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Gastroenterology for Geriatric Patients (S Katz and A Afzali, Section Editors)

Esophageal Dysphagia in the Elderly

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Abstract

Purpose of review With a globally aging population, dysphagia is a growing health concern among elderly. Increasing reflux disease has contributed to an increased prevalence of dysphagia from peptic strictures and esophageal cancer. Dysphagia can lead to malnutrition and aspiration pneumonia, causing considerable morbidity and mortality. This review article focuses on recent advances in the approach and management of esophageal dysphagia.
Recent findings Endoscopic functional luminal imaging probe is a novel test that complements upper endoscopy, esophagram, and esophageal manometry for evaluation of esophageal dysphagia. Opioid induced esophageal dysfunction (OIED) is an emerging clinical entity that can mimic achalasia. Strictures refractory to dilation can be treated with intralesional steroid injections, electrosurgical incision, or esophageal stents. Peroral endoscopic myotomy (POEM) is gaining in popularity for treatment of achalasia and other spastic disorders of esophagus.
Summary Treatment of esophageal dysphagia may include proton pump inhibitors, endoscopic dilation, or surgery and requires a personalized approach based on risks and benefits. POEM is a valuable therapy for achalasia, but further studies are needed to evaluate its use, and other alternatives, for treatment of OIED and spastic esophageal disorders.

Introduction

Dysphagia, defined as difficulty in swallowing, is a growing health concern in our aging population. Elderly are at increased risk for developing dysphagia due to age-related physiological motor changes and susceptibility to certain diseases, such as stroke. The prevalence of dysphagia in persons aged 65 years or older ranges from

25 to 38% in the independently living [1–3] to 50–60% in dependent or institutionalized patients [2, 4]. There has been an increasing prevalence of GERD, which contributes to peptic strictures and esophageal cancer [5]. Furthermore, the US Census Bureaus' 2014 National Projections indicates that the population of adults aged 65 and over is expected to grow from 15 to 24% over the next several decades and will equate to 74 million people by 2030 due to aging of the baby boom generation [6].

Dysphagia can lead to dehydration, malnutrition, and aspiration pneumonia, which increases hospitalizations and mortality, as well as affects this populations' quality of life [3, 7]. Malnutrition has been reported in 18.6% of independently living elderly with dysphagia [3]. Dysphagia can lead to weight loss and nutritional deficiencies, which increases risk for opportunistic infections and overall frailty. Patients with dysphagia have a threefold increased risk of aspiration pneumonia and a 11-fold increased risk of pneumonia if aspiration is confirmed [3]. Moreover, aspiration pneumonia increases with age, leading to 90% of pneumonia admissions in those 90 years and older [7]. Dysphagia also significantly affects quality of life in the elderly and often goes undiagnosed. In a study on 360 elderly patients with dysphagia symptoms, 50% of patients reported their dysphagia made their life less enjoyable [8]. Despite 59% of patients changing their eating habits (e.g., eating slower), 50% ate less due to discomfort, 33% were still hungry or thirsty after a meal, and 44% experienced weight loss over 12 months. Additionally, 40% experienced anxiety or panic during mealtimes due to food sticking in their throat or the sensation of choking. Surprisingly, only 36% had been formerly diagnosed with dysphagia and only 32% had received treatment for dysphagia [8]. This study points to the potential under-diagnosis of dysphagia in our elderly population. As our aging population grows, it is imperative to elicit dysphagia symptoms to establish early diagnosis and treatment.

Oropharyngeal versus esophageal dysphagia

Dysphagia can be classified as either oropharyngeal or esophageal. Oropharyngeal dysphagia is due to difficulty in forming or moving a bolus from the oral cavity to the esophagus [9]. Evaluation of oropharyngeal dysphagia requires fiberoptic endoscopic evaluation of swallowing and video fluoroscopic swallowing study, also known as modified barium swallow. Whereas esophageal dysphasia is due to difficulty in passing a bolus from within the esophagus into the stomach, this article will focus on esophageal etiologies of dysphagia (Table 1).

