Esophageal Diseases:
Eosinophilic Esophagitis,
Esophageal Motor Disorders and
Functional Disorders of the Esophagus

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Esophageal Symptoms

• Symptoms
  – Transit related - Antegrade and Retrograde
    • Food impaction
    • Regurgitation
    • Aspiration
    • Malnutrition
  – Perception related
    • Discomfort
      – Chest pain / pressure
      – Heartburn
      – Thermal
Esophageal Anatomy
Etiologies of Esophageal Symptoms

Structural abnormality
(dysphagia- usually solid food)

Endoscopy

- Ring
- Stricture
- Eosinophilic esophagitis
- Infectious esophagitis
- Pill or caustic esophagitis
- Dermatologic disorders
- Extrinsic compression
- Primary or secondary tumor
Etiologies of Esophageal Symptoms

Structural abnormality (dysphagia- usually solid food)

Endoscopy- Esophagram

- Ring
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- Infectious esophagitis
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- Extrinsic compression
- Primary or secondary tumor
Eosinophilic Esophagitis

• “Allergic esophagus” – infiltrative eosinophilia
• Increasing incidence vs underrecognized
• Signs/symptoms:
  – Dysphagia, food impaction, abdominal/chest pain, vomiting, regurgitation
• Clinical characteristics
  – Male predominance (70%-80% of cases)
  – Family or personal history of allergy/atopy
    • Asthma, rhinitis, eczema, food allergy

Mechanical properties of the Esophageal Wall

3D geometry of the esophageal body during volume distention using the EndoFLIP

Distensibility of the esophageal body during volume distention using the EndoFLIP

Management of Eosinophilic Esophagitis

- Medical therapy can lead to resolution of symptoms and stricture
- Treatment
  - PPI
  - Steroids (fluticasone, prednisone)
  - Diet (wheat, egg, soy, milk, peanuts, and/or seafood)
  - Allergy evaluation?
  - Dilation

Dilation therapy
Dilation will be performed at the post PPI therapy EGD if the Esophageal diameter (ED) is less than 9mm. Protocol will be to dilate to 13 mm or evidence of first mucosal tear.

**Dilation protocol is standardized to every 2-3 weeks with a goal of 17 mm using savary dilator with guidewire placement via endoscopy- 3 sessions- for first 12 weeks.

- PPI dose- Omeprazole 40 mg per day- will allow patients to be enrolled on their current BID/Double dose regimen
- Steroids- Budesonide dose- 1 mg BID

[ED- Esophageal diameter estimated during endoscopy, RCT- trial comparing steroids plus dilation to dilation alone]
Etiologies of Esophageal Symptoms

Propulsive Disorder
(usually dysphagia for solids & liquids or GERD)
Functional Esophageal Tests

- Peristaltic weakness
- Aperistalsis
- Nutcracker/Jackhammer
- Spasm
- Achalasia
- Functional Obstruction
- GERD

Structural abnormality
(usually solid food only)

- Ring
- Stricture
- Eosinophilic esophagitis
- Infectious esophagitis
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- Dermatologic disorders
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- Functional Obstruction
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Structural abnormality
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- Ring
- Stricture
- Eosinophilic esophagitis
- Infectious esophagitis
- Pill or caustic esophagitis
- Dermatologic disorders
- Cricopharyngeal bar
- Extrinsic compression
- Primary or secondary tumor

Sensory abnormality
(solids & liquids)

- EGD Negative
- Functional
- Nonspecific EMD
- Psychological

Overlap with propulsive disorders and GERD
Functional Imaging of Esophageal Peristalsis

**MANOMETRY**

![Diagram showing manometric port and manometric sleeve with pressure readings in mmHg.](image-url)
Functional Imaging of Esophageal Peristalsis

HIGH-RESOLUTION MANOMETRY
Functional Imaging of Esophageal Peristalsis

**ESOPHAGEAL PRESSURE TOPOGRAPHY**

![Manometric port](image)

![Clouse Plot](image)
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 velocity*
    • *Contractile activity*
  – Defines intra-luminal pressurization patterns
Esophageal Pressure Topography: The Method: Procedure

