

Stanford Gastroenterology & Hepatology Division
MEDICINE

Gastroparesis & Functional Dyspepsia: What you need to know

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Normal Gastric Function

- Body/Fundus
 - Liquid emptying
 - Accommodation/storage
- Antrum
 - Mixing and grinding food to <2mm (chyme)
- Pylorus
 - Contracts postprandially to allow grinding
- Pacemaker
 - Interstitial Cells of Cajal

Evaluating Gastric Emptying

- Gastric Emptying Scintigraphy
- Wireless Capsule Motility
- Spirulina Breath Test

Types of Gastric Neuromuscular Dysfunction

Anatomic Location	Physiologic Abnormality	Symptoms
Fundus	Impaired Gastric Accommodation	Diastolic Dysfunction: - Fullness - Early Satiety
Antrum	Antral hypomotility	Systolic Dysfunction: - Delayed gastric emptying - N/V
Pylorus	Pylorospasm	Functional Outlet Obstruction
Duodenum	Duodenal dysmotility	Functional Outlet obstruction
Interstitial Cells of Cajal	Tachygastria, Bradygastria, dysrhythmia	Gastric Arrhythmias - Nausea - Gastric motor dysfunction

** Any dysfunction can give rise to GI symptoms without causing a delay in gastric emptying

Gastroparesis & FD Defined

Gastroparesis

- Abnormal gastric emptying in the absence of a mechanical obstruction
- Symptoms¹:

Symptom	Idiopathic (%)	Type 1DM (%)	Type 2DM (%)
Nausea	84.3	84.6	84.9*
Vomiting	59.8	89.5*	91.5*
Bloating	57.5	56.4	62.7
Early Satiety	57.5	47.4	74.6*
Abdominal pain	76.0	60.3*	69.5
Weight loss	46.5	52.6	52.5

Functional Dyspepsia

- Botherome postprandial fullness, early satiety, epigastric pain or epigastric burning in the absence of structural abnormalities
- Postprandial Distress (PDS)= meal related symptoms
- Epigastric Pain Syndrome (EPS) = pain/burning that may or may not be related to meals
- Nausea or vomiting can be present

1. Data from Parkman, H et al. Clin Gastroenterol Hepatol. 2011; 9(12);
2. Stanghellini V et al. Gastroenterol 2016;150:1380-92

Causes of Gastroparesis

	Idiopathic (N=254)
Age	41.0 ± 14.2
Gender (%F)	88.6%
Race (%Caucasian)	90.2%
BMI (Mean)	25.7 ± 6.9
- BMI < 18	7.5%
- BMI 18-24	46.1%
- BMI 25-30	20.9%
- BMI > 30	25.6%

Soykan I et al. Dig Dis Sci 1998
Parkman HP et al. Clin Gastroenterol Hepatol 2011

Functional Dyspepsia

- Upper abdominal pain or discomfort in the absence of a structural abnormality
 - Postprandial distress: pain related to eating
 - Impaired gastric accommodation (~40%)
 - Delayed (20-30%) or rapid (~10%) gastric emptying
 - Epigastric pain syndrome: pain unrelated to eating
 - Visceral hypersensitivity (up to 87%)
- Prevalence ~25% of the population

Tack et al. Gastroenterol 1991.
Thumshirn et al. Gut 1999.
Coffin, B et al. Gastroenterol 1994.

How is Idiopathic Gastroparesis Different From Functional Dyspepsia?

Does It Matter?

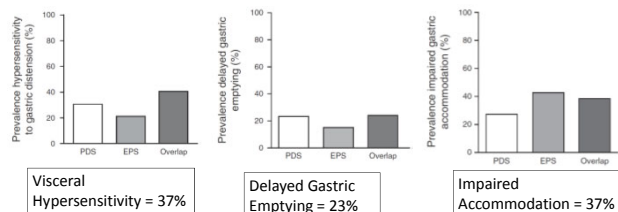


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FD Symptoms & Pathophysiology



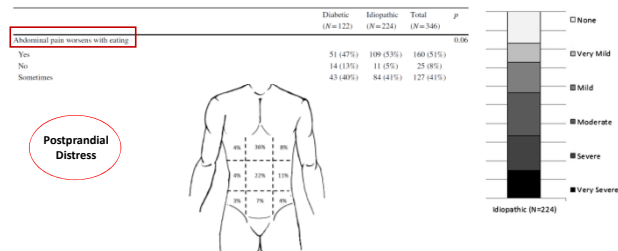
Vanheul H et al. Am J Gastroenterol 2017;112:132-140

