

# New Approaches in Achalasia and Gastroparesis

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# Financial Disclosures

- I have nothing to disclose

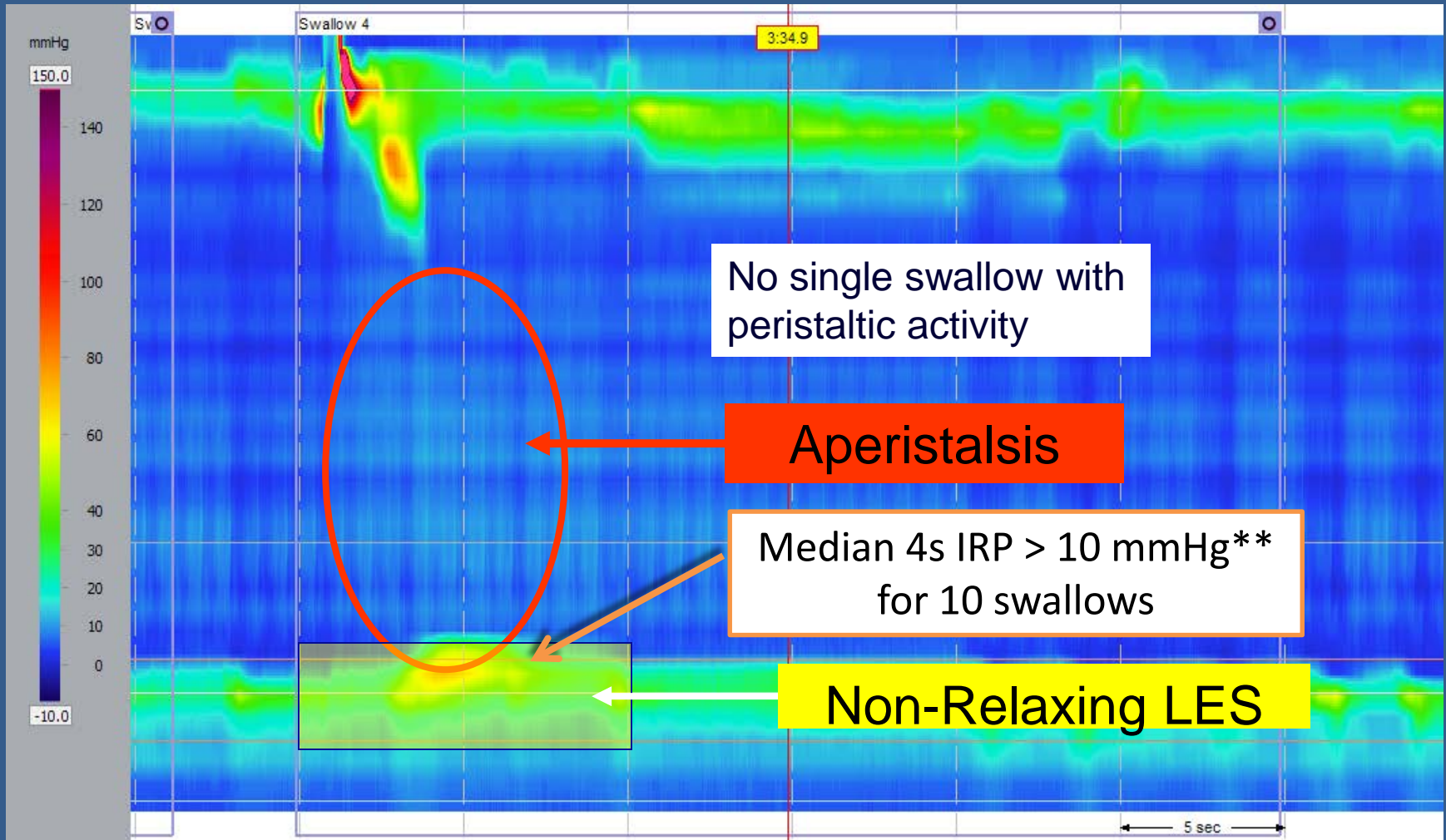


# Achalasia and Gastroparesis

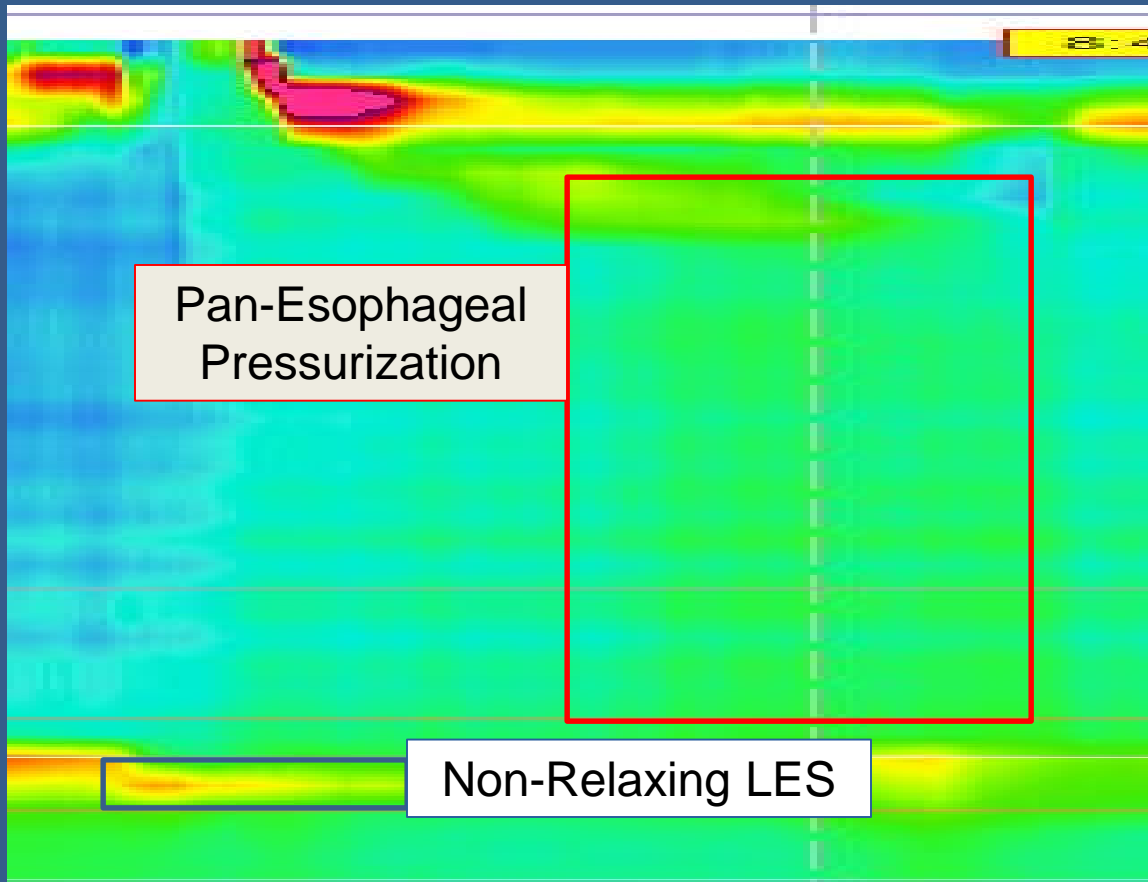
- Heterogeneous Disorders
- Diagnostic Pitfalls
- Treatments
  - Poor medical therapies
  - Movement toward definitive therapies