- Spans from the pharynx to the stomach with sensor separation of no more than a centimeter within and around the sphincters.
  - Greater than 32 pressure sensors
  - Temporal frequency response matched to the zone of the esophagus
- The immediate advantages of HRM are:
  - 1) a simplified procedural set up with improved sphincter localization,
  - 2) elimination of movement artifact
  - 3) simplified data interpretation and
  - 4) ability to perform more sophisticated analysis of esophageal function.
Pressure Topography of Esophageal Motility

The Chicago Classification

IRP ≥ upper limit of normal AND
absent peristalsis

No

Yes

IRP ≥ upper limit of normal AND
some instances of intact or weak
peristalsis

Yes

IRP ≥ upper limit of normal AND
absent peristalsis
OR reduced distal latency
OR DCI > 8,000 mmHg-cm-s

Yes

IRP is normal AND
absent peristalsis

No

IRP is normal AND
Minor Peristaltic Abnormalities
*outside of normative range/clinical
significance less clear

No

Normal

Achalasia
• Subtypes I,II,III

EGJ Outflow Obstruction
• Achalasia variant versus
mechanical obstruction

Absent Peristalsis

Yes

Diffuse esophageal spasm (DES)
• ≥ 20% of swallows with reduced DL(<4.5s)
Jackhammer esophagus
• ≥ 20% of swallows with DCI > 8,000 mmHg-cm-s and normal DL

Yes

Rapid contraction
• ≥ 20% of swallows with rapid CFV (>9 cm/s) and normal DL

Hypertensive Peristalsis
• ≥ 20% of swallows with DCI > 5,000 mmHg-s-cm and normal DL

Weak Peristalsis
• ≥ 30% of swallows with small (2-5 cm) breaks in the 20-mmHg IBC
• ≥ 20% of swallows with large (>5 cm) breaks in the 20-mmHg IBC

Frequent Failed Peristalsis
• ≥ 30% of absent swallows

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some instances of intact or weak peristalsis

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✓ EGJ Outflow Obstruction
• Achalasia variant versus mechanical obstruction
Clinical Evolution of Achalasia

Assessing clinically relevant phenotypes

Early
Type II or III

Chronic
Type II/III--I

Late
Type I
High-Resolution Manometry: Achalasia subtypes

- **Type I**: IRP = 22.3 mmHg
- **Type II**: IRP = 24.2 mmHg
- **Type III**: IRP = 29.8 mmHg

5 seconds

EGJ

- **Gastroesophageal reflux disease (GERD)**
- **Diverticulum**

EGJ

- **Achalasia**
- **Contraction**
High-Resolution Manometry: EGJ Outflow Obstruction

A: EGJOO: achalasia phenotype

- Locus of diverticulum above EGJ
  - IRP = 22.3 mmHg

B: EGJOO: Mechanical

- Normal peristalsis
- Compartmentalized pressurization
  - IRP = 27.2 mmHg

- Barium tablet localized 12 mm restriction

- Large diverticulum 4 cm above EGJ
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>
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<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>96*</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>29 (29.3)</td>
<td>29*</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>95.3</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>23 (9.4)</td>
<td>69.3</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>90</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>85.7 - 81</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>114 (64.7)</td>
<td>100 - 95</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>18 (10.2)</td>
<td>40 - 86</td>
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</tbody>
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LHM, laparoscopic heller myotomy; PD, pneumatic dilatation.
Utilizing HRM/EPT in the Management of Achalasia

Symptoms of dysphagia ± chest pain and bland regurgitation

Upper Endoscopy

- Obstructive process: ring, stricture, etc.
- Normal
- Esophageal dilatation
- EGJ resistance
- Retained food
- Diverticulum

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

EPT Diagnosis

EGJ Outflow Obstruction
- EGD ± 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
Pressure Topography of Esophageal Motility

The Chicago classification

- IRP is normal **AND** absent peristalsis
- OR reduced distal latency
- OR DCI > 8,000 mmHg-cm-s

- Absent Peristalsis
- Diffuse esophageal spasm (DES)
  - ≥ 20% of swallows with reduced DL(<4.5s)
- Jackhammer esophagus
  - ≥ 20% of swallows with DCI > 8,000 mmHg-s-cm and normal DL
A) Normal: No breaks/ NL DCI

