Achalasia
A Systematic Review

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THE constellations of dysphagia (difficulty swallowing), chest pain, and reflux symptoms may be caused by a variety of diseases of the esophagus such as gastroesophageal reflux disease, malignancy, mechanical obstruction (strictures, rings, or diverticula), and achalasia and other motility disorders.

Achalasia is derived from the Greek khalasis, translated as "not loosening or relaxing." A common historical definition of achalasia is the inability of the lower esophageal sphincter to relax in the setting of absent peristalsis. An initial trial of acid suppression (6-8 weeks) is reasonable, but when dysphagia symptoms persist or are dominated by the report of dysphagia, endoscopy should be performed to evaluate for mechanical obstruction or inflammatory processes. When these are not found, achalasia should be considered, especially in the setting of dysphagia primarily to liquids. Liquids can pool and accumulate above a tight, "unrelaxing" lower esophageal sphincter, whereas they are usually less of an issue in the setting of structural causes of dysphagia.

Recent advances in diagnostic testing for achalasia, especially high-resolution esophageal manometry, have provided new insights into the pathogenesis and clinical manifestation of this disorder. The purpose of this review is to highlight the epidemiology, pathogenesis, and clinical approach to patients with achalasia, emphasizing published evidence pertinent to both primary care clinicians and specialist physicians.

Evidence Acquisition and Synthesis
The literature was reviewed based on an initial broad MEDLINE search using the terms (((esophageal motility) OR achalasia) OR high-resolution esophageal manometry) and (((esophageal reflux) OR gastroesophageal reflux disease) OR GERD) and (((esophageal obstruction) OR mechanical obstruction) OR obstruction) and (((esophageal dilation) OR pneumatic dilation) OR dilation) and (((esophageal myotomy) OR endoscopic myotomy) OR laparoscopic myotomy). A total of 93 articles were included in the final literature review addressing facets of achalasia epidemiology, pathophysiology, diagnosis, treatment, and outcomes. Nine randomized controlled trials focusing on endoscopic or surgical therapy for achalasia were included (734 total patients).

FINDINGS A diagnosis of achalasia should be considered when patients present with dysphagia, chest pain, and refractory reflux symptoms after an endoscopy does not reveal a mechanical obstruction or an inflammatory cause of esophageal symptoms. Manometry should be performed if achalasia is suspected. Randomized controlled trials support treatments focused on disrupting the lower esophageal sphincter with pneumatic dilation (70%-90% effective) or laparoscopic myotomy (88%-95% effective). Patients with achalasia have a variable prognosis after endoscopic or surgical myotomy based on subtypes, with type II (absent peristalsis with abnormal pan-esophageal high-pressure patterns) having a very favorable outcome (96%) and type I (absent peristalsis without abnormal pressure) having an intermediate prognosis (81%) that is inversely associated with the degree of esophageal dilatation. In contrast, type III (absent peristalsis with distal esophageal spastic contractions) is a spastic variant with less favorable outcomes (66%) after treatment of the lower esophageal sphincter.

CONCLUSIONS AND RELEVANCE Achalasia should be considered when dysphagia is present and not explained by an obstruction or inflammatory process. Responses to treatment vary based on which achalasia subtype is present.
resolution manometry) OR Chicago classification) OR esophageal peristalsis. Articles published from January 2004 to February 2015 in English were included.

This search yielded 6194 references, of which 5788 were in English. Case reports (n = 521) and review articles (n = 899) were excluded. Articles were further searched using terms specific for epidemiology, genetics, diagnosis, manometry, surgery, pneumatic dilation, botulinum toxin, and per-oral endoscopic myotomy. Other pertinent articles and guidelines were obtained through citations or were known to the authors. We reviewed titles and abstracts to determine relevance to the article sections and ultimately included 93 articles in the review (n = 4276 excluded). A total of 9 randomized controlled trials were included when evaluating endoscopic and surgical treatment modalities (comprising 734 total patients). Details are shown in the eFigure in the Supplement.

