

Gastroesophageal reflux disease: Important considerations for the older patients

Maxwell M Chait

Maxwell M Chait, Hartsdale Medical Group, Hartsdale, NY 10530, United States

Author contribution: Chait MM contributed solely to this paper. Correspondence to: Maxwell M Chait, MD FACP, FACG, AGAF, FASGE, 180 East Hartsdale Avenue, Hartsdale, NY 10530, United States. mdgi77@aol.com

Telephone: +1-914-7252010 Fax: +1-914-7256488

Received: October 28, 2010 Revised: November 29, 2010

Accepted: December 6, 2010

Published online: December 16, 2010

Abstract

Gastroesophageal reflux disease (GERD) is the most common upper gastrointestinal disorder seen in the elderly. The worldwide incidence of GERD is increasing as the incidence of *Helicobacter pylori* is decreasing. Although elderly patients with GERD have fewer symptoms, their disease is more often severe. They have more esophageal and extraesophageal complications that may be potentially life threatening. Esophageal complications include erosive esophagitis, esophageal stricture, Barrett's esophagus and adenocarcinoma of the esophagus. Extraesophageal complications include atypical chest pain that can simulate angina pectoris; ear, nose, and throat manifestations such as globus sensation, laryngitis, and dental problems; pulmonary problems such as chronic cough, asthma, and pulmonary aspiration. A more aggressive approach may be warranted in the elderly patient, because of the higher incidence of severe complications. Although the evaluation and management of GERD are generally the same in elderly patients as for all adults, there are specific issues of causation, evaluation and treatment that must be considered when dealing with the elderly.

© 2010 Baishideng. All rights reserved.

Key words: Gastroesophageal reflux disease; Older patient; Elderly

Peer reviewers: Shinji Nishiwaki, MD, PhD, Director, Department of Internal Medicine, Nishimino Kosei Hospital, Yorocho, Yoro-gun, Gifu 503-1394, Japan; Kaushal Kishor Prasad, MD, PDCC, Associate Professor, Chief, Division of GE Histopathology, Department of Superspeciality for Gastroenterology, Postgraduate Institute of Medical Education and Research, Sector-12, Chandigarh, UT 160012, India

Chait MM. Gastroesophageal reflux disease: Important considerations for the older patients. *World J Gastrointest Endosc* 2010; 2(12): 388-396 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v2/i12/388.htm> DOI: <http://dx.doi.org/10.4253/wjge.v2.i12.388>

INTRODUCTION

Gastroesophageal reflux disease (GERD) is the most common upper gastrointestinal disorder encountered in the elderly patient. It is highly prevalent worldwide with a prevalence of 10%-20% in the western world^[1-4]. It is estimated that GERD affects 18.6 million people in the United States^[5,6]. The prevalence of weekly symptoms has increased to an annual rate of approximately 5% in North America^[4]. In the US adult population, 10%-20% of people have symptoms at least once weekly and 15%-40% of people have symptoms at least once monthly^[4]. Among adult patients with GERD who seek medical care, up to 20% have serious complications^[7]. There has been an increasing incidence of GERD and its complications, including Barrett's esophagus and adenocarcinoma of the esophagus, throughout the world^[8-9]. No causal relationship has been demonstrated between *Helicobacter pylori* (*H. Pylori*) infection and gastroesophageal reflux disease. In fact, there is an inverse relationship of the prevalence of GERD to that of *H. Pylori* infection^[10-11].

GERD has direct impact on quality of life, especially in the elderly. GERD patients reported a lower quality of life than unaffected individuals, especially in those with nighttime GERD^[12]. In one study, 78% of GERD

patients reported nocturnal symptoms and 63% of those patients reported that sleep was negatively affected^[13].

GERD has a significant economic impact. In the US direct costs of medical consultations, testing and treatment total 9.3 billion dollars. In addition, indirect costs in the US of absenteeism and interference with job performance, which is termed presenteeism, total 75 billion dollars^[14-15].

Although there is a tendency to reduced symptom frequency of the usual complaints of heartburn and acid regurgitation in older patients, the frequency of GERD complications, such as erosive esophagitis, esophageal stricture, Barrett's esophagus, and esophageal cancer is significantly higher^[6]. For example, Collen *et al* found an increase of esophagitis and Barrett's esophagus in patients over 60 years of age compared to those younger, 81% versus 47%^[16]. Huang *et al*^[17] found more severe gastroesophageal reflux and esophageal lesions in elderly patients, as compared to younger patients. Therefore, elderly patients with GERD are at greater risk than younger patients for developing serious complications of GERD.

PATHOGENESIS

GERD is defined as symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus^[18]. A newer definition has been adopted which states that GERD is a condition that develops when reflux of gastric contents causes troublesome symptoms and/or complications^[19]. The abnormalities that appear to play a pathogenic role in GERD tend to be more severe in the elderly patient and lead to the increased rate of GERD complications.

Injury to the esophagus is due to reflux of gastric acid and pepsin. However, duodenogastric reflux of bile may also cause esophageal injury^[20]. The pathogenic abnormalities causing GERD include a defective antireflux barrier, abnormal esophageal clearance, reduced salivary production, altered esophageal mucosal resistance, and delayed gastric emptying.

The lower esophageal sphincter (LES) is the antireflux barrier^[6]. GERD most often occurs as a result of transient LES relaxations (tLESRs), where the drop in LES pressure is not accompanied by swallowing. The tLESRs promote acid reflux and the constellation of GERD problems. Incompetence of the LES was shown by Huang *et al*^[17] to be more prevalent in the elderly. Furthermore, multiple medications more frequently taken by the elderly for co-morbid illnesses, such as hypertension, cardiovascular disease, and pulmonary disease and depression are well known to decrease LES pressure. These include nitrates, calcium channel blockers, benzodiazepines, anticholinergic agents, and antidepressants. The frequency of hiatal hernia and the loss of the diaphragmatic "pinch" which impairs the function of the LES and the clearance of refluxed acid from the distal esophagus also appear to increase with age^[21].

