

Chapter 1

Dysphagia: How to Recognize and Narrow the Differential



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Introduction

As M.F.K Fisher once wrote, “First we eat, then we do everything else.” Though the ability to swallow effortlessly is often taken for granted, dysphagia is a common patient concern with significant impact on quality of life. It can be a challenging symptom to diagnose with causes ranging from benign strictures to chronic allergic disease to widespread malignancy. Narrowing down the differential diagnosis of dysphagia can be difficult by history. This chapter will focus on signs and symptoms that can be used to help pinpoint the underlying cause of dysphagia. Additionally patient-reported outcomes that aid in disease monitoring and treatment will be reviewed.

The word dysphagia stems from Greek terms *dys* (difficulty) and *phagia* (to eat) [1]. This debilitating symptom affects humans across the globe with prevalence rates reported as high as 22% [2]. However, it can be a complex symptom to assess as there is often overlap with other esophageal and pharyngeal symptoms such as globus, heartburn, and regurgitation. Causes of dysphagia vary worldwide. In western nations such as the United States, esophageal adenocarcinoma and eosinophilic esophagitis (EoE) are increasing in incidence. With the introduction and increasing use of proton pump inhibitors, reflux related strictures are decreasing. Contrastingly, eastern nations are noting an increase in squamous cell carcinoma [3].

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Dysphagia Overview

Dysphagia is divided into several main categories, oropharyngeal vs. esophageal and mechanical vs. dysmotility. As apparent in the term, oropharyngeal dysphagia stems from abnormal processes affecting the mouth and pharynx. Patients with oropharyngeal dysphagia have problems transferring liquid or food boluses to the esophagus. Associated symptoms that may help distinguish oropharyngeal dysphagia from esophageal dysphagia include functions related to neuromuscular dysfunction such as drooling, food spillage from the mouth, inability to masticate, piecemeal swallowing, difficulty initiating a swallow, nasal regurgitation, need for repeat swallows, coughing, sialorrhea, xerostomia, dysarthria, dysphonia, or choking [4, 5]. Esophageal dysphagia encompasses all disorders that originate below the upper esophageal sphincter, causing issues with transit to the stomach. Patients classically complain of the sensation of slowed movement of food or liquids boluses in the chest though occasionally may refer symptoms to the neck from a more distal source of obstruction. The onset of symptoms is after the swallow as opposed to during the swallow. These patients do not have respiratory symptoms as the site of obstruction is distal to the airway. Patients with esophageal dysphagia may also tolerate more and/or larger boluses due to the capacious nature of the esophageal body when compared to the pharynx.

Mechanical dysphagia occurs typically through compromise of the lumen diameter. As a result, these patients will note that bolus size and consistency are the most important variables in producing symptoms. As a result, hard, dry, or chunky foods such as meat or rice and also pills cause symptoms in mechanical causes of dysphagia, whereas softer foods and liquids are not problematic unless the narrowing is almost to the point of obstruction. In contrast, motility disorders that cause dysphagia will typically involve both solids and liquids. This is because intact sphincter and esophageal body function are required for passage of all bolus consistencies. Early on in a disease such as achalasia, however, solid dysphagia may dominate with liquids becoming problematic later as lower esophageal sphincter dysfunction worsens. In some esophageal diseases, there may be a combination of dysmotility and mechanical obstruction. For example, a Zenker's diverticulum may form poor upper esophageal sphincter compliance but in turn compress the proximal esophagus.

It is also important to consider the sensory component of dysphagia. Disorders of esophageal hypersensitivity such as functional dysphagia may yield a sense of food sticking or slow transit when in fact motor function is normal and the patient is sensing physiologic passage of the bolus. Conversely, in disorders such as achalasia, where sensory function may be lessened, patients may not be cognizant of bolus impedance until large or multiple boluses have become obstructed.

Oropharyngeal Dysphagia

The most common cause of oropharyngeal dysphagia is neurologic dysfunction in older patients and myopathies, rings, or webs in younger patients [3]. Muscle weakness, drooling, focal weakness, hemiplegia, vision changes, vertigo, tinnitus, fatigability, tremor, ataxia, and trouble speaking are symptoms that may point toward a neurologic deficit, particularly of cranial nerves leading to oropharyngeal dysphagia. Additional attending symptoms with dysphagia are common as a single cranial nerve will typically innervate muscles that contribute to multiple aspects of the swallowing phases as well as speaking. Thus phases such as preparation of the bolus, elevation of the palate, and speaking may all be involved in a single cranial nerve injury. Thus a careful history evaluates all aspects of the swallowing phases. Liquids typically cause more difficulty, particularly with attending respiratory symptoms such as cough. This is because the normal mechanisms that protect the airway are commonly affected in oropharyngeal dysphagia; they are less successful in preventing liquid than solid penetration of the laryngeal vestibule.

