Approach to Patients with Esophageal Dysphagia

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KEYWORDS

• Dysphagia • Endoscopy • Manometry

KEY POINTS

- Patients present to a physician with complaints of difficulty swallowing, and the approach to evaluating these problems can be challenging for those who do not manage this complaint regularly.
- Dysphagia refers to difficulty with swallowing where there are problems with the transit of food from the mouth to the hypopharynx or through the esophagus.
- The most important step in assessing dysphagia is to determine whether it is oropharyngeal or esophageal in origin; potential causes and subsequent investigation and management can differ greatly.
- Numerous tools are available to aid with the determination of the cause of dysphagia and assist with the formulation of a logical treatment algorithm.

INTRODUCTION

Dysphagia refers to difficulty with swallowing where there are problems with the transit of food from the mouth to the hypopharynx or through the esophagus. Dysphagia can be classified based on the location and by the physiologic circumstances in which it occurs. Dysphagia is classified as oropharyngeal or esophageal dysphagia based on location.[1] In terms of physiology, dysphagia can be classified based on the transport of an ingested bolus. The transport depends on the consistency and size of the bolus, the caliber of the lumen, the integrity of peristaltic contraction, and whether there is deglutitive inhibition of both the upper and lower esophageal sphincter (LES). Structural dysphagia is caused by an oversized bolus or a narrow lumen; motor dysphagia is secondary to abnormalities of peristalsis or impaired deglutitive inhibition

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Abbreviations

CT	Computed tomography
EGD	Esophagogastroduodenoscopy
EUS	Endoscopic ultrasound
HRM	High-resolution manometry
LES	Lower esophageal sphincter

of the sphincters. The most important initial step in assessing dysphagia is to determine whether it is oropharyngeal or esophageal in origin, because their potential causes and subsequent investigation and management can differ greatly. Patients with oropharyngeal dysphagia present with symptoms of cough after swallowing and nasopharyngeal regurgitation.[1] It is seen commonly in patients with a history of head and neck surgery or radiation treatment, stroke, and other neurologic conditions, such as Parkinson's disease and motor neuron disease. This article provides an outline for approaching patients with esophageal dysphagia in terms of etiologies and clinical evaluation. The article discusses initially the physiology of esophageal swallowing, followed by pathophysiology and clinical evaluation of patients with various etiologies of esophageal dysphagia.

PHYSIOLOGY OF ESOPHAGEAL SWALLOWING

Swallowing begins with a voluntary (oral) phase that includes preparation during which food is masticated and mixed with saliva. Once the food is transferred to the esophagus through a complex physiologic transfer and relaxation of the upper esophageal sphincter, peristaltic contractions propel the food through the esophagus. The LES relaxes as the food enters the esophagus and remains relaxed until the peristaltic contraction has delivered the bolus into the stomach.[2] Peristaltic contractions elicited in response to a swallow are called primary peristalsis and involve sequenced inhibition followed by contraction of the musculature along the entire length of the esophagus. Local distention of the esophagus anywhere along its length activates secondary peristalsis that begins at the point of distention and proceeds distally. Tertiary esophageal contractions are nonperistaltic, disordered esophageal contractions. The distal esophagus and LES are composed of smooth muscle and are controlled by excitatory and inhibitory neurons within the esophageal myenteric plexus.[2] Peristalsis results from the patterned activation of inhibitory followed by excitatory ganglionic neurons, with progressive dominance of the inhibitory neurons distally. The function of the LES is supplemented by the right diaphragmatic crus, which acts as an external sphincter during inspiration, cough, or abdominal straining.[2]

PATHOPHYSIOLOGY AND ETIOLOGIES OF ESOPHAGEAL DYSPHAGIA

Solid food esophageal dysphagia becomes apparent when the esophageal lumen is narrowed to less than 13 mm; the normal diameter of the lumen varies from 2 to 3 cm. However, dysphagia can occur even with larger diameters when patients have motility disorders. The most common structural causes of dysphagia are Schatzki's rings, eosinophilic esophagitis, and peptic strictures. Disorders of motility could be secondary to abnormalities of peristalsis and/or deglutitive inhibition. In general, the etiologies of esophageal dysphagia can be divided broadly into either mechanical or dysmotility (**Box 1**). However, in a number of conditions, dysphagia could be mediated by both mechanical and dysmotility mechanisms.