Structure and Normal Function of the Esophagus

The esophagus is an 18- to 26-cm muscular hollow tube that transports food from the oropharynx into the stomach (Figure 1). There are 4 primary layers of esophageal tissue—the mucosa, submucosa, muscularis propria, and adventitia. The esophagus originates at the level of the cricoid cartilage and normally terminates below the hiatus in the right crura of the diaphragm. The muscularis propria gradually changes from predominant skeletal muscle in the upper esophagus to predominantly smooth muscle in the distal esophagus, with mixing of muscle types along the length of the esophagus (Figure 1). Both circular and longitudinal muscle layers are present, and within the diaphragmatic hiatus there exists a 2- to 4-cm thickened circular muscle layer, the lower esophageal sphincter. Esophageal innervation consists of both parasympathetic and sympathetic nerves, with peristalsis regulated via the parasympathetic pathway from the vagus nerve and the intrinsic enteric nervous system.

Despite the seemingly simple task of food transport, the mechanism and control of esophageal function is complex, largely owing to the neural coordination required with the oropharynx and transition through different anatomical domains with mixed muscle types. Once a food or liquid bolus enters the esophagus, primary peristalsis strips the food bolus down the length of the esophagus. Peristaltic contraction in the striated muscle esophagus is dependent on central mechanisms that involve sequential activation of excitatory activity of lower motor neurons in the vagal nucleus am-
biguus (Figure 2).\textsuperscript{1} This promotes peristaltic propagation through a sequenced top-to-bottom excitation mediated by release of acetylcholine at the motor end plates (Figure 2).\textsuperscript{1}

Primary peristalsis in esophageal smooth muscle is preceded by inhibition, which stops a progressing peristaltic wave when another swallow is initiated.\textsuperscript{2,3} This involves patterned activation of preganglionic neurons in the dorsal motor nucleus of the vagus that project onto inhibitory and excitatory neurons in the esophageal myenteric plexus (Figure 2). Under normal circumstances, the inhibitory pathway is activated first to relax the esophagus to promote filling and transport through the esophagus. The inhibitory neurons activated by the preganglionic neurons from the caudal dorsal motor neuron release nitric oxide to promote deglutitive inhibition. This is followed by sequential activation of excitatory neurons, which releases acetylcholine in response to activation by preganglionic neurons arising from the rostral dorsal motor nucleus.

The direction and rate of propagation is modulated by the increasing inhibitory influence in the distal esophagus, called the latency gradient.\textsuperscript{2,3} This essentially delays contractions in the distal esophagus and allows propagation to proceed in an aboral direction. Secondary peristalsis related to distension of the esophagus will elicit a local reflex independent of the vagal input from the dorsal
Box. Symptoms Suggestive of Achalasia That May Prompt Referral for Esophageal Motility Testing*

**Esophageal Symptoms**
- Dysphagia (90% of patients)
- Heartburn (75% of patients)
- Regurgitation or vomiting (45% of patients)
- Noncardiac chest pain (20% of patients)
- Epigastric pain (15% of patients)
- Odynophagia (<5% of patients)

**Other Associated Signs and Symptoms**
- Cough or asthma (20%-40% of patients)
- Chronic aspiration (20%-30% of patients)
- Hoarseness or sore throat (33% of patients)
- Unintentional weight loss (10% of patients)

*Data from Tsubo et al,33 Sinan et al,34 and Nig et al.35

Epidemiology and Genetics of Achalasia

Achalasia has an annual reported incidence of approximately 1/100 000 worldwide.10-13 In Iceland, 62 cases of achalasia were diagnosed over the course of 51 years (overall incidence, 0.6/100 000 per year; mean prevalence, 8.7 cases/100 000).14 Gennaro et al14 recently reported an incident rate in Italy of 1.59 cases/100 000 per year (2001-2005). Due to the chronicity of achalasia, the estimated prevalence of achalasia is approximately 9/100 000 to 10/100 000.11,12 In the United States, rates of hospitalization for achalasia depend on patient age, ranging from 0.25/100 000 (<18 years) to a high of 37/100 000 (>85 years).15 Although the incidence is low, the chronicity of achalasia significantly affects patients’ health-related quality of life, work productivity, and functional status compared with the general US population.16

