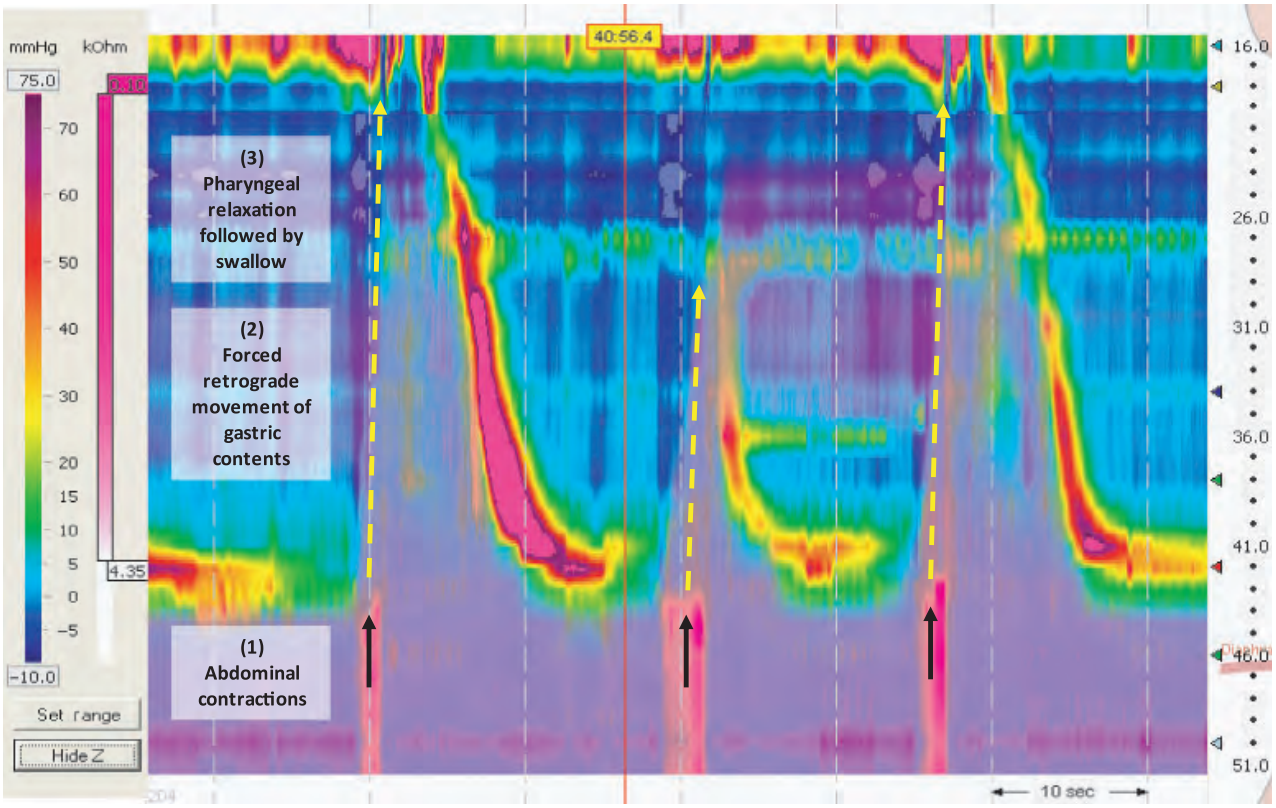

Figure 6 Rumination during postprandial observation period in a patient referred for investigation of 'vomiting' after meals that had been resistant to all medical therapy. On eating, the patient complained of dyspeptic symptoms, and then abdominal contractions were observed which forced gastric contents into the esophagus and back to the mouth. The patient then swallowed. Rumination is a voluntary, albeit subconscious, learned behavior. This patient responded after only one session of biofeedback therapy.