If patients present with a known history of neurologic disease such as Parkinson's disease, cerebrovascular accident, multiple sclerosis, or amyotrophic lateral sclerosis, oropharyngeal dysphagia should be suspected. Similarly, patients with striated muscle dysfunction such as with myasthenia gravis or polymyositis commonly have oropharyngeal dysphagia. On the other hand, these and other neuromuscular diseases may present with dysphagia before more evident neurologic symptoms develop [3]. Anatomic abnormalities such as osteophytes may cause oropharyngeal compression but there are no specific differentiating symptoms to raise suspicion for these. A proper oral examination is critical in dysphagia to assess for poor dentition and loss of salivation (often a medication side effect) as probable causes. A full list of potential causes of oropharyngeal dysphagia can be seen in Table 1.1 and a suggested algorithm is seen in Fig. 1.1.

Patients with pharyngeal dysphagia often indicate the sensation of bolus holdup in the cervical esophagus with multiple swallows required to transfer the bolus. However, distal esophageal obstruction can also cause symptoms in the cervical region; this occurred in up to 30% of patients in one study [6]. Thus this is not a specific indicator of location and does not definitively distinguish clinically between oropharyngeal and esophageal dysphagia.

Esophageal Dysphagia

Patients with esophageal dysphagia often indicate food and/or liquids moving slowly or getting stuck in the chest. Classically, dysphagia to solids alone was thought to indicate a structural issue, whereas dysphagia to liquids and solids was

Table 1.1 Differential diagnosis of oropharyngeal dysphagia

<p><i>Neurologic</i></p> <ul style="list-style-type: none"> Cerebrovascular accident Parkinson's disease Multiple sclerosis Central nervous system tumor Botulism Supranuclear palsy Amyotrophic lateral sclerosis Myotonic dystrophy Postpolio syndrome Tardive dyskinesia Acute demyelinating process Guillain Barré syndrome Rabies Lead poisoning 	<p><i>Anatomic</i></p> <ul style="list-style-type: none"> Diverticulum Malignancy Thyromegaly Osteophyte Prior head or neck surgery Cervical web Cricopharyngeal bar <p><i>Iatrogenic</i></p> <ul style="list-style-type: none"> Medication induced Radiation injury Post-surgical Corrosive
<p><i>Muscular</i></p> <ul style="list-style-type: none"> Myasthenia gravis Polymyositis Pharynx or neck infection Mixed connective tissue disease Sarcoidosis Myotonic dystrophy Upper esophageal sphincter dysfunction Paraneoplastic syndromes 	<p><i>Oral</i></p> <ul style="list-style-type: none"> Poor dentition Loss of salivation Sjogren's syndrome

thought to indicate a motility disorder [4]. A recent study reviewed consecutive esophageal manometries in 200 patients with non-obstructive dysphagia and found that achalasia occurred significantly more often in patients with mixed dysphagia than solid food dysphagia [7]. A lack of strong follow-up studies remains. However, clinical application of this teaching may not be unreasonable with the caveat that in any patient with longstanding dysphagia of any type, workup for a motility disorder should eventually be pursued.

There are further clinical clues in dysphagia patients that are often useful. Patients with esophageal dysmotility such as achalasia or Chagas disease often note regurgitation [1, 8]. An associated history of food impaction is classically seen in structural causes such as eosinophilic esophagitis or peptic strictures [3]. In patients who require endoscopic removal of food impaction, it is more likely than not to be from eosinophilic esophagitis in younger patients, with prevalence rates in this subgroup reported to be up to 54%. [9] In older patients, a Schatzki ring is more typical. Dysphagia to solids without food impaction may indicate esophageal webs. Furthermore, it is apparent via clinical observation that patients with mechanical causes of dysphagia tend to feel symptoms at the start of the meal with a single poorly chewed bolus whereas patients with motility disorders feel symptoms later in the meal when several boluses have become compounded in the esophagus. Indeed, some of these patients will describe a stacking effect. Furthermore, patients with mechanical obstruction may regurgitate the single lodged bolus for relief whereas those with motility disorders will regurgitate a

