Esophageal and Gastric Motility Disorders in the Elderly

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KEYWORDS

• Oropharyngeal dysphagia • Gastroparesis • Dyspepsia • Nausea and vomiting
• Dysphagia • Parkinson's disease

KEY POINTS

- Gastrointestinal and motility disorders in the elderly are more commonly a sequelae of systemic disease or medication side effects rather than related to age.
- Many medications have unwanted gastrointestinal side effects; polypharmacy is a significant concern in the elderly.
- Dysphagia is common in elderly and can be oropharyngeal and/or esophageal, requiring a dedicated motility workup using barium swallow studies and esophageal motility testing to determine the cause.
- Gastroparesis in the elderly is mostly due to complications of diabetes or some neurologic diseases like Parkinson's disease; its treatment is limited given the cardiac and neurologic side effects of currently available medications.
- Opiates cause several gastrointestinal disturbances, including esophageal dysmotility, gastric emptying delay, and constipation and should be used sparingly and with caution in the elderly population.

INTRODUCTION

Similar to other organ systems, the gastrointestinal (GI) tract experiences age-related physiologic changes. Some disorders are a result of structural and functional changes owing to age, but most upper GI disorders are secondary to age-related disease burden and the medications used to treat those diseases.[1] Older patients report symptoms infrequently, a phenomenon often leading to delayed diagnosis and more severe complications.[2] Clinicians need to not only be aware of the more

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common GI diseases effecting elderly patients, but keep these conditions in the forefront when evaluating older patients to ensure prompt diagnosis.

ESOPHAGEAL DISEASE

Physiology of the Aging Esophagus

To diagnose and treat upper GI tract disorders in the elderly, one must first understand how the physiology of the upper GI tract changes with increasing age. The term presbyesophagus, first coined in 1964, was used to describe a tortuous esophagus more often seen in older individuals.[3] More specifically, this term describes age-related changes, including decreased esophageal contractile amplitudes, polyphasic waves in the esophageal body, incomplete lower or upper sphincter relaxation, and esophageal dilation. With endoscopy, and the advent of more sophisticated testing modalities like esophageal high-resolution manometry, we have now come to understand that this term, in its original understanding, is obsolete.

Varied data exist on the change in esophageal physiology with age. Although initial studies showed significant alterations in motility, a subsequent retrospective study failed to show significant age-related changes.[4,5] Healthy subjects over age 75 were found to have lower basal lower esophageal sphincter (LES) tone, a lower percentage of swallows with complete LES relaxation, and an increase in the mean integrated relaxation pressure, which measures relaxation at the esophagogastric junction.[6] The increase in peristaltic velocity when upright seen in the younger patients was not seen in this older cohort. There was also an increase in the time to recovery of LES tone back to baseline after swallow-induced relaxation in the older subjects.

Gastroesophageal Reflux Disease

Gastroesophageal reflux disease (GERD)—defined as symptoms or lesions resulting from the reflux of gastric contents into the distal esophagus—is the most commonly seen upper GI condition by primary care providers. GERD accounts for nearly one-third of visits to primary care in patients over age 65.[7] Roughly 20% of these patients experience symptoms of GERD once weekly, and nearly 60% have symptoms monthly.[8] GERD is more prevalent in the elderly owing to medications that decrease LES tone, the increased prevalence of hiatal hernia, and impaired esophageal motility.[9] Impaired saliva production and decreased salivary bicarbonate concentration impair esophageal acid clearance.[10] Decreased physical activity and more time recumbent increases reflux.[11]

Older adults can also have poor primary and secondary peristalsis, leading to increased acid exposure time. Esophageal manometry and pH impedance data show that both the frequency and duration of esophageal acid exposure increases with age.[12] Despite the increase in the prevalence of GERD in the elderly, symptom reporting is low owing to decreased pain perception in this age group.[13,14] Endoscopic studies show a worse reflux complications, such as esophagitis and peptic strictures in the elderly.[15–17] Older patients also more frequently present with atypical symptoms of GERD, as well as extraesophageal manifestations like asthma, chronic cough, globus, and laryngitis.[18]