Evaluation of dysphagia

History and physical

A detailed history helps differentiate between oropharyngeal and esophageal dysphagia. Patients with oropharyngeal dysphagia, also called transfer dysphagia, will report difficulties initiating a swallow and propelling solids and/or liquid from the hypopharyngeal area through the upper esophageal sphincter [10]. This often results in coughing or choking with eating or deglutitive cough, defined as repetitive swallows to clear the pharynx. In contrast, patients with esophageal dysphagia more often describe a sensation of food "stuck in their chest or epigastrium" after food or liquids have easily passed the upper esophageal sphincter, often associated with chest pain or reflux. These patients may attempt repeated swallows, drinking large quantities of fluids, or regurgitate to relieve the discomfort [10]. Additionally, history regarding if dysphagia is progressive versus intermittent, if related to solids or liquids, and if associated with other symptoms, such as weight loss or odynophagia, is helpful in narrowing a differential

Table 1. Etiologies of esophageal dysphagia

Structural disorders	Motor disorders	Functional disorder
Intrinsic disease • Strictures: peptic, radiation-induced, anastomotic, caustic ingestion • Mucosal Schatzki ring • Esophageal web • Eosinophilic esophagitis • Esophagitis: reflux-induced, pill-esophagitis, CMV, HSV, Candida • Malignancy: primary or metastatic • Foreign body Systemic disease • Crohn's disease • Plummer-Vinson • Dermatologic: Pemphigus vulgaris, Bullous pemphigoid, Lichen planus, Stevens-Johnson syndrome • Extrinsic compression: mediastinal mass, vascular compression (dysphagia lusoria), spinal osteophytes	Primary dysmotility • Achalasia • Diffuse esophageal spasm • Hypercontractile (Jackhammer) esophagus • Esophagogastric junction outflow obstruction (a heterogenous group of etiologies) • Minor motor disorders (ineffective esophageal motility, fragmented peristalsis) Secondary dysmotility • Scleroderma & other connective tissue diseases • Opioid induced esophageal dysfunction • Thyroid dysfunction • Amyloidosis • Paraneoplastic syndrome • Chagas disease • Medications	Functional dysphagia—an entity that is unable to be explained by structural or motor disturbances

diagnosis. Patients with structural abnormalities often have dysphagia with solids alone whereas those with motility disorders have dysphagia to both solids and liquids. On physical exam, special attention to the oral cavity including dentition, head, and neck can provide clues to the diagnosis. Careful examination for dermatological conditions like lichen planus and epidermolysis bullosa, which could present with recurrent esophageal strictures, are warranted.

Esophagram

Fluoroscopic esophagram can define the contour of esophagus and may be helpful in detecting strictures, diffuse esophageal spasm, diverticulum, ulceration, or luminal narrowing due to malignancy or achalasia [11, 12]. Esophagram has a sensitivity of 90–95% in showing structural abnormalities, including esophageal carcinoma, peptic stricture, mucosal rings, and severe reflux esophagitis [13]. Barium esophagram has been shown to be more sensitive than endoscopy to detect more subtle strictures and fibrostenotic changes in eosinophilic esophagitis (EoE) [14]. Some motility disorders are more easily identifiable, such as the "bird beak" appearance in achalasia and "corkscrew sign" in diffuse esophageal spasm [15••]. Barium esophagram has a sensitivity of 56% for esophageal dysmotility and specificity of 91% for normal esophageal motility [13].

Timed barium esophagram

Timed barium esophagram (TBE) is helpful for assessing esophageal emptying with good inter-observer agreement [16]. The degree of esophageal clearance

can be assessed both qualitatively based on shape of esophagus and quantitatively based on height of the barium column from the esophagogastric junction (EGJ). In normal individuals, barium completely empties from the esophagus within 1 min for most patients and within 5 min for all patients [17]. TBE is particularly helpful for diagnosis of achalasia and assessment of response to treatment like esophageal dilation or myotomy. A barium column height of 2 cm at 5 min has been shown to have a sensitivity of 85% and a specificity of 86% in differentiating untreated achalasia from esophagogastric junction outflow obstruction (EGJOO) and non-achalasia dysphagia. Furthermore, combining liquid and a barium tablet increases the diagnostic yield to 100% in untreated achalasia patients [18]. In contrast to lower esophageal sphincter (LES) pressure, esophageal stasis was a better predictor of treatment failure in patients with long-standing achalasia with sensitivities of 20% versus 88%, respectively [19]. TBE is used to confirm successful myotomy for achalasia [20]. Typically, reduction of 50% or more in the height of barium column at 5 min is considered good response to treatment [21].

Esophagogastroduodenoscopy

Generally, esophagogastroduodenoscopy (EGD) is the initial diagnostic test and gold standard to rule out mechanical or anatomic etiology unless oropharyngeal dysphagia is suspected [22–24]. The decision to pursue EGD prior to esophagram should be based on the pretest probability of obstruction versus motility disorder. Patients with progressive worsening of dysphagia or presence of alarm features, such as weight loss, should undergo EGD immediately, whereas patients who have suspected esophageal dysmotility without alarm features can undergo esophagram before EGD. Esophagram prior to EGD is cost effective for the diagnosis of abnormal esophageal motility while initial evaluation with EGD is cost effective for GERD or anatomic obstruction [25].