Box 1
Etiologies of esophageal dysphagia

Mechanical causes

Benign strictures

- Peptic stricture
- Schatzki's ring
- Esophageal webs
- Anastomotic stricture
- Eosinophilic esophagitis
- Post fundoplication
- Radiation-induced strictures
- Postendoscopic mucosal resection
- Extrinsic compression from vascular compression (dysphagia lusorio)
- Extrinsic compression from benign lymph nodes or enlarged left atrium

Malignant strictures

- Esophageal adenocarcinoma
- Squamous cell cancer
- Extrinsic compression from malignant lymph nodes

Dysmotility

- Achalasia
- Hypotensive peristalsis
- Hypertensive peristalsis
- Nutcracker esophagus
- Diffuse esophageal spasm
- Functional obstruction

CLINICAL ASSESSMENT

The history and clinical assessment give clues to the etiologies of dysphagia and the evaluation required. Dysphagia to the type of food provides clues to the etiologies of dysphagia. Intermittent dysphagia that occurs only with solid food implies structural dysphagia, whereas constant dysphagia with both liquids and solids strongly suggests a motor abnormality.[2] Dysphagia that is progressive over the course of weeks to months raises concern for neoplasia. Episodic dysphagia to solids that is unchanged over years indicates a benign disease process such as a Schatzki's ring or eosinophilic esophagitis. Food impaction with a prolonged inability to pass an ingested bolus even with ingestion of liquid is typical of a structural dysphagia. Chest pain frequently accompanies dysphagia whether it is related to motor disorders, structural disorders, or reflux disease. A prolonged history of heartburn preceding the onset of dysphagia is suggestive of peptic stricture and, less commonly, esophageal adenocarcinoma. A history of head and neck surgery, ingestion of caustic agents or pills, previous radiation or chemotherapy, or associated mucocutaneous diseases may help to isolate the cause of dysphagia. With accompanying odynophagia, which

usually is indicative of ulceration, infectious, or pill-induced esophagitis should be suspected. A strong history of allergy increases concerns for eosinophilic esophagitis.

CLINICAL INVESTIGATIONS

The initial clinical investigations depends on the suspected etiology. If mechanical causes, such as an obstructing mass lesion or stricture, are suspected, upper endoscopy is the initial investigation of choice. In contrast, if motility disorders such as achalasia are suspected, high-resolution manometry is the initial investigation. Radiographic evaluation with a barium swallow remains a useful investigation in some situations when upper endoscopy evaluation is normal.

Barium Swallow

The sensitivity of barium radiography for detecting esophageal strictures is greater than that of endoscopy, particularly for esophageal webs and rings, and remains the best initial evaluation strategy for dysphagia. The advantages are that it is noninvasive, can be done in patients who are poor candidates for endoscopic evaluation, and provides a good functional assessment of the esophagus. Barium swallow may also demonstrate anatomic abnormalities such as a stricture and Schatzki's ring.[3] The major drawback is that it is usually followed by endoscopic evaluation. A timed barium swallow is, however, used to follow up on treatment after achalasia as the height of the barium column at 1 minute after contrast ingestion 6 months after treatment was found to correlate with symptom scores.[3]

Upper Endoscopy

Upper esophagogastroduodenoscopy (EGD) is the first-choice investigation in patients with dysphagia, particularly with mechanical etiologies for dysphagia. It can diagnose intraluminal tumors, strictures and inflammatory disorders such as reflux disease, eosinophilic esophagitis, and pill-induced ulceration. In a systematic review of endoscopic findings in eosinophilic esophagitis, esophageal rings accounted for 44%; strictures, 21%; narrow-caliber esophagus, 9%; linear furrows, 48%; white plaques or exudates, 27%; pallor or decreased vasculature, 41%; and erosive esophagitis, 17%.[4] The endoscopic examination was normal in 17% of cases of eosinophilic esophagitis.[4] In patients who present for routine endoscopy for any indication, the prevalence of eosinophilic esophagitis is 6.5%, and in those undergoing an EGD for dysphagia, the prevalence is 10% to 15%.[5] In addition to the ability to take mucosal biopsies, EGD also has the opportunity of therapeutic potential with dilatation, which is useful for esophageal web, peptic stricture, anastomotic stricture, radiation-related stricture, and Schatzki's ring. In addition, it is a useful adjunct in the evaluation of underlying motility disorder. It may show the presence of a dilated esophagus, sigmoid esophagus with lack of contractions, and a tight LES, suggesting achalasia. Also, in evaluation of patients with achalasia, EGD is always performed to rule out pseudoachalasia secondary to tumors of the gastroesophageal junction and gastric cardia. Also, in achalasia patients who are unfit for surgical treatment, pneumatic balloon dilatation and botulinum toxin injection may offer alternative treatment. Recently, per oral endoscopic myotomy offers an exciting option in patients with achalasia.[6]