Proton pump inhibitors (PPIs) are the mainstay of acid suppression treatment for GERD; however, more attention has been paid in recent years to potential side effects of long-term use. Although conflicting data exist, PPIs have been linked to increased risk of infections like *Clostridium difficile*,[19] pneumonia,[20] bone fractures,[21] and kidney disease.[22,23] Although dementia was once conjectured to be a side effect of PPIs, newer data suggest no association.[24,25]

Dysphagia

Dysphagia, the subjective sensation of difficulty with swallowing, is common in the elderly. An estimated 14% to 33% of community-dwelling elderly patients experience dysphagia with rates as high as 70% in nursing homes.[26–28] Dysphagia can affect not only quality of life, but also lead to malnutrition, which impacts overall health status leading to frailty.

Oropharyngeal dysphagia is characterized by difficulty initiating a swallow, and is most often due to diseases affecting the structures of the oral cavity, pharynx, and upper esophageal sphincter. Multiple conditions can cause this. Poor dentition can affect mastication. Xerostomia (dry mouth) can affect bolus formation and transfer. Conditions common to the elderly resulting in dry mouth are poorly controlled diabetes, atrophic gastritis, and medications such as anticholinergics and antihistamines, impairing transfer of food bolus into the esophagus.[29] Patients with neurologic disorders like cerebrovascular accidents, amyotrophic lateral sclerosis, and myasthenia gravis may experience dysphagia owing to decreased lingual control, impaired or absent swallowing reflex, or weakened laryngopharyngeal musculature.[30] Dysphagia is also a hallmark of more advanced Parkinson's disease.[31]

Esophageal dysphagia in the elderly may be structural or functional in etiology. Structural causes of dysphagia include malignancies, benign strictures (such as reflux-induced strictures), hernias, rings, webs, cricopharyngeal bars, and esophageal diverticula. Functional causes of esophageal dysphagia include age-related changes in primary motility disorders (with achalasia being the most well-studied), motility disorders that are secondary to another medical disorder or age-related changes in peristaltic function. One study found that, with age, even when overall esophageal function is preserved, a functional reduction in percentage of swallows with complete LES relaxation can be seen.[6] Ineffective esophageal motility, a minor disorder of peristalsis according to Chicago Classification v3.0, is characterized by weak peristalsis in more than 50% of swallows.[32] Ineffective esophageal motility can be due to longstanding GERD, esophageal involvement of connective tissue disorders like scleroderma or Sjogren's syndrome, and idiopathic owing to smooth muscle fibrosis and dysfunction, all of which is more common in older adults.[33,34]

Gastroesophageal hernias, particularly paraesophageal hernias, may cause dysphagia through an esophageal outlet obstruction. Paraesophageal hernias (**Fig. 1**) comprise 5% to 10% of all hiatal hernias, and are more common to the elderly.[35,36] Although some are asymptomatic, many patients present with postprandial pain, dysphagia, and dyspnea. Previously standard management of paraesophageal hernias was prophylactic repair to prevent higher risk emergent surgery owing to gastric volvulus; however, newer data suggest there may be only some indications for repair in asymptomatic patients.[37] Laparoscopic paraesophageal hernias repair is safe in older individuals with good patient satisfaction and limited morbidity.[38,39] In very high-risk surgical patients, gastropexy is the preferred method of treatment.

Cricopharyngeal bars and hypopharyngeal diverticula are both functional and structural abnormalities in the pharynx that can result in dysphagia. Cricopharyngeal bar, a defect in the esophagus at the level of the cricopharyngeus muscle, can lead to decreased compliance and narrowing of the upper esophageal sphincter.[40] Zenker's diverticulum (**Fig. 2**)—an outpouching of the mucosa and submucosa through Killian's triangle, an area of muscular weakness between the cricophayngeus and the thyropharyngeus muscles near the upper esophageal sphincter—is more common in older males, usually in the seventh or eighth decades of life.[41] Zenker's diverticulum is

