New Approaches in Achalasia and Gastroparesis

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Financial Disclosures

• I have nothing to disclose
Achalasia and Gastroparesis

• Heterogeneous Disorders

• Diagnostic Pitfalls

• Treatments
  - Poor medical therapies
  - Movement toward definitive therapies
Type I Achalasia

- Aperistalsis
- Non-Relaxing LES

- No single swallow with peristaltic activity
- Median 4s IRP > 10 mmHg** for 10 swallows
Type II Achalasia

- PEP seen in ≥ 20% of swallows
- No swallows with normal peristalsis
- Median 4s IRP for 10 swallows > 15 mmHg

Pan-Esophageal Pressurization

Non-Relaxing LES
Type III Achalasia

- No normal peristalsis
- Spastic contractions in ≥ 20% of swallows
- Median 4s IRP > 15 for 10 swallows

Incomplete LES Relaxation

DL < 4.5 Sec
Functional EGJ Outlet Obstruction (EGJOO)

40% resolve dysphagia spontaneously

6% evolve to achalasia over 10 months

2) Hoeij et al. Neurogastroenterol Motil 2015
Achalasia Spectrum

Type I Achalasia

Type II Achalasia

Sodikoff et al. Neurogastroenterol Motil 2016
# Achalasia Subtypes: Response to Therapy

<table>
<thead>
<tr>
<th>Achalasia Subtype</th>
<th>Type I (n=16)</th>
<th>Type 2 (n=46)</th>
<th>Type 3 (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success with Botox</td>
<td>0%</td>
<td>86%</td>
<td>22%</td>
</tr>
<tr>
<td>Success with Dilation</td>
<td>38%</td>
<td>73%</td>
<td>0%</td>
</tr>
<tr>
<td>Success with myotomy</td>
<td>67%</td>
<td>100%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Pandolfino et al. Gastroenterology 2008
Diagnosis of Achalasia

- High Resolution Esophageal Manometry remains gold standard
- Referral for EM is delayed by mean 4.7 years
- 15% consulted ≥ 5 physicians before diagnosis

HRM Superior to Standard Manometry

Prevalence of Motility Disorders Using Standard Manometry (SM) vs High Resolution Manometry (HRM)

<table>
<thead>
<tr>
<th>Disorder</th>
<th>SM</th>
<th>HRM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Motility Disorder</td>
<td>52%</td>
<td></td>
</tr>
<tr>
<td>Achalasia</td>
<td>28%</td>
<td>26%</td>
</tr>
<tr>
<td>EGJOO</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Non-Specific Hypermotility Disorders</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>Hypomotility Failure</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>UES Disorders</td>
<td>7%</td>
<td>7%</td>
</tr>
</tbody>
</table>

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Roman et al. Am J Gastroenterol 2016
Timed Barium Esophagram (TBE)

- Column Ht > 2 cm at 5 min
  - 85% Sens, 86% Spec for Achalasia

- Differentiate Achalasia from EGJOO

- Also provides Objective Measurement of Emptying after intervention

EGJ Distensibility in Achalasia

Normal Controls

**EGJ Distensibility**

- **6.3 ± 0.7 mm²/mmHg**

Untreated Achalasia

**EGJ Distensibility**

- **0.7 ± 0.9 mm²/mmHg**

Rohof et al. Gastroenterology 2012
Achalasia with Normally Relaxing EGJ?

- Eckhardt Score ≥ 7
- Low or Normal 4s IRP
- EGJ-DI 0.8
- Achalasia Treatments improved median Eckardt to 2

Ponds et al. Neurogastroenterol and Motil 2016
Achalasia Treatments

Temporizing

- **Medical Therapies**
  - Nitrates, Ca-Blockers, Peppermint Oil
  - Ineffective

- **Endoscopic**
  - Botox Injection
  - Pneumatic Dilation

Definitive

- **Lap Heller Myotomy**
- **POEM**
POEM Outcomes

Remission Rates After POEM

Success Rate (Eckhardt < 3)

Remission Rates After POEM

3 months 6 months 12 months

LHM vs POEM

p=0.001

% With Symptom Score < 2

Dysphagia Solids 71%
Dysphagia Liquids 92%
Heartburn 84%

POEM After Failed LHM

- 80% of pts improved w/ POEM
- Compare to 57% rate in pts treated with PD after LHM