Manometry

Manometry is the most sensitive currently available technique to diagnose esophageal motility disorders.[7] High-resolution esophageal manometry (HRM) is a revolutionary step beyond conventional manometry, the traditional method of assessing

esophageal motility. HRM has been developed with up to 36 recording points.[8] This enables pressure measurements of 1 cm or less apart along the entire esophagus. In HRM, the distal end of the catheter is passed into the gastric compartment below the LES and the catheter can provide recording from the stomach through the esophagus into the oropharynx.[8] During an HRM study, plots are generated, also known as "Clouse" plots. These plots are presented as a color spectrum on a plot of esophageal position (*y*-axis) against time (*x*-axis) produces a pressure topograph of swallowing generated by computer software during 10 wet (5 mL water) swallows.[8] HRM helps in the diagnosis of specific motility disorders; for example, the manometric finding of aperistalsis and incomplete LES relaxation without evidence of a mechanical obstruction solidifies the diagnosis of achalasia in the appropriate setting.[9]

Diagnostic Algorithm

In patients presenting with dysphagia, the initial evaluation includes EGD to rule out important etiologies such as cancer and stricture. In addition, evaluation for eosinophilic esophagitis needs to be performed with biopsies of the esophagus. Barium swallow evaluation can be performed in elderly patients who are not candidates for EGD. In patients with normal EGD and biopsies with dysphagia, HRM is required for evaluation.

Esophageal Cancer

The possibility of the cause for dysphagia being cancer of the esophagus is the greatest concern in the majority of patients who present with difficulty swallowing. In the United States, 18,000 people were diagnosed with esophageal cancer in 2014 and 15,000 patients died owing to esophageal cancer in the United States in 2014. The most common symptoms for patients who present with esophageal cancer are dysphagia (74%) and weight loss (57.3%).[10] The evaluation of the patient who is suspected or confirmed of having esophageal cancer can involve the following studies:

- Upper endoscopy
- Endoscopic biopsy
- Barium esophagram
- CT
- Endoscopic ultrasound (EUS)
- Bone scan
- Positron emission tomography

The patient with esophageal cancer presenting with dysphagia and weight loss usually describes difficulty swallowing solids, but often retains the ability to swallow liquids until the tumor is very advanced. The weight loss in esophageal cancer patients often exceeds what would be expected from the degree of dysphagia. Upper endoscopy is often the initial procedure or study performed in this patient population. Endoscopic evaluation allows direct visualization and simultaneous acquisition of tissue samples when indicated. The pattern of cell type of esophageal cancer is changing. In 2000, pathologic evaluation of esophageal cancers revealed squamous cell carcinoma in approximately 52% of patients and adenocarcinoma in 42% of patients.[10] Currently, The National Cancer Institute describes more than 50% of esophageal cancers as adenocarcinoma, primarily arising from Barrett's esophagus, and fewer than one-half of cancers as squamous cell carcinoma. The remaining tumors are usually sarcomas or small cell cancers. Benign gastrointestinal tumors such as gastrointestinal stromal tumors can be found within the esophagus. Endoscopy with biopsy is highly sensitive and specific for the diagnosis of esophageal cancer.

Box 2
Percentage of esophageal cancer patients by stage at time of diagnosis

Stage 1: 13.3%

Stage 2: 34.7%

Stage 3: 35.7%

Stage 4: 12.3%

Staging of esophageal cancer after establishing tissue diagnosis is necessary for planning treatment options and strategies. CT is used to evaluate the mass and involvement of surrounding structures. Additionally, CT can be very helpful in identifying metastatic tumors. EUS is being used with increasing frequency owing to the ability of this technology to define clearly the layers of the esophageal wall involved with the tumor. EUS is also highly sensitive in identifying adjacent nodal metastases and can guide needle biopsies of nodes suspected of containing metastatic disease. Positron emission tomography is used frequently to evaluate the patient for local and distant metastatic disease. Less frequently, nuclear medicine bone scans are used to evaluate the patient for bone metastases.

Esophageal cancer can be a highly lethal disease and the overall disease-free survival at 1 year after diagnosis is only 43%. Most patients are diagnosed with stage 2 (34.7%) or stage 3 (35.7%) disease (**Box 2**).[10]

SUMMARY

Patients frequently present to a physician with complaints of difficulty swallowing. The approach to evaluating systematically these problems can be challenging for those who do not manage this type of patient regularly. The potential for life-threatening malignancies is present and makes this evaluation a priority. Numerous excellent tools are available to aid with the determination of the cause of dysphagia and assist with the formulation of a logical treatment algorithm.

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