During endoscopic evaluation, biopsies should be obtained from the distal and proximal esophagus to evaluate for EoE [26, 27]. If a stricture is found, biopsies should be taken to rule out malignancy. Biopsies for GERD have shown limited value [28]. If EGD and biopsies are unrevealing, high-resolution esophageal manometry is the next step in evaluation of esophageal dysphagia to assess for esophageal motor disorders [29–34].

High-resolution manometry

High-resolution manometry (HRM) has replaced conventional esophageal manometry and assesses esophageal motility by measuring the amplitude of contractions and relaxation in the esophagus and its sphincters in relation to time. Esophageal motility disorders are classified according to the updated Chicago Classification [35•]. The major motility disorders include:

1. Achalasia—high integrated relaxation pressure (IRP) with failed or spastic esophageal peristalsis
2. EGJOO—high IRP with normal esophageal peristalsis
3. Diffuse esophageal spasm (DES)—normal IRP with short distal latency in 20% of swallows
4. Jackhammer esophagus—normal IRP with high amplitude contractions in 20% of swallows

Elevated IRP ≥ 15 indicates impaired LES relaxation. Minor motility disorders include ineffective esophageal motility (IEM) where 50% or more of swallows are weak or failed, and fragmented peristalsis where 50% or more of swallows are fragmented with large breaks in peristalsis. The clinical significance of these minor motility disorders is unclear.

The rapid drinking challenge (RDC) of 200 mL of water within 30 s is an additional tool used during HRM to assess LES relaxation and bolus clearance [36]. An IRP of 8 mmHg or greater is indicative of EGJOO, whereas an IRP of 12 mmHg or greater suggests achalasia (sensitivity 85%, specificity > 95%) [37, 38]. Moreover, the esophageal pressurization seen during RDC correlates well with TBE barium column height at 5 min and can be a measure of esophageal stasis in achalasia [36].

Endoscopic functional luminal imaging probe

Endoscopic functional luminal imaging probe (EndoFLIP) is a novel transoral catheter that has been commercially available since 2009 and can be used at the time of EGD to assess esophageal and EGJ distensibility by volumetric distension [39, 40•, 41, 42]. Topographic plots (panometry) showing EGJ distensibility index < 2.8 mm^2/mmHg or contractility pattern with absent or repetitive retrograde contractions are considered abnormal. Currently, it is considered complimentary to HRM for the evaluation of non-obstructive dysphagia. EGJ distensibility assessed by EndoFLIP correlates with esophageal emptying and may be a screening tool for achalasia [40•, 43]. Nicodeme et al. showed that reduced esophageal distensibility predicted risk of food impaction and need for esophageal dilation in patients with EoE [44]. EndoFLIP is also useful in assessing response to interventions, such as POEM for achalasia or EoE treatment [45, 46].

Esophageal disorders and targeted treatment

Benign esophageal strictures

When approaching benign strictures, strictures should first be classified as simple or complex. Simple strictures are short (< 2 cm) in length, focal and straight, and traversable with a normal adult endoscope (> 9-mm luminal diameter) [47]. Etiologies of simple strictures include peptic stricture and Schatzki ring, and typically only 1–3 dilations are needed with a low recurrence rate. In contrast, complex benign strictures are longer (> 2 cm), angulated and tortuous, irregular, and severely narrowed (< 9 mm) [48]. These often have deep, transmural fibrosis and fall into the categories of radiation-induced, ischemic, anastomotic, caustic ingestion-related, or iatrogenic (e.g., post endoscopic submucosal dissection or radiofrequency ablation). Complex strictures are often refractory to dilation and require frequent sessions. Refractory strictures are defined as the inability to successfully remediate the anatomic problem to a diameter of at least 14 mm over 5 sessions at 2-week intervals [49]. Recurrent strictures are defined as the inability to maintain a satisfactory lumen for 4 weeks once the target of 14 mm has been achieved [49].

Dilators can be categorized into 2 groups: fixed-diameter push-type dilators (bougie dilators) and radial expanding balloon dilators. Bougie dilators provide both radial and longitudinal forces while balloon dilators provide mainly

radial force [50]. The most commonly used dilators are the wire-guided Savary-Gilliard thermoplastic dilators with a tapered tip and the wire-guided through-the-scope (TTS) balloon dilators. Maloney dilators are flexible, tungsten-weighted rubber bougies with a tapered tip that can be used for self-dilations [51]. When Maloney, balloon and Savary dilators were compared, perforation was most common with blind passage of Maloney bougies for complex strictures [52]. Perforation rates for all dilations are generally 2–3% with a mortality of 1% [53, 54]. Randomized control trials comparing bougie dilators with TTS balloons for benign strictures have shown no difference in efficacy or safety [55, 56]. Thus, the choice of dilator can be based on the endoscopist's preference. Savary dilators can be considered for very small diameter strictures as the smallest TTS balloon size is 6 mm, although biliary TTS balloons could also be used. The additional benefit to Savary dilators is the tactile assessment during the dilation. Balloon dilators can be considered if multiple strictures are present [57].