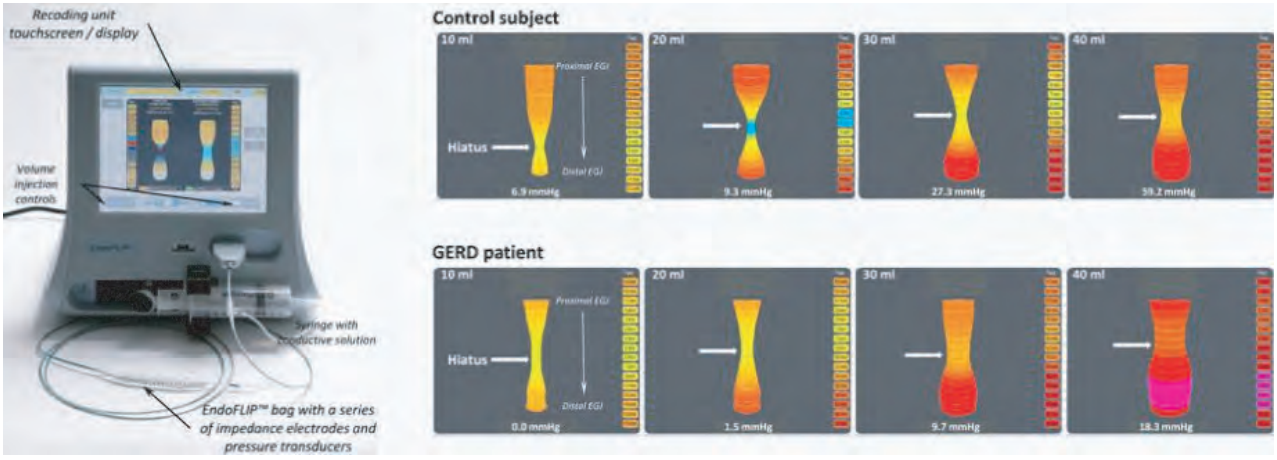

Figure 7 The Endo-FLIP® system monitors the cross-sectional diameter of a bag with a series of impedance electrodes and pressure transducers along its length during a sequence of volumetric distensions. The bag is placed across the EGJ and, typically, an hourglass shape is observed. The examples illustrate the greater EGJ distensibility with larger hiatal diameter and lower intra-bag pressures at 20–40 ml distension volumes in a GERD patient compared to control. EGJ = Esophago-gastric junction Reproduced with permission from Kwiatek *et al.* J Gastrointest Surgery 2010.[46]

Esophageal distensibility and sensitivity can be assessed by impedance planimetry, a technique that measures cross-sectional area of the esophagus in response to distension. In a recent case series, abnormal esophageal stiffness and visceral hyperalgesia to distension was found in 143/189 (75%) patients with 'functional chest pain' in whom conventional manometric and pH-studies were normal. Typical symptoms were reproduced in 105 (56%) subjects.[44] These findings suggest that treatment directed at relaxing the esophageal wall and reducing esophageal sensitivity may be targets for treatment in this patient group. Esophageal sensitivity can be assessed also using electricity, temperature, infusion of acid, and other chemicals; however, distension is a clinically relevant stimulus in patients with dysmotility and/or PPI resistant GERD and no other technique has shown comparable results in clinical studies.

Esophago-gastric junction distensibility can also be measured by impedance planimetry (Endo-FLIP®; Crospon Medical Devices, Galway, Ireland).[45] This technique has confirmed that the EGJ is more distensible (i.e. opens more easily) in GERD patients than healthy controls and that this property is normalized after fundoplication (Fig. 7).[46] The utility of this device in GERD diagnosis is not certain; however, there is considerable interest in its use as a 'clever bougie' in anti reflux surgery to ensure that hiatal repair and fundoplication wrap form a reflux barrier that is neither too 'loose', nor too 'tight'.[47] In addition, Endo-FLIP® can identify and quantify outlet obstruction at the EGJ due to complications or a 'tight' repair after antireflux surgery, achalasia and also in other conditions such as eosinophilic esophagitis.[48]

CONCLUSION

The success of scientific medicine is based on the identification and treatment of the pathophysiological basis of disease. In the past management options in functional esophageal disease have been limited; however now, as in many other areas of medicine, technology is driving progress. New instruments are available to assess every aspect of esophageal motor and sensory function. In addition, new methodologies with application of HRM/EPT and, in particular, HRIM to assess motility and function during and after a test meal can identify the causes of swallowing problems, reflux, and other postprandial symptoms. This information has the potential to direct personalized clinical management.

ACKNOWLEDGMENTS

Mark Fox and Rami Sweis contributed to and approved the manuscript. Mark Fox and the HRM Working Group are grateful to the academic and industry sponsors of the 'Advances in Clinical Oesophageal Measurement' conference, Ascona 10–15. April 2011: The University of Zurich and the Swiss Federal Institute of Technology Zurich, Centro Stefano Franscini, United European Gastroenterology Foundation, Given Imaging/Sierra Scientific Instruments, Medical Measurement Systems and Sandhill Scientific Instruments.

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Neurogastroenterology & Motility

Neurogastroenterol Motil (2012) **24** (Suppl. 1), 57–65

REVIEW ARTICLE

Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography[1]

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Chicago Classification Criteria of Esophageal Motility Disorders Defined in High Resolution Esophageal Pressure Topography (EPT)[1]

[1] Endorsed by:

- The American Neurogastroenterology and Motility Society (ANMS)
- The European Society of Neurogastroenterology and Motility (ESNM) Steering Committee
- The European Society of Esophagology (ESE)
- The International Society for Diseases of the Esophagus (ISDE)
- German Society for Neurogastroenterology and Motility
- Groupe Français de Neuro-Gastroentérologie (GFNG) scientific board
- Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)
- Working Group for Neurogastroenterology and Motility of the German Society for Digestive and Metabolic Diseases

Statements of support from (organizations that do not endorse outside documents):

- The American Gastroenterological Association Institute (AGAI)
- The British Society of Gastroenterology (BSG) Oesophageal, Neurogastroenterology and Motility and Associated GI Physiologists subcommittees
- The United European Gastroenterology Federation (UEGF)

[2]Members of the International High Resolution Manometry Working Group are listed in the Appendix.

