New Esophageal Function Testing (Impedance, Bravo pH Monitoring, and High-Resolution Manometry): Clinical Relevance

Jason A. Wilson, MD, and Marcelo F. Vela, MD, MSCR

Corresponding author
Marcelo F. Vela, MD, MSCR
Division of Gastroenterology and Hepatology, Medical University of South Carolina, 25 Courtenay Drive, ART 7100A, MSC 290, Charleston, SC 29425, USA.
E-mail: velaaqui@musc.edu

Current Gastroenterology Reports 2008, **10:**222–230
Current Medicine Group LLC ISSN 1522-8037

Esophageal testing aims to quantify gastroesophageal reflux or characterize esophageal motility. Reflux monitoring traditionally has been based on the detection of acidic reflux by a transnasal catheter that measures esophageal pH. Recently there have been two major developments in this field: the wireless Bravo pH capsule (Medtronic, Inc., Minneapolis, MN), which allows catheter-free monitoring, and impedance-pH measurement, a catheter-based technique that enables detection of acidic and nonacidic reflux. The assessment of esophageal motility has relied on conventional manometry for many years. Two new procedures also recently became available to assess esophageal motility: high-resolution manometry, which uses many closely spaced pressure sensors and provides spatiotemporal plots of esophageal pressure changes, and impedance manometry, a test that directly measures bolus transit and provides conventional manometric data. The advantages, disadvantages, and clinical importance of these new esophageal tests are discussed in this review.

Introduction

Twenty-four–hour pH monitoring to detect acidic reflux has been considered the gold standard to document gastroesophageal reflux disease (GERD), but this test has some limitations. The procedure requires placement of a transnasal catheter that may not be well tolerated and can limit patient activity. This can result in avoidance of refluxogenic behaviors during testing and lead to decreased sensitivity. The procedure may also lack sensitivity (eg, the presence of esophagitis does not necessarily predict a positive pH study). Furthermore, standard pH monitoring evaluates only reflux with a pH less than 4. Nonacidic reflux (pH > 4) cannot be detected, and this type of reflux may be clinically significant.

Conventional manometry, which has limitations but has been considered the gold standard to evaluate motility disorders, provides data on esophageal pressures and peristalsis but does not offer information about esophageal bolus transit. Patients with abnormal esophageal pressures may have normal bolus transit, and vice versa. Conventional manometry lacks sensitivity and specificity, many symptomatic patients have normal or equivocal studies, and normal asymptomatic individuals may have abnormal motility patterns (ie, ineffective esophageal motility). Because of these limitations, considerable controversy exists regarding the clinical relevance of nonachalasia motility disorders diagnosed by manometry.

This review discusses the new technologies available to perform esophageal testing: Bravo (wireless) pH (Medtronic, Inc., Minneapolis, MN) and impedance-pH monitoring for reflux detection, as well as impedance manometry and high-resolution manometry (HRM) for esophageal motility evaluation. These new technologies have the potential to overcome some of the limitations of conventional manometry and 24-hour pH testing.

Reflux Monitoring Tests

Catheter-based pH monitoring

Conventional ambulatory pH monitoring is performed by a transnasal catheter that records esophageal pH over a 24-hour period. A reflux episode is defined by a drop in pH to less than 4.0. Although the sensitivity and specificity of this test are greater than 90% in some studies [1,2], other data point to much lower sensitivity with a normal pH test in 29% of patients with erosive esophagitis [3].

Causes of decreased sensitivity may include incorrect pH probe placement, changes in patient behavior related to transnasal catheter placement that may result in decreased reflux during testing, and pH electrode inaccuracy. Transnasal catheter tolerance can be an issue. In a study of 54 patients that compared behavior on and off testing, 61% reported that the catheter bothered them during most of the testing time, often resulting in a decreased number of meals, lower activity, and fewer reflux symptoms [4]. Similar results were reported in a study of 114 patients who underwent 24-hour pH monitoring; a total of 65% reported decreased activity on the day of testing [5]. The pH catheter may move during the test, as demonstrated in a study of 43 patients in whom fluoroscopy found that the pH probe location may change by as much as 2 cm as a result of body position, swallowing, and talking [6]. This can impact test results because a more distal location may overestimate reflux, whereas more proximal placement will miss reflux episodes [7,8].

Standard ambulatory pH testing also lacks specificity. This method cannot distinguish between a pH drop below 4.0 caused by acidic reflux and ingestion of acidic food [9]. This was demonstrated in a study of 60 patients who underwent impedance-pH testing off acid-suppressive medication; all studies were initially read by exclusively analyzing pH, with subsequent analysis using the impedance information to detect swallows [10•]. A total of 81% of acidic gastroesophageal reflux episodes detected by pH alone were associated with impedance-detected swallows, and GERD was diagnosed erroneously in 22% of patients because of increased esophageal acid exposure detected by pH alone.

There have been concerns about the inaccuracy of antimony electrodes (the current standard in pH probes) compared with glass electrodes. One study found that a catheter using an antimony pH electrode measured pH values that were 0.6 U lower than a reference bench top electrode [11]. However, the recently introduced methodology for improved calibration appears to have increased the accuracy to an acceptable level [12]. The specificity of standard ambulatory pH monitoring is further limited by its inability to detect any nonacidic (pH > 4.0) reflux.

Bravo pH monitoring

A new technology has been developed that monitors esophageal pH wirelessly, obviating the need for a transnasal catheter. The Bravo system uses a small recording capsule that is endoscopically attached to the distal esophagus and transfers pH data via radiofrequency signals to an external recording device. Bravo has similar and possibly improved accuracy for detecting esophageal pH compared with catheter-based pH monitoring [11]. Also, Bravo is better tolerated by adult [13] and pediatric [14] patients, it enables testing under more physiologic conditions with less limitations on diet and activity [15], and it allows for prolonged monitoring (up to 96 hours) [16••].

