

Esophageal and Gastric Motility Disorders: A case based approach

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Conflicts of Interest:

- None

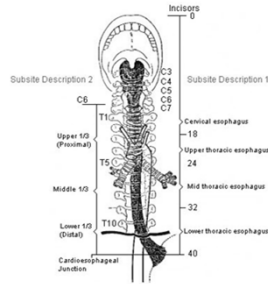
Overview

- Esophageal anatomy
- Dysphagia-case based approach
- Reflux disease-case based approach
- Gastric physiology
- Gastroparesis-case based approach

Dysphagia-Case based approach

Esophagus: Anatomy

- 25 cm muscular tube.
- Extends from upper esophageal sphincter to stomach.
- Proximal 1/3rd consist of striated muscles while distal 2/3rd is formed by smooth muscles.
- Lined squamous epithelium.



Terminology

- **Dysphagia:** derived from the Greek word *dys* (difficulty, disordered) and *phagia* (to eat).
- **Odynophagia:** painful swallowing.
- **Globus Sensation:** Sensation of lump in throat between meals.

History

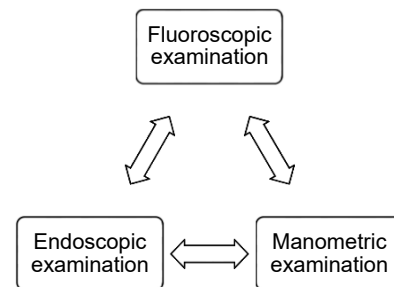
Oropharyngeal

- **Oral:**
 - Drooling of saliva
 - Food spillage
 - Sialorrhea
 - Piecemeal swallows
 - Associated dysarthria
- **Pharyngeal:**
 - Choking/cough during swallow
 - Associated dysphonia

Esophageal

- **Food stuck in suprasternal notch or retrosternal region**
- **Motility:**
 - dysphagia to solids and liquids
 - Associated with heartburn or chest pain.
- **Mechanical:**
 - progressive dysphagia to solids; may involve liquids at later stages

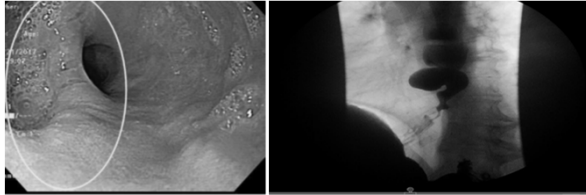
Dysphagia Assessment



Case Study 1:

78-year-old female with no significant medical history presenting with:

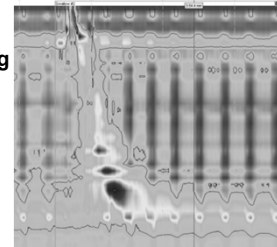
- Dysphagia to both solids and liquids
- Chest pain
- Denies any heartburn
- 50 lb weight loss



- Epiphrenic diverticulum
- Resistance at GEJ
- Epiphrenic diverticulum
- Beaking at GEJ

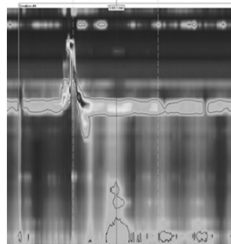
Case Study 1:

- Mean DCI: 2380
- Mean LES IRP: 32 mm Hg
- Mean DL: 3.8 sec



Case Study 1:

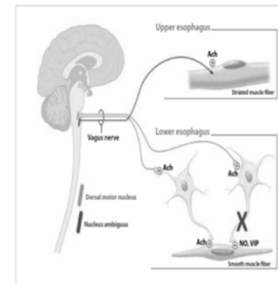
- Post extended myotomy and diverticulectomy
- Fairly doing



Achalasia

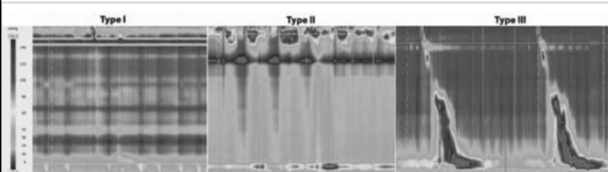
- Rare esophageal motility disorder
- Esophageal aperistalsis
- Impaired LES relaxation