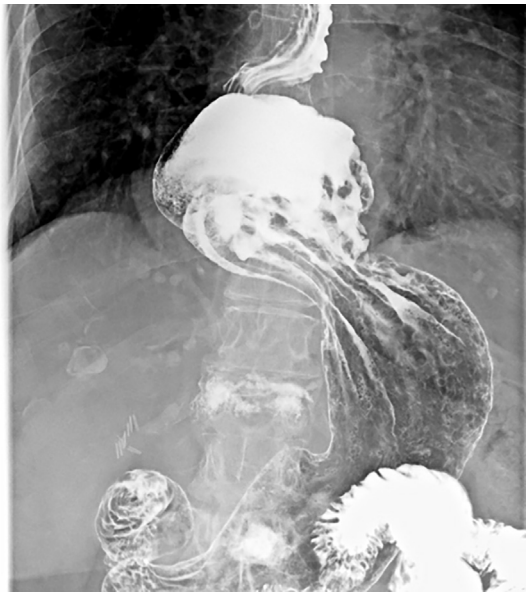

Fig. 1. Barium radiograph of a paraesophageal hernia in an elderly patients with dysphagia.

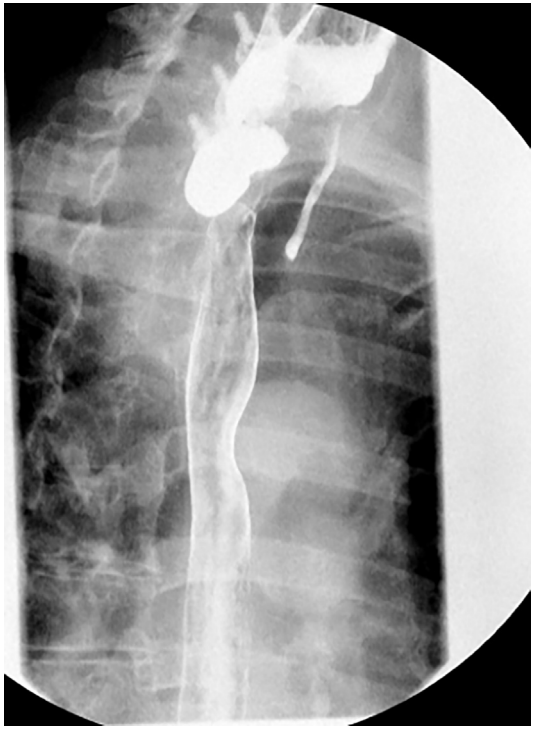

Fig. 2. Esophagram showing a right-sided Zenker's diverticulum in an 80-year-old patient with oropharyngeal dysphagia and halitosis. Patient had a myotomy performed at the level of the upper esophageal sphincter with complete symptom resolution.

caused by increased intraluminal pressure in the oropharynx during swallowing against inadequate relaxation of the cricopharyngeal muscle.[42] Symptoms include dysphagia, regurgitation, chronic cough, aspiration, halitosis, and weight loss.[43] Given the increased prevalence in the elderly, if a Zenker's diverticulum or cricopharyngeal bar is suspected, dedicated imaging with a modified barium swallow is performed initially to make a diagnosis. Rarely, a condition called distal idiopathic hyperskeletal hyperostosis causes direct compression of esophagus by cervical osteophytes is also seen more commonly in the elderly.