Evidence supporting genetic underpinnings for achalasia come from twin and sibling studies and from the association of achalasia with other diseases such as Parkinson disease, Allgrove syndrome, and Down syndrome.17-19 Familial adrenal insufficiency with alacrima and achalasia (Allgrove syndrome) is a rare genetic syndrome associated with defects in the A4AS gene (chromosome 12q13) and subsequent defective tryptophan–aspartic acid repeat protein.20,21 A few reports have described familial achalasia, most recently in a single family with an autosomal dominant pattern with 6 affected members.22 Polymorphisms in the nitric oxide synthase gene have been investigated, but polymorphisms were found to be no different between patients with achalasia and controls.23 Because of a possible autoimmune etiology of achalasia, studies have suggested possible roles of interleukin polymorphisms (IL-23 and IL-10).24,25 Currently, genetic testing for achalasia has no role in clinical management outside of research endeavors.

Pathophysiology

Achalasia is associated with functional loss of myenteric plexus ganglion cells in the distal esophagus and lower esophageal sphincter.26 The cause for an initial reduction of inhibitory neurons in achalasia is unknown. Initiation of neuronal degeneration may be an autoimmune process triggered by an indolent viral infection (herpes, measles) in conjunction with a genetically susceptible host.27 Patients with achalasia are more likely to have concomitant autoimmune diseases than the general population28 and the prevalence of serum neural autoantibodies is higher.29,30 lending further credence to an autoimmune etiology. The inflammatory reaction is associated with a T-cell lymphocyte infiltrate that leads to a slow degradation of ganglion cells. The distribution and end result of this plexitis is variable and may be modified by the host response or the etiologic stimulus. Achalasia can also be one manifestation of the widespread myenteric plexus destruction in Chagas disease, a consequence of infection with the parasite *Trypanosoma cruzi*.30

The consequence of the myenteric plexus inflammation is degeneration or dysfunction of inhibitory postganglionic neurons in the distal esophagus, including the lower esophageal sphincter.31,32 These neurons use nitric oxide and vasoactive intestinal peptide as neurotransmitters, and their dysfunction results in an imbalance between excitatory and inhibitory control of the sphincter and adjacent esophagus. Unopposed cholinergic stimulation can result in impaired relaxation of the lower esophageal sphincter, hypercontractility of the distal esophagus, and rapidly propagated contractions in the distal esophagus. Longitu-
dinal muscle contractions and esophageal shortening can persist in achalasia. There is variable expression of these abnormalities among individuals, and only impaired deglutitive relaxation of the lower esophageal sphincter is universally required as a defining feature of achalasia.

### Symptoms and Signs

The most common symptoms of achalasia are listed in the Box and may prompt referral for a motility evaluation after more common disorders are ruled out, such as gastroesophageal reflux disease, mechanical obstruction (stricture, rings), or malignancy. Progressive dysphagia to both solids and liquids is the hallmark symptom associated with a diagnosis of achalasia. The prevalence of weekly dysphagia among US adults is approximately 4% and is associated with a broad differential diagnosis and workup (Table 1). Esophageal motility testing should only be done after a structural or mechanical obstruction has been ruled out and oropharyngeal causes are not apparent. In a single-center review of all patients with manometry over a period of 24 years (1984-2008), Tsuboi et al found that patients with achalasia most commonly presented with dysphagia and heartburn. Other common symptoms included chest pain, regurgitation, cough or asthma, odynophagia, and epigastric pain.

Respiratory symptoms are also common in patients with achalasia, because primary motor abnormalities result in decreased clearance of food and liquid from the esophagus, predisposing patients to aspiration. Sinan et al found that of 110 patients with achalasia, 40% reported at least 1 respiratory symptom daily. Another study of 38 patients with achalasia found that 71% had sore throat, hoarseness, or postnasal drip and 61% had cough. The dysphagia preceded respiratory symptoms by an average of 24 months, indicating the progressive nature of symptoms with lack of treatment. It is also important to consider a diagnosis of connective tissue disease (eg, scleroderma) in patients with chronic respiratory issues and abnormalities of esophageal motility.

Demographic and clinical factors may affect clinical symptoms. Dysphagia and regurgitation are common among all ages, but younger patients with achalasia have been found to have a higher prevalence of heartburn and chest pain than older patients. Obese patients (body mass index $\geq 30$) may have more frequent symptoms of choking and vomiting, possibly related to increased abdominal pressure. Chest pain was more commonly reported by women than men in a single-center retrospective review of 213 patients with achalasia. However, another group reported similar reports of chest pain regardless of age or sex.

