Achalasia Treatment Options
POEM The New Gold Standard?

Marc F. Catalano, MD, FACG, FACP, AGAF, FASGE
Professor of Medicine
Department of Internal Medicine
Division of Gastroenterology and Hepatology
The University of Texas, McGovern Medical School
Objectives

- Review the pathogenesis of Achalasia
- Discuss the clinical features of Achalasia
- Discuss the workup of Achalasia
- Discuss the current options for the management of Achalasia
- Describe new developments in the treatment of Achalasia
Histopathology of Achalasia

Histologic examination shows a decrease in the neurons of the myenteric plexus (Auerbach’s plexus)

There is a preferential decrease in the nitric oxide producing cells

➤ These contribute to LES relaxation

There is a relative sparing of the cholinergic neurons

➤ Responsible for maintaining the LES tone

The loss of these inhibitory neurons leads to an increased tone in the LES and aperistalsis of the esophagus
History of Achalasia

First Rx description 1674 – Sir Thomas Willis. Sponge tipped carved whalebone to dilate the esophagus

It was not actually called Achalasia until a 1927 article by Arthur Hurst

- The treatment of achalasia of the cardia: so-called “cardiospasm”
- Achalasia is Greek for lack of relaxation

In 1913 Ernest Heller performed the first surgical intervention for Achalasia and the procedure still bears his name

Ellis et al described the first transthoracic approach in 1958
Secondary Achalasia - Infection

Secondary Achalasia can be due to Chagas disease

Chagas disease occurs mainly in Central and South America

It is due to an infection by the protozoan parasite Trypanosoma Cruzi - carried by Rhodnius Prolixus

Infection results in the loss of ganglion cells in Auerbach’s plexus
When evaluating patients for Achalasia, it is important to rule out the possibility of malignancy, which can mimic Achalasia.

Things that may suggest malignancy include:

- Presence of symptoms for less than six months
- Onset after age 60
- Excessive weight loss
- Difficulty passing endoscope past GEJ
Achalasia - Incidence

- Has an annual incidence of 1.6 per 100,000 people
- The relative infrequency of the disease has made it more difficult to study in comparison to more common disease processes
- Occurs equally in men and women
- Usually occurs in individuals age 20-50
Clinical Manifestations of Achalasia

- Dysphagia (solids and liquids)
- Mild weight loss (usually < 10 kg)
- Patients may sense a lump in their throat (globus)
- Regurgitation
- Chest pain
- Heartburn
- Hiccups
Onset of symptoms is slow and gradual. The average time between onset of symptoms and diagnosis is over four years.

In patients with suspected achalasia, there are three important tools in diagnosing Achalasia:

- Barium swallow
- Endoscopy
- Manometry
Barium Swallow

- Barium swallow is an excellent tool in the diagnosis of achalasia
- Classic appearance shows a dilated esophagus which tapers to a classic “bird’s beak” appearance
- The diagnostic accuracy of a barium swallow was 95% in one study
Manometry – Three Classic Findings

- Aperistalsis of esophageal body (<40 mmHg or absent)
- Elevated resting LES pressure (often above 45 mmHg)
- Incomplete LES relaxation
  - The LES should drop to < 8 mmHg above gastric (IRP <15)
  - In Achalasia LES relaxation in response to a swallow may be incomplete or absent

Normal

Achalasia
Achalasia – Types I-III

Type I - Classic Achalasia
Type II - Achalasia with Pan-Esophageal Compression
Type III - Spastic Achalasia
Upper GI Endoscopy

- All patients with suspected achalasia should undergo endoscopy to rule out malignancy
- On entering the esophagus, it is usually large and will potentially have retained food
- While the LES does not open spontaneously, it can be passed with gentle pressure
Additional modalities such as CT scan or endoscopic ultrasound (EUS) can be helpful in the workup of a patient for Achalasia if another cause is suspected (such as malignancy)
Aims

- Reduce LES pressure
- Facilitate esophageal emptying
- Relieve functional obstruction

Modalities

- Oral pharmacologic agents
- Chemical denervation by endoscopic injection of Botox
- Pneumatic dilation
- Surgical myotomies
- Self-expanding metallic stents
- Esophagectomy
- Per-oral endoscopic myotomy (POEM)
Pharmacologic Treatment - Achalasia

