Esophageal Motility Disorders

*Current classification and treatment*

Peter J. Kahrilas, M.D.
Northwestern University
Chicago, USA

**REVIEW ARTICLE**

Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography


EMD #68 v5/15/13 PK  Bredenoord AI et al, Neurogastroenterol Motil 2012;24(suppl 1):57-65
Normal Esophageal Motility

Pressure topography plot with key metrics

- Swallow
- Distal contractile integral (DCI) < 8,000 mmHg-s-cm
- Latency (DL) > 4.5s
- IRP window (IRP < 15 mmHg)

Interpreting Clinical EPT Studies

The tools of analysis

- IRP (Integrated Relaxation Pressure)
  - The best validated metric of deglutitive relaxation
  - Advantages of a sleeve-type recording
  - Accounts for both nadir and persistence of relaxation
Deglutitive EGJ Relaxation Measures

*Sensitivity in detecting achalasia*

<table>
<thead>
<tr>
<th>EGJ relaxation measure</th>
<th>Achalasia sensitivity (n=62)</th>
<th>False -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single sensor nadir (&lt;7 mmHg)</td>
<td>52%</td>
<td>48%</td>
</tr>
<tr>
<td>High resolution nadir (&lt;10 mmHg)</td>
<td>69%</td>
<td>31%</td>
</tr>
<tr>
<td>4s Integrated Relaxation Pressure (&lt;15 mmHg)</td>
<td>97%</td>
<td>3%</td>
</tr>
</tbody>
</table>

*Ghosh SK et al. Am J Physiol 2007;293:G878*
Fitting Chicago Classification to EPT Studies

Hierarchical analysis

**Probably Achalasia**

- IRP ≥ 15 mmHg & absent peristalsis

**Achalasia**

- Type I: classic
- Type II: with esophageal compression
- Type III: spastic

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**Achalasia Subtypes**

- **Type I** (classic)
  - IRP = 22.3 mmHg
- **Type II**
  - Panesophageal pressurization
  - IRP = 28.9 mmHg
- **Type III** (spastic)
  - Compartmentalized pressurization
  - IRP = 52.3 mmHg
- **Type IV**
  - EGJ outflow obstruction

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Kahrilas PJ et al, Gastroenterology 2013; In Press
Achalasia treatment outcome by EPT subtype

*Type I (classic), Type II (pressurization), Type III (spastic)*

<table>
<thead>
<tr>
<th>Publication</th>
<th>N, (Rx type)</th>
<th>Type I</th>
<th>Type II</th>
<th>Type III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pandolfino 2008 [1]</td>
<td>99 (PD, LHM, Botox)</td>
<td>56% (n=21)</td>
<td>96% (n=49)</td>
<td>29% (n=29)</td>
</tr>
<tr>
<td>Salvador 2010 [2]</td>
<td>246 (LHM)</td>
<td>85% (n=96)</td>
<td>95% (n=127)</td>
<td>69% (n=23)</td>
</tr>
<tr>
<td>Pratap 2011 [3]</td>
<td>51 (PD)</td>
<td>63% (n=24)</td>
<td>90% (n=24)</td>
<td>33% (n=3)</td>
</tr>
<tr>
<td>Rohof 2013 [4]</td>
<td>176 (RCT: PD, LHM)</td>
<td>86% (PD) 81% (LHM) (n=44)</td>
<td>100% (PD) 95% (LHM) (n=114)</td>
<td>40% (PD) 86% (LHM) (n=18)</td>
</tr>
</tbody>
</table>


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Pre and Post-treatment esophageal pressure topography in achalasia

**Type II achalasia**

**Weak peristalsis**

Length along the esophagus (cm)

0 5 10 15 20 25 30 35

UES Proximal break

Pan-esophageal pressurization

Peristaltic remnant

Distal break

EGJ

mmHg


EMD #57 v3/31/13 PJK
Pre and Post-treatment esophageal pressure topography in achalasia

**Pre-myotomy**
- Type III (spastic) achalasia
  - Pan-esophageal pressurization
  - Early latency (spastic) contraction
- EGJ

**Post-myotomy**
- Distal esophageal spasm
  - DL = 2.1 s

**Pre-treatment achalasia subtype**
- Type I: 1
- Type II: 2
- Type III: 6

**Post-treatment pattern**
- EGJ outflow obstruction
- Type I achalasia
- Premature contraction
- Frequent failed peristalsis
- Weak peristalsis
- Absent peristalsis

**Number of patients**
Evolution of achalasia over a 2-year period,

*Myenteric plexus inflammation at LES*

Finally treated with laparoscopic Heller myotomy

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Evolution of achalasia over a 2-year period,

*Myenteric plexus inflammation at LES*

Finally treated with laparoscopic Heller myotomy

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ACG Regional Postgraduate Course - Williamsburg, VA
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Achalasia Treatments

