Diagnosis and treatment of gastroesophageal reflux disease in the elderly

ABSTRACT

Gastroesophageal reflux disease poses special diagnostic and therapeutic challenges in the elderly. These patients may not report the classic symptoms of dysphagia, chest pain, and heartburn, and they are more likely to develop severe disease and complications such as esophageal ulceration and bleeding. Therapeutic options include lifestyle changes, medication, and surgery. Polypharmacy and changes in renal, hepatic, and gastrointestinal function can complicate treatment. Proton pump inhibitors can help optimize disease management.

KEY POINTS

The most common primary presenting symptoms of GERD in the elderly are regurgitation, dysphagia, dyspepsia, vomiting, and noncardiac chest pain, rather than heartburn.

Because the elderly commonly take multiple drugs for various comorbidities, drug interactions and treatment responses must be carefully assessed in this patient population.

Nonpharmacologic measures may be helpful but often do not relieve nighttime GERD symptoms.

GASROESOPHAGEAL REFUX DISEASE (GERD) is not only more common in the elderly, but its diagnosis and treatment are more challenging. The presenting symptoms are likely to be different than those reported by younger patients, and the disease is more likely to lead to complications. In addition, treatment is more likely to be complicated by drug interactions.

This review focuses on the management of GERD in the elderly, with an emphasis on proton pump inhibitors.

WHY IS GERD SO COMMON IN THE ELDERLY?

GERD is a common chronic disorder in Western society and is the most common esophageal disease in the elderly.1,2 Approximately one third of all adults experience the classic symptoms of heartburn or regurgitation at least once a month, with the prevalence rising to 59% in persons older than 65.2-4 Although the same pathophysiologic factors are responsible for GERD in all age groups, age-related changes in the normal antireflux mechanisms may abet both the development and the progression of this disease (FIGURE 1). Delayed esophageal clearance and gastric emptying, decreased salivary secretion, and loss of lower esophageal sphincter tone can increase the total amount of time that the esophagus is in contact with refluxed gastric acid.2,5,6 Gastric acid hypersecretion and diminished esophageal mucosal resistance can promote GERD development without increasing reflux frequency.2,5
Age-related changes that may lead to GERD

Patient age has been correlated with the severity of GERD, but it has been difficult to obtain unequivocal evidence showing that the antireflux mechanism in healthy elderly people is impaired.\textsuperscript{7-9} One recent investigation reported a possible age-related decline in esophageal motility and clearance.\textsuperscript{10} In this study, volunteers ranging in age from 70 to 80 exhibited abnormal peristalsis and reflux episodes of significantly longer duration than...
did 20-to-30-year-olds and 50-to-60-year-olds. Together, these changes may contribute to the higher incidence of severe esophagitis seen in the elderly.

As reported by several investigators, gastric acid secretion does not decline with age; in fact, it may increase. On the other hand, salivary secretion has been shown to decline slightly with advancing age, and mucosal resistance or clearance mechanisms may be compromised due to long-term use of medications such as nonsteroidal anti-inflammatory drugs. As a result, the defense mechanisms of the esophageal mucosa may be altered. Moreover, medications such as theophylline, nitrates, calcium channel blockers, benzodiazepines, anticholinergics, lidocaine, and prostaglandins, which the elderly are more likely to be taking, have all been shown to decrease lower esophageal sphincter tone and increase gastroesophageal reflux. This could, in part, explain the age-related increase in esophageal acid exposure.

Whether advanced age causes changes in lower esophageal sphincter pressure has also been difficult to answer. A recent study identified a possible age-related shortening of the intra-abdominal segment of the lower esophageal sphincter in the elderly. The lower esophageal sphincter may gradually migrate toward the thoracic cavity with age. This shortening may well precede hiatal hernia development and contribute to the higher frequency and increased severity of gastroesophageal reflux and of esophagitis that occurs with age.

Chronic pain is especially prevalent in the elderly and is often treated with nonsteroidal anti-inflammatory drugs. Circumstantial evidence has linked the use of aspirin with GERD. An esophageal stricture may impede passage of a nonsteroidal anti-inflammatory tablet into the stomach, facilitating local mucosal injury. However, in the absence of an esophageal stricture, the mechanism whereby nonsteroidal anti-inflammatory drugs may exacerbate GERD remains unclear.