### Diagnosis

Diagnosis of achalasia requires recognition of symptoms and appropriate use and interpretation of diagnostic testing (Table 1). Diagnoses can be difficult to make, and many patients have symptoms for many years prior to correct diagnosis and treatment. This is most common when patients present with symptoms that mimic gastroesophageal reflux disease, such as heartburn, chest pain, and regurgitation. In contrast, when patients primarily present with dysphagia, a careful history and evaluation

<table>
<thead>
<tr>
<th>Table 1. Differential Diagnosis of Dysphagia Symptoms and Initial Testing</th>
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<tr>
<td><strong>Signs and Symptoms</strong></td>
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<tr>
<td><strong>Esophageal Dysphagia</strong></td>
</tr>
<tr>
<td>Structural esophageal disorders</td>
</tr>
<tr>
<td>Peptic stricture</td>
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<tr>
<td>Esophageal (Schatzki) ring or webs</td>
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<tr>
<td>Eosinophilic esophagitis</td>
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<tr>
<td>Malignancy</td>
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<tr>
<td>Radiation- or medication-induced strictures</td>
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<tr>
<td>Foreign body or food impaction</td>
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<tr>
<td>Vascular compression</td>
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<tr>
<td>Mediastinal mass/external compression</td>
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<tr>
<td><strong>Motility esophageal disorders</strong></td>
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<tr>
<td>Achalasia and esophagogastric junction outflow obstruction</td>
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<tr>
<td>Absent contractility</td>
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<tr>
<td>Distal esophageal spasm</td>
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<tr>
<td>Hypercontractile esophagus (jackhammer)</td>
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<tr>
<td>Minor disorders of peristalsis</td>
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<tr>
<td>Scleroderma</td>
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<tr>
<td>Gastroesophageal reflux disease</td>
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<tr>
<td><strong>Oropharyngeal Dysphagia</strong></td>
</tr>
<tr>
<td>Structural oropharyngeal disorders</td>
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<tr>
<td>Malignancy</td>
</tr>
<tr>
<td>Spinal osteophytes</td>
</tr>
<tr>
<td>Zenker diverticulum</td>
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<tr>
<td>Proximal strictures, rings, or webs</td>
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<tr>
<td>Radiation injury</td>
</tr>
<tr>
<td>Oropharynx infection</td>
</tr>
<tr>
<td>Thyroid enlargement</td>
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<tr>
<td><strong>Neuromuscular (systemic) disorders</strong></td>
</tr>
<tr>
<td>Cerebral vascular accident</td>
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<tr>
<td>Multiple sclerosis</td>
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<tr>
<td>Parkinson disease</td>
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<tr>
<td>Myasthenia gravis</td>
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<td>Amyotrophic lateral sclerosis</td>
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<tr>
<td>Muscular dystrophy</td>
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<td>Dermatomyositis</td>
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<td>Thyroid disorders</td>
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*pH testing indicates ambulatory pH and reflux monitoring.*
of swallowing by watching the patient drink water can be helpful in distinguishing between oropharyngeal dysphagia and esophageal dysphagia. Patients with oropharyngeal dysphagia will typically struggle to move the bolus into the esophagus during water swallows and will often have coughing and immediate regurgitation. Primary oropharyngeal symptoms should first prompt an evaluation for oropharyngeal etiologies, with a modified barium cookie swallow study performed by speech pathology (Table 1).

Patients with intact oropharyngeal swallowing and dysphagia should be evaluated for esophageal causes, and the differential should focus on distinguishing between a structural mechanical obstruction and a motility disorder (Table 1). Mechanical obstruction should be ruled out first, via either upper gastrointestinal tract endoscopy or radiologic imaging, prior to evaluation for abnormal motility. Patients with a previous fundoplication or bariatric procedure (lap-band, gastric bypass) may also present with signs and symptoms that mimic achalasia, and it is extremely difficult to make the diagnosis of achalasia in the context of these operations. In these cases, it is important to look for mechanical causes of obstruction, such as anastomotic stricture, tight lap-band, and an obstructed fundoplication.