Overlapping FD in Idiopathic Gastroparesis

Idiopathic Gastroparesis	Total (N=243)	
Rome III categories	No.	Percent
Functional dyspepsia	209	86.0%
- Postprandial Distress Syndrome (PDS) [Impaired accommodation, Delayed gastric emptying]	221	91.0%
- Epigastric Pain Syndrome (EPS) [Visceral hypersensitivity]	3	1.2%
Irritable bowel syndrome (IBS)	157	64.6%

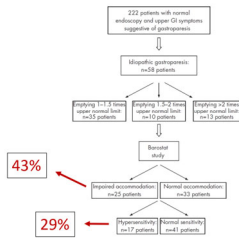
Parkman H et al. Gastroenterol 2011;140:103-115

Abdominal Pain in Idiopathic Gastroparesis



Parkman HP et al. Dig Dis Sci 2019;64:2242-2255.

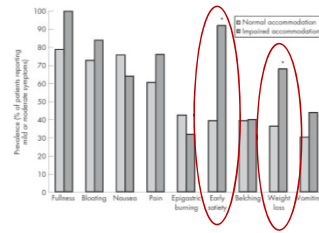
Overlapping Abnormalities in IG



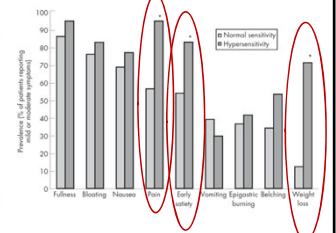
Karamanolis G et al. Gut 2007;56:29-36

GP Symptoms: Accommodation & Sensation

Impaired Gastric Accommodation



Visceral Hypersensitivity



Karamanolis G et al. Gut 2007;56:29-36

Does "Severe" GP Separate from FD?

Early Satiety ¹	Mild (n=53)	Moderate (n=46)	Severe (n=99)	p
4 hour gastric retention (%)	26.1 ± 19.2	28.8 ± 15.4	33.9 ± 21.3	0.1

Idiopathic GP ²	Normal (N=129)	Severely Delayed* (N=73)	
Average GCSI	2.8±1.0	3.2±1.0	0.006
GCSI subscales			
Bloating	2.8±1.7	3.2±1.5	0.08
Nausea/Vomiting	2.3±1.4	2.8±1.4	0.006
Postprandial fullness	3.4±1.1	3.6±1.1	0.14
PAGI-QOL	2.6±1.1	2.1±0.9	0.003

* Severely delayed GE = 4hr retention > 35%

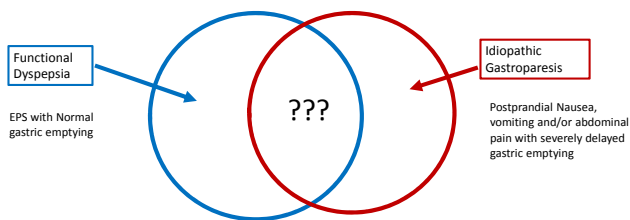
1. Parkman H et al. Neurogastroenterol Motil 2017; 29(4)
2. Nguyen L et al. DOW 2011.

Comparative Pathophysiology of GP & FD

Pathophysiology	Functional dyspepsia		
	Gastroparesis	Epigastric pain syndrome	Postprandial distress syndrome
Visceral hypersensitivity	?	+	?
Delayed gastric emptying	+	+	+
Rapid gastric emptying		+	+
Gastric dysrhythmias	+		+
Fundic accommodation	+		+
Weak antral pump	+		+
Antroduodenal discoordination	+		+
Duodenal neuromuscular dysfunction	+		+
Duodenal sensitization		+	+
Abnormal duodenal feedback	+		+
Sensitivity to acid, bile, and fats		+	+

Kim B and Kuo B. J Neurogastroenterol Motil 2019;25:27-35

Do FD & GP Represent a Spectrum or Distinct Disorders?



