Evaluation of GERD: Symptoms and Disease Classification

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Gastroesophageal reflux, or retrograde movement of gastric contents across the lower esophageal sphincter (LES), is relatively common, seen in almost two-thirds of adults in the United States [4]. It is physiologically normal and in fact occurs several times each day in normal healthy individuals. Whenever the pressure gradient between stomach and esophagus is high enough to overcome the LES pressure, retrograde movement of gastric contents will occur. Typically this occurs in the form of a transient lower esophageal sphincter relaxation (TLESR) [2]. This is caused by shortening of the LES during gastric distension, as commonly happens after meals [12]. In most individuals, TLESRs are often brief and asymptomatic. In some cases, TLESRs can be more frequent, longer lasting, or more acidic, allowing excessive exposure of the esophageal mucosa to gastric acid [8]. Over time, this can lead to failure of the LES and symptomatic gastroesophageal reflux. The esophagus, upon receipt of acidic refluxate, will attempt to clear contents back toward the stomach with peristaltic activity. However, the effectiveness of this is variable depending upon underlying esophageal function. Gastroesophageal reflux disease, over time, can cause ineffective motility of the esophagus, in turn worsening the effect of reflux on the esophageal mucosa.

The typical symptoms of gastroesophageal reflux are heartburn and regurgitation. Heartburn is defined as a burning sensation in the retrosternal area [11]. Heartburn is caused when acids enter the squamous epithelium of the distal esophagus and stimulate nerve endings, producing a sensation of pain. In comparison, the columnar epithelium of the stomach is impervious to damage by acid. Regurgitation is defined as the perception of flow of refluxed gastric content (including acid) into the mouth or hypopharynx [11]. This results from either TLESRs or permanent damage to the lower esophageal sphincter causing complete failure of the LES to

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J. Grams et al. (eds.), *The SAGES Manual of Foregut Surgery*,
https://doi.org/10.1007/978-3-319-96122-4_6

close. Regurgitation can be severe, with full column regurgitation of acidic gastric content and/or food.

Reflux can be seen in the presence of a normal LES that has transient lower esophageal sphincter relaxations. If an increased number of episodes occur, TLESRs can lead to microscopic changes to the LES. This can lead to destruction of the LES and worsening reflux or GERD.

There are also a number of atypical reflux symptoms. These are often accompanied by typical symptoms of GERD but are sometimes isolated. These include pulmonary symptoms such as chronic sore throat, cough, hoarseness, and asthma [3]. Dysphagia can also be an atypical symptom of GERD but does need further workup because dysphagia suggests possible underlying esophageal motility disorder or cancer. Dental erosions have been found to be associated with GERD as well [7]. Many patients with atypical GERD present initially to otolaryngologists, dentists, and allergists and may not see a surgeon until their symptoms become quite severe. It is important to keep GERD in the differential for patients that present with these atypical symptoms.

Despite this, it is important to realize that GERD is not a typical sole cause of these diseases but rather is often found to exacerbate them [11]. Patients can have a constellation of typical and atypical reflux symptoms, with no appreciable esophageal damage present. Gastroesophageal reflux disease (GERD) is the term used for reflux symptoms causing esophageal damage [11]. GERD can also be used to classify symptoms severe enough to impact quality of life.

Disease Classification

There are two types of epithelium in the upper digestive tract: squamous epithelium of the esophagus and columnar or oxyntic epithelium of the stomach. The latter is not damaged by acidic gastric contents. The squamous epithelium of the esophagus is damaged when exposed to pathologically high levels of acid.

This damage can manifest in a variety of ways. One result of chronic acid exposure is esophagitis. Esophagitis can be diagnosed with EGD and biopsy, although the characteristic findings of esophagitis (widened intracellular spaces, basal cell hyperplasia, intraepithelial eosinophils) are not specific to reflux esophagitis. Furthermore, the absence of these histologic changes does not rule out the presence of GERD. Thus, the diagnosis of GERD must be made in concert with clinical symptoms.

Esophagitis is classified as either erosive esophagitis or nonerosive esophagitis. Erosive esophagitis causes significant full-thickness mucosal damage of the esophagus, which can lead to ulcer formation. Ulcerations are visible on EGD, and the Los Angeles classification system is useful to determine the severity of esophagitis. The healing of these ulcers can in turn lead to stricture formation in the distal esophagus.

Erosive esophagitis is the most common macroscopic abnormality seen during EGD in patients with GERD. Despite that, it is still only seen in a minority of

patients. On EGD, it is seen as a break in the mucosa. This can be either superficial (erosions) or full thickness (ulcerations). When it is full-thickness damage to the mucosa, it leads to more complications (strictures and ulcers) and an increased likelihood of disease that is refractory to medical management. As these areas cyclically break down and heal, strictures often form in the distal esophagus. Erosions have been classified by the Los Angeles classification system into grades A–D of severity, based upon percentage of circumference affected and size of mucosal break [5]. Esophagitis can also be found histopathologically, but the specificity of this to diagnose GERD is less reliable.

The majority of patients suffering from GERD have nonerosive esophageal reflux disease or NERD. Nonerosive disease is defined as reflux-associated symptoms in the absence of mucosal breaks at endoscopy [11]. This is less likely than erosive disease to cause long-term structural damage to the esophagus. They also typically have fewer complications (strictures, etc.) than patients with erosive reflux disease. Patients with NERD can have excellent acid control on proton pump inhibitors (PPI). In fact, PPI use has been successful in moving patients from erosive to nonerosive reflux disease in large numbers. Histologically, biopsies of the esophagus of patients with NERD will have early signs of damage such as dilated intracellular spaces [9, 10]. These are visible early on only using electron microscopy and as damage progresses will become visible on light microscopy as well [10].

Another potential result of squamous epithelial cell exposure to acid is columnar metaplasia. Columnar metaplasia can occur early in the disease course and can be seen in the majority of patients with chronic GERD [1]. Gastric reflux can damage the squamous epithelium to the stem cell layer, which is significantly deep to alter the proliferation of the squamous epithelial cells, leading to columnar metaplasia [1, 6]. Columnar metaplasia, or Barrett's esophagus, begins in the distal-most esophagus but can extend proximally as damage continues, leading to visible metaplasia or columnar-lined esophagus. This can progress to dysplastic Barrett's esophagus and finally adenocarcinoma of the esophagus [1]. Long-segment Barrett's esophagus is one of the most reliable risk factors for development of esophageal adenocarcinoma [11].

A patient with reflux symptoms will often undergo upper endoscopy to evaluate the extent of damage from reflux. This will allow designation of erosive versus nonerosive disease. Additionally, tissue biopsies of the gastroesophageal junction can evaluate for signs of esophagitis as well as columnar metaplasia indicative of Barrett's esophagus.

Summary

Reflux symptoms are relatively common. Gastroesophageal reflux disease is the presence of esophageal damage accompanying reflux symptoms.

GERD can be characterized by erosive and nonerosive esophagitis.

Erosive esophagitis is more likely to lead to stricture, ulcers, and metaplasia in the distal esophagus, as a result of full-thickness mucosal injury.

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