Pathophysiology of GERD: Ineffective Esophageal Motility

While gastroesophageal reflux disease (GERD) is probably the most common disorder of the upper gastrointestinal system in adults (1), impaired esophageal motility is a common finding in patients with gastroesophageal reflux disease (2). Absent or incomplete peristaltic contractions result in little or no volume clearance (3) suggesting that distorted motility of the esophageal body may contribute to the pathogenesis of GERD. Continuing the series on the pathophysiology of GERD this article addresses the role of esophageal motility in patients with gastroesophageal reflux disease.

ESOPHAGEAL MOTILITY TESTING

Occasionally endoscopy and barium esophagram reports contain information about esophageal motility. Still, esophageal manometry is considered the gold standard in evaluating and quantifying esophageal motility. Esophageal manometry in patients with GERD is recommended to investigate the presence of esophageal motility abnormalities associated with GERD and to locate the lower esophageal sphincter (LES) for adequate placement of esophageal pH testing devices.

The manometric systems can be classified into water-perfused and solid-state depending on the characteristics of the transducers used to measure pressure. Water-perfused systems use a complex assembly of tubes inside a catheter and water pumps that transmit the intraesophageal pressure through water columns to external pressure sensors. In solid-state systems small pressure transducers are mounted on a catheter allowing direct measurement of intraesophageal pressure. Both systems provide information on intraesophageal pressures and peristaltic sequence of contractions during swallowing.

During esophageal manometry the patient is traditionally in a recumbent position and is given a predefined amount of liquids. The supine position may be considered non-physiologic for swallowing but it has the advantage of eliminating the influence of gravity on bolus movement, thus providing the “maximum” challenge to the esophageal musculature. The supine position is also required by water-perfused systems for a proper alignment of the external transducers to the esophagus, a shortcoming eliminated when using solid-state systems.

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Richter, et al have published normal values for esophageal manometry in 95 healthy volunteers (4). Based on this study and simultaneous video-fluoroscopic and manometric studies by Kahrilas, et al (3) contractions with amplitudes less to 30 mmHg were considered manometrically ineffective (5) (Figure 1). Manometric swallows with amplitudes greater or equal to 30 mmHg in the distal esophagus and onset velocity (i.e. velocity of the onset of the contraction) exceeding 8 cm/sec were considered simultaneous. Manometric normal swallows have been defined as swallows with amplitude greater or equal to 30 mmHg in the distal esophagus and onset velocity less or equal to 8 cm/sec (Table 1).

During routine clinical esophageal manometry patients are given 10 liquid swallows. Normal esophageal manometry has been defined by the presence of not more than 2 manometric ineffective and 1 manometric simultaneous swallows (4). Ineffective esophageal manometry (IEM) has been defined as the presence of 3 or more out of 10 manometric ineffective swallows (6) and distal esophageal spasm (DES) as the presence of 2 or more out of 10 manometric simultaneous swallows (7). There are also specific manometric criteria to identify achalasia (i.e. absent esophageal peristalsis with or without high LES resting and residual pressure), nutcracker esophagus (i.e. normal esophageal manometry with an average distal esophageal amplitude exceeding 180 mmHg), hypertensive lower esophageal sphincter (i.e. mid-respiratory LES resting pressure exceeding 45 mmHg) and poorly relaxing LES (i.e. average LES residual pressure exceeding 8 mmHg).

It is important to acknowledge that, with the exception of achalasia, the above mentioned esophageal motility abnormalities are not established diseases of the esophagus since no underlying pathologic changes have been identified. Thus, their presence should be regarded only as possible explanations for the patient symptoms or clinical picture.

**THE ROLE OF ESOPHAGEAL MOTILITY IN GERD**

Esophageal manometry became available many years before both flexible endoscopy and esophageal pH testing. In the past manometry was considered an important tool for the diagnosis of GERD since low LES pressure was believed to be a good marker of the potential for gastric content to reflux into the esophagus (8). The availability of esophageal pH testing (9) and endoscopy (10) to diagnose GERD have led to a decline in the popularity of esophageal manometry as a means to diagnose GERD. This has been further emphasized by the recognition that transient lower sphincter relaxations (TLESR’s) (11,12) are a major mechanism by which reflux occurs, independent of the resting LES pressure.

Leite, et al (6) first defined ineffective esophageal motility (IEM) as the presence of at least 30% wet swallows with distal amplitudes of <30 mmHg or lack of peristalsis. Ineffective esophageal manometry was found to be a specific pattern in over 90% (60/61) of patients previously defined as non-specific esophageal motility disorder. In the same studies the authors found that the 35 patients with IEM who also underwent pH studies had significantly higher recumbent percent time pH less than 4 and esophageal acid clearance times compared to patients with normal esophageal manometry.

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try, distal esophageal spasm and nutcracker esophagus. Based on the results of this study a possible association between IEM and recumbent GER was suggested.

Founad, et al also reported on the association of IEM and GERD in 98 patients with GERD and respiratory symptoms (13). IEM was found to be the most prevalent esophageal motility abnormality in these patients regardless of their presenting symptom (asthma, laryngitis, chronic cough) and the authors found a significantly increased esophageal acid clearance time in patients with respiratory symptoms (1.51 min/reflux) compared to those presenting with heartburn (0.72 min/reflux). The results of this study suggest that patients with GERD and IEM may have a higher risk of developing respiratory symptoms given the delayed esophageal acid clearing.