The "rule of 3" has typically been used for dilations within a single session and was originally created for bougie dilations but extrapolated to balloon dilations. The rule states that once moderate resistance is encountered, no more than 3 dilations of increasing diameter should be done during that session [51]. Although some studies have shown non-adherence to the rule of 3 does not increase the risk of perforation [58], general practice is to air on the side of caution and have an individualized treatment approach to each stricture.

If conventional stricture dilation fails, the following options can be considered:

1. Dilation with intralesional steroid injection (4-quadrant injection of triamcinolone 40 mg/ml diluted 1:1 with saline in aliquots of 0.5 mL) can be considered for peptic strictures [59, 60]. The theory behind this treatment is to inhibit the inflammatory response and decrease production of fibrous tissue formation.
2. Electrosurgical incision therapy where a needle-knife is used to make longitudinal incisions in the stricture can be considered for anastomotic strictures or refractory Schatzki's rings [61, 62].
3. Esophageal stent placement to provide persistent radial force leading to tissue remodeling. Types of stents include self-expanding plastic stent (SEPS), partially covered self-expending metal stent (SEMS), fully covered SEMS, and biodegradable stents. Typically, stents are sutured in place; however, the duration of optimal stent placement is unknown. For shorter strictures, a 4–8-week duration is suggested versus a longer duration for long or ischemic strictures. The 2016 ESGE guidelines support the use of fully covered SEMS for refractory benign esophageal strictures but with a maximum duration of 3 months [63•]. Biodegradable stents that maintain a radial force for 6–8 weeks before disintegrating over 8–12 weeks showed the same efficacy and safety profile as SEPS and SEMS [64, 65]. The overall clinical success rate for all stent types for treatment of refractory-benign esophageal strictures is approximately 40% [64]. The average migration rate is 26–29% [64, 66], and adverse event rate is 21% for all stent types [64]. Immediate and early complications of stent placement include perforation, malposition, and chest pain while late complications include GERD, stent migration, food impaction, and trachea-esophageal fistula formation [67].

Aspiration and bleeding can be early or late complications [67].

4. Self-dilations with 14–18-mm Maloney bougie dilators are a safe treatment option for refractory-benign simple esophageal strictures [68].

Malignant esophageal strictures

Malignant esophageal strictures are most often related to intrinsic obstruction from esophageal cancer but could be related to extrinsic compression from other malignancies, such as lung cancer or lymphoma [47]. Endoscopic treatment of malignant strictures is typically with esophageal metal stent placement for palliation of dysphagia [69]. Recurrent dysphagia can occur in 30–40% of patients due to stent migration, tumor/tissue overgrowth, or food obstruction. The latest 2016 ESGE guidelines on esophageal stents recommends fully or partially covered SEMS for malignant dysphagia over laser therapy, photodynamic therapy, and esophageal bypass [63•]. This is a palliative measure that is not recommended as a bridge to surgery or prior to preoperative chemotherapy. Although more expensive, SEMS are preferred over rigid plastic stents due to lower complication rates [70]. Randomized control trials have shown covered SEMS are superior to both uncovered SEMS and covered SEPS due to less tumor ingrowth and stent migration, respectively [71, 72].

GERD-related dysphagia

Pathological GERD is defined by at least one of the following criteria: grade C or D esophagitis, peptic stricture, Barrett's esophagus > 1 cm, or esophageal acid exposure time > 6% on pH testing [28]. GERD can lead to structural changes, such as esophagitis, and also impairs esophageal peristalsis and amplitude of contractions, both of which can lead to dysphagia [73]. The gold standard for detection of reflux is 24-h esophageal impedance pH monitoring [28]. Wireless pH monitoring can be used in patients with intolerance of the transnasal impedance catheter or for those with a negative pH impedance and > 24-h testing is indicated [28]. Treatment with proton pump inhibitors (PPIs) is typically initiated in those who are symptomatic, although empiric trials for those who are asymptomatic but reflux is suspected are reasonable. Anti-reflux therapy may improve ineffective esophageal motility, although rarely completely normalizes [74, 75].

