Esophageal Motility Testing: The Present and the Future

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13.1 Introduction

The primary functions of the esophagus are to transport swallowed materials from the pharynx to the stomach and to prevent the reflux of injurious gastric contents into the esophagus and airways [1]. The motor activities that allow the esophagus to accomplish these tasks are governed by complex neuromuscular interactions in three physiologically distinct neuromuscular units: the upper esophageal sphincter (UES), the body of the esophagus, and the lower esophageal sphincter (LES) [2]. Manometric techniques measure the amplitudes and timing of the pressure changes that, in general, reflect the force and timing of the circular muscle contraction or relaxation [3, 4].

Motor function can be assessed by a variety of recording techniques including radiology, scintigraphy manometry, and most recently intraluminal electrical impedance monitoring. Some of these are complementary. The gold standard, however, for the assessment of motor disorders remains manometry. Manometric measurement of esophageal pressure is the most direct method for the assessment of motor function [5]. Since its introduction in the early 1950s, esophageal manometry has contributed to a better understanding of esophageal motor function and has currently become a widely performed technique in clinical practice [6]. The first manometry systems used a catheter that contained water-perfused channels, which

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opened to the lumen at several points along the catheter. These water-perfused pressure channels were driven by a pneumatic pump and connected to external pressure sensors [6]. Water-perfused manometry catheters were hindered by large intervals between the pressure sensors, which could result in an inadequate assessment of sphincter pressure and peristaltic abnormalities. This shortcoming was partly overcome by adding a sleeve sensor, which measured the highest pressure exerted along a segment of several centimeters [7]. This allowed for a reliable measurement of the esophagogastric junction (EGJ), even though the EGJ moves up and down the catheter during inspiration or during swallowing. However, the esophageal pressure was still measured with a low level of detail, and the addition of more pressure channels was limited by the need of a larger diameter of the catheter and a significant amount of water being administered to a patient during the measurement. Furthermore, the response rate of water-perfused manometry is relatively low which results in difficulties when measuring rapidly changing pressures. Smaller caliber capillaries have partly overcome these shortcomings, making it now possible to create catheters with much more pressure sensors [7].

In the last 10 years, a new system to perform esophageal manometry was developed and introduced in both research and clinical setting: the high-resolution manometry. High-resolution manometry (HRM) is the current gold standard technique to assess esophageal motility. It utilizes closely spaced pressure sensors to create a dynamic representation of pressure change along the entire length of the esophagus. Data acquisition is easier than with conventional manometry, and interpretation is facilitated by esophageal pressure topography (Clouse) plots [8]. Along with the technological innovation, an international consensus process has evolved over recent years to define esophageal motility disorders using HRM, Clouse plots, and standardized metrics. This classification, titled the Chicago Classification (CC), was firstly published in 2009 [9] and updated in 2012 [10]. In recognition of many studies performed in the last years, the international HRM Working Group met in Chicago in May 2014 in conjunction with Digestive Disease Week to discuss new data in the context of working toward an update of the CC (v3.0) that was published in the first months of 2015 [11].

13.2 Where Esophageal Pressure Topography Come From?

In the 1990s, Ray Clouse and his colleagues gave birth to high-definition manometry (or high-resolution manometry) when they decreased the spacing between pressure sensing sites along the manometry catheter from 3 to 5 cm to 1 cm. Thus, they were able to increase the number of pressure sensors and to lengthen the sensing segment of the catheter so it spanned from the pharynx to the stomach. At last, it was possible to simultaneously see motor function of the upper esophageal sphincter (UES), esophagus, and lower esophageal sphincter (LES) with each swallow, giving us a complete spatial and temporal depiction of esophageal motor function for the first time [12, 13]. The true genius of his method was to convert the pressure data into a topographical plot. The convention at the time was to display manometry

