Evaluation of Esophageal Motor Disorders in the Era of High-Resolution Manometry and Intraluminal Impedance

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The past few years were an exciting time in the study of esophageal motor disorders because new technologies emerged to study esophageal motor function and bolus transit. Although conventional manometry was long considered the "gold standard" for defining esophageal motor disorders, many technologic improvements occurred due to advances in transducer technology, computerization, and graphic data presentation. In addition, a relatively new technology, intraluminal impedance, was incorporated into manometric modalities. The most sophisticated systems now include combined high-resolution manometry with high-resolution impedance. Although these techniques provide more detailed information about esophageal function, whether they improve our ability to diagnose and treat patients more effectively is debatable. However, more recent data support that these advances actually improve our ability to diagnose and treat esophageal motor disorders. This article provides an update on these technologies in clinical practice and how they may be helpful in the future.

Introduction

Despite the recent emergence of new technologies enhancing the ability to study esophageal motor function and bolus transit, the approach to a patient with dysphagia should always begin with a basic history and physical examination. The initial goal is to differentiate oropharyngeal from esophageal dysphagia, which can be done by history in about 85% of cases [1]. Although the patient's sense of the anatomic location of the problem does not correlate well with the actual location of the defect, symptoms associated with immediate bolus transfer issues (coughing, aspiration, nasopharyngeal regurgitation) typically localize the dysfunction at or above the upper esophageal sphincter (UES). The history is complemented by watching the patient swallow and performing a detailed neurologic examination to assess cranial nerve function. Based on the history and physical examination, patients suspected of having oropharyngeal dysphagia should be referred for a modified videofluoroscopy study to evaluate oropharyngeal bolus transfer and to rule out mechanical obstruction at the UES. This tool may be the only requirement in the analysis of these patients if the problem is straightforward and treatment is determined by the pattern of abnormality encountered [2].

If the initial history is inconsistent with oropharyngeal dysphagia or the modified videofluoroscopy is unrevealing, the next step is to rule out mechanical or anatomic obstruction (eg, a web, ring, stricture, or mass lesion) [2]. This is done with upper endoscopy or barium swallow under fluoroscopy. Once obstruction is ruled out, the workup should focus on defining esophageal motor function and bolus transit abnormalities. Traditionally this assessment was performed with conventional manometry and/or a barium esophagram. Unfortunately, both modalities have well-documented limitations. Fluoroscopy requires patient exposure to ionizing radiation and provides no quantifiable data on peristalsis or sphincter pressure profiles. Conventional manometry characterizes the esophageal pressure profile but does not provide direct information on bolus transit or esophageal emptying. Additionally, conventional manometry is limited by a lack of standardized methodology and conflicting analysis paradigms. As a result, there is a high degree of interobserver variability in analytic observations, even when performed by industry leaders [3].

Given the aforementioned limitations, two new technologies were developed that address these issues and therefore may offer a more robust evaluation of dysphagia: high-resolution manometry (HRM) and impedance. HRM is an evolution of the prior manometric technique, whereas impedance is a new technology that provides much of the same information as fluoroscopy (eg, bolus transit) but without exposing the patient to ionizing radiation. These two techniques have advanced our understanding of esophageal motility and are evolving into clinically relevant tools in their own right. Thus, this article describes 1) the technology behind these new methodologies, and 2) how they can be used to improve clinical outcomes.

High-Resolution Manometry

Technology

By definition, HRM is not a new technology. Instead, it represents a refinement in methodology that provides greater resolution while simplifying data interpretation. The concept of HRM is to use an ample number of pressure sensors within the esophagus such that intraluminal pressure can be monitored as a continuum. Conventional manometry utilizes three to eight pressure sensors positioned within the esophageal lumen to assess the contractile pattern during fluid swallows. In contrast, HRM uses a vastly increased number of sensors with decreased spacing between them to comprehensively define the intraluminal pressure environment and minimize the impact of spacing between sensors. The practical requirements for high resolution typically mean having pressure sensors spaced less than 1 cm apart such that pressure values between sensors can be estimated by interpolation without significant loss of contractile information [4].

