Achalasia: Inject, Dilate, or Surgery?

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Northwestern University
Chief, Division of Gastroenterology and Hepatology
Northwestern Medicine
Northwestern Memorial Hospital

Chicago Classification 3.0

Disorders of EGJ Outflow Obstruction

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

Major Disorders of Peristalsis
- Entities not seen in normal controls
  - IRP ≥ upper limit of normal AND sufficient evidence of peristalsis such that criteria for type III achalasia are not met
    - Yes
    - No
  - IRP is normal AND reduced distal latency (DL) OR DCI >8,000 mmHg-cm-s
    - Yes
    - No
  - IRP is normal AND 100% failed peristalsis
    - Yes
    - No

Minor Disorders of Peristalsis
- Impaired bolus clearance
  - IRP is normal AND >50% of swallows are ineffective based on DCI values or large breaks
    - Yes
    - No

Normal Esophageal Motor Function
- IRP is normal AND >50% of swallows are effective without criteria for spasm or jackhammer
  - Yes

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 < 4.5 s)
- Jackhammer esophagus
  - ≥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)

Ineffective Motility (IEM)
- ≥50% ineffective swallows
- Fragmented peristalsis
  - ≥50% fragmented swallows and not meeting criteria for IEM (mean DCI > 450 mmHg-cm-s)

Rapid contraction and Hypertensive peristalsis are not considered distinct clinical-pathological entities in CC v3.0
Pressure Topography of Esophageal Motility

Disorders of EGJ Outflow Obstruction

Major Disorders of Peristalsis
• Entities not seen in normal controls

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

Yes

EGJ Outflow Obstruction
• Incompletely expressed achalasia
• Mechanical obstruction

IRP ≥ upper limit of normal AND
100% failed peristalsis or spasm

No

IRP ≥ upper limit of normal AND
sufficient evidence of peristalsis such that criteria for type III achalasia are not met

Yes

IRP is normal AND
100% failed peristalsis

Yes

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

Does the Chicago Classification provide insight into Natural History?

Early
Type II or III
EGJOO

Chronic
Type II/III–I

Late
Type I/
Absent Contractility

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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

Esophageal Physiology: Neuromuscular Control

Esophageal Physiology: Neuromuscular Control

Symptoms of dysphagia ± chest pain and bland regurgitation

Upper Endoscopy

Obstructive process: ring, stricture, etc.

Normal

High Resolution Manometry

*esophagram may be helpful when manometry is technically difficult to perform

EPT Diagnosis

EGJ Outflow Obstruction
- EGJ = EUS/CT to rule out obstructive process
- Potentially achalasia phenotype with preserved peristalsis

Absent Peristalsis
- If clinical scenario c/w achalasia, a timed barium esophagram should be performed
- Potentially advanced GERD or scleroderma
- Potentially achalasia phenotype with hypotensive LES

Achalasia I
- Severe dilatation is associated with poor treatment response
- Consider myotomy as initial therapy

Achalasia II
- Best treatment response
- Esophagram can be 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

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### Response Rates of Achalasia 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>29*</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29 (29.3)</td>
<td></td>
</tr>
<tr>
<td>Salvador (LHM)</td>
<td>I</td>
<td>96 (39)</td>
<td>85.5</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>127 (51.6)</td>
<td>69.3</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>23 (9.4)</td>
<td></td>
</tr>
<tr>
<td>Pratap (PD)</td>
<td>I</td>
<td>24 (47.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>24 (47.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>3 (5.8)</td>
<td>33.3</td>
</tr>
<tr>
<td>Rohof (PD &amp; LHM)</td>
<td>I</td>
<td>44 (25)</td>
<td>88.8</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>40</td>
</tr>
</tbody>
</table>

LHM, laparoscopic heller myotomy; PD, pneumatic dilatation.


### Response Rates of Achalasia Treatments

*Patients categorized by pressure topography subtype*

<table>
<thead>
<tr>
<th>Study</th>
<th>OR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pandolfino</td>
<td>0.07 (0.00, 1.87)</td>
<td>12.58</td>
</tr>
<tr>
<td>Crepin (2014)</td>
<td>0.18 (0.01, 3.18)</td>
<td>6.43</td>
</tr>
<tr>
<td>Salvador (2010)</td>
<td>0.59 (0.11, 2.78)</td>
<td>58.48</td>
</tr>
<tr>
<td>Rohof (2013)</td>
<td>0.32 (0.07, 1.38)</td>
<td>21.51</td>
</tr>
<tr>
<td>Overall (p = 0.05, P = 0.835)</td>
<td>0.26 (0.12, 0.58)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>OR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pandolfino</td>
<td>1.00 (1.14, 6788.86)</td>
<td>1.13</td>
</tr>
<tr>
<td>Crepin (2014)</td>
<td>3.35 (0.12, 92.89)</td>
<td>9.88</td>
</tr>
<tr>
<td>Salvador (2010)</td>
<td>8.82 (2.63, 29.55)</td>
<td>59.87</td>
</tr>
<tr>
<td>Rohof (2013)</td>
<td>2.04 (0.20, 20.87)</td>
<td>34.03</td>
</tr>
<tr>
<td>Overall (p = 0.05, P = 0.444)</td>
<td>4.66 (2.72, 17.28)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