- UES
- EGJ relaxation
- DCI = 2,761 mmHg-s-cm

B) Jackhammer: No breaks/ Abnormal DCI

- DCI = 20,452 mmHg-s-cm

C) Absent Peristalsis

- DCI = 7 mmHg-s-cm

D) Absent/Failed Peristalsis

- DCI = 32 mmHg-s-cm

E) Weak Peristalsis- IEM

- DCI = 325 mmHg-s-cm

F) Weak Peristalsis- TZ Defect

- DCI = 4121 mmHg-s-cm
Conclusion: Hypertensive Contractility

- 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
  - Many patients may respond to treating visceral sensitivity
A: Latency described with conventional manometry

B: Latency measured with EPT
Normal swallow

C: DES: Rapid Premature Contraction

DL = 4.4 s
CFV = 6 cm/s

D: DES: Premature Contraction

CFV = 6 cm/s
DL = 4.4 s

E: Rapid Contraction with Normal latency

CFV = 15 cm/s
DL = 7.0 s

CFV
DL
CVP

mmHg

150
100
50
30
10
0

Time (s)

Length along the esophagus (cm)

Axial position (cm)

Time (s)
Conclusions: Spasm

- There is a difference between rapid contractions and spastic contractions.
  - Does the contraction occur too early [latency]?
  - Should consider whether contraction is altered by deglutitve inhibition.
  - A trial of smooth muscle relaxants is warranted in patients with true spasm and treatment similar to achalasia may be warranted.
Pressure Topography of Esophageal Motility

The Chicago classification

- **Rapid contraction**
  - ≥ 20% of swallows with rapid CFV (>9 cm/s) and normal DL

- **Hypertensive Peristalsis**
  - ≥ 20% of swallows with DCI > 5,000 mmHg-s-cm and normal DL

- **Weak Peristalsis**
  - ≥ 30% of swallows with small (2-5 cm) breaks in the 20-mmHg IBC
  - ≥ 20% of swallows with large (>5 cm) breaks in the 20-mmHg IBC

- **Frequent Failed Peristalsis**
  - ≥ 30% of absent swallows

IRP is normal AND Minor Peristaltic Abnormalities *outside of normative range/clinical significance less clear*
Peristaltic Defect

Gaps in the peristaltic wavefront

\( X = 7.1 \text{ cm} \)

\( T = 3.3 \text{ s} \)
Pill Esophagitis with Chest Pain
Transition Zone Defect
GERD: Pitfalls

• Patients may have a good response to PPI and not have GERD.
• Patients may have a positive pH study and not have GERD.
• Patients may have a good symptom correlation on pH-impedance testing and not have GERD.
• Be careful with belching, regurgitation and nausea/vomiting.
tLESR

Liquid reflux

LES relaxation and crural inhibition
• 23 year old female with sore throat, acid taste and regurgitation with meals.
  – She has a good response to PPI in terms of the acid taste but still has regurgitation
  – EGD was c/w a gaping EGJ and a small hiatus hernia.
  – pH-impedance was c/w normal acid exposure and a symptom index of 90% fro regurgitation / SAP 100%.
Rumination # 1 HRM only

Increased IGP pressure

Liquid reflux
Rumination #2 HRIM

Liquid reflux

EGJ relaxed

Increased IGP pressure
Rumination #2 HRIM

- Increased IGP pressure
- Liquid reflux
- Regurgitation with swallowing
GERD: Pitfalls

• 43 year old female with chest pain, belching and regurgitation with meals.
  – She has a good response to PPI in terms of the heartburn but continues to have severe debilitating belching
  – EGD was c/w a normal EGJ and a small hiatus hernia.
  – pH-impedance was c/w normal acid exposure and a positive symptom index of 60% for belching/regurgitation.
GERD: Pitfalls
Supragastric Belching

Air reflux

No LES relaxation
Model for Symptom Generation in UGI Disorders

Physiologic Event
Gastroesophageal Reflux
Swallowing Bolus
Post-prandial accommodation

Normal Function
Functional heartburn/chest pain
Functional Dysphagia/Globus
Functional Dyspepsia
Functional Nausea/Vomiting

Abnormal Function
Gastroesophageal Reflux Disease
EGJ Obstruction/Dysmotility
Gastroparesis/GOO
Impaired accommodation

