Achalasia: “a New Disease in the 21st century”

- Better defined due to high-resolution manometry
  - Impaired relaxation is more accurately assessed and we can appreciate
  - Aperistalsis can be better defined
    - Absent peristalsis
    - Pan-esophageal pressurization
    - Spasm
    - Variant with intact peristalsis

- Treatment strategy
  - More options are available that allow one to tailor therapy
**Chicago Classification 3.0**

Disorders of EGJ Outflow Obstruction
- Entities not seen in normal controls

**Major Disorders of Peristalsis**
- Incompletely expressed achalasia
  - IRP ≥ upper limit of normal AND sufficient evidence of peristalsis such that criteria for type III achalasia are not met
  - Yes

- IRP ≥ upper limit of normal AND 100% failed peristalsis or spasm
  - No

**Minor Disorders of Peristalsis**
- Impaired bolus clearance
  - Yes

- Normal Esophageal Motor Function
  - IRP is normal AND 100% failed peristalsis
  - No

**Achalasia**
- Type I: 100% failed peristalsis [no PEP]
- Type II: 100% failed peristalsis [+ PEP]
- Type III: >20% premature contractions

**EGJ Outflow Obstruction**
- Incompletely expressed achalasia
- Mechanical obstruction

**Distal esophageal spasm (DES)**
- ≥ 20% premature contractions (DL<4.5s)
- ≥ 20% of swallows with DCI >8,000 mmHg-cm-s and normal DL

**Absent Contractility**
- No scorable contraction by DCI and DL criteria (should consider achalasia with borderline IRP and/or bolus pressurization)

**Pressure Topography of Esophageal Motility**

The Chicago Classification 3.0

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John E. Pandolfino, MD, MSCI, FACG

**Esophageal Physiology: Neuromuscular Control**

Concept of Inhibitory and Excitatory Balance

A: EGJ Outflow Obstruction
B: Type II Achalasia
C: Type I Achalasia
D: Type III achalasia

![Image of physiological conditions and pressure scale](image)

**Symptoms of dysphagia ± chest pain and bland regurgitation**

**Upper Endoscopy**
- Obstructive process: ring, stricture, etc.
- Normal

**High Resolution Manometry**
- EPT Diagnosis
  - EGJ Outflow Obstruction
  - Absent Peristalsis
  - Achalasia I
    - Severe dilatation is associated with poor treatment response
    - Consider myotomy as initial therapy
  - Achalasia II
    - Normal without barium retention or esophageal dilatation
    - Frequently misdiagnosed with conventional manometry
  - Achalasia III
    - Worst treatment response
    - May benefit from treatment directed at spasm
    - Often diagnosed as DES on esophagram
  - DES
    - Extremely rare
    - Difficult to treat
    - Many cases are misdiagnosed Type III achalasia

**Utilizing HRM/EPT in the Management of Achalasia**

- Esophageal dilatation
- EGJ resistance
- Retained food

*esophagram may be helpful when manometry is technically difficult to perform*
ACHALASIA: Treatment Options

- Medication
  - Nitrites
  - Calcium channel blockers
  - Phosphodiesterase inhibitors (sildenafil, etc.)

- Botulinum toxin injection

- Pneumatic dilation

- Laparoscopic Heller myotomy

- Emerging Treatments
  - Peroral endoscopic myotomy (POEM)

EGJ Distensibility in Achalasia

<table>
<thead>
<tr>
<th>EndoFLIP bag volume (ml)</th>
<th>Distensibility Index (EGJ-DI) (CSA [mm²]/Pressure [mmHg])</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HV</td>
</tr>
<tr>
<td>30</td>
<td>5.1 (0.8, 21.7)</td>
</tr>
<tr>
<td>40</td>
<td>8.2 (1.7, 18.7)</td>
</tr>
</tbody>
</table>

Volume: 40 ml
CSA= 24 mm²
Pressure =22.8 mmHg

EGJ EDI 40= 1.05

Volume: 40 ml
CSA= 21 mm²
Pressure =63.1 mmHg

EGJ EDI 40= 0.33

Volume: 40 ml
CSA= 137 mm²
Pressure =19.2 mmHg

EGJ EDI 40= 7.1
PNEUMATIC DILATION

- Same day procedure
- Graded dilation:
  3.0 - 3.5 - 4.0 cm balloons
- Endoscopy
- Balloon placement by fluoroscopy
- Gradual dilation until “waist” flatter
- 8-10 psi x 15-60 seconds
- Post dilation esophagram
- Observe x 2-3 hours