The ideal system for esophageal studies should span from the pharynx to the stomach with sensor separation of no more than 1 cm within and around the sphincters, and a temporal frequency response matched to the zone of the esophagus in which the sensors reside. Currently, three devices fulfill these requirements (Medical Measurement Systems: Enschede, The Netherlands; Sandhill Scientific: Highlands Ranch, CO; Sierra Scientific Instruments: Los Angeles, CA). These systems each consist of 32 to 36 solid-state transducers spaced at 1-cm intervals, adequate to assess intraluminal activity from the pharynx to the stomach without the need to reposition the recording assembly.

The wealth of data collected by HRM devices can by simplified for interpretation by presentation in esophageal pressure topography format. This design, which was not possible using conventional manometry due to the wide spacing between sensors, is more akin to an imaging technique (Fig. 1*A*, Fig. 1*B*, Fig. 1*C*). Not only does it simplify data interpretation through pattern recognition, but it also allows for standardization of methodology because sensors span the entire length of the esophagus without significant gaps. Thus, tracing interpretation is no longer dependent on sensor positioning relative to anatomic landmarks.

Two sensor configurations are available in solid-state HRM catheters: unidirectional and circumferential. As the names imply, unidirectional sensors record pressure from just one side of the three-dimensional cylinder while circumferential sensors derive an average pressure from integration of multiple pressure-sensing elements around the cylinder. In the esophageal body, sensor type does not appear to make a significant difference. Through the upper and lower esophageal sphincters there is substantial asymmetry with contraction and relaxation, and therefore circumferential sensors are of theoretical benefit [5,6].

Clinical advantages

Procedural

HRM offers several intuitive advantages over conventional manometry. In conventional manometry, a standard pull-through technique is necessary to locate the lower esophageal sphincter (LES) and place manometry sensors relative to this landmark. In HRM, the narrowly spaced pressure sensors provide a comprehensive assessment of the esophagus and therefore do not need to be placed relative to anatomic landmarks. As a result, studies are both quicker and easier to perform. Additionally, variability in sensor placement is eliminated, thus increasing the reproducibility of studies.

One failure of conventional manometry is the inability to account for anatomic changes in a dynamic esophagus, such as esophageal shortening or hiatus hernia, which are lost in the inter-sensor “blind spots.” Once again, the global esophageal assessment provided by HRM accurately defines the dynamic change in the esophagus and confidently localizes mobile landmarks, such as the LES or crural diaphragm [7,8]. Thus, HRM studies can be performed with more accuracy and less artifact than conventional manometry.

Management

Although the improvements in the procedural aspects of HRM are directly related to the increased number of sensors and the reduced spacing between them, the true clinical advantages of HRM derive from the methodology of data presentation originally described by Clouse and Staiano [4]. By coupling sophisticated algorithms to display the manometric data as pressure topography plots, HRM permits the visualization of esophageal contractility with color continuums representing isobaric conditions. In this format, the different esophageal contractile segments can be spatially delineated and independently analyzed (Fig. 1*A*). This process of interpretation is more intuitive and more easily learned by trainees naïve to either conventional or high-resolution manometric formats [9].