Received: 6 August 2011
Accepted for publication: 14 September 2011

Abstract

Background *The Chicago Classification of esophageal motility was developed to facilitate the interpretation of clinical high resolution esophageal pressure topography (EPT) studies, concurrent with the widespread adoption of this technology into clinical practice. The Chicago Classification has been an evolutionary process, molded first by published evidence pertinent to the clinical interpretation of high resolution manometry (HRM) studies and secondarily by group experience when suitable evidence is lacking.*

Purpose *This publication summarizes the state of our knowledge as of the most recent meeting of the International High Resolution Manometry Working Group in Ascona, Switzerland in April 2011. The prior iteration of the Chicago Classification was updated through a process of literature analysis and discussion. The major changes in this document from the prior iteration are largely attributable to research studies published since the prior iteration, in many cases research conducted in response to prior deliberations of the International High Resolution Manometry Working Group. The classification now includes criteria for subtyping achalasia, EGJ outflow obstruction, motility disorders not observed in normal subjects (Distal esophageal spasm, Hypercontractile esophagus, and Absent peristalsis), and statistically defined peristaltic abnormalities (Weak peristalsis, Frequent failed peristalsis, Rapid contractions with normal latency, and Hypertensive peristalsis). The Chicago Classification is an algorithmic*

scheme for diagnosis of esophageal motility disorders from clinical EPT studies. Moving forward, we anticipate continuing this process with increased emphasis placed on natural history studies and outcome data based on the classification.

Keywords *achalasia, esophageal motility disorders, esophageal pressure topography, manometry.*

INTRODUCTION

High resolution esophageal pressure topography (EPT) is an evolutionary technology incorporating the combination of high resolution manometry (HRM) and pressure topography plotting in the form of Clouse plots introduced in 2000 for the clinical evaluation of esophageal motility.[1] Prior to that, EPT had been developed and utilized as a highly innovative research modality.[2–6] The HRM Working Group first met in San Diego during DDW 2008 with the objective of adapting EPT to the clinical evaluation of esophageal motility. Since then, a series of HRM Working Group meetings have ensued on a more-or-less annual basis to review, critique, and plan the iterative process of developing a practical classification for esophageal motility disorders based on EPT-specific metrics and criteria. The classification scheme was initially branded 'The Chicago Classification' in 2008[7] following a series of seminal publications defining key EPT metrics and interpretation criteria optimized for clinical EPT studies emanating from a group of investigators at Northwestern University in Chicago.[8–11] Since then, two iterations of the Chicago Classification have been published summarizing the incremental development of the classification scheme.[8,12,13] The most recent meeting of the HRM Working Group was in Ascona, Switzerland in conjunction an international congress focused on the clinical evaluation of esophageal disease. This article summarizes the Chicago Classification of esophageal motility disorders emanating from that meeting at the Ascona congress.

CLINICAL HRM STUDY

As with conventional esophageal manometry, current HRM studies are comprised of a series of test water swallows. With HRM devices, the recording assembly is comprised of multiple closely spaced pressure sensors suitable for capturing the entirety of the deglutitive response spanning from the pharynx to the proximal stomach. Hence, only a single trans-nasal positioning of the device is necessary to accomplish the study and positioning is correct when both esophageal sphincteric regions are visualized and clearly delineated from adjacent regions. By convention, an EPT study comprised a series of ten test swallows of 5 ml water each, swallowed in a supine posture. Although it is certainly feasible to conduct studies in alternative postures and swallowing alternative substances, the metrics, normal values, and analysis for the Chicago Classification are currently entirely based on this convention. One avenue for further development is to expand beyond this convention. However, the diagnostic utility of such modifications will need to be established through future research.

EPT-SPECIFIC METRICS

The terms necessary to utilize the Chicago Classification of EPT studies are detailed in Table 1. Each metric has been developed to characterize a specific feature of deglutitive esophageal function for individual test swallows. The conceptual framework for developing these metrics (and the classification in general) was that it be based on physiological principles and that identified dysfunction is prioritized in a hierarchical fashion: (i) achalasia/EGJ dysfunction, (ii) motility patterns never observed in normal subjects, and (iii) peristaltic abnormalities out of the range of normal values. The overall scheme is that single test swallows are first individually scored utilizing the metrics in Table 1. The summary of that analysis for all ten swallows is then utilized to fit classification criteria and result in a manometric diagnosis.