Bravo enables pH measurement during increased activity. A study of 10 GERD patients undergoing Bravo pH monitoring to measure acidic reflux over 2 days (1 day with and 1 without a 60-minute period of exercise) found a threefold increase in esophageal acid exposure on exercise days [17]. Another potential advantage of Bravo is that because the capsule is fixed to the esophageal mucosa, the movement artifact seen with catheter displacement in conventional testing may be eliminated [18].

The Bravo system allows monitoring beyond the standard 24-hour time period. Forty-eight–hour Bravo pH monitoring in 44 healthy controls and 41 GERD patients revealed normal acid exposure on the first day but abnormal exposure on the second day in 12 patients and 7 controls [19]. Improved sensitivity in distinguishing controls from GERD patients was achieved by using the data from the worst of the 2 days. Prolonged pH monitoring permits evaluation off and on therapy in a single test. Four-day Bravo pH monitoring in 18 patients with suspected GERD who were tested off and on acid suppression (no therapy for the first day, rabeprazole on days 2–4) revealed significant reduction in acid exposure on the first day of treatment; only one patient failed to achieve normal acid exposure time during the 4-day period [16••]. The 4-day testing approach has also been used successfully to compare response to histamine 2-receptor antagonists versus proton pump inhibitors (PPIs) [20].

The Bravo system has some limitations. A recent study found early capsule detachment in 11 of 100 patients undergoing 48-hour Bravo pH monitoring; inclusion of these data resulted in abnormal acid exposure times in all 11 patients [21]. The Bravo capsule may cause discomfort, particularly in patients with functional heartburn [22]. The need for endoscopy to attach the Bravo sensor increases the cost and adds the risks related to endoscopy and conscious sedation. Whether Bravo is cost-effective compared with standard pH testing has not been studied. Finally, similar to conventional monitoring, the Bravo system cannot detect nonacidic (pH > 4) reflux, which may be clinically significant.

In summary, the Bravo system is better tolerated by adults and children, enables more physiologic behavior during testing, and permits prolonged monitoring. All of these advantages can increase the sensitivity and specificity compared with conventional pH testing [17,21,23]. Prolonged monitoring also enables testing off and on acid suppression in a single test [16••]. Limitations include possible early detachment, patient discomfort, increased cost, the risks of endoscopy and sedation, and the inability to detect nonacidic reflux.

Multichannel intraluminal impedance and pH

Intraesophageal impedance, determined by measuring electrical conductivity across a pair of closely spaced electrodes within the esophageal lumen, depends on the conductivity of material through which the current travels. By placing

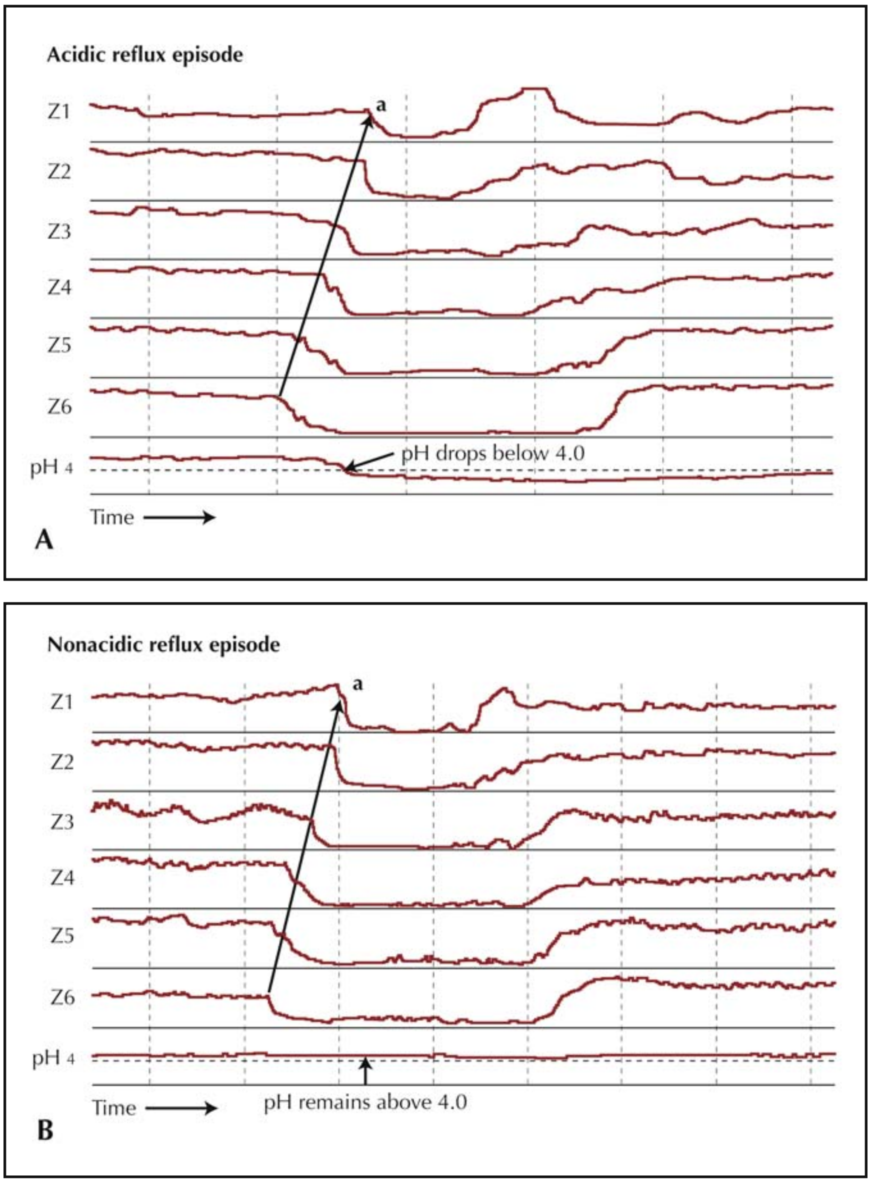

Figure 1. Acidic reflux and nonacidic reflux detected by multichannel intraluminal impedance and pH monitoring. Impedance changes in six measuring segments spanning the esophagus (Z1–Z6) and pH changes from a single sensor in the distal esophagus are shown in the "Y" axis. The *horizontal dotted line* marks a pH of 4.0. **A**, Acidic reflux. A typical impedance reflux pattern is seen, with sequential drops in impedance starting at the most distal measuring segment and proceeding toward the proximal esophagus. Return of impedance to baseline (signifying clearance of refluxate) begins proximally and progresses downward. *Point a* indicates the most proximal level reached by this reflux episode. Arrival of the refluxate into the distal esophagus causes a fall in pH to below 4.0, making this an acidic reflux episode. **B**, Nonacidic reflux. The height reached by this typical impedance pattern of reflux is indicated by *point a*. This is not accompanied by a fall in pH to below 4.0; therefore, this is considered an episode of nonacidic reflux.