Visualized with topography as a continuum in two axial planes, HRM readily allows the determination of

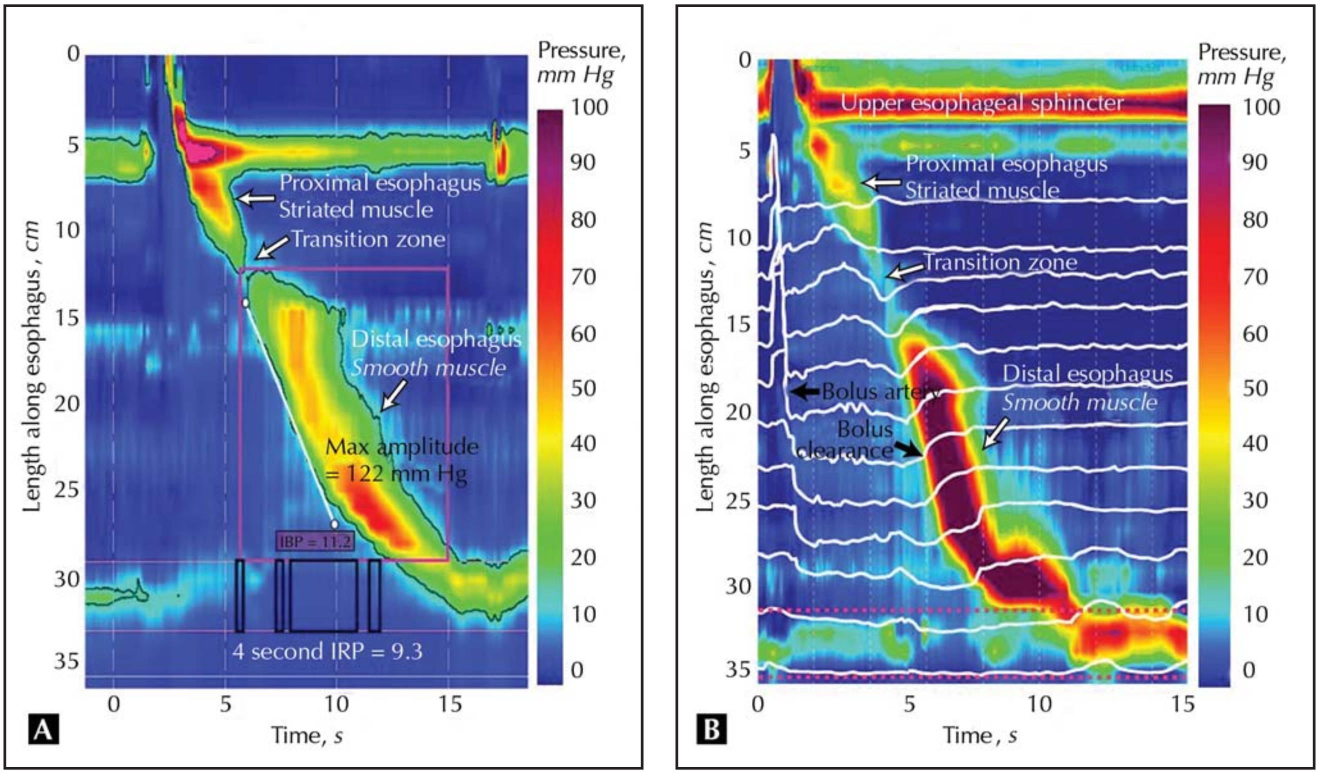

Figure 1. High-resolution manometry (HRM) alone or coupled with intraluminal impedance monitoring. (**A**) The typical pressure topography of the upper and lower esophageal sphincters with the intervening esophagus during a normal swallow (ManoScan system; Sierra Scientific Instruments, Los Angeles, CA). The relative timing of sphincter relaxation and segmental contraction and position of the transition zone are shown. The *pink box* on the pressure isocontour plot illustrates the domain for calculating the distal contractile integral (DCI). This can be estimated by multiplying the length of the box, time duration on the x-axis of the box, and mean pressure of the box domain using the Smart-Mouse tool in ManoView Analysis software. The contractile front velocity (CFV) is also measured using the Smart-Mouse tool to determine the slope of the *white line* (*ds/dt*). Alternatively, the CFV and DCI are calculated using the automated analysis paradigms in ManoView. Esophagogastric junction (EGJ) relaxation is also analyzed using the ManoView integrated relaxation pressure (IRP) tool, but can be measured manually with the isobaric contour tool. The default settings on the automated IRP tool establish a 4- to 6-cm by 10-second domain after the swallow and calculate the lowest mean eSleeve pressure for 4 noncontiguous seconds of relaxation within that window (*black boxes*). The intrabolus pressure (IBP) is also measured using an automated tool (IBP2) in ManoView and represents the average of the maximal 3-second IBP 1 cm above the proximal EGJ margin. (**B**) Classic impedance combined with esophageal pressure topography: impedance data overlaid on top of a standard esophageal pressure topography plot (Medical Measurement Systems, Enschede, The Netherlands). The combined catheter incorporates 36 unidirectional strain gauge pressure sensors spaced at 1-cm intervals and 14 impedance recording rings (12 impedance segments) spaced at 2-cm intervals spanning the distal 26 cm of the assembly. Data from simultaneous impedance