abstract

Gastroesophageal reflux disease is a common condition responsible for significant morbidity in older adults. It causes disease in the esophagus, and it is increasingly recognized as a cause of extra-esophageal symptoms such as chronic cough, adult-onset asthma, and hoarseness. Despite significant symptoms, endoscopy may be negative. Endoscopy-negative reflux disease may be a unique disease entity within the acid reflux group of disorders that includes erosive esophagitis and Barrett's esophagus. Regardless of the symptoms or endoscopic findings, treatment remains geared to reducing the contact time between acid and sensitive tissue through lifestyle modification measures, acid suppression, and improved upper gastrointestinal motility.

Key words: *GERD, extra-esophageal reflux, endoscopy-negative reflux disease, acid suppression, older adults*

Gastroesophageal Reflux Disease in Older Adults: An Update

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Introduction

Gastroesophageal reflux disease (GERD), the abnormal reflux of gastric and duodenal contents into the esophagus, is common. Almost 50% of the North American population experience symptoms once a month and 10% have symptoms daily.[1] Patients most commonly complain of pyrosis and regurgitation, but other symptoms such as chest pain and nausea are occasionally observed.[1] As well, there is increasing recognition that extra-esophageal symptoms such as chronic cough, hoarseness, and asthma may be due to acid reflux.[1,2,3,4]

GERD in Older Adults

GERD appears to occur more often in the older population. Consultations for GERD and related complaints increase from 355 per 10,000 in those aged 25–44 years, to 789 per 10,000 in those aged 75–84 years.[5] Older patients, however, are less likely to complain of frequent or severe symptoms.[6] They complain less than younger patients with the same degree of injury, and endoscopy and esophageal pH monitoring indicate that older patients have more severe disease with reduced symptoms.[2,7–10]

Although there are only minor intrinsic changes in the functional nature of esophageal tissue due to aging,[1,11] and there have been no documented age-related changes in 24-hour pH esophageal recordings,[1] other changes exist to account for this increased GERD in this patient population. Older patients have a greater tendency to increased recumbency and experience more nocturnal and supine reflux events. They have decreased bicarbonate secretion and saliva volume. There is increased incidence of comorbid conditions that may affect esophageal motility such as diabetes mellitus and Parkinson's disease. Additionally, aging adults are on more medications that can impair esophageal motility and saliva production.[5,12]

Extra-Esophageal Manifestations of GERD

Extra-esophageal reflux (EER) symptoms are being increasingly recognized. Symptoms include pulmonary, otolaryngologic, and oral findings such as asthma (particularly adult-onset), chronic cough, hoarseness, laryngitis, and dental erosions (Table 1). Observational studies have demonstrated the prevalence of extra-esophageal manifestations of GERD although it has been difficult to prove causality because classic GERD, symptoms and EER symptoms are common and could occur simultaneously without causal association. Additionally, it is difficult to measure gastric acid in the affected extra-esophageal compartments.[3] Furthermore, a significant number of people who experience EER do not have typical GERD symptoms such as pyrosis or regurgitation.[3,4] Nevertheless, successful treatment of EER symptoms often occurs with standard antireflux therapy. As well, a high percentage of people with classic GERD symptoms experience at least one EER symptom, further suggesting an association.[3]

GERD has been implicated as a significant factor in up to two-thirds of adult patients with difficult-to-control asthma and is the main cause of 10–20% of

chronic coughing cases, 80% of cases of persistent hoarseness, and nearly 50% of patients with globus.[3]

There are two possible mechanisms for the development of EER, and both may occur simultaneously. First, there may be a direct noxious effect of refluxed gastric contents.[3,4] The actual noxious agent may be the acid itself or pepsin in the refluxate.[3] Pulmonary symptoms occur from microaspirations of these substances. Contact between the stimuli and the affected mucosa initiates an inflammatory pathway resulting in symptoms. In the second mechanism, the acid may activate receptors in the esophagus that initiate vagally-mediated reflexes, causing a variety of symptoms such as esophageal muscular contractions causing chest pain, bronchoconstriction triggering asthma, and reflex coughing and throat clearing producing chronic coughing, hoarseness, and laryngitis.[3,4]

In general, there is poor correlation of any of these EER symptoms with endoscopic features of reflux. Many studies have shown endoscopic esophagitis in only 10–27% of patients with EER.[4] A recent prospective study, however, demonstrated that approximately 50% of patients with EER had varying degrees of endoscopic evidence of GERD.[4]

Endoscopy-Negative Reflux Disease

It is recognized that many patients who complain of reflux symptoms have no evidence of esophageal mucosal defects on endoscopy.[13,14] It has also been noted that many patients with no symptoms may have significant GERD, including complications such as Barrett's esophagus.[13] Thus, while GERD is usually considered a condition with a spectrum of signs and symptoms, it may represent separate, unique disorders of endoscopy-negative reflux disease (ENRD), erosive esophagitis, and Barrett's esophagus.[13] ENRD has been defined several ways but in general it is a condition in which patients have a normal esophagus at endoscopy yet still experience pyrosis.