a series of conducting electrodes in a catheter that spans the length of the esophagus, changes in impedance can be recorded in response to movement of intraesophageal material in antegrade or retrograde direction [24,25]. Assisted by the observation that the esophageal muscle wall, air, and any given bolus material (ie, swallowed food, saliva, or refluxed gastric contents) all produce a different change in impedance, the technique enables very detailed characterization of gastroesophageal reflux episodes, including composition (air, liquid, or mixed), proximal extent (height), velocity, and clearance time. During combined multichannel intraluminal impedance and pH (MII-pH) monitoring, impedance is used to detect retrograde bolus movement, whereas pH measurement establishes the acidity (acidic or nonacidic) of the reflux episode. Figure 1 shows examples of acidic and nonacidic reflux.

Based on the very detailed information that MII-pH monitoring provides, it was recognized as the most sensitive tool for measuring reflux by a recently convened panel of experts, the "Porto Consensus" [25]. Assessment of reflux with MII-pH has been found to be reproducible [26], and normal values for ambulatory 24-hour MII-pH monitoring obtained by three independent multicenter studies are very similar [27–29]. Although MII-pH is undoubtedly the most accurate method for reflux detection, the clinical indications for its use and its role in managing GERD patients are still evolving because the clinical relevance of nonacidic reflux must be discerned further, and there is a paucity of high-quality controlled studies examining the benefit of treating nonacidic reflux. It must be remembered that nonacidic reflux occurs predominantly in the postprandial period (when food buffers the stomach contents) or during pharmacologic acid suppression.

An early study of 12 patients evaluated the potential importance of nonacidic reflux by performing two 2-hour MII-pH recordings under refluxogenic conditions (left lateral decubitus after a meal). The patients were tested before and after treatment with omeprazole twice daily for 7 days [30]. Omeprazole did not significantly reduce the total number of reflux episodes (acidic and nonacidic reflux combined). However, after omeprazole treatment, the percentage of acidic reflux decreased from 45% to 3%, whereas nonacidic reflux increased from 55% to 97%. Heartburn and acidic taste were more commonly linked to acidic reflux but were also associated with nonacidic reflux, and regurgitation was reported equally after both kinds of reflux. It is important to note that this was a small study performed in a laboratory for a short period of time and under conditions designed to maximize reflux. Therefore, the findings may not reflect those seen in prolonged ambulatory conditions. Nonetheless, this was the first study to demonstrate ongoing nonacidic reflux as a potential cause of symptoms in acid-suppressed patients.

The association between symptoms and reflux assessed by 24-hour MII-pH has been the subject of two large, multicenter studies. In one study of 144 patients with persistent reflux symptoms despite twice-daily PPI administration, the association between symptoms and acidic or nonacidic reflux episodes was evaluated using the symptom index (SI) as the primary outcome measure [31]. On PPI therapy, 11% of patients had a positive SI for acidic reflux, 37% had a positive SI for nonacidic reflux, and 52% had a negative SI. Another study evaluated 134 patients with ongoing reflux symptoms (60 patients were being treated with a PPI, the other 74 were off therapy) [32]. The main outcome measure was the symptom association probability (SAP). This study found a positive SAP for 37% of the 60 patients on treatment. The SAP was positive due to nonacidic reflux in 17%, acidic reflux in 5%, and both acidic and nonacidic reflux in 15%. The discrepancy in the proportion of patients with a positive symptom association seen between the two studies may be partially explained by the outcome measure chosen, as the SAP is thought to be more stringent than the SI.

MII-pH has been used to measure the effects of therapies for acidic and nonacidic reflux. A study of 18 individuals (9 normal and 9 GERD patients) used 2-hour MII-pH recordings in refluxogenic conditions to compare the effect of 40 mg of baclofen (a γ-aminobutyric acid-B inhibitor that inhibits transient lower esophageal sphincter [LES] relaxations) versus placebo for treating acidic and nonacidic reflux [33]. Baclofen decreased acidic and nonacidic reflux in both study groups and reduced the median number of acid- and non–acid-related symptoms in the GERD patients.

Only a few uncontrolled studies have evaluated the long-term outcome of treating nonacidic reflux. A telephone interview survey assessed the clinical outcome in 17 patients who underwent fundoplication to treat symptomatic nonacidic reflux, which was documented by MII-pH performed on acid-suppressive medication [34•]. After a mean follow-up of 14 months, all but one of the patients were asymptomatic or markedly improved. Similar therapeutic success was reported in a retrospective study of six patients treated by fundoplication for nonacidic reflux–related cough that had persisted despite twice-daily PPI therapy [35]. Both studies were small, retrospective, and uncontrolled, and outcomes were based on subjective measures (ie, patient symptoms). However, these data suggest that treating nonacidic reflux is helpful.

MII-pH has also been used to study belching, which may be caused by air from the stomach or excessive air swallowing. In patients with excessive aerophagia, belching is typically supragastric and characterized by rapid intake and expulsion of air from the esophagus before it reaches the stomach. Impedance can distinguish these supragastric belches from normal gastric belches, and this information can potentially identify patients who would benefit from behavioral therapy [36].

