Combined MII and pH (MII-pH)

Gastroesophageal reflux (GER) testing using combined MII-pH is a technique approved by the FDA in July 2002. MII can detect bolus volume presence independent of the pH of the refluxate. Thus, combined MII-pH represents a shift in the reflux-testing paradigm. GER of all types is detected by MII and is only characterized as acid or non-acid by its pH. Simultaneous measurements of manometry and impedance have been used to validate reflux detection by MII when reflux was identified by the presence of a manometrically defined “common cavity” (1).

The ability of combined MII-pH to detect and characterize non-acid GER represents an important advance for clinical testing of non-acid reflux (2). It is not dependent on presence of bilirubin in the refluxate (a limitation of the Bilitec technique) (3), is not affected by gastric emptying time of an ingested material (a limitation of scintigraphic methods [4,5]) and does not require stationary-supine postures (a limitation of manometric measurements detecting common cavities [1]). Although non-acid reflux may have a limited role in development of erosive lesions within the esophagus it is quite likely to be clinically important in patients with early post-prandial symptoms, patients with persistent symptoms on acid suppressive therapy, patients with atypical (supraesophageal) symptoms and in infants. The interest for non-acid GER testing in infants is sustained by the fact that the acid output is decreased compared with adults and the feeding patterns (drinking milk or formula every 2–3 hours) maintain long periods of time with the stomach full and with buffering of intragastric acid concentrations (6,7,8).

Combined MII-pH classifies GER by: (1) content of reflux into liquid, gas and mixed reflux events and (2) pH characteristics of the content into acid, non-acid, minor acid and acid re-reflux. Using multiple impedance measuring sites MII can also identify the height of the refluxate (i.e. most proximal impedance...
Channel in which GER impedance changes are noted). An acid MII-GER reflux event is a MII-detected reflux event in which a drop of pH from above 4.0 to below 4.0 is noted (Figure 1a). Non-acid reflux is a MII-detected reflux event during which the pH stays above 4.0 and doesn’t drop more than 1 pH unit (B). Minor acid reflux is a MII-detected reflux event during which pH stays above 4.0 but the pH drops more than 1 unit (C). An acid re-reflux event is another type of acid reflux that occurs while intra-esophageal pH is already below 4.0. It is detected by MII and the pH may or may not go further below 4.0 (Figure 1d).

Currently available systems using combined MII-pH employ impedance rings mounted on pH catheters (Sandhill Scientific Inc., Highlands Ranch, CO). The dimensions of combined MII-pH catheters are similar to those of traditional pH catheters (2.1 mm diameter)
and therefore do not change patient comfort compared to traditional pH testing. Different MII-pH catheters can be used depending on the clinical scenario (Figure 2). The “classic” 6MII-1pH assembly will readily detect acid and non-acid reflux. Normative data for this design have been established in a multicenter study (see below). A modified design 6MII-2pH (esophageal + gastric) catheter for use in patients on therapy will concomitantly assess intragastric acid control on therapy. Studies establishing normative data on therapy are currently being conducted. A bifurcated adjustable catheter (4MII-1pH + 2MII-1pH) may be preferred to evaluate pharyngeal reflux concomitantly with distal esophageal reflux. Normative data for this technique have yet to be established although our previous experience with bifurcated pH probes reveals that acid reflux rarely reaches the pharynx in normal volunteers (9).