Gastroparesis & FD Treatments

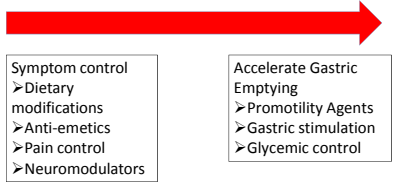
Gastroparesis

- Dietary Modifications
- Pharmacologic
 - Prokinetics
 - Anti-emetics
 - Neuromodulators
- Surgical
 - J tube
 - Pyloric intervention
 - Gastric stimulation
 - Gastrectomy
- CAM
 - Acupuncture
 - Herbal (Iberogast, Rikkunshito)

Functional Dyspepsia

- Dietary Modifications
- Pharmacologic
 - Acid suppression
 - Prokinetics
 - Fundic relaxation
 - Neuromodulators
- CAM
 - Acupuncture
 - Herbal (FDgard, Iberogast)

Current Therapeutic Approach to Gastroparesis



Treatment of Gastroparesis

- Dietary Modifications
 - Low fat diet- fat delays gastric emptying
 - Low residue- avoid nondigestible fibers
 - Small frequent meals
 - May require jejunal tube feeds and/or venting gastrostomy if severe
- Maintain hydration and electrolytes
- Maintain glycemic control in diabetics
 - Acute hyperglycemia > 275 mg/dL associated with delayed gastric emptying¹

Fraser RJ et al. Diabetologia 1990

Treatment Delayed Gastric Emptying

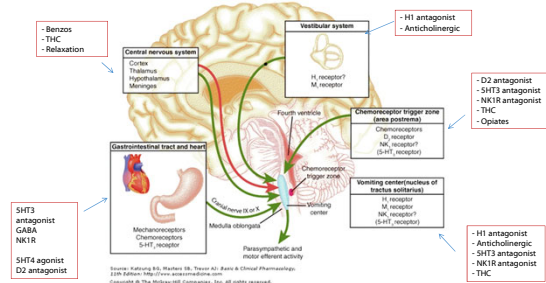
- Dopamine antagonists (D₂-receptor)
- Serotonin agonist 5-HT₄ (i.e. tegaserod, cisapride)
- Cholinergic agonists (i.e. Neostigmine, bethanechol)
- Macrolides-motilin agonist
 - Improves gastric emptying with minimal affect on symptoms Meganty et al. Am J Gastroenterol 2003
- Intrajugular Botulinum Toxin
- Jejunal feeding tube

Acceleration of gastric emptying is NOT associated with improvement in symptoms

Symptom Directed Therapy: Gastroparesis & Functional Dyspepsia



Management of Nausea/Vomiting



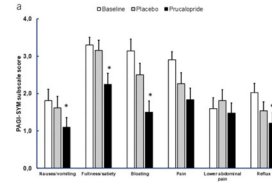
Antiemetics

Antiemetic Class	Example
H1 antagonist	Diphenhydramine Meclizine Promethazine Cycproheptadine
Muscarinic (cholinergic) M1 antagonist	Scopolamine
D2 antagonist	Metoclopramide Domperidone Prochlorperazine Trimethobenzamide
5-HT3 antagonist	Ondansetron Granisetron Dolasetron Palonosetron (IV)
Neurokinin (NK1) antagonist	Aprepitant Fosaprepitant (IV)
Cannabinoid (CB1) agonist	Dronabinol
Benzodiazepine	Lorazepam Alprazolam

Promotility Agents

Prucalopride & Idiopathic Gastroparesis

- Crossover study of Prucalopride 2 mg daily vs. Placebo x 4 weeks (N=28)

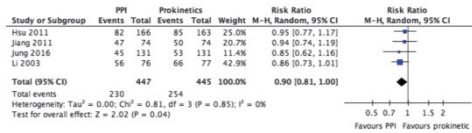


Carbone F et al. Am J Gastroenterol 2019;003:10

ACG and CAG Clinical Guideline: Management of Dyspepsia

Paul M. Moayyedi, MB, ChB, PhD, MPH, FACP, Brian E. Lacy, MD, PhD, FACP, Christopher N. Andrews, MD, Robert A. Enns, MD, Colin W. Howden, MD, FACP and Nimish Vakil, MD, FACP

- PPIs more effective than promotility agents in FD



Moayyedi P et al. Am J Gastroenterol 2017;112:988-1013

Surgical Therapies for Gastroparesis

Surgical Intervention

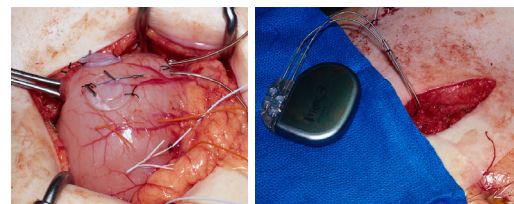
- Gastric Electrical Stimulation
- Pyloromyotomy
- Gastrectomy

Table 1. Response to surgical intervention for GP: patient improvement.