recordings are overlaid on the color esophageal pressure topography plots to highlight the correlation between bolus transit and contractile activity. Bolus entry is identified by a decrease in impedance of at least 50% compared with baseline and bolus clearance as a subsequent, sustained (≥ 5 seconds), 50% or greater increase in impedance toward the original baseline. This swallow is characterized by intact proximal and distal esophageal segments. There is a seamless pressure wave through the distal esophagus with pressures greater than 20 mm Hg (highlighted by the outer *orange isobaric contour line*). EGJ relaxation is normal and evidence of preserved crural contraction is illustrated on the color isocontour plot. Bolus transit through the distal segment of the esophagus is normal as the impedance tracing rises to greater than 50% of the original baseline, which corresponds to the intact pressure front depicted on the color isocontour plot.

parameters of esophageal function: contractile velocity (contractile front velocity), global contractile vigor (distal contractile integral), intrabolus pressure, basal LES pressure, and the LES relaxation pressure (integrated relaxation pressure) (Fig. 1*A*). These variables allow standardization and organization of analysis methodology yielding a structured approach to swallow classification [10•].

Achalasia

Apart from improving the sensitivity of manometry in the detection of achalasia, HRM has also defined a clinically relevant subclassification of achalasia [11•]. A diagnosis of achalasia requires both aperistalsis and impaired deglutitive esophagogastric junction (EGJ) relaxation. In its most obvious form, this occurs in the setting of esophageal dilatation with negligible pressurization within the esophagus. However, despite the absence of peristalsis, pressurization within the esophagus can be substantial. In fact, a very common pattern is achalasia with esophageal compression and pan-esophageal pressurization. The other, less common, pattern is spastic achalasia in which there is a spastic contraction within the distal esophageal segment. In a series of 99 consecutive patients with newly diagnosed achalasia, 21