HELLER MYOTOMY

- Requires 1-2 days of hospitalization
- Needs to be performed by an experienced surgeon with esophageal training.
- Recovery is longer in terms of post-operative pain and ability to return to normal activity and advance diet.
- More expensive
Pneumatic Dilation versus Laparoscopic Heller’s Myotomy for Idiopathic Achalasia


Figure 2. Kaplan–Meier Curves for the Rate of Treatment Success.
Per Oral Endoscopic Myotomy (POEM)

International Experience with POEM

<table>
<thead>
<tr>
<th>Location of primary investigators</th>
<th>No. of patients</th>
<th>Hypermotility found</th>
<th>Inability to diagnose</th>
<th>LES pressure, mm Hg</th>
<th>LES pressure, normalizing</th>
<th>Dysphagia, resolving in % of patients</th>
<th>Dysfunction of esophageal motility, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yokohama, Japan</td>
<td>2012</td>
<td>17</td>
<td>41 (20.62)</td>
<td>6.1 (3.10)</td>
<td>16 (1.72)</td>
<td>52 (4.15)</td>
<td>5 (60)</td>
</tr>
<tr>
<td>Shanghai, China (combined)</td>
<td>2012</td>
<td>205</td>
<td>44 (9.17)</td>
<td>18.2 (1.18)</td>
<td>-</td>
<td>85 (3)</td>
<td>7 (97)</td>
</tr>
<tr>
<td>Hamburg, Germany (2 centers)</td>
<td>2012</td>
<td>16</td>
<td>45 (28.76)</td>
<td>12.0 (1.17)</td>
<td>7.6 (0.27)</td>
<td>21.2 (1.6)</td>
<td>8 (67)</td>
</tr>
<tr>
<td>North, U.S. (Combined)</td>
<td>2012</td>
<td>11</td>
<td>42 (3.64)</td>
<td>10</td>
<td>7.1 (1.1)</td>
<td>45 (7.6)</td>
<td>8 (67)</td>
</tr>
<tr>
<td>North, Canada</td>
<td>2012</td>
<td>18</td>
<td>39 (2.14)</td>
<td>9.0 (1.0)</td>
<td>6 (6)</td>
<td>45 (7.6)</td>
<td>8 (67)</td>
</tr>
<tr>
<td>Hong Kong, China (Combined)</td>
<td>2013</td>
<td>16</td>
<td>47 (2.45)</td>
<td>16.6 (1.16)</td>
<td>5.5 (9)</td>
<td>43 (0.52)</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Chicago, U.S. (Combined)</td>
<td>2012</td>
<td>18</td>
<td>39 (2.24)</td>
<td>9.0 (1.4)</td>
<td>7 (7)</td>
<td>106 (56)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Naples, Italy (combined)</td>
<td>2012</td>
<td>28</td>
<td>35 (2.30)</td>
<td>14.2 (1.10)</td>
<td>6.7 (0.7)</td>
<td>74 (21)</td>
<td>10 (70)</td>
</tr>
<tr>
<td>Nice, France (Combined)</td>
<td>2012</td>
<td>13</td>
<td>40 (2.40)</td>
<td>8.3 (1.6)</td>
<td>6.6 (0.6)</td>
<td>20 (15)</td>
<td>6 (46)</td>
</tr>
<tr>
<td>European MCT (6 centers)</td>
<td>2013</td>
<td>79</td>
<td>45</td>
<td>13 (2.23)</td>
<td>6 (6)</td>
<td>21 (6.9)</td>
<td>12 (9)</td>
</tr>
<tr>
<td>Misawa, Japan (combined)</td>
<td>2012</td>
<td>65</td>
<td>52 (2.19)</td>
<td>9.3 (1.7)</td>
<td>7 (95)</td>
<td>46 (15)</td>
<td>10 (70)</td>
</tr>
<tr>
<td>Yokohama, Japan (5 centers)</td>
<td>2012</td>
<td>300</td>
<td>43 (2.87)</td>
<td>14.5</td>
<td>8 (5)</td>
<td>25 (15)</td>
<td>12 (8)</td>
</tr>
<tr>
<td>Dutch MCT (5 centers)</td>
<td>2012</td>
<td>17</td>
<td>14.3</td>
<td>12.2</td>
<td>6.3 (1.19)</td>
<td>49 (12)</td>
<td>8 (57)</td>
</tr>
<tr>
<td>Amsterdam, The Netherlands (3 centers)</td>
<td>2012</td>
<td>13</td>
<td>40</td>
<td>20 (1.6)</td>
<td>7 (95)</td>
<td>46 (15)</td>
<td>10 (70)</td>
</tr>
</tbody>
</table>
Northwestern Experience with POEM

