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In search of reliability in the description of gastroesophageal reflux disease (GERD)

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Abstract

The prevalence of gastroesophageal reflux disease (GERD) in populations of Western countries is fairly high: around 15% of persons complain of weekly symptoms of GERD. The figure is lower in Asia, in the range of 3% to 6%; however, there is a worldwide increase in the prevalence of GERD. Reliability in the description of GERD has been explored in consensus workshops based on analysis of literature that followed the methodology of evidence-based medicine. This method applies to description of esophageal and extraesophageal symptoms and complications, pH and impedance monitoring in the esophagus, grading of erosive esophagitis, and assessment of the size of a segment of columnar metaplasia. On the other hand, there is still not enough reliability in assessment of esophageal lesions in nonerosive esophagitis, in endoscopic analysis of the esophago-gastric (EG) junction with very short segments of metaplasia, and in evaluation of the risk of adenocarcinoma in the esophagus and the distinction of tumors arising from the esophagus or from the gastric cardia at the EG junction.

Key words Gastrooesophageal reflux · Esophagitis · Columnar metaplasia · Adenocarcinoma

Prevalence of symptoms and complications of GERD

The symptoms of gastroesophageal reflux disease (GERD) have a high prevalence in Western countries; however, a large proportion (65%) of persons with such symptoms do not consult a doctor and practice self-medication. The proportion of severe cases is small (4%), and other cases (31%) present with mild symptoms. In 60% of the persons with gastroesophageal reflux symptoms, when an endoscopy is performed the esophageal mucosa is either normal or shows slight, not reliable alterations; this is called nonerosive reflux disease (NERD). In 30% of patients, endoscopy displays mucosal breaks, which is called erosive esophagitis and is considered as a complication; strictures or stenoses are unusual nowadays. Finally, in 10% the esophagus is lined with a gastric type of metaplastic epithelium called Barrett esophagus.

The prevalence of GERD symptoms, defined as weekly symptoms (heartburn and regurgitation), has been analyzed in cross-sectional population studies in cross sectional populations studies. As referred in the literature [1–8], the prevalence is high in Western. The prevalence is high in Western countries and was found in the United States at 17.8% in Olmsted County by Locke in 1999 or 23% in the white population of Houston by El Serag in 2004. A high (21%) prevalence was also reported in Argentina by Chiocca in 2005. In Europe, the prevalence is also high in northern countries, and was found to be 16.7% in Sweden by Terry in 2000 and 31% in Norway by Nilsson in 2004. Lower figures were reported in Southern Europe: 9.8% in Spain (Diaz Rubio in 2004). In countries of Western Asia, the prevalence of GERD in population studies is lower, ranging from 2.5% to 6.7%; 2.5% was found in Hong Kong by Wong in 2003, 4.1% in Korea by Cho in 2004, and 6.6% in Japan by Fujiiwara in 2005. Less reliable data are available on the prevalence of esophagitis in the general population. In Japan, a study was conducted in 4723 persons: heartburn was found in 15.4%, and endoscopy was normal in 75.5% of the persons with heartburn. In another study conducted in Japan, in 2760 persons the prevalence of GERD was 17.9% and that of NERD was 10.9%. Nonerosive reflux disease (NERD) appears to be the most common form of GERD among Asian patients, accounting for 50%–70% of cases with GERD.

An increasing incidence of GERD occurred in the period 1980–2000, as shown in cross-sectional and in longitudinal population-based studies. The trend is attributed to increased weight at a young age and the increased use of drugs depressing the pressure of the lower esophageal sphincter. The increase varies from 25% to 300% in Western countries, as shown in the statistics of medical visits in ambulatory medical care in the United States or primary care practice...
in the UK. This increasing trend also occurs in Asian populations in surveys conducted in Singapore and in China.

**Progress in reliability for the evaluation of symptoms**

Workshops have been devoted to developing improved reliability in the evaluation and classification of symptoms in persons complaining of GERD [9–13]. There is a common methodology to delineate the points of consensus: a series of statements is selected after a review of the literature according to criteria of evidence-based medicine. The propositions are submitted to successive voting by a group of experts from various countries. Their response is graded from complete agreement to complete disagreement. The Marrakech Workshop held in 2002 assessed the levels of strengths between 28 participants from 10 countries. In the Montreal Workshop held during the World Congress of Gastroenterology in Montreal in 2005, the consensus was reached through a modified Delphi process, with repeated voting on 51 statements between 44 experts. At the final vote, 94% of the statements were approved by 90% of the group.