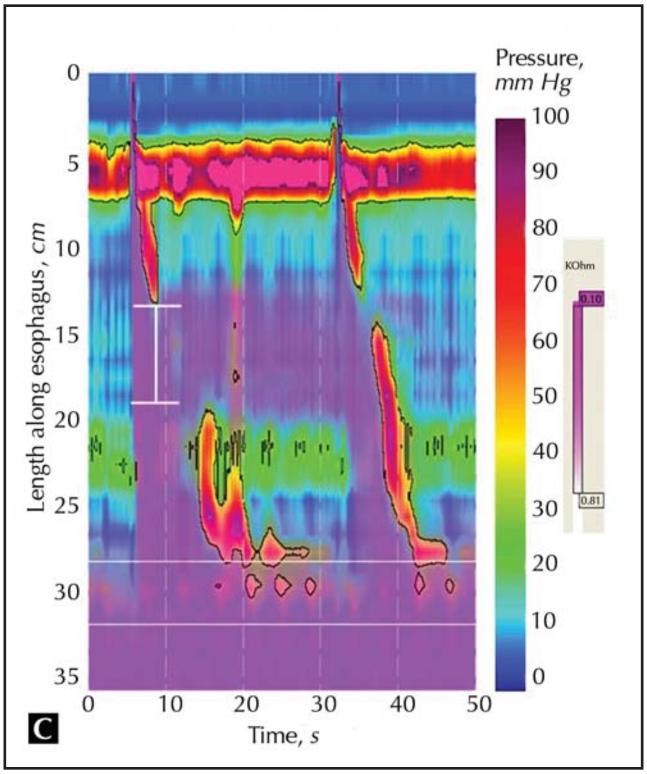

Figure 1. *(Continued)* (**C**) Color isocontour impedance combined with esophageal pressure topography. The HRM catheter incorporates impedance rings through the upper esophageal sphincter and into the stomach (Sierra Scientific Instruments). The impedance signal is converted to a specific color that has a preset range to distinguish a liquid bolus. The color spectrum (*purple*) is used because the transparency allows simultaneous impedance data to be overlaid on top of the typical color topography plot for HRM. This patient has a 6-cm defect starting below the proximal segment and extending through the transition zone into the second segment. The defect is associated with proximal stasis, and the patient responds to a feeling of regurgitation by performing a second dry swallow. Note the complete bolus clearance with the intact contractile front during the dry swallow.

patients had a pattern with negligible pressurization; 49 patients had the pattern of compression and pan-esophageal pressurization; and 29 had the pattern of spastic achalasia [11•]. Logistic regression analysis found pan-esophageal pressurization to be a predictor of positive treatment response whereas spastic achalasia was predictive of negative treatment response. Furthermore, it appeared that these patterns also predicted response to different therapies, and thus may be clinically useful for selecting appropriate candidates for surgery.

EGJ obstruction

A major advancement of HRM-derived esophageal pressure topography is the ability to accurately measure and define intrabolus pressure (IBP) within the esophagus during swallowing. IBP is the primary determinant of bolus transit through the EGJ because it is derived from the interplay of forward peristaltic forces behind the bolus competing against the downstream resistance of the EGJ. Unfortunately, this parameter has been largely ignored during conventional manometry due to limitations in accurately distinguishing contraction from compartmentalized pressurization. Esophageal pressure topography is not limited in this respect and can actually describe various IBP patterns associated with obstruction or reduced compliance in the esophagus.

Recently, our group reviewed 400 consecutive high-resolution manometries and found that 37 patients had impaired EGJ relaxation with intact peristalsis and distal esophageal compartmentalized pressurization to greater than 15 mm Hg. In addition, seven patients had severe functional obstruction evident by impaired EGJ relaxation with a compartmentalized pressure to greater than 30 mm Hg (severe functional obstruction) [10•]. In some cases, these patterns were associated with clearly identified mechanical abnormalities of the EGJ leading to outflow obstruction: 15 were post-fundoplication, five had peptic stricture, and three had eosinophilic esophagitis. The remainder of the subjects had no clearly defined pathology. Some of these patients may represent evolving or variant achalasia, whereas the others likely have pathology at the EGJ that reduces compliance and impedes esophageal emptying. Thus, these patients theoretically should respond to therapies focused on improving EGJ compliance or opening. Future research should focus on defining normal IBP values and determining whether this variable has value as a predictor of treatment outcome.

Refining classification of esophageal motor disorders

With the improvements in defining esophageal motor function, interest has increased in redefining esophageal motor disorders based on esophageal pressure topography. The first attempt at devising a new classification was based on a systematic analysis of motility patterns in 75 control subjects and 400 consecutive patients [10•], reviewed in two recent publications [12,13]. Individual swallows are analyzed in a stepwise fashion for the extent of EGJ relaxation, propagation velocity of peristalsis, weakness (or vigor) of peristaltic contraction,

Table 1. Classification of individual swallows based on pressure topography criteria*