Eosinophilic esophagitis

Eosinophilic esophagitis (EoE) is a disease characterized by esophageal dysfunction and eosinophil-predominant inflammation as a result of a T cell–mediated response in the esophageal mucosa due to food antigens [76, 77]. The diagnosis is based on a combination of clinical symptoms and characteristic histologic findings. While children often present with esophageal inflammation, adults present with esophageal fibrostenotic disease [76, 78]. The diagnosis of EoE is made when esophageal biopsies show > 15 eosinophils per high-power field [77, 79]. Six to eight biopsies from the distal and mid/proximal esophagus are recommended to provide a high level of sensitivity [80]. It is important to keep in mind that esophageal eosinophilia can also be seen with GERD, Crohn's disease, celiac disease, achalasia, drug hypersensitivity, and graft-versus-host reaction [76, 81]. An endoscopic reference score with good inter-observer agreement (EREFS) has been created to standardize and grade

endoscopic findings of edema, rings, exudates, furrows, and strictures often seen on endoscopy in EoE patients [82]. The 2018 updated international consensus guidelines have removed response to PPIs from the diagnostic criteria, but rather consider PPIs as a treatment option [79, 83••]. The goal of EoE treatment is to decrease esophageal eosinophilia to improve symptoms and inflammation.

Proton pump inhibitors

PPIs can induce histologic remission in 50% of patients and clinical remission in 61% of patients with EoE [84, 85]. PPI-responsive esophageal eosinophilia (PPI-REE) is a subtype of EoE that responds to PPI monotherapy [86]. PPI therapy has also been shown to reduce T helper 2 cell–mediated inflammation in EoE patients, similar to steroid therapy [86]. Typically high doses of PPI twice daily are initially used [86], but 70–80% of PPI-responsive patients are able to be maintained on lower doses of PPI once or twice daily [79, 87].

Swallowed steroids

Swallowed topical corticosteroids, such as viscous budesonide (2 mg daily) and fluticasone (880 μg twice a day), are effective treatment options [88–90]. Typically this dose is tried for 8 weeks prior to transitioning to lower maintenance doses [91]. Several meta-analyses have shown topical corticosteroids induce histologic remission but may not improve clinical symptoms [92–95]. Histologic response rates can range from 50 to 90%. Cessation of treatment often leads to relapse of symptoms [96]. A recent 5-year retrospective study on non-PPI-responding EoE patients showed that higher cumulative doses of swallowed topical corticosteroids and longer durations of treatment were associated with higher rates of complete remission compared with placebo (16.1% vs 1.3%); however, complete remission remains < 20% [97]. In general, systemic steroids are not recommended given their side-effect profile and no significant clinical benefit [98].

Elimination diets

The 6-food group elimination diet (SFGED), based on the most common food allergens, eliminates wheat, milk, soy, egg, nuts/legumes, and seafood and can achieve clinical and histologic remission in over 70% of patients [99–101]. This diet is often challenging for patients to adhere to [102] and has led to a more common practice of eliminating milk and wheat first, given these are the most frequent sensitivities, followed by removal of other foods. Additionally, 65–85% of patients who respond to the SFGED have only 1 or 2 causative foods and thus, elimination of the most common foods first is a reasonable approach to limit unnecessary dietary restrictions [101, 103]. Alternatively, a four-food group elimination diet that eliminates milk, wheat, eggs, and legumes has been proposed [104].

Maintenance therapy

EoE is a chronic, relapsing disease that requires maintenance therapy. Most PPI-REE patients remain in long-term remission on low-dose PPI at 1 year, and those who relapse regain histologic remission after dose escalation [105]. Data is limited on PPI efficacy after 1 year. In general for all EoE patients, symptoms typically

recur in 3 to 6 months after stopping dietary or pharmacologic therapy [79]. The feared complication in persistent untreated eosinophilic inflammation is tissue remodeling with fibrin deposition causing stricture formation and subsequent food bolus impactions [84, 106, 107]. Budesonide is helpful in reducing tissue remodeling in the long-term. Up to 30% of patients may have refractory EoE defined as non-responsiveness in clinical, endoscopic or histology assessment after first-line therapy [108]. These patients may need prolonged combination of PPIs and steroids. Overall swallowed topical steroids in the short-term and long-term is considered safe [91], with mild oral candidiasis being the most common adverse effect seen in up to 10% of patients [93].

Esophageal dilation

EoE patients with severe or persistent dysphagia and/or history of food impaction should undergo endoscopic dilation. As with other esophageal strictures addressed above, dilations should be performed gradually, using the "rules of 3" and often over several sessions. Although once thought that dilation in EoE patients has a high risk of perforation, a recent meta-analysis of 468 EoE patients who underwent a total of 671 dilations showed no increased frequency of esophageal perforation from dilation (1 out of 671, 0.1%) [109], which is comparable to esophageal dilation for other strictures (0.1–0.2%) [76]. Additionally, there is no significant difference in complications with bougie versus TTS balloon dilations, with the overall complication rate of 5% predominated by post-procedural pain [110]. A total of 58% of patients need repeat dilations within 1 year [110].