# Type I Achalasia



# Type II Achalasia



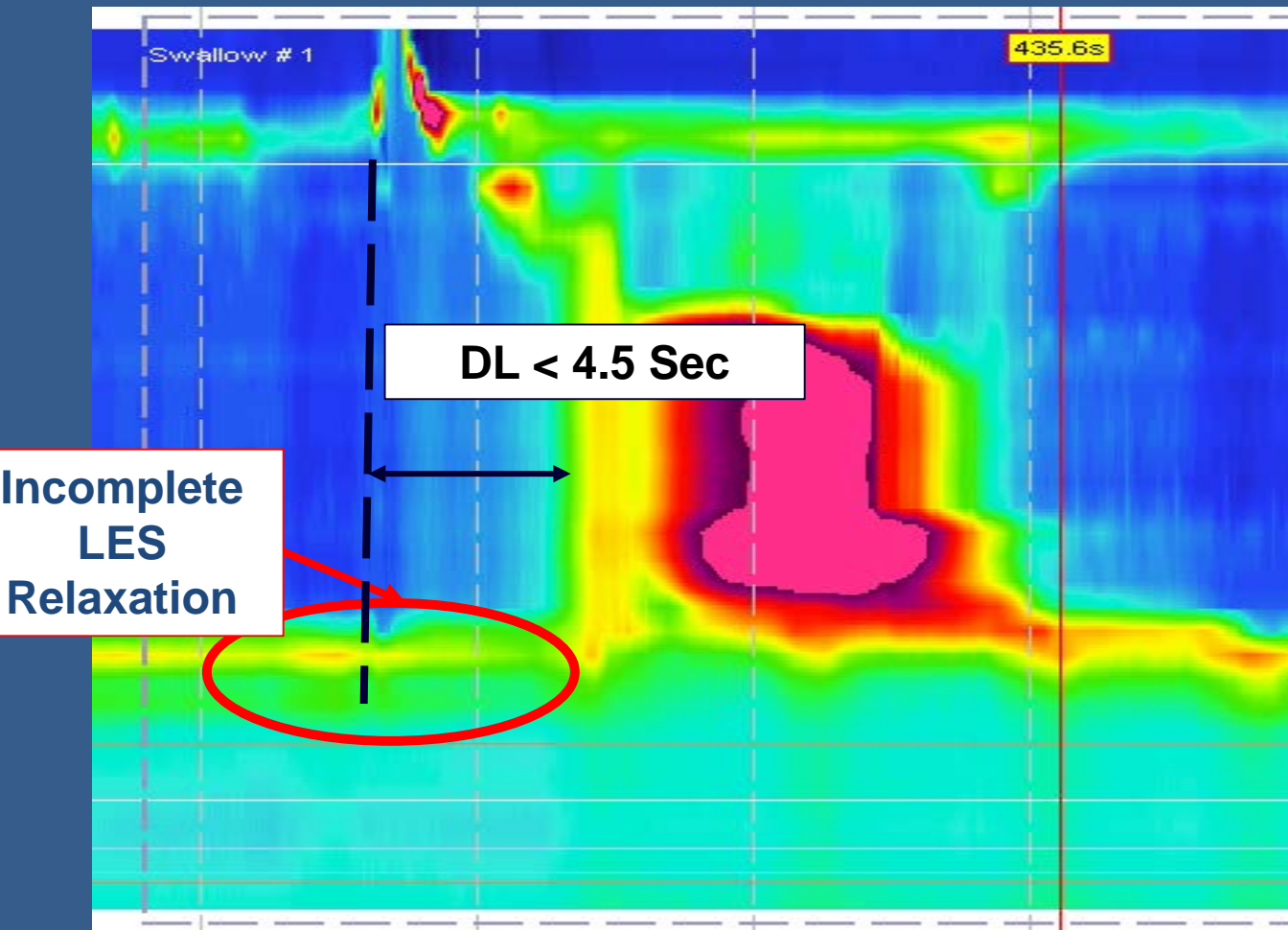
PEP seen in  $\geq 20\%$  of swallows

No swallows with normal peristalsis

Median 4s IRP for 10 swallows  $> 15$  mmHg



# Type III Achalasia



No normal peristalsis

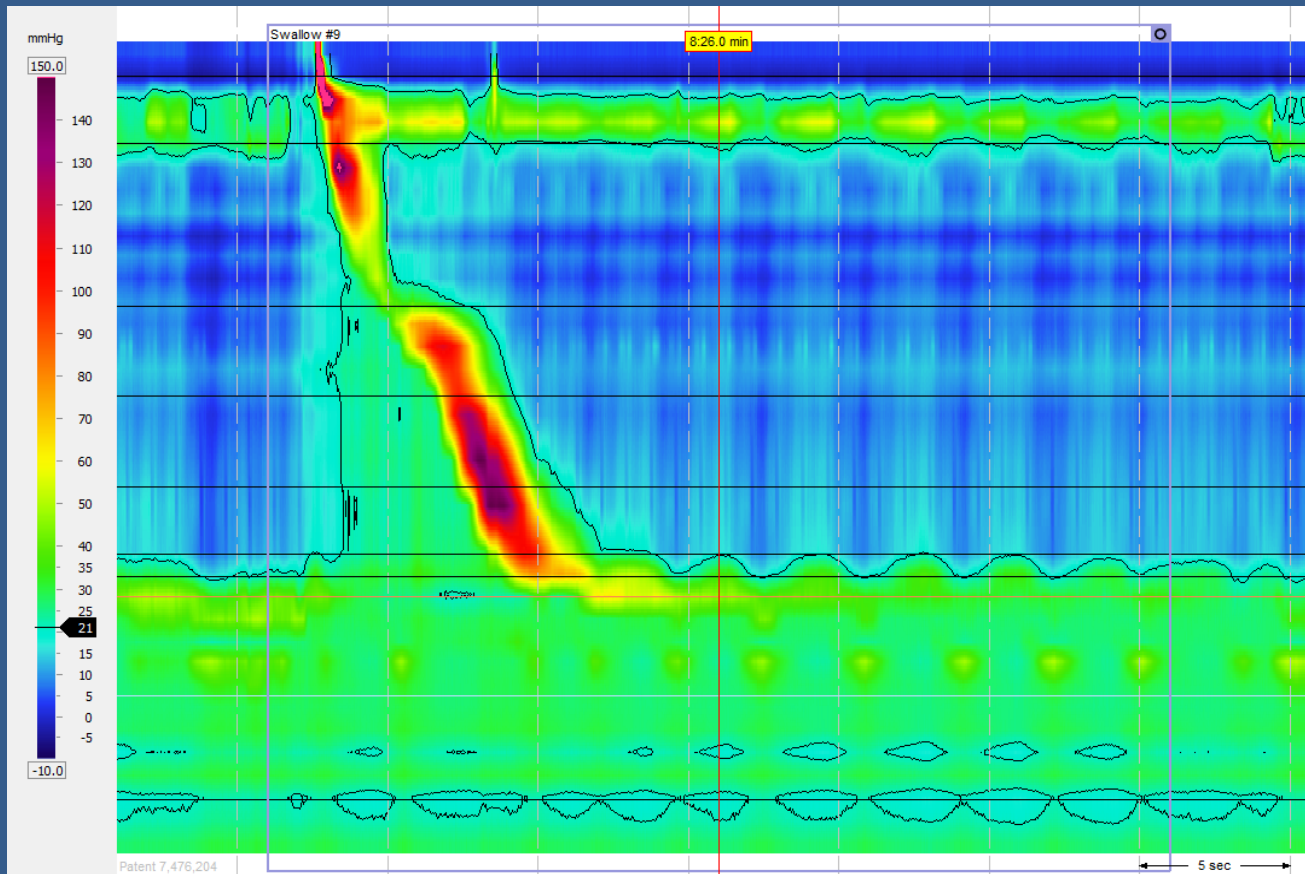
Spastic contractions in  $\geq 20\%$  of swallows

Median 4s  
IRP > 15 for 10 swallows





# Functional EGJ Outlet Obstruction (EGJOO)



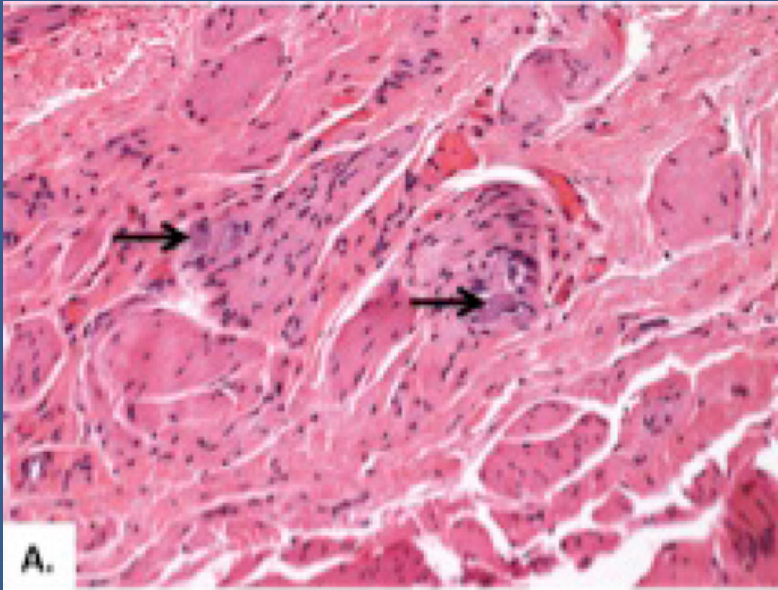
40% resolve  
dysphagia  
spontaneously

6% evolve to  
achalasia over  
10 months

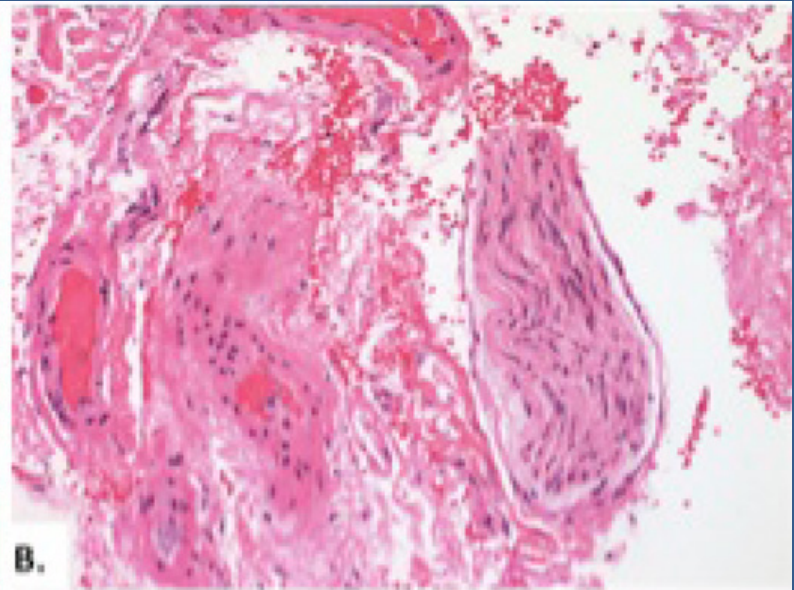
1) Perez-Fernandez et al. Neurogastroenterol Motil 2016 2) Hoeij et al. Neurogastroenterol Motil 2015



