Esophageal Motor Abnormalities

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High Resolution Manometry
Pivotal Advance

- Late Ray Clouse, MD
- Suspected widely spaced recording points from water perfused systems were missing important data
- Developed spatiotemporal contour plots and converted amplitudes to colors
- Software developed to provide “best fit” data between sensors
- Solid state catheters with 36 high-fidelity circumferential sensors
  - Entire esophagus could now be visualized
- Additional refinements (3D HRM, impedance, video) and applications (anorectal, gastric and small bowel)

Esophageal Pressure Topography

- High-Resolution Manometry Catheter
- Spans from the pharynx to the stomach with sensor separation of no more than a centimeter within and around the sphincters.
- Temporal frequency response matched to the zone of the esophagus
- Compared to water perfusion, the immediate advantages of HRM are:
  - 1) simplified procedural set up with improved sphincter localization
  - 2) elimination of movement artifact
  - 3) simplified data interpretation
  - 4) ability to perform more sophisticated analysis of esophageal function

Sierra Scientific Instruments  Medical Measurement Systems  Sandhill Scientific Inc.
Functional Imaging of Esophageal Peristalsis

HIGH-RESOLUTION MANOMETRY

Clouse Plot

True Functional Imaging of Esophageal Peristalsis

ESOPHAGEAL PRESSURE TOPOGRAPHY
**Pressure Topography of Esophageal Motility: What does it add?**

- More akin to an imaging modality
  - Defines important anatomical landmarks and abnormalities
  - Refines measurement of important motor events
    - EGJ relaxation
    - Peristaltic timing velocity
    - Contractile activity/force/amplitude
  - Defines intra-luminal pressurization patterns
  - Permits pattern recognition

**3 Main Steps in Diagnostic Approach to a High Resolution Manometry Test**

1. Assess EGJ anatomy and function
2. Assess esophageal body function
3. Review pressurization patterns

These 3 steps will permit diagnosis of most esophageal motor abnormalities

* Some changes in prioritization with recent Chicago Classification update (v3.0)

**Anatomy of a High Resolution Esophageal Manometry Test**
**STEP 1 | Assess the EGJ Anatomy and Function**

- Determine if hiatus hernia is present
- Confirm that the catheter has crossed the EGJ and diaphragm

Integrated relaxation pressure: The IRP will determine whether outflow obstruction at the EGJ is evident. Disorders are separated at this point, determined by those with or without outflow obstruction at the EGJ.

**Integrated Relaxation Pressure (IRP):** Mean EGJ pressure measured with a sleeve for 4 contiguous or non-contiguous seconds of relaxation in the 10-second window following deglutitive UES relaxation.

- The upper limit of normal using ManoScan is 15 mmHg.

**Assess the EGJ Anatomy and Function**
STEP 2 | Assess Esophageal Body Function

• Peristaltic integrity: either intact, weak or failed
• Contractile deceleration point (CDP): anatomic separation point (between tubular esophagus and phrenic ampulla)
• Distal Latency (DL): timing of esophageal peristalsis
  • will define the swallow as premature or normal latency
• Distal contractile index (DCI): vigor of the distal esophageal contraction
• Contractile front velocity (CFV): speed of esophageal contractions
  • previously used to define rapid contraction
  • no longer considered meaningful

Peristaltic Breaks: Gaps in the 20 mmHg isobaric contour of the peristaltic contraction between the UES and EGJ, measured in axial length.

Contractile Deceleration Point (CDP): The inflection point along the 30 mmHg isobaric contour where propagation velocity slows, demarcating the tubular esophagus from the phrenic ampulla.

Distal Latency (DL): Interval between UES (1) relaxation and the CDP (2), expressed in seconds. Normal DL is >4.5 sec.
STEP 3 | Pressurization Patterns

Each swallow should be evaluated using the IBC tool to document an isobaric pressurization above 30 mmHg.