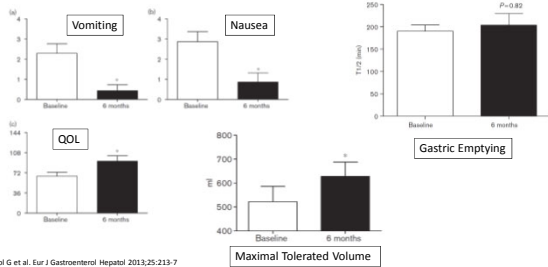
Treatment	Number of studies	Patient improvement (unweighted)	Number of patients	Patient improvement (weighted)
GES	9	69.0 ± 11.7*	441	69.8 ± 8.9*
Pyloric intervention	5	82.1 ± 5.7*	141	81.6 ± 7.0*
Gastrectomy	7	73.0 ± 15.3	263	67.3 ± 17.4

Zoll B et al. Journal Surgical Research 2018

Gastric Electrical Stimulation



Gastric Electrical Stimulation (GES) Improves Symptoms but NOT Emptying



Gourcelot G et al. Eur J Gastroenterol Hepatol 2013;25:213-7

Endoscopic Pyloromyotomy

Author	N	Patient Population	Outcome Measures	Follow up (months)	Gastric Emptying	Response Rate
Khshab 2017	30	11 DM, 12 PS, 7 ID	^A Patient reported change in symptoms	6 (7-11)	Improved: 37% vs. 17%	86% (26/30)
Gonzalez 2017	29	15 ID, 7 DM, 5 PS, 2 scleroderma	^B GCSI Improvement	Acute: 3 Midterm: 6	69% (18/23) normalization	79% (23/29) 69% (18/26)
Rodriguez 2017	47	27 ID, 12 DM, 8 PS	GCSI, Decrease medication use	3	Improved: 37% vs. 20%	GCSI & Meds ↓
Xu 2018	16	13 PS, 3 DM	^C * GCSI decrease > 50%	14.5 (5-19)	Improved	81% (13/16)
Khoury 2018	*189	69 ID, 43 DM, 40 PS, 4 other	GCSI (5/7 studies)	1-3 months	55% normalization	81.5%

1. Khshab M et al. Gastrointest Endosc. 2017; 85: 123-8.
2. Gonzalez JM et al. Aliment Pharmacol Ther. 2017; 46: 364-369
3. Rodriguez JM et al. Surg Endosc. 2017; 31: 5383-5388
4. Xu J et al. Canadian J of Gastroenterology Hep 2018;
5. Khoury T et al. J Gastroenterology and Hepatology 2018; 33: 1820-1833

^A Patients reported resolution, improvement, no change or worse symptoms
^B GCSI improvement not clearly defined
^C Only patients with total GCSI > 21 included
* Pooled data from 7 studies

Predictors of Response: G-POEM

Variable	Outcome
Etiology of GP (Idiopathic vs. Diabetic)	3 months: 93% vs. 57% 6 months: 92% vs. 43% OR 3.8 (95%CI 1-14.4)
Female sex	Failure to respond OR 1.8 (95% CI 1.2-2.5)
Symptom severity (GCSI > 21 < 30)	OR 0.74 (95%CI 0.54-1.003)
GES (2 hour retention < 78%)	PPV for success 100%

1. Gonzalez JM et al. Aliment Pharmacol Ther 2017; 46: 364-369
2. Xu J et al. Canadian J of Gastroenterology Hep 2018;

CAM for Nausea and Vomiting



Stanford University

Herbal Therapies

Herbals

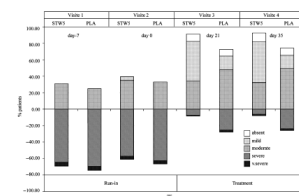
- Ginger (NK1)
- Ginseng (5HT3)
- Artichoke Leaf

Herbal blends

- Rikkunshito (5HT3, ghrelin)
 - › Bitter orange, Ginseng root, Zingiberis Rhizoma, Jujubae fruit, Crow-dipper, Atractylodis rhisoma, Licorice root, Porio cocos
- STW5 (Iberogast)
 - › Bitter candytuft, Angelica root, milk thistle fruit, caraway fruit, celandine herb, licorice root (5HT3), chamomile flower (5HT4), lemon balm leaf, and peppermint leaf
- Padma Digestin
 - › Pomegranate seed, lesser galangal, long pepper, cardamom fruit, and cassia bark
 - › Increases contractility of the antrum

Iberogast-Functional Dyspepsia

- Meta-analysis of Iberogast (n=199) vs. Placebo (n=198)



Melzer J et al. Aliment Pharmacol Ther 2004;20:1279-1987