# Achalasia Spectrum



Type I Achalasia



Type II Achalasia

Sodikoff et al. Neurogastroenterol Motil 2016





# Achalasia Subtypes: Response to Therapy

Achalasia Subtype	Type 1 (n=16)	Type 2 (n=46)	Type 3 (n=21)
Success with Botox	0%	86%	22%
Success with Dilation	38%	73%	0%
Success with myotomy	67%	100%	0%

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  $\geq 5$  physicians before diagnosis

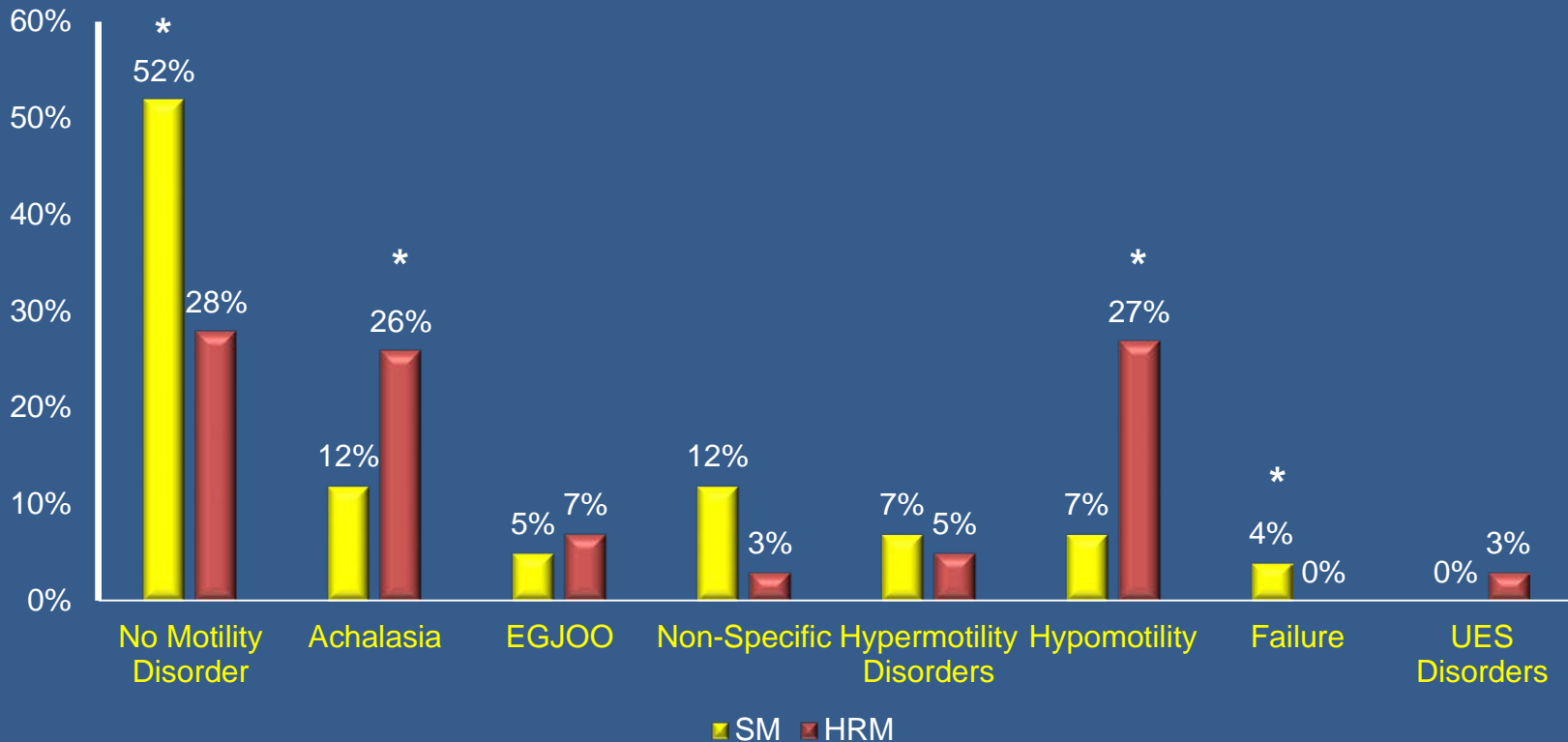


Eckardt et al. Dig Dis Sci 1997



# HRM Superior to Standard Manometry

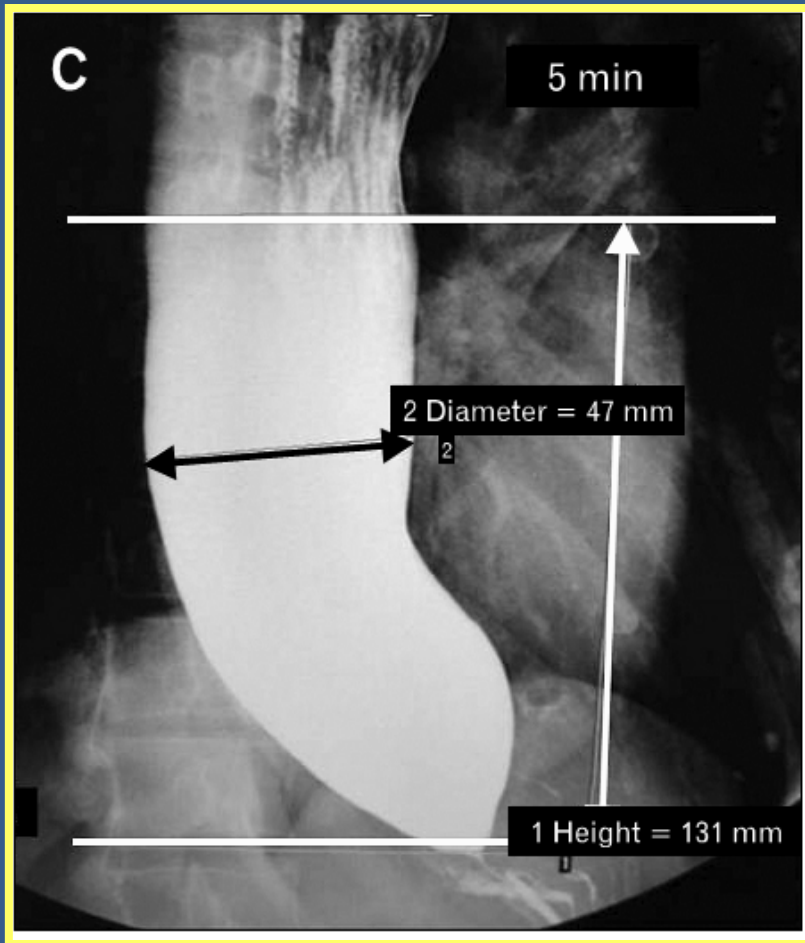
Prevalence of Motility Disorders Using Standard Manometry (SM) vs High Resolution Manometry (HRM)