Abnormalities of deglutitive lower esophageal sphincter (LES) relaxation are fundamental in disordered esophageal motility making this a crucial evaluation. However, from the vantage point of intraluminal manometry, the LES cannot be distinguished from other potential contributions to intraluminal pressure at the level of the esophagogastric junction (EGJ), most notably, the crural diaphragm and outflow obstruction. The latter is a novel term used to describe pathology that partially obstructs bolus passage across the EGJ leading to high intra-bolus pressure as a consequence of increased viscous resistance. Consequently, the terminology 'esophagogastric junction relaxation' was adopted. The EPT metric developed to optimally distinguish normal from impaired EGJ relaxation is the Integrated Relaxation Pressure (IRP).[9,11] The IRP is a complex metric as it involves accurately localizing the margins of the EGJ, demarcating the time window following deglutitive upper sphincter relaxation within which to anticipate EGJ relaxation to occur, applying an e-sleeve measurement within that

Table 1 Esophageal pressure topography metrics utilized in the Chicago classification. All pressures referenced to atmospheric pressure except the integrated relaxation pressure (IRP), which is referenced to gastric pressure

Pressure topography metrics	
Metric	Description
Integrated relaxation pressure (mmHg)	Mean EGJ pressure measured with an electronic equivalent of a sleeve sensor for four contiguous or non-contiguous seconds of relaxation in the ten-second window following deglutitive UES relaxation
Distal contractile integral (mmHg-s-cm)	Amplitude x duration x length (mmHg-s-cm) of the distal esophageal contraction >20 mmHg from proximal (P) to distal (D) pressure troughs
Contractile deceleration point [(CDP) (time, position)]	The inflection point along the 30 mmHg isobaric contour where propagation velocity slows demarcating the tubular esophagus from the phrenic ampulla
Contractile front velocity (cm s^{-1})	Slope of the tangent approximating the 30 mmHg isobaric contour between P and the CDP
Distal latency (s)	Interval between UES relaxation and the CDP
Peristaltic breaks (cm)	Gaps in the 20 mmHg isobaric contour of the peristaltic contraction between the UES and EGJ, measured in axial length

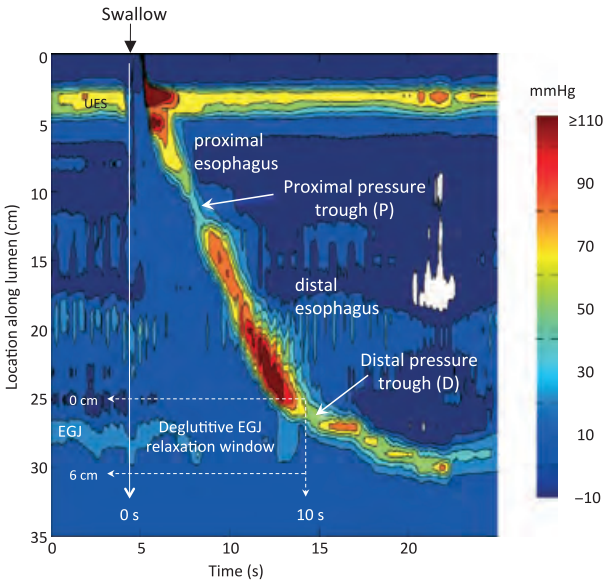

Figure 1 Esophageal pressure topography (Clouse plot) illustrating a normal peristaltic contraction and key landmarks used in the Chicago Classification of esophageal motility. For further description, see Table 1. P is the proximal pressure trough separating the proximal and distal contractile segments; D is the trough separating the distal esophagus from the esophagogastric junction.

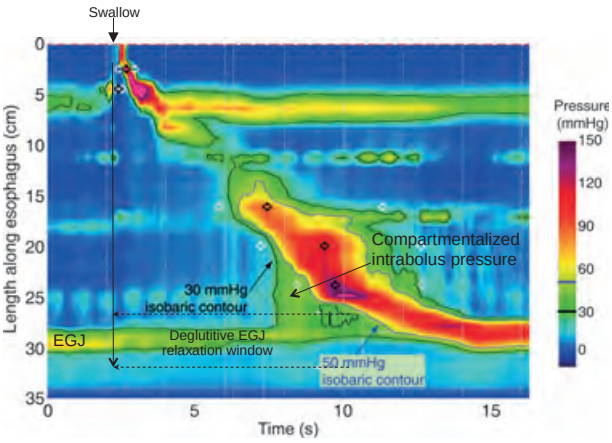

Figure 2 Example of elevated intrabolus pressure with high IRP and normal peristalsis. To illustrate the point, two isobaric contours are highlighted, 30 mmHg (black line) and 50 mmHg (blue line). Note that the EGJ pressure never falls below 30 mmHg and never goes above 50 mmHg indicating that the IRP is between these boundaries (actual value 43 mmHg). Hence, compartmentalized intrabolus pressure develops between the advancing peristaltic contraction and the EGJ outflow obstruction. In circumstances such as this the contractile front velocity must be measured at an isobaric contour value that is greater than EGJ pressure (50 mmHg in this case) so as to not erroneously high intrabolus pressure as indicative of a rapid contraction.

