



Gastroesophageal Reflux Disease: Current Evaluation and Management

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Abstract

Gastroesophageal reflux disease (GERD) is the most common upper gastrointestinal disorder in the westernized countries. The worldwide incidence of GERD is increasing as the incidence of *H.Pylori* is decreasing. There are a variety of 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 (ENT) 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. Evaluation and management of GERD are generally the same for all adults. However, there are specific issues of causation, evaluation and treatment that must be considered when dealing with the elderly. In the majority of patients GERD can be successfully managed.

Keywords: Gastroesophageal Reflux Disease (GERD)

Introduction

Gastroesophageal reflux disease (GERD) is the most common upper gastrointestinal disorder in westernized countries. It is highly prevalent worldwide with a prevalence of 10%-20% in the Western world [1-4]. It is estimated that it affects 18.6 million people in the United States [5]. 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 *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. 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 [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].

There are differences among age groups in adults with GERD. 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]. 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. found more severe gastroesophageal reflux and esophageal lesions in elderly patients, as compared to younger patients [17].

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].

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), the drop in LES pressure 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. to be more prevalent in the elderly [17]. Multiple medications more frequently taken 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 appear to increase with age also [21].

Esophageal acid clearance is often impaired due to disturbances of esophageal motility and saliva production. There is a significant decrease in the amplitude of peristaltic contraction and an increase in the frequency of nonpropulsive and repetitive contractions more often in the elderly as compared to younger individuals, often referred to as presbyesophagus [21]. Salivary production slightly decreases

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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 adversely affect esophageal motility as well as the LES. Many diseases can negatively affect esophageal motility and often 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 and are important considerations in 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 same medications taken by patients that adversely affect esophageal motility as well as the LES negatively affect gastric dysmotility with delayed gastric emptying and duodenogastric reflux [20].

Direct esophageal injury can occur, 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, especially in the elderly. Acid injury can occur without the usual warning symptom of significant heartburn and acid reflux [7]. There is an age-related decrease in esophageal pain perception with advancing age [21]. This may be due to atrophic gastritis which is more common in the elderly [23]. It is often 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 of GERD that are associated with more severe esophageal and extraesophageal complications of GERD [12,13]. Obesity is a significant problem that 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 [12,25]. Nocturnal gastroesophageal reflux and the recumbent, supine position remove the protective effect of gravity in GERD, especially in the infirmed and elderly patient [26,27]. Nocturnal GERD allows for more gastroesophageal reflux and further increase esophageal injury and GERD complications, especially in elderly and infirmed 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]. In a study by Labins, *H.Pylori* infection revealed a possible protective effect 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. 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 to both solids and liquids or more to liquids than solids, it may be related to esophageal dysmotility due to disease states, such as Parkinson's disease, cerebrovascular disease, dementia and diabetes. However, when it occurs to solids more than liquids, it may be structural in nature 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. This signals a more severe problem, such as severe esophagitis, esophageal ulcer, esophageal stricture, Barrett's esophagus and esophageal cancer.

Extraesophageal symptoms include atypical chest pain that can simulate angina pectoris; ear, nose, and throat (ENT) manifestations such as globus sensation, laryngitis, and dental problems; and pulmonary problems such as chronic cough, asthma, and pulmonary aspiration and sleep apnea [33].

Complications

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

Esophageal complications

The most common complication of GERD in the elderly is esophagitis. It may progress from non-erosive esophagitis (NERD) to severe esophageal erosions, ulcerations and hemorrhage [33]. Esophageal strictures occur 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 more 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 adenocarcinoma of the esophagus and

Table 1: Complications of Gastroesophageal reflux disease.

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

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 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, Laserphotoablation, 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 noted with increasing frequency [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 relegating symptoms to GERD alone.

Ear, nose, and throat (ENT) complications of GERD have been noted with increasing frequency. Laryngitis is the most common ENT complication of GERD. In upto 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 have also been noted with increasing frequency. They include asthma, chronic cough, chronic bronchitis, pulmonary fibrosis, aspiration pneumonia and sleep apnea. They are noted 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 patient. The mechanism for the development of pulmonary complications is not only pulmonary aspiration of refluxed material. It is also 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 is essentially the same in all 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 often warranted in the older patient [7]. Barium swallow upper GI series and upper GI endoscopy are used to evaluate dysphagia and mucosal injury. Upper GI endoscopy is superior to the barium swallow exam. 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. Wireless probes have improved compliance [40]. Multichannel intraluminal impedance with pH sensor allows the detection of pH episodes irrespective of their pH values (acid and nonacid reflux). It is useful in the postprandial period in patients with persistent symptoms while on therapy and in those patients with atypical symptom [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. 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 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 days, and observed for improvement in their clinical response [42]. However, it does not supplant the use of upper GI 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 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].