recordings in a two-dimensional (2-D) space with pressure waves stacked sequentially from caudal to cephalad in the y-axis. The authors added a z-axis and stacked the pressure waves sequentially in the z-axis with gastric pressures to the front and pharyngeal pressures in the back. Amplitude was therefore on the y-axis and time on the x-axis. They developed an interpolation technique that filled in pressure data between pressure waves to give a 3-D pressure contour. They then assigned colors to pressures, with high pressures represented by warmer colors (reds and yellows) and low pressures by cold colors (blues and greens). Finally, they collapsed the color contour back into a 2-D space with time on the x-axis, position relative to the nares on the y-axis, and pressure depicted as color. This is a color topographical map of esophageal pressure that has been called the Clouse plot or esophageal pressure topography (EPT). In concept, it is like topographical maps of weather radar images that assign color to atmospheric pressure. Once one is comfortable with what the EPT means, it is apparent that many motor disturbances are recognizable as distinct patterns. These tools, as will be seen later, have changed how we categorize and define esophageal motor disorders in the new millennium [12, 13].

13.3 The Present

13.3.1 Metrics and Swallow Pattern Characterization

The primary objective of the CC is to apply standardized HRM metrics to categorize esophageal motility disorders in patients with nonobstructive dysphagia and/or esophageal chest pain. The CC is based on the scoring of ten 5-ml water swallows performed in supine position. Esophagogastric junction (EGJ) relaxation, esophageal contractile activity, and esophageal pressurization are evaluated for each swallow [11].

The terms necessary to better understand the Chicago Classification are detailed in Table 13.1. Each metric has been developed to characterize a specific feature of

Table 13.1 Esophageal pressure topography metrics utilized in the Chicago Classification

Pressure topography metrics	
Metric	Description
Integrated relaxation pressure (IRP, mmHg)	Mean EGJ pressure measured with an electronic equivalent of a sleeve sensor for four contiguous or non-contiguous seconds of relaxation in the 10-s window following deglutitive UES relaxation
Distal contractile integral (DCI, mmHg-s-cm)	Amplitude × duration × length (mmHg-s-cm) of the distal esophagus contraction > 20 mmHg from proximal to distal pressure troughs
Contractile deceleration point (CDP)	Inflection point along the 30-mmHg isobaric contour where propagation velocity slows demarcating the tubular esophagus from the frenic ampulla
Distal latency (DL, s)	Interval between UES relaxation and CDP

Legend: *EGJ* esophagogastric junction, *UES* upper esophageal sphincter

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 [11].

13.3.2 Esophagogastric Junction

During HRM analysis, EGJ pressure is dynamically monitored during normal respiration with defined axial resolution (usually 1 cm) and without artifacts attributable to swallow-induced sphincter movement [14] or to EGJ conformational changes that may spontaneously occur [15]. However, even within the domain of EPT, there are still a number of variables regarding the methodology for assessing EGJ relaxation, morphology, and competence (barrier function). Progress in the understanding of the optimal methodology for assessing the EGJ among these functional domains has been considerable with the widespread adoption of HRM into clinical practice.

With HRM and Clouse plots, the relative localization of the two constituents of the EGJ, the lower esophageal sphincter (LES) and the crural diaphragm (CD), defines EGJ morphologic subtypes [16]. The EGJ morphology was simply classified in three types: *type I EGJ morphology*, in which there is complete overlap of the CD and LES with no spatial separation evident on the Clouse plot and no double peak on the associated spatial pressure variation plot; *type II EGJ morphology*, in which the LES and CD are separated (double-peaked spatial pressure variation plot), but the nadir pressure between the two peaks does not decline to the gastric pressure; *type III EGJ morphology*, in which the LES and CD are clearly separated as evidenced by a double-peaked spatial pressure variation plot and the nadir pressure between the peaks equal to or less than the gastric pressure; with type IIIa the pressure inversion point remains at the CD level, while in type IIIb, it is located at the LES level [11]. Recently Tolone and coworkers [17] evaluated, by means of HRM and impedance with pH monitoring, 130 consecutive patients and identified 46.2 % type I EGJ, 38.5 % type II, and 15.4 % type III patients. Patients with type III EGJ had a higher number of reflux episodes (61 versus 45, $p < 0.03$, versus 25, $p < 0.001$), a greater mean AET (12.4 versus 4.2, $p < 0.02$, *versus* 1.5, $p < 0.001$), and a greater positive symptom association (75 % versus 72 %, $p = 0.732$ versus 43.3 %, $p < 0.02$) compared to patients with types II and I, respectively. They concluded that increasing separation between LES and CD could cause a gradual and significant increase in reflux. Thus, they demonstrated that EGJ morphology assessment may be useful to predict an abnormal impedance-pH testing in gastroesophageal reflux disease (GERD) patients [17]. Similarly, the same group [18] evaluated the vigor of EGJ and its relationship with GERD by adopting a new HRM metric, namely, the contractile integral (CI). The EGJ-CI was calculated using the distal contractile integral toolbox during three consecutive respiratory cycles. They observed that