Fig. 1.1 Oropharyngeal dysphagia

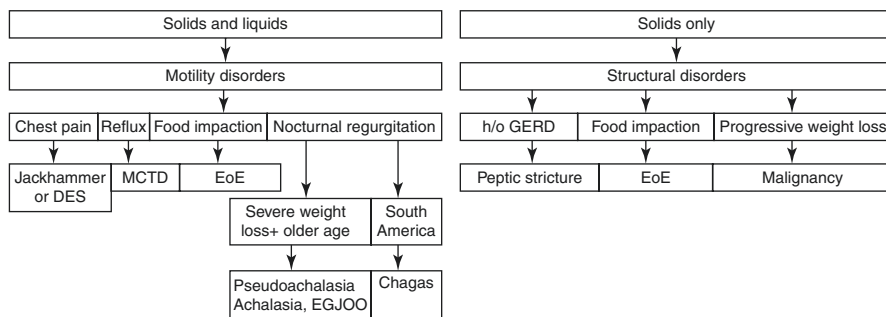
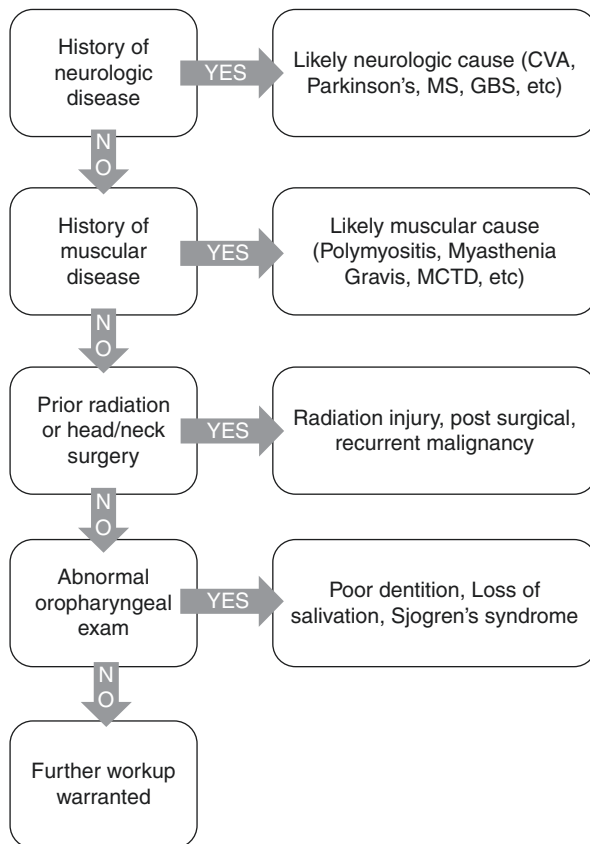


Fig. 1.2 Esophageal dysphagia

larger quantity of food and beverage. The absence of regurgitation and vomiting may indicate a patent esophagus such as patients with ineffective esophageal motility, early to moderate scleroderma, or reflux-related esophageal dysmotility. Figure 1.2 notes an algorithm for narrowing the differential diagnosis for esophageal dysphagia based on clinical details.

Regarding structural causes of dysphagia, investigators have used balloon distension techniques to evaluate the accuracy of patient symptom localization. In one study of 139 patients with esophageal strictures, the majority of patients (74%) were able to localize symptoms to within four centimeters of the esophageal lesion as seen on barium esophagram. Patients were significantly more likely to report symptoms from distal lesions being more proximal than vice versa [10]. In another study of 16 distal esophageal rings, only 75% of patients felt any symptom when a marshmallow was impacted at the site. Of these patients, 11 of the 12 reported symptoms more proximal to the implicated area [11]. Further studies reveal similar findings of proximally referred symptoms [12, 13]. Thus patient localization of dysphagia is likely only clinically useful when localized distally, to the substernal area. The broad list of potential causes of esophageal dysphagia is outlined in Table 1.2. Medication lists should be scrutinized as various drugs can lead to oropharyngeal and esophageal dysphagia via both anticholinergic pathways and localized mucosal effects [5, 14] (Table 1.3). For instance, opiates have been described to cause a range of motility disorders from esophagogastric outflow obstruction to type III achalasia [15, 16].