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

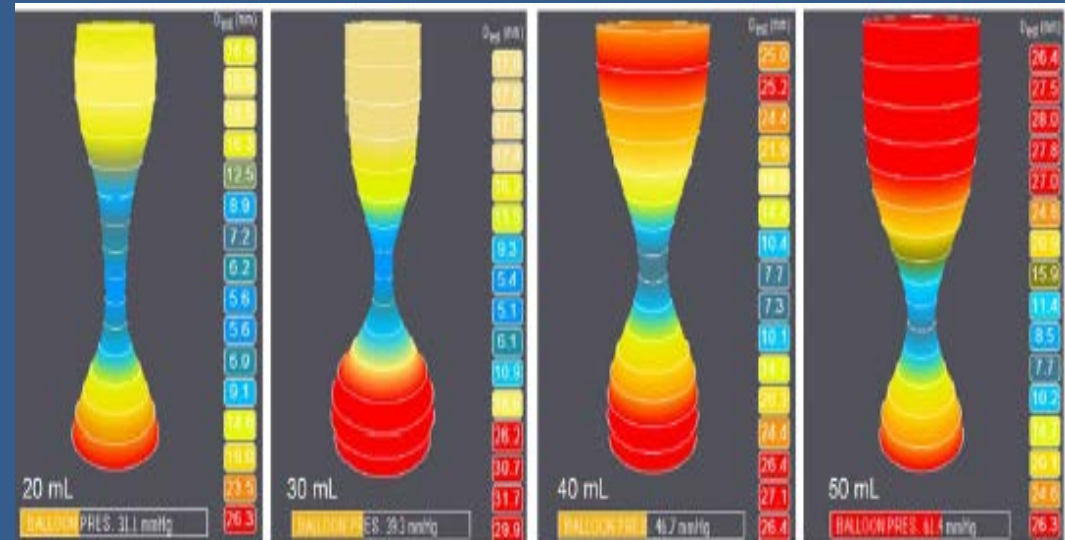
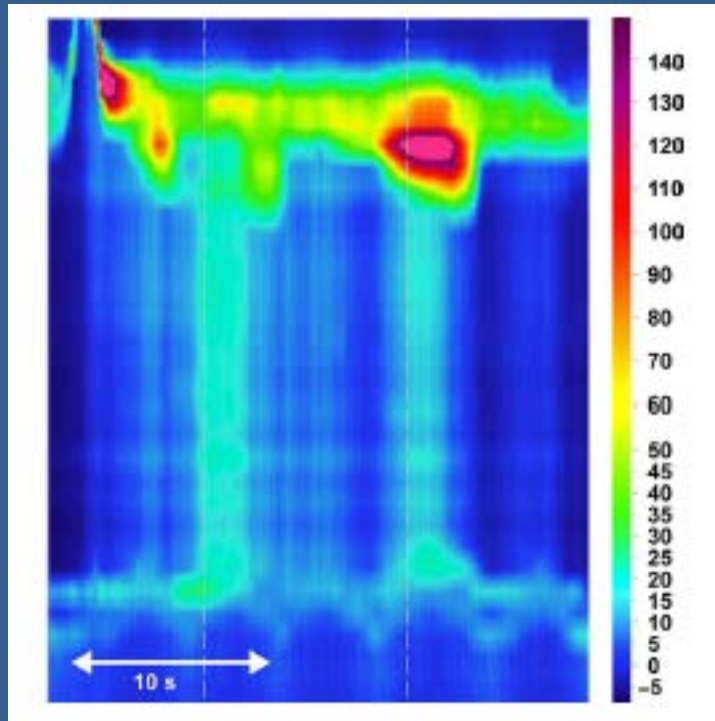
1) Neyaz J Neurogastroenterol Motil 2013 2) Vaezi Am J Gastroenterol 1999 3) Blonski Am J Gastroenterol 2018







# Achalasia with Normally Relaxing EGJ?



- Eckhardt Score  $\geq 7$
- 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