Aim: Relaxation of the smooth muscle to lower LESP

- Calcium channel blocker (10-30 min prior meals)
- Nitrates
- Anti-cholinergics
  - atropine
  - dicyclomine
  - cimetropium
- Beta-adrenergic agonists
  - terbutaline
- Theophylline

Modest success, not recommended as first line therapy. 50-70% initial response, < 50% at 1 year. Tachyphylaxis and side effects limit their use
Botulinum neurotoxin type A
Inhibits the release of acetylcholine
The idea for the use of Botox came from an understanding of the pathophysiology of Achalasia
By blocking the release of Ach from the presynaptic channels in the ganglia of Auerbach’s plexus – restores balance of neurotransmitters
Endoscopic injection is done in the area of the lower esophageal sphincter (LES).

The standard technique is to inject 1 mL (20 to 25 units BT/mL) into each of four quadrants.

Complications include:

- Mediastinitis
- Esophageal mucosal ulceration
- Pneumothorax
### Botulinum Toxin Treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th># pts enrolled</th>
<th>% LESP dec post Rx</th>
<th>Remission 1 mo</th>
<th>Remission 6 mo</th>
<th>Remission 12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pasricha</td>
<td>Random</td>
<td>21</td>
<td>33%</td>
<td>90%</td>
<td>44%</td>
<td>--</td>
</tr>
<tr>
<td>Fishman</td>
<td>Prospect</td>
<td>60</td>
<td>--</td>
<td>70%</td>
<td>--</td>
<td>36%</td>
</tr>
<tr>
<td>Gordon</td>
<td>Prospect</td>
<td>16</td>
<td>--</td>
<td>75%</td>
<td>48%</td>
<td>--</td>
</tr>
<tr>
<td>Vaezi</td>
<td>Random</td>
<td>24</td>
<td>21%</td>
<td>60%</td>
<td>50%</td>
<td>32%</td>
</tr>
<tr>
<td>Annese</td>
<td>Random</td>
<td>16</td>
<td>49%</td>
<td>100%</td>
<td>--</td>
<td>12.5%</td>
</tr>
<tr>
<td>Pasricha</td>
<td>Prospect</td>
<td>31</td>
<td>45%</td>
<td>90%</td>
<td>64%</td>
<td>--</td>
</tr>
<tr>
<td>Martinek</td>
<td>Prospect</td>
<td>49</td>
<td>65%</td>
<td>93%</td>
<td>--</td>
<td>41%</td>
</tr>
<tr>
<td>Zaninotto</td>
<td>Random</td>
<td>40</td>
<td>--</td>
<td>--</td>
<td>66%</td>
<td>34%</td>
</tr>
</tbody>
</table>

BOTOX has downside of not being as effective as other interventions (short and long-term)

Studies report symptomatic relief as high as 90%. The effects generally fall to 50% or lower at one year and continue to diminish after that

Current consensus on BOTOX: should only be used on patients who are not fit for other interventions
Pneumatic Dilation

The best predictors of success:

- Post-dilation pressure (some report the difference between pre and post-dilation pressures)
- Older age, female gender

The biggest concern with pneumatic dilation is esophageal perforation - reported to be as low as 1.6% while other studies have reported an incidence of around 10% (one study: 21% perforation rate)

Post PD abnormal acid exposure 15% (LHM 23%)
EndoFlip: Pre-Post Treatment Assessment

Untreated
Volume: 40 ml
CSA= 24 mm²
Pressure =22.8 mmHg
EGJ distensibility index = 1.05

Good Response
Volume: 40 ml
CSA= 137 mm²
Pressure =19.2 mmHg
EGJ distensibility index = 7.1

Poor Response
Volume: 40 ml
CSA= 21 mm²
Pressure =63.1 mmHg
EGJ distensibility index = 0.33
First described by Ernest Heller in 1913 where he used an abdominal approach to perform an anterior myotomy

First laparoscopic myotomy 1991 – Sir Alfred Cuschieri

In addition to laparoscopic myotomy, thoracoscopic myotomy has also been described

Thoracic approach does have certain drawbacks
Layers of the Esophagus

Muscle Layers

Stylized cross section of oesophagus showing Longitudinal Rugae

Muscularis Mucosa

Blood Vessels & Glands

Circular Muscle

Neural Plexus

Longitudinal Muscle

Stratified Squamous Epithelium

Lymphoid Tissue
Current consensus - considered the gold standard operation

Surgeon weakens the LES by cutting its muscle fibers – primary alternative to pneumatic dilation for Achalasia