Future therapies

Current studies are being conducted to see if small-molecule (CRTH2 antagonists) or biologic agents could be used as future therapies for EoE [76, 84]. In phase II trials, antibody against IL13 had been shown to reduce histologic and endoscopic scores and these benefits were extended even onto steroid-refractory EoE patients [111]. Several biologic agents such as mepolizumab (anti-IL-5 monoclonal antibody), omalizumab (anti-IgE monoclonal antibody), and infliximab (anti-TNF-alpha monoclonal antibody) are being considered but have not yet shown benefit [84]. These are currently not recommended for standard therapy. Immunomodulators, such as azathioprine and 6-mercaptopurine, are being considered as steroid sparing agents for inducing and maintaining remission in EoE but data is limited to case series [112]. Additionally, antihistamines and leukotriene receptor antagonists (e.g., montelukast) have shown no therapeutic effect for EoE [79, 84, 113].

Achalasia

Achalasia is a primary esophageal motor disorder characterized by impaired relaxation of the LES and absence of esophageal body peristalsis [114]. Type I achalasia is characterized by absent contractility, type II achalasia by pan-esophageal pressurization, and type III achalasia by spastic contractions [115]. This sub-classification of achalasia is helpful in determining treatment options, which include pharmacotherapy, endoscopic management, laparoscopic Heller myotomy (LHM), and peroral endoscopic myotomy (POEM). Type II achalasia is most responsive to treatment (96% success rate), compared to type I achalasia

(81% success rate, which worsens as esophageal dilation progresses), and type III achalasia (66% success rate) due to spasm that is not treated by LES directed therapies [116]. In general, type I achalasia is treated with LHM or POEM, type II achalasia with LMH, POEM, or pneumatic dilation (PD) based on surgical candidacy, and type III achalasia with POEM.

Pharmacologic treatments consisting of muscle-relaxant drugs, such as calcium channel blockers, nitrates, or phosphodiesterase inhibitors, generally have limited efficacy and are associated with several limiting side effects [117]. The recent 2018 ISDE achalasia guidelines recommend against the use of medication for treatment given no convincing evidence these are effective for symptomatic relief in adults [15]. Thus, these agents are reserved as a bridge to more durable therapy or for patients unwilling or unable to undergo more definitive treatment with either surgical myotomy or PD [117, 118]. In contrast, endoscopic treatment has long consisted of botulinum toxin injections and PD but more recently included POEM.

Botox

Botulinum toxin injections (BTI) at the EGJ induce a short-term paralysis of the LES. Standard protocol consists of injecting 100 units of Botox into 4 quadrants just above the squamocolumnar junction [119]. Studies report symptom relief of 78% at 1 month [120] however drops to 35–41% after 1 year [119, 120]. Unfortunately, repeat treatments are less effective than initial treatment [15]. Additionally, repeated BTI can cause an inflammatory reaction that obscures the mucosal-muscle plane near the LES and increases the risk of surgical complications if surgical myotomy is later pursued [121–123]. Although there lacks strong evidence that BTI or PD reduces technical feasibility of POEM or affects outcomes [15], in general, BTI should be reserved for patients who are not surgical candidates, especially frail elderly individuals.

Pneumatic dilation

Achalasia balloon dilators are air-insufflated large-diameter (30, 35, and 40 mm) polyethylene balloon dilators positioned across the EGJ with the use of fluoroscopy [51]. Graded pneumatic dilation (PD), defined as repeated PDs with increasing dilation size, increases durability of symptom relief from 62 to 90% at 6 months and 28 to 44% at 6 years compared with single PD [124]. Risk factors for failure after single PD include younger age, male gender, wider esophageal diameter, and poor emptying on post-treatment TBE [124]. Graded PD is an effective and safe treatment [15] with perforation rate of around 2% [125], but as low as 0.5% at high-volume centers [126]. Generally, these perforations can be managed conservatively [127, 128]. Risk factors for perforation include older age and larger balloon size [128, 129]. GERD can occur in 15–30% of patients following PD [128, 129].

Longer term success rates have been as high as 85% at 5 years and are comparable to LHM success rates [124, 130••]; however, 25% of PD patients require repeat dilations [130••]. Overall, PD has the best outcomes in type II achalasia [128] and the least efficacy in type III achalasia [129]. Patients who do not respond to PD should be referred for LHM or POEM [15]. Alternatively, PD can be used as first line for patients who did not respond to LHM [15]. Previous

PD does not affect the results of myotomy [121].