An increasingly sedentary lifestyle and the presence of presbyesophagus secondary to stroke or diabetes or both may also increase the risk of GERD in the elderly.

### COMPLICATIONS ARE MORE FREQUENT AND SEVERE IN THE ELDERLY

Although complications of GERD—including ulceration, stricture, gastrointestinal bleeding, Barrett’s esophagus, and adenocarcinoma—can occur in patients of all ages, epidemiologic data indicate that complications are more frequent and severe in older persons. This is consistent with cumulative injury from years of acid reflux. Patients with Barrett’s esophagus, esophageal ulcers, or stricture are thus more likely to be older than those with less severe esophagitis.

In addition, delayed esophageal clearance, impaired swallowing, use of anticholinergic medications, and use of hypnotics, all of which are common in the elderly, can lead to increased risk of aspiration of gastric contents and thereby cause recurrent respiratory symptoms.

Several studies investigating the prevalence and severity of GERD in relation to age showed no age-related increase in the frequency of symptoms indicative of severe GERD. However, elderly patients actually experience significantly more esophageal mucosal disease and more advanced disease than do younger patients. Because minimally symptomatic patients are less likely to seek medical attention, this lack of correlation between disease severity and symptom perception may make elderly patients more prone to develop severe GERD and its complications before coming to the attention of a physician. The reasons for diminished symptom recognition in the elderly are unknown but may include impaired sensory perception, atypical pain localization, central nervous system disease, or depression.

### HOW TO DIAGNOSE GERD

**Symptoms**

GERD symptoms in the elderly can mimic those of a variety of cardiac, infectious, viral, peptic, and inflammatory disorders. The elderly are more likely to have comorbidities, which may prevent them from identifying GERD-related symptoms. Also, elderly patients may have impaired sensory perception, perhaps stemming from changes in the...
In older patients who report no classic GERD symptoms, pulmonary complaints (e.g., coughing, hoarseness, and wheezing) may provide diagnostic clues. Hematemesis and anemia may indicate that the esophagus is ulcerated and bleeding and, therefore, that GERD has entered a more severe stage.

**Endoscopy**
A correlation between symptoms and GERD severity for any patient age group has never been established. Thus, endoscopy remains the diagnostic tool of choice to assess the esophageal mucosa unequivocally. Endoscopy provides visual evidence of reflux esophagitis, erosive esophagitis, Barrett's esophagus, infectious esophagitis, and cancer. Furthermore, it enables the physician to grade GERD severity and disease prognosis objectively.

Because the severity of symptoms described by the typical elderly patient tends to be significantly less than that of younger patients, endoscopy may be more important for disease assessment in the older patient.

Endoscopically observed peptic ulcer disease warrants testing for *Helicobacter pylori* infection.

**24-hour pH monitoring**
A reliable and objective measurement of disease pathophysiology may be obtained with 24-hour pH studies. Ambulatory 24-hour pH monitoring quantifies the extent of gastroesophageal reflux. It can sometimes confirm the diagnosis in patients whose endoscopic findings are apparently normal and in patients with atypical symptoms. The test can help clinicians correlate the episodes of reflux with patients' awareness of their symptoms. In elderly patients who present with atypical symptoms, pH monitoring has been used to diagnose pathological reflux, which can severely damage the esophagus.

Although traditionally the 24-hour pH study has been considered an accurate test (sensitivity and specificity have been rated as high as 96%), more current studies have questioned its accuracy, suggesting that pH monitoring should be used in conjunction with endoscopy, esophageal manometry, or other measures.
Manometry is used chiefly as a preoperative measure and for elderly patients who report atypical symptoms such as chest pain.2

## TREATMENT STRATEGY

Whether the patient is young or old, GERD does not resolve spontaneously and often requires long-term therapy. Therapeutic options include simple lifestyle changes, medication, and antireflux surgery (TABLE 3).2,25 The goal is to control symptoms, and this is most often achieved by reducing the amount of time the esophagus is exposed to refluxed gastric acid.2

## IMPORTANCE OF PATIENT EDUCATION

Educating the patient about the mechanism and cause of reflux is an essential first step in any therapeutic strategy.5,22 Patients should be informed about specific lifestyle factors that affect reflux activity and consequences of exposure of the esophagus to gastric acid.5 Potential drug interactions and, specifically, contraindicated drugs, must be reviewed with the patient if he or she is taking other medications.5