**Esophagogastroduodenoscopy**

Esophagogastroduodenoscopy with mucosal biopsy should be performed in most patients presenting with solid food dysphagia, liquid food dysphagia, or both. This is done to rule out erosive gastroesophageal reflux disease, eosinophilic esophagitis, structural lesions (strictures, webs, or rings), and esophageal cancer or “pseudoachalasia.” Endoscopic features of an esophageal motility disorder include a dilated or tortuous esophagus, food impactions and fluid pooling in the esophagus, and resistance to intubation of the gastroesophageal junction. Patients with achalasia may also develop candidiasis attributable to esophageal stasis, and evidence of candidiasis in the context of intact immune function should prompt an evaluation for esophageal dysmotility. Although endoscopy may suggest achalasia, other testing must be performed to confirm the diagnosis.

**Barium Esophagram**

The classic “bird’s-beak” appearance of achalasia on a barium swallow study is a well-known image in clinical medicine (Figure 3C). Other radiographic features suggestive of an esophageal motility disorder include esophageal dilation, contrast filling the esophagus, a “corkscrew appearance,” and aperistalsis.

**Esophageal Manometry**

Esophageal manometry to assess esophageal pressures and contractile activity along the length of a flexible catheter has become the standard for diagnosing and classifying achalasia. Major technological advances have occurred during the last decade, wherein conventional water-perfused or strain gauge systems with a line tracing output have been replaced by more reproducible high-resolution manometry systems that present pressure data in the context of esophageal pressure topography plots (Figure 2 and Figure 3). These methods were originally developed by Clouse and led to an improved understanding of peristaltic contractile activity. Seminal work that characterized high-resolution manometry metrics using Clouse plots in both asymptomatic and symptomatic individuals eventually led to the creation of a new classification scheme for motility disorders, called the Chicago Classification (Figure 4).

One important advantage of esophageal pressure topography has been the ability to further refine conventional diagnoses, such as achalasia, into clinically relevant phenotypes. The diagnosis of achalasia is classically made by demonstrating impaired relaxation of the lower esophageal sphincter and absent peristalsis in the absence of esophageal obstruction near the lower esophageal sphincter attributable to a stricture, tumor, vascular structure, implanted device, or infracting process. Three distinct subtypes of achalasia (types I, II, and III) are defined with high-resolution manometry that have both prognostic and potential therapeutic implications (Figure 3). If criteria for achalasia subtypes are not met, a validated hierarchical analysis is used to determine if patients have nonachalasia motor disorders, as shown in Figure 4. However, a possible diagnosis of achalasia should be considered when patients present with an esophagogastric junction outflow obstruction, because this may represent an incomplete or early form of the disease. Similarly, it is also important to consider achalasia in patients with absent contractility, as these cases may be confused with scleroderma owing to the complexities of measuring relaxation of the lower esophageal sphincter. Equivocal cases may require further workup with endoscopic ultrasound in the case of EGJ outflow obstruction to rule out a subtle obstruction and a barium esophagogram in the case of absent contractility to document bolus retention, which would favor a diagnosis of achalasia.

**Treatment**

There are no curative therapies for achalasia; a summary of treatment modalities is listed in Table 2. Nine randomized trials have compared endoscopic and surgical treatments for achalasia (Table 3). Physiologically, many treatments are directed at reducing contractility in the lower esophageal sphincter to allow for adequate esophageal emptying. The primary goal of management should be based on early diagnosis to prevent late complications of the disease and preserve remaining esophageal structure and function.

**Medical Treatment**

Oral calcium channel blockers or nitrates cause a prompt reduction in lower esophageal sphincter pressure of up to 47% to 64%, with mild benefit for dysphagia. These medications can have limiting adverse effects (headache, orthostatic hypotension, or edema) and do not halt disease progression. Consequently, they are poor long-term treatment options and should be reserved for patients who are poor candidates for surgical or endoscopic therapy. Nifedipine (10-30 mg, given 30-45 minutes before meals) or isosorbide dinitrate (5-10 mg, given 15 minutes before meals) may be useful as short-acting temporizing treatments. Absorption and effect of oral medications can be unpredictable in achalasia.