10 s time box (Fig. 1) and then finding the 4 s during which the e-sleeve value was least. The IRP is the mean pressure during those 4 s, necessarily being influenced not only by LES relaxation, but also by crural diaphragm contraction and intrabolus pressure (i.e. outflow obstruction) in the post-deglutitive period. These 4 s are not necessarily continuous but can be scattered over the 10 s time window. Given the intricacies of this measurement, it is not surprising that normal values are specific for specific sensor types and arrays. The upper limit of normal for the IRP using the Given Imaging (Sierra) HRM assembly is 15 mmHg.[9] Consistent with conventional manometry, IRP is referenced to intragastric pressure. Fig. 2 is an example of outflow obstruction with a high IRP, high intrabolus pressure, but normal peristalsis. The closest

equivalent to the IRP in conventional manometry is the 'LES relaxation pressure.'

The EPT metric devised to summarize the vigor of the distal esophageal contraction is the Distal Contractile Integral (DCI), measured for the segment spanning from the proximal to distal pressure trough or to the EGJ (Fig. 1). When the contraction is conceptualized as a solid, with pressure amplitude conferring height to the isobaric contours in Fig. 1, the DCI can be conceptualized as the volume of the pressure from P to D (or to the proximal margin of the EGJ when D is not clearly discernible), thereby being sensitive to the length of that span, and the amplitude and duration of the contraction at each locus along the way.[10] To exclude the effects of intrabolus pressure in the DCI computation, the first 20 mmHg is ignored.[10,13] Consequently, if a swallow was not associated with any recorded pressure >20 mmHg in the P to D span, the DCI for that swallow would be zero. However, keep in mind that the DCI was devised primarily to identify swallows of excessive contractile vigor making the upper rather than the lower limit of normal the more relevant limit. The upper limit of normal defined by the 95th percentile in a normal population is 5000 mmHg-s-cm, whereas when defined as the value never encountered in a normal population it is 8000 mmHg-s-cm.[13,14] The nearest equivalent of the DCI in conventional manometry is the 'peristaltic amplitude.'

The next three variables in Table 1, the Contractile Deceleration Point (CDP), the Contractile Front Velocity (CFV), and the Distal Latency (DL) all pertain to the rate of contractile propagation in the distal esophagus. Fundamental to understanding these is the CDP, a concept introduced to account for the transition from peristaltic propagation to the late phase of esophageal emptying illustrated with combined pressure topography and fluoroscopy in Fig. 3. The late phase of esophageal emptying proceeds much more slowly than does peristalsis and is both mechanistically and visually distinct.[15] Consequently the CFV is measured for the segment preceding the CDP to be reflective of the peristaltic mechanism proper. Similarly, the DL is measured from the time of upper sphincter relaxation to the CDP, again making it reflective of peristaltic timing and the period of deglutitive inhibition[16,17] rather than the late phase of esophageal emptying.[18]

The last pressure topography characteristic detailed in Table 1 is of the presence and length of breaks in the 20 mmHg isobaric contour, sometimes referred to as pressure troughs or the transition zone between the proximal and distal esophageal segments.[2,19,20] Large (≥5 cm) and to a lesser degree small (2–5 cm) gaps represent loci of extreme hypotensive peristalsis and have been shown to correlate with incomplete bolus transit at those loci.[21,22]

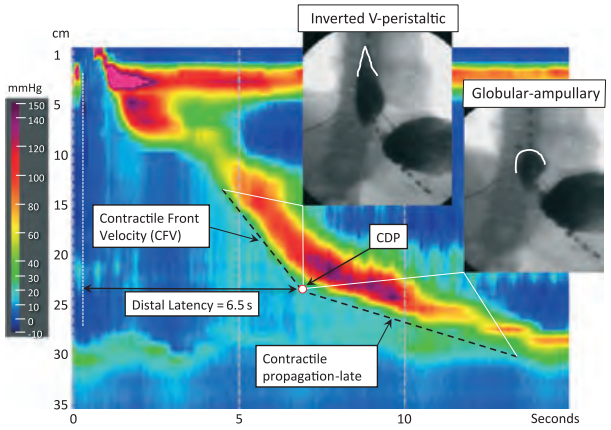

Figure 3 Functional significance of the Contractile Deceleration Point (CDP). Prior to the CDP, esophageal emptying is by a peristaltic stripping wave, imaged fluoroscopically as an inverted 'V' with the point of the 'V' corresponding to the upstroke of the peristaltic contraction at each locus. Peristalsis ends in the region of the CDP. After that, esophageal emptying is completed through formation and emptying of the globular shaped phrenic ampulla. This proceeds much more slowly and is not completed until the LES has recovered its pre-swallow position within the hiatal canal. The contractile front velocity (CFV) is calculated only on the segment of the EPT tracing preceding the CDP.