Impedance-pH monitoring has some limitations. It is catheter-based, which, like conventional pH testing, can result in patient discomfort, change in behavior on the day of testing, limited duration of monitoring, and technical difficulties with catheter positioning. In addition to these catheter-based difficulties, low baseline impedance (seen in some patients with severe reflux or Barrett's esophagus) can make the tracing very difficult to read. Finally, interpreting the additional impedance data is more laborious and requires an additional skill set beyond reading standard pH tracings. Table 1 summarizes characteristics of the available reflux monitoring tests.

Esophageal Motility Tests

Conventional manometry

Standard esophageal manometry is typically performed with a catheter that contains five pressure transducers (usually solid-state) placed 5 cm apart. The catheter is placed transnasally so that the distal pressure transducer is located in the LES, with the additional pressure transducers located 5, 10, 15, and 20 cm above the LES. Swallows are then evaluated with the patient in the supine position with small volumes of liquid or viscous boluses. For each swallow, the corresponding pressures are recorded at the measuring sites in the esophageal body and LES [37]. Manometry provides data on esophageal pressures and peristalsis but does not evaluate esophageal function (ie, bolus transit) [38]. Manometry lacks sensitivity and specificity; many symptomatic patients have normal or equivocal studies, and normal individuals may have abnormal motility patterns (ie, ineffective esophageal motility [IEM]) [39]. Despite decades of clinical use, achalasia stands out among the esophageal motility disorders as the most clearly defined (clinically, manometrically, and radiographically) and the most successfully treated. The other manometric disorders are poorly defined, can occur in asymptomatic individuals, and may be inconsistent over time [39,40].

Table 1. Summary of reflux monitoring tests

Test characteristics	Standard pH testing	MII-pH	Bravo*
Catheter-based	Yes	Yes	No
Cost	Reference standard	Added cost of impedance catheter	Added cost of Bravo and upper endoscopy
Patient discomfort	Reference standard	Same as standard pH testing	Less discomfort
Interpretation	Reference standard	Requires additional knowledge	Same as standard pH testing
Detects nonacidic reflux	No	Yes	No
Detects supragastric belches	No	Yes	No
Prolonged monitoring	No	No	Yes

*Medtronic, Inc., Minneapolis, MN.
MII-pH—multichannel intraluminal impedance and pH.

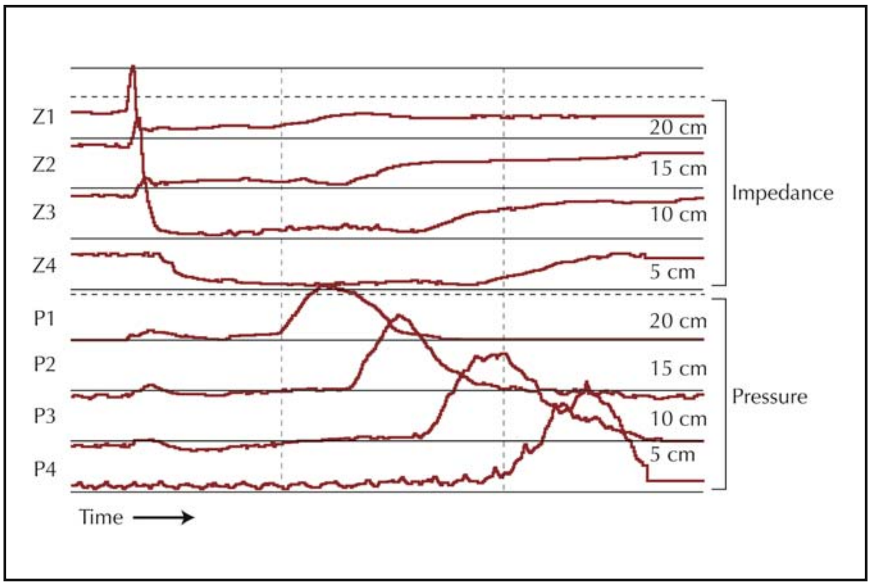

Figure 2. Multichannel intraluminal impedance and manometry. Impedance is measured in four channels (Z1–Z4) located 5, 10, 15, and 20 cm above the lower esophageal sphincter. Pressure sensors (P1–P4) at the same location simultaneously record manometric data (the pressure sensor in the lower esophageal sphincter is not shown in this figure). The impedance tracing reveals a typical swallow pattern characterized by sequential drops in impedance starting at the most proximal channel and proceeding toward the distal esophagus. The peristaltic wave detected by manometry, also moving from proximal to distal esophagus, induces bolus clearance. This clearance is appreciated in the impedance channels as a return to baseline beginning in the proximal esophagus and moving downward.

Multichannel intraluminal impedance and esophageal manometry

Intraesophageal impedance testing performed in conjunction with manometry can provide additional information about bolus transit, and this information strongly correlates with bolus transit assessed by videofluoroscopy [41]. It is hoped that MII and esophageal manometry (MII-EM) may help to better define the nonachalasia abnormal motility patterns and possibly guide therapy. The impedance measuring segments are incorporated directly into the standard manometry catheter so that from the patient's perspective, there is no added inconvenience. Normal values for MII-EM have been established by a multicenter study [42]. A tracing of MII-EM during a swallow is shown in Figure 2.

A large prospective study used MII-EM to evaluate the relationship between manometric findings and bolus transit in 350 patients with heterogeneous symptoms [43]. Impedance revealed abnormal bolus transit in all patients with achalasia (n = 24) and scleroderma (n = 4), but transit was abnormal in only 45% of patients with distal esophageal spasm (DES, n = 33) and 49% of patients with IEM (n = 71). Almost all the patients (> 95%) with normal manometry, nutcracker esophagus, and isolated LES abnormalities demonstrated normal bolus transit. A different group of researchers used MII-EM to evaluate 40 patients with nonobstructive dysphagia [44]. Abnormal transit was found in 35% of normal manometry (n = 20), 67% of DES (n = 4), 85% of IEM (n = 13), and 100% of achalasia (n = 3) patients. In both studies, all achalasia patients had abnormal transit, so impedance did not change the original diagnosis. In the nonachalasia patients, impedance identified bolus transit abnormalities in patients with normal and abnormal manometric findings.