Reflux esophagitis develops in 20-30% of patients treated by surgical myotomy

When compared to open techniques, similar rates of complications with much shorter hospital stay and recovery times
## Surgical Myotomy

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Method of surgery</th>
<th># patients</th>
<th>Length F/U</th>
<th>Good - Exc Resp</th>
<th>GERD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bessell</td>
<td>Prospect</td>
<td>Lap HM</td>
<td>167</td>
<td>5 years</td>
<td>77%</td>
<td>15%</td>
</tr>
<tr>
<td>Vella</td>
<td>Retrospect</td>
<td>88% Lap, 12% Open</td>
<td>73</td>
<td>6 years</td>
<td>57%</td>
<td>36%</td>
</tr>
<tr>
<td>Dang</td>
<td>Retrospect</td>
<td>81% Lap, 9% Open</td>
<td>22</td>
<td>3 years</td>
<td>76%</td>
<td>18%</td>
</tr>
<tr>
<td>Raiser</td>
<td>Retrospect</td>
<td>Lap or Thoracoscopy</td>
<td>35</td>
<td>1-4 years</td>
<td>97%</td>
<td>14%</td>
</tr>
<tr>
<td>Hunt</td>
<td>Retrospect</td>
<td>Lap</td>
<td>70</td>
<td>2.9 years</td>
<td>81%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Frantzides</td>
<td>Retrospect</td>
<td>Lap</td>
<td>53</td>
<td>3 years</td>
<td>92%</td>
<td>9%</td>
</tr>
<tr>
<td>Zaninotto</td>
<td>Prospect</td>
<td>Lap</td>
<td>100</td>
<td>2 years</td>
<td>92%</td>
<td>7%</td>
</tr>
</tbody>
</table>
Achalasia - sigmoid esophagus

- Markedly dilated esophagus with tortuous, angulated shape
- Previously believed that this would require esophagectomy or at the very least preclude fundoplication
- Extended Myotomy
  - Surgical
  - Endoscopic
Response to Achalasia Treatment

Figure 3. Type II achalasia has a higher success rate compared with type I achalasia (P < .01) and type III achalasia (P < .001), as shown in a Kaplan–Meier curve.

Figure 4. Kaplan–Meier curves comparing PD and LHM are shown for the 3 subtypes for up to 60 months after treatment. Success rates are comparable in type I achalasia (P = .84). Pneumodilation has a significantly higher success rate in type II achalasia (P = .03). Success rates, however, are high for both treatments. In type III patients the largest difference is observed, which, however, is not statistically significant (P = .12).

To fundoplicate, or not to fundoplicate, that is the question...

- Up to 30% of pts complain of significant heartburn
- 24 hr. pH probe or endoscopy demonstrate that 60% of pts have significant reflux
- “Objective analysis reveals an unacceptable rate of GERD in laparoscopic Heller Myotomy without an anti-reflux procedure. Therefore it is recommend performing a concurrent anti-reflux procedure.”

[Diagram of stomach with different fundoplication techniques: Nissen, Dor, Toupet]
A new approach to Achalasia: POEM

- Submucosal endoscopic esophageal myotomy: a novel experimental approach for the treatment of achalasia
  - Published in Endoscopy, 2007
- It has also been referred to as POEM: Per-oral Endoscopic Myotomy
- It is considered a form of NOTES
- Gaining traction at select centers in U.S.
- Leading expert, Dr. Haruhiro Inoue, from Shohawa University, Northern Yokohama Hospital in Japan – reported on over 1500 cases
Impaired EGJ relaxation (IRP >15 mmHg)
- Achalasia
  - Classic Achalasia (Type I)
  - Achalasia With Esophageal Compression (Type II)
  - Spastic Achalasia (Type III)
- EGJ Outflow Obstruction

Normal EGJ relaxation (IRP <15mmHg)
- Jackhammer Esophagus (DCI >8000)
- Diffuse Esophageal Spasm (DL <4.5)
The POEM Procedure – Two Step Process

The Tunnel (including mucosotomy)