The pathophysiology of ENRD is not well understood. Acid reflux may still be involved through the activation of nociceptors on deep mucosal nerves that are accessed not by exposure through mucosal denudation, but through dilated intercellular spaces that occur in ENRD and erosive esophagitis.[13] As well, there may be mechanosensitivity pathways that are involved in symptom production. Esophageal longitudinal muscle thickening may occur and cause chest pain or heartburn. Such contractions have been shown on esophageal ultrasound but they are undetectable by usual esophageal manometry.[13]

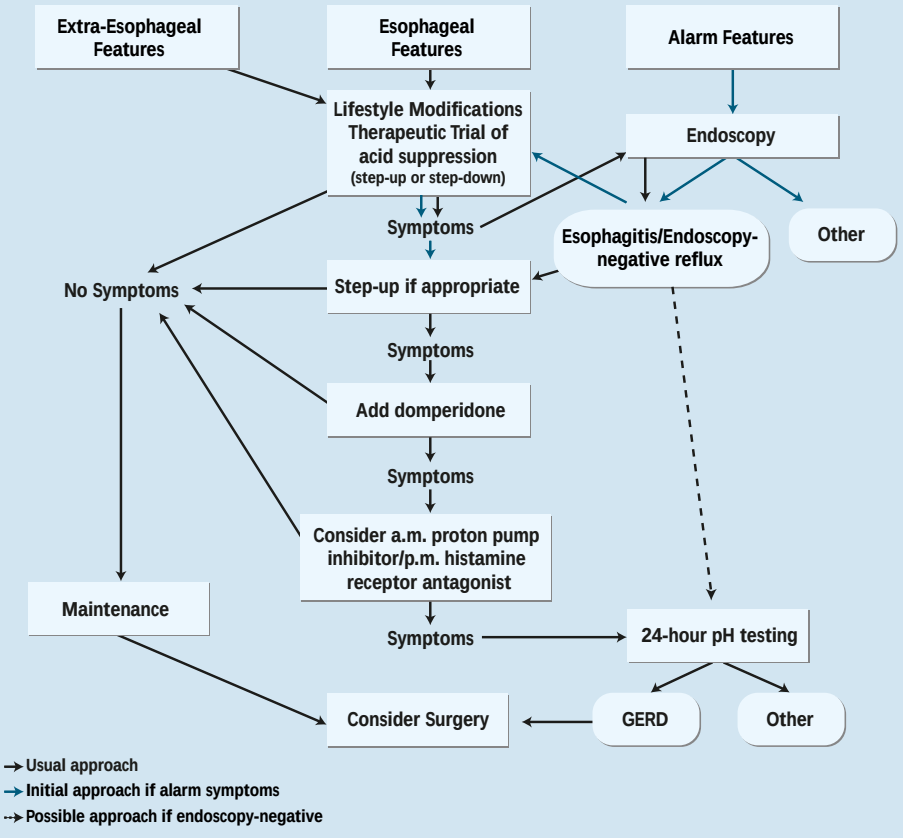
Table 1: Symptoms of GERD

Esophageal Symptoms	Extra-esophageal Symptoms	Alarm Symptoms
Heartburn	Chest pain	Dysphagia
Regurgitation	Cough	Weight loss
	Hoarseness	Bleeding
	Asthma	Anemia

Treatment

The diagnosis and treatment of GERD are based on the patient's symptoms (Figure 1). When complaints are typical, such as pyrosis or regurgitation, a trial of therapy is reasonable.[15] This is not appropriate, however, for patients with worrisome features such as gastrointestinal bleeding, unexplained weight loss, iron deficiency anemia, a palpable mass, or an abnormal upper gastrointestinal barium study.[5] In these cases, endoscopy is warranted to exclude malignancy and other

Figure 1: An Approach to the Management of Gastroesophageal Reflux Disease (GERD)



