TECHNICAL REVIEW

Esophageal-reflux monitoring (CME)

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It is neither practical nor necessary to initiate a diagnostic evaluation of every patient with symptoms of GERD. Management, by and large, is focused on empiric therapy, with lifestyle modification and medication if the clinical presentation is compatible with uncomplicated GERD symptoms. Further testing is only required when complications are suspected, patients fail therapy, or the diagnosis must be confirmed before a change in treatment strategy.

Documenting the role of reflux in GERD symptoms, however, is not an easy task. Certainly, evidence of esophagitis on endoscopy is highly specific; however, the majority of patients with GERD will have a normal endoscopy. Therefore, in most cases, our diagnostic focus must be redirected to concentrate on documenting abnormal gastroesophageal reflux. This endeavor is also not straightforward, because there currently is no criterion standard for defining abnormal reflux. The diagnosis of GERD would be simple if the causative factor, gastric refluxate, were easily measured and a reliable threshold for symptom generation and complications were known. Unfortunately, this is not the case, and our current armamentarium consists of techniques that are limited in their ability in that they only provide surrogate information that reflux is occurring.

Ambulatory pH monitoring provides evidence for reflux by measuring periods when the pH drops below a certain threshold, whereas combined multichannel intraluminal impedance and pH (MII-pH) detects reflux by measuring the direction and extent of changes in impedance along a catheter and qualifies reflux as acid or nonacid based upon the concomitant pH changes. Although these techniques are helpful in clinical practice, it is important to understand their limitations. It must also be kept in mind that, currently, there is no consensus regarding the optimal technique or methodology, because there are no well-done randomized controlled trials that compare pH alone with combined pH and impedance in predicting clinical outcomes. With these limitations, the focus of this technical review on ambulatory pH monitoring will be concentrated on reviewing 3 specific issues: (1) the appropriate equipment and methodology for clinical studies, (2) the accuracy and quality of the information obtained, and (3) how ambulatory reflux monitoring can help guide clinical practice. Our ultimate goal is to familiarize practicing gastroenterologists with the current techniques available and also to highlight how these tools can improve management in the context of their imperfections.

REVIEW METHODOLOGY

Key words, including ‘‘pH monitoring,’’ ‘‘pH electrodes,’’ ’’reflux testing,’’ ‘‘impedance,’’ ‘‘Bravo,’’ ‘‘esophageal acid exposure,’’ and ‘‘nonacid reflux’’ were used to search the PubMed database through February 2008, with limits set to human trials published in English. A manual search from relevant articles was also performed for each specific section of the review. Data were classified according to the guidelines of the U.S. Preventive Services Task Force, with 5 classifications (A, B, C, D, and insufficient) used to determine the strength of evidence and magnitude of net benefit for each recommendation (Appendix 1). The quality of evidence is graded separately by using 3 classifications (good, fair, and poor). There was a paucity of large-scale randomized controlled data that compared various modalities and measurement parameters; thus, most of the evidence is classified as fair.

TECHNICAL ASPECTS

Reflux monitoring can be performed by using a variety of devices, and, currently, there is no uniform consensus regarding the optimal system. These reflux monitoring systems differ in many ways and can be categorized based on the following characteristics: (1) pH-electrode type, (2)

Abbreviations: ISFET, ion-sensitive field effect; LES, lower-esophageal sphincter; MII, multichannel intraluminal impedance; MII-pH, combined multichannel intraluminal impedance and pH; PPI, proton pump inhibitor; SAP, symptom association probability; SCJ, squamocolumnar junction; SI, symptom index.