patients with a defective EGJ-CI had more frequently a positive impedance-pH monitoring or esophageal mucosal breaks at endoscopy ($p < 0.05$) than patients with a normal EGJ-CI and concluded that a defective EGJ-CI at HRM is associated with evidence of GERD at reflux monitoring or endoscopy [18]. These data reinforced the need of performing HRM to better understand the mechanisms of GERD and suggested a potential diagnostic application of HRM for GERD diagnosis, at least as complementary test, and not only for positioning the pH electrode before reflux monitoring or for excluding achalasia in case of gastroesophageal surgery, in particular anti-reflux surgery.

During swallowing, EGJ relaxation is evaluated using the integrated relaxation pressure (IRP). This has been and will continue to be defined as the mean of the 4 s (contiguous or non-contiguous) of maximal deglutitive relaxation in the 10-s window beginning at deglutitive UES relaxation. The IRP is referenced to gastric pressure. The IRP represents a realistic alternative to the "nadir LES residual pressure" obtained during a standard manometry. Lin et al. [19] evaluated in a large group of patients the difference between single-sensor-detected EGJ relaxation and IRP to diagnose achalasia. They observed that the single-sensor method of assessing EGJ relaxation had a sensitivity of only 52 % for diagnosing achalasia. The 4-s IRP using a cutoff of 15 mmHg performed optimally with 98 % sensitivity and 96 % specificity in the detection of achalasia. This is important because failing to detect impaired EGJ relaxation in these patients would result in giving them a wrong diagnosis.

13.3.3 Disorders with EGJ Outflow Obstruction

The most fundamental assessment of deglutitive contractility in the Chicago Classification is of whether or not an EGJ outflow obstruction is present as defined by an IRP > 15 mmHg. Disorders of the EGJ outflow are subdivided into achalasia subtypes and EGJ outflow obstruction based on the contractile and pressurization patterns in the body of the esophagus. Three clinically relevant subtypes of achalasia have been defined in the different versions of the Chicago Classification [9–11]: type I achalasia was characterized by 100 % failed contractions and no esophageal pressurization; type II achalasia was defined as 100 % failed contraction and panesophageal pressurization for at least 20 % of swallows; and type III achalasia was defined as the presence of preserved fragments of distal peristalsis or premature contractions for at least 20 % of the swallows [10, 11]. Some studies showed that the adoption of the Chicago Classification can improve our capability to diagnose and treat patients with achalasia. However, recent data highlighted that the use of a specific rigid cutoff (15 mmHg) to define normal from abnormal should be considered with caution. Indeed, the last iteration of the CC (v3.0) suggested assessment of EGJ relaxation by means of the median instead than by the mean value of IRP with ten swallows in order to minimize the effect of occasional outliers. Moreover, Lin et al. [19] recently showed that the critical IRP threshold may vary among achalasia subtypes and might range between 10 and 17 mmHg, specifically in type I achalasia, suggesting that IRP threshold might be reduced [19]. Similarly, Salvador and coworkers [20] observed

that in a larger group of 139 patients with endoscopic, radiological, and manometric characteristics of achalasia, 10.9% of the cases had an IRP value lower than 15 mmHg. To note, the authors showed that all patients had a positive outcome after laparoscopic Heller myotomy. Therefore, they suggested that some patients might also be correctly classified as a different type of achalasia deriving on clinical, radiological, and manometric pattern even if they had a borderline IRP [20]. Finally, another important consideration is that the cutoff for the upper limit of normal is technology specific ranging from a low value of 15 mmHg for the Sierra design transducers to as high as 28 mmHg for the Unisensor design. Thus, the diagnostic accuracy for detecting EGJ outflow obstruction for each device varies and further emphasizes the need of caution when applying a rigid cutoff value.