Classification	Criteria
Normal	< 3 cm defect in the 30-mm Hg isobaric contour distal to the TZ, CFV < 8 cm/s, IBP < 15 mm Hg, and DCI < 5000 mm Hg•s•cm
Hypotensive peristalsis	Normal wave-front propagation with ≥ 3-cm defect in the 30-mm Hg isobaric contour distal to the TZ
Absent peristalsis	No propagating contractile wave front and minimal (< 3 cm) contractile activity or pressurization > 30-mm Hg isobaric contour
Hypertensive peristalsis	Normal-appearing wave-front propagation with DCI > 5000 mm Hg•s•cm
Spasm	Rapidly propagated contraction (CFV ≥ 8 cm/s)
	Focal—1 distal esophageal segment
	Diffuse—both distal esophageal segments
Elevated IBP	IBP > 15 mm Hg compartmentalized between the EGJ and the peristaltic wave front
Panesophageal pressurization	Esophageal pressurization from the UES to the EGJ with > 30 mm Hg IBP

*Distal segment contraction is referenced to atmospheric pressure.
CFV—contractile front velocity; DCI—distal contractile integral; EGJ—esophagogastric junction; IBP—intrabolus pressure; TZ—transition zone; UES—upper esophageal sphincter.
(*Adapted from* the High-Resolution Manometry Consensus Group and *modified from* Fass et al. [14].)

and abnormalities of intrabolus pressure (Table 1). These results are then synthesized into a global diagnosis that is customized to esophageal pressure topography. The first classification system incorporating these parameters was formulated through the efforts of a high-resolution manometry working group (Table 2). The resultant classification objectifies the identification of three unique subtypes of achalasia: distal esophageal spasm, EGJ obstruction, and nutcracker esophagus. Although this classification provides a working basis for evaluating esophageal pressure topography, it is evolving and requires further clinical validation and input from the working group.

Multichannel Intraluminal Impedance

Technology

Intraluminal impedance was created to provide information on bolus transit and avoid the requirement of radiation found in fluoroscopy. Impedance monitoring works by using an alternating-current generator to apply an electrical potential between two metal electrode rings separated by an isolator. The electrical current can only be bridged through the conduction of electrical charges through the surrounding material adjoining the two metal electrode rings. Air, saline, refluxate, and the esophageal wall each have unique impedance characteristics, thereby allowing easy identification of the material residing between the metal electrodes. Air is highly resistant to current flow and thus has very high impedance, whereas saline and gastric juice have low resistance to flow and a very low impedance value. Esophageal mucosa has an intermediate impedance range, and thus serves as a baseline during monitoring [14–16].

Clinical advantages

Procedural

By dispersing the impedance electrodes along a catheter and defining impedance changes over adjacent pairs of rings, one can determine the direction of bolus transit within the esophagus and document whether complete bolus clearance has occurred [14,17,18]. Studies using combined fluoroscopy and impedance have validated the convention that liquid bolus entry is signaled by a 50% drop in impedance at the recording site, and bolus clearance is signaled by a return to at least 50% of baseline [15,16] (Fig. 1*B*). Studies assessing the correlation between simultaneous barium videoesophagram and impedance revealed agreement in more than 97% of swallows for determining normal bolus transit or retrograde escape and stasis [19]. Thus, impedance serves as an excellent substitute for fluoroscopy in the assessment of esophageal emptying and normative data have been validated in a multicenter study of healthy volunteers [20].