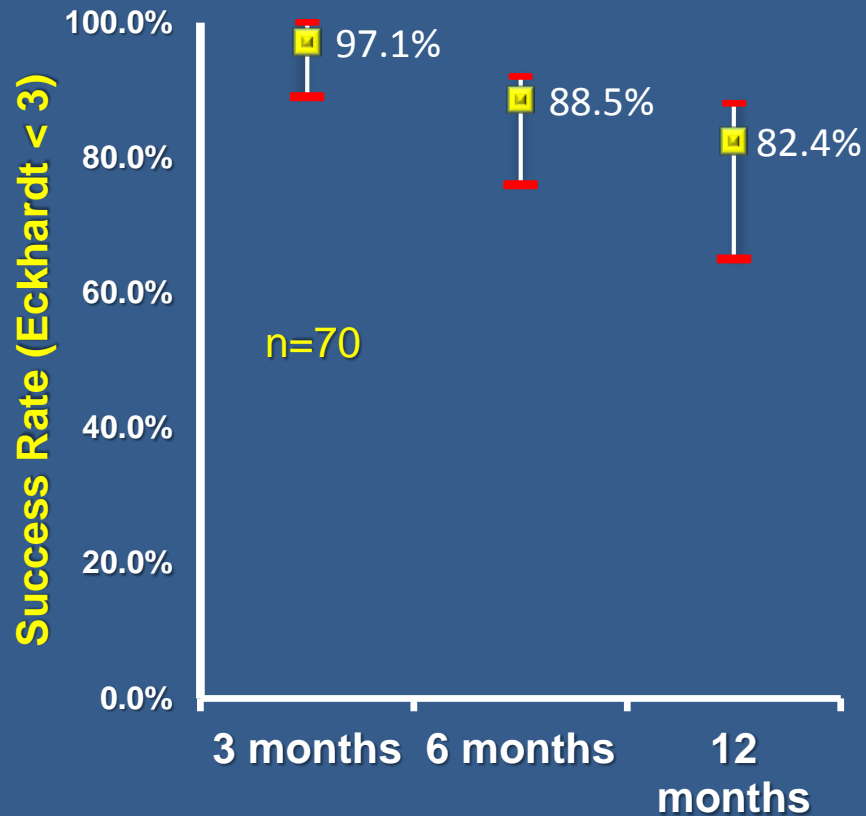
## Definitive

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

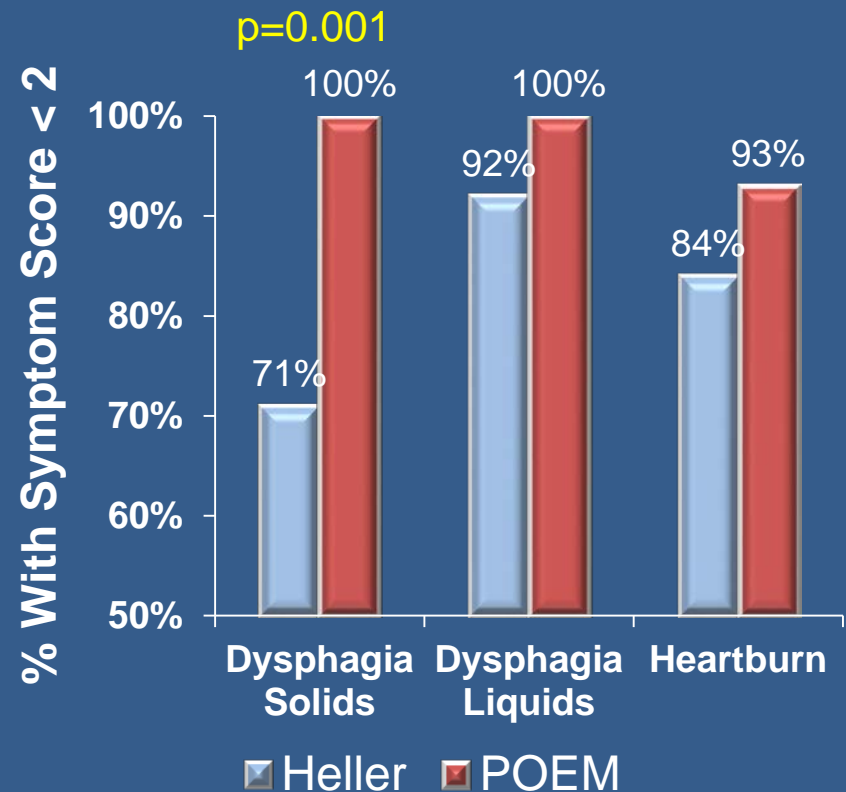


# POEM Outcomes

## Remission Rates After POEM



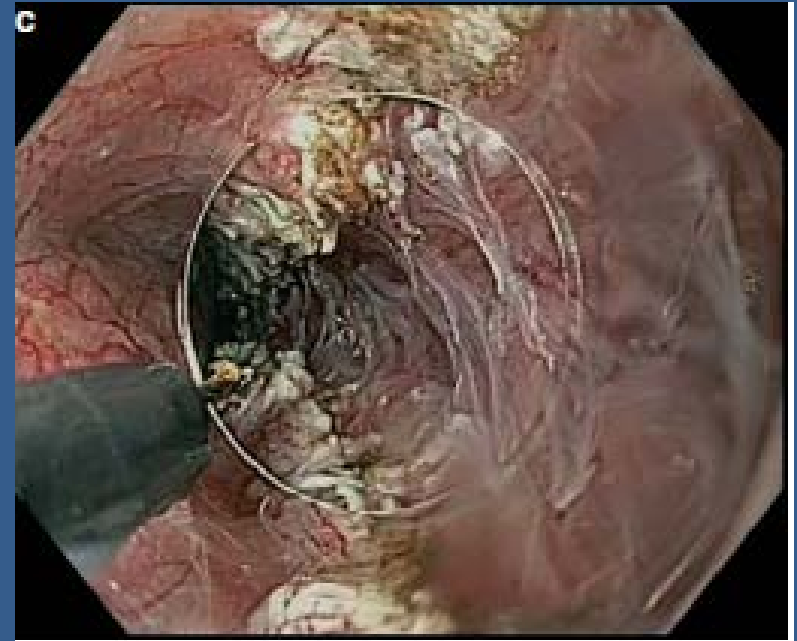
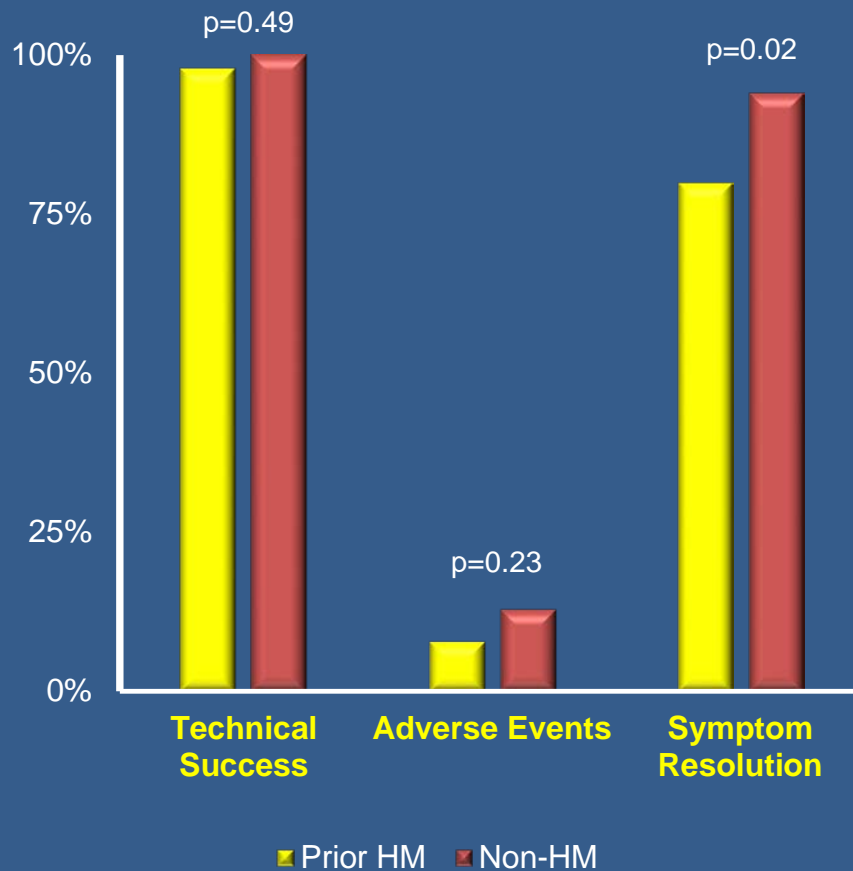
## LHM vs POEM



1) Von Renteln et al. Gastroenterology 2013 2) Bhayani et al. Ann Surg 2013



# POEM After Failed LHM



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

1) Ngamruengphong et al. Clin Gastroenterol and Hepatol 2017 2) Saleh et al. Neurogastroenterol and Motil 2016



# 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

1) Camilleri et al. Am J Gastroenterol 2013 2) Parkman et al. Gastroenterology 2011



# Histology and Etiology of GP

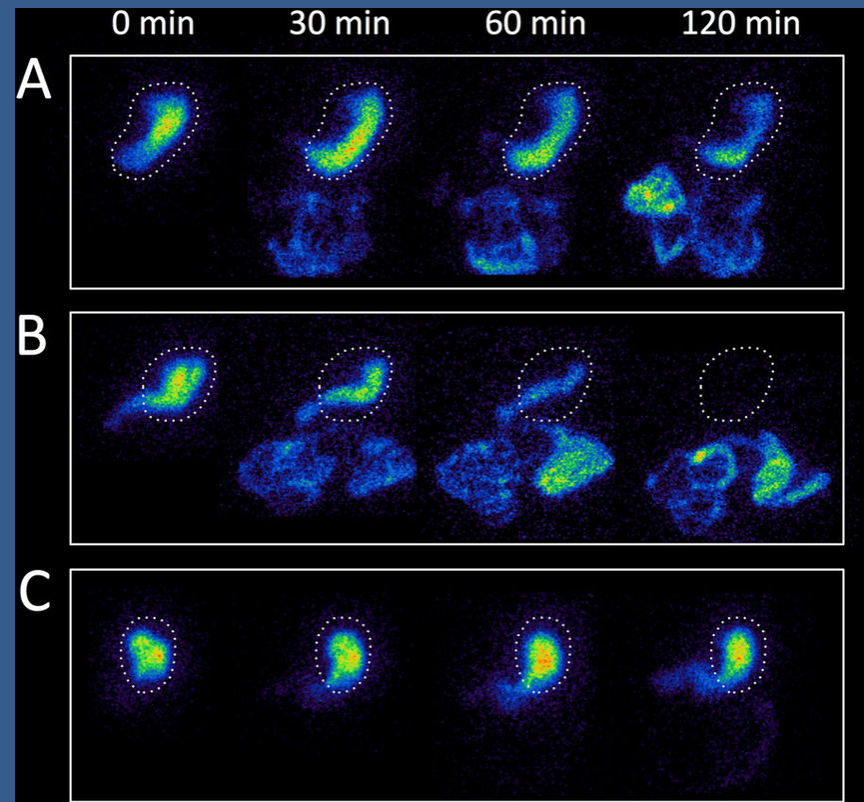
- **Diabetic GP**
  - Fewer ganglion Cells
  - Less dense ganglia than Idiopathic GP
- **Response to GES Therapy**
  - Inversely related to ganglia density

Heckert et al. Neurogastroenterol and Motil 2017



# Diagnosis of Gastroparesis

- **No obstruction**
- **Delayed Gastric Emptying**
  - Gastric Scintigraphy
  - WMC
  - Spirulina Breath Test



# Common Mistakes with GES

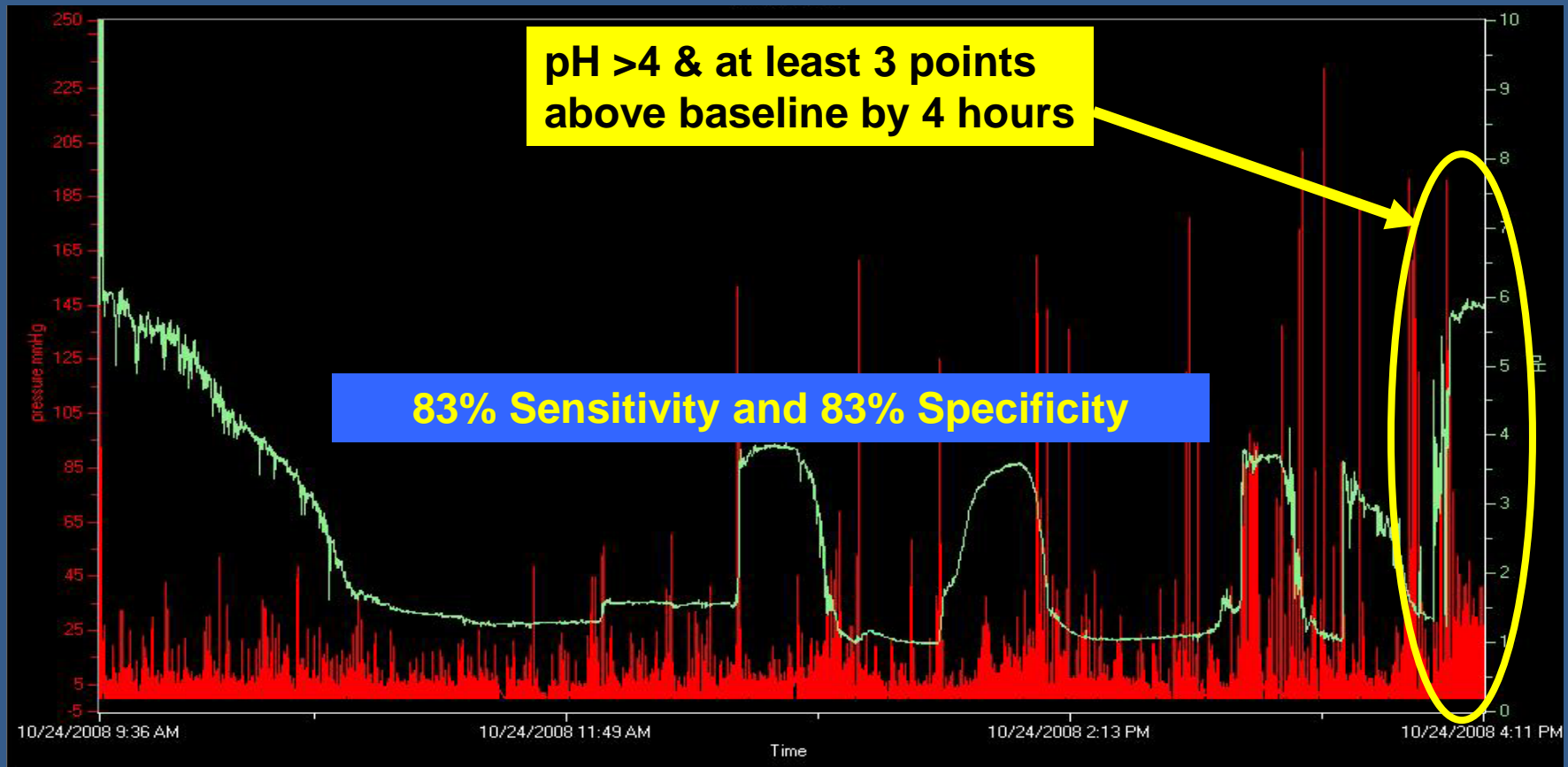
- **Not done long enough**
  - 4 hr study
  - ↑ diagnostic yield by 25%
  - Correct measure is % retention
- **Fails to use correct test meal**
  - Eggbeaters with jam and toast