A different condition characterized by an impaired EGJ relaxation is defined EGJ outflow obstruction (EGJ-OO). The EGJ-OO exhibits not only an IRP greater than 15 mmHg but also a preserved peristalsis and elevated intrabolus pressure above the EGJ during peristalsis [21]. The finding of an elevated intrabolus pressure proximal to the sphincter is important because it validates the physiological significance of impaired EGJ relaxation. From a physiological perspective, elevated intrabolus pressure is the consequence of the impaired relaxation. A recent work suggested that when EGJ outflow obstruction occurs as a consequence of incomplete relaxation, it is accompanied by a relative increase in the ratio of peristaltic amplitude in the distal part of the esophagus, whereas this is not the case with mechanical obstruction [22]. With the term EGJ-OO, the CC includes a heterogeneous group of patients with some individuals having an incomplete phenotype of achalasia or an undetected mechanical cause of EGJ-OO such as hiatus hernia, esophageal stenosis, or eosinophilic esophagitis. Consequently, it is a patient group that merits further evaluation with mucosal biopsies and imaging studies to exclude inflammatory or malignant etiologies, be that with computerized tomography or endoscopic ultrasound. Only after these possibilities have been fully explored should it be accepted as atypical achalasia [23]. On this topic, van Hoeij et al. [24] evaluated 34 patients with primary EGJ-OO. They concluded that EGJ-OO is an unclear motility disorder with poor clinical significance. Indeed, the authors observed that 10% of patients had unrelated symptoms and 15% had spontaneous symptom relief. Moreover, one hundred percent of patients showed no stasis during esophageal radiogram, whereas treated patients showed a beneficial response to botox injections. Finally, less than 10% of patients developed achalasia during follow-up [24].

13.3.4 EPT Metrics to Score Individual Swallows

The main HRM deglutitive peristaltic metrics used to evaluate esophageal contractile function are the distal contractile integral (DCI) and the distal latency (DL) (Fig. 13.1, Table 13.1) [10, 11]. They are used to characterize each of the ten 5-ml test swallows in order to obtain the final diagnosis. In particular, the DL physiologically represents an indirect measurement of deglutitive inhibition and thus of normal peristalsis. The DL is measured as the interval from UES relaxation to the

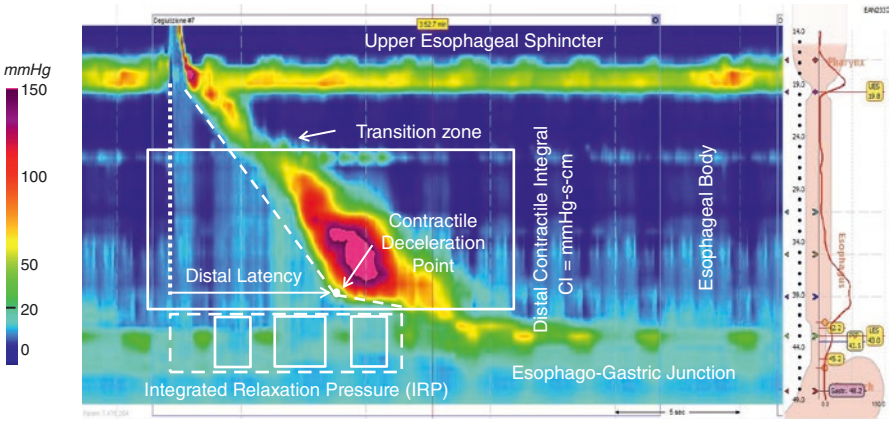

Fig. 13.1 High-resolution manometry tracing showing an example of a peristaltic wave. In the picture are well-represented both upper and lower esophageal sphincters and the swallowing-induced lower esophageal sphincter relaxation