Esophageal acid clearance is impaired in the elderly

due to disturbances of esophageal motility and saliva production. In elderly patients, there is a significant decrease in the amplitude of peristaltic contraction and an increase in the frequency of nonpropulsive and repetitive contractions compared to younger individuals, often referred to as presbyesophagus^[21]. Salivary production slightly decreases with age and is associated with a significantly decreased salivary bicarbonate response to acid perfusion of the esophagus^[22]. Many of the medications noted above taken by elderly patients adversely affect esophageal motility as well as the LES. Many diseases that can negatively affect esophageal motility appear with greater frequency with advancing age, such as Parkinson's disease, cerebrovascular disease, cardiovascular disease, pulmonary disease and diabetes mellitus.

Gastric dysmotility with delayed gastric emptying and duodenogastric reflux of bile plays a significant role in GERD pathogenesis in elderly patients and is an important consideration in elderly patients that poorly respond to acid reducing medication. Delayed gastric emptying and duodenogastric reflux may be a significant cause of non-erosive reflux disease (NERD) and non-ulcer dyspepsia (NUD). Many of the medications taken by elderly patients that adversely affect esophageal motility as well as the LES also negatively affect gastric dysmotility with delayed gastric emptying and duodenogastric reflux^[20].

Direct esophageal injury occurs more frequently in the elderly, because of medications given for co-morbid illnesses such as cardiovascular diseases, cerebrovascular disease, arthritis and osteoporosis that can directly injure the esophageal mucosa. These medications include nonsteroidal anti-inflammatory drugs (NSAIDs), potassium tablets, iron supplements and bisphosphonates.

Reduced pain perception can increase the rate of GERD complications in the elderly, because acid injury can occur without the usual warning symptom significant heartburn and acid reflux symptoms^[7]. Gastric acid secretion per se does not decrease with age alone. However, there is a decrease in esophageal pain perception with advancing age^[21]. In addition, atrophic gastritis is more common in the elderly^[23]. It may be associated with anti-parietal cell antibodies and pernicious anemia. *H. pylori* is also associated with decreased acid production and reduced acid reflux symptoms^[10-11].

Lifestyle factors can be associated with increased gastroesophageal reflux and more complications of GERD^[7]. Tobacco smoking, caffeine, alcohol and fatty foods adversely affect GERD. Obesity, sedentary lifestyle and nocturnal gastroesophageal reflux are important mechanisms that are associated with more severe esophageal and extraesophageal complications of GERD in the elderly^[12-13]. Obesity is a significant problem which increases acid reflux and thus increases GERD and its complications^[24]. Nocturnal effects on GERD are reported by up to 78% of patients, with 75% of patients reporting that it negatively affects their ability to sleep^[12]. Nocturnal gastroesophageal reflux and the recumbent, supine position remove the protective effect of gravity in GERD

Table 1 Complications of gastroesophageal reflux disease

Esophageal
Erosive esophagitis
Esophageal stricture
Barrett's esophagus
Esophageal adenocarcinoma
Extraesophageal
Atypical noncardiac chest pain
ENT complications
Globus sensation
Pharyngitis
Sinusitis
Otitis media
Dental erosions
Hoarseness
Laryngitis
Vocal cord granulomas
Subglottic stenosis
Laryngeal cancer
Pulmonary complications
Chronic cough
Asthma
Chronic bronchitis
Pulmonary fibrosis
Aspiration pneumonia
Sleep apnea

ENT: ear, nose, and throat.

in the elderly patient^[26-27]. Nocturnal GERD allows for more gastroesophageal reflux and further increases esophageal injury and GERD complications, especially in elderly patients who often spend more time in bed due to comorbid illness, such as dementia, Parkinson's disease, cerebrovascular disease, cardiovascular disease, pulmonary disease and diabetes mellitus.

The worldwide variation in incidence of GERD may be inversely related to the prevalence of *H. Pylori* infection^[11]. Studies have found a negative association between the prevalence of *H. Pylori* infection and GERD that is more marked with the more virulent CagA strains^[27]. Additionally, they have shown a negative association of *H. Pylori* status and the complications of GERD including Barrett's esophagus and esophageal adenocarcinoma^[27]. A study by Labins revealed a possible protective effect of *H. Pylori* infection in the subgroup analysis of patients with severe esophagitis^[10]. In a study from China, a stepwise relationship was found between increasing grade of esophagitis and decreasing prevalence of *H. Pylori*^[28]. In a Swedish study, *H. Pylori* was found to be associated with a significantly decreased risk of adenocarcinoma of the esophagus^[29]. A subgroup analysis showed that the negative association was only apparent for the CagA positive strains of *H. Pylori*.

CLINICAL PRESENTATION

The most common symptoms of GERD are heartburn and acid regurgitation^[30]. Other common symptoms include water brash, belching, and nausea. Important symptoms that herald more severe disease include dysphagia,

odynophagia, anemia, unexplained weight loss, and gastrointestinal bleeding^[31].

Heartburn is characterized by epigastric and retrosternal burning pain that may radiate to the neck, throat, and back. It often occurs after large meals, exercise, or reclining. Remarkably, the frequency of severe heartburn seems to decline with age, possibly due to a decrease in esophageal pain perception and atrophic gastritis. Dysphagia, difficulty in swallowing, is an important symptom that has been reported in 7% to 22% of the general population. In the frail elderly nursing home patient dysphagia is reported in 40% to 50% of patients^[32]. When it occurs in response to both solids and liquids or more to liquids than solids, it may be related to esophageal dysmotility due to disease states more common in the elderly, such as Parkinson's disease, cerebrovascular disease, dementia and diabetes. However, when it occurs in response to solids more than liquids, it may be structural in nature and due to severe esophagitis, esophageal stricture or esophageal cancer

Other important symptoms that signify more severe disease are odynophagia, anemia, unexplained weight loss, and gastrointestinal bleeding. These may signal problems such as severe esophagitis, esophageal ulcer, esophageal stricture, Barrett's esophagus or esophageal cancer.