Achalasia: HRM led to the identification of three discernible achalasia types. Each subgroup represents a distinct clinical entity, each with significantly different biomechanics and treatment outcomes. Type I patients do significantly better with Heller myotomy than with pneumatic dilatation, and Type III patients exhibit the worst prognostic outcome.

Achalasia TYPE I

There is no significant pressurization within the body of the esophagus. Therefore, this would be classified as failed peristalsis with abnormal IRP. In the absence of esophageal body contractility, the IRP threshold of >10 mmHg is used to distinguish Type I Achalasia from absent peristalsis.

Major Disorders of Esophageal Peristalsis

- Achalasia
- Hypertensive LES/EGJ Outflow obstruction
- (Nutcracker esophagus)
- Jackhammer esophagus
- Distal esophageal spasm (DES)
- Absent peristalsis

Pressure Topography of Esophageal Motility
Chicago Classification 3.0 Changes

- Use median rather than mean cutoff value for IRP
- Use lower IRP cutoff for type I achalasia (platform specific)
- Panesophageal pressurization with ≥ 20% swallows with 100% failed contractions is type II achalasia irrespective of IRP
- Emphasize heterogeneity of conditions potentially causing EGJ outflow obstruction
- Modify hypercontractile esophagus to ≥20% swallows with DCI 5000–8000 mmHg x s x cm
- Substitute ‘absent contractility’ for ‘aperistalsis’ or ‘absent peristalsis’ to differentiate from other scenarios where peristalsis is absent (e.g., achalasia)
- Rename ‘minor disorders of peristalsis’
- Eliminate small breaks (2–5 cm) in the 20-mmHg isobaric contour as a criterion of abnormality
- Eliminate rapid CFV (>9 cm/s) as a criterion of abnormality
- Eliminate the designation of ‘hypertensive peristalsis’ (DCI 5000–8000 mmHg x s x cm) (no more Nutcracker)
- Adopt the ‘ineffective esophageal motility’ (IEM) designation from conventional manometry
- Eliminate ‘frequent failed peristalsis’ as a distinct diagnostic entity
- Incorporate new data from studies of multiple repetitive swallows into the criteria for IEM

Disorders with EGJ Outflow Obstruction

The Chicago Classification

- Achalasia
  - Subtype I: No contractility
  - Subtype II: ≥ 20% PEP
  - Subtype III: ≥ 20% spasm (DL<4.5s)

- EGJ Outflow Obstruction
  - Incompletely expressed achalasia
  - Mechanical obstruction

- IRP ≥ ULN AND 100% failed peristalsis or spasm
- IRP < upper limit of normal AND some instances of intact or weak peristalsis

Nutcracker (DCI 5000–8000 mmHg x s x cm)

EIGE 2015;27;160-74.
Achalasia

- Dysphagia, wt loss, regurgitation, halitosis, GERD sx
- Immune-mediated disease targeting esophageal myenteric plexus (neurons and ganglia)
  - Antineuronal Abs, inflammatory cells, cytokines, immunoglobulins, complement
  - Achalasia subtypes may represent differential degree of immune activation/selectivity (cell vs humoral)
  

High-Resolution Manometry: Achalasia subtypes

- Type I
- Type II
- Type III

Clinical Evolution of Achalasia

Assessing clinically relevant phenotypes

Achalasia types may not be a progression as once thought

IRP = 22.3 mmHg
IRP = 24.2 mmHg
IRP = 29.8 mmHg
Achalasia Mimics

- Malignancy (Pseudoachalasia)
- Chaga’s disease
- Amyloidosis
- Postvagotomy
- Neurofibromatosis
- Sarcoidosis
- MEN IIb