Table 13.2 Characterization of esophageal contractility

Contraction vigor (20-mmHg isobaric contour)	
Failed	DCI <100 mmHg-s-cm
Weak	DCI >100 mmHg-s-cm but <450 mmHg-s-cm
Ineffective	Failed or weak
Normal	DCI >450 mmHg-s-cm but <8000 mmHg-s-cm
Hypercontractile	DCI >8000 mmHg-s-cm
Contraction pattern	
Premature	DL <4.5 s
Fragmented	Large break (>5 cm length) in the 20-mmHg isobaric contour with DCI >450 mmHg-s-cm
Intact	Not achieving the above diagnostic criteria
Intrabolus pressure pattern (30-mmHg isobaric contour)	
Panesophageal pressurization	Uniform pressurization of >30 mmHg extending from UES to EGJ
Compartmentalized esophageal pressurization	Pressurization of >30 mmHg extending from the contractile front to EGJ
EGJ pressurization	Pressurization restricted to the zone between the LES and CD in conjunction with the LES-CD separation
Normal	No bolus pressurization >30 mmHg

Legend: *DCI* distal contractile integral (mmHg-s-cm), *DL* distal latency (s), *EGJ* esophagogastric junction, *LES* lower esophageal sphincter, *CD* crural diaphragm

contractile deceleration point (CDP) [10, 11]; a value less than 4.5 s defines a premature contraction. The contractile vigor is measured by using the DCI. This metric applies an algorithm to quantify the contractile pressure exceeding 20 mmHg for the region spanning from the transition zone to the EGJ [10, 11]. As described in Table 13.2, the integrity of the contraction associated with each swallow describes

how completely that contraction is propagated from the upper sphincter to the EGJ, irrespective of the vigor of the contraction or latency. These qualifiers fall under the contraction pattern that is subsequently characterized.

Contraction Vigor Although an ineffective contraction was originally defined in conventional manometry on the basis of low-amplitude peristalsis, this criterion was not used to define weak peristalsis in the v2.0 of the CC [10]. The CC v3.0 clarified the distinction between contractile vigor and pattern and opted to clearly separate these concepts, basing the evaluation of contractile vigor entirely on the DCI and using a cutoff value of 100 mmHg-s-cm for failed peristalsis and a cutoff value of 450 mmHg-s-cm for weak peristalsis. The value for the weak peristalsis was derived directly from the study of Xiao and coworkers [25] that showed a positive percent agreement in predicting ineffective swallows of 83 % and a negative percent agreement of 90 % in a validation sample of 100 patients. Both failed and weak peristaltic contractions are ineffective. At the other extreme of contractile vigor, it was accepted to keep the cutoff for hypercontractility at 8000 mmHg-s-cm, but to eliminate the "hypertensive" designation for contractions with DCI between 5000 [10] and 8000 mmHg-s-cm, because it has no apparent clinical significance [11].

Contraction Pattern Hence, the CDP (the inflection point in the contractile front propagation velocity in the distal esophagus) is a key landmark in the assessment of the contraction pattern. However, in some instances like atypical peristaltic architecture or compartmentalized pressurization, the CDP can be difficult to localize, and so far the HRM Working Group decided to add two caveats for localizing the CDP in the last version of CC: (i) the CDP must be localized to within 3 cm of the LES, and (ii) in instances of compartmentalized pressurization, the CDP needs to be localized along an isobaric contour line of greater magnitude than the compartmentalized intrabolus pressure. Moreover, the HRM Working Group defined that breaks in the 20-mmHg isobaric contour should be considered into the chapter of "contraction pattern." Kumar et al. [26] observed that small breaks (<3 cm) in the 20-mmHg isobaric contour are frequently encountered in normal subjects, and therefore the HRM Working Group suggested that these should be considered normal [11]. On the other hand, Roman et al. [27] showed that large breaks (>5 cm) in the 20-mmHg isobaric contour were significantly more common in patients with dysphagia than in controls (14 % versus 4 %, $p=0.02$), and this concept was considered in the CC v3.0. Finally, in a recent study, Porter et al. [28] adopted the term "fragmented" to characterize those contractions with a large break in the 20-mmHg isobaric contour, but normal or elevated DCI (>450 mmHg-s-cm).

13.3.5 Major Motility Disorders

Major motility disorders are defined as patterns of motor function that are not encountered in controls in the context of normal EGJ relaxation. The hierarchical Chicago Classification v3.0 is reported in Table 13.3 [11].

