American Neurogastroenterology and Motility Society Workshop
Sponsored by Medtronic

Management of Esophageal Diseases
In the Era of Personalized Medicine

Saturday, November 3, 2018 • 8:30 am – 4:00 pm

Northwestern University
303 E. Superior
Lurie Medical Research Building, Baldwin Auditorium, Chicago, IL 60611
Agenda: Esophageal Diseases in the Era of Personalized Medicine

8:00  Registration and continental breakfast
8:30–9:00  A new paradigm in managing esophageal complaints: Focusing on index endoscopy – John Pandolfino
9:00–9:45  Esophageal function tests: When and how. John Pandolfino and Dustin Carlson
  o FLIP protocol
  o Using Bravo capsule during index endoscopy
  o Shifting role of HRIM in the era of FLIP
9:45–10:45  Simulation cases (4 cases): Dustin Carlson and John Pandolfino
  o Dysphagia to solids and liquids
  o Regurgitation not responding to PPI
  o Chest pain, dysphagia, and food impaction
  o Heartburn and regurgitation
10:45–11:15  Break
11:15–12:15  Simulation cases (4 cases): Dustin Carlson and John Pandolfino
  o Odynophagia and dysphagia
  o PPI refractory heartburn
  o Nocturnal regurgitation and dysphagia
  o Heartburn and regurgitation
12:15–1:00  Lunch • Q&A with C. Prakash Gyawali and John Pandolfino
1:00–2:00  Credentialing in manometry – John Pandolfino
  o Passing the manometry test
  o What is the optimal protocol and technique required for certification?
2:00–3:00  Difficult cases in HRIM and reflux testing – C. Prakash Gyawali
3:00–4:00  Debriefing and Q&A session with Panel – C. Prakash Gyawali and John Pandolfino
4:30–6:00  Reception hosted by ANMS
Esophageal Symptoms
Diagnostic Approach

• Heartburn, regurgitation, dysphagia, chest pain and food impaction.

• Differential Diagnosis:
  – GERD, EoE, Obstruction, Motor Disorder, Functional Esophageal Disorder

• All roads lead to endoscopy
  – r/o mechanical obstruction, reflux injury, EoE
  – Negative- NERD, motility disorder, functional
Approach to patient with esophageal complaints:
- Dysphagia, Regurgitation, Chest pain, Food impactions
- Diff Dx: GERD, EoE, EMD/Achalasia - difficult to distinguish on history

Visit 1: potentially prescribe a 4-8 week course of PPI and schedule endoscopy

Visit 2: EGD

Esophagitis LA B or higher

- yes
  - Escalate antireflux therapy
  - may need pH-impedance on meds if fails therapy

- no
  - Stricture

- yes
  - Dilation therapy based on morphology and etiology

- no
  - Eosinophilic esophagitis

- yes
  - Biopsies - target EoE treatments

- no
  - Hiatus hernia > 3 cm

- yes
  - May cause reflux and dysphagia
  - May require surgery - will need preop w/u motility and potentially reflux testing

- no
  - Normal or suspect EMD

Visit 3: Follow up in clinic

Visit 4: Esophageal Function testing

Visit 5: Debrief Schedule endoscopy or Surgery
Approach to patient with esophageal complaints: - Dysphagia, Regurgitation, Chest pain, Food impactions

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Molecular and Cellular Mechanisms

Physiologic and Mechanical Consequences
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Line Plots (pressure vs time) of Conventional and High Resolution Manometry

HRM Plotted in Esophageal Pressure Topography

Catheter Configuration

UES

Proximal trough

Middle trough

Distal trough

CDP

1st

2nd

3rd

4th LES

EGJ

EGJ relaxation

Clouse Plots

mmHg

0

10

20

30

40

Time (seconds)

10 s
Achalasia Subtypes: Contractile and Pressure Profiles

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

Color Pressure scale (mmHg)
Distal Esophageal Spasm

Defining Relevant Phenotypes

- **Rapid Premature Contraction**
  - Time (s): 2 s
  - CFV: 45 cm/s
  - DL: 3.0 s

- **Premature Contraction**
  - Time (s): 2 s
  - CFV: 6 cm/s
  - DL: 4.4 s

- **Rapid Contraction**
  - Time (s): 2 s
  - CFV: 15 cm/s
  - DL: 7.0 s
  - Distance: 5.5 cm

*Pandolfino JE, et al. Gastroenterology 2011*
Esophageal pressure Topography

Jackhammer Esophagus- Treatment

A: Jackhammer standard swallow-no pain
B: Jackhammer- Normal protocol swallow + sildenafil
C: Jackhammer-Spasms during chest pain event
D: Jackhammer-Absent Contractility After POEM

Color Pressure scale (mmHg)
Chicago Classification 3.0

Disorders of EGJ Outflow Obstruction

- Incompletely expressed achalasia
- Mechanical obstruction
- >50% ineffective swallows
- Fragmented peristalsis
- >50% fragmented swallows and not meeting criteria for IEM (mean DCI >450 mmHg-s-cm)
- Distal esophageal spasm (DES)
- ≥20% premature contractions (DL<4.5s)
- Jackhammer esophagus
- ≥20% of swallows with DCI >8,000 mmHg-s-cm and normal DL