Hypertensive LES

- Presentation: Chest pain/dysphagia/globus
  - May be an achalasia variant
- Dx: LES pressure > 35 mmHg AND failure to relax below IRP of 15 mmHg
  - Normal peristalsis
- More important than pressures: failure of full relaxation at LES
  - Incomplete bolus transfer
- Can overlap with other spastic esophageal conditions
  - May need additional provocation (bread swallow, multiple rapid swallows, solid swallows)
  - EUS recommended prior to therapy to exclude infiltrative or compressive disease (eg malignancy)

EGJ Outflow Obstruction

- EGJ Outflow Obstruction: Achalasia phenotype
- EGJ Outflow Obstruction: Mechanical

- EGJ Outflow Obstruction: Compartmentalized pressurization
- Normal peristalsis
- EGJ Outflow Obstruction: Obstruction

- Barium tablet localized 12 mm restriction EGJ
- Large diverticulum 4 cm above EGJ
- Locus of diverticulum above EGJ

- EGJ Outflow Obstruction: Normal relaxation
- EGJ Outflow Obstruction: Mechanical obstruction
Major Disorders of Peristalsis
The Chicago Classification

Non-achalasia motor abnormalities

Hypercontractile Esophagus The diagnostic criteria for hypercontractile peristalsis have been redefined as at least one propagated swallow-induced contraction with a DCI of >8,000 mmHg·s·cm, as that value is extremely rare in asymptomatic subjects. The repetitive contractions sometimes seen in this presentation have led to the reference of “Jackhammer” esophagus.

Distal Esophageal Spasm Distal Latency (DL) has been proposed as an improved measure to represent simultaneous contractions. The DL is currently used to define DES, although further evaluation of clinical outcomes is needed to support this metric.

Borderline Esophageal Motor Function This category represents a range of abnormalities including borderline-normal to those conditions similar to ineffective esophageal motility (IEM) or absent contractility.

Nutcracker Esophagus

- Prolonged hypertensive contractions with normal swallow waveform propagation
- Etiology: possible hypercholinergic state leading to incoordination of smooth muscle fibers
- Presentation: chest pain (may be mistaken with GERD or cardiac CP), dysphagia (solids or liquids), exacerbation with hot or cold, ENT symptoms (high dysphagia, globus)
- May exist with other abnormalities (LES HTN)
- Dx: DCI >5000 (cont ampl x duration x length)
**Hypercontractile or Jackhammer Esophagus (aka Spastic Nutcracker)**

- Offshoot of Nutcracker
  - 4% manometry referrals; r/o mechanical obst
- Presentation: Chest pain/dysphagia
- Dx:
  - At least one DCI > 8000
  - Repeated high amplitude contractions
  - Normal DL (≥ 4.5 sec)

**Distal Esophageal Spasm (DES)**

- Unknown etiology; likely related to defects in inhibitory neural pathways of esophagus
  - Rarest manometric diagnosis (3%)
  - Classic corkscrew esophagus very rare
- Presentation: Chest pain/dysphagia
  - Symptom correlation poor
- Dx:
  - Normal median IRP (LES relaxation), ≥ 20% premature contractions with DCI > 450 mmHg x s x cm
  - Some normal peristalsis may be present
Treatment of Achalasia

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>SHEEHAN (74%)</th>
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</thead>
<tbody>
<tr>
<td>Pandolfino, et al.</td>
<td>Normal: No breaks/ NL DCI</td>
<td>31 (41.85)</td>
<td>56.5</td>
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<td></td>
<td>DCI= 20,452 mmHg-s-cm</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Abnormal DCI</td>
<td>49 (65.6)</td>
<td>60.3</td>
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<tr>
<td></td>
<td>DCI= 7 mmHg-s-cm</td>
<td></td>
<td></td>
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<tr>
<td>Salvador, et al.</td>
<td>Absent Peristalsis</td>
<td>23 (30.6)</td>
<td>60.3</td>
</tr>
<tr>
<td>Pratap, et al.</td>
<td>Absent/Failed Peristalsis</td>
<td>34 (44.7)</td>
<td>60</td>
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<tr>
<td>Rohof, et al.</td>
<td>Weak Peristalsis- IEM</td>
<td>2 (2.6)</td>
<td>61.1</td>
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<tr>
<td></td>
<td>Weak Peristalsis- TZ Defect</td>
<td>10 (13.0)</td>
<td>40</td>
</tr>
</tbody>
</table>