Table 13.3 The Chicago Classification v3.0

Achalasia and EGJ outflow obstruction	Criteria
Type I achalasia (classic achalasia)	Elevated median IRP (>15 mmHg[a]), 100 % failed peristalsis (DCI < 100 mmHg-s-cm) *Premature contractions with DCI values less than 450 mmHg-s-cm satisfy criteria for failed peristalsis*
Type II achalasia (with esophageal compression)	Elevated median IRP (>15 mmHg[a]), 100 % failed peristalsis, panesophageal pressurization with ≥20 % of swallows *Contractions may be masked by esophageal pressurization, and DCI should not be calculated*
Type III achalasia (spastic achalasia)	Elevated median IRP (>15 mmHg[a]), no normal peristalsis, premature (spastic) contractions with DCI >450 mmHg-s-cm with ≥20 % of swallows *May be mixed with panesophageal pressurization*
EGJ outflow obstruction	Elevated median IRP (>15 mmHg[a]), sufficient evidence of peristalsis such that criteria for types I–III achalasia are not met[b]
Major disorders of peristalsis (not encountered in normal subjects)	
Aperistalsis (absent contractility)	Normal median IRP, 100 % failed peristalsis *Achalasia should be considered when IRP values are borderline and when there is evidence of esophageal pressurization* *Premature contractions with DCI values less than 450 mmHg-s-cm meet criteria for failed peristalsis*
Distal esophageal spasm (DES)	Normal median IRP, ≥20 % premature contractions with DCI >450 mmHg-s-cm[a]. Some normal peristalsis may be present
Hypercontractile esophagus (jackhammer)	At least two swallows with DCI >8000 mmHg-s-cm[a, c] *Hypercontractility may involve, or even be localized to, the LES*
Minor disorders of peristalsis (characterized by contractile vigor and contraction pattern)	
Ineffective esophageal motility (IEM)	≥50 % ineffective swallows *Ineffective swallows can be failed or weak (DCI < 450 mmHg-s-cm)* *Multiple repetitive swallow assessment may be helpful in determining peristaltic reserve*
Fragmented peristalsis	≥50 % fragmented contractions with DCI > 450 mmHg-s-cm
Normal esophageal motility	Not fulfilling any of the above classifications

Modified from Kahrilas et al. [11]

[a]Cutoff value dependent on the manometric hardware; this is the cutoff for the Sierra device

[b]Potential etiologies: early achalasia, mechanical obstruction, esophageal wall stiffness, or manifestation of hiatal hernia

[c]Hypercontractile esophagus can be a manifestation of outflow obstruction as evident by instances in which it occurs in association with an IRP greater than the upper limit of normal

Aperistalsis It (absent peristalsis) is defined by the combination of a normal IRP and 100 % failed contractions [11]. As mentioned previously, the contractions with DCI <100 mmHg-s-cm meet the criteria for failed peristalsis, but type I achalasia should be considered in cases of borderline IRP [19].

Distal Esophageal Spasm (DES) It should be considered when 20% or more esophageal contractions resulted premature with a DL value lower than 4.5 s [29] in a context of normal EGJ relaxation [11].

Hypercontractile Disorders The definition of hypercontractile esophagus (jackhammer esophagus, Fig. 13.2) is, in the last version of CC, identified as the only one hypercontractile disorder of the esophageal contraction [11]. The jackhammer esophagus (the nickname is quietly explicative) was previously defined as the occurrence of at least one swallow with DCI >8000 mmHg-s-cm in the CC v2.0 [30]. However, more recently, the HRM Working Group observed that an 8000-mmHg-s-cm DCI might occur in control subjects, and the previously indicated threshold of one swallow was insufficient and of uncertain relevance. Thus, the Working Group proposed to define jackhammer esophagus as the occurrence of >20% of swallows with a DCI >8000 mmHg-s-cm and normal latency. Further, the authors of CC v3.0 clarified that the hypercontractility can involve the LES or even might be restricted to the LES. In keeping, the authors suggested that it is necessary to expand the DCI measurement including the EGJ in such instances [11].