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spacing and position of the pH electrode, (3) the need for an indwelling transnasal catheter, and (4) incorporation of MII to enable measurement of nonacid reflux. In addition, there is also no consensus regarding the optimal technique in terms of duration of pH monitoring, position of the pH electrodes within the upper-GI tract, and how to instruct patients regarding meals and activities. Given that these issues could potentially alter accuracy and reproducibility, this section will review these variables and their potential impact on performance of reflux monitoring in clinical practice (Table 1).

pH monitoring electrodes

pH monitoring systems use 2 electrodes that function as a galvanic cell. One electrode acts as a reference electrode with a constant potential, and the other acts as an indicator electrode whose potential is sensitive to changes in hydrogen ion concentration. The electrodes are typically connected to a device that can translate the potential difference between the 2 electrodes into a concentration gradient of hydrogen ions (pH). Several types of pH electrodes are available for ambulatory esophageal pH recording: (1) antimony monocrystalline electrodes, (2) combined glass electrodes (built-in reference electrode), and (3) ion-sensitive field effect (ISFET). Glass electrodes are generally the most accurate of the electrodes available[1]; however, they are limited by a restriction to a single sensor and require careful handling. Although antimony pH electrodes are inferior to glass in terms of sensitivity, drift, temperature effect, and response rate, they are cheaper and smaller, which makes them more suited for ambulatory clinical studies. The lack of accuracy and significant hysteresis make antimony electrodes unsuitable for research studies and intragastric pH measurement.[2,3] ISFET electrodes are now becoming clinically available in various systems, and these catheters may soon replace antimony as the electrode of choice in clinical studies. They combine the accuracy and stability of glass catheters with the flexibility and size of antimony-electrode catheters and, thus, may represent the best of both worlds.[4] Regardless, all of these electrodes can be used satisfactorily for clinical esophageal pH monitoring.[3,5,6] (grade B, fair)

Wireless pH electrodes

The Bravo pH monitoring system (Medtronic, Minneapolis, Minn) uses a radiotelemetry pH sensing capsule that is attached to the mucosa of the distal esophagus. The oblong capsule is 25 mm in length and has an antimony pH electrode and a reference electrode located at its distal tip, with an internal battery and transmitter located within the epoxy covered capsule. The capsule simultaneously measures pH and transmits data via a radiofrequency signal to a pager-sized receiver clipped onto the patient's belt. The performance of the catheter-free wireless pH electrode in measuring esophageal-acid exposure has been validated against catheter-based antimony pH electrode systems in simultaneous controlled trials.[7-9]

TABLE 1. Summary of technical aspects of pH monitoring

pH electrode type

- All pH electrodes are adequate for clinical ambulatory studies that assess distal esophageal-acid exposure.
- The accuracy of the Bravo wireless antimony pH electrode has been validated.

Position and placement of the electrode

- Distal esophageal-acid exposure should be measured 5 cm above the proximal aspect of the LES or 6 cm above the SCJ.
  - Catheter-based systems (pH alone or combined pH and impedance) should use manometric assessment of the proximal aspect of the LES for placement.
  - Transoral wireless capsule placement can be placed with both endoscopic measurements (6 cm above the SCJ) and transnasal manometric landmarks (9 cm above the proximal aspect of the LES).
- Proximal esophageal pH measurement is technically limited and not helpful for routine clinical use.
- Gastric pH should be measured 7-10 cm below the LES; although gastric pH monitoring can provide information regarding the efficacy of acid-suppressive medications or suggest poor compliance, its clinical significance is not clear.

Duration of studies

- Ambulatory pH studies should be performed with a goal of 24 h.
- Extending ambulatory pH monitoring beyond 24 h improves sensitivity of reflux correlation and can be used to perform studies while "off" and while "on" medical therapy.

Diet and activity

- Diet and activity should not be limited during the study period; however, a careful diary must be kept to reduce false positives that may occur with ingestion of acidic foods in-between meals.
- Monitoring with impedance-pH enables distinction between swallowed acidic material and reflux.

The main advantages of this system are the lack of a catheter and that its position can be fixed. Tolerability has been shown to be better with the wireless system when compared with catheter-based pH monitoring in both randomized[10] and uncontrolled comparison studies.[11] However, there are some drawbacks to the wireless system that deserve mention. Accuracy of a single sensor may overestimate reflux by including swallow events, and early detachment can also alter results and may require repeated placement. Furthermore, additional endoscopic procedures may be required for patients who report severe chest pain (5%), odynophagia, or failure of the capsule to detach.[11-13] Thus, wireless pH monitoring