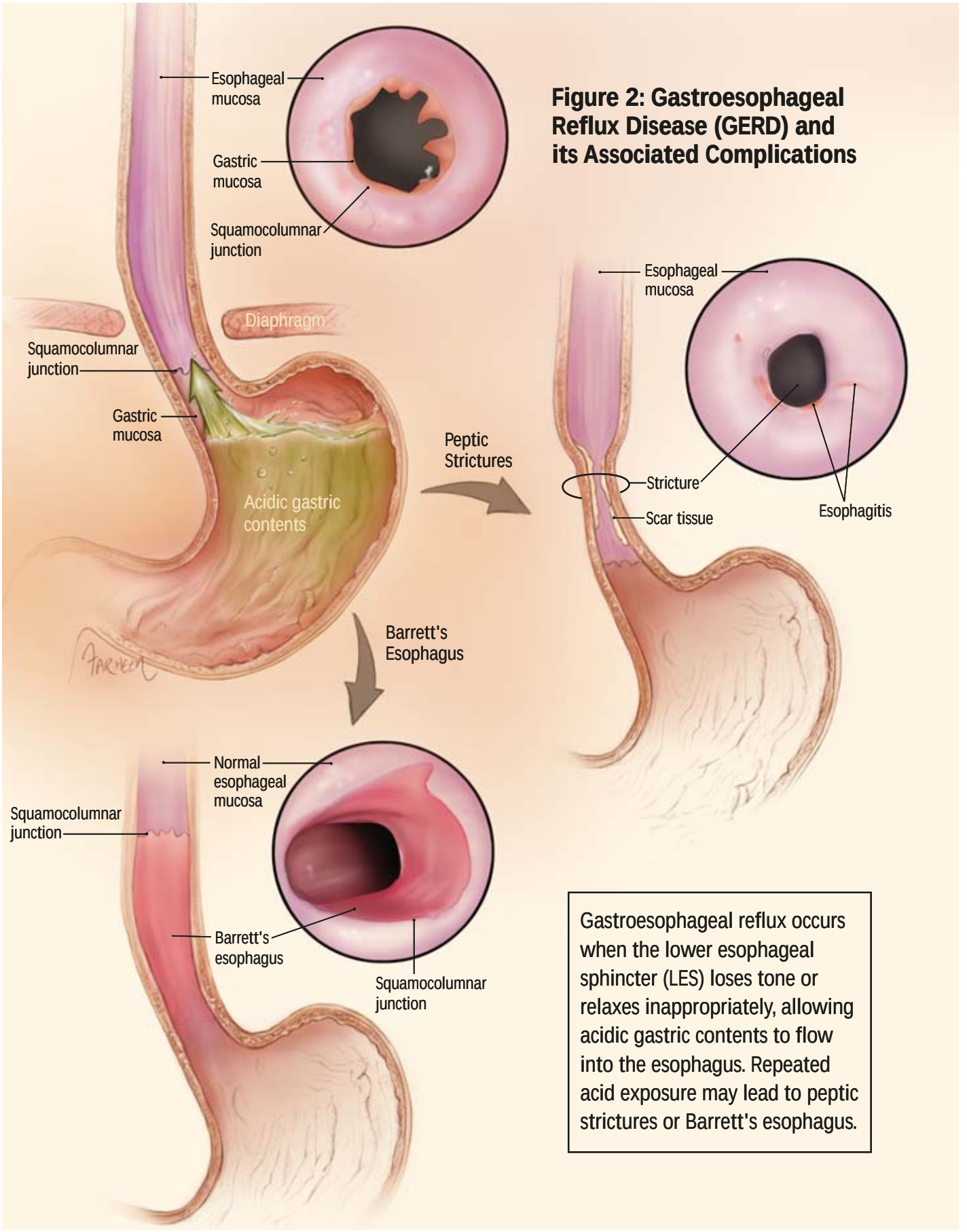


Figure 2: Gastroesophageal Reflux Disease (GERD) and its Associated Complications

Gastroesophageal reflux occurs when the lower esophageal sphincter (LES) loses tone or relaxes inappropriately, allowing acidic gastric contents to flow into the esophagus. Repeated acid exposure may lead to peptic strictures or Barrett's esophagus.

more serious disease. It is also usually considered prudent to investigate patients who present with typical GERD features for the first time over the age of 55 years.[5] Endoscopy should also be performed in patients with typical GERD features who do not respond to standard antireflux therapy.[5]

The approach to management of patients with EER symptoms is not well defined. As a patient with EER features is likely to have a normal endoscopy, it is reasonable to initiate a trial of antireflux therapy if non-reflux causes of their symptoms have been excluded.[5]

The concern with empirical management is that one might overlook serious underlying pathology, particularly a gastric or esophageal malignancy. Two studies have shown that, while a diagnosis of an upper gastrointestinal malignancy might be delayed, there is no difference in staging of a tumour at time of diagnosis and outcome is unaffected if an empiric approach is applied.[16,17]

Treatment includes both lifestyle modification as well as pharmacological management. Both elements are aimed at reducing acid contact with the esophageal (and supra-esophageal) tissue. The goal of therapy is to eliminate symptoms, heal mucosal damage, and prevent recurrence of symptoms and complications. Lifestyle recommendations include[1,15]:

- elevation of the head of the bed (10–15 cm) to reduce nocturnal reflux events
- avoidance of postprandial recumbency (2–3 hrs)
- cessation of smoking and alcohol (which reduce lower esophageal sphincter tone)
- avoidance of foods such as tea, coffee, colas, and peppermints (which also affects lower esophageal sphincter tone [LES])
- weight loss (to reduce abdominal pressure on the LES).