Extrasophageal symptoms occur more commonly in the elderly. They include atypical chest pain that can simulate angina pectoris; ear, nose, and throat (ENT) manifestations such as globus sensation, laryngitis, and dental problems; pulmonary problems such as chronic cough, asthma, and pulmonary aspiration and sleep apnea^[33].

COMPLICATIONS

Complications of GERD that are potentially severe are more common in the elderly. Among patients with GERD seeking medical care in the United States, 20% have complications^[7]. Complications may be esophageal or extraesophageal in nature and may vary from mild esophagitis to major life threatening problems such as recurrent pulmonary aspiration, Barrett's esophagus, and esophageal cancer^[7,9] (Table 1).

Esophageal complications

As in younger patients, the most common complication of GERD in the elderly is esophagitis. This may progress from non-erosive esophagitis (NERD) to severe esophageal erosions, ulcerations and hemorrhage^[33]. Esophageal stricture occurs in up to 10% of patients who have reflux esophagitis, especially in elderly men. Esophageal strictures are often associated with the use of NSAIDs. Treatment with esophageal dilatation and aggressive antireflux therapy is usually effective.

An important and increasingly common esophageal complication is Barrett's esophagus, in which columnar epithelium replaces squamous epithelium in the distal esophagus^[34]. Barrett's esophagus is a premalignant condition highly associated with the development of adenocarcino-

ma of the esophagus and the gastric cardia. It is found in approximately 10%-15% of patients with GERD symptoms who undergo endoscopic examinations. It is more common in elderly Caucasian men over the age of 60^[9]. Although its pathogenesis remains uncertain, acid reflux appears to injure the squamous epithelium and promote epithelial repair by columnar metaplasia of the esophageal mucosa. Because of the frequency and importance of Barrett's esophagus, upper GI endoscopy should be considered in all elderly patients with recurrent reflux symptoms. Patients with Barrett's esophagus must be evaluated with multiple biopsies to look for the presence of dysplasia, which is the precursor of invasive cancer. Continued endoscopic surveillance and aggressive measures, especially in high-grade dysplasia, are warranted to prevent adenocarcinoma of the esophagus. These measures include endoscopic ablative techniques such as endoscopic mucosal resection, electrocautery fulguration, laser photoablation, photodynamic therapy. Surgical esophagectomy in good operative risk patients with severe dysplasia is warranted^[9].

Adenocarcinoma of the esophagus is among the fastest growing carcinomas by incidence in the United States where it has become the most common form of esophageal cancer^[9]. The incidence of adenocarcinoma in patients with Barrett's esophagus is approximately 1% per year. Patients with esophageal cancer typically present in the seventh or eighth decade of life with weight loss and dysphagia. Although the overall survival rate of patients with adenocarcinoma of the esophagus is less than 10%, those with early stage cancer identified in surveillance programs usually have a higher survival rate^[35].

Extraesophageal complications

Extraesophageal complications of GERD are more common in the elderly^[33]. These include atypical noncardiac chest pain; ear, nose, and throat (ENT) manifestations, such as globus sensation, laryngitis, otitis media, sinusitis, pharyngitis, hoarseness, vocal cord granulomas, subglottal stenosis, laryngeal cancer, dental erosions; pulmonary problems, such as asthma, chronic cough, chronic bronchitis, pulmonary fibrosis, aspiration pneumonia and sleep apnea.

Atypical noncardiac chest pain has been related to GERD in up to 60% of cases. In 50% of cases symptoms are related directly to reflux injury and in 10% symptoms are related to esophageal dysmotility. Atypical noncardiac chest pain due to GERD may often be indistinguishable from angina pectoris^[36]. Therefore, a cardiac evaluation is indicated in these elderly patients before ascribing symptoms to GERD alone.

Ear, nose, and throat (ENT) complications of GERD are frequent in the elderly with laryngitis being the most common. In up to 10% of patients with hoarseness, acid peptic injury from reflux is the cause. Acid injury can also cause globus sensation, otitis media, sinusitis, pharyngitis, hoarseness, dental erosions, vocal cord granulomas, subglottal stenosis and laryngeal cancer. Prolonged antireflux

therapy may be necessary and is often effective in these patients. However, prompt relapses occur when therapy is discontinued^[37].

Pulmonary complications of GERD are common in the elderly. Conditions include asthma, chronic cough, chronic bronchitis, pulmonary fibrosis, aspiration pneumonia and sleep apnea are all seen more frequently in the elderly. In up to 21% of patients with chronic cough, GERD is the cause^[38]. Remarkably, chronic cough can be the only symptom of GERD in some patients. The mechanism for the development of pulmonary complications is not only pulmonary aspiration of refluxed material but also involves a neurally mediated reflex bronchoconstriction due to esophageal irritation by acid^[38]. As with ENT manifestations, antireflux therapy is often helpful with a prompt recurrence occurring upon discontinuation of therapy.