Laparoscopic Heller myotomy

Laparoscopic Heller myotomy (LHM) used to treat type I and II achalasia has the best outcomes [15]. It should also be considered over other therapies for patients with significantly dilated or tortuous esophagus, esophageal diverticula, or previous EGJ surgery. The use of partial fundoplication, typically with an anterior 180° (Dor) or 270° (Toupet) fundoplasty, at the time of LHM has shown to help prevent GERD [15], which occurs in 23% of patients [128]. LHM combined with fundoplication provided 90% symptom relief at 35 months with a complication rate of 6% and decreased post-operative GERD from 31.5 to 8.8% [120]. LHM efficacy is comparable to PD; success rates decrease to approximately 75% at 5 years [131].

Peroral endoscopic myotomy

Peroral endoscopic myotomy (POEM) is a new endoscopic technique involving submucosal dissection from the esophageal body across the LES and into the gastric cardia developed by Inoue et al. in 2008 [132•] that is increasingly being practiced as a less invasive alternative to surgical laparotomy for achalasia [133]. A meta-analysis showed an overall pooled success rate of 93% over variable follow up periods with a 14% complication rate, including pneumothorax and pneumoperitoneum, typically managed conservatively [134]. POEM efficacy and safety have been shown to be comparable with LHM [135] with shorter hospitalization and recovery time [136].

POEM is particularly helpful for spastic achalasia type III as it allows for a longer myotomy than LHM [137]. A retrospective study comparing POEM to LHM in type III achalasia patients showed higher clinical response with POEM (98% vs 81%) and lower adverse events (6% vs 27%) [137]. POEM is now recommended as an effective option by the 2018 ISDE guidelines, but is associated with higher incidence of GERD compared to LHM with fundoplication [15, 138]. The prevalence of GERD post-POEM is approximately 12–37% [139•, 140]. POEM is also a safe and effective option for patients who have failed LHM with a clinical response rate of 81–94% [141, 142] and no difference in adverse events compared with those without previous LHM [141]. No randomized control trials have been performed comparing POEM with PD or POEM with LMH.

Esophagectomy

About 10–15% of patients will have progressive symptoms despite PD or surgical myotomy and result in end-stage achalasia, characterized by severe esophageal dilation and possible sigmoid deformity [143, 144]. Esophagectomy is the last resort for patients with persistent symptoms who have failed all other treatments [15, 145], about 5% of patients [144].

Diffuse esophageal spasm and hypercontractile (jackhammer) esophagus

Diffuse esophageal spasm (DES) is characterized by spastic peristalsis with normal LES relaxation, technically defined by distal latency less than 4.5 s (premature contractions) in 20% or more of swallows on HRM [35]. Jackhammer esophagus is characterized by hypercontractile peristalsis, technically

defined by distal contractile integral (DCI) greater than 8000 mmHg/s/cm on 20% or more swallows on HRM [35].

Treatment options are limited for both disorders. Nitrates, hydralazine, phosphodiesterase inhibitors, and calcium channel blockers have modest effect but with significant side effects [146]. Peppermint oil is a safe topical smooth muscle relaxant shown in small studies to decrease the number of simultaneous and spontaneous esophageal contractions with no effect on resting LES pressures [146]. Peppermint tablets have also been tried with some success for DES patients [147].

In a double-blind, randomized, sham control trial, botox injections were shown to be superior to saline injections in improving symptoms in patients with DES and jackhammer esophagus for at least 6 months [148]. The response decreased to 30% at 1 year. POEM is rising in popularity as a treatment option for spastic esophageal disorders. In a recent meta-analysis, the clinical success of POEM for DES was 88% and 72% for jackhammer esophagus with no difference in safety of POEM for achalasia type III, DES and jackhammer esophagus [149].

Opioid-induced esophageal dysfunction

Opioid-induced esophageal dysfunction (OIED) is an emerging entity. Chronic opiates have been shown to cause elevated LES pressure and spastic paralysis on HRM that could resemble EGJOO or type III achalasia [150•, 151, 152]. Treatment involves withdrawal of opiates. Methylnaltrexone has not shown any effects on esophageal LES or peristalsis [153]. PD tried for those with esophageal dysmotility resembling type III achalasia did not improve symptoms [151]. If withdrawal of opiates is not possible, then reduction of doses and considering BTI or POEM has been proposed; although strong evidence is lacking [152].