APPLYING EPT METRICS TO SCORE INDIVIDUAL SWALLOWS

The metrics detailed in Table 1 are applied to characterize each test swallow in terms of the integrity of the contraction, the contraction pattern, and intrabolus pressure pattern as summarized in Table 2. Note that not every test swallow can be scored in terms of contraction pattern as this domain pertains only to swallows with either intact peristalsis or weak peristalsis with small breaks in the 20 mmHg isobaric contour. Furthermore, in other instances, the contraction pattern can exhibit one to two or even all three of the patterns described (e.g. a hypercontractile, rapid, premature contraction).

As delineated in Table 2, the integrity of the contraction associated with each swallow describes how completely that contraction spans from the upper sphincter to the EGJ, irrespective of the vigor of the contraction, velocity of propagation, or latency. These qualifiers fall under the contraction pattern that is subsequently characterized. Weak contractions can be subtyped according to the location of the breaks (proximal, middle, or distal pressure troughs), although

Table 2 Esophageal pressure topography scoring of individual swallows

Integrity of contraction	
Intact contraction	20 mmHg isobaric contour without large or small break
Weak contraction	a) Large break in the 20 mmHg isobaric contour (>5 cm in length) b) Small break in the 20 mmHg isobaric contour (2–5 cm in length)
Failed peristalsis	Minimal (<3 cm) integrity of the 20 mmHg isobaric contour distal to the proximal pressure trough (P)
Contraction pattern (for intact or weak peristalsis with small breaks)	
Premature contraction	DL < 4.5 s
Hypercontractile	DCI > 8000 mmHg-s-cm
Rapid contraction	CFV > 9 cm s^{-1}
Normal contraction	Not achieving any of the above diagnostic criteria
Intrabolus pressure pattern (30 mmHg isobaric contour)	
Panesophageal pressurization	Uniform pressurization extending from the UES to the EGJ
Compartmentalized esophageal pressurization	Pressurization extending from the contractile front to a sphincter
EGJ Pressurization	Pressurization restricted to zone between the LES and CD in conjunction with hiatus hernia
Normal pressurization	No bolus pressurization >30 mmHg

given the absence of evidence suggesting unique implications to one or another subtype, these subtypes are currently not distinguished in the classification of weak peristalsis.[21] Similarly, a contraction characterized as hypercontractile (DCI >8000 mmHg-s-cm) can be subtyped as single peaked or multipeaked or non-multipeaked and synchronized with respiration or not.[14] However, the unique feature of hypercontractile contractions is that they are never observed in normal individuals, irrespective of subtype and in the absence of clinical differentiation among these subsets, these distinctions are not carried forward into the overall classification.

The final characterization of the test swallows summarized in Table 2 pertains to the pattern of intrabolus pressure, using the threshold of 30 mmHg relative to atmospheric pressure to identify potentially significant intrabolus pressure.[23–26] A fundamental distinction, the importance of which cannot be overemphasized, is between intrabolus pressure, recorded from within a compartment trapped between two loci of greater amplitude contraction and rapid contraction, which implies no necessary downstream obstruction. The extreme example is panesophageal pressurization, spanning from the upper sphincter to the EGJ and potentially occurring early (within 2 s) or late (>2 s) relative to the pharyngeal contraction.[27] When occurring in the context of achalasia, panesophageal pressurization is the consequence of a distinct motor pattern characterized by contraction of both sphincters and of the intervening esophageal longitudinal muscle, but without lumen-obliterating contraction of the circular muscle in the intersphincteric span.[28]

APPLYING THE CHICAGO CLASSIFICATION OF ESOPHAGEAL MOTILITY

After characterization of the test swallows, the summary of that analysis is used to fit the Chicago Classification of esophageal motility detailed in Table 3 and illustrated as a flow diagram in Fig. 4. An important caveat to this is that this classification is of primary esophageal motility disorders and is not intended to include post-surgical studies, for instance after fundoplication, laparoscopic gastric banding, or Heller myotomy. Although EPT studies are certainly done in those clinical circumstances, and the findings of those studies can be characterized in the terms of Tables 1 and 2, the interpretation of post-operative studies needs to be considered in the context of the specific operative history, each of which can be associated with a unique set of potential secondary motility disturbances. Similarly, in the case of achalasia, subtyping applies to patients prior to having definitive achalasia treatment to disrupt the LES. Again, EPT studies are certainly done after treatment for achalasia, and the findings of those studies can be characterized in the terms of Tables 1 and 2, but the interpretation needs to be considered in the context of the individual's specific treatment history. Finally, the classification detailed in Table 3 and Fig. 4 pertains to peristaltic function of the distal esophageal segment; it does not include the pharynx, UES, proximal esophageal segment, or the EGJ in the context of reflux barrier function. These topics are slated for future discourse.