Major Disorders of Peristalsis
- Entities not seen in normal controls

Minor Disorders of Peristalsis
- Impaired bolus clearance

Normal Esophageal Motor Function

- ≥50% of swallows are effective without criteria for spasm or jackhammer
- Rapid contraction and Hypertensive peristalsis are not considered distinct clinical-pathological entities in CC v3.0

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)

Jackhammer esophagus
- ≥20% of swallows with DCI >8,000 mmHg-s-cm 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-s-cm)
Approach to patient with esophageal complaints:
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- Hiatus hernia > 3 cm
  - yes: May require surgery- will need preop w/u motility and potentially reflux testing
  - no

- Achalasia or suspect EMD
  - yes: Treat EGJOO/Achalasia – PD/BoTox or if spastic or hypercontractile- try smooth muscle relaxants
  - no

- Wireless pH Monitoring

Visit 3: Debrief at 1 week post-EGD
May require HRIM PP or Behavior Intervention/NM therapy
Impedance Planimetry
- Evolution of the FLIP to FLIP Topography and Panometry
- Mechanical Properties and Contractile Patterns
Impedance Planimetry
- Evolution of the FLIP to FLIP Topography and Panometry
- Mechanical Properties and Contractile Patterns
Normal control

CC 3.0: Normal motility: IRP = 13 mmHg, DL = 7.4s, DCI = 2200 mmHg-s-cm
FLIP cases: Normal Control
EGJ-distensibility index (EGJ-DI) Analysis

- \[ \text{EGJ-DI} = \frac{\text{Narrowest CSA}_{\text{EGJ}}}{\text{intra-balloon pressure}} \]

- Achalasia: Reduced \( \text{EGJ-DI}^{1,2} \)

**EGJ-distensibility index (EGJ-DI)**

**Analysis: Sweet Spot**

- **EGJ-DI** = Narrowest $\text{CSA}_{\text{EGJ}}$ / intra-balloon **pressure**
- **Sweet spot**: 4.0-7.5

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<tr>
<th>Diameter (mm)</th>
<th>CSA (mm²/mmHg)</th>
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*Esophageal Center at Northwestern*
EGJ-distensibility index (EGJ-DI)
Analysis: Sweet Spot

- **EGJ-DI** = Narrowest $\text{CSA}_{\text{EGJ}}$ / intra-balloon pressure
- Normative Data in 20 asymptomatic controls

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Graph showing distribution of CSA values against pressure levels.
EGJ-distensibility index (EGJ-DI)

- Untreated achalasia
- Treated achalasia - ES < 3, No retention
- Treated achalasia - ES > 3, + Retention

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Esophageal Center at Northwestern
**FLIP cases:** 48 yo M: dysphagia, regurgitation

CC 3.0: Type I achalasia: IRP = 29 mmHg, DL = NA, DCI = NA
FLIP cases: Patient with Achalasia Type I
**FLIP™ Panometry: Contractile patterns**

- **Repetitive, ANTEGRADE contractions (RACs)**
- **Absent contractility**
- **Contractility, No RACs or RRCs**
- **Repetitive, RETROGRADE contractions (RRCs)**

---

**Pressure (mmHg)**

- 150
- 120
- 90
- 60
- 30
- 0

**Diameter (mm)**

- 30
- 25
- 20
- 15
- 10
- 5

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*Esophageal Center at Northwestern*
Relationship: HRM and FLIP™ Panometry

High-Resolution Manometry
N = 145

Abnormal
n = 111 (77%)
- Achalasia: 70 (48%)
- EGJO: 38 (26%)
- Jackhammer: 3 (2%)

Normal
n = 34 (23%)
- IEM: 5 (15%)
- Normal motility: 29 (20%)

Panometry

Abnormal
n = 106 (95%)
- HRM Dx (% HRM dx):
  - Achalasia: 70 (100%)
  - EGJO: 33 (87%)
  - Jackhammer: 3 (100%)

Normal
n = 5 (5%)
- HRM Dx (% HRM dx):
  - EGJO: 5 (13%)

Panometry Dx:
- EGJO-9
- Spasm-8

Abnormal
n = 17 (50%)
- Panometry Dx:
  - EGJO-9
  - Spasm-8

Normal
n = 17 (50%)
- HRM Dx (% HRM dx):
  - IEM: 3 (60%)
  - Normal motility: 14 (48%)

Esophageal Center at Northwestern

**Evaluation of esophageal motility with FLIP panometry**

<table>
<thead>
<tr>
<th>EGJ Distensibility</th>
<th>Distension-induced contractility pattern</th>
<th>Panometry Diagnosis</th>
<th>Esophageal Disease State</th>
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<tbody>
<tr>
<td>Abnormal EGJ-DI and/or Abnormal Max Diameter</td>
<td><strong>RRCs +/- [RACs or other contractility]</strong></td>
<td>Yes</td>
<td><strong>EGJOO with Retrograde Contractile Response</strong></td>
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<td><strong>Other Contractility +/- RACs</strong></td>
<td>No</td>
<td><strong>EGJOO with Absent Contractile Response</strong></td>
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<td>Yes</td>
<td><strong>EGJOO with Diminished/Disordered Contractile Response</strong></td>
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                  - no
                    - Wireless pH Monitoring
                      - yes
                        - Visit 3: Debrief at 1 week post-EGD
                          - May require HRIM PP or Behavior Intervention/NM therapy

Assessed during 1st endoscopy visit