Achalasia

Achalasia is a rare esophageal motor disorder defined by the functional loss of myenteric plexus ganglion cells in the distal esophagus, causing lack of swallow-induced LES relaxation with abnormal motility of the esophageal body, leading to impaired esophageal clearance.[44,45] Patients present with dysphagia and even regurgitation of undigested food. The true etiology of achalasia is unknown. Although more common between the ages of 20 and 40 years, achalasia has a secondary peak in those above the age of 65[46] (**Fig. 3**). Sequelae are cumulative, and complications of the disease are more often seen in older individuals. Without treatment, achalasia can lead to irreversible structural changes in the esophagus. End-stage achalasia is characterized by severe dilation (>6 cm diameter) and tortuosity of the esophagus resembling what is termed sigmoid esophagus.[47] Other complications include epiphrenic diverticula, candida esophagitis, malnutrition, aspiration pneumonia, and squamous esophageal cancer. Treatment of achalasia depends on multiple disease and patient factors, but treatment options include per oral endoscopic myotomy, laparoscopic Heller myotomy, pneumatic dilation, botulinum toxin injection, and medications like nitrates and calcium channel blockers.[48] Typically, treatment should be targeted toward the type of achalasia.[49,50] For older individuals, pneumatic dilation is preferred, although per oral endoscopic myotomy has also been found to be safe.[51,52] In poor surgical or endoscopic candidates, botulinum toxin injection can also be considered.[53]

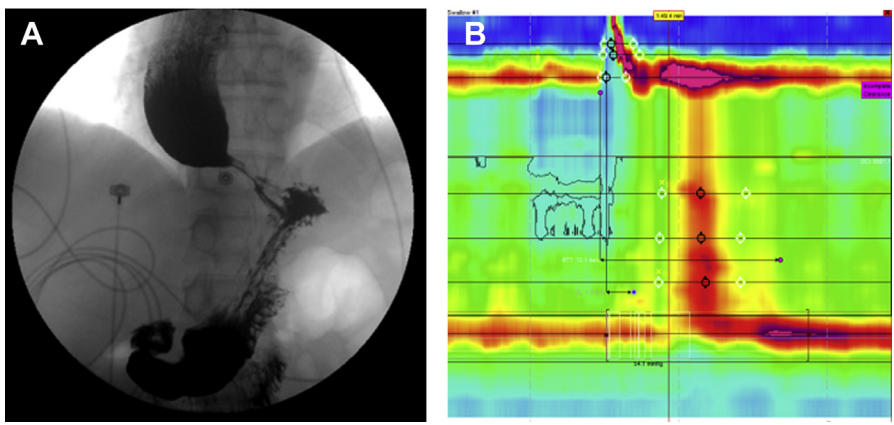

Fig. 3. (*A*) Barium swallow image of a patient with suspected achalasia showing a narrowing at the esophagogastric junction. (*B*) High-resolution manometry image shows a hypertensive LES with pan-pressurization and a high integrated relaxation pressure consistent with type II achalasia. (*B*) Failed relaxation of the LES with elevated integrated relaxation pressure median of 34 mm Hg (upper limit of normal, <15).

Medications for LES relaxation in poor surgical candidates like nitrates and calcium channel blockers can be considered, but are only moderately effective and carry cardiovascular side effects.

GASTRIC DISEASES IN ELDERLY

Physiology of the Aging Stomach

Physiologic changes in the stomach are subtle, and data are conflicting. Gastric motility is regulated by the interaction of smooth muscle cells and the interstitial cells of Cajal. An age-related decline in the number of interstitial cells of Cajal may account for early satiety and decreased food intake in the elderly.[54,55] Age-associated changes in the migratory motor complexes of the eighth and ninth decades of life occurs; however, other investigators have not demonstrated an age-related change in antral motility either in the fasting or postprandial state.[56,57] Other data may suggest that gastric emptying of liquids and mixed meals may be impaired in the elderly owing to changes in fundic accommodation and activity.[58]

Gastroparesis

Gastroparesis, defined as delayed gastric emptying in the absence of a mechanical obstruction, is most commonly caused by type 1 and type 2 diabetes, although idiopathic causes, rarely systemic diseases such as amyloidosis and neurologic diseases, and medication side effects can also contribute.[59] Over 10% of the US population has diabetes in 2020.[60] The resultant chronic peripheral neuropathy is the most common extrinsic neurologic disorder that leads to GI motor dysfunction.[61] Symptoms include nausea, vomiting, postprandial fullness, early satiety, and bloating or epigastric pain, and can lead to weight loss, malnutrition, and impaired glycemic control. As many as 12% of patients with diabetes have reported symptoms attributable to gastroparesis.[62] The incidence of gastroparesis increases with age.[63] Unfortunately, once present, despite subsequent adequate glucose control, symptoms of gastroparesis tend to persist and can significantly impact quality of life.