EVALUATION

Diagnostic testing in older patients is essentially the same as for younger patients with GERD^[39]. However, because of the higher incidence of complications in the elderly that may be severe and life threatening, an aggressive approach with prompt evaluation is warranted^[7]. Barium swallow upper GI series and upper GI endoscopy are used to evaluate dysphagia and mucosal injury. Endoscopy is superior to the barium swallow exam, but must be used with caution in the elderly frail patient. Capsule endoscopy is evolving as a modality to evaluate the upper GI tract. It is less invasive than routine upper GI endoscopy and may be an alternative in the elderly patient. In patients with atypical symptoms or when quantification of reflux is required, ambulatory pH monitoring is helpful, but may be difficult to perform in the elderly patient. Wireless probes may improve compliance^[40]. Multichannel intraluminal impedance measurement with a pH sensor allows the detection of pH episodes irrespective of their pH values (acid and nonacid reflux). This is useful in the postprandial period, in patients with persistent symptoms while on therapy and in those patients with atypical symptoms^[41]. Esophageal manometry is often used in patients with markedly atypical symptoms, for locating the LES for pH testing, and in those for whom surgery is contemplated. However, it is not useful for the evaluation of GERD in the majority of patients.

The proton pump inhibitor (PPI) test has become a useful noninvasive test in elderly GERD patients for the evaluation atypical chest pain. Patients are given a course of high dose PPI agent, such as omeprazole 60 mg per day for 7 d, and observed for improvement in their clinical response^[42]. However, this does not supplant the use of endoscopy in patients with significant symptoms, such as odynophagia and dysphagia.

Diagnostic testing should be performed in patients in whom the diagnosis remains uncertain; in patients with atypical symptoms such as chest pain, ENT problems, or pulmonary complications; in patients with significant

Table 2 Noninvasive treatment of gastroesophageal reflux disease¹**Lifestyle modification**

Elevation of head of bed
 Avoid eating within 3 h of bedtime
 Avoid tobacco, alcohol, caffeine, fatty food, peppermint
 Avoid harmful medications if possible, such as NSAIDs, beta blockers
 Calcium-channel blockers, theophylline, potassium tablets, bisphosphonate

Medications**Antacids****Motility agents:**

Metoclopramide, erythromycin, bethanechol, cisapride, GABA

B-receptor agonists**H₂ receptor antagonists:**

Cimetidine, famotidine, nizatidine, ranitidine

PPI agents¹:

Esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole, dexlansoprazole

GABA: Gamma-aminobutyric acid B-receptor agonist; NSAIDs: non-steroidal anti-inflammatory drugs; H₂: histamine₂; PPI: proton pump inhibitor; ¹Most often successful.

symptoms that are often associated with complications such as dysphagia, odynophagia, unexplained weight loss, GI hemorrhage, and anemia; in patients who have an inadequate response to therapy, whether medical or surgical; in patients with recurrent symptoms; and in patients prior to consideration of antireflux surgery^[43].

There are important considerations relating to diagnostic and treatment methods in elderly patients^[44]. In cognitively impaired patients, a Mini-Mental State Examination may be indicated. Informed consent to procedures may be difficult to obtain in patients who suffer from cognitive dysfunction. With the exception of a true life-threatening emergency, every attempt should be made to obtain consent for testing procedures from the patient, if competent, or the surrogate. In cases where a guardian cannot be reached, administrative consent should be obtained. Timing of tests and type of intervention should be tailored, especially for the frail elderly patient, depending upon functional status, its impact on outcome, and the available diagnostic strategies. However, intervention should not be withheld because of age alone.

Older patients are more likely to have pacemakers with or without defibrillators. Recommendations for management of patients who require endoscopy and have pacemakers and internal defibrillators are not well defined. Cardiology consultation may often be indicated. If required, alternative means of tissue removal, destruction, or hemostasis should be considered to simplify management of patients. For example, to control hemorrhage in the bleeding patient with a defibrillator one may need to use such methods as hemo-clips, ligation devices, and injection of epinephrine and sclerosing agents. The general principle of geriatric pharmacology of starting with low doses of medication and slowly advancing to larger doses is an important dictum in conscious sedation of the elderly patient during endoscopy. Initial dosages should be lower and titration should be more gradual^[44].

Deeper sedation that requires an anesthesiologist may be warranted in difficult cases.

In contrast to younger patients, endoscopy should be considered as the initial diagnostic test in elderly patients with heartburn, regardless of the severity or duration of complaints. This aggressive approach is warranted because of the higher incidence of cumulative acid injury over time and the higher incidence of complications of Barrett's esophagus and esophageal cancer in the elderly^[16].

TREATMENT

Treatment of GERD in the elderly patient is essentially the same as in all adults with GERD^[33]. However, a more aggressive approach to treatment is necessary in the elderly patient, because of the higher incidence of complications^[16]. This aggressive approach must be balanced with the constraints of dealing with an older often frailer patient with comorbidities. The treatment goals, as in all patients with GERD, are elimination of symptoms, healing of esophagitis, managing or preventing complications, and maintaining remission^[43]. The vast majority of patients can be treated successfully with the noninvasive methods of lifestyle modification and medication^[43] (Table 2).

Although lifestyle modification remains a cornerstone of initial therapy in GERD, it may not be sufficient to control symptoms in the majority of patients, especially in those with complications. However, patients should try to lose weight, be more active, elevate the head of their bed before going to sleep, avoid eating within three hours of bedtime, stop tobacco smoking, decrease dietary fat and volume of meals and avoid dietary irritants such as alcohol, peppermint, onion, citrus juice, coffee, and tomatoes.

Potentially harmful medications that can aggravate the symptoms and effects of GERD in the elderly, such as NSAIDs, potassium tablets, bisphosphonates, beta blockers, theophylline and calcium-channel blockers should be avoided if possible. If these agents must be continued because of comorbid illness, the regimen should be modified on an individual basis, such as switching potassium tablets to an elixir or using an alternative medication or dosing frequency in the osteoporotic patient on bisphosphonates. All medications should be given with 6-8 ounces of water in an upright position.

Over-the-counter antacids, histamine (H₂) blockers and PPI agents on an as-needed basis may be helpful for those individuals who have mild disease. However, for the majority of patients, and certainly for those patients with complications, one must use prescription agents for more effective therapy^[7].