A study of 71 patients with a manometric diagnosis of DES found that 49% had abnormal bolus transit [45]. Those with chest pain had higher contraction amplitudes and a higher proportion of swallows with normal bolus transit compared with patients presenting with dysphagia. The authors speculated that the clinical approach to patients

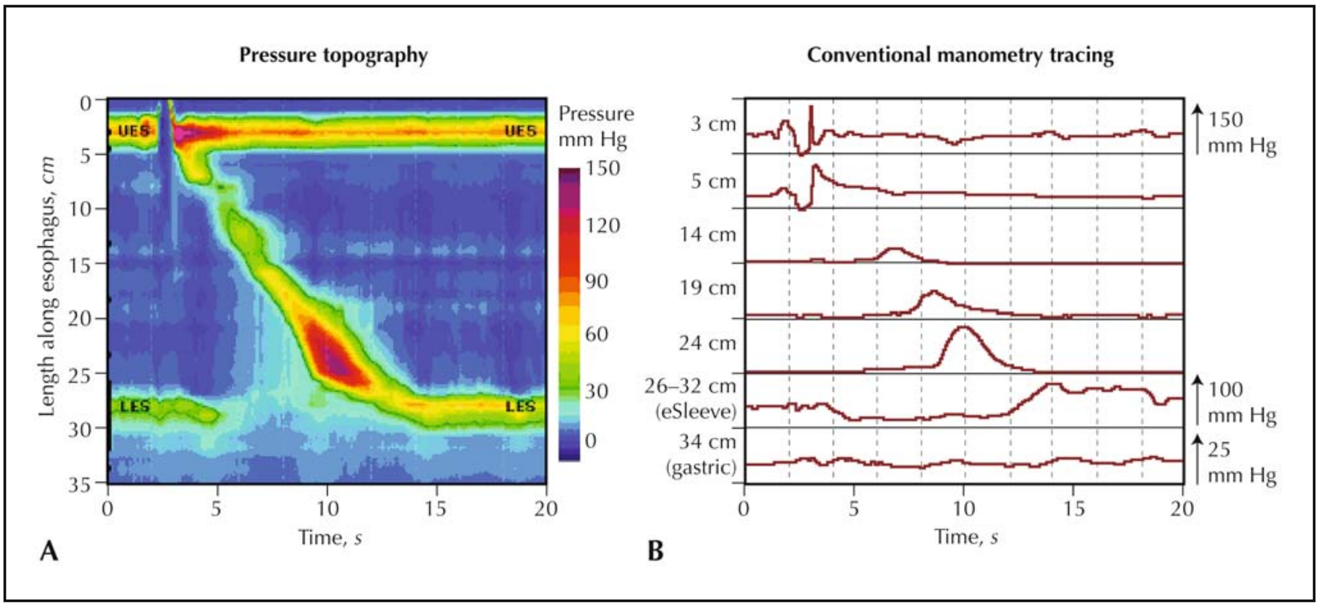

Figure 3. High-resolution manometry. **A**, Pressure topography during a normal swallow. Color coding of pressures allows easy recognition of two high-pressure zones: the upper esophageal sphincter (UES) and lower esophageal sphincter (LES). Both sphincters relax at the onset of the swallow; UES relaxation is shorter in duration. A peristaltic wave progresses from proximal to distal esophagus between the two sphincters. **B**, A conventional manometry tracing of the same swallow is shown for comparison. (*Courtesy of* John Pandolfino.)

with DES may be different for patients with chest pain, high amplitudes, and normal transit compared with patients with dysphagia, low amplitudes, and abnormal transit. The additional information regarding functional abnormalities may eventually guide therapy. However, controlled studies assessing the clinical outcomes of treating patients based on MII-EM findings are not available. A recent report of seven patients treated with bethanechol for severe bolus transit abnormality in the setting of manometrically defined IEM found increased contraction pressures and improved bolus transit after treatment [46]. It is hoped that further studies examining treatment of esophageal disorders diagnosed by MII-EM will provide added insight in the near future.

Rumination, defined as the chronic voluntary regurgitation of recently ingested food into the mouth with subsequent remastication and swallowing, is difficult to document using conventional esophageal tests. A recent case report described the use of MII-EM to diagnose rumination, based upon the detection of increased intragastric pressure followed by retrograde bolus movement from stomach to esophagus [47].

The limitations of MII-EM are similar to those of MII-pH, as the technology is subject to the same catheter-related limitations and low baseline impedance problems. Interpreting MII-EM is also more complex and time consuming compared with conventional manometry. Finally, the technology assesses bolus transit but not esophageal anatomy, so additional testing is needed to obtain this information.

High-resolution manometry

Similar to conventional manometry, the high-resolution technique requires a transnasal catheter and uses sensors to record esophageal and sphincter pressures during swallows. Conventional manometry has limited spatial resolution, as motility assessment is based upon pressure changes at sensors spaced 5 cm apart. The high-resolution catheter contains more pressure-measuring sites that are spaced less than 2 cm apart, and advances in computer processing have allowed this increased amount of data to be displayed as "spatiotemporal" plots rather than simple line graphs (Fig. 3) [48•]. High-resolution manometry (HRM) may provide improved assessment of esophageal and esophagogastric junction dynamics and a simpler way to perform manometry, both in correct catheter placement and in interpretation of the results.

Conventional manometry requires a "pull-through" of the catheter across the high-pressure zone to identify the LES and position the catheter. The presence of a hiatus hernia can make identifying the LES difficult [49]. Furthermore, the LES pressure sensor can be displaced during movement caused by esophageal contractions and shortening. When LES or catheter movement occurs during HRM, the closely spaced sensors continuously monitor the high-pressure zone and reliably measure LES pressures [50]. This obviates the need for a pull-through that shortens the procedure time and facilitates more accurate positioning of a pH probe for reflux monitoring. The "spatiotemporal" data display is considered to be more intuitive and may decrease interpretation time [51]. The same principles apply to assessment of upper esophageal sphincter, which moves during swallowing. Studies in healthy volunteers have recently defined normal findings for upper esophageal sphincter relaxation [52], esophageal peristalsis [48•], and esophagogastric junction dynamics [53].