Visceral Sensitivity
Modulates perception of event

Hypoalgesia Normal Allodynia Hyperalgesia

Hypervigilance
Selective attention to sensations
Fear of symptoms/consequences

Psychological
Obsessive/compulsion to monitor symptoms
Anxiety reinforces importance of monitoring

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Model for Symptom Generation in UGI Disorders

Abnormal Motor Function

Case 1: Functional Heartburn

Case 2: Visceral Hypersensitivity
Functional Esophageal Diseases

Rome Classification

- Functional heartburn
  - Burning retrosternal discomfort or pain
  - Absence of evidence that gastroesophageal reflux is the cause of the symptom
  - Absence of histopathology-based esophageal motility disorders
  - Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Galmiche JP et al. Gastroenterology
2006;130:1459
Patient with retrosternal discomfort (heartburn/chest pain) or regurgitation

- Alarm features?
  - yes → EGD ± biopsy
  - no → PPI Trial

- PPI Trial
  - yes → Heartburn resolved?
    - yes → Reflux disease: titrate PPI therapy
    - no → PPI Trial
  - no → Heartburn resolved?
    - yes → Reflux disease: titrate PPI therapy
    - no → pH or impedance-pH monitoring (off of PPIs)

- pH or impedance-pH monitoring (off of PPIs)
  - yes → Esophageal manometry
  - no → Esophageal manometry

- Esophageal manometry
  - yes → Meets esophageal motor disorder criteria?
    - yes → Achalasia DES
    - no → yes
  - no → yes

- Meets esophageal motor disorder criteria?
  - yes → Achalasia DES
  - no → Positive symptom association?
    - yes → NERD
    - no → yes

- Positive symptom association?
  - yes → NERD
  - no → yes

- NERD

- >5% esophageal acid exposure?
  - yes → yes
  - no → no

- Esophagitis EoE
  - yes → yes
  - no → no
Medical Management

NOT FDA APPROVED

• Anti-depressants
  – amitriptyline, nortriptyline, desipramine
    • 10 to 25 mg at bedtime with escalation of 10 to 25 mg
      increments to a target of 50-75 mg
  – Trazadone
    • 25mg QHS up to 100 mgHg
  – SSRIs

• 5HT agonists-antagonists- not currently available
Gut-directed Hypnotherapy

Are you getting sleepy?

- Deep physical relaxation and deep mental concentration
- Alters focus of attention, changes meaning about sensations arising from the gut and encourages body to restore itself to a healthier state
- Shown to produce cognitive change and improve pain tolerance
- Modifies physiological arousal and hypersensitivity over long-term
- Initially performed in a doctors office but can eventually be self-guided
- The most scientifically supported non-drug treatment for Functional GI disorders
Globus: Definition

• **Globus Sensation**
  • Persistent or intermittent, nonpainful sensation of a lump or foreign body in the throat
  • Occurrence of the sensation between meals
  • Absence of dysphagia or odynophagia

• **Rome III: Functional Esophageal Disorders**
  • *Absence of evidence that gastroesophageal reflux is the cause of the symptom*
  • *Absence of histopathology-based esophageal motility disorders*
  • *Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.*
Patient with sensation of a lump in the throat

History/Physical Exam

Laryngoscopy

Abnormal

Treat

Normal/LPR

Low threshold for treating GERD

No Response

Response

Endoscopy

Negative

Abnormal

Dx: GERD

Titrate dose

Re-evaluate at 1 year

Dx: Globus

Negative

1-HRM

2-pH study off medication

Dx: Achalasia

-DES

-Absent Peristalsis

Optimize TX

-No response

pH-MII on PPI

Negative

Dx: Refractory GERD

Lee et al. WJG 2012;18: 2462
Kahrilas PJ & Smout AJPM. Am J Gastroenterol 2010;105:747
Approach to Patients with Esophageal Diseases

- **Key Clinical Take Home Points:**
  - Esophageal symptoms can have a number of overlapping etiologies and the interaction between organic and functional influence should not be ignored.
  - Most of these disorders can be managed by a careful systematic evaluation that focuses on ruling out the most dangerous causes first and then focusing on the most likely cause.
  - Diagnose and treat in parallel.