1) Guo et al. Dig Dis Sci 2001 2) Abell et al. Am J Gastroenterol 2008



# Wireless Motility Capsule





# Gastroparesis Treatments

## Medical

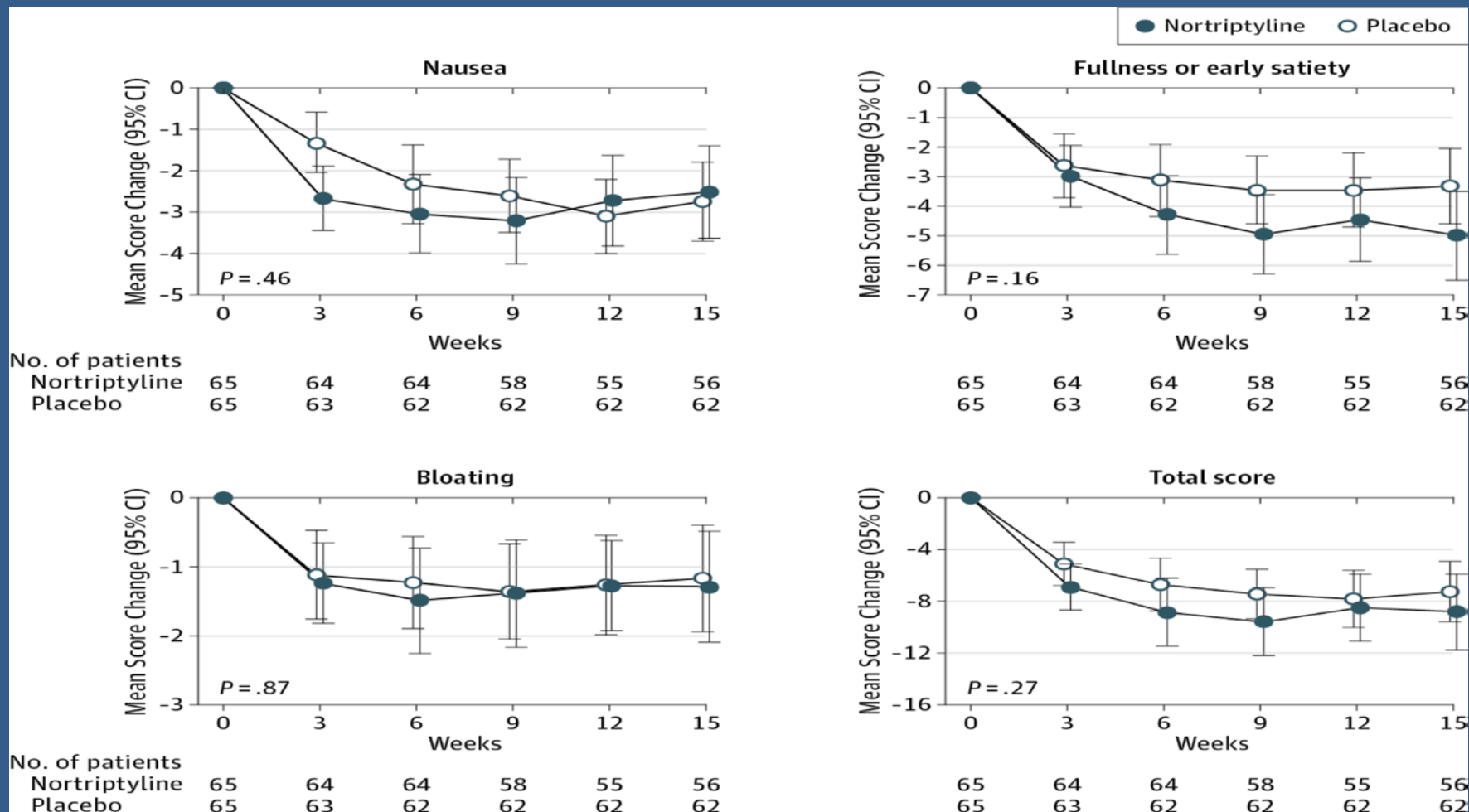
- **Ineffective**
  - TCA's
  - Botox
- **Problematic**
  - Metoclopramide
  - Domperidone
  - Erythromycin
- **Symptom Alleviation**
  - Ondasetron

## Definitive

- **Gastric Electrical Stimulation**
- **Endoscopic Pyloromyotomy?**



# TCA's for Gastroparesis

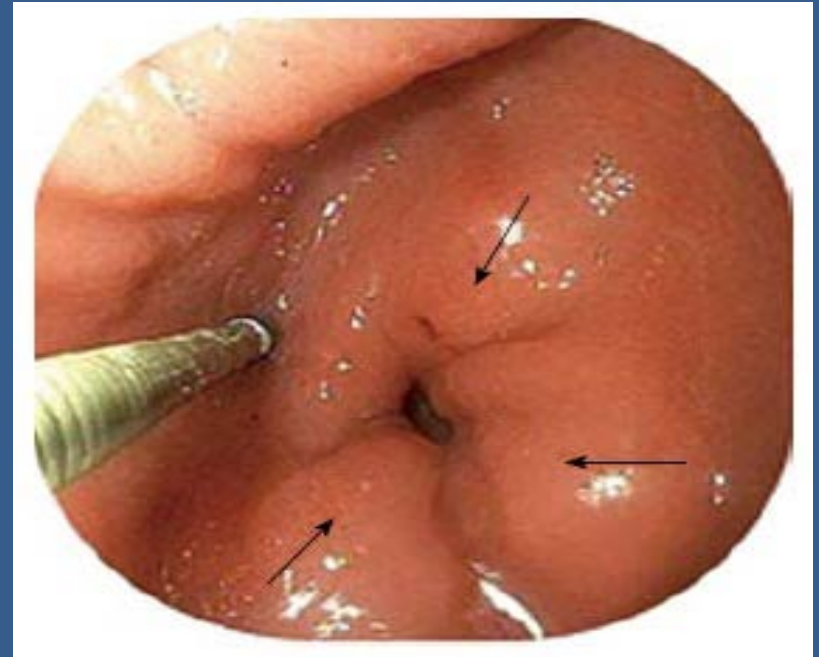


Parkman et al. JAMA 2010



# Pyloric Botox Injection

- Open Label Studies
  - Benefit in symptoms and GE
- (2) RCT's
  - Improvement no better than placebo



1) Camilleri et al. Am J Gastroenterol 2013 2) Friedenburg et al. Am J Gastroenterol 2008 3) Ukleja et al. World J Gastrointest Endosc 2015



