Achalasia and Nutrition: Is it Simple Physics or Biology?

INTRODUCTION

Achalasia is a rare esophageal motility disorder that is characterized manometrically by esophageal aperistalsis and impaired relaxation of the lower esophageal sphincter (LES) in response to deglutition. Thus, primary symptoms at presentation include dysphagia and regurgitation of undigested food with varying degrees of weight loss. Achalasia was first described by Sir Thomas Willis in 1674 with recent evidence suggesting an annual incidence and prevalence of approximately 2/100,000 and 10/100,000 respectively. The disease can occur at any age, but is usually diagnosed between 30 and 60 years with a mean age at diagnosis of > 50 years.

The underlying etiology of achalasia is loss of myenteric neurons that coordinate esophageal peristalsis and LES relaxation. Despite its initial description in 1674, the inciting event that leads to loss of these inhibitory neurons is still unclear. Thus, the most common form of achalasia is idiopathic achalasia. However, approximately 2-4% of patients with suspected achalasia have pseudoachalasia (due to malignancies or secondary achalasia from extrinsic processes such as prior tight fundoplication). Similar clinical presentation can also occur with other diseases (see Table 1).

In this review article, we provide a brief overview of the clinical presentation, diagnosis, and management options in patients with achalasia followed by a detailed review of nutritional aspects that are often overlooked in these patients.
CLINICAL PRESENTATION

Patients with achalasia exhibit a varied clinical presentation, however, progressive dysphagia to solids followed by liquids is usually the first clinical symptom. Other symptoms include regurgitation that is often non-responsive to adequate proton pump inhibitor (PPI) trial, weight loss, chest pain, and respiratory symptoms (cough, hoarseness, shortness of breath, and sore throat). Table 2 shows the most common symptoms in patients with achalasia and their prevalence based on available data. Chest pain is more frequent in younger female patients. Although achalasia as a disease entity overall is rare, it is important for primary care providers to have a low clinical threshold for referral to specialists given that in early stages of the disease, dysphagia may be very subtle and can be misinterpreted as dyspepsia or poor gastric emptying. In addition, these patients will often have heartburn due to food stasis and can lead to an erroneous diagnosis of gastro-esophageal reflux disease (GERD), which is often unresponsive to PPI therapy, and might result in inappropriate referral for anti-reflux surgery (which would significantly exacerbate the underlying problem). Weight loss in these patients is also widely variable with average loss of 20 ± 16 lbs; it is unclear why certain patients with achalasia lose significantly more weight compared to others.

Table 1. Clinical Presentations that Mimic Achalasia

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<thead>
<tr>
<th>Chagas Disease</th>
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<tr>
<td>o Infection with Trypanosoma cruzi</td>
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<tr>
<td>As part of other complex syndromes such as:</td>
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<tr>
<td>o Allgrove or Triple A syndrome</td>
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<tr>
<td>• Alacrima</td>
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<tr>
<td>• Achalasia</td>
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<tr>
<td>• Adrenocorticotropic hormone deficiency</td>
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<tr>
<td>o Down's syndrome</td>
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<td>o Familial visceral neuropathy</td>
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DIAGNOSIS

The diagnosis of achalasia can be relatively straightforward with a well-documented clinical history, radiography/endoscopy, and esophageal motility testing. Manometry is the gold standard diagnostic test for establishing the diagnosis of achalasia and can also help characterize motor patterns with treatment outcome implications. It is required regardless of findings on barium esophagram and esophagogastroduodenoscopy (EGD). Table 3 identifies the advantages and disadvantages of the various methods used in diagnosing achalasia.

Esophageal Manometry

Characteristic findings for achalasia on conventional manometry is absence of esophageal peristalsis and incomplete LES relaxation on deglutition (usually residual pressures of >10mmHg). However, most academic centers have now replaced conventional manometry with high-resolution manometry (HRM) with esophageal pressure topography (EPT), which allows for improvement in pressure sensing technology. This has allowed clinicians to develop a subclassification of achalasia into 3 clinical groups based on the pattern of esophageal contractility:

- Type I (classic achalasia; quiescent esophageal body)
- Type II (isobaric pan-esophageal pressurization)
- Type III (simultaneous contractions)