Normative data for the 6MII-1pH assembly have been established in a multicenter study involving Graduate Hospital (Philadelphia), Cleveland Clinic, Mayo Clinic (Rochester), University of Southern California (Los Angeles) and the Catholic University in Leuven, Belgium. Sixty healthy adult volunteers underwent 24-h ambulatory MII-pH studies. This study indicates that normal volunteers have less non-acid reflux compared to acid-reflux, MII-detected acid refluxate presence time (percent time) is significantly less than percent time intraesophageal pH <4 and minor amounts and number of nonacid reflux events

![Figure 2](image)

**Figure 2.** Placement of various combined MII-pH catheters: (A) “classic” 6MII-1pH probe placed relative to LES, (B) 6MII-2pH (esophageal and gastric pH) probe placement relative to LES and (C) bifurcated 4MII-1pH + 2MII-1pH probe placement relative to LES and UES.
occur at nighttime in the supine position. Non-acid GER occurred predominantly in the 2-hour post-prandial periods. Furthermore 37% of distal (5 cm above LES) reflux episodes, either acid or non-acid, reach the proximal (15 cm above LES) esophagus in normal volunteers. In the same study it was also observed that acid clearance (pH) time is different than acid bolus (MII) clearance time suggesting that neutralizing acid pH in the esophagus depends on other mechanisms (i.e. swallowing of saliva, mucosal characteristics, etc.) than only refluxate appearance and disappearance from the esophageal lumen.

Some of the advantages of combined MII-pH over traditional pH testing are supported by the following reports. Studying the effects of omeprazole on 2-h postprandial gastroesophageal reflux Vela MF, et al (10) found that although the proton pump inhibitor dramatically reduced the number of acid GER episodes the total number of MII-detected GER events did not change but became predominantly non-acid. This observation underscores the effect of acid suppressive therapy to shift the balance of acid vs. non-acid reflux events without influencing the total number of GER events in the postprandial individual (Figure 3A). Studying the (continued on page 27)
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Figure 5. Patient in which persistent chest pain episodes were not associated with any type of reflux. The antegrade changes in impedance are produced by swallows.

Figure 6. Patient with chest pain preceded by gas GER. Gas GER episodes are identified by rapid increase in impedance to above 5000 Ohm in at least two channels.

effects of baclofen, a GABA antagonist that decreases the frequency of transient lower esophageal sphincter relaxations (TLESR), Vela MF, et al (11) found that this medication reduced the number of all GER episodes in a 2-h postprandial period; both acid and non-acid GER. These studies suggest that combined MII-pH should be the preferred test to document reduction of gastroesophageal reflux (Figure 3B).

Using combined MII-pH in clinical practice helps clarify symptoms attributed to GERD. To date using combined MII-pH in our motility laboratory we have identified different clinical applications, particularly related to patients with persistent symptoms on PPI therapy. One such scenario involves non-acid reflux as a cause of persistent regurgitation in patients being considered for surgery (Figure 4). In other patients we have identified gas reflux (belch) preceding the vast majority of chest pain episodes leading to treatment with simethicone (Figure 5). An increased number of non-acid GER episodes were identified in an 8-month old infant with subglotic stenosis that was subsequently referred for Nissen fundoplication. In yet another patient we were able to identify that none of the persistent chest pain episodes on acid suppressive therapy were related to any form of GER, clarifying for the patient that the cause of her symptoms was not related to GERD (Figure 6).

Current recommendations for GERD testing suggest an initial empiric trial of PPI’s in patients with symptoms suggestive of GERD (12). If patients respond to this trial the diagnosis is established and continuation of acid suppressive therapy is recommended. Before MII-pH became available patients not responding to the PPI trial would often undergo ambulatory pH testing either while continuing therapy or after at least a 7 days “wash-out” period to evaluate if their symptoms were associated with GER. This approach left the question of possible non-acid GER symptoms unresolved. Since combined MII-pH can identify both acid and non-acid GER we propose using MII-pH testing on therapy at this
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Figure 7. Proposed GERD diagnostic algorithm.

In summary combined MII-pH is a promising technique using a new principle for gastroesophageal reflux testing to identify liquid, gas, and mixed reflux and categorize it into acid and non-acid. By its ability to better discriminate GER and the association of symptoms with acid and non-acid GER combined MII-pH should become a useful tool in evaluating patients with persistent symptoms on acid suppressive therapy, patients with atypical symptoms and possible GER in infants.

References