# 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**

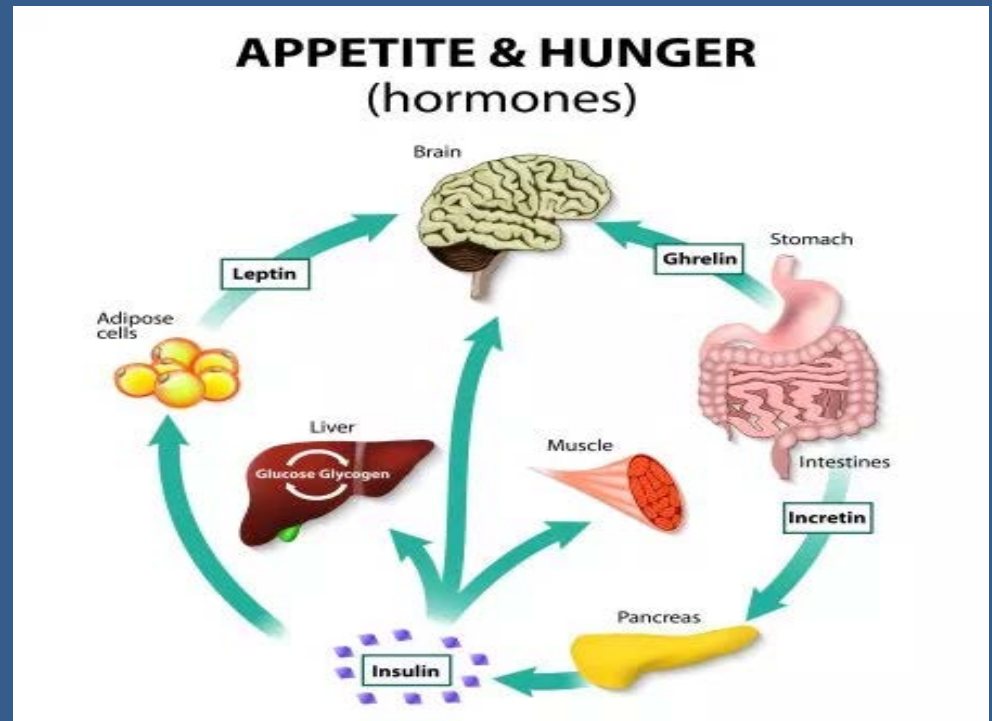
- Fewer GI side effects
- Long QT

1) Camilleri et al. Am J Gastroenterol 2013 2) Richard et al. Am J Gastroenterol 1993



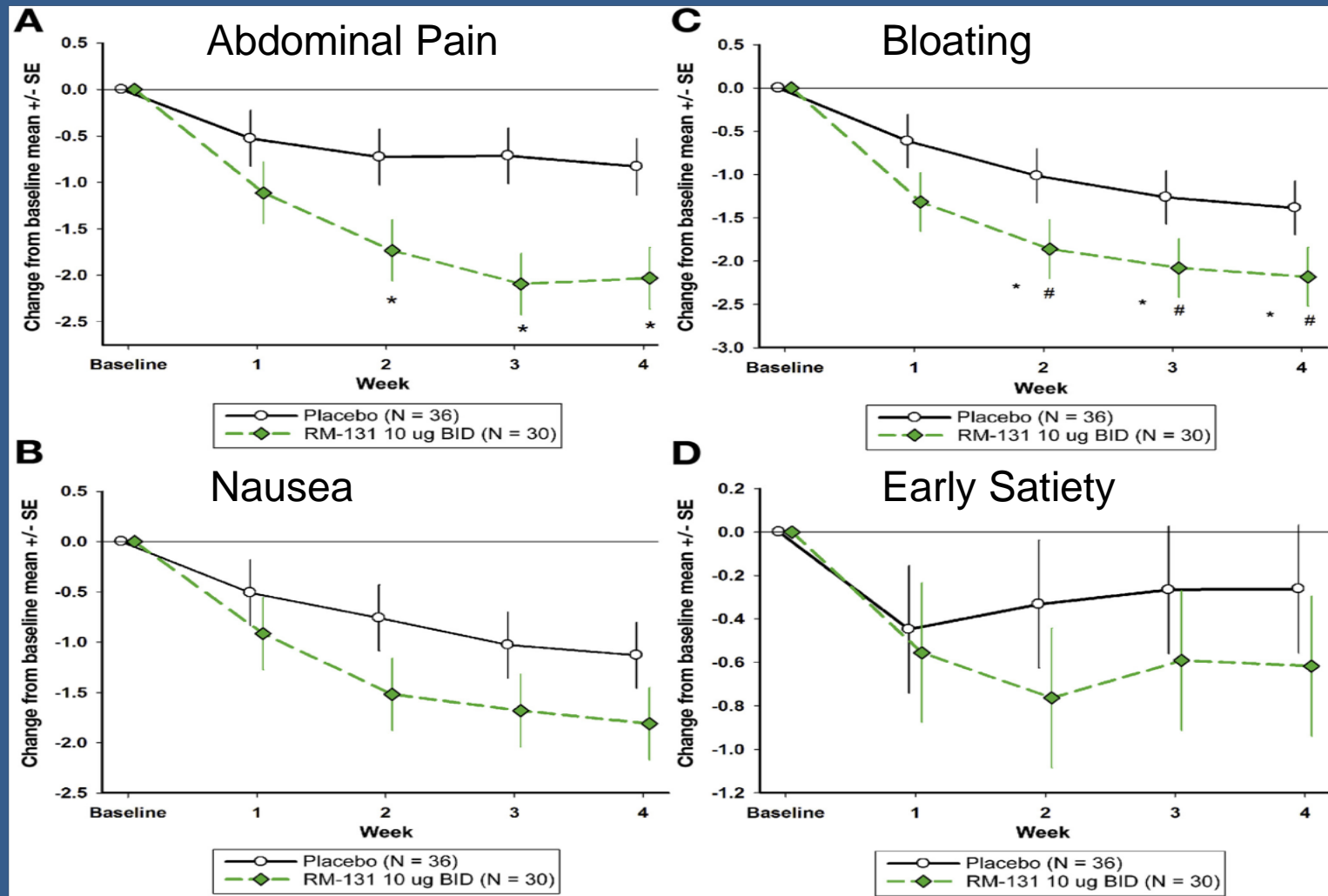
# Ghrelin Agonists

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





# Relamorelin

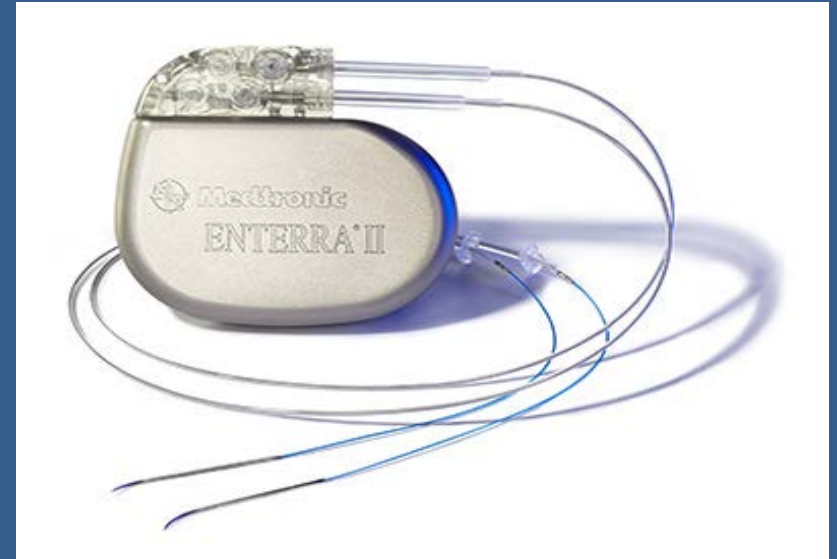


Lembo et al. Gastroenterology 2016



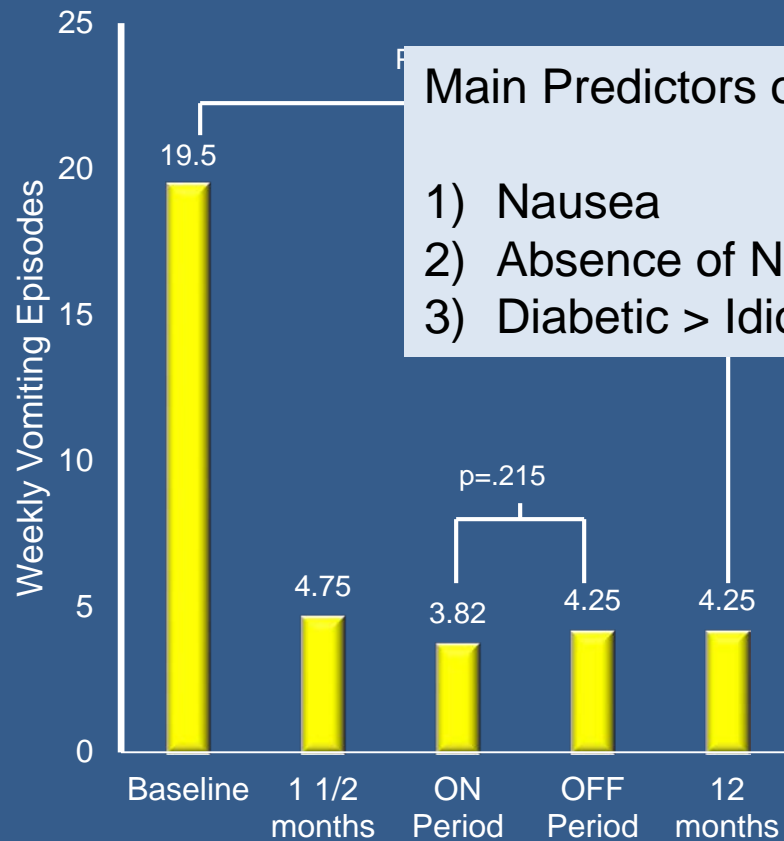
# Gastric Electrical Stimulation (GES)