Patient-Reported Outcomes

Patient-reported outcome (PRO) measures are uninfluenced expressions of a patient's experience that are captured in a standardized format to allow assessment of patient-centered outcomes [17]. They can be critical in disease monitoring and treatment response [18]. Thus, PRO measures are used widely in the approval process for medications as well as devices. In fact, most randomized controlled trials funded by the National Institute of Health are required to include PRO measures

Table 1.2 Differential diagnosis of esophageal dysphagia

<i>Motility</i> Achalasia Hypertensive esophageal sphincter Diffuse esophageal spasm Jackhammer esophagus Eosinophilic esophagitis Ineffective esophageal motility Chagas disease Pseudoachalasia Reflux-related dysmotility Scleroderma Lupus Mixed connective tissue disease Medication induced	<i>Anatomic and structural</i> Malignancy Benign tumors Esophageal polyp Esophageal rings Cervical webs Eosinophilic esophagitis Foreign body Strictures Osteophytes Vascular compression Mediastinal or hilar lymphadenopathy Post-surgical
<i>Infectious</i> Candida esophagitis Viral esophagitis	<i>Other</i> Functional dysphagia

Table 1.3 Medications implicated in causing oropharyngeal and esophageal dysphagia [5, 14]

Opioids
Olanzapine, clozapine
Amitriptyline
Botulinum toxin
Procainamide
Amiodarone
Iron
Potassium
Non-steroidal anti-inflammatory medications
Tetracyclines, macrolides
Bisphosphonates
Calcium channel blockers
Nitrates
Alcohol
Theophylline
Cholesterol-lowering medications
Phenothiazines
Cytotoxins

[17, 18]. Over the past three decades, there have been over 40 different PROs developed specifically for diseases that cause dysphagia. A recent systematic review of dysphagia-related PROs evaluated the following categories to assess for rigor: conceptual model, content validity, reliability, construct validity, scoring and interpretation, burden, and presentation. Of the 34 studies that met criteria for extraction and analysis, there were 7 studies thought to be of satisfactory analysis. These outcome measures assess mechanical and neuromyogenic oropharyngeal dysphagia, esophageal cancer, achalasia, and eosinophilic esophagitis [18].

General Dysphagia

In 2004 the National Institutes of Health (NIH) launched a patient-reported outcomes initiative to develop publicly available banks to measure patient experience. A gastrointestinal symptom scale was developed by the NIH, and disrupted swallowing was measured via seven questions. This concise questionnaire was not targeted toward any specific esophageal disease but encompassed general dysphagia. It was practical in its ease of availability to the public, the short 7-day recall period, and a reading level that did not exceed that of a sixth grader [19]. The Mayo Dysphagia Questionnaire (MDQ) is another PRO developed for general dysphagia. It was more extensive and consists of 28 items, encompassing dysphagia severity and frequency, presence of allergies, gastroesophageal reflux disease and treatment, and esophageal surgery and dilation history. This takes about 6 minutes to complete and has been used in various clinical trials [20].

Oropharyngeal Dysphagia

Given the high prevalence of oropharyngeal dysphagia in patients over 50 years of age, a quality of life outcomes tool for oropharyngeal dysphagia is definitely justified. Unsurprisingly, numerous PROs have been developed [21]. The first validated dysphagia-specific PRO for patients with head and neck cancer was developed at M.D. Anderson in 2001. The MDADI (M.D. Anderson Dysphagia Inventory) consists of a self-administered questionnaire assessing 20 items that encompass global, emotional, functional, and physical well-being. This has been used in various studies assessing outcomes in head and neck cancer patients [22]. The SWAL-QOL is a quality of care outcomes tool for oropharyngeal dysphagia that assesses ten main categories including symptom frequency, eating duration and desire, fear, mental health, and fatigue. The complementary SWAL-CARE is a medications implicated in causing shorter and more patient-friendly assessment specifically looking into quality of care and patient satisfaction. Brief versions of these PROs can be seen in Table 1.4 [23].

