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Assessing Old and New Diagnostic Tests for Gastroesophageal Reflux Disease

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A detailed critique of objective measurements of gastroesophageal reflux disease (GERD) would improve management of patients suspecting of having reflux, leading to rational selection of treatment and better outcomes. Many diagnostic tests for GERD have been developed over the past decades. We analyze their development, positive- and negative-predictive values, and ability to predict response to treatment. These features are important for development of medical, surgical, and endoscopic therapies for GERD. We discuss the value of available diagnostic tests and review their role in management of patients with persistent reflux symptoms despite adequate medical or surgical treatment. This is becoming a significant health economic problem, due to the widespread use of proton pump inhibitors. GERD is believed to cause nonesophageal symptoms, such as those provoked by ear, nose, throat, or respiratory disorders. We analyze the value of GERD diagnostic tests in evaluation of these troublesome, nonesophageal symptoms.

Keywords: GERD; Mucosal Impedance; Reflux Monitoring.

Gastroesophageal reflux disease (GERD) is a common condition affecting up to 20% of the Western world.[1] It is a challenge to identify patients with GERD, because of suboptimal performance of diagnosis tests. Patients suspected of having GERD are first tested for a response to acid-suppressive therapy, often with a proton pump inhibitor (PPI). This approach, known as the PPI trial, is used based on symptoms believed to be caused by GERD. Heartburn and regurgitation are the 2 cardinal symptoms of GERD, although the disease can cause other symptoms, such as chest pain or pulmonary, ear, nose, or throat symptoms.[2]

However, neither patients' symptoms nor response to PPI are strongly associated with a final diagnosis of GERD. Heartburn and regurgitation have suboptimal sensitivity (30%–76%) and specificity (62%–96%) in identification of patients with GERD.[3,4] GERD is found in only 54% of patients with a dominant symptom of heartburn and in only 29% of patients with a predominant symptom of regurgitation.[5] This is likely due to the significant overlap among GERD, gastroparesis, functional dyspepsia, and eosinophilic esophagitis, which all cause symptoms of heartburn and regurgitation. Symptoms alone are therefore not adequately sensitive or specific to guide therapeutic strategies. Alternatively, response or lack of response to an initial trial of PPI therapy does not rule in or out GERD as the possible etiology of continued symptoms.

Diagnostic tests for GERD are used in presurgical or endoscopic interventions (to ensure that patients have GERD) and for patients with continued symptoms despite an initial PPI trial. Continued symptoms with PPI use is the most common and the most challenging indication for a diagnosis of GERD. Given the complexity of patient presentations and technical advances in the field of GERD research, it is important yet challenging to determine whether reflux contributes to symptoms in patients who do not respond to aggressive acid suppression. Optimizing strategies to improve appropriate GERD diagnosis is critical to improve patient outcomes and reduce unnecessary cost from suboptimal diagnostic testing and a greater understanding of the pathophysiology and treatment of GERD symptoms in the presence of normal esophageal acid exposure.

We review technical developments in tests in for GERD over the past decades (Figure 1), and analyze their ability to identify or exclude GERD and adequately predict response

Abbreviations used in this paper: **DGER, duodenogastroesophageal reflux; EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; MI, mucosal impedance; NBI, narrow-band imaging; NERD, nonerosive reflux disease; PPI, proton pump inhibitor; PSPW, postreflux swallow-induced peristaltic wave; SAP, symptom association probability; SI, symptom index.**