Loss of inhibitory neurons secreting VIP and NO leads to unopposed excitatory activity and failure of LES relaxation



DA Patel. An Overview of Achalasia and Its Subtypes. Gastroenterology & Hepatology. Volume 13, Issue 7 July 2017

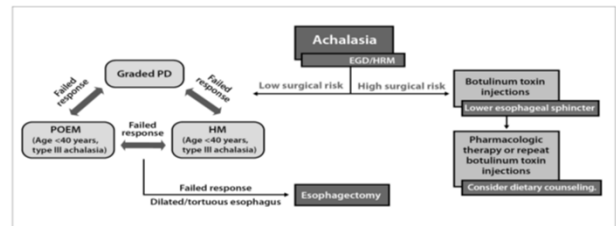
Achalasia: Subtypes



Type I is characterized by a quiescent esophageal body, type II has pan-esophageal pressurization, and type III is characterized by simultaneous contractions.

DA Patel. An Overview of Achalasia and Its Subtypes. Gastroenterology & Hepatology. Volume 13, Issue 7 July 2017

Achalasia: Treatment Algorithm



DA Patel. An Overview of Achalasia and Its Subtypes. Gastroenterology & Hepatology. Volume 13, Issue 7 July 2017

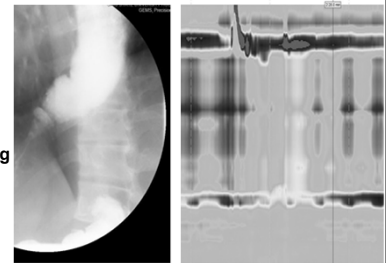
Achalasia: Treatment Options

Treatment Options	Pros	Cons
Medications (CaCB/Nitrates)	<ul style="list-style-type: none"> On Demand Minimal risk For non-operative candidates 	<ul style="list-style-type: none"> Least effective Not durable
Botulinum toxin injection	<ul style="list-style-type: none"> Good option for nonoperative candidates Short procedure time 	<ul style="list-style-type: none"> Durability of 6–12 months
Pneumatic dilation	<ul style="list-style-type: none"> Most effective nonsurgical option Short recovery time Durability 2–5 years Procedure time <30 minutes 	<ul style="list-style-type: none"> Perforation (1%–5%)
Surgical myotomy	<ul style="list-style-type: none"> Durability 5–7 years Procedure time ~90 minutes 	<ul style="list-style-type: none"> General anesthesia required Hospital stay of 1–2 days
Esophagectomy	<ul style="list-style-type: none"> For end-stage disease 	<ul style="list-style-type: none"> High morbidity and mortality

Case Study 2:

24-year-old female presented with dysphagia to solids and liquids.

- Mean DCI: NA
 - Mean LES IRP: 24 mm Hg
 - Mean DL: NA
- Diagnosis??**

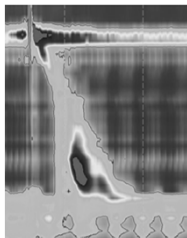


Type 2 Achalasia. Patient sent for myotomy

Case Study 3:

64-year-old female with CAD, chronic backache on morphine is presenting dysphagia and spasmodic pain in the neck and chest.

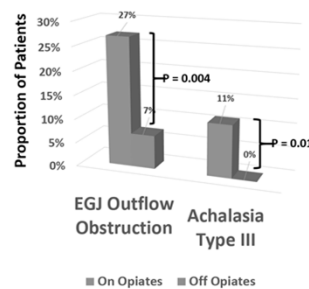
- Mean DCI: 2765
- Mean LES IRP: 18 mm Hg
- Mean DL: 3.8s



Diagnosis?? **Opioid induced esophageal dysfunction**

Opioid-induced esophageal dysfunction

Opioid-induced esophageal dysfunction is often characterized by EGJ outflow obstruction and type III achalasia pattern.