ACHALASIA: Treatment Options

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

• Botulinum toxin injection

• Pneumatic dilation

• Laparoscopic Heller myotomy

• Emerging Treatments
  - Peroral endoscopic myotomy (POEM)

Recommendations: Treatment

• **Definitive treatment of achalasia include pneumatic dilation and Heller's myotomy which have equal long-term outcomes and the choice between the two forms of therapy should be based on practices and institutional expertise as well as patient preference**
  - (Strong recommendation, high quality evidence).

• **Younger males may benefit more from myotomy or initial dilation with the larger balloon sizes of 3.5 cm**
  - (Weak recommendation, moderate quality evidence).

• **Pharmacologic therapy for achalasia (botulinum toxin, nitrates, calcium channel blockers) should be reserved for those who cannot undergo definitive treatment with either pneumatic dilation or surgical myotomy**
  - (Strong recommendation, high quality evidence).
ACHALASIA: Treatment Options

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

- Botulinum toxin injection

- Pneumatic dilation
  - Gradual dilation: 3.0 - 3.5 - 4.0 cm balloons
  - Endoscopy
  - Balloon placement by fluoroscopy
  - Gradual dilation until “waist” flattens
  - 8-10 psi x 15-60 seconds
  - Post dilation esophagram?
  - Observe x 2-3 hours

PNEUMATIC DILATION
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

Pneumatic Dilation versus Laparoscopic Heller’s Myotomy for Idiopathic Achalasia
G. Boeckxstaens, M.D., Ph.D., V. Annese, M.D., Ph.D.,
S. Bruley des Varannes, M.D., Ph.D., S. Chaussade, M.D., Ph.D.,
M. Costantini, M.D., Ph.D., A. Cuttitta, M.D., J. Elizalde, M.D.,
U. Fumagalli, M.D., Ph.D., M. Gaudric, M.D., Ph.D.,
W. Rohof, M.D., A. Smout, M.D., Ph.D., J. Tack, M.D., Ph.D.,
A. Zwierman, Ph.D., G. Zaninotto, M.D., Ph.D.,
and O. Busch, M.D., Ph.D., for the European Achalasia Trial Investigators*
Pneumatic Dilation versus Laparoscopic Heller Myotomy for Idiopathic Achalasia

**Figure 2.** Kaplan–Meier Curves for the Rate of Treatment Success.


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Pneumatic Dilation versus Laparoscopic Heller Myotomy for Idiopathic Achalasia

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Pneumatic Dilation versus Laparoscopic Heller Myotomy for Idiopathic Achalasia

Clockwise from bottom:
- Esophagus
- Stomach
- EJG
- Hydraulic dilator: EsoFLIP®

14 paired impedance planimetry electrodes at 0.5-cm spacing

Moonen et al Gut 2016
Hydraulic dilation

- EsoFLIP® ES-330 catheter (Crospon, Inc. Galway, Ireland)

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>75</td>
<td>75</td>
</tr>
</tbody>
</table>

- Dilation repeated
- (7/10 patients)
- Held for 30-60 s

Final EGJ measurement at 30 mL

Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Hydraulic dilation</th>
<th>Pneumatic dilation</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean +/- SD</td>
<td>48 +/- 15</td>
<td>44 +/- 17</td>
<td>0.529</td>
</tr>
<tr>
<td>Gender: F/M</td>
<td>4/6</td>
<td>4/6</td>
<td>1.0</td>
</tr>
<tr>
<td>Achalasia subtype, n (%)</td>
<td></td>
<td></td>
<td>0.515</td>
</tr>
<tr>
<td>Type I</td>
<td>2 (20)</td>
<td>3 (30)</td>
<td></td>
</tr>
<tr>
<td>Type II</td>
<td>5 (50)</td>
<td>7 (70)</td>
<td></td>
</tr>
<tr>
<td>Type III</td>
<td>1 (10)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>FLIP Dx</td>
<td>2 (20)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Median IRP, mmHg</td>
<td>28 (23 – 31)</td>
<td>35 (29 – 54)</td>
<td>0.043</td>
</tr>
<tr>
<td>Basal EGJ pressure, mmHg</td>
<td>30 (16 -49)</td>
<td>29 (22 – 45)</td>
<td>0.965</td>
</tr>
<tr>
<td>EGJ-DI, mm²/mmHg</td>
<td>0.87 (0.74 – 1.2)</td>
<td>1.0 (0.66 – 1.2)</td>
<td>0.897</td>
</tr>
<tr>
<td>Baseline ES</td>
<td>6.5 (5 – 8)</td>
<td>6.5 (4 – 8)</td>
<td>0.631</td>
</tr>
</tbody>
</table>