Three retrospective studies have showed treatment outcome implications based on the subtype of achalasia suggesting type II having the best prognosis, followed by subtype I; subtype III can be difficult to treat.
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**Table 2. Prevalence of Symptoms in Patients with Achalasia**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Percent of Patients with Achalasia</th>
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<tr>
<td>Dysphagia for solids and liquids</td>
<td>82-100%</td>
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<tr>
<td>Regurgitation of undigested food</td>
<td>76-91%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>35-91%</td>
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<tr>
<td>Chest pain</td>
<td>25-64%</td>
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<tr>
<td>Heartburn</td>
<td>27-42%</td>
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<tr>
<td>Nocturnal cough</td>
<td>37%</td>
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<tr>
<td>Aspiration</td>
<td>8%</td>
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</table>

**Endoscopy**

All patients with suspected achalasia are recommended to have an upper endoscopy to exclude mechanical obstruction or pseudoachalasia that can mimic achalasia. At endoscopy, the esophageal body usually appears normal or can be dilated, but can occasionally have friable mucosa with even superficial ulcers secondary to chronic stasis or candida esophagitis. The LES is closed even with insufflations of air, showing the appearance of puckering, but the endoscope can pass this area with gentle pressure. If there is high concern for malignancy due to rapid progression of symptoms, biopsies and endoscopic ultrasound or chest CT are obligatory.

**Barium Esophagram**

Barium esophagram is a non-invasive test for examination of the esophagus that, although less sensitive compared to manometry, can still provide important clinical information with ruling out structural abnormalities and estimating the diameter of the esophagus. Typical findings in achalasia is the presence of smooth tapering of the lower esophagus leading to a closed LES, resembling a “bird’s beak” as showed in Figure 1. In more advanced stages of the disease, it can also show a “mega-esophagus,” with massive dilatation of the esophageal body, which can have significant implications for treatment. Furthermore, in 1997, de Oliverira et al. described timed barium esophagram with films taken at 1, 2, and 5 minutes after the last swallow of barium for evaluating esophageal emptying in patients with achalasia. This and subsequent studies found that the rate of barium emptying was predictive of long term success after treatment.

**MANAGEMENT**

Treatment for achalasia is aimed towards palliation of symptoms, as there are no curative therapies for achalasia at present. The goal of management is to reduce LES pressure to allow adequate esophageal emptying and prevent late complications of the disease such as severe malnutrition and recurrent aspiration pneumonia. Current therapeutic options include pharmacologic treatment, pneumatic dilatation, surgical myotomy and more recently per-oral endoscopic myotomy (POEM). We briefly review these options below.

**Pharmacologic Treatment**

Pharmacological therapy is primarily aimed at lowering LES pressure. Two of the most common agents are calcium channel blockers and nitrates. These medications can decrease LES pressure by 47-64%, but are often limited due to their adverse effects including headaches, orthostatic hypotension, and edema. In a study comparing the effect of sublingual nifedipine to sublingual isosorbide dinitrate, both drugs decreased LES pressure, but the effect of nitrate was slightly better than that of nifedipine (65% vs. 49%, respectively). However, patients often develop tachyphylaxis and will lose response to these medications after short-term benefit. Thus, these treatment options are reserved for patients:

1. As bridge to more effective therapy
2. Who have failed botulinum toxin injections
3. Who are not candidates for pneumatic dilatation or surgery.

Another pharmacologic option is injection of
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**Per-Oral Endoscopic Myotomy (POEM)**
Per-oral endoscopic myotomy (POEM) is the newest treatment option available at some centers and consists of an endoscopic approach to esophagomyotomy. It involves creating a submucosal tunnel through an esophageal mucosal incision approximately 10cm proximal to esophagogastric junction and then dissecting the muscle fibers beginning at 3cm distal to the mucosal entry site and extending 2cm in to the cardia.

Treatment success has been reported as high as 90% with significant decreases in LES pressure with improved quality of life measurements and low complication rates. There have been no randomized trials comparing PD to laparoscopic HM to POEM and long term outcomes after POEM still need to be studied.