Diabetes decreases gastric emptying owing to less frequent antral contractions during phase 3 of the interdigestive motor complex and postprandial period. Histopathology of the vagus nerve of patients with diabetes has shown a significant decrease in the density of unmyelinated axons, and smaller caliber of the surviving axons, indicating an overall decrease in the innervation.[64] Loss or dysfunction of the interstitial cells of Cajal plays a major role in disordered gastric emptying in diabetes.[65] Diabetes causes antroduodenal dyscoordination and pylorospasm, preventing gastric contents from emptying into the small bowel for further digestion.[66] Diabetes and gastroparesis can also predispose patients to development of small intestinal bacterial overgrowth from small bowel stasis or rapid transit from uncoordinated small bowel activity.[61]

Gastroparesis may also result from commonly used medications. PPIs, taken by approximately 10% of elderly patients, may delay gastric emptying.[67] Opiates and anitcholinergics lead to delayed gastric emptying.[68,69] Ironically, although elevated blood glucose can delay gastric emptying, some antihyperglycemic medications like the exenatides as glucagon-like peptide receptor agonist impair gastric emptying by inhibiting glucagon secretion to promote satiety.[69–71] It is critical to review the medication lists of older patients to not only evaluate for polypharmacy and drug interactions, but also to monitor side effects of medications used commonly in the treatment of diseases more prevalent in the elderly.

Treatment of Gastroparesis

Treatment of gastroparesis can be complicated. First and foremost, control of glucose is critical, because gastric emptying is delayed with elevated blood sugar.[70] Although there are an increasing number of medications becoming available for the treatment of gastroparesis, in older adults many medications carry undesired side effects. Cisapride, a 5-HT_4 receptor agonist, was initially used for the treatment of gastroparesis, but later removed from the market owing to an increased risk of arrhythmia.[72] Bethanechol, a muscarinic receptor agonist, decreases fundic contractions allowing for improved gastric accommodation, as well as increasing pyloric contractility to improve gastric emptying.[73] Metoclopramide, a dopamine D2 receptor antagonist, is the only medication approved by the US Food and Drug Administration (FDA)for the treatment of gastroparesis.[74] Side effects of parkinsonism and tardive dyskinesia ultimately led to an FDA black box warning in 2009.[75,76] As a result, there is maximum duration of use of 3 months, and use is heavily cautioned in patients older than 65 years of age. Metoclopramide, cisapride, and bethanechol all have side effects of tardive dyskinesia, confusion, and drowsiness, which are more likely in an elderly population.[77,78] Domperidone—which is only available in the United States via an Investigational New Drug program—is a more selective peripheral dopamine antagonist with less central penetration, but side effects can include QT prolongation and with significant cardiac disease in older adults, and this agent must be used with extreme caution.[79] Tegaserod, used for constipation-predominant irritable bowel syndrome, significantly improves gastric emptying; however, it is only approved for female patients under 65 years of age, and therefore not applicable to our elderly population.[80] Prucalopride, a selective 5-HT_4 receptor agonist, is FDA approved for the treatment of chronic idiopathic constipation and has also shown efficacy for the treatment of gastroparesis in Europe, but is not yet FDA approved for this purpose.[81] Unlike cisapride and tegaserod, prucalopride does not interact with the cardiac hERG potassium channels or serotonergic receptors in blood vessels responsible for the major cardiovascular events seen with the former drugs.[82] Relamorelin, a potent investigational synthetic ghrelin analog, accelerates gastric emptying, and has been shown to decrease gastric retention of solids in patients with diabetes, and may be a viable option for nondiabetic gastroparesis with few side effects.[83,84]

Motilin agonists, azithromycin and erythromycin are potent prokinetics used for gastroparesis; however, tachyphylaxis development limits their use.[85] Erythromycin can have significant drug interactions with medications metabolized by CYP3A4, and can cause QT prolongation, so it should only be used with caution in an older population with an increased prevalence of cardiac disease. Approved in 2000 for the management of diabetic and idiopathic gastroparesis, gastric electrical stimulation delivers high-frequency, lower energy electrical stimulation. Gastric stimulators may be an option in few patients if operable candidates.[86]