13.3.6 Minor Motility Disorders

The clinical significance of minor motility disorders continues to be debated. The prior classification for "peristaltic abnormalities" encountered significant dissatisfaction in the clinical community because of its complexity and unclear relevance. In the place of "peristaltic abnormalities" [10], the new version of CC v3.0 adopted the terminologies "ineffective esophageal motility," popularized in conventional manometric diagnoses, and "fragmented peristalsis" [11].

Ineffective Esophageal Motility (IEM) In 2008, Blonski et al. [31], by means of conventional manometry, defined ineffective esophageal motility (IEM) on the

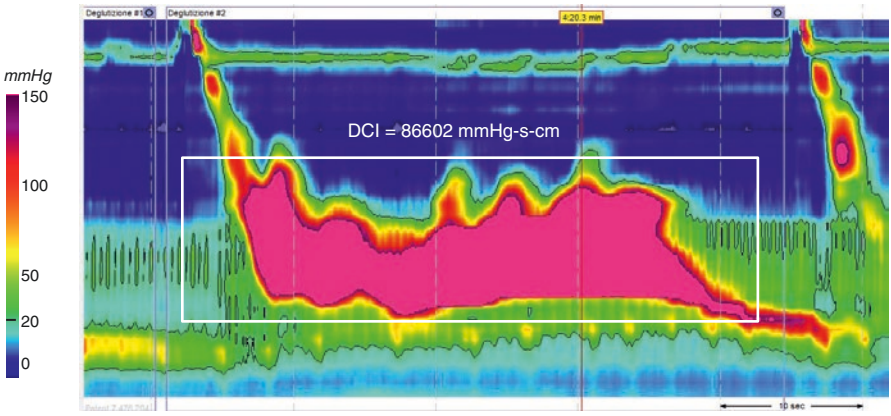

Fig. 13.2 High-resolution manometry tracing showing an example of jackhammer esophagus

basis of 50 % or more ineffective esophageal swallows which were in turn defined as esophageal contractions exhibiting amplitudes <30 mmHg at pressure sensors positioned 3 or 8 cm above the LES. The unifying feature of swallows contributing to the diagnosis of IEM is poor bolus transit in the distal esophagus. Thus, the Working Group proposed to define IEM as ≥50 % ineffective swallows based on a DCI <450 mmHg-s-cm, in accordance with Xiao and coworkers' results [25]. No distinction need to be made between failed swallows and weak swallows, thereby eliminating the former designation of "frequent failed peristalsis."

Fragmented Persistalsis The Working Group proposed to define "fragmented peristalsis" as ≥50 % fragmented contractions (large breaks >5 cm in the 20-mmHg isobaric contour) with the added stipulation of not meeting IEM criteria. Large breaks are significantly more common in patients with dysphagia than in controls (14 versus 4 %, $p=0.02$) [27]. It has been shown that the proportion of failed or fragmented contractions was greater in patients with GERD than in controls [28, 31]. The new definitions of the minor disorders of peristalsis are detailed in Table 13.3 [11].

13.4 The Future

13.4.1 The Near Future: Multiple Rapid Swallows

The recent introduction in clinical and research practice of HRM and impedance-manometry has represented a major advance in defining and characterizing esophageal motor abnormalities in GERD patients [32–34]. Several studies have shown that esophageal dysmotility prevalence parallels the increasing severity of GERD presentation [35–37], and, of particular relevance, those patients had failed and hypotensive peristaltic contractions, which resulted in incomplete esophageal emptying [36, 38]. Moreover, intermittent and nonspecific alterations of esophageal motility are frequently encountered in patients with GERD. However, the true impact and frequency of these abnormalities are not clear, even because standard manometric protocols based on single wet swallows are affected by intrinsic limitations, considering that active esophageal contractions may not be necessary to allow liquid transport, especially if it happens in the upright-seated position [39]. On that ground, recent studies highlighted the importance of including provocative tests, aimed at increasing esophageal workload, during HRM studies, in order to enhance the description and interpretation of esophageal motility [40, 41].