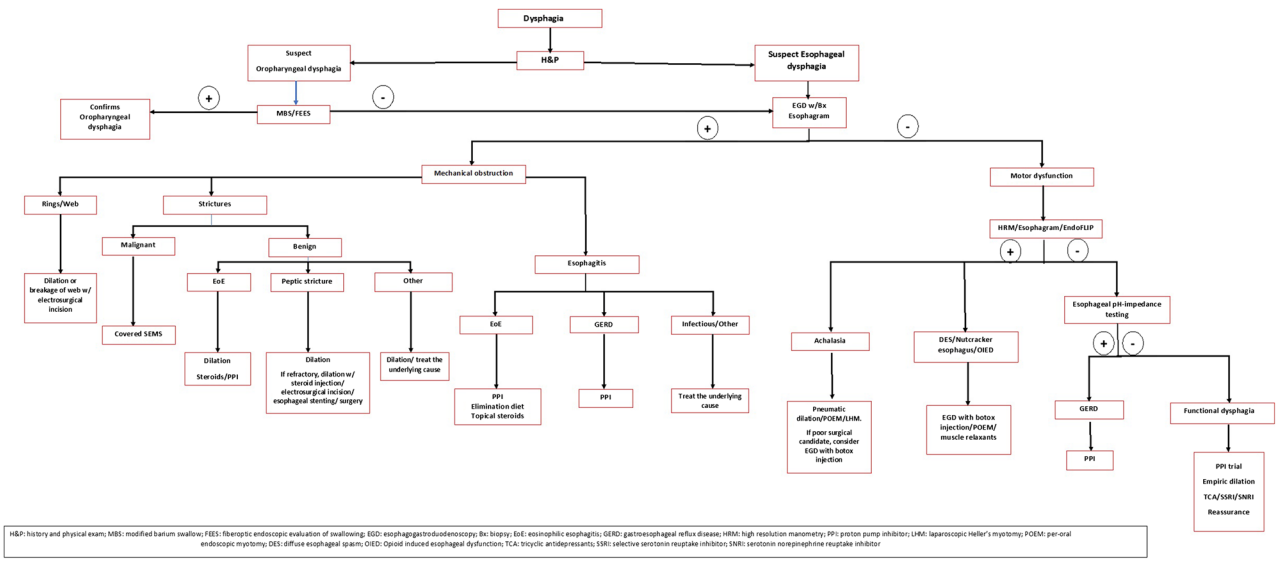

Fig. 1. Dysphagia algorithm.

Functional dysphagia

Functional dysphagia is the sensation of abnormal bolus transit through the esophagus that is unable to be explained by structural, mucosal or motor disturbances [154, 155]. An arbitrary requirement of at least 3 months of symptoms occurring at least once a week with an onset of at least 6 months before diagnosis is used to establish chronicity [28, 155]. A study evaluating over 5000 US households estimated the national prevalence of functional dysphagia to be approximately 7.5% [156]. As this is a diagnosis of exclusion, patients should undergo an EGD with esophageal biopsies for EoE, HRM, pH impedance study, and potentially barium esophagram to evaluate for subtle strictures [155]. While the underlying mechanisms remain unclear, it is theorized that visceral hypersensitivity and hypervigilance drive patient's symptoms [155, 157]. The following management options could be considered for treatment of functional dysphagia:

1. Minimize opioids and/or other motility altering medications
2. Trial of high dose acid suppression for 4–8 weeks to treat any reflux
3. Consider empiric esophageal dilation with 50–54-Fr bougie to treat subtle rings or strictures [158, 159]
4. Targeting visceral hypersensitivity by modulating peripheral and central perception [155]. Various classes of pain modulators include low-dose TCAs (e.g., imipramine 25–50 mg daily), SSRIs (e.g., sertraline 50–200 mg daily), SNRIs (e.g., venlafaxine 75 mg daily), mirtazapine, and trazodone [157, 160•]. Antidepressants have been shown to reduce functional chest pain by 18–67% and reduce functional heartburn by 23–61% [160•]. Fewer studies have looked at globus sensation and functional dysphagia but amitriptyline 25 mg daily has shown to be effective in small studies [161].
5. Reassurance and lifestyle modifications, such as eating upright, chewing food thoroughly, following food with liquids, and avoiding precipitating foods

Conclusion

In summary, a wide variety of disorders can lead to esophageal dysphagia in the elderly. Thorough evaluation with various tools including history, EGD, esophagram, HRM, and EndoFLIP can help determine a structural versus motor versus functional disorder. We propose the following algorithm (Fig. 1) to help navigate the various esophageal disorders and their specific treatment.

Compliance with Ethical Standards

Conflict of Interest

Megan Q. Chan declares that she has no conflict of interest. Gokulakishnan Balasubramanian declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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