Table 1.4 SWAL-QOL and SWAL-CARE abbreviated versions

<i>Burden</i>	<i>Mental Health</i>
Dealing with my SP is very difficult	My SP depresses me
SP is a major distraction in my life	I get impatient dealing with my SP
	Being so careful when I eat or drink annoys me
<i>Eating Duration</i>	My SP frustrates me
It takes me longer to eat than other people	I've been discouraged by my SP
It takes me forever to eat a meal	
	<i>Social</i>
<i>Eating Desire</i>	I do not go out to eat because of my SP
Most days, I don't care if I eat or not	My SP makes it hard to have a social life
I don't enjoy eating anymore	My usual activities have changed BOM SP
I'm rarely hungry anymore	Social gatherings are not enjoyable BOM SP
	My role with family/friends has changed BOM ^a SP
<i>Symptom Frequency</i>	
Coughing	<i>Fatigue</i>
Choking when you eat food	Feel exhausted
Choking when you take liquids	Feel weak
Having thick saliva or phlegm	Feel tired
Gagging	
Having excess saliva or phlegm	<i>Sleep</i>
Having to clear your throat	Have trouble falling asleep
Drooling	Have trouble staying asleep

Table 1.4 (continued)

Problems chewing	
Food sticking in your throat	<i>Advice (SWAL-CARE)</i>
Food sticking in your mouth	Food I should eat
Food/liquid dribbling out your mouth	Foods I should avoid
Food/liquid coming out your nose	Liquids I should drink
Coughing food/liquid out your mouth	Liquids I should avoid
	Techniques to help get food down
<i>Food Selection</i>	Techniques to help me avoid choking
Figuring out what I can eat is a problem for me	When I should contact a swallowing clinician
It is difficult to find foods I both like and can eat	My treatment options
	What to do if I start to choke
<i>Communication</i>	Signs that I am not getting enough to eat or drink
People have a hard time understanding me	Goals of the treatment for my SP
It's been difficult for me to speak clearly	
	<i>Patient Satisfaction (SWAL-CARE)</i>
<i>Fear</i>	Had confidence in your swallowing clinicians
I fear I may start choking when I eat food	Swallowing clinicians explained treatment to you
I worry about getting pneumonia	Swallowing clinicians spent enough time with you
I am afraid of choking when I drink liquids	Swallowing clinicians put your needs first
I never know when I am going to choke	

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**BOM* because of my, *SP* swallowing problem. Item content is abbreviated. The SWAL-QOL and SWAL-CARE are available free of charge upon request

Esophageal Cancer

Despite recent advances in neoadjuvant chemotherapy, the mortality rate of esophageal cancer remains dismal. Thus quality of life is a critical consideration for patients when assessing treatment options, and patient-reported outcomes are of utmost value in this disease. Though there have been several PROs developed for esophageal cancer, FACT-E (Functional Assessment of Cancer Therapy Esophageal Cancer subscale) is one of the most comprehensive. FACT-E focuses on physical, social, and emotional well-being as well as esophageal symptom frequency. This PRO has been used in various clinical investigations. [24] The EORTC QLQ-OG25 was developed to assess health-related quality of life in patients with esophageal and stomach cancer. This 25-item questionnaire assesses 6 critical patient outcomes: dysphagia, eating restriction, reflux, odynophagia, pain, and anxiety [25, 26].

Achalasia

Though achalasia treatment response is often evaluated by the well-known Eckardt symptom score, a quality of life assessment has been developed. The MADS (Measure of Achalasia Disease Severity) assessment encompasses food tolerance, behavior modifications, pain, heartburn, distress, lifestyle limitation, and satisfaction [27]. Though it is patient friendly and has shown to be valid and reliable, it has not been widely adapted in achalasia treatment outcomes studies.

Eosinophilic Esophagitis

Eosinophilic esophagitis is a young disease described barely 30 years ago, with an increasing incidence and prevalence. In concordance with this trend, there have been several PROs developed for eosinophilic esophagitis in the recent years. The EoE Activity Index (EEsAI) PRO is a widely used global assessment of EoE that includes seven items that evaluate frequency and duration of dysphagia, severity of dysphagia, and behavioral adaptations to various foods. The recall period is 7 days and 24 hours; completion time is 8 minutes. This is currently being used in clinical trials [28]. Other PRO measures which are not as widely used in EoE include the DSQ which assesses solid food avoidance, dysphagia, and actions to improve dysphagia in a daily electronic diary and the Straumann Dysphagia Index (SDI) which is a non-validated PRO which assesses frequency and intensity of dysphagia events [28, 29].

Summary

Proper oropharyngeal mechanisms and esophageal propagation of food and liquid boluses are essential to daily life. Unfortunately dysphagia is a common patient complaint and can stem from a plethora of causes. A careful review of the patient's history, physical exam, and clinical presentation can often narrow down the differential. It is critical to separate the symptoms into either oropharyngeal dysphagia or esophageal dysphagia, as treatment options differ significantly. Patient-reported outcome measures have been well studied in various esophageal disorders and should be followed to evaluate quality of life in these cumbersome diseases.

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