Motility agents, such as cisapride, metoclopramide, erythromycin, bethanechol and the gamma-amino butyric acid B-receptor (GABA) agonist Baclofen have helped to improve LES tone and esophagogastric motility in selected patients^[44]. However, their success is limited in patients with more severe disease. For patients with diabetes, cisapride and metoclopramide have been used with moderate success in improving gastric emptying and re-

Table 3 Potential effects of prolonged acid suppression with histamine₂ receptor antagonists and PPI agents

Reduced absorption of nutrients and calcium
B ₁₂ , iron, calcium
Osteoporosis
Bacterial proliferation
Community acquired pneumonia
<i>Clostridium difficile</i>
Drug metabolism interference
Acid effects on drug absorption
PPI Effects on CYP2C19 pathway interference
Clopidogrel
Histamine ₂ receptor antagonists effects on cytochrome P-450 3A4 system
Warfarin, phenytoin, benzodiazepines, theophylline
Drug side effects
Delirium, especially cimetidine
Neurologic
Antiandrogen
Cardiac side effects
Hematologic

PPI: proton pump inhibitor.

ducing GERD symptoms. However, cisapride is only available on a restricted-use basis due to potentially fatal cardiac arrhythmias. Metoclopramide must be used with caution in the elderly, because it can cause side effects, such as muscle tremors, spasms, agitation, insomnia, drowsiness, and tardive dyskinesia, in up to one-third of patients. Erythromycin use is limited by its side effects and tachyphylaxis. Bethanechol has not proved useful in GERD. Gamma-amino butyric acid B-receptor (GABA) agonists, such as Baclofen, reduce tLESRs and improve gastric emptying. However, side effects that are more common in the elderly, such as somnolence, confusion, dizziness, light-headedness, weakness and trembling, limit their use in the older patient. Newer agents are under investigation^[45].

Histamine H-2 receptor antagonists, including cimetidine, ranitidine, famotidine, and nizatidine, are helpful in patients with GERD, by providing good acid suppression and symptom relief. These drugs are remarkably similar in their action and equally effective at equivalent doses. However, high doses of up to four times daily may be necessary in some patients with severe symptoms. Reducing dosage because of renal insufficiency, which is more common in the elderly, is often necessary. In addition, all these agents, especially cimetidine, can cause delirium in the older patient. Drug-drug interactions with histamine H-2 receptor antagonists through metabolism of the hepatic cytochrome P-450 3A4 system may be potentially harmful in elderly patients who use medications such as warfarin, phenytoin, benzodiazepines, and theophylline. Side effects of these agents, especially cimetidine, are more common in the elderly and in those with comorbid illnesses. Side effects include central nervous system side effects, such as mental confusion, delirium, headache, and dizziness; antiandrogen side effects of gynecomastia and impotence; cardiac side effects of sinus bradycardia, atrioventricular block, and prolongation of the QT interval;

and hematological side effects of anemia, neutropenia, and thrombocytopenia. However, most side effects are reversible with dosage reduction or withdrawal of the offending agent^[7].

Proton pump inhibitors (PPIs), such as esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole, and dexlansoprazole are the most effective medical therapeutic agents for the treatment of GERD. Proton pump inhibitors provide excellent acid suppression and effective symptom relief^[43]. These agents are particularly useful in elderly persons who often require more acid suppression due to more severe disease and complications. In older patients who are unable to swallow pills, capsules may be opened and the granules mixed in water or juice or sprinkled on applesauce or yogurt. For example, lansoprazole is available as an orally dissolving tablet and both lansoprazole and omeprazole powder are available as oral suspensions, which may be useful for those with swallowing disorders or those who require tube feedings.

Maintenance therapy is most often required, because relapses are common in elderly patients with GERD, especially those with associated complications. Long-term treatment with adequate doses of medication is the key to effective care in the elderly. For the majority of patients with esophageal strictures, the use of acid suppression and esophageal dilatation are effective. Aggressive acid suppression is effective in the majority of patients with GERD-related atypical chest pain. ENT complications, such as hoarseness, show dramatic response to these agents when adequate doses are used for prolonged periods. In patients with GERD-mediated asthma, significant improvement will occur with acid suppression by H₂ blockers and PPIs. Maintenance therapy is required in all of these patients because relapses occur very soon after cessation of therapy. In patients with Barrett's esophagus, chronic medical therapy is warranted, although its success remains controversial^[45].

POTENTIAL EFFECTS OF PROLONGED ACID SUPPRESSION

Prolonged acid suppression by Histamine H-2 receptor antagonists and PPI agents may potentially affect nutrient and calcium absorption, bacterial proliferation, and drug metabolism in the older patient. However, with adequate monitoring, long term maintenance with PPI agents remains quite safe in the elderly population^[46] (Table 3).

Vitamin B₁₂, iron and calcium absorption can be affected. The effect on B₁₂ and iron absorption appears to be insignificant, but periodic monitoring for anemia and reduced B₁₂ and iron stores may be warranted^[47].

Reduction of calcium absorption and the potential development or worsening of osteoporosis and resultant bone fracture is a significant but controversial issue. Reduction in bone density and increased incidence of hip fractures has been reported with both PPI agents and Histamine H-2 receptor antagonists^[48]. If these agents are used for maintenance therapy, patients should be monitored for

Table 4 Invasive treatment of gastroesophageal reflux disease endoscopic therapy

Evolving techniques
Non-biodegradable polymer
Radiofrequency treatment of the gastroesophageal junction
Endoscopic suturing
Implantable gastric electrodes
Botulinum injection of the pylorus
Ablative techniques for Barrett's esophagus
Endoscopic mucosal resection
Electrocautery fulguration
Laser photoablation
Photodynamic therapy
Surgery
Laparoscopic fundoplication

osteoporosis as per recommended guidelines and given adequate intake of calcium and vitamin D. If osteoporosis is detected, treatment with appropriate agents, such as bisphosphonates should be offered. Withdrawal of acid suppression agents with worsening bone health in elderly patients must be considered.