The organization of Table 3 is prioritized top to bottom, with the most significant diagnoses bolded on

Table 3 The Chicago classification of esophageal motility

Diagnosis	Diagnostic Criteria
Achalasia	
Type I achalasia	Classic achalasia: mean IRP > upper limit of normal, 100% failed peristalsis
Type II achalasia	Achalasia with esophageal compression: mean IRP > upper limit of normal, no normal peristalsis, panesophageal pressurization with ≥20% of swallows
Type III achalasia	Mean IRP > upper limit of normal, no normal peristalsis, preserved fragments of distal peristalsis or premature (spastic) contractions with ≥20% of swallows
EGJ outflow obstruction	Mean IRP > upper limit of normal, some instances of intact peristalsis or weak peristalsis with small breaks such that the criteria for achalasia are not met†
Motility Disorders	(Patterns not observed in normal individuals)
Distal esophageal spasm	Normal mean IRP, ≥20% premature contractions
Hypercontractile esophagus (Jackhammer esophagus)	At least one swallow DCI > 8000 mmHg-s-cm with single peaked or multipeaked contraction‡
Absent peristalsis	Normal mean IRP, 100% of swallows with failed peristalsis
Peristaltic abnormalities	(Defined by exceeding statistical limits of normal)
Weak peristalsis with large peristaltic defects	Mean IRP <15 mmHg and >20% swallows with large breaks in the 20 mmHg isobaric contour (>5 cm in length)
Weak peristalsis with small peristaltic defects	Mean IRP <15 mmHg and >30% swallows with small breaks in the 20 mmHg isobaric contour (2-5 cm in length)
Frequent failed peristalsis	>30%, but <100% of swallows with failed peristalsis
Rapid contractions with normal latency	Rapid contraction with ≥20% of swallows, DL >4.5 s
Hypertensive peristalsis (Nutcracker esophagus)	Mean DCI > 5000 mmHg-s-cm, but not meeting criteria for hypercontractile esophagus
Normal	Not achieving any of the above diagnostic criteria

†May be a variant form of achalasia, indicative of wall stiffness consequent from an infiltrative disease, or manifestation of hiatal hernia in which case it can be sub typed to CD or LES. ‡The locus of the multipeaked contraction can be in either of the distal two contractile segments or very rarely in the LES, but this is usually in the third contractile segment. May coexist with EGJ outflow obstruction.

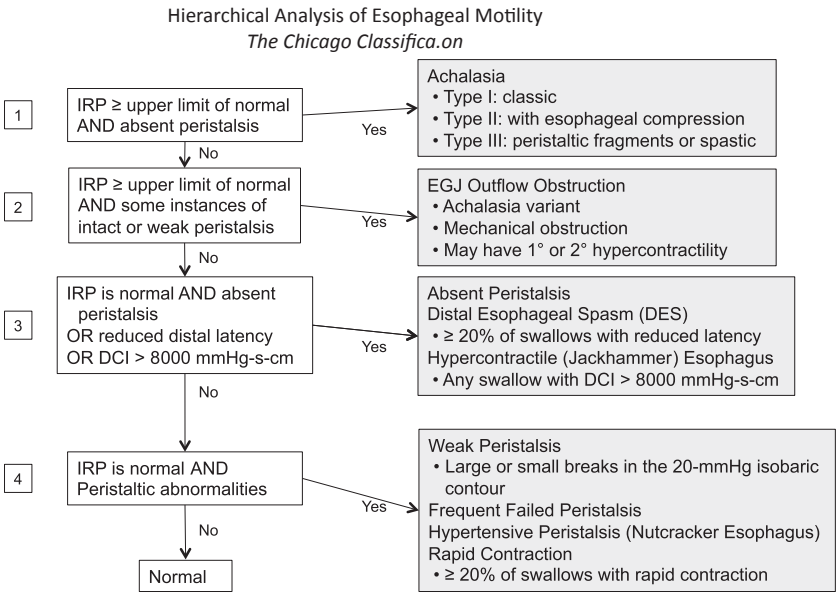

Figure 4 Flow diagram illustrating the hierarchical analysis of EPT studies according to the Chicago Classification. Note that primary motility disorders should be considered as a cause of dysphagia and/or chest pain after first evaluating for structural disorders, eosinophilic esophagitis and, where appropriate, cardiac disease. The first branch point identifies patients meeting criteria for achalasia (elevated IRP and absent peristalsis), which is then sub-classified. Patients meeting partial criteria for achalasia or exhibiting swallow-induced contractions with short latency or hypercontractility to a degree never encountered in normal subjects are then characterized. Note that some of these patients likely have variant forms of achalasia. The last branch point in the algorithm is to identify individuals with abnormalities of peristalsis defined by being outside of statistical norms. However, these abnormalities may be encountered in a normal population and their ultimate clinical significance remains to be established.

top leading to the hierarchical analysis illustrated in Fig. 4. A unifying attribute of the bolded diagnoses in the top half of Table 3 and the first two branch points of Fig. 4 is that they are not encountered in normal subjects. Although the clinical implications of the conditions at the second branch point of Fig. 4 are generally less clear than in the case of achalasia, each is strongly associated with symptoms, particularly dysphagia, supporting the validity of the designations. The evidence is less clear for the non-bolded entities comprising the lower half of Table 3. In these instances, the conditions identified are uniformly outside of statistical norms, but the strength of association with esophageal symptoms is less and there are instances in which each may be encountered in normal subjects.