Management

Refining classification of esophageal motor disorders

Intraluminal impedance is combined with conventional manometry to provide a methodology to describe both motor function and bolus transit. Recently, Tutuain and Castell [21] described their experience in a series of 350 patients presenting for evaluation of esophageal function. Their results revealed that all patients with manometrically defined achalasia and scleroderma have abnormal bolus transit. In contrast, only half the patients with ineffective esophageal motility and distal esophageal spasm (DES) had abnormal bolus transit, whereas most patients with intact peristalsis and various LES abnormalities had normal bolus transit. The authors theorized

Table 2. Esophageal pressure topography classification of distal esophageal motility disorders

With normal EGJ relaxation (IRP < 15 mm Hg with ≥ 70% of swallows)	
Disorder	**Criteria**
Aperistalsis	100% swallows with absent peristalsis
Hypotensive peristalsis	
Intermittent	> 30% of swallows with hypotensive or absent peristalsis
Frequent	≥ 70% of swallows with hypotensive or absent peristalsis
Hypertensive peristalsis	Normal CFV, mean DCI > 5000 and < 8000 mm Hg•s•cm or LES after-contraction >180 mm Hg
Spastic nutcracker	Normal CFV, mean DCI > 8000 mm Hg•s•cm
Distal esophageal spasm	Spasm (CFV > 8 cm/s) with ≥ 20% of swallows
Segmental	Spasm limited to Segment 2 or Segment 3
Diffuse	Spasm involving both Segment 2 and Segment 3
Functional esophageal obstruction	Max-IBP > 15 mm Hg with ≥ 30% of swallows not associated with EGJ obstruction
With impaired EGJ relaxation (IRP ≥ 15 mm Hg with ≥ 30% swallows)	
Disorder	**Criteria**
Achalasia	
Classic achalasia	Mean IRP ≥ 15 mm Hg, absent peristalsis
Achalasia with esophageal compression	Mean IRP ≥ 15 mm Hg, absent peristalsis, and panesophageal pressurization with ≥ 20% of swallows
Spastic achalasia	Mean IRP ≥ 15 mm Hg, absent peristalsis, and spasm (CFV > 8 cm/s) with ≥ 20% of swallows
Functional EGJ obstruction*	Normal CFV, max-IBP > 15 mm Hg with ≥ 30% of swallows compartmentalized above EGJ
Functional LES obstruction*	Normal CFV, max-IBP > 15 mm Hg with ≥ 30% of swallows compartmentalized above the LES with hiatus hernia
Functional CD obstruction	Normal CFV, max-IBP > 15 mm Hg with ≥ 30% of swallows compartmentalized above the CD with hiatus hernia

*May represent an achalasia variant.
CD—crural diaphragm; CFV—contractile front velocity; DCI—distal contractile integral; EGJ—esophagogastric junction; IBP—intrabolus pressure; IRP—integrated relaxation pressure; LES—lower esophageal sphincter; TZ—transition zone; UES—upper esophageal sphincter.
(*Adapted from* the High-Resolution Manometry Consensus Group and *modified from* Fass et al. [14].)

that impedance could potentially categorize esophageal motor abnormalities into more clinically relevant groups based on abnormalities of bolus transit and pressure as opposed to pressure alone.

To provide more focused information regarding a clinical role for impedance, Tutuian et al. [22] analyzed 71 subjects with DES and characterized them based on motor function and ability to obtain complete bolus transit. They found that DES patients with chest pain had higher contraction amplitudes and were more likely to have normal bolus transit than DES patients with dysphagia as the primary complaint. These observations are intriguing because it appears that impedance may help define treatment strategies for various patient groups: chest pain patients with extremely high contractile amplitudes may be a subpopulation amenable to treatments with nitrates and calcium channel blockers, whereas patients with impaired bolus transit may require alternative therapies. Thus, the stage is set for defining clinically relevant subtypes based on impedance data and prospective interventional outcome trials.

Rumination and belching

In contrast to studying antegrade bolus transit, intraluminal impedance has been adapted to study other esophageal motor diseases that focus on retrograde bolus transit, such as gastroesophageal reflux disease, rumination, and belching [23•]. Multichannel intraluminal impedance combined with manometry can help distinguish rumination from regurgitation related to an incompetent antireflux barrier or another esophageal motor disease [23•]. For example, regurgitation of ingested food followed by remastication then swallowing appears on combined impedance-manometry as increased intragastric pressure by manometry with subsequent impedance changes consistent with regurgitation of food and reswallowing. Similarly, this technique can also be used to differentiate the various causes of belching. Recently, Bredenoord et al. [24] used impedance to describe a group of patients with belching that originates from air being sucked into the esophagus with immediate expulsion, termed a "supragastric belch." This phenomenon is not related to an increase in gastric belching similar to that seen with transient LES relaxations. This distinction can be made by combined manometry-impedance based upon the lower esophageal sphincter tone.