- High Frequency Low Energy
- Does not alter rate of gastric emptying
- Implanted along greater curve
- Humanitarian Use Protocol

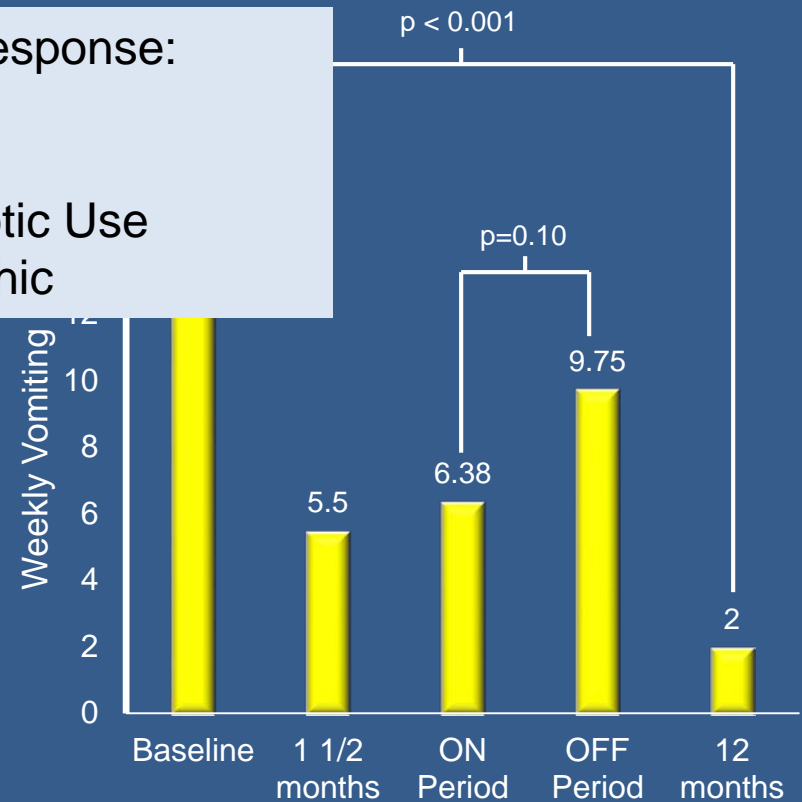


# GES in Gastroparesis

GES in Patients with DG



GES in Patients with IG



Main Predictors of Response:

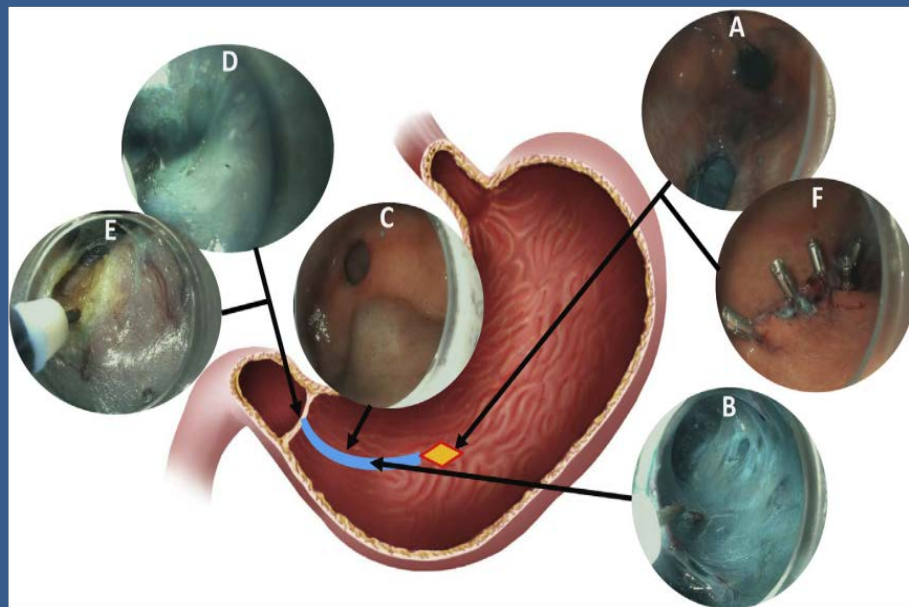
- 1) Nausea
- 2) Absence of Narcotic Use
- 3) Diabetic > Idiopathic

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

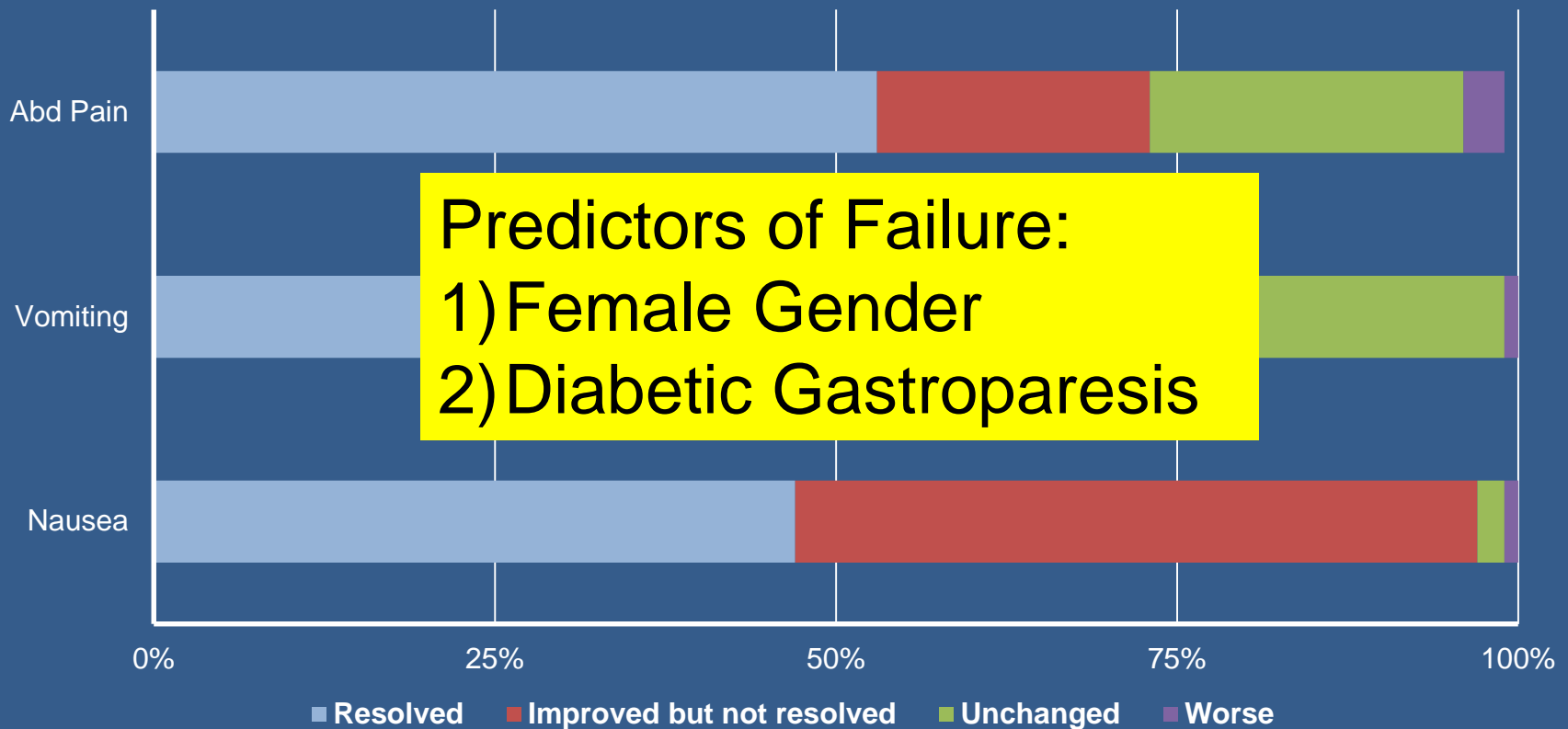


Mekaroonkamol Clin Gastroenterol and Hepatol 2019



# G-POEM in Mixed Gastroparesis

Response to G-POEM at 6 months



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
- **Gastroparesis**
  - 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?