The Myotomy
Equipment for POEM

- Antibiotic irrigation
- Single channel endoscope
- Cap fitted at end of scope
- CO2 insufflation
- High pressure water pump (ERBE Jet2)
- Injection needle
- Methylene blue, saline solution
- Energy source to cut/coag (ERBE VIO 300D)
- Endo knife
- Clips, Apollo Overstitch
Anti-fungal agent 3 days prior
2-3 days clear liquid diet
General paralytic agent – Anesthesia
Clear stomach and esophagus of debris
Gentamycin lavage
Prepare Injection mixture (300cc)
Identify anatomy: GEJ distance, diverticula, locate anterior/posterior positions
Availability and familiarity of Veres needle and chest tube placement
Equipment

- **ERBE VIO 300**
  
  APC/electrosurgical system – APC pulsed mode

- **ERBE JET**

- **ERBE Knife – Hybrid T, TT**
Two P.O.E.M Technique Variations

- Balloon dilation for blunt dissection of tunnel (SMT) followed by TT knife to complement dissection and perform the myotomy

- Hybrid knife – T type for submucosal tunnel dissection and subsequent myotomy
Esophageal Lumen orientation

By convention
- 12 O’clock = anterior esophageal wall
- 6 O’clock = posterior esophageal wall

Myotomy is generally performed at 2-5 O’clock

Imprints of recognizable extrinsic structures such as the spine (when visible)

Pooling of instilled water along the posterior wall

Ballottement of the anterior wall of the cardia (in thin patients)
POEM Technique: The Tunnel

- Choose appropriate ERBE Knife (Hybrid T-Type)
- Create a 2 cm Mucosotomy after injection of submucosal space separating the muscle layers
- Enter submucosal space 15 cm above the GE junction
- Using a solution of saline and Methylene blue, a tunneled dissection is carried distally to 2-3 cm past the GE junction
- Exit Tunnel every 2-3 cm progression to assess direction and integrity of mucosa, re-confirming location of muscle from mucosal layer
- Identify palisading vessels lower esophagus, careful coagulation current
- Spindle veins in submucosa/muscularis – careful advancement avoiding cutting large vessels (coag graspers for hemostasis)
- Bundle(s) of longitudinal muscle fibers running in the submucosa and inserting into the circular layer of the muscularis propria (sling fibers)
- Wider submucosal space with large perforating vessels as tunnel is advanced into cardia
The myotomy is begun 5 cm past the Mucosotomy, 10 cm proximal to the GE jct.

Myotomy of inner circular, but can include the outer longitudinal preserving the serosa.

Careful dissection of inner circular until plane between circular/outer long. I.D.

Lift the inner circ. from outer long. with Hybrid T knife then apply short burst of current.

Proceed slowly preserving outermost barrier (serosa or longitudinal muscle layer).

Control all bleeding with coag (knife or grasper).

Start proximally and work distally into the cardia.

After completion of myotomy inspect length of myotomy by retroflexion in the stomach I.D. blue discoloration of cardia mucosa from submucosal injection.


Appropriate closure of Mucosotomy with clips or OverStich completes procedure.
POEM - Technique

- Myotomy is carried distally down to 2-3cm past the GE junction (beyond sling fibers)
- Myotomy only takes the inner circular fibers while leaving the outer longitudinal fibers intact
- At the end of the procedure, the scope is removed from the submucosal tunnel and the entry site is closed with endoscopic clips

Lower Esophageal Sphincter

- Intrinsic distal esophageal muscles – tonically contracted
- Muscular Sling fibers of the gastric cardia
- Diaphragmatic crura
- Transmitted pressure of the abdominal cavity
POEM Procedure: Areas of Concern

- Vessels – careful dissection and proper use of Coag Graspers

- Myotomy of LES – Sling fibers, difficult orientation and identification

- Preservation of mucosal layer

- Preservation outermost barrier
Timed Barium Esophagram (TBE)
# POEM Long-term Efficacy

<table>
<thead>
<tr>
<th></th>
<th>Total Pt #</th>
<th>F/U (mo)</th>
<th>Clinical Success</th>
<th>Eckardt Score (pre/post)</th>
<th>LESP mmHg (pre/post)</th>
<th>Clinical GERD (sx’s or PPI use)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inoue</td>
<td>500</td>
<td>36</td>
<td>88.5%</td>
<td>6.0/1.7</td>
<td>28.7/14</td>
<td>21.3%</td>
</tr>
<tr>
<td>Hu</td>
<td>32</td>
<td>30</td>
<td>96.8%</td>
<td>7.8/1.4</td>
<td>37.9/12.9</td>
<td>25.8%</td>
</tr>
<tr>
<td>Chen</td>
<td>26</td>
<td>24.6</td>
<td>100%</td>
<td>8.3/0.7</td>
<td>31.6/12.7</td>
<td>19.2%</td>
</tr>
<tr>
<td>Sharata</td>
<td>75</td>
<td>20.1</td>
<td>97%</td>
<td>6/1</td>
<td>22.2/11.7</td>
<td>19.1%</td>
</tr>
<tr>
<td>Minami</td>
<td>28</td>
<td>16</td>
<td>100%</td>
<td>6.7/0.7</td>
<td>71.2/21</td>
<td>21.4%</td>
</tr>
<tr>
<td>Teitelbaum</td>
<td>41</td>
<td>15</td>
<td>92%</td>
<td>7/1</td>
<td>28/11</td>
<td>15%</td>
</tr>
<tr>
<td>Von Renteln</td>
<td>70</td>
<td>12</td>
<td>82.4%</td>
<td>6.9/1</td>
<td>27.6/8.9</td>
<td>29%</td>
</tr>
</tbody>
</table>

*Eckardt Score: dysphagia (0-3), regurgitation (0-3), chest pain (0-3), weight loss (0-3)*
## Comparison of Techniques

<table>
<thead>
<tr>
<th></th>
<th>POEM</th>
<th>LHM</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scarring</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Selective Circular Myotomy</td>
<td>Possible</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Concurrent Anti-Reflux procedure</td>
<td>No</td>
<td>Fundoplication</td>
<td>No</td>
</tr>
<tr>
<td>Dissection/disruption of the diaphragmatic hiatus</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Postoperative incidence of GERD</td>
<td>(+++) GERD - 20-30%</td>
<td>(++) GERD 15%</td>
<td>(+/-)</td>
</tr>
<tr>
<td>Myotomy extension to the proximal esophageal body</td>
<td>Possible</td>
<td>Difficult</td>
<td>Impossible</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>Intermediate</td>
<td>Relatively long</td>
<td>Very short</td>
</tr>
<tr>
<td>Cost</td>
<td>Intermediate</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>C.R. - Achalasia</td>
<td>Good/excellent</td>
<td>Good</td>
<td>Fair</td>
</tr>
<tr>
<td>C.R. Spastic esophageal disorders</td>
<td>Good</td>
<td>Fair</td>
<td>Poor</td>
</tr>
</tbody>
</table>
POEM: Expanded Indications

Nutcracker Esophagus (Jackhammer)  Diffuse Esophageal Spasm
POEM: Complications

- Perforation: mediastinum, peritoneum
- Bleeding: common (immediate or delayed).
  - Immediate: resolution high with electrocautery.
  - Delayed: hemo-peritoneum, hemothorax
- Mucosal injury: repaired with different modalities
- Mediastinitis: rare
POEM: Complications

Perforation
POEM - Post Heller Myotomy or PD

- POEM after Heller myotomy is safe with minimal morbidity
- Symptom improvement is excellent
- Radiographic changes on timed barium esophagrams do not always show significant improvement
Maneuvers to overcome scar due to prior intervention

- Cut the muscle to progress tunnel
- Create a tunnel 90 degrees from the current trajectory
- Shorter tunnel
- Repeat injections of methylene blue to separate layers
Steps for POEM - Summary

- Sub-mucosal injection (cushion)
- Mucosotomy
- Creation of sub-mucosal tunnel
- Verification of the integrity of the sub-mucosal flap
- Myotomy – selective inner circular if possible
- Closure of Mucosotomy
Final Tips: P.O.E.M

- Pneumoperitoneum
- Pneumothorax
- Hemothorax
- Confirmation of tunnel extension through GE junction (GEJ) into cardia important
Achalasia is a process that affects the myenteric plexus of the esophagus leading to high resting LES pressures and esophageal aperistalsis.

Medical therapy is ineffective.

Botox should be reserved for patients who are not able to undergo other interventions.

Pneumatic dilation is effective, but has the risk of perforation.
Laparoscopic Heller Myotomy has excellent clinical results. Should be accompanied by either Dor or Toupet fundoplication (not a Nissen)

The myotomy should extend at least 5 cm on the esophagus to 2 cm on the stomach, and possibly longer

Submucosal endoscopic myotomy (POEM) definitely shows promise, but we lack long-term results and comparative studies to make definitive statements