Upper GI endoscopy should not be withheld due to age alone. It should be considered earlier 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 is essentially the same 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 times frailer patient with comorbidities. The treatment goals 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 (Table 2) [43].

Noninvasive therapy

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 beds 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, 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 biphosphonates. All medications should be given with 6-8 ounces of water in an upright position.

Over-the-counter antacids, histamine₂ (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 reducing GERD symptoms. However, cisapride is only available on a restricted use basis due to potentially fatal cardiac arrhythmias. Metoclopramide must be used with caution, especially 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) agonist, such as Baclofen reduces tLESRs and improves gastric emptying. However, side effects that are more common in the elderly, such as somnolence, confusion, dizziness, lightheadedness, weakness and trembling, limit its use in the older patient. Newer agents are under investigation [45].

Histamine₂ receptor antagonists, including cimetidine, ranitidine, famotidine, and nizatidine, are helpful in patients with GERD, by providing good acid suppression and symptom relief. They 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 in renal insufficiency is often necessary. Also, all these agents can cause delirium in the older patient, especially cimetidine. Drug-drug interactions with histamine₂ receptor antagonists through metabolism of the hepatic cytochrome P-450 3A4 system may be potentially harmful in 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].

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 persons who often require more acid suppression due to more severe disease and complications. In

Table 2: Noninvasive Treatment of Gastroesophageal Reflux Disease*

Lifestyle Modification	Elevation of head of bed
	Avoid eating within 3 hours 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
	H ₂ receptor antagonists: cimetidine, famotidine, nizatidine, ranitidine
	PPI agents*: 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.
*Most often successful

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. Medications such as Lansoprazole are 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 patients with GERD, especially those with associated complications. Long-term treatment with adequate doses of medication is the key to effective. For the majority of patients with esophageal strictures, the use of acid suppression and esophageal dilatation are effective therapy. Aggressive acid suppression is effective in the majority of patients with GERD-related atypical chest pain. ENT complications, such as hoarseness, have dramatic responses to these agents when adequate doses are used for prolonged periods. In patients with GERD-mediated asthma, significant improvement with acid suppression by H₂ blockers and PPIs will occur. 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 Histamine₂ receptor antagonists and PPI agents may potentially affect nutrient and calcium absorption, bacterial proliferation, and drug metabolism in patients taking these medications on a long-term basis. However, with adequate monitoring, long-term maintenance with PPI agents remains quite safe in the elderly population (Table 3) [46].

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 Histamine₂ receptor antagonists [48]. If these agents are used for maintenance therapy, patients should be monitored for osteoporosis as per recommended guidelines and given adequate intake of calcium and vitamin D. If osteoporosis is detected, treatment with appropriate

agents, such as biphosphonates should be offered. Withdrawal of these agents with worsening bone health 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 controversial issue in patients with long-term acid suppression therapy. 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 their use in this regard remains controversial [49,50].

Interference 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 affect this pathway, such as dexlansoprazole, lansoprazole or pantoprazole or switching to a Histamine₂ receptor antagonist may be warranted [51].

Histamine₂ receptor antagonists can cause delirium in the older patient, especially cimetidine. Drug-drug interactions with histamine₂ receptor antagonists through metabolism of the hepatic cytochrome P-450 3A4 system may be potentially harmful in 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].

Invasive therapy

Although the vast majority of patients with GERD can be successfully managed with medical therapy, invasive methods of surgery and endoscopic treatment of GERD may be warranted in some cases. Surgery is an option for some patients with GERD [52]. Surgery is contemplated now with more frequency 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 H₂ 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 more 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 Enteryx, a biocompatible, non-biodegradable polymer into

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

Table 4: Invasive Treatment of Gastroesophageal Reflux Disease.

Endoscopic therapy		Surgery
Evolving techniques	Ablative techniques for Barrett's esophagus	Laparoscopic fundoplication
<ul style="list-style-type: none"> - Non-biodegradable polymer - Radiofrequency treatment of the gastroesophageal junction - Endoscopic suturing - Implantable gastric electrodes - Botulinum injection of the pylorus 	<ul style="list-style-type: none"> - Endoscopic mucosal resection - Electrocautery fulguration - Laser photoablation - Photodynamic therapy 	

the gastric cardia and radiofrequency energy delivery to the gastroesophageal junction, the Stretta Procedure, for the treatment of GERD are available for use only 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 yet other techniques being evaluated to reduce gastroesophageal reflux. Further evaluation of these therapeutic techniques is warranted (Table 4) [57].

Conclusion

GERD and its associated complications are common. 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 patients with GERD. However, with appropriate management, GERD and its associated complications can be treated successfully in majority of patients.

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