Bacterial proliferation with an increased incidence of community acquired pneumonia and the development of gastrointestinal infection, such as *Clostridium difficile* associated colitis, has been reported and is important, although a controversial issue in the elderly patient. These patients have a higher incidence of comorbidities and more often are in hospitals or long term care facilities. This would predispose them to frequent and more serious infections. Restriction of acid suppressant use in this regard remains controversial^[49-50].

Interference of acid suppressant agents with drug metabolism is an issue. Acid inhibition may affect absorption of some drugs. Recently, interference with drug metabolism has become an issue with clopidogrel, which is often used for anticoagulation in the elderly. Omeprazole competitively interferes with conversion of clopidogrel to its active metabolite through the CYP2C19 pathway. The significance of this interference remains controversial, but switching to another PPI that may not significantly use this pathway, such as pantoprazole, lansoprazole or rabeprazole or switching to a Histamine H-2 receptor antagonist may be warranted^[51].

Histamine H-2 receptor antagonists, especially cimetidine, can cause delirium in the older patient. Drug-drug interactions with histamine H-2 receptor antagonists through metabolism of the hepatic cytochrome P-450 3A4 system may be potentially harmful in elderly patients who use medications such as warfarin, phenytoin, benzodiazepines, and theophylline. Side effects of these agents, especially cimetidine, are more common in the elderly and in those with comorbid illnesses. Side effects include central nervous system side effects, such as mental confusion, delirium, headache, and dizziness; antiandrogen side effects of gynecomastia and impotency; cardiac side effects of sinus bradycardia, atrioventricular block, and prolongation of the QT interval; and hematological side effects of anemia, neutropenia, and thrombocytopenia. However, most side

effects are reversible with dosage reduction or withdrawal of the offending agent^[7].

Although the vast majority of elderly patients with complications associated with GERD can be successfully managed with medical therapy, invasive methods of surgery and endoscopic treatment may be warranted in some cases. Surgery is an option for some patients with GERD^[52] and is now more frequently considered because of the ability to perform antireflux surgery laparoscopically. It is indicated in patients with intractable GERD, difficult-to-manage strictures, severe bleeding, nonhealing ulcers, recurrent aspiration, and GERD requiring large maintenance doses of PPI agents or H-2 receptor antagonists. Barrett's esophagus alone is not an indication for surgery. However, surgery is warranted for high grade dysplasia and esophageal adenocarcinoma. Given that there appears to be no greater increase in postoperative morbidity or mortality in the elderly with this type of surgery, healthy elderly patients should not be denied surgery on the basis of age alone^[53]. Careful patient selection with complete preoperative evaluation, including upper GI endoscopy, esophageal manometry, pH testing, and gastric emptying studies, should be done prior to surgery.

Endoscopic therapy of GERD has had little success. Implantation of a biocompatible, non-biodegradable polymer (Enteryx) into the gastric cardia and radiofrequency energy delivery to the gastroesophageal junction, the Stretta Procedure, are available for the treatment of GERD on an investigational basis only^[54-55]. Endoscopic suturing below the gastroesophageal junction is possible and has been used with some success to treat GERD^[56]. However, further investigation and perfection of this technique is warranted. Pyloric injections of botulinum toxin in patients with refractory GERD and gastroparesis has had limited short term success. Endoscopic ablative techniques for treatment of Barrett's esophagus are evolving. They include endoscopic mucosal resection, electrocautery fulguration, laser photoablation and photodynamic therapy. Implantable gastric electrodes and botulinum injection of the pylorus to improve gastric emptying are further techniques being evaluated to reduce gastroesophageal reflux. Additional evaluation of these therapeutic techniques is warranted^[57] (Table 4).

CONCLUSION

GERD and its associated complications are common in the older patient. The elderly tend to have fewer symptoms with more severe complications that may be life threatening. There are important considerations regarding causation, evaluation and treatment in the older as compared to the younger patient. However, with appropriate management, GERD and its associated complications can be treated successfully in majority of elderly patients.