Most people require antacids. It is reasonable for patients with mild symptoms to use over-the-counter (OTC) antacids or histamine receptor antagonists (H2RAs). These medications may be particularly beneficial if used before provocative activities (e.g., meals and exercise). Up to 20% of patients respond to such treatments.[15]

It is quite common, however, for patients to require stronger acid suppression than that provided by OTC therapies. Esophageal mucosa lacks the features that protect gastric mucosa from acid damage, such as bicarbonate secretion, mucous production, and epithelial cell migration to cover areas of denudation.[7,18] Therefore, greater and longer-term acid suppression is required in patients with GERD than in those with peptic ulcer disease.

Four H2RAs are available for the treatment of GERD and they are listed in Table 2. It is clear from the literature, however, that proton pump inhibitors (PPIs) provide the best acid suppression and are often required for the treatment of GERD. There are five PPIs available (Table 2) and all are equally effective. They have been shown to result in up to 95% of patients experiencing complete symptom resolution and mucosal healing,[1] and are capable of doing so faster that H2RAs.[15]

It is well documented that esophagitis will recur in most patients if treatment is stopped, with recurrence being faster for more severe disease.[19,20] Approximately 89% of patients relapse within six months of reduction or discontinuation of their therapy.[19] Full-dose PPIs, therefore, are often required for maintenance.[15,19]

Side effects of PPIs appear to be mild and uncommon. There was concern with the introduction of PPIs that long-term use might give rise to carcinoid tumours because of constant antral G-cell stimulation by the profound acid suppression. While hypergastrinemia does occur (levels two to four times normal), no cases of gastrinoma attributable to PPIs have been reported within the 10 years of their use throughout North America, Europe, and Australia.[15,21] Similarly, gastric acid contributes to production of a relatively sterile proximal gastrointestinal tract, yet bacterial overgrowth does not seem to occur either.[15]

Table 2: Acid Suppression Medications Used in the Treatment and Maintenance of GERD

Drug	Doses
Histamine Receptor Antagonists (H2RA)	
cimetidine	800mg q.h.s. to 600mg b.i.d.
famotidine	20mg b.i.d.
ranitidine	150mg b.i.d.
nizatidine	150mg b.i.d.
Proton Pump Inhibitors (PPIs)	
esomeprazole	20–40mg o.d.
lansoprazole	30mg o.d.
omeprazole	20–20mg b.i.d.
pantoprazole	40mg o.d.
rabeprazole	20mg o.d.

Occasionally, acid suppression alone is insufficient to suppress reflux symptoms, and a prokinetic agent may be added to the medical regimen. The rationale is that the prokinetic agent will assist in clearing the acid from the esophagus, reducing contact time between the acid and the mucosa. Metoclopramide, a dopamine antagonist, is known to have extrapyramidal side effects and is not a good choice for long-term therapy. Domperidone (also a dopamine antagonist), however, does not cross the blood-brain barrier and lacks the neurological side effects of metoclopramide. A typical dose of domperidone is 10mg t.i.d. or q.i.d. but may be increased to 20mg q.i.d. if necessary.[22]

If the diagnosis of GERD is verified and maximal medical therapy is insufficient or impractical, antireflux surgery (fundoplication) may be considered.[19]

Complications of GERD

Complications of GERD include peptic stricture of the esophagus and Barrett's esophagus (Figure 2). Peptic strictures can be dilated but can recur without maintenance therapy; long-term acid suppression with PPI therapy is indicated in this situation. The time between dilation and symptomatic recurrence is lengthened by the use of PPIs.[11,15]

Barrett's esophagus is a condition in which the squamous epithelium of the esophagus is replaced by intestinal columnar epithelium. It is thought to be an adaptive mechanism to repeated acid exposure. Structural change does not occur and endoscopy with biopsy is required for diagnosis. This is a premalignant condition with a risk of esophageal cancer 30 times greater than baseline.[23] Although they will not reverse metaplasia, PPIs are indicated in this condition as well.

Summary

GERD is a common medical condition in the general population, and may be more prevalent in older than in younger people. Symptoms of GERD include the typical features of reflux and heartburn, but also extraesophageal symptoms such as asthma, hoarseness, and non-cardiac chest pain. Management of GERD, whether there is mucosal injury or not and whether the symptoms are esophageal or extraesophageal, is based on acid suppression for both treatment and maintenance therapy.

No competing financial interests declared.

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