**Surgical Myotomy**
Laparoscopic Heller myotomy (HM) combined with an antireflux fundoplication (Dor vs. posterior Toupet) is also a highly effective treatment option with studies showing efficacy rates in the 88-95% range. Although laparoscopic HM is superior to a single pneumatic dilatation in terms of efficacy and durability, the difference is significantly less when compared with a graded approach to pneumatic dilatation using repeated dilatations. Thus, pneumatic dilatation and surgical myotomy should both be offered to low surgical risk patients as the initial therapy. Surgery might have a more favorable clinical response in younger male patients or patients with tortuous esophagus, esophageal diverticula or previous surgery on the gastroesophageal junction.

**Pneumatic Dilation**
Pneumatic dilatation (PD) involves use of a rigid balloon that is positioned across the lower esophageal sphincter with or without fluoroscopy with the goal of disrupting the circular muscle fibers of the LES (Figure 2). The most commonly used balloon is the Rigiflex dilator, which comes in three different diameters (3.0, 3.5, and 4.0 cm). Multiple randomized controlled trials have shown efficacy from 62-90% and is arguably the most effective non-surgical treatment option in these patients. It is also very well tolerated with a recent systematic review concluding that using modern technique, the risk of perforation was < 1% and comparable to the risk of perforation during Heller myotomy. Predictors of favorable clinical response to PD include older age (>45 years), female gender, narrow esophagus, LES pressure after dilation of <10 mmHg, and type II pattern on high-resolution manometry (HRM).

**ACHALASIA AND NUTRITION**

**Weight Loss: Is it Related to Physiology or Inflammation?**
Why some patients with achalasia lose weight and other patients do not is unknown due to paucity of focus in this area. One of the first studies evaluating clinical response in achalasia with pneumatic dilatations noted weight loss in approximately 91% of patients (n= 264) with 16 patients reporting > 20kg and 18 patients reporting < 5kg of weight loss. However, this might have been skewed given most patients in this study noted duration of symptoms ranging from 2 to >20 years prior to diagnosis and treatment with pneumatic dilatation. This “diagnosis latency” of achalasia is very
common; many patients have had symptoms for years before seeking medical treatment. Subsequently, 3 to 13 years after treatment, these patients rapidly gained weight and weight loss was only observed in <6% of patients.²⁶ Thus, post-therapy patients that have lost weight are able to gain it back.

What is interesting about achalasia is that despite the mechanical obstruction in all, many do not lose weight, and in fact, some are obese. One small surgical series reported 3 patients with achalasia and morbid obesity (BMI of 43.3, 60, and 52.7), who did not have typical symptomatic presentation with dysphagia, but all 3 reported significant respiratory symptoms with nocturnal cough and recurrent aspiration.²⁷ The question of sub-types of achalasia and weight loss may be of physiologic interest. In a retrospective study assessing clinical, radiological, and manometric profiles of 145 patients with untreated achalasia, the authors reported that 31% of patients with classic achalasia reported weight loss compared to 43% of patients with vigorous achalasia.⁸ Although the degree of weight loss was not significantly different between the two at 20 ± 16 lbs, patients with vigorous achalasia had a significantly higher percent with normal LES pressure (49% vs. 13%).⁸ Thus, it is not clear if LES physiology is related to presence or absence of weight loss, as one would expect patients with higher LES pressure to report more weight loss.

Another prospective study evaluating 213 achalasia patients (110 men and 103 women) investigated differences in clinical presentation based on gender. They noted that mean duration of symptoms, age at diagnosis, and mean weight loss (3.2 kg) were not significantly different between men and women; however, they did not differentiate between the sub-types of achalasia.²⁸

Interestingly, a recent cross-sectional study evaluating 623 patients with dysphagia in Iran tried to explore the sensitivity, specificity, and predictive accuracy of presenting esophageal symptoms to normal or abnormal esophageal motility testing.²⁹ They noted that no clinical symptoms were sensitive enough to
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discriminate between normal and abnormal esophageal motility testing, but did find that presence of dysphagia, non-cardiac chest pain, hoarseness, vomiting, and weight loss had high specificity and high accuracy in distinguishing esophageal motor disorders from normal findings. Eighty-five out of 623 (14%) had achalasia; the type II achalasia group reported more frequent weight loss (26%), followed by Type I (11%), then Type III (1%). Why patients with type II would be at higher risk of losing weight remains a mystery.