REFERENCES

- 1 Shaheen NJ, Hansen RA, Morgan DR, Gangarosa LM, Ringel

- Y, Thiny MT, Russo MW, Sandler RS. The burden of gastrointestinal and liver diseases, 2006. *Am J Gastroenterol* 2006; **101**: 2128-2138
- 2 **Fujiwara Y**, Higuchi K, Watanabe Y, Shiba M, Watanabe T, Tominaga K, Oshitani N, Matsumoto T, Nishikawa H, Arakawa T. Prevalence of gastroesophageal reflux disease and gastroesophageal reflux disease symptoms in Japan. *J Gastroenterol Hepatol* 2005; **20**: 26-29
 - 3 **Wong WM**, Lai KC, Lam KF, Hui WM, Hu WH, Lam CL, Xia HH, Huang JQ, Chan CK, Lam SK, Wong BC. Prevalence, clinical spectrum and health care utilization of gastro-oesophageal reflux disease in a Chinese population: a population-based study. *Aliment Pharmacol Ther* 2003; **18**: 595-604
 - 4 **El-Serag HB**. Time trends of gastroesophageal reflux disease: a systematic review. *Clin Gastroenterol Hepatol* 2007; **5**: 17-26
 - 5 **Sandler RS**, Everhart JE, Donowitz M, Adams E, Cronin K, Goodman C, Gemmen E, Shah S, Avdic A, Rubin R. The burden of selected digestive diseases in the United States. *Gastroenterology* 2002; **122**: 1500-1511
 - 6 **Johnson DA**, Fennerty MB. Heartburn severity underestimates erosive esophagitis severity in elderly patients with gastroesophageal reflux disease. *Gastroenterology* 2004; **126**: 660-664
 - 7 **Chait MM**. Complications of gastroesophageal reflux disease in the elderly. *Annals of Long Term Care* 2005; **13**: 8-32
 - 8 **Robertson D**, Aldersley M, Shepherd H, Smith CL. Patterns of acid reflux in complicated oesophagitis. *Gut* 1987; **28**: 1484-1488
 - 9 **Lagergren J**, Bergström R, Lindgren A, Nyrén O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *N Engl J Med* 1999; **340**: 825-831
 - 10 **Labenz J**, Jaspersen D, Kulig M, Leodolter A, Lind T, Meyer-Sabellek W, Stolte M, Vieth M, Willich S, Malfertheiner P. Risk factors for erosive esophagitis: a multivariate analysis based on the ProGERD study initiative. *Am J Gastroenterol* 2004; **99**: 1652-1656
 - 11 **Chait MM**. The association and clinical implications of gastroesophageal reflux disease and H pylori. *Practical Gastroenterology* 2006; **30**: 40-48
 - 12 **Farup C**, Kleinman L, Sloan S, Ganoczy D, Chee E, Lee C, Revicki D. The impact of nocturnal symptoms associated with gastroesophageal reflux disease on health-related quality of life. *Arch Intern Med* 2001; **161**: 45-52
 - 13 **Shaker R**, Castell DO, Schoenfeld PS, Spechler SJ. Nighttime heartburn is an under-appreciated clinical problem that impacts sleep and daytime function: the results of a Gallup survey conducted on behalf of the American Gastroenterological Association. *Am J Gastroenterol* 2003; **98**: 1487-1493
 - 14 American Gastroenterological Association (AGA). The burden of gastrointestinal disease. Bethesda, Md: AGA, 2001
 - 15 **Brook RA**, Wahlqvist P, Kleinman NL, Wallender MA, Campbell SM, Smeeding JE. Cost of gastroesophageal reflux disease to the employer: a perspective from the United States. *Alim Pharmacol Ther* 2007; **26**: 889-898
 - 16 **Collen MJ**, Abdulian JD, Chen YK. Gastroesophageal reflux disease in the elderly: more severe disease that requires aggressive therapy. *Am J Gastroenterol* 1995; **90**: 1053-1057
 - 17 **Huang X**, Zhu HM, Deng CZ, Porro GB, Sangaletti O, Pace F. Gastroesophageal reflux: the features in elderly patients. *World J Gastroenterol* 1999; **5**: 421-423
 - 18 **DeVault KR**, Castell DO. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol* 2005; **100**: 190-200
 - 19 **Vakil N**, van Zanten SV, Kahrilas P, Dent J, Jones R. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006; **101**: 1900-1920; quiz 1943
 - 20 **Ferrioli E**, Oliveira RB, Matsuda NM, Braga FJ, Dantas RO. Aging, esophageal motility, and gastroesophageal reflux. *J Am Geriatr Soc* 1998; **46**: 1534-1547
 - 21 **Fass R**, Pulliam G, Johnson C, Garewal HS, Sampliner RE. Symptom severity and oesophageal chemosensitivity to acid in older and young patients with gastro-oesophageal reflux. *Age Ageing* 2000; **29**: 125-130
 - 22 **Sonnenberg A**, Steinkamp U, Weise A, Berges W, Wienbeck M, Rohner HG, Peter P. Salivary secretion in reflux esophagitis. *Gastroenterology* 1982; **83**: 889-895
 - 23 **Hurwitz A**, Brady DA, Schaal SE, Samloff IM, Dedon J, Ruhl CE. Gastric acidity in older adults. *JAMA* 1997; **278**: 659-662
 - 24 **Jacobson BC**, Somers SC, Fuchs CS, Kelly CP, Camargo CA Jr. Body-mass index and symptoms of gastroesophageal reflux in women. *N Engl J Med* 2006; **354**: 2340-2348
 - 25 **Orr WC**. Reflux events and sleep: are we vulnerable? *Curr Gastroenterol Rep* 2006; **8**: 202-207
 - 26 **Mody R**, Bolge SC, Kannan H, Fass R. Effects of gastroesophageal reflux disease on sleep and outcomes. *Clin Gastroenterol Hepatol* 2009; **7**: 953-959
 - 27 **Sharma P**. Recent advances in Barrett's esophagus: short-segment Barrett's esophagus and cardia intestinal metaplasia. *Semin Gastrointest Dis* 1999; **10**: 93-102
 - 28 **Zhang J**, Chen XL, Wang KM, Guo XD, Zuo AL, Gong J. Relationship of gastric Helicobacter pylori infection to Barrett's esophagus and gastro-oesophageal reflux disease in Chinese. *World J Gastroenterol* 2004; **10**: 672-675
 - 29 **Ye W**, Held M, Lagergren J, Engstrand L, Blot WJ, McLaughlin JK, Nyrén O. Helicobacter pylori infection and gastric atrophy: risk of adenocarcinoma and squamous-cell carcinoma of the esophagus and adenocarcinoma of the gastric cardia. *J Natl Cancer Inst* 2004; **96**: 388-396
 - 30 **Traube M**. The spectrum of the symptoms and presentations of gastroesophageal reflux disease. *Gastroenterol Clin North Am* 1990; **19**: 609-616
 - 31 **Räihä JJ**, Impivaara O, Seppälä M, Sourander LB. Prevalence and characteristics of symptomatic gastroesophageal reflux disease in the elderly. *J Am Geriatr Soc* 1992; **40**: 1209-1211
 - 32 **Chait MM**, Saffel D. Gastroesophageal reflux disease in the elderly. *Pharmacy Times*, 2006: 101-107
 - 33 **Richter JE**. Gastroesophageal reflux disease in the older patient: presentation, treatment, and complications. *Am J Gastroenterol* 2000; **95**: 368-373
 - 34 **Spechler SJ**. Barrett's esophagus. *Semin Oncol* 1994; **21**: 431-437
 - 35 **van der Burgh A**, Dees J, Hop WC, van Blankenstein M. Oesophageal cancer is an uncommon cause of death in patients with Barrett's oesophagus. *Gut* 1996; **39**: 5-8
 - 36 **Ruigómez A**, García Rodríguez LA, Wallander MA, Johansson S, Graffner H, Dent J. Natural history of gastro-oesophageal reflux disease diagnosed in general practice. *Aliment Pharmacol Ther* 2004; **20**: 751-760
 - 37 **Wong RK**, Hanson DG, Waring PJ, Shaw G. ENT manifestations of gastroesophageal reflux. *Am J Gastroenterol* 2000; **95**: S15-S22
 - 38 **Irwin RS**, French CL, Curley FJ, Zawacki JK, Bennett FM. Chronic cough due to gastroesophageal reflux. Clinical, diagnostic, and pathogenetic aspects. 1993. *Chest* 2009; **136**: e30
 - 39 **Wong WM**, Wong BC. Definition and diagnosis of gastroesophageal reflux disease. *J Gastroenterol Hepatol* 2004; **19** Suppl 3: S26-S32
 - 40 **Pandolfino JE**, Bianchi LK, Lee TJ, Hirano I, Kahrilas PJ. Esophagogastric junction morphology predicts susceptibility to exercise-induced reflux. *Am J Gastroenterol* 2004; **99**: 1430-1466
 - 41 **Hong SK**, Vaezi MF. Gastroesophageal reflux monitoring: pH (catheter and capsule) and impedance. *Gastrointest Endosc Clin N Am* 2009; **19**: 1-22
 - 42 **Fennerty MB**. Use of a therapeutic trial as a diagnostic test for GERD. *Practical Gastroenterology*. 2004; **28**: 45-50
 - 43 **Kahrilas PJ**. Clinical practice. Gastroesophageal reflux disease. *N Engl J Med* 2008; **359**: 1700-1707
 - 44 **Chait MM**. Lower gastrointestinal bleeding in the elderly. *World J Gastrointest Endosc* 2010; **2**: 147-154