Multiple rapid swallows (MRS) that consist in the administration of five swallows (1–2 ml per swallow) in rapid sequence (less than 10 s) represent the simplest provocative maneuver. Indeed, when multiple swallows are rapidly administered, esophageal peristalsis is deeply inhibited, and pronounced LES relaxation ensues. After the last swallow of the series, a robust esophageal

contraction is expected [42]. Abnormal responses consist of incomplete inhibition (when contraction fragments are seen during the period of expected inhibition) or suboptimal contraction (when the post-MRS sequence fails to demonstrate augmentation of smooth muscle contraction) [42, 43]. In particular, Shaker et al. [44] showed that the strength of smooth muscle contraction augments almost twofold with MRS in normal controls and that lack of strong contraction is significantly more prevalent in GERD patients who develop postoperative dysphagia [43, 44]. Therefore, this alteration is considered to represent an inadequate peristaltic reserve of the esophageal smooth muscle [43]. To date, Martinucci and coworkers showed an inverse correlation between MRS response and acid exposure time in patients with negative endoscopy heartburn [45]. Considering these data, MRS has been proposed to be included in routine HRM studies. Indeed, it is simple, cheap, and easy to perform, and, above all, assessing the response to such a provocative test may increase the ability of HRM studies to detect clinically relevant esophageal dysfunction in patients with minor defects of peristalsis or with dysphagia without any finding of achalasia or EGJ-OO. This "low-volume challenge test" should be also suggested in patients with GERD-related symptoms to better define which patients will develop impairment of esophageal clearance. Finally, swallow challenges during the HRM study such as free drinking or a test meal, to trigger motility abnormalities, may improve the diagnostic yield of the study.

13.4.2 Future Role of the HRM Working Group

The real goal of the HRM Working Group is to update the classification every 3 years according to the main literature research projects. This is required to maintain a classification that takes into account relevant new developments in the esophageal motility pathophysiology. The future aim of the HRM Working Group will be to consider pharyngeal and UES functions that are still not included in the CC v3.0. Recent studies suggest the utility of combined impedance-HRM, but not HRM by itself, in detecting the main mechanism involved in GERD pathogenesis, which is the transient lower esophageal sphincter relaxation (Fig. 13.3), and in predicting the risk of aspiration in patients with oropharyngeal swallowing disorders [46–48]. Impedance measurement might also complement the analysis of esophageal function in patients without significant pressure abnormalities to evaluate the impact of esophageal body motility on bolus flow [49, 50] and might also be incorporated into future versions of the CC. Prospective trials taking into account provocative tests such as MRS, applesauce, and solid meal are needed to better recognize borderline diagnostic conditions. Finally, outcome studies about medical and surgical treatment of esophagogastric junction (both in GERD and in achalasia) are necessary.

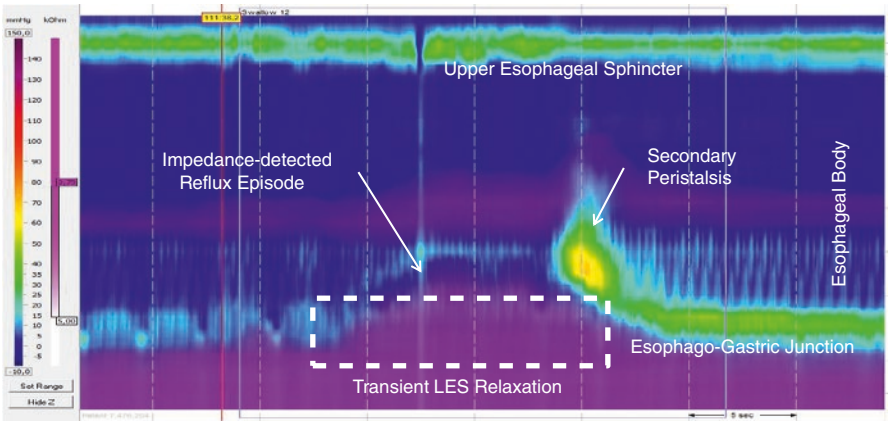

Fig. 13.3 High-resolution impedance-manometry tracing showing an example of a transient lower esophageal sphincter relaxation accompanied by an impedance-detected reflux episode

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