Although lifestyle habits may be ingrained and difficult to change in elderly patients, an educated patient is more likely to make the necessary changes.5

## LIFESTYLE CHANGES

Simple interventions such as sleeping on an incline with the head elevated can significantly reduce esophageal exposure to acid during the night.6,22 Reducing intake of specific foods and beverages, losing weight, avoiding tight-fitting clothes, and other simple interventions (TABLE 3) can lessen the reflux of gastric juices and consequently help control GERD.22,25 Although nonpharmacologic measures may be helpful, they often do not relieve nighttime GERD symptoms.

## MEDICATIONS

When treating the elderly, one must carefully assess drug interactions and treatment responses. Older patients take more prescription and nonprescription medications than any other age group. They are also at greater risk of developing medication-induced cognitive dysfunction.26,27 In addition, age-related changes in drug metabolism and gastrointestinal, hepatic, and renal function can complicate treatment.

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*GERD, gastroesophageal reflux disease; NS, not significant

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**TABLE 2**

Occurrence of GERD* symptoms in the elderly by age group

<table>
<thead>
<tr>
<th>GERD SYMPTOM</th>
<th>PERCENT OF PATIENTS, GROUPED BY AGE</th>
<th>PVALUE</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>60-70 YEARS (N = 61)</td>
<td>71-80 YEARS (N = 96)</td>
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<tr>
<td>Heartburn</td>
<td>46</td>
<td>32</td>
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<td>Regurgitation</td>
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<td>51</td>
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<td>Dysphagia</td>
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<td>22</td>
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<td>Respiratory symptoms</td>
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<td>42</td>
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<tr>
<td>Dyspepsia</td>
<td>62</td>
<td>59</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Chest pain</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>Anorexia</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

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See the patient information handout on page 766
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TABLE 3

Treatment options for GERD

Pretreatment
Educate the patient about the mechanism and causes of reflux

Lifestyle changes
Lose weight
Sleep with head slightly elevated
Avoid tight clothing
Stop smoking
Avoid foods that precipitate reflux, such as citrus fruits, fatty foods, chocolate, peppermint, onions, and garlic
Eat small meals
Avoid eating late in the day
Avoid medications that reduce lower esophageal sphincter pressure or tone, such as hormones, (estrogens, progesterone, glucagons), anticholinergics, theophylline, calcium channel blockers, and meperidine
Use antacids

Medical therapies
Mucosa-coating agents
Sucralfate
Prokinetic drugs
Cisapride (limited to investigational use)
Metoclopramide
Histamine H₂ receptor antagonists
Cimetidine
Famotidine
Nizatidine
Ranitidine
Proton pump inhibitors
Omeprazole
Lansoprazole
Rabeprazole
Pantoprazole

Surgical therapies
Fundoplication
Crural tightening
Hiatal hernia repair

The ideal medication for GERD in the elderly would be one that is well tolerated, can be taken once daily, and does not interact with other medications. In addition, a drug with pharmacokinetic and pharmacodynamic properties that are not significantly altered in patients with renal or hepatic impairment would be preferred. Cost may also play a role in the selection of medication, given the lack of a drug program for Medicare.

Currently, four types of drugs are used to treat GERD in the elderly: cytoprotective agents, prokinetic agents, histamine H₂ receptor antagonists, and proton pump inhibitors.

Cytoprotective agents
Sucralfate (Carafate), a mucosa-coating agent, is useful in geriatric patients, but it may reduce absorption of certain drugs. Concomitant medications must be given 2 hours after sucralfate.

Prokinetic agents
Cisapride and metoclopramide can reduce the detrimental effects of acid reflux by increasing esophageal peristalsis and by reducing gastric emptying time. These agents may also help reduce symptoms by increasing the resting pressure of the lower esophageal sphincter.

Cisapride (Propulsid), a prokinetic drug indicated for symptoms of nighttime reflux, is no longer freely available. Marketing for this drug was stopped on July 14, 2000, owing to reports of cardiac arrhythmias and deaths in patients taking cisapride. The concomitant use of drugs such as macrolide antibiotics andazole antifungals, which inhibit the metabolism of cisapride by cytochrome P-450, may elevate serum levels of cisapride, which poses a significant risk to cardiac stability.