The correlation between IEM and GERD is supported by data published by Ho, et al in 89 patients with GERD (14). They found an overall high prevalence of IEM in GERD patients (49%) as well as significantly increased percent time pH <4 (recumbent 4.4% and upright 6.7%) and esophageal acid clearance times (12.5 min/reflux) compared to patients with other motility findings. Beside the association of GERD and IEM these data suggest that the presence of IEM in GERD patients may reflect a more severe form of GERD.

In a retrospective study, Chrysos, et al (15) report data collected from a group of 147 patients with documented GERD. Analyzing symptoms, grade of mucosal injury on endoscopy, esophageal manometry and esophageal barium transit during esophagograms the authors report lower esophageal body amplitudes and more delayed esophageal transit in patients with GERD compared to controls. In this cohort of patients they found worse esophageal motor function and more prolonged esophageal transit in patients with dysphagia, severe esophagitis and Barrett’s esophagus compared to those lacking these findings. Of interest also was the inverse relationship between the duration of GERD and amplitude of esophageal contractions at 5, 10 and 15 cm above the LES.

In a large retrospective study, Shiino, et al (16) evaluated the relationship between duration of gastro-esophageal reflux disease and degree of acid reflux to data obtained from esophageal manometry in 768 GERD patients. Measuring esophageal contraction amplitudes at 3 and 8 cm above the LES they found no correlation between the duration of symptoms and contraction amplitudes (r = -0.07 and r = -0.06 respectively) as well as a poor correlation between Johnson-DeMeester reflux score and contraction amplitudes (r = -0.18 and r = -0.17 respectively). Based on these data the authors concluded that the duration of GERD and degree of acid reflux have little influence on esophageal motility.

Along the same line, Vinjirayer, et al (17) reported their experience in 84 patients who underwent both esophageal manometry and pH testing. They found no difference in the prevalence of esophageal motility abnormalities between patients with normal and abnormal distal esophageal acid exposure (30% vs. 35%; p = 0.79) and no difference in the prevalence of motility abnormalities in patients with esophageal or supra-esophageal symptoms (32% vs. 25%; p = 0.75). Based on these results the authors cautiously concluded that, even though an association of GERD and IEM cannot be excluded, IEM does not stand alone as a significant marker for the presence of GERD.

While accepting the association of IEM and GERD with the prevalence of IEM ranging between 25%–50% (continued on page 18)
Identifying the presence of IEM in patients with GERD has been advocated as an important point in the pre-operative work-up due to concerns that patients with underlying motility abnormalities might be at higher risk of developing post-operative dysphagia (23,24). More recent publications though, suggest that the presence of esophageal motility abnormalities may not predict the development of dysphagia, regardless of whether full or partial fundoplications are performed (25,26).

**COMBINED IMPEDANCE AND MANOMETRY TESTING**

Part of these controversies may be due to the limitations of esophageal manometry to provide complete information on esophageal motility. While esophageal manometry measures the amplitude and sequence of contractions generated in the esophagus it offers only indirect information on the function of the esophagus; i.e. bolus transit/clearance. Recently multichannel intraluminal impedance (MII) has become clinically available to study bolus movement without the use of radiation (27). This technique uses differences in resistance to alternating current between air, bolus and esophageal wall to determine intraesophageal bolus transit (28). Combined with manometry (multichannel intraluminal impedance and manometry; MII-EM) it provides information about both pressures and their functional implications (bolus transit) (29).

Combined MII-EM studies in both healthy volunteers and patients with IEM found that some swallows with contraction amplitude less than 30 mmHg in the distal esophagus (manometric ineffective swallows) have incomplete while other manometric ineffective swallows have complete bolus transit (Figure 2). Factors influencing whether manometric ineffective swallows have complete bolus transit include the distal esophageal amplitude (average amplitude at two distal esophageal sites) and number of sites with amplitudes less than 30 mmHg (30). The total number of manometric swallows with amplitude less than 30 mmHg appears to influence
whether or not patients with IEM have normal or abnormal bolus transit (Figure 3).

Studying 70 patients with manometrically defined IEM we found that only one third of these patients have impaired bolus transit for both liquid and viscous solutions while the remaining two third have normal bolus transit for liquid, viscous or both (30). Also, the current 30 mmHg criteria to separate manometric normal from ineffective swallows is only 85% sensitive and 65% specific in identifying complete bolus transit. These data suggest that current manometric criteria to identify impaired esophageal motility are too sensitive and most likely need to be revised.

SUMMARY

While there is some controversy on the relationship of ineffective esophageal motility (IEM) and GERD, these two conditions appear to be associated with 25%–50% of GERD patients having manometric criteria of IEM. Currently, the question whether the motility abnormality is the result or cause of GERD is still debated.

The opportunity to obtain concomitant information on both esophageal contractions and esophageal bolus transit is likely to revise the current definition of ineffective esophageal motility and may offer new insights in the association of esophageal reflux and motility abnormalities.

References