Table 2. Summary of esophageal motility tests

Test characteristics	Standard manometry	MII-EM	HRM
Catheter-based	Yes	Yes	Yes
Interpretation	Reference standard	Requires additional knowledge	Requires additional knowledge
Predicts bolus transit	No	Yes	Unclear
Evaluation of esophageal sphincters	Reference standard	Same as standard manometry	Improved
Detects segmental abnormalities	No	No	Yes

HRM—high-resolution manometry; MII-EM—multichannel intraluminal impedance and esophageal manometry.

Two studies that compared HRM with conventional manometry demonstrated a high degree of diagnostic concordance and cited examples of possibly clinically relevant dysmotility identified only by HRM, such as segmental abnormalities of the esophageal body [54,55]. The relevance of these potential missed findings is uncertain, as clinical studies are limited.

Whether HRM is capable of assessing bolus transit is unclear. In a comparison with videofluoroscopy used as the reference standard, HRM predicted abnormal bolus transport with a sensitivity of 90% and specificity of 100% [54]. In contrast, conventional manometry accurately predicted abnormal transit with a sensitivity and specificity of 70% and 89%, respectively. No head-to-head comparisons of HRM and impedance have been done, but if the two techniques predicted bolus transit equivalently, HRM might be the preferred technology because of the more reliable and accurate data regarding the LES and focal areas along the esophageal body.

In summary, HRM enables more reliable localization of the LES during movement and in the presence of hiatus hernia, permits analysis of segmental esophageal defects, and may be able to predict bolus transit. Disadvantages include a higher cost compared with conventional manometry. Also, the supplementary data could result in overdiagnosis of clinically insignificant dysmotility. As with impedance-based techniques, the clinical usefulness of HRM awaits further definition. A classification scheme for esophageal motor abnormalities identified by HRM recently has been proposed [56]. Future clinical studies that evaluate the implementation of these diagnostic criteria and the treatment of motility disorders diagnosed by HRM are anticipated. Table 2 summarizes characteristics of the available tests of esophageal motility.

Summary of Clinical Applications for Bravo, Impedance, and HRM

It is important to emphasize that no controlled outcome studies have evaluated these technologies' role in managing GERD or other esophageal disorders. In the absence of clinical outcomes data, the practical aspects of each technology must be considered. Bravo offers obvious advantages compared with catheter-based pH monitoring. As a result, it has become widely accepted in academic and community practices. A limitation of the Bravo technique is its inability to detect nonacidic reflux. The empiric treatment of reflux symptoms with a PPI is now standard practice in the primary care setting. As a result, most patients with reflux referred to a gastroenterologist are already on PPI therapy, and there is good evidence that this therapy suppresses acid production in most patients [13]. In the case of continued symptoms despite PPI therapy, evaluation for nonacidic reflux by impedance pH is important. This test can help ascertain whether the persistent symptoms are due to ongoing reflux (acidic or nonacidic) and can identify patients in whom symptoms are not reflux-related and thus require evaluation for other pathology. However, as the Bravo technique obviates the need for a catheter and enables prolonged monitoring, it should be the preferred approach when the clinician requires information only about acidic reflux. An example of this situation is the patient without even partial symptom relief on empiric PPI therapy, in whom the pretest probability of an association between reflux and symptoms is very low [18]. In this setting, a negative pH test off therapy can direct the diagnostic evaluation toward other nonreflux etiologies while allowing discontinuation of the PPI.

Impedance manometry provides bolus transit assessment in addition to manometric data. It is hoped that this technique can further clarify the clinical significance of nonachalasia motility disorders diagnosed by manometry. HRM may also enhance the evaluation of esophageal dysmotility. The closely spaced sensors permit the accurate measurement of segmental esophageal body pressures and esophageal sphincter pressures and movement. The LES is more easily identified without the need for a pull-through, also enabling more accurate placement of a pH sensor. It is unknown if HRM can predict bolus transit with the same accuracy as impedance manometry. If it can, it may become the dominant technology used to evaluate esophageal motility. Catheters capable of performing HRM combined with impedance may become available in the future.

Conclusions

The perfect test to evaluate GERD and esophageal motility disorders does not exist, so the clinician must carefully consider the advantages and limitations of each technology. Bravo wireless pH monitoring, impedance-pH monitoring, HRM, and impedance manometry all provide obvious practical advantages compared with the standard methods of pH and manometric testing. As a result, these new technologies are becoming established in clinical practice. The clinical indications for these procedures and their role in managing esophageal disease await further elucidation.

Disclosures

Dr. Vela has served on the speakers' bureau for AstraZeneca Pharmaceuticals. No further potential conflicts of interest relevant to this article were reported.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Jamieson JR, Stein HJ, DeMeester TR, et al.: **Ambulatory 24-h esophageal pH monitoring: normal values, optimal thresholds, specificity, sensitivity, and reproducibility.** *Am J Gastroenterol* 1992, **87:**1102–1111.
2. Richter JE, Bradley LA, DeMeester TR, Wu WC: **Normal 24-hr ambulatory esophageal pH values. Influence of study center, pH electrode, age, and gender.** *Dig Dis Sci* 1992, **37:**849–856.
3. Schlesinger PK, Donahue PE, Schmid B, et al.: **Limitations of 24-hour intraesophageal pH monitoring in the hospital setting.** *Gastroenterology* 1985, **894:**797–804.
4. Fass R, Hell R, Sampliner RE, et al.: **Effect of ambulatory 24-h esophageal pH monitoring on reflux-provoking activities.** *Dig Dis Sci* 1999, **44:**2263–2269.
5. Mearin F, Balboa A, Dot J, et al.: **How standard is a standard day during a standard ambulatory 24-h esophageal pH monitoring?** *Scand J Gastroenterol* 1998, **33:**583–585.
6. Aksglaede K, Funch-Jensen P, Thommessen P: **Intra-esophageal pH probe movement during eating and talking. A videoradiographic study.** *Acta Radiol* 2003, **44:**131–135.
7. Pouderoux P, Lin S, Kahrilas PJ: **Timing, propagation, coordination, and effect of esophageal shortening during peristalsis.** *Gastroenterology* 1997, **112:**1147–1154.
8. Anngiansah A, Sumboonnanonda K, Wang J, et al.: **Significantly reduced acid detection at 10 centimeters compared to 5 centimeters above the lower esophageal sphincter in patients with acid reflux.** *Am J Gastroenterol* 1993, **88:**842–846.
9. Agrawal A, Tutuian R, Hila A, et al.: **Ingestion of acidic foods mimics gastroesophageal reflux during pH monitoring.** *Dig Dis Sci* 2005, **50:**1916–1920.
10.• Hila A, Agrawal A, Castell DO: **Combined multichannel intraluminal impedance and pH esophageal testing compared to pH alone for diagnosis both acid and weakly acidic gastroesophageal reflux.** *Clin Gastroenterol Hepatol* 2007, **5:**172–177.