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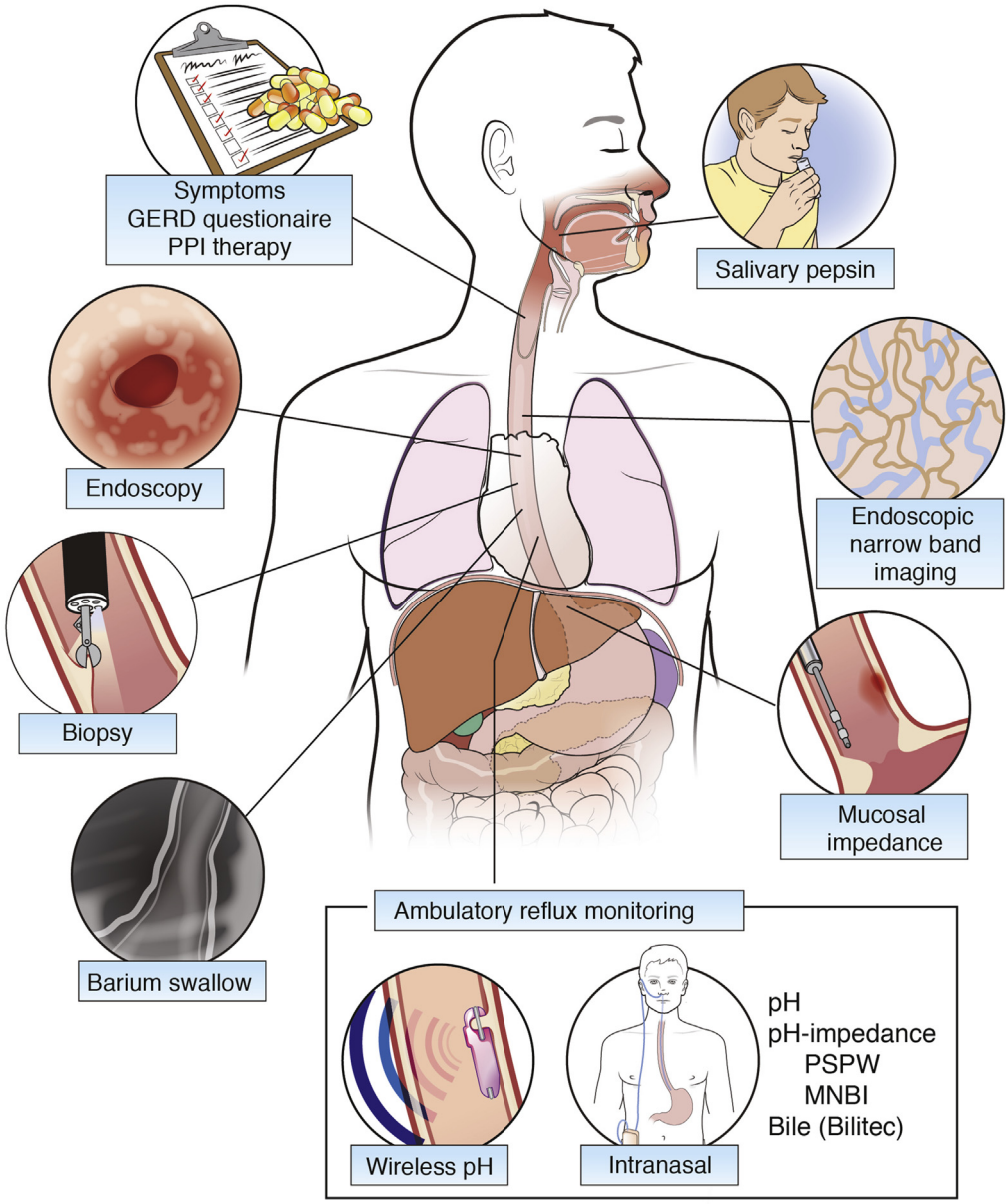

Figure 1. Diagnostic tests for GERD.

to treatment (Table 1). These abilities are important for development of medical (new acid blockers and antireflux drugs), surgical, and endoscopic therapies in GERD.

Endoscopy and Biopsies

In patients with symptoms of GERD, an early endoscopy should be considered if their symptoms provide evidence for complicated disease (ie, dysphagia, weight loss, hematemesis), eosinophilic esophagitis, infection, or pill-induced injury.[6] Failure to respond to appropriate antisecretory medical therapy should also prompt evaluation with esophagogastroduodenoscopy. Furthermore, endoscopy should be used to diagnose Barrett's esophagus in high-risk patients (white men with a high body mass index, 50 years or older, with chronic GERD symptoms).[7] Additionally, endoscopy is often performed as part of the preoperative evaluation of patients being considered for antireflux surgery or for the placement of wireless esophageal pH monitoring devices. GERD can be diagnosed with confidence when endoscopy reveals esophagitis, but endoscopy may be normal in approximately two-thirds of untreated patients with heartburn and regurgitation. There can be significant interobserver variations in mild esophagitis (Los Angeles Classification of GERD grade A). Therefore, many experts consider only grades B or higher as objective evidence of GERD.[8]

In patients with typical reflux symptoms, endoscopic findings may include esophagitis, strictures, Barrett's esophagus, and typical features of eosinophilic esophagitis (EoE). Endoscopy identifies these disorders with high levels of specificity.[9] However, endoscopy detects GERD with a low