

## Diagnosis and Treatment of Gastroesophageal Reflux Disease

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Gastroesophageal Reflux Disease (GERD) is one of the most common disorders in medical practice, which carries a risk of significant morbidity and potential mortality from resultant complications [1,2]. It has been estimated that as many as 21% to 60% of the US population have monthly symptoms attributable to this condition [3] and the average annual number of physician visits for GERD has been estimated to be 9,455,000 between 1998 and 2001 [4]. There are several studies that have evaluated the financial burden of GERD for patients and the impact of GERD on work productivity, and they conclude that the costs are substantial for patients and that GERD causes significant losses by reduced productivity both at work as well as during regular daily activities [5,6].

While many patients are self-diagnosed and self-managed and do not seek medical attention for their symptoms, others suffer from more severe disease with esophageal damage ranging from erosive - ulcerative esophagitis to Barrett's esophagus [7]. According to the American Gastroenterological Association (AGA) [8] position statement, there can be no standard definition of GERD because the threshold of distinction between physiologic reflux and reflux disease is ultimately arbitrary. Therefore, GERD is defined by consensus. The vast majority of authors [1] conclude that GERD must be defined as symptoms and possible complications that can be produced by the gastric content when it enters the esophagus and beyond (larynx, pharynx and oral cavity). The Montreal consensus, elaborated by a panel of world experts, has also been used frequently to define GERD [9]. The Montreal consensus defined GERD as "a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications." Symptoms are "troublesome" if they adversely affect an individual's wellbeing. Esophageal GERD syndromes are categorized as those that are symptom based and those that are defined by tissue injury, while the extraesophageal syndromes are classified as either established or assumed association with GERD, acknowledging that while the available evidence is sufficient to link these syndromes to reflux, it is insufficient to establish a causal relation [8,9].

There are several key points to keep in mind regarding the diagnosis and treatment of GERD.

1. The first key point regarding the diagnosis of GERD is the wide variety of symptoms that have been related to this condition, like heartburn, regurgitation, chest pain, dysphagia, chronic cough, asthma, chronic laryngitis, dyspepsia, bloating and epigastric pain. However, it is well known that these symptoms can be attributed to other conditions as well. It is recommended that patients with typical symptoms likely to be caused by reflux like heartburn and regurgitation should be treated empirically with proton pump inhibitors (PPIs). If the patient has symptoms that can very well be caused by other diseases, we should first evaluate this possibility before starting empiric therapy for GERD (e.g. chest pain, asthma) [9-11].
2. With respect to the complementary diagnostic tests, a large number of them are not necessary to diagnose GERD. In the

presence of typical GERD symptoms upper endoscopy with or without biopsy is not necessary, but it is recommended in the presence of alarm symptoms and in case of patients at high risk for complications. Barium radiographs or video fluoroscopy are not indicated for the diagnosis of GERD and are only recommended for the evaluation of dysphagia. Esophageal manometry is recommended for preoperative evaluation of selected patients. Ambulatory esophageal reflux monitoring is the only test that can reveal association of symptoms with episodes of reflux, reflux frequency and the presence of abnormal esophageal acid exposure, but it is only indicated when the diagnosis of GERD is in question, in case of refractory symptoms on PPI therapy and before considering surgical therapy on patients with non-erosive disease. Screening on *Helicobacter pylori* infection is not necessary because eradication is not required for treatment of GERD [12-18].

3. Regarding treatment, apart from the usual changes in lifestyles, it is accepted that the medication of choice are PPIs in an 8 weeks course and dosage modified depending on patient's symptoms. Several studies have demonstrated that on-demand therapy with PPIs is the most cost-effective method for non-erosive reflux disease. Randomized controlled trials have shown that PPIs are more effective than both H2RAs and placebo in controlling symptoms from erosive reflux disease (83% compared to 60% and 27%, respectively) over 4 to 8 week period. In addition to controlling symptoms and esophagitis, PPI therapy has been shown to normalize the impaired quality of life caused by GERD. However, patients on long-term PPI therapy should be re-evaluated periodically to determine the need and to weigh potential risks versus benefits of therapy [19-21]. There are currently seven available PPIs (omeprazole, lansoprazole, omeprazole-sodium bicarbonate, rabeprazole, pantoprazole, esomeprazole, and dexlansoprazole). Gralnek et al. [22] performed a meta-analysis that showed no significant difference in efficacy for symptom relief between the different PPIs.

Surgical treatment of GERD is an option in patients with long term therapy that respond to PPIs. Prior to surgery it is recommended to perform manometry and ambulatory pH monitoring in patients without erosive esophagitis. Surgical therapy performed by an experienced surgeon has been demonstrated to be as

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effective as medical therapy for selected patients [23,24]. On the short to medium term laparoscopic fundoplication surgery is more effective than medical management for the treatment of GERD, but surgery has the disadvantage of carrying some risks and long term benefits remains uncertain [25].

4. During the follow up of patients with GERD, PPI therapy has to be optimized, tailoring the dose of PPI according to the patient's symptoms. Moreover, possible changes in the symptoms of the patient may be alarm signs and an indication to perform tests as described above.
5. There are several signs and complaints that have been considered extraesophageal symptoms of GERD. Chronic cough, laryngitis and asthma are accepted to have an established association with reflux disease [26]. The problem is that extraesophageal symptoms are nonspecific and may be produced by multiple causes. Additionally, there are patients with possible extraesophageal symptoms but without signs of esophageal GERD, and in those cases the relationship remains uncertain. Given the nonspecific nature of the extraesophageal symptoms and the fact that diagnostic tests don't have sufficient sensitivity and specificity, empirical therapy with PPIs has become the common practice.

Laryngopharyngeal reflux (LPRD) should be suspected when clinical history and findings are suggestive. LPRD could be defined as retrograde reflux of gastric contents beyond the esophagus up to the laryngeal and pharyngeal level, but patients usually show no lesions when evaluated by upper digestive endoscopy. LPRD may be suspected when patients have conditions such as asthma, chronic cough, and laryngeal disorders including paroxysmal laryngospasm and laryngeal granuloma [27,28]. In these cases, the response to treatment with PPIs can give us the diagnosis.

Despite all attempts to find a gold standard test for GERD, the diagnosis of GERD is based on the symptomatology of the patient. If the patient has typical symptoms of GERD a presumptive diagnosis can be made and empirical treatment with PPIs can be started. This strategy saves many diagnostic tests that may be burdensome for our patients as well as society. Diagnosis and treatment of GERD should be driven and supported by the highest available evidence to result in cost-effective diagnostic and treatment algorithms. This aspect is the more important to keep health care affordable in this era of increasing costs of health care and economic difficult times.

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