*General principles*

- Early treatment is desirable
  - Prevents disease progression and complications
- Dysphagia responds to Rx better than chest pain
- Botox can be a useful temporizing measure
  - Doubt in diagnosis
  - Elderly, frail patient
- Pneumatic dilation and LHM are both highly effective and highly operator dependent procedures
  - Leverage regional expertise
  - Comparative data from the literature are not necessarily locally or even regionally applicable
- Peroral Endoscopic Myotomy (POEM) is a promising new technique

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**Botox®**

*Know when to say, “when”*
Pneumatic Dilators used for Treating Achalasia

Microvasive® Rigiflex Dilator (3.0, 3.5, or 4.0 cm)
Passed over guidewire, imaged with fluoroscopy

Microvasive™ Pneumatic Dilation
35 mm dilator
Microvasive™ Pneumatic Dilation

35 mm dilator

“Waist” locating the LES

Effacement of “Waist”
### Achalasia Treatments

**Pneumatic dilation**

#### Advantages
- Outpatient procedure
- Can repeat
- Can be long-term solution
- Halts disease progression
- Rare post-Rx reflux

#### Disadvantages
- 1% perforation risk requiring surgical repair
- Less efficacious than myotomy
- Less predictable than myotomy
- May need 2 or even 3 successive dilations

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### Laparoscopic Heller Myotomy with Dor Fundoplication

![Laparoscopic Heller Myotomy with Dor Fundoplication](image)

- Mucosa through myotomy
- Esophagus
- Right crus of diaphragm
Achalasia Treatments

Laparoscopic Heller myotomy

Advantages

• The most effective treatment
• The most definitive treatment
• Halts disease progression

Disadvantages

• Usually requires hospitalization
• 1% perforation risk requiring intervention
• Operative morbidity and mortality
• Expensive
• Post-Rx reflux in > 50%

Success rates of pneumatic dilation and laparoscopic Heller myotomy

The European Achalasia Trial, 2 year results

<table>
<thead>
<tr>
<th></th>
<th>Heller myotomy (n=97)</th>
<th>Pneumatic dilation (n=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful treatment (%)</td>
<td>97%</td>
<td>78%</td>
</tr>
<tr>
<td>Eckardt score</td>
<td>1.1 ± 0.1</td>
<td>1.3 ± 0.1</td>
</tr>
<tr>
<td>LES pressure (mmHg)</td>
<td>14 ± 1</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>Timed barium swallow (cm)</td>
<td>3.4 ± 0.6</td>
<td>4.8 ± 0.7</td>
</tr>
</tbody>
</table>


EMD #43 v1/25/11 PJK
Complication rates of pneumatic dilation and laparoscopic Heller myotomy for achalasia

Northwestern experience 2000-2011 (n=463 patients)

<table>
<thead>
<tr>
<th></th>
<th>LHM (n=295)</th>
<th>PD (n=272)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforation rate per procedure, n (%)</td>
<td>6 (2.0%)</td>
<td>1 (0.37%)</td>
</tr>
<tr>
<td>Perforation rate per patient treated, n (%)</td>
<td>6 (2.0%)</td>
<td>1 (0.51%)</td>
</tr>
<tr>
<td>30-Day mortality, n (%)</td>
<td>2 (0.68%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Perforation after prior achalasia treatment, n (%)</td>
<td>1 (2.6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Surgical intervention for perforation, n (%)</td>
<td>2 (33%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Average hospital stay after perforation, days</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Post-perforation deaths, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Relationship between series size and perforation rate for (modern) pneumatic dilation in achalasia

Funnel plot

Number of patients in series (n) vs. Procedural esophageal perforations (%)

Northwestern experience: Used all 35 mm dilations
European Achalasia trial: With the first 13 cases (7.2%)
Per-Oral Esophagomyotomy (POEM)

Novel alternative to LHM or PD for achalasia

...laparoscopic Heller-Dor myotomy still requires 5 abdominal skin incisions for trocar placement. Pasricha initially reported a method of submucosal endoscopic myotomy with no skin incision in an experimental model [1]. Subsequently, Inoue modified the technique and applied it clinically...[2].


POEM

(1) Enter into the submucosa in the mid esophagus

View through transparent distal cap on endoscope

After about 10 ml injection, ≈ 2 cm incision placed ≈13 cm above EGJ

Courtesy of H. Inoue
(2) Creation of submucosal tunnel ≈ half esophageal circumference

Tunnel down to EGJ using endoscopic submucosal dissection technique

(3) Myotomy begun ≈ 3 cm distal to entry, ≈ 7 cm above EGJ

Lift inner circular muscle bundle toward tunnel cavity and cut with triangle tip knife
POEM

(3) Myotomy completion

Complete incision of thickened inner muscular layer of through the narrowed EGJ extending ~ 2cm on to the stomach

POEM

(4) Clipping
Achalasia Treatments

*Per-Oral Endoscopic Myotomy (POEM)*

**Advantages**
- Incisionless (NOTES)
- Surgical efficacy without surgical morbidity
- (Should) halt disease progression
- Potential to ‘customize’

**Disadvantages**
- New
- Learning curve situation
- Limited data on morbidity, mortality, post-op reflux
- Long term?

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**Fitting Chicago Classification to EPT Studies**

*Hierarchical analysis*

1. Probably Achalasia
   
   \[ \text{IRP} \geq 15 \text{ mmHg} \text{ & absent peristalsis} \]

   Yes

   No, but...