This study demonstrated that swallowing acidic material can mimic reflux and lead to overdiagnosis of GERD. Impedance pH is capable of distinguishing acidic reflux from acidic food swallows.

11. Pandolfino JE, Zhang Q, Schreiner MA, et al.: **Acid reflux event detection using the Bravo wireless vs the Slimline catheter pH systems: why are the numbers so different?** *Gut* 2005, **54:**1687–1692.
12. Pandolfino JE, Ghosh S, Zhang Q, et al.: **Slimline vs glass pH electrodes: what degree of accuracy should we expect?** *Aliment Pharmacol Ther* 2006, **15:**331–340.
13. Wenner J, Jonsson F, Johansson J, Oberg S: **Wireless esophageal pH monitoring is better tolerated than the catheter-based technique: results from a randomized cross-over trial.** *Am J Gastroenterol* 2007, **102:**239–245.
14. Croffie JM, Fitzgerald JF, Molleston JP, et al.: **Accuracy and tolerability of the Bravo catheter-free pH capsule in patients between the ages of 4 and 18 years.** *J Pediatr Gastroenterol Nutr* 2007, **45:**559–563.
15. Ward EM, Devault KR, Bouras EP, et al.: **Successful oesophageal pH monitoring with a catheter-free system.** *Aliment Pharmacol Ther* 2004, **19:**449–454.
16.•• Hirano I, Zhang Q, Pandolfino JE, et al.: **Four-day Bravo pH capsule monitoring with and without proton pump inhibitor therapy.** *Clin Gastroenterol Hepatol* 2005, **3:**1083–1088.

Demonstrated that the Bravo system could be used for prolonged monitoring (4 days); this longer duration of monitoring allows for combined testing on and off therapy.

17. Pandolfino JE, Bianchi LK, Lee TJ, et al.: **Esophagogastric junction morphology predicts susceptibility to exercise-induced reflux.** *Am J Gastroenterol* 2004, **99:**1430–1436.
18. Hirano I: **Review article: modern technology in the diagnosis of gastro-oesophageal reflux disease—Bilitec, intraluminal impedance and Bravo capsule pH monitoring.** *Aliment Pharmacol Ther* 2006, **23(Suppl 1):**12–24.
19. Pandolfino JE, Richter JE, Ours T, et al.: **Ambulatory esophageal pH monitoring using a wireless system.** *Am J Gastroenterol* 2003, **98:**740–749.
20. Suzuki T, Yamaguchi T, Odaka T, et al.: **Four-day continuous gastric pH monitoring following anti-acid secretory drug administration: cross-over test to assess the early effects.** *Aliment Pharmacol Ther* 2008, **27:**66–71.
21. Iqbal A, Lee YK, Vitamvas M, Oleynikov D: **48-hour pH monitoring increases the risk of false positive studies when the capsule is prematurely passed.** *J Gastrointest Surg* 2007, **11:**638–641.
22. Lee YC, Wang HP, Chiu HM, et al.: **Patients with functional heartburn are more likely to report retrosternal discomfort during wireless pH monitoring.** *Gastrointest Endosc* 2005, **62:**834–841.
23. des Varannes SB, Mion F, Ducrotte P, et al.: **Simultaneous recordings of oesophageal acid exposure with conventional pH monitoring and a wireless system (Bravo).** *Gut* 2005, **54:**1682–1686.
24. Silny J: **Intraluminal multiple electric impedance procedure for measurement of gastrointestinal motility.** *J Gastrointest Motil* 1991, **3:**151–162.
25. Sifrim D, Castell D, Dent J, et al.: **Gastro-oesophageal reflux monitoring: reflux and consensus report on detection and definitions of acid, non-acid, and gas reflux.** *Gut* 2004, **53:**1024–1031.
26. Bredenoord AJ, Weusten BL, Timmer R, Smout AJ: **Reproducibility of multichannel intraluminal electrical impedance monitoring of gastroesophageal reflux.** *Am J Gastroenterol* 2005, **100:**265–269.
27. Shay S, Tutuian R, Sifrim D, et al.: **Twenty-four hour ambulatory simultaneous impedance and pH monitoring: a multicenter report of normal values from 60 healthy volunteers.** *Am J Gastroenterol* 2004, **99:**1037–1043.
28. Zerbib F, des Varannes SB, Roman S, et al.: **Normal values and day-to-day variability of 24-h ambulatory oesophageal impedance-pH monitoring in a Belgian-French cohort of healthy subjects.** *Aliment Pharmacol Ther* 2005, **22:**1011–1021.
29. Zentilin P, Liritano E, Dulbecco P, et al.: **Normal volumes of 24-h ambulatory intraluminal impedance combined with pH-metry in subjects eating a Mediterranean diet.** *Dig Liver Dis* 2006, **38:**226–232.
30. Vela MF, Camacho-Lobato L, Srinivasan R, et al.: **Intraesophageal impedance and pH measurement of acid and non-acid reflux: effect of omeprazole.** *Gastroenterology* 2001, **96:**647–655.