An investigational limited-access program has been established for patients whose disease has failed to respond to other standard treatment options and who meet defined eligibility criteria.

Metoclopramide (Reglan), which increases lower esophageal sphincter pressure, is indicated for symptomatic GERD and esophageal lesions refractory to conventional therapy. Its use is limited by any history of renal impairment as well as by its sedating and extrapyramidal side effects.

Histamine H₂ receptor antagonists
These drugs, cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axid), and ranitidine (Zantac), are commonly used to treat GERD. They reduce acid secretion by 60% to 70% by binding to H₂ receptors on parietal cells and blocking the stimulation of acid production. Short-term use (up to 12 weeks)
Proton pump inhibitors are the most effective treatment for GERD

**Endoscopic healing**

**Relief of symptoms**

<table>
<thead>
<tr>
<th>% of patients</th>
<th>Placebo</th>
<th>Sucralfate</th>
<th>Histamine H₂ receptor antagonist</th>
<th>Proton pump inhibitor</th>
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</table>

**FIGURE 2. Summary of reports on the efficacy of medications for GERD.**


Proton pump inhibitors are safe, but do have some interactions

at a dosage twice that used in treating duodenal ulcers can heal mild to moderate esophagitis in 50% of patients and can relieve GERD symptoms in 60%, 22, 25

Histamine H₂ receptor antagonists have a relatively short duration of activity (4 to 8 hours), and patients may develop tolerance to them regardless of the route of administration. Also, acid suppression is incomplete in response to meals. As a result, these drugs are less effective in patients with advanced GERD, even when higher doses and longer treatment periods are used. 34

These drugs have other disadvantages. Cimetidine can occasionally cause confusion in the elderly. It alters the steady-state kinetics of oral theophylline, slowing its clearance by 25%. Also, the histamine H₂ receptor antagonists interact with other drugs, notably antacids. In one study, the ingestion of magnesium and aluminum hydroxide was shown to reduce the bioavailability of famotidine, ranitidine, and cimetidine by 20% to 25%. Magnesium and aluminum hydroxide also caused a 12% decrease in the bioavailability of nizatidine. 2, 35

Proton pump inhibitors

Proton pump inhibitors can contribute to the optimal defense strategy in the elderly. 36 They
are the most effective medications available for suppressing gastric acid, healing erosive esophagitis, and resolving GERD symptoms.

The proton pump inhibitors are the most effective acid suppressants currently available (FIGURE 2). These agents irreversibly bind to the proton pump hydrogen-potassium adenosine triphosphatase (H+,K+ ATPase) in parietal cells and block enzyme function. By blocking this final step in the pathway of acid secretion, all proton pump inhibitors function independently of the mechanism of parietal cell stimulation. They can provide fast control of acid output, leading to relatively complete esophagitis healing and GERD symptom relief. Proton pump inhibitors can also improve dysphagia and reduce the occurrence of esophageal strictures and the need for esophageal dilatation.

At one time, there was concern that long-term use of proton pump inhibitors might increase the risk of gastric mucosal tumors by elevating serum gastrin levels. However, widespread clinical use for more than a decade has not substantiated this supposed risk. One meta-analysis of various therapies for erosive or ulcerative esophagitis that were given for up to 12 weeks showed that proton
pump inhibitors not only had higher healing rates than histamine H₂ receptor antagonists (83.6% vs 51.9%), but they worked twice as fast (a healing rate of 11.5%/week vs 5.9%/week). Another study showed that lansoprazole was superior to ranitidine in the healing of gastric ulcers associated with non-steroidal anti-inflammatory drug use. Yet another advantage of proton pump inhibitors is that they can be taken once a day, which can help increase medication compliance.

An important consideration for any patient taking multiple medications is drug interactions. The currently available proton pump inhibitors are safe, although drug interactions through the cytochrome P-450 enzyme system of the liver may occur. Preliminary evidence suggests that rabeprazole and pantoprazole may induce the lowest incidence of these interactions (Table 3).

Long-term omeprazole therapy for GERD has been associated with increased incidence of atrophic gastritis in H pylori positive patients and decreased serum vitamin B₁₂ levels. Yearly monitoring of vitamin B₁₂ in such patients is recommended. However, continuing treatment with gastric antisecretory drugs (including proton pump inhibitors) does not decrease iron stores or cause iron deficiency, and monitoring of iron and ferritin levels is not necessary.