5’-Phosphodiesterase inhibitors, such as sildenafil, have also been used (off-label) to treat achalasia and spastic disorders of the esophagus. Sildenafil lowers esophagogastric junction pressure and attenuates distal esophageal contractions by blocking the en-
zyme that degrades cyclic guanosine monophosphate induced by nitric oxide. Sildenafil is a viable alternative in patients not responding to or proving intolerant of calcium channel blockers or nitrates. However, minimal long-term treatment data exist pertinent to using 5′-phosphodiesterase inhibitors to treat achalasia.

Botulinum Toxin

Botulinum toxin injection into the muscle of the lower esophageal sphincter was initially proposed as an achalasia treatment based on its ability to block acetylcholine release from nerve endings. Using this technique, Pasricha et al.54 reported improved dysphagia in 66% of patients with achalasia for 6 months. No increase in efficacy has been demonstrated with greater doses.55 The effect is temporary and is eventually reversed by axonal regeneration; subsequent clinical series report minimal continued efficacy after 1 year.54,65-67 Most patients relapse and require re-treatment within 12 months, and repeated treatments have been shown to make subsequent Heller myotomy more challenging.58 Thus, botulinum toxin injection should rarely be used as a first-line therapy for achalasia and is primarily reserved for patients who are not candidates for definitive therapy.

Pneumatic Dilation

A pneumonic dilator is a noncompliant, cylindrical balloon that is positioned fluoroscopically across the lower esophageal sphincter and inflated with air using a handheld manometer. The reported efficacy of pneumatic dilation in randomized controlled trials ranges from 62% to 90% (Table 3). Patients with a poor result or rapid recurrence of dysphagia are unlikely to respond to additional dilations, but subsequent response to myotomy is not influenced. Although the reported incidence of perforation from pneumatic dilation ranges from 0% to 16%, a recent systematic review on the

Figure 3. Conceptual Model of Esophageal Disease Presentation and Progression Based on Phenotypes Described Using High-Resolution Manometry and Barium Esophagrams

Some patients may present with an esophagogastric junction (EGJ) outflow obstruction pattern (panel A) in which there is impaired lower esophageal sphincter (LES) relaxation with evidence of propagating contractions. This may represent the point where the esophageal body is progressing to aperistalsis and there is variable loss of the excitatory (blue circles) and inhibitory (red circles) influence. As preferential loss of the inhibitory neurons continues to progress, the manometric pattern may progress to a type II pattern (panel B) associated with impaired LES relaxation and panesophageal pressurization, akin to a filled water balloon being squeezed.42 Type I achalasia (panel C) is the classic presentation of achalasia, in which there is complete loss of contractile activity in the body of the esophagus; this is typically a later phase of disease progression where there is evidence of moderate to severe esophageal dilatation. Type III achalasia (panel D) is associated with premature simultaneous contractions that compartmentalize the bolus before it can empty the esophagus, as evidenced by the corkscrew appearance on esophagram. This may represent a distinct entity that does not fall into the typical presentation of progressive neuron loss seen with the progression of EGJ outlet obstruction to type II achalasia, to type I achalasia. Corresponding barium esophagrams are also shown for each subtype. Barium esophagrams and esophageal pressure topography plots reproduced with permission from the Esophageal Center at Northwestern Medicine.
### Figure 4. Chicago Classification Version 3.0 for Esophageal Motility Disorders, Including Achalasia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Criteria</th>
<th>Type I: 100% failed peristalsis</th>
<th>Type II: 100% failed peristalsis with panesophageal pressurization</th>
<th>Type III: ≥20% premature contractions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achalasia</td>
<td>LES relaxation zupper limit of normal AND 100% failed peristalsis or spasm</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Esophageal junction outflow obstruction</td>
<td>LES relaxation zupper limit of normal AND sufficient evidence of peristalsis such that criteria for type I-III achalasia are not met</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Distal esophageal spasm (DES)</td>
<td>LES relaxation is normal AND premature contractions or hypercontractile vigor</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ineffective esophageal motility (IEM)</td>
<td>LES relaxation is normal AND 100% failed peristalsis</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Fragmented peristals</td>
<td>LES relaxation is normal AND ≥50% of swallows are ineffective based on contractile vigor measurements</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Normal esophageal motor function</td>
<td>LES relaxation is normal AND &gt;50% of swallows are effective without criteria for spasm or jachamper esophagus</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Modified from Kahrilas et al. Classification algorithm based on results of high-resolution manometry with ten 5-mL water swallows. Note that achalasia should be considered in patients presenting with esophageal junction outflow obstruction and absent contractility. Failed peristalsis denotes swallows with a distal contractile integral (DCI) less than 100 mm Hg·sec·cm (the DCI quantifies the distal contractile pressure exceeding 20 mm Hg from the transition zone to the proximal aspect of the lower esophageal sphincter [LES] [amplitude × time × length in units of mm Hg·sec·cm·]). Panesophageal pressurization denotes uniform pressurization greater than 30 mm Hg extending from the upper esophageal sphincter to the esophagogastric junction. Contractile vigor denotes the strength of distal contraction as defined by the DCI. Ineffective esophageal motility (IEM) is diagnosed when a patient exhibits greater than 50% ineffective swallows (ineffective swallows are either failed [DCI <100 mm Hg·sec·cm] or weak [DCI <450 mm Hg·sec·cm]). Fragmented swallow denotes a swallow with DCI greater than or equal to 450 mm Hg·sec·cm and a greater than 5-cm break in the pressure domain, corresponding to an intact esophageal contraction, required to push a swallowed bolus forward.