- First case in August 2010
- 165 cases over the last five years

<table>
<thead>
<tr>
<th>First 120 Cases</th>
<th>Pre-op</th>
<th>1-year post-op</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eckardt score</td>
<td>7</td>
<td>1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Clinical success (Eckardt &lt; 4)</td>
<td>-</td>
<td>92%</td>
<td>-</td>
</tr>
<tr>
<td>4-sec IRP (mmHg)</td>
<td>30.2</td>
<td>11.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>5min column height on TBE (cm)</td>
<td>13</td>
<td>4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Symptomatic GER</td>
<td>-</td>
<td>11%</td>
<td>-</td>
</tr>
<tr>
<td>Esophagitis &gt; Grade A</td>
<td>-</td>
<td>17%</td>
<td>-</td>
</tr>
</tbody>
</table>

Response Rates of Treatments

Patients categorized by pressure topography subtype

<table>
<thead>
<tr>
<th>Author</th>
<th>Subtype</th>
<th>No. patients [%]</th>
<th>Success rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pandolfino</td>
<td>I</td>
<td>21 (21.2)</td>
<td>56%</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>49 (49.5)</td>
<td>39%</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29 (29.3)</td>
<td>39%</td>
</tr>
<tr>
<td>Salvador (LHM)</td>
<td>I</td>
<td>96 (39)</td>
<td>84.6%</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>127 (51.6)</td>
<td>98.3%</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>23 (9.4)</td>
<td>69.5%</td>
</tr>
<tr>
<td>Pratap (PD)</td>
<td>I</td>
<td>24 (47.1)</td>
<td>63%</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>24 (47.1)</td>
<td>63%</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>3 (5.8)</td>
<td>33%</td>
</tr>
<tr>
<td>Rohof (PD &amp; LHM)</td>
<td>I</td>
<td>44 (25)</td>
<td>85.7%</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>114 (64.7)</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>18 (10.2)</td>
<td>50%</td>
</tr>
</tbody>
</table>

LHM, Laparoscopic heller myotomy; PD, pneumatic dilatation.
Response Rates of POEM versus LHM

• Comparator Trial in Type III

**Procedural characteristics and outcomes**

<table>
<thead>
<tr>
<th></th>
<th>POEMn=49</th>
<th>LHMn=26</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median length of myotomy (cm)</td>
<td>16 (7–26)</td>
<td>8 (6–10)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Median procedure time (min)</td>
<td>102 (43–245)</td>
<td>204 (189–331)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Adverse events, n (%)</td>
<td>2 (4) 1 (2) 3 (6)</td>
<td>1 (4) 6 (23) 7 (27)</td>
<td>&lt;0.01 &lt;0.01</td>
</tr>
<tr>
<td>Mean length of stay, days (SD)</td>
<td>3.3 (1.9)</td>
<td>3.2 (2.3)</td>
<td>0.68</td>
</tr>
<tr>
<td>PPI therapy, n (%)</td>
<td>19 (38.8)</td>
<td>12 (46.1)</td>
<td>0.7</td>
</tr>
<tr>
<td>Eckardt stage II or III, n (%)</td>
<td>1 (2.0)</td>
<td>5 (19.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Need for subsequent therapy, n (%)</td>
<td>0</td>
<td>2 (7.7)</td>
<td>0.11</td>
</tr>
<tr>
<td>Clinical response, n (%)</td>
<td>48 (96)</td>
<td>21 (80.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Duration of follow-up, months (SD)</td>
<td>8.6 (1.7)</td>
<td>21.5 (3.9)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Summary: Achalasia in the 21st century

- Achalasia can be more accurately defined and subtyped into clinically relevant phenotypes that may alter management.
  - Counsel patients on prognosis
  - Consider further imaging
- New techniques are evolving that can help tailor therapy based on bolus emptying and distensibility.
  - Consider POEM for type III achalasia
- Warning: need to follow these patients closely as they can worsen under the radar