

# Impedance pH Guided Approach to Proton Pump Inhibitor-refractory Non-erosive Reflux Disease

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**Article:** Diagnostic utility of impedance-pH monitoring in refractory non-erosive reflux disease  
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Patients with persistent symptoms despite proton pump inhibitor (PPI) make a therapeutic challenge for the clinical gastroenterologist. There are multiple mechanisms causing PPI failure; proper PPI dosing, patients compliance, functional heartburn (FH) and esophageal hypersensitivity, weakly acidic or alkaline reflux, residual acid reflux, bile acid reflux, nocturnal acid breakthrough and so on.<sup>1</sup> Most patients with gastroesophageal reflux disease who do not respond to a PPI have either non-erosive reflux disease (NERD) or FH.<sup>2</sup>

Combined multichannel intraluminal impedance (MII)-pH helps clarify the association of symptoms with reflux events in patients who do not respond to PPIs. It can determine if there is ongoing pathological acid or non-acid reflux despite the PPI.<sup>3,4</sup> Combined MII-pH has demonstrated that about one-half of patients with persistent symptoms on therapy do not have a temporal correlation between their symptoms and any type of reflux. In addition, about 40% of patients with persistent symptoms on PPI

therapy have a temporal association between their symptoms and reflux, primarily of the non-acid type.<sup>2</sup>

Using impedance pH metry, Savarino et al<sup>5</sup> classified NERD patients into 3 groups; pH positive NERD, hypersensitive esophagus and functional heartburn.<sup>5</sup> Those with symptomatic non-acid reflux were classified as having a hypersensitive esophagus. This means that patients who earlier classified as FH with conventional pH testing were now reclassified as hypersensitive esophagus. In one study, the number of patients in the FH subgroup decreased from 43% to 26%.<sup>5</sup> The results of impedance pH testing can thus guide to the next therapeutic step in management of reflux.

For patients with symptomatic non-acid reflux, either pathological NERD or hypersensitive esophagus, the therapeutic target is to decrease reflux episodes or esophageal hypersensitivity. Baclofen which reduces the transient lower esophageal sphincter relaxation, or a pain such as antidepressant can be tried. Anti-re-

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flux surgery can be considered as another treatment option if medical therapy is not effective and positive symptom correlation is clearly defined based on the impedance pH results. Based on the results of MII-pH monitoring, one study found that most patients with documented positive symptom association who underwent anti-reflux surgery, reported no symptoms during a median follow-up time of 14 months after surgery. These results indicate that MII-pH monitoring on therapy helps identify patients with persistent reflux symptoms who may benefit from anti-reflux surgery.<sup>6</sup>

The treatment options for the FH may be different. FH represents a heterogeneous group of patients with different pathophysiological mechanisms. Although a subset of patients with esophageal hypersensitivity may respond to acid suppressive therapy, this disorder is similar to the visceral hyperalgesia described in a variety of other functional gastrointestinal disorders including functional dyspepsia and irritable bowel syndrome.<sup>7</sup>

The current issue of the journal has published a prospective study<sup>8</sup> using MII-pH testing. Sixty symptomatic NERD patients refractory to PPI were evaluated. Approximately 60% of these patients had positive reflux-symptom association, primarily due to nonacid reflux. Nearly half of NERD patients on PPI were further sub-divided into FH and hypersensitive esophagus equally. The strength of this study was its prospective design. As expected, the results are not significantly different from previous studies. As mentioned in their study, cut-off reference values in classifying impedance results are still controversial. It can challenge the clinical implication of sub-classification of NERD.

In summary, combined MII-pH can help guide stepwise diagnostic approach to the patients with gastroesophageal reflux

disease refractory to PPIs. However, whether the improved understanding of symptoms to reflux and non-reflux events translates into better treatment outcomes is still controversial. The approach to the pathophysiology of heterogeneous subgroups of NERD will help in making better therapeutic strategy.

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