LHM, laparoscopic Heller myotomy; PES, pneumatic dilatation.
Treatment of Achalasia: 2015

- POEM (Per-oral endoscopic myotomy)
  - Short-term success 82-100%
  - LES pressures reliably lowered
  - Lack of long-term data/comparisons to laparoscopic Heller myotomy (current data suggests equivalence)

Treatment of other Esophageal Hypertensive Conditions

- Nutcracker/Jackhammer
  - Trial of nitrates (SL or oral) + PPI
  - Calcium channel blockers (diltiazem, sildenafil) PRN
  - Tricyclic antidepressants
- Hypertensive LES/EGJ Outflow obstruction
  - Balloon dilation or botox injection
  - SAA
  - POEM
- DES
  - PPI + Botox injection
  - Surgical myotomy (when all else fails)

POEM for Spastic Disorders

- 73 patients
  - 9 DES; 10 Jackhammer, 54 type III (spastic) achalasia
  - Dysphagia, regurg, chest pain
  - 11 medcens
- 100% completion
  - 118 mins (mean)
  - 19 cm tunnel (mean)
  - 16 cm myotomy (mean)
  - 3.4 hospital days (mean)
- 8 AEs (11%) none severe

POEM for Spastic Disorders

Hypertensive Contractility Caveats

- There is no clear discriminator of symptomatic hypercontractility
- Propagation can appear normal
- Therapy focused on reducing peristaltic amplitude in altering symptoms is extremely limited
  - Smooth muscle relaxants
  - BOTOX
  - Treat visceral sensitivity

Minor Disorders of Peristalsis
Non-hypertensive Esophageal Motility Disorders

The Chicago classification

- Ineffective motility
  - ≥ 50% ineffective swallows

- Fragmented Peristalsis
  - ≥ 50% fragmented swallows with large (>5 cm) breaks in the 20-mmHg IBC and not effective

Minor Disorders of Peristalsis: Impaired clearance
Minor Disorders of Peristalsis

Symptoms of dysphagia ± chest pain and bland regurgitation

Upper Endoscopy
- Obstructive process e.g. stricture, etc.
- Normal

Esophageal dilatation
- EGJ resistance
- Retained food
- Diverticulum

High Resolution Manometry
* Esophagram may be helpful when manometry is technically difficult to perform

Utilizing HRM/EPT in the Management of Esophageal Symptoms

EGJ Outflow Obstruction
- Absent contractility
  - Achalasia I: Severe dilatation associated with poor treatment response
  - Achalasia II: Best treatment response
  - Achalasia III: Worst treatment response
- DES: Extremely rare

EGD ± EUS/CT to rule out obstructive process
- If clinical scenario c/w achalasia, a timed barium esophagram should be performed
- Consider myotomy as initial therapy
- Esophagram can be normal without barium retention or esophageal dilatation
- May benefit from treatment directed at spasm
- Difficult to treat
- Many cases misdiagnosed Type III achalasia
- Potentially achalasia phenotype with preserved peristalsis
- Potentially advanced GERD or scleroderma
- Potentially achalasia phenotype with hypotensive LES
- Frequently misdiagnosed with conventional manometry
- Often diagnosed as DES on esophagram

Approach to Patients with Esophageal Symptoms

Key Take Home Points
- Esophageal symptoms can have a number of overlapping etiologies
- Interaction between organic and functional influence should not be ignored
- Most disorders can be managed by a careful systematic evaluation
  - Exclude most dangerous causes first and then focus on the most likely cause
- Diagnose and treat in parallel
- Embrace the evolving technology available to you