* Rapid contraction and hypertensive peristalsis are not considered distinct clinical pathological entities in Chicago Classification version 3.0.

#### Myotomy

Heller myotomy, which divides the circular muscle fibers of the lower esophageal sphincter, is the standard surgical approach for achalasia. Laparoscopy is the preferred surgical approach because of its lower morbidity and comparable long-term outcome compared with that achieved with thoracotomy. 

Laparoscopic Heller myotomy is superior to a single pneumatic dilation in terms of efficacy and durability, with reported efficacy rates in the 88% to 95% range. However, the superiority of surgical myotomy over pneumatic dilation is less evident when compared with a graded approach to pneumatic dilation using repeat dilations as mandated by the clinical response. An antireflux repair has been shown to significantly decrease gastroesophageal reflux disease, and this can range from an anterior 180° fundopasty (Dor) to a 270° partial fundoplication (Toupet). There is general agreement that a full 360° Nissen fundoplication is contraindicated, as 1 randomized trial showed that 15% of patients had recurrent dysphagia.

### References

Table 3. Randomized Clinical Trials Evaluating Treatment Modalities for Achalasia (2004-2015)

<table>
<thead>
<tr>
<th>Source</th>
<th>Inclusion Criteria</th>
<th>Sample Size, No.</th>
<th>Comparison</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Richards et al,57 2004</td>
<td>Patient’s diagnosis of untreated achalasia</td>
<td>43</td>
<td>LHM vs LHM with Dor fundoplication</td>
<td>No significant difference in postoperative LES pressure or postoperative dysphagia Pathologic GERD: 48% for LHM vs 9% for LHM + fundoplication</td>
</tr>
<tr>
<td>Rebecchi et al,58 2008</td>
<td>Patients with achalasia, including previous treatment with botulinum toxin and pneumatic dilation</td>
<td>144 (138 for long-term analysis)</td>
<td>LHM with Dor fundoplication vs LHM with total fundoplication</td>
<td>Incidence of GERD after 60-mo follow-up: 2.8% for Dor vs 0% for total (P = NS) Recurrence of dysphagia: 2.8% for Dor vs 15% for total (P &lt; .001)</td>
</tr>
<tr>
<td>Rawlings et al,59 2012</td>
<td>Patients with achalasia (untreated or previously treated with botulinum toxin or pneumatic dilation)</td>
<td>60</td>
<td>LHM with Dor fundoplication vs LHM with Toupet fundoplication</td>
<td>Reflux symptoms: no difference Positive 24-h pH testing: no difference Improvement in dysphagia: no difference</td>
</tr>
<tr>
<td>Kostic et al,60 2007</td>
<td>Patients with newly diagnosed untreated achalasia</td>
<td>51</td>
<td>Pneumatic dilation vs LHM with Toupet fundoplication</td>
<td>Cumulative number of treatment failures at 12 mo: 6 treatment failures in pneumatic dilation group vs 1 treatment failure in LHM group (P = .04)</td>
</tr>
<tr>
<td>Novais et al,61 2010</td>
<td>Patients with newly diagnosed achalasia</td>
<td>94</td>
<td>Pneumatic dilation vs LHM</td>
<td>Clinical response at 3 mo: 73.1% for pneumatic dilation vs 88.3% for LHM (P = .08) Manometric response at 3 mo: no difference between groups Incidence of GERD (24-h pH measurement): 31% for pneumatic dilation vs 5% for LHM (P = .0001)</td>