Values are median (range) unless otherwise specified
Symptomatic outcomes

Results: Clinical outcomes

Hydraulic dilation

Positive outcome 77% (7/9)

Pneumatic dilation

Positive outcome 88% 8/9

Per Oral Endoscopic Myotomy (POEM)

1 2 3 4 5

Fukuoka univ.
International Experience with POEM

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

### Northwestern Experience with POEM

<table>
<thead>
<tr>
<th>Location of primary investigation</th>
<th>Year</th>
<th>Age (mean, range)</th>
<th>Markevitch length (transrectal cm)</th>
<th>Echardt score (before/after)</th>
<th>4-sec IRP (mmHg) (before/after)</th>
<th>5min column height on TBE (cm) (before/after)</th>
<th>Symptomatic GER (%)</th>
<th>Esophagitis &gt; Grade A (%)</th>
<th>Follow-up (months)</th>
<th>Pre-op</th>
<th>1-year post-op</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shanghai, China** (Shovel)</td>
<td>2013</td>
<td>65 (64-75)</td>
<td>10.3 (7-13)</td>
<td>8.5 (3-17)</td>
<td>7.8 (16-37)</td>
<td>27.2 (11-138)</td>
<td>3 (1-4)</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Elective, Frankfurt (Dr. Chollet)</td>
<td>2012</td>
<td>45 (39-73)</td>
<td>12.3 (8-17)</td>
<td>7.8 (16-37)</td>
<td>27.2 (11-138)</td>
<td>3 (1-4)</td>
<td>100</td>
<td>111</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rome, Italy* (Kharasch)</td>
<td>2012</td>
<td>11</td>
<td>41 (30-65)</td>
<td>7.1 (1-13)</td>
<td>43.5 (16-69)</td>
<td>3 (0-0)</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Portland, Oregon** (Chesner)</td>
<td>2012</td>
<td>18</td>
<td>59 (22-86)</td>
<td>9 (6-12)</td>
<td>45 (16-68)</td>
<td>6 (0-0)</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hong Kong, China** (Woo)</td>
<td>2013</td>
<td>18</td>
<td>47 (22-87)</td>
<td>10.8 (7-13)</td>
<td>5.5 (1)</td>
<td>4.5 (0-9)</td>
<td>3 (0-0)</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oxford, England** (Rajput)</td>
<td>2012</td>
<td>14</td>
<td>68 (52-94)</td>
<td>9 (6-14)</td>
<td>9 (2-14)</td>
<td>7 (1-14)</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Northeast Japan** (Miyamoto)</td>
<td>2011</td>
<td>28</td>
<td>92 (19-84)</td>
<td>14.8 (9-17)</td>
<td>6.7 (12)</td>
<td>7.1 (2-23)</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>South Korea** (Eul)</td>
<td>2013</td>
<td>13</td>
<td>49 (13-64)</td>
<td>4.4 (1-5)</td>
<td>4 (1-0)</td>
<td>3 (2-5)</td>
<td>3 (0-0)</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>European multicenter** (van Rassen)</td>
<td>2011</td>
<td>75</td>
<td>45 (26-65)</td>
<td>13 (6-28)</td>
<td>6 (1-1)</td>
<td>25 (8-9)</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Akita City, Japan** (Shibatani)</td>
<td>2011</td>
<td>60</td>
<td>52 (18-82)</td>
<td>9 (3-17)</td>
<td>7.9 (2)</td>
<td>4.2 (5-13-4)</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Yokohama, Japan** (Tanaka)</td>
<td>2013</td>
<td>300</td>
<td>43 (3-93)</td>
<td>14 (1)</td>
<td>6.1 (3-13)</td>
<td>27.3 (13-64)</td>
<td>12 (5-88)</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aachen, Switzerland** (Majtan)</td>
<td>2013</td>
<td>21</td>
<td>19 (7-70)</td>
<td>1.2 (0-17)</td>
<td>4.6 (1-13)</td>
<td>4.6 (1-22)</td>
<td>100</td>
<td>100</td>
<td>99</td>
<td>15</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*First 120 Cases
# Response Rates of POEM versus LHM

• Comparator Trial in Type III

## Procedural characteristics and outcomes

<table>
<thead>
<tr>
<th>Characteristic</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 (45–345)</td>
<td>264 (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>1&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 (98)</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>


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**Per Oral Endoscopic Myotomy (POEM)**

Tailored: failed Heller Myotomy
Clinical Pearls: 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
- Pneumatic Dilation and Surgical Myotomy are equivalent if one considers requirement of multiple PDs equivalent to HM.
- New techniques are evolving that can tailor therapy based on subtype.
  - Consider POEM for type III achalasia
- Medical therapy should be reserved for patients who are not surgical candidates or as adjunct therapies in those patients who have undergone definitive therapy.
- No therapy is perfect and patients may require re-intervention and should be followed closely.