2. Major motor disorder
   
   \[ \text{IRP} \geq 15 \text{ mmHg OR absent peristalsis OR reduced latency OR DCI >8,000 mmHg-s-cm} \]

   - Type I achalasia: classic
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   - Type III achalasia: (includes spastic)
Fitting Chicago Classification to EPT Studies

Hierarchical analysis

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   - Yes

2. Major motor disorder
   - IRP ≥ 15 mmHg OR absent peristalsis OR reduced latency OR DCI > 8,000 mmHg-s-cm
   - Yes

   - Absent peristalsis
   - Distal esophageal spasm
     - Pseudorelaxation?
     - Spastic achalasia with low LESP?
   - EGJ outflow obstruction
     - may be an achalasia variant
   - Hypercontractile (Jackhammer) esophagus

Latency vs contraction velocity as criterion for DES

Latency is a much more specific abnormality

- Propagation velocity = 15 cm/s
- Distal contraction latency (DL) = 7.0 s
Phenotypes of rapid propagation

Refining the diagnosis of DES

Rapid Contraction

Weak Contraction

Latency vs contraction velocity as criterion for DES

Latency is a much more specific abnormality

Normalized length along the esophagus

Propagation velocity = 25 cm/s
Distal contraction latency (DL) = 3.0 s
1070 consecutive patients with clinical EPT studies

91 Patients with rapid propagation

Premature Contractions (n=24) [Distal latency < 4.5 s]

Rapid Contractions (n=67) [CFV > 9 cm/s / normal latency]

- Spastic achalasia
- DES
- Weak peristalsis – segmental contraction
- Functional EGJ obstruction
- Weak peristalsis
- Hypertensive peristalsis
- Normal

Jackhammer esophagus (DCI>8,000 mmHg-s-cm)

Repetitive contractions not synchronized with respiration

DCI = 12,957 mmHg-s-cm

Phosphodiesterase type 5 inhibitors for EMD

Background

• Sildenafil potentiates the activity of endogenous NO by inhibiting an enzyme (PDE-type V) that catalyzes the second messenger (cGMP) mediating NO action
• Reduces esophageal contractile amplitude for several hours
• Less consistent effect on peristaltic propagation
• Potentially useful for EMD with hypercontractility


Phosphodiesterase type 5 inhibitors for EMD

Case reports with EPT

45 minutes post-sildenafil 25 mg

Pre-sildenafil
Severe swallow-related chest pain

50 minutes post-sildenafil, solid challenge

Phosphodiesterase type 5 inhibitors for EMD

Case reports with EPT

Pre-sildenafil
Severe dysphagia and chest pain
Solid swallow challenge

45 minutes post-sildenafil 25 mg
Reduced dysphagia, no chest pain


Fitting Chicago Classification to EPT Studies

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   IRP ≥15 mmHg & absent peristalsis
   Yes
   No, but...

2. Major motor disorder
   IRP ≥15 mmHg OR absent peristalsis
   OR reduced latency OR DCI >8,000 mmHg·s·cm
   Yes
   No

3. Not major motor disorder
   But... Peristaltic abnormalities
   No

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### Fitting Chicago Classification to EPT Studies

**Hierarchical analysis**

1. **Probably Achalasia**
   - IRP $\geq 15$ mmHg & absent peristalsis
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   - No, but...

2. **Major motor disorder**
   - IRP $\geq 15$ mmHg OR absent peristalsis OR reduced latency OR DCI >8,000 mmHg-s-cm
   - Yes
   - Absent peristalsis
   - Distal esophageal spasm
   - Pseudorelaxation?
   - Spastic achalasia with low LESP?
   - EGJ outflow obstruction
   - may be an achalasia variant
   - Hypercontractile (Jackhammer) esophagus

   - No

3. **Not major motor disorder**
   - But... Peristaltic abnormalities
   - No
   - Normal

   - Weak peristalsis
   - with large or small 20 mmHg isobaric contour breaks
   - Frequent failed peristalsis
   - Hypertensive peristalsis (nutcracker esophagus)
   - Rapid contraction

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### Esophageal Motility: Impact of HRM/EPT

**Circa 2013**

- EPT has clarified the diagnosis of achalasia and defined criteria for EGJ outflow obstruction as a distinct diagnosis
- Spasm remains difficult, but EPT may sort out subsets of reduced-latency and hypercontractile conditions amenable to specific therapies
- EPT findings should be prioritized:
  1. impaired EGJ relaxation,
  2. reduced latency contractions,
  3. extreme hypo- or hypercontractility,
  4. then....
Esophageal Motor Disorders, What’s New?

Treatment

- POEM (per-oral endoscopic myotomy) is potentially superior to existing achalasia treatments
- Phosphodiesterase-type 5 inhibitors are potentially useful to treat hypercontractile EMD