31. Mainie I, Tutuian R, Shay S, et al.: **Acid and non-acid reflux in patients with persistent symptoms despite acid suppressive therapy: a multicenter study using combined ambulatory impedance-pH monitoring.** *Gut* 2006, **55:**1398–1402.
32. Zerbib F, Roman S, Ropert A, et al.: **Esophageal pH-impedance monitoring and symptom analysis in GERD: a study in patients off and on therapy.** *Am J Gastroenterol* 2006, **101:**1956–1963.
33. Vela MF, Tutuian R, Katz PO, et al.: **Baclofen decreases acid and non-acid post-prandial gastro-oesophageal reflux measured by combined multichannel intraluminal impedance and pH.** *Aliment Pharmacol Ther* 2003, **17:**243–251.
34.• Mainie I, Tutuian R, Agrawal A, et al.: **Combined multichannel intraluminal impedance-pH monitoring to select patients with persistent gastro-oesophageal reflux for laparoscopic Nissen fundoplication.** *Br J Surg* 2006, **93:**1483–1487.

Provided some initial subjective outcome data for patients selected by MII-pH for Nissen fundoplication.

35. Tutuian R, Mainie I, Agrawal A, et al.: **Nonacid reflux in patients with chronic cough on acid-suppressive therapy.** *Chest* 2006, **130:**386–391.
36. Bredenoord AJ, Weusten BL, Sifrim D, et al.: **Aerophagia, gastric, and supragastric belching: a study using intraluminal electrical impedance monitoring.** *Gut* 2004, **53:**1561–1565.
37. Richter JE, Wu WC, Johns DN, et al.: **Esophageal manometry in 95 healthy adult volunteers: variability of pressure with age and frequency of 'abnormal' contractions.** *Dig Dis Sci* 1987, **32:**583–592.
38. Frieling T, Hermann S, Kuhlbusch R, et al.: **Comparison between intraluminal multiple electric impedance measurement and manometry in the human oesophagus.** *Neurogastroenterol Motil* 1996, **8:**45–50.
39. Reidel WL, Clouse RE: **Variation in clinical presentation of patients with esophageal contraction abnormalities.** *Dig Dis Sci* 1985, **30:**1065–1071.
40. Achem SR, Crittenden J, Kolts B, et al.: **Long-term clinical and manometric follow-up of patients with nonspecific esophageal motor disorders.** *Am J Gastroenterol* 1992, **87:**825–830.
41. Iman H, Shay S, Ali A, et al.: **Bolus transit patterns in healthy subjects: a study using simultaneous impedance monitoring, videoesophagram, and esophageal manometry.** *Am J Physiol Gastrointest Liver Physiol* 2005, **288:**1000–1006.
42. Tutuian R, Vela MF, Balaji NS: **Esophageal function testing with combined multichannel intraluminal impedance and manometry: multicenter study in healthy volunteers.** *Clin Gastroenterol Hepatol* 2003, **1:**174–182.
43. Tutuian R, Castell DO: **Combined multichannel intraluminal impedance and manometry clarifies esophageal function abnormalities: study in 350 patients.** *Am J Gastroenterol* 2004, **99:**1011–1019.
44. Conchillo JM, Nguyen NQ, Samson M, et al.: **Multichannel intraluminal impedance monitoring in the evaluation of patients with non-obstructive dysphagia.** *Am J Gastroenterol* 2005, **100:**2624–2632.
45. Tutuian R, Mainie I, Agrawal A, et al.: **Symptom and function heterogenicity among patients with distal esophageal spasm: studies using combined impedance-manometry.** *Am J Gastroenterol* 2006, **101:**464–469.
46. Agrawal A, Hila A, Tutuian R, et al.: **Bethanechol improves smooth muscle function in patients with severe ineffective esophageal motility.** *J Clin Gastroenterol* 2007, **41:**366–370.
47. Tutuian R, Castell DO: **Rumination documented by using multichannel intraluminal impedance and manometry.** *Clin Gastroenterol Hepatol* 2004, **2:**340–343.
48.• Ghosh SK, Pandolfino JE, Zhang Q, et al.: **Quantifying esophageal peristalsis with high-resolution manometry: a study of 75 asymptomatic volunteers.** *Am J Physiol Gastrointest Liver Physiol* 2006, **290:**G988–G997.

Provided an initial approach to evaluate esophageal motility with HRM.

49. Dent J: **Approaches to driving the evolving understanding of lower oesophageal sphincter mechanical function.** *J Smooth Muscle Res* 2007, **43:**1–14.
50. Pandolfino JE, Kahrilas PJ: **American Gastroenterological Association medical position statement: clinical use of esophageal manometry.** *Gastroenterology* 2005, **128:**207–208.
51. Fox MR, Bredenoord AJ: **Oesophageal high-resolution manometry—moving from research into clinical practice.** *Gut* 2008, **57:**405–423.
52. Ghosh SK, Pandolfino JE, Zhang Q, et al.: **Deglutitive upper esophageal sphincter relaxation: a study of 75 volunteer subjects using solid-state high-resolution manometry.** *Am J Physiol Gastrointest Liver Physiol* 2006, **291:**G525–G531.
53. Pandolfino JE, Ghosh SK, Zhang Q, et al.: **Quantifying EGJ morphology and relaxation with high-resolution manometry: a study of 75 asymptomatic volunteers.** *Am J Physiol Gastrointest Liver Physiol* 2006, **290:**G1033–G1040.
54. Fox MR, Hebbard G, Janiak P, et al.: **High-resolution manometry predicts the success of oesophageal bolus transport and identifies clinically important abnormalities not detected by conventional manometry.** *Neurogastroenterol Motil* 2004, **16:**533–542.
55. Clouse RE, Staiano A, Alrakawi A, et al.: **Application of topographical methods to clinical manometry.** *Am J Gastroenterol* 2000, **95:**2677–2679.
56. Pandolfino JE, Ghosh SK, Rice J, et al.: **Classifying esophageal motility by pressure topography characteristics: a study of 400 patients and 75 controls.** *Am J Gastroenterol* 2008, **103:**27–37.