Future Directions

The new technologies described here represent modifications of existing techniques and new tools that can improve accuracy and detail in describing esophageal function. They should not be viewed as competing technologies, because each method provides a valuable improvement over the existing technology. Although pressure gradients are the primary determinants of bolus transit, an inherent flaw of HRM is that it represents an indirect estimation of bolus transit [25]. As a result, efforts have focused on combining these techniques because they are largely complementary (Fig. 1*B*, Fig. 1*C*).

Recently, our group used a high-resolution impedance and manometry catheter (HRIM) designed by Medical Measurement Systems incorporating 32 point-pressure sensors spaced at 1-cm intervals with 12 impedance recording sites spaced at 2-cm intervals to study HRM predictors of bolus transit [26] (Fig. 1*B*). We analyzed 10 saline swallows each among 16 asymptomatic volunteers and eight patients with dysphagia. Impedance data were used to determine bolus transit success or failure, and peristaltic integrity and isobaric contour defect size were assessed using manometric data. Notably, none of the 24 patients had increased lower esophageal sphincter pressures or evidence of hiatus hernia. With this approach, we found that a peristaltic contraction wave that reaches 20 mm Hg or greater along its entire course was associated with bolus transit success in all identified cases. This is an improvement on the previously accepted pressure threshold of 30 mm Hg identified using conventional manometry [27,28]. In cases in which the peristaltic integrity was compromised, we found that the largest defect in the 20-mm Hg and 30-mm Hg isobaric contour associated with successful bolus transit measured 1.7 cm and 3.0 cm, respectively, in length. Meanwhile, the smallest defect predictive of bolus transit failure measured 2.1 cm and 3.2 cm, respectively. We concluded that an esophageal contraction wave with defects less than 2 cm in the 20-mm Hg contour or less than 3 cm in the 30-mm Hg contour are associated with normal bolus transit, whereas defects greater than 3 cm predict abnormal bolus transit [26].

Beyond research, HRIM technology may be clinically beneficial to the individual patient with complex pressure profiles. As detailed previously, progress is being made in understanding how specific patterns may be predictive of bolus transit. In cases in which the pressure profile does not match a specific pattern, impedance data are useful to directly determine bolus transit failure and to localize it to specific esophageal segments. As a result, the manometric analysis can focus on the specific impedance segments showing retained bolus. In addition, various display formats for the combined data are being developed to improve measurement and visualization of the bolus transit data. Figure 1*C* represents an example of combined HRM and impedance using a color-scale isocontour to describe bolus transit (Sierra Scientific Instruments). In this example, bolus transit is abnormal secondary to a 6-cm defect in the contractile wavefront. The bolus is not cleared until the patient swallows secondary to a sensation of regurgitation.

Conclusions

HRM and multichannel intraluminal impedance are new technologies in the evaluation of esophageal function that improve upon the flaws of prior methodologies and thereby increase diagnostic accuracy. They have proven helpful in difficult management cases and have refined the diagnosis and management of achalasia, functional obstruction, and rumination. Additionally, in combination they have also helped better discern threshold peristaltic pressure values for abnormal bolus transit. Thus, these tools alone and in combination continue to enhance research and the delivery of quality care to our patients.

Disclosure

Dr. Pandolfino has served as a consultant to AstraZeneca, Satiety, Medtronic, and Crospon; he has also served on the speakers' bureaus for AstraZeneca and Santarus. No other potential conflicts of interest relevant to this article were reported.

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