</tr>
<tr>
<td>Boeckxstaens et al,57 2011</td>
<td>Patients with newly diagnosed achalasia</td>
<td>201 (LHM = 106, pneumatic dilation = 95)</td>
<td>Pneumatic dilation vs LHM with Dor fundoplication</td>
<td>Decrease in Eckardt score of s3 at 12 mo and 24 mo: (1) 90% for 12-mo pneumatic dilation vs 93% for LHM (P = .46) and (2) 86% for 24-mo pneumatic dilation vs 90% for LHM (P = .46) LES pressure, esophageal emptying, quality of life, complications: (1) no difference in LES pressure, quality of life, or esophageal emptying and (2) 4% perforation rate with pneumatic dilation and 12% mucosal tear rate with LHM</td>
</tr>
<tr>
<td>Persson et al,56 2015</td>
<td>Patients with newly diagnosed achalasia</td>
<td>53 (LHM = 25, pneumatic dilation = 28)</td>
<td>Pneumatic dilation vs LHM with posterior fundoplication</td>
<td>Treatment failure: (1) 4% for LHM vs 32% for pneumatic dilation at 3 y and (2) 8% for LHM vs 36% for pneumatic dilation at 5 y</td>
</tr>
<tr>
<td>Mikaeli et al,60 2006</td>
<td>Patients with newly diagnosed achalasia</td>
<td>54</td>
<td>Botulinum toxin 1 mo before pneumatic dilation vs pneumatic dilation alone</td>
<td>Cumulative 1-y remission rate: 77% for botulinum toxin + pneumatic dilation vs 62% for pneumatic dilation alone (P = .10)</td>
</tr>
<tr>
<td>Bakhshipour et al,64 2009</td>
<td>Patients with achalasia with failed 30- and 35-mm pneumatic dilation or botulinum toxin</td>
<td>34</td>
<td>Pneumatic dilation vs pneumatic dilation + botulinum toxin</td>
<td>Symptoms at 1, 6, and 12 mo: no significant difference in symptom scores at all time intervals</td>
</tr>
</tbody>
</table>

Abbreviations: GERD, gastroesophageal reflux disease; LES, lower esophageal sphincter; LHM, laparoscopic Heller myotomy.
Prognosis and Follow-up

Multiple publications now support the prognostic value of achalasia subtypes: (1) patients with type II achalasia have the best prognosis from treatment involving myotomy or pneumatic dilatation (96% success rate)\(^{81}\); (2) the treatment response of patients with type I is less robust, at 81%\(^{81}\) (and is reduced further as the degree of esophageal dilatation increases); and (3) patients with type III have a worse prognosis (66%\(^,\)\(^{81}\)) likely because the associated spasm is less likely to respond to therapies directed at the lower esophageal sphincter.\(^{52,71,82-84}\)

The optimal approach in providing follow-up for patients with achalasia is focused on periodic evaluation of symptom relief, nutrition status, and esophageal emptying by timed barium swallows.\(^{1980;238(6):G485-G490.}\) Achalasia treatment is not curative, and up to 20% of patients have symptoms that may require additional treatments within 5 years.\(^{19-22}\) Up to 6% to 20% of treated patients may have progressive dilatation to megaesophagus or end-stage disease.\(^{93}\) Management of care of these patients is difficult, and options include botulinum toxin injection, repeat pneumatic dilatation, or repeat myotomy. Esophagectomy is ultimately reserved as a final option in patients with severe esophageal dilatation and symptoms not responding to dilation and myotomy.

ARTICLE INFORMATION

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