Ratuapli S, et al. Opioid-Induced Esophageal Dysfunction (OIED) in Patients on Chronic Opioids. *Am J Gastroenterol* 2015; 110:979-984;

Achalasia syndromes beyond the CC v3.0

CC v3.0 diagnosis	IRP > ULN?	Oesophageal contractility	Notes
Oesophagogastric junction outflow obstruction	Yes	Sufficient peristalsis to exclude type I, II or III achalasia	<ul style="list-style-type: none"> • Heterogeneous group • Early or incomplete achalasia • Can resolve spontaneously • Recording artefacts
Absent contractility	No	Absent contractility	<ul style="list-style-type: none"> • Can be achalasia • Abnormal FLIP distensibility index supports achalasia • Oesophageal pressurization with swallows or MRS supports achalasia
Distal oesophageal spasm	Yes or no	≥20% premature contractions (DL < 4.5s)	Might be spastic achalasia
Jackhammer	Yes or no	≥20% of swallows with DCI > 8,000 mmHg·s·cm	Might be spastic achalasia if DL < 4.5s with ≥20% swallows
Opioid effect (not in CC)	Yes	Normal, hypercontractile or premature	Can mimic EGJOO, type III achalasia, DES or jackhammer
Mechanical obstruction (not in CC)	Yes	Absent, normal or hypercontractile	EUS, CT or MRI of the EGJ might clarify the aetiology

Kahrilas, P. J. et al. (2017) Advances in the management of esophageal motility disorders. in the era of high-resolution manometry: a focus on achalasia syndromes. *Nat. Rev. Gastroenterol. Hepatol.* doi:10.1038/nrgastro.2017.132

GERD-Case based approach

Gastroesophageal Reflux Disease Definition

GERD is a condition that develops when the reflux of gastric content causes troublesome symptoms or complications.

- Mild symptoms once in > 2 days/week
- Moderate/Severe once in >1 day/week

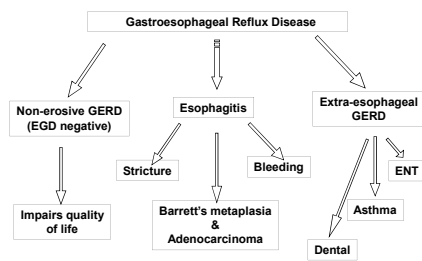
Vakil N, van Zanten SV, Kahrilas P, et al. Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol.* 2006;101:1900-1920.

Risk factors:

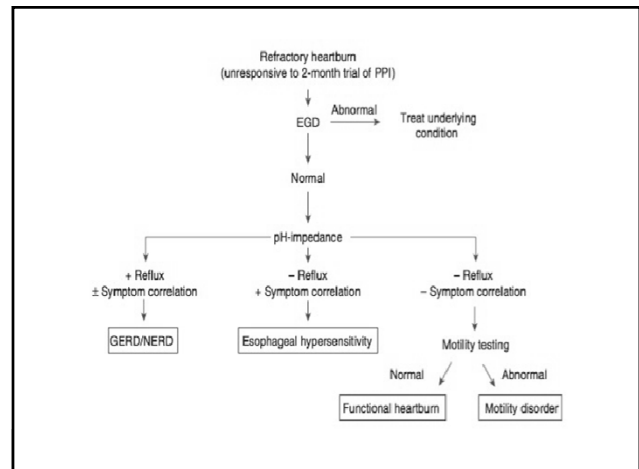
- Obesity
- Family history for GERD
- Tobacco smoking
- Alcohol consumption
- Associated psychosomatic complaints

Locke GR, et al. *The American Journal of Medicine.* 1999;106(6):642-649
 Hampel H. *Ann Intern Med.* 2005;143(3):199-211.

Impact of Gastroesophageal Reflux Disease



Irvine EJ, Hunt RH. *Evidence-Based Gastroenterol.* BC Decker Inc. Hamilton and London. 2001.



Goals for Treatment of GERD

- Eliminate symptoms
- Heal erosive esophagitis
- Prevent the relapse of erosive esophagitis and complications from GERD

Life-Style Modifications include:

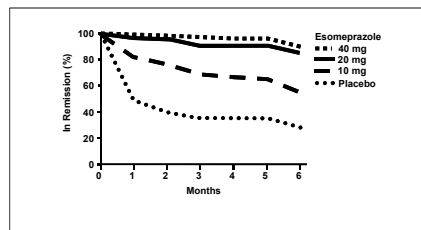
- Elevate the head of the bed on 4" to 6" blocks.
- Advise weight loss for obese patients.
- Avoid recumbency for 3 hours after meals.
- Avoid bedtime snacks.
- Avoid fatty foods, chocolate, peppermint, onions, and garlic.
- Avoid cigarettes and alcohol.
- Avoid drugs that decrease LES pressure and delay gastric emptying.