Small Intestinal Bacterial Overgrowth

Small intestinal bacterial overgrowth, is defined by an increased proliferation of enteric flora within the small bowel. Patients can present with bloating, abdominal pain, bowel disturbance, and weight loss.[87] Polypharmacy may be a contributing factor, with the use of PPIs, narcotics, steroids, and anticholinergic medications associated with positive xylose breath testing diagnostic of small intestinal bacterial overgrowth.[88] Although this study only found an increase in small intestinal bacterial overgrowth in older women, there may be an age-associated change in microbiota leading to small intestinal bacterial overgrowth in elderly.

CONDITIONS PREDISPOSING THE ELDERLY TO GASTROINTESTINAL MOTILITY DISTURBANCES

Cardiovascular Disease

Heart disease is the leading cause of death for both men and women in the United States.[89] Rampant obesity, hypertension, dyslipidemia, and inactivity are contributing to a worsening epidemic. Cardiovascular issues can affect GI motility. Cardiomyopathy from hypertension, inherited structural abnormalities, valvulopathies, or infiltrative disease can lead to an enlarged heart and dilated aortic root. The aortic arch crosses in front of the esophagus in the superior mediastinum, and the lower esophagus lies anteriorly to the left atrium. Enlargement in either of these structures can lead to exterior compression on the esophagus that is otherwise collapsed when no food is present in the lumen. These points of compression can lead to intermittent obstruction and symptoms of dysphagia.

Stroke

Globally, stroke is the second leading cause of death behind ischemic heart disease.[90] Risk of stroke increases with age, and more than 60% of patients hospitalized for stroke are over the age of 65.[91] Dysphagia after a stroke owing to damage to the cortex and subcortical structures is a common and early complication and is an independent predictor of poor outcome and institutionalization.[92,93] As many as 50% of patients have persistent dysphagia at 6 months.[94] Stroke patients with dysphagia have a higher mortality, primarily related to the increase in risk of aspiration pneumonia.[95]

Neuromuscular Diseases

Neuromuscular disorders are more prevalent in the elderly, and can affect GI motility. The myenteric and submucosal plexi control smooth muscle activity of the GI tract, and depend on neurotransmitters like dopamine, serotonin, and acetylcholine, all of which impact GI function. Diseases and medications that affect the production or degradation of these neurotransmitters can have a significant effect on GI motility, making GI side effects common and critical in multiple disorders.

Parkinson's Disease and Parkinsonism

Enteric neurons produce dopamine, which regulates GI motility. Parkinson's disease, a disorder of dopamine production, results in significant GI disturbances, and may originate in the gut.[96] PD affects 1% of the population over the age of 60.[97] GI symptoms are present in nearly 60% to 80% of these patients, with some symptoms present up to 5 years before the development of the typical motor symptoms—a phenomenon called Braak's hypothesis.[98] GI complications are among the most common reasons for patients with PD to present for emergency evaluation, and older age in PD is associated with more GI complications. Although constipation is most prevalent, upper GI motility disorders including dysphagia, gastroparesis, small intestinal bacterial overgrowth, and malnutrition are also common.[99]

Dysphagia is a key feature of Parkinson's pathology. Xerostomia and drooling are common.[96] Dysphagia in PD can result from dyscoordination of muscular contraction at any phase of deglutition. Disorder of the oropharyngeal phase is most common, affecting nearly one-third of patients, is due to decreased motor control of the tongue, delayed swallowing reflex, and laryngeal movement deficits.[100] Esophageal dysphagia can result from aperistalsis, esophageal spasm, and slower esophageal transit. Incomplete bolus clearance is worsened by impaired LES relaxation leading

to an increased risk of aspiration.[101] PD patients with dysphagia are at risk for aspiration with a nearly 70% mortality rate.[102]