POEM Failure

- 9.8% Failure Rate
- 63% responded to repeat POEM
- 45% to LHM
- 20% to PD

Van Hoeij et al. Gastrointest Endosc 2018
Gastroparesis Subgroups

**Diabetic (29%)**
- Women
- > 5 years of Disease
- 5% and 1% incidence in DM1 and DM2

**Post-Surgical (13%)**
- Vagal Nerve Injury
- Fundoplication
- Roux-En-Y GastroJ

**Idiopathic (36%)**
- Women
- 86% overlap with Functional Dyspepsia
- Post-Viral

Histology and Etiology of GP

• **Diabetic GP**
  - Fewer ganglion Cells
  - Less dense ganglia than Idiopathic GP

• **Response to GES Therapy**
  - Inversely related to ganglia density

Heckert et al. Neurogastroenterol and Motil 2017
Diagnosis of Gastroparesis

- No obstruction
- Delayed Gastic Emptying
  - Gastric Scintigraphy
  - WMC
  - Spirulina Breath Test
Common Mistakes with GES

• **Not done long enough**
  - 4 hr study
  - ↑ diagnostic yield by 25%
  - Correct measure is % retention

• **Fails to use correct test meal**
  - Eggbeaters with jam and toast

Wireless Motility Capsule

pH >4 & at least 3 points above baseline by 4 hours

83% Sensitivity and 83% Specificity
Gastroparesis Treatments

**Medical**
- **Ineffective**
  - TCA's
  - Botox
- **Problematic**
  - Metoclopramide
  - Domperidone
  - Erythromycin
- **Symptom Alleviation**
  - Ondasetron

**Definitive**
- Gastric Electrical Stimulation
- Endoscopic Pyloromyotomy?
TCA’s for Gastroparesis

Parkman et al. JAMA 2010
Pyloric Botox Injection

- **Open Label Studies**
  - Benefit in symptoms and GE

- **(2) RCT’s**
  - Improvement no better than placebo

The Problem Drugs

- **Metoclopramide**
  - 30-50% sx improvement
  - Tardive Dyskinesia
  - Long QT
  - Women, non-diabetics more likely to have SE

- **Domperidone**
  - 40-50% sx improvement
  - Long QT

- **Erythromycin**
  - Improves sx’s and GET
  - Tachyphylaxis
  - Long QT
  - IV > Oral Effectiveness

- **Azithromycin**
  - Fewer GI side effects
  - Long QT

Ghrelin Agonists

- **Stimulates hunger**
  - ↑ proximal gastric tone
  
  - Stimulates Phase III MMC’s
    
  - ↑ Gastric Emptying
Relamorelin

Lembo et al. Gastroenterology 2016
Gastric Electrical Stimulation (GES)

- High Frequency Low Energy
- Does not alter rate of gastric emptying
- Implantated along greater curve
- Humanitarian Use Protocol
GES in Gastroparesis

GES in Patients with DG

GES in Patients with IG

Main Predictors of Response:
1) Nausea
2) Absence of Narcotic Use
3) Diabetic > Idiopathic

1) McCallum Clin Gastroenterol and Hepatol 2010
2) McCallum Neurogastroenterol and Motil 2013
3) Maranki Dig Dis Sci 2008
Pyloroplasty: A Definitive Therapy?

- Targets pylorospasm
- Same principles as POEM

Mekaroonkamol Clin Gastroenterol and Hepatol 2019
G-POEM in Mixed Gastroparesis

Response to G-POEM at 6 months

Predictors of Failure:
1) Female Gender
2) Diabetic Gastroparesis

1) Khashab et al. Gastrointest Endosc 2017 2) Gonzalez et al. Aliment Pharmacol and Ther 2017
Conclusions: Heterogenous Disorders

• Achalasia
  - Types I-III and EGJOO
  - May represent spectrums of same disease

• Gastropareasis
  - IG, DG, and PSG
  - May represents separate disease states
Pitfalls in Diagnosis

• Achalasia
  - Delays in Manometric Diagnosis
  - EGJOO and Achalasia with normal manometric EGJ Relaxation

• Gastroparesis
  - Incorrect GE Study Protocols
Less than Optimal Medical Therapies

- **Achalasia**
  - Ca channel blockers, nitrates

- **Gastroparesis**
  - Botox
  - Drugs with side effects
Definitive Treatments

• **Achalasia**
  - POEM and LHM

• **Gastroparesis**
  - Gastric Electrical Stimulation
  - Relamorelin?
  - G-POEM?