- 45 **Boeckstaens GE**, Beaumont H, Mertens V, Denison H, Ruth M, Adler J, Silberg DG, Sifrim D. Effects of lesogaberan on reflux and lower esophageal sphincter function in patients with gastroesophageal reflux disease. *Gastroenterology* 2010; **139**: 409-417
- 46 **Laine L**, Ahnen D, McClain C, Solcia E, Walsh JH. Review article: potential gastrointestinal effects of long-term acid suppression with proton pump inhibitors. *Aliment Pharmacol Ther* 2000; **14**: 651-668
- 47 **McColl KEI**. Effect of proton pump inhibitors on vitamins and iron. *Am J Gastroenterol* 2009; **104**: S5-S9
- 48 **Laine L**. Proton pump inhibitors and bone fractures? *Am J Gastroenterol* 2009; **104**: S21-S26
- 49 **Dial MS**. Proton pump inhibitor use and enteric infections. *Am J Gastroenterol* 2009; **104**: S17-S20
- 50 **Vakil N**. Acid inhibition and infections outside the gastrointestinal tract. *Am J Gastroenterol* 2009; **104**: S10-S16
- 51 **Ray WA**, Murray KT, Griffin MR, Chung CP, Smalley WE, Hall K, Daugherty JR, Kaltenbach LA, Stein CM. Outcomes with concurrent use of clopidogrel and proton-pump inhibitors: a cohort study. *Ann Intern Med* 2010; **152**: 337-345
- 52 **Spechler SJ**. Comparison of medical and surgical therapy for complicated gastroesophageal reflux disease in veterans. The Department of Veterans Affairs Gastroesophageal Reflux Disease Study Group. *N Engl J Med* 1992; **326**: 786-792
- 53 **Trus TL**, Laycock WS, Wo JM, Waring JP, Branum GD, Mauren SJ, Katz EM, Hunter JG. Laparoscopic antireflux surgery in the elderly. *Am J Gastroenterol* 1998; **93**: 351-353
- 54 **Johnson DA**, Ganz R, Aisenberg J, Cohen LB, Deviere J, Foley TR, Haber GB, Peters JH, Lehman GA. Endoscopic, deep mural implantation of Enteryx for the treatment of GERD: 6-month follow-up of a multicenter trial. *Am J Gastroenterol* 2003; **98**: 250-258
- 55 **Triadafilopoulos G**, DiBaise JK, Nostrant TT, Stollman NH, Anderson PK, Wolfe MM, Rothstein RI, Wo JM, Corley DA, Patti MG, Antignano LV, Goff JS, Edmundowicz SA, Castell DO, Rabine JC, Kim MS, Utey DS. The Stretta procedure for the treatment of GERD: 6 and 12 month follow-up of the U.S. open label trial. *Gastrointest Endosc* 2002; **55**: 149-156
- 56 **Mahmood Z**, McMahon BP, Arfin Q, Byrne PJ, Reynolds JV, Murphy EM, Weir DG. Endocinch therapy for gastroesophageal reflux disease: a one year prospective follow up. *Gut* 2003; **52**: 34-39
- 57 **Dellon ES**, Shaheen NJ. Persistent reflux symptoms in the proton pump era: the changing face of gastroesophageal reflux disease. *Gastroenterology* 2010; **139**: 7-13

S- Editor Zhang HN L- Editor Hughes D E- Editor Liu N