Medical treatment options:

Proton Pump Inhibitors:

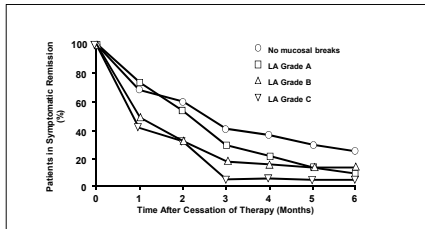
- Higher healing rates in mild to moderately severe reflux esophagitis(80% to 100%).
- Improves dysphagia.
- Decreases the need for esophageal dilation in patients who have peptic esophageal strictures.
- About 70% may have nocturnal acid breakthrough that requires H2RA.

Maintenance of Healing Erosive Esophagitis



Pooled from Johnson DA, et al., *Am J Gastroenterol*, 2001;96:27-34 and Vakili NB, et al., *Aliment Pharmacol Ther*, 2001;15:927-935.

GERD Is a Chronic Condition Likely to Relapse



Lundell LR, et al. *Gut*. 1999;45:172-180.

Appropriateness of PPI use

Reason for use	
Long-term PPI therapy appropriate	<ul style="list-style-type: none"> Barrett's esophagus Healing and maintenance of healed Los Angeles grade C or D erosive esophagitis^a PPI-responsive esophageal eosinophilia Idiopathic, H. pylori and NSAID/aspirin negative) peptic ulcer disease Zollinger-Ellison disease^{b,c} PPI-responsive GERD/non-erosive reflux disease^{d,e} Long-term non-selective NSAID users at high-risk for upper GI complications or long-term cox-2 inhibitor users with a prior episode of GI bleeding^f Anti-platelet therapy in patients at high-risk for upper GI complications (age > 65 years or concomitant use of corticosteroids or anticoagulants or history of peptic ulcer disease) Steatorrhea refractory to enzyme replacement therapy in chronic pancreatitis
Short-term PPI therapy appropriate (4- to 12-week course)	<ul style="list-style-type: none"> Healing of Los Angeles grade A or B erosive esophagitis^a Eosinophilic esophagitis H. pylori eradication (in combination with antibiotics)^{g,h} Stress ulcer prophylaxis in high-risk patients (i.e., critically ill patients with respiratory failure or coagulopathy) Functional dyspepsia Treatment and maintenance of peptic ulcer disease^e Prior to endoscopy for acute upper GI bleeding
PPI use not appropriate	<ul style="list-style-type: none"> Nonhealing endoscopic treatment of a high-risk ulcer or bleed Corticosteroid users without concomitant NSAID therapy To prevent bleeding from hypertensive gastropathy in cirrhotic patients Acute pancreatitis Stress ulcer prophylaxis in non-critically ill hospitalized patients that are not at high-risk for ulcer formation and GI bleeding
PPI use of uncertain benefit	<ul style="list-style-type: none"> PPI non-responsive GERD Extra-digestive GERD

Yadlapati and Kahrilas *BMC Medicine* (2017) 15:36

Table 2 Quality of evidence and risks of adverse effects associated with long-term proton pump inhibitors (PPIs)

Potential adverse effect	Nature of evidence	Risk estimate
Causality established, idiosyncratic, rare	Acute interstitial nephritis	Observational, case-control OR 5.16 (2.21–12.05)
Causality proven but of minimal significance	Fundic gland polyps	Observational OR 2.2 (1.3–3.8) [6]
Weak association, causality probable	B12 deficiency	Observational, case-control OR 1.65 (1.58–1.73) [7]
	Small intestinal bacterial overgrowth	Meta-analysis OR 2.28 (1.23–4.21) [8]
	Spontaneous bacterial peritonitis in cirrhotic patients	Systematic review/meta-analysis OR 2.17 (1.46–3.23) [9]
Weak association, causality		1.78–5.10 [10] 3.50 2.64 [11] 2.93 ^a [12] 3.90 1.90 [13] 1.52 1.24 ^b 1.92 ^b

Decisions to start, properly dose, continue, or discontinue PPI therapy should be personalized based on indication, