Diagnosis and Management of Achalasia: Past, Present, & Future

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Achalasia

• Motor disorder of esophagus
  Aperistalsis
  Impaired LES relaxation
• Causes dysphagia, pain, regurgitation
• Leads to weight loss, pulmonary complications
• Increased risk of esophageal CA
## Epidemiology

- Prevalence 7.9-12.6/ 100,000
- Incidence 0.4-1.1/ 100,000
- Mean age at diagnosis 30 to 60 years
- Peak age in 40’s

## Cancer Risk

- Achalasia series report 0-33% increased risk of esophageal CA (mostly SCCA)
- Swedish population-based study of 1062 achalasia patients with 9864 pt-years f/u → 16-fold increased risk of esoph CA
- Surveillance not recommended – would require >400 endoscopies to find one cancer
Historical Perspective

1674  Sir Thomas Willis (England) -- Successful treatment of “cardiospasm” with serial esophageal dilation using a sponge attached to a whale bone (baleen)
**Lower Esophageal Sphincter**

- High pressure zone 2 to 4 cm long at GEJ
- Parasympathetic and sympathetic innervation mostly in myenteric plexus
- Provides barrier to reflux of gastric juice

**Pathophysiology of Achalasia**

- Dysfunction of myenteric plexus
  - Early: lymphocytic inflammation
  - Late: loss of ganglion cells
- Selective loss of inhibitory neurons (VIP/NO)
- Sparing of stimulatory cholinergic innervation
- Failure of LES to relax with swallow
### Clinical Presentation

- Progressive solid food dysphagia (variable for liquids)
- Chest pain – more frequent early decreases with progressive dilation
  Regurgitation of undigested, nonbilious food (esp. at night)
- Heartburn – not relieved with acid suppression

### Clinical Features

- Eating maneuvers augment food passage
  - Head back, upright posture, valsalva
  - Warm, carbonated/alcoholic beverages
- Food fermentation → acidification with esophageal ulceration/heartburn
- Pulmonary complications -- aspiration
- Weight loss – up to 84% of patients
### Differential Diagnosis

- **Pseudoachalasia**
  Over 50% 2º to GEJ/cardia tumor
  Other causes: pseudocysts, GEJ obstruction after hiatal surgery, paraneoplastic syndromes
- **Scleroderma**
  Aperistalsis with low LES pressure
- **Neurologic disorders (Parkinson’s)**
- **Chagas’ Disease**

### Evaluation

- **Manometry**
- **Barium esophagogram**
- **EGD**
- +/- pH study
Esophageal Manometry

- Used to assess esophageal motility and LES function (pressure, length, relaxation)
- Multichannel water-perfused or solid state catheter connected to pressure transducers
- Records pressure at various points along the esophagus during bolus swallow

Normal Manometry
Normal High-Res Manometry

Manometry in Achalasia

- Aperistalsis of body
- Incomplete relaxation of LES
- Normal to elevated LESP
- Simultaneous low amplitude contractions
Manometry

High-Res Manometry: Type I Achalasia
High-Res Manometry: Type II Achalasia

High-Res Manometry: Type III Achalasia
Barium Swallow

- Dilated, possibly tortuous esophagus (late finding)
- “Bird’s beak” tapered appearance of distal esophagus
- Air fluid level with retained food

Endoscopy

- Necessary to rule out malignancy
- Requires retroflexed view of cardia/GEJ
- Scope should pass through easily – if not, consider malignancy
- EUS may help to evaluate esophageal wall when CA suspected
### pH Study

- May help when diagnosis is in question, especially when heartburn is major sx
- Interpretation may be difficult due to fermentation
- Achalasia shows gradual decline in pH vs. rapid drop seen with GERD

### Management

- Pharmocologic
- Botox injection
- Pneumatic dilation
- Surgical myotomy
  - Laparoscopic
  - Endoscopic
- Esophagectomy
**Pharmacologic Therapy**

- Goal – decrease LES pressure to allow esophagus to empty
- Nitrates – use limited by side effects
- Nifedipine – reduces LESP but minimal improvement in symptoms vs. placebo in 2 out of 3 RCT’s
- Reserved for mild disease or patients unable to tolerate dilation/surgery

<table>
<thead>
<tr>
<th><strong>Botulinum Toxin</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrasphincteric injection of LES</td>
</tr>
<tr>
<td>Blocks release of acetylcholine at neuromuscular junction</td>
</tr>
<tr>
<td>70-100% effective at 1 month</td>
</tr>
<tr>
<td>Ease of administration and low rate of adverse effects contribute to popularity</td>
</tr>
<tr>
<td>Most benefit seen in elderly, debilitated patients</td>
</tr>
</tbody>
</table>
### Botulinum Toxin – The Downside

- Usually requires repeat injection at 6 to 9 months – 30% remission at 1 year
- Response to repeat injections limited by antibody formation
- Reported to increase scarring of distal esophagus, increasing difficulty of surgery
- Long term results inferior to dilation in several RCT’s

### Treatment Strategies

- **Medical Therapy (Nitrates, nifedipine)**
- **Botulinum Toxin**
- **Endoscopic pneumatic dilation**
  - **Advantages**: Effective symptom relief, outpatient procedure
  - **Disadvantages**: Repeat dilations often needed, increased risk of esophageal perforation
- **Laparoscopic Heller Myotomy**
  - **Advantages**: durable symptom relief
  - **Disadvantages**: invasive surgical procedure

Pneumatic Esophageal Dilation

• 3-4 cm balloon rapidly inflated in distal esophagus under fluoro guidance
• Relies on rupture of LES fibers

Pneumatic Esophageal Dilation

• Trials with f/u > 2 years report good to excellent results in 65-80%
• Repeat dilation required in > 50%
• West et. al. reported on 125 patients
  12 year f/u → 50% remission with median 4 tx
  15 year f/u → 40% remission Am J Gastro 2002
• Improved results in older patients (over 40) and those with post-dilation LESP < 10
### Complications of Dilation

- **Perforation**  
  Most series report 0 to 4%

- **Gastroesophageal reflux**  
  Symptomatic in 7-17% of cases

### Surgery vs. Dilation

<table>
<thead>
<tr>
<th>Dilation</th>
<th>Myotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>- outpatient procedure</td>
<td></td>
</tr>
<tr>
<td>- minimal pain</td>
<td></td>
</tr>
<tr>
<td>- Rapid return to work</td>
<td></td>
</tr>
<tr>
<td>- May treat any patient population (frail, pregnant, ect...)</td>
<td></td>
</tr>
<tr>
<td>- Less expensive</td>
<td></td>
</tr>
<tr>
<td>- Does not preclude myotomy</td>
<td></td>
</tr>
<tr>
<td>- single procedure</td>
<td></td>
</tr>
<tr>
<td>- dysphagia relief is longer at the cost of more heartburn</td>
<td></td>
</tr>
<tr>
<td>- may be more effective treatment in younger patients</td>
<td></td>
</tr>
</tbody>
</table>
Surgery vs. Dilation

- Over a two year horizon, the clinical success of pneumatic dilation and laparoscopic myotomy are comparable in a recent large European randomized trial.

- However, at 5 year follow-up, surgery is favored due to higher rate of recurrent dysphagia requiring retreatment with increased complications in patients undergoing endoscopic dilation.

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### Surgical Therapy – Historical Perspective

- 1913 Heller: Anterior and posterior myotomy via abdominal approach
- 1918 Groeneveldt: Single anterior myotomy
- 1958 Ellis: Thoracic approach
- 1991 Cuschieri: Laparoscopic myotomy
- 1992 Pellegrini: Thoracoscopic approach

### Surgery – Laparoscopic vs. Open

- Laparoscopic approach associated with significant reduction in
  - Length of stay
  - Post-operative narcotic use
  - Time to return to work
- Long term efficacy and LES pressure/relaxation equivalent in retrospective comparison studies
Laparoscopic vs. Thoracoscopic

- Lap approach → better symptom relief and less reflux in 3 large retrospective series
- Thoracoscopic limited by need for single lung ventilation and postop chest tube
- Easier to extend myotomy onto cardia with laparoscopic approach
- Thoracic approach used for hostile abdomen or when need to extend myotomy higher onto esophagus

Surgical Principles

- Goal – decrease LES pressure and improve esophageal emptying
- Transect longitudinal and circular fibers of esophagus, and sling fibers of cardia
- Myotomy should extend 1 to 2 cm on stomach and up to normal esoph muscle
- Cut edges of muscle should be widely separated to prevent reapproximation
Addition of Antireflux Procedure

- Prompted by reports of up to 40% reflux rate after thorascopic approach
- Partial fundoplication
  - Anterior wrap (Dor)
  - Posterior wrap (Toupet)
- No difference in rates of dysphagia or reflux b/w two procedures

Surgical Technique

Dissection of Gastrohepatic Ligament and Crura
Surgical Technique

Performing the Myotomy

Fundoplication

Dor

Toupet
## Complications of Surgery

- Overall low morbidity
- Esophageal/ gastric mucosal perf (4-5%)  
  Usually inconsequential when recognized at time of operation
- Other complications (3%)  
  Pneumothorax, bleeding, abscess

## LHM: Long-Term Results

<table>
<thead>
<tr>
<th></th>
<th>RHM (n=33)</th>
<th>LHM (n=11)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Follow-up Interval, median (range), years</strong></td>
<td>9.1 (3.9-12.8)</td>
<td>9.9 (4.4-14.8)</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>Dysphagia, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent or mild</td>
<td>26 (79)</td>
<td>8 (80)</td>
<td>1.00</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>7 (21)</td>
<td>2 (20)</td>
<td></td>
</tr>
<tr>
<td><strong>Heartburn, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent or mild</td>
<td>26 (79)</td>
<td>9 (90)</td>
<td>0.66</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>7 (21)</td>
<td>1 (10)</td>
<td></td>
</tr>
<tr>
<td><strong>PPI use, No (%)</strong></td>
<td>18 (56.3)</td>
<td>8 (80%)</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>GERD-HRQL score, median (range)</strong></td>
<td>11 (0-36)</td>
<td>12 (6-20)</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>Satisfied, No. (%)</strong></td>
<td>32 (95.5)</td>
<td>10 (90.9)</td>
<td>0.44</td>
</tr>
<tr>
<td>Heller again, No. (%)</td>
<td>30 (90.9)</td>
<td>10 (90.9)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**LHM: Long-Term Results**

<table>
<thead>
<tr>
<th>Primary Author</th>
<th>Patients (No.)</th>
<th>Follow-up (years)</th>
<th>Absent or Mild Dysphagia (%)</th>
<th>Retreatment (%)</th>
<th>Mild to Mod Heartburn (%)</th>
<th>PPI Use (%)</th>
<th>Satisfaction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cowgill</td>
<td>47</td>
<td>10.6</td>
<td>92</td>
<td>12.8</td>
<td>NR</td>
<td>NR</td>
<td>92</td>
</tr>
<tr>
<td>Jeansonne</td>
<td>17</td>
<td>11.2</td>
<td>94</td>
<td>17.7</td>
<td>23.5</td>
<td>NR</td>
<td>94</td>
</tr>
<tr>
<td>Kilic</td>
<td>46</td>
<td>6.4</td>
<td>80</td>
<td>20</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Sasaki</td>
<td>34</td>
<td>7.8</td>
<td>100</td>
<td>5.9</td>
<td>0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Zaninotto</td>
<td>177</td>
<td>10.0</td>
<td>82</td>
<td>9.6</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

**Per Oral Endoscopic Myotomy**

- **Per Oral Endoscopic Myotomy (POEM)**
  - Submucosal plane accessed via esophageal mucosotomy
  - Totally endoscopic procedure
  - Allows complete surgical myotomy under direct visualization

- *Has the potential to offer the advantages of both surgical myotomy and endoscopic balloon dilation*
Per Oral Endoscopic Myotomy

- Described by Inoue in 2009
- Surgical principles
  - Mucosal flap
  - Submucosal dissection
  - Adequate distal myotomy
  - Secure closure of mucosotomy
- Supine position
- General anesthesia
- CO2 insufflation


POEM Technique

- Inspect and washout esophagus/stomach
- Identify GE junction
- Inject mucosa at 12 o’clock position 13cm proximal to GE junction
- Mucosotomy should be at least 3cm proximal to start of myotomy
- Incise mucosa
- **Use TT knife**
- Enter submucosal space
### POEM Technique

- Submucosal dissection past 2cm on cardia
- GE junction usually narrows and then widens on gastric side
- The scope length can also be checked to approximate the GE junction
- Important to go back into the stomach lumen and look for the length of dissection
- Transillumination

### POEM Technique

- Complete circular myotomy created using electrocautery
- Begin ~6cm above GEJ
  - At least 2cm distal to mucosotomy
- Extend 2cm onto the gastric cardia
### POEM Technique

- Close mucosal incision with clips or suturing device
- Upper GI series POD #0 or 1
- Follow-up: 2 weeks, 6 weeks, 6 months, 1 year

### POEM Outcomes

- Between August 2012 and October 2013, 26 patients underwent POEM, 25 for achalasia and 1 long myotomy for diffuse esophageal spasm
- Median age: 54 years
- Median BMI: 28.4 kg/m²
- 14/26 (54%) male
Operative Experience

- Successfully completed in all cases
- Mean operative time: 105 ± 30 minutes
- Median of 7 (5-16) endoscopic clips were required for mucosotomy closure
- Pneumoperitoneum requiring Veress needle decompression occurred in 9 (35%) cases
- No intraoperative complications or esophageal leaks
- Median hospital stay: 1 (1-2) day

Dysphagia

![Dysphagia Score Chart]