Nearly 20% of patients with PD experience nausea and vomiting, felt to be a side effect of the antiparkinsonian medications rather than the disease itself.[103] Carbidopa, often coadministered with levodopa, can worsen nausea.[104] Nausea can be present in untreated patients, likely secondary to gastroparesis, which is present in up to 90% of Parkinson's patients.[105] Delayed gastric emptying is due to decrease stomach motility, leading to nausea, early satiety, weight loss, abdominal pain, and bloating.[106] Although dysphagia can improve with medication optimization, gastroparesis symptoms maybe worsened by levodopa, a medication most commonly used to treat the disorder.[61] Delayed gastric emptying effects absorption of PD medications, impairing improvement in motor symptoms, but continuous delivery formulations of these medications per enteral tubes can help.[107]

Other treatments of gastroparesis in PD are mostly focused on symptom management.[108] Metoclopramide and other dopaminergic antagonists often used in gastroparesis treatment are contraindicated in PD because they worsen motor symptoms.[109] Domperidone, a peripheral dopamine antagonist, does not mostly cross the blood–brain barrier and has shown 100% efficacy in treating nausea and vomiting in PD, but is only available by an Investigational New Drug program owing to cardiac risk.[110]

OPIATES AND THE UPPER GASTROINTESTINAL TRACT

Nearly one-half of older adults report pain that interferes with normal function, and more than 50% of nursing home patients report daily pain.[111,112] Persons over age 65 comprise 25% of chronic opiate users.[113] Opioid pain medications lead to dyspepsia, nausea and vomiting, esophageal dysmotility, and the well-known opiate-induced constipation–narcotic bowel syndrome.[114] In the esophagus, opiates can lead to esophagogastric junction outlet obstruction, wherein esophageal peristalsis is otherwise normal, but there is impaired LES relaxation. Although this phenomenon can be seen in early or evolving achalasia, it can also be a result of mechanical obstruction, or a side effect seen in opiate use. The frequency of type III (spastic) achalasia is much higher in patients using opiates, and may in fact be the predominating cause.[115] Opiate medications also lead to delayed gastric emptying, but have been paradoxically used to treat abdominal pain but should be avoided.[116,117] Opiates in older adults can lead to changes in cognition and, therefore, neuromodulators may be more beneficial instead.

SUMMARY

There are expected to be more than 80 million patients aged 65 and older in the United States in 2040.[118] Although there are some age-related physiologic changes, the majority of GI motility disorders in the elderly result from effects of systemic diseases. Oropharyngeal dysphagia can result from stroke, Parkinson's disease, and other neuromuscular disease. Esophageal dysphagia can be due to structural changes such as hernias, motility disorders like achalasia, or severe or complicated GERD. Gastroparesis is also a significant concern for the elderly, but the majority of treatment medications have undesired and even dangerous side effects in this demographic. Perhaps most important, polypharmacy and medication side effects can create or exacerbate many upper GI motility disorders in the elderly. It is important to investigate GI symptoms in the elderly to diagnose their underlying pathology, but particular care needs to be taken in choosing a treatment regimen in these patients.

DISCLOSURE

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CLINICS CARE POINTS

- A multidisciplinary approach in caring for the geriatric population is paramount.
- Careful attention to polypharmacy and the side effect profiles of many medications such as commonly misused opiates in the elderly should be provided and their use should be minimized if possible.
- An important part of every care plan for the elderly should include a careful history of their medications and their interactions and possible GI and CNS side effects.
- Several noninvasive diagnostic tests are now available to enhance our physiologic workup of GI symptoms in the elderly and guide treatments with measurable positive outcomes.
- These tests include esophageal manometry and pH testing, barium swallow studies both for upper and lower esophageal disorders, gastric emptying scintigraphy for gastroparesis, Anorectal manometry and balloon expulsion testing to evaluate constipation and fecal incontinence and several breath tests used to evaluate for small bowel bacterial overgrowth.
- Age is not necessarily a precursor to GI distress or dysmotility, but systemic illnesses seen more commonly in geriatrics can lead to GI dysmotility.

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