The most fundamental measurement for utilizing Table 3 is the IRP. More so than any other measurement, this influences diagnostic categorization. However, the IRP is also the most technology-sensitive of the Table 1 metrics. Consequently, it is important to emphasize that the designation 'greater than the upper limit of normal' is used in Table 3 in differentiating abnormal from normal EGJ relaxation. The IRP was described and evaluated using the Sierra (Sierra Scientific Instruments Inc., Los Angeles, CA, USA) adult version circumferential HRM sensing device (subsequently acquired by Given Imaging) and the upper limit of normal for the IRP using this device is a mean of 15 mmHg in a supine posture.[9] Appropriate cutoff values for other sensing devices need to be established.

One of the novel features of the classification in Table 3 compared to conventional manometric diagnoses is the differentiation of achalasia into three subtypes [27,29,30] with the addition of 'EGJ outflow obstruction' as an additional potential achalasia phenotype.[24] This sub-categorization is based upon the recognition that these subtypes carry implications either to the efficacy of treatment,[27,29,30] the certainty of diagnosis,[24,31] and very likely, the evolution of the disease. Hence, 'classic achalasia' includes the spectrum from a hugely dilated esophagus to one with borderline characteristics of 'Type II' and distinguishing 'Type III' from 'EGJ outflow obstruction' ultimately depends upon the point at which one judges a residual contraction in the distal esophagus as a 'fragment of peristalsis' in one case or 'weak peristalsis with a small break' in the other. Such judgments can be subjective. However, this is the clinical reality and these nuances should not distract the practitioner from the bright side, which is that the overwhelming majority of cases are more neatly defined.

Other novelties of the classification in Table 3 pertain to the definition of 'distal esophageal spasm' and the differentiation of 'hypercontractile esophagus' from 'hypertensive peristalsis.' In the case of 'distal esophageal spasm' the revised criterion stems from the observation that the conventional criterion based on contraction velocity was heterogeneous and very non-specific, encompassing many instances of 'weak peristalsis'. On the other hand, the criterion based of distal contractile latency performed much better.[32] In the case of 'hypercontractile esophagus', nicknamed 'jackhammer esophagus' because the contractions are usually repetitive, the distinction is that, not only are the contractions vigorous, but to a degree not observed in normal subjects.[14] On the other hand, 'hypertensive peristalsis', popularly known as 'nutcracker esophagus' requires only that the contraction amplitude exceed the 95th percentile of normal which is, by definition, observed in 5% of a normal population.

Finally, the classification of weak peristalsis in Table 3 differentiates 'frequent failed peristalsis' from frequent occurrences of weakened peristaltic contractions with either small or large breaks. These categorizations are based upon an analysis of a large clinical dataset that found weakened peristalsis but not 'frequent failed peristalsis' to correlate with an increased prevalence of dysphagia.[21] Of note, both patterns of contraction are associated with impaired bolus transit as determined by concurrent high resolution impedance manometry.[21,33]

SUMMARY

The Chicago Classification of esophageal motility was developed to facilitate the interpretation of clinical EPT studies, concurrent with the widespread adoption of HRM and EPT into clinical practice. The Chicago Classification has been, and will continue to be, an evolutionary process, molded first by published evidence and secondarily by group experience when suitable evidence is lacking. This publication summarizes the state of our knowledge as of the most recent meeting of the International High Resolution Manometry Working Group in Ascona, Switzerland in April 2011. The major changes in this document from the prior iteration [13] are largely attributable to research studies published since the prior iteration, in many cases research conducted in response to prior deliberations of the International High Resolution Manometry Working Group. Moving forward, we anticipate continuing this process with increased emphasis placed on natural history studies and outcome data based on the developing classification.

ACKNOWLEDGMENTS

Albert J Bredenoord is supported by The Netherlands Organisation for Scientific Research (NWO). Mark Fox and Werner Schwizer are supported by the Zurich Centre for Integrative Human Physiology. Peter J Kahrilas and John E Pandolfino are supported by R01 DK56033 and R01 DK079902 from the US Public Health Service.

DISCLOSURES

There are no financial or professional disclosures relevant to either the meetings of the HRM working group or the synthesis of this paper for any of the authors. AJB received speaking fees from MMS International and AstraZeneca and received grant support from Movetis, Shire, Endostim, and AstraZeneca. JEP serves as a consultant for Given Imaging.

AUTHOR CONTRIBUTIONS

AJB assisted in critiquing, editing, and refining the paper; MF assisted in critiquing, editing, and refining the paper; PJK performed the initial literature search, wrote the initial draft of the paper and managed the integration of coauthor contributions; JEP assisted in critiquing, editing, and refining the paper; WS assisted in critiquing, editing, and refining the paper. All members of the HRM Working Group reviewed the final manuscript and approved of its content.

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APPENDIX

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