Furthermore, if weight loss is not predicted by physiology, it may be related to an inflammatory process by an increase in cytokines (such as in patients with IBD). A recent study evaluated histopathologic patterns among achalasia subtypes and noted that type I achalasia specimens had significantly more myenteric plexus ganglion cell loss compared to type II, suggesting that type I achalasia likely represented disease progression from type II. Whether a higher degree of histopathologic inflammation in type II achalasia patients might explain the weight loss in this group compared to type I needs further study. In addition, it is also possible that certain patients eat significantly less and make calorie-poor choices compared to other patients; unfortunately, these patients are rarely referred to dietitians for appropriate nutritional education until after achalasia is treated.

NUTRITIONAL IMPLICATIONS

Nutrition in patients with achalasia has often been overlooked. In fact, there are currently no published studies or reviews in this area. The advice that is often given is “eat what you can tolerate.” This is likely due to high treatment success in achalasia, which often allows the patient to resume their regular diet without significant alterations almost immediately. However, dietary modifications should be highly considered as adjunctive treatment in patients that undergo other less effective treatment modalities such as Botox injections or pharmacologic treatment with medications as it could potentially assist with maintaining adequate nutrition. We prospectively evaluated the nutritional status of 19 patients with untreated achalasia with 80% reporting having altered their diet due to swallowing difficulties; 90% reported consuming less than usual. In addition, 80% of patients reported an estimated weight loss of 40 pounds over the course of approximately 6 months. Studies are now underway to assess the magnitude and mechanism of nutritional deficiencies in achalasia as well as prospectively assess response to therapy.

Physiologically, a low fiber diet (defined as maximum of 10g fiber/day) could be considered in these patients similar to patients who have small bowel stricture. Soluble fiber increases the viscosity of the bolus, which reduces absorption and insoluble fiber possess high water-binding capacity and increases the bulk of the bolus. However, in the setting of luminal narrowing, as in achalasia due to high LES pressure, a low fiber diet would be physiologically advantageous to allow easier passage through a small narrowing. Fiber bulking agents should also be avoided until treated. Some patients may need to switch to high calorie/protein liquids also. It is also prudent to consider prompt referral to a registered dietitian in patients

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<tr>
<th>Medications</th>
<th>Dosing</th>
<th>Efficacy</th>
<th>Side effects</th>
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| Sub-lingual nifedipine | 10-30mg should be administered 30-45 min prior to meals and at bedtime. | 50-90% of patients | • Develop tachyphylaxis  
• 30% had side effects including hypotension, peripheral edema, headache, and dizziness |
| Sub-lingual isosorbidide dinitrate (unavailable in US) | 5mg administered 10-15 min before meals (can use nitroglycerin 0.4mg sublingual as an alternate). | 53-87% of patients | |
| Botulinum Toxin (BT-A) | 20-25 units of the toxin are injected through a 5-mm sclerotherapy needle into each quadrant of the LES (total of 80-100 units) | >80% have clinical response at 1 month, but fades over time with <60% in remission at 1 year. | • Transient chest pain (16-25%)  
• Reflux symptoms (<5%) |

Table 4. Pharmacological Options in Patients with Achalasia
who are having difficulty regaining weight. In those with significant weight loss, refeeding will need to be done cautiously to prevent refeeding syndrome. Thiamine supplementation (as well as other vitamins and minerals) might also be needed in patients with persistent vomiting.

Eating frequent, small, low-fiber meals with higher liquid content should be encouraged until they are able to get definitive treatment for achalasia. In those who continue to have trouble meeting their nutrient requirements orally, gastric access for enteral feeding may be necessary, but rarely needed due to effective therapeutic options available for achalasia. However, given the paucity of data regarding nutrition in achalasia patients, we strongly recommend future focus in this very important clinical area.

CONCLUSION

Achalasia is one of the most studied motility disorders of the esophagus and is characterized by impaired LES relaxation. Patients often present with dysphagia, significant regurgitation, and some have a tremendous degree of weight loss. Despite significant resources allocated to understanding the physiology and treatment options in patients with achalasia, it is still unclear why certain patients with achalasia lose significantly more weight compared to others. Although achalasia cannot be permanently cured, excellent palliation of symptoms is possible in > 90% of patients with currently available treatment modalities. In patients who are not candidates for more definitive therapies such as pneumatic dilatation, Heller myotomy, or POEM, we advocate combination of botulinum toxin injection and focus on dietary alterations with eating small, frequent, low-fiber meals with higher liquid content to help maintain nutritional needs.

References