Dysphagia Score

- Preoperative
- 6 weeks postop
- 6 months postop

* Denotes significant difference from preoperative score.
Disease Specific QoL

**GERD-HRQL**

Global QoL: 6 Months
### POEM vs. LHM

#### Population: Preoperative Descriptors

<table>
<thead>
<tr>
<th></th>
<th>Heller n = 64</th>
<th>POEM n = 37</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), yr</td>
<td>57 (20)</td>
<td>56 (16)</td>
<td>0.7</td>
</tr>
<tr>
<td>Female, %</td>
<td>52</td>
<td>48</td>
<td>0.8</td>
</tr>
<tr>
<td>Eckardt Score, mean (SD)</td>
<td>5.9 (2.4)</td>
<td>5.4 (2.2)</td>
<td>0.5</td>
</tr>
<tr>
<td>Manometry, median (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting pressure</td>
<td>37</td>
<td>41</td>
<td>0.2</td>
</tr>
<tr>
<td>Relaxation pressure</td>
<td>20</td>
<td>19</td>
<td>0.4</td>
</tr>
<tr>
<td>Distal esophageal contraction amplitude</td>
<td>32</td>
<td>29</td>
<td>0.9</td>
</tr>
<tr>
<td>Symbol score &gt;2, %</td>
<td>19</td>
<td>10</td>
<td>0.5</td>
</tr>
<tr>
<td>Heartburn</td>
<td>62</td>
<td>32</td>
<td>0.06</td>
</tr>
<tr>
<td>Dysphagia to solid</td>
<td>49</td>
<td>30</td>
<td>0.4</td>
</tr>
<tr>
<td>Dysphagia to liquid</td>
<td>45</td>
<td>17</td>
<td>0.01</td>
</tr>
<tr>
<td>Reflux</td>
<td>23</td>
<td>13</td>
<td>0.6</td>
</tr>
<tr>
<td>Chest pain</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### POEM vs. LHM: Operative Data

#### Operative Details

<table>
<thead>
<tr>
<th></th>
<th>Heller n = 64</th>
<th>POEM n = 37</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time, min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>160</td>
<td>120</td>
<td>0.003</td>
</tr>
<tr>
<td>Range</td>
<td>100-280</td>
<td>60-215</td>
<td></td>
</tr>
<tr>
<td>Full-thicknesss injury, n</td>
<td>8</td>
<td>4</td>
<td>0.1</td>
</tr>
<tr>
<td>Esophagus</td>
<td>3</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Return to the OR, n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Length of stay, mean days (SD)</td>
<td>2.5 (1.9)</td>
<td>1.1 (0.6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

OR indicates operating room.

POEM vs. LHM: Acid Reflux

### Long-Term pH Testing

<table>
<thead>
<tr>
<th></th>
<th>Heller n = 31 (48%)</th>
<th>POEM n = 23 (76%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeMeester score, median</td>
<td>2</td>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>DeMeester score &gt;14.7%</td>
<td>10</td>
<td>9</td>
<td>0.4</td>
</tr>
<tr>
<td>Number of reflux episodes, median</td>
<td>4</td>
<td>12</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Testing >6 mo after surgery


### POEM vs. LHM: Conclusions

- POEM is less invasive than LHM and enhances recovery with decreased pain, shorter length of hospital stay, and faster return to work

- Similar efficacy and post-operative reflux compared to LHM at 1 year
POEM Outcomes

- 18 patients with 1 year follow-up
  - 3 intraoperative perforations managed with clips
  - Durable dysphagia relief at 11 months in all patients
  - 46% had positive pH study at 6 months


POEM: What’s next?

- Procedure has proven safe and effective in the short-term
- Comparison of outcomes with pneumatic dilation and laparoscopic myotomy (dysphagia relief and reflux)
- Long-term studies to assess durability and cost-effectiveness
Persistent or Recurrent Dysphagia

- Seen in 8 to 13%
- DDX includes incomplete myotomy, CA, stricture from reflux, severe dysmotility
- Evaluation similar to achalasia workup
- Treatment may include dilation or repeat myotomy (70-80% successful)

Esophagectomy

- Required in 1 to 2% of cases
- Indications: tortuous megaesophagus, failure of myotomy, stricture from reflux
- Orringer et. al. reported on 93 patients
  - 10% leak rate/ 2% mortality
  - 50% required dilation of anastomosis
  - 95% eating well
### Summary

- Rare disorder of esophageal motility
- Progressive and debilitating
- Treatment aimed at reducing LES pressure and improving esophageal clearance
- Myotomy and dilation most effective trx
- Laparoscopic approach favored, endoscopic emerging
- Addition of antireflux procedure controversial
- Esophagectomy rarely required