GERD is defined as a condition that develops when the reflux of stomach contents causes troublesome symptoms, with or without complications. The symptoms are divided into esophageal or extraesophageal. Among esophageal symptoms, heartburn is a burning pain provoked by acid or nonacid reflux, and regurgitation is the perception of flow of refluxed gastric content in the mouth or hypopharynx. Noncardiac chest pain can occur without accompanying heartburn or regurgitation and is classified as an esophageal symptom that can be caused by reflux more frequently than by disorders of esophageal motility. Accepted extraesophageal symptoms of reflux include laryngitis, cough, asthma, and dental erosions. There has been debate about laryngitis because the confirmation of mucosal inflammation by laryngoscopy is often unreliable. In addition, the gastropharyngeosophageal reflux must be assessed during pharyngeal pH monitoring studies at 1 to 4 cm above the upper esophageal sphincter.

Pharyngeal acid reflux also occurs in persons without laryngitis. The occurrence of pharyngeal acid reflux has been compared in 181 healthy controls and in 184 patients with reflux laryngitis and was found to be significantly higher in the group with reflux laryngitis [5]. The severity of the symptoms of GERD is graded as “mild” or “severe” by the number of days in a week in which symptoms occurred. Scales for reflux syndrome were developed to assess the clinical impact of antisecretory agents. The 7-point modified Likert scale is graded from no pain to severe pain. The Gastrointestinal Symptoms Rating Scale (GSRS) takes in account the altered quality of life and the concern of the person who is afraid of having a severe disease [14].

The primary complication of GERD is chronic inflammation of the esophageal mucosa, called erosive reflux esophagitis when there are mucosal breaks. Erosive esophagitis with deep ulcers can cause hemorrhage. Strictures resulting from the fibrotic healing of circumferential and deep ulcers are less frequent. The replacement of the squamous epithelium by a metaplastic gastric epithelium (Barrett esophagus) is classified and graded as a severe stage of esophageal complications. Reflux esophagitis is not associated with a significant increased risk for squamous cell cancer. On the other hand, an increased risk of adenocarcinoma is associated with columnar metaplasia.

**Progress in reliability for the description of erosive esophagitis**

Erosive esophagitis is detected at endoscopy in up to 30% of patients complaining of GERD symptoms. An endoscopic grading of erosive esophagitis provides a reliable assessment of the severity of chronic inflammation in the squamous epithelium was established during the Los Angeles Workshop organized by The International Working Group for the Classification of Oesophagitis (IWGCO), during the World Congress of Gastroenterology at Los Angeles in 1994 [11]. Here also the method to obtain an evidence-based consensus was applied, and the four-grades scale proposed was tested by 46 endoscopists from different countries using endoscopic video recordings from 22 patients with the full range of severity of reflux esophagitis. First, the terminology “mucosal break” replaced the term erosion or ulceration, which could not reach reliability in their definition. The mucosal breaks were classified in four grades: A, mucosal breaks no longer than 5 mm; B, mucosal breaks more than 5 mm long; C, mucosal breaks involving less than 75% of the circumference; and D, mucosal breaks involving 75% or more of the circumference. The reliability of the Los Angeles grading was also correlated with 24-h esophageal pH monitoring, and the severity of esophageal acid exposure was significantly \( P < 0.001 \) related to the severity grade of esophagitis. The grading was also applied to clinical therapeutic trials with proton pump inhibitors (PPI). The outcome of treatment with PPI – symptom relief and healing of lesions – was also related to the endoscopic grading of esophagitis.

**Progress in reliability for the assessment of reflux**

The reliability of attributing esophageal symptoms to gastroesophageal reflux improved with the development of ambulatory 24-h esophageal pH monitoring [15] with a transnasal catheter. The distal probe of the catheter is placed 5 cm proximal to the lower esophageal sphincter, whose position has been determined by manometry; the proximal probe is located 10 cm above the distal probe. Acid reflux is characterized by a rapid drop in pH below 4.0 that occurs for a longer time in the distal than in the proximal probe. Recently, the Bravo capsule offers a wireless alternative with data recording by teletransmission. The capsule is placed with endoscopy and allows a 48-h monitoring. Acid reflux in the esophagus is considered abnormal when the fraction of time where pH < 4 is recorded is more than 4% (catheter) or 5.3% (capsule) of the total recording time. The