The various proton pump inhibitors have different pharmacokinetic properties and different potential drug interactions (Table 4). The pharmacodynamics of gastric acid suppression is also of importance in any medication that is taken long-term.

Omeprazole (Prilosec), the first proton pump inhibitor, is supplied as 10-, 20-, or 40-mg delayed-release capsules containing the active drug in enteric-coated granules. Omeprazole is rapidly absorbed, with peak plasma levels occurring within 0.5 to 3.5 hours. The plasma half-life in healthy subjects is between 30 minutes and 1 hour, and the total body clearance is 500 to 600 mL/minute.

Omeprazole can prolong the elimination of diazepam, warfarin, and phenytoin. Reports have also suggested that it interacts with other drugs metabolized by the cytochrome P-450 system, including cyclosporine, disulfiram, and the benzodiazepines. Dosages may require adjustment when these drugs are taken concomitantly with omeprazole. The absorption of drugs that are dependent on gastric pH for their bioavailability may also be affected by the concomitant administration of omeprazole.

Lansoprazole (Prevacid) is supplied as 15- or 30-mg delayed-release capsules that contain the active drug in enteric-coated granules. This agent's rapid absorption leads to mean peak plasma levels in only 1.7 hours. The drug does not accumulate, and its pharmacokinetic properties are unaltered by repeated dosing.

A 10% increase in the clearance of theophylline has been reported in patients receiving lansoprazole. The absorption of drugs dependent on gastric pH for their bioavailability may be affected by the concomitant administration of lansoprazole.

Rabeprazole (Aciphex) is supplied as 20-mg, delayed-release, enteric-coated tablets. Peak plasma concentrations of rabeprazole occur during a range of 2 to 5 hours, and no appreciable accumulation is evident at dosages of up to 40 mg daily. The pharmacokinetic properties of rabeprazole are not altered by repeated dosing. The plasma half-life ranges from 1 to 2 hours. A more rapid onset of action is one of the main characteristics of rabeprazole.

The metabolism of cyclosporine is inhibited by rabeprazole, and the drug may influence the bioavailability of pH-dependent compounds.

Pantoprazole (Protonix), the newest proton pump inhibitor, has been available in oral form in Europe for about 5 years, where it has been shown to be well tolerated in the elderly. It is supplied as 40-mg enteric-coated tablets and as a freeze-dried powder for reconstitution for intravenous administration. Pantoprazole is expected to be the only proton pump inhibitor available for intravenous administration in the United States, which may make it useful in meeting special needs of elderly patients.

Pantoprazole does not accumulate, and its pharmacokinetic properties are not altered by repeated dosing. The increase in pantoprazole inhibitors may be more cost-effective than surgery for GERD.
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Clearance time in the elderly may not be clinically significant or require dosage adjustment.51,52 Because pantoprazole absorption is unaffected by food intake, it has a minimal effect on meal or medication schedules.51 It may be safe in patients with renal or hepatic impairment, with no dosage adjustment required.53,54 Intravenous and oral pantoprazole show dose equivalence in inhibiting gastric acid secretion and healing erosive esophagitis.35,56 The bioavailability of pH-dependent compounds may be influenced by pantoprazole. Extensive clinical evaluation to date has revealed no clinically significant drug interactions between pantoprazole and commonly used drugs.57

SURGERY

Surgery should be considered in elderly patients who have an extremely low lower esophageal sphincter resting pressure, who are unresponsive to the available medications, or who have developed complications from severe GERD.6,22,25,58

Laparoscopic Nissen-Rossetti fundoplication, currently the procedure of choice, provides excellent long-term relief of GERD symptoms with few complications in 85% to 90% of patients.2,58 Although patient age and the risk of complications must be considered when evaluating any patient for surgery, a recent study showed that current laparoscopic methods are safe and effective for treating GERD in the elderly.22,59 However, because the medical decision analysis by Sonnenberg and colleagues showed the cost of Nissen fundoplication to be approximately equal to 14.5 years of therapy with a proton pump inhibitor, it may be more cost-effective to treat the elderly GERD patient with a proton pump inhibitor.60 Many authorities consider proton pump inhibitor use to be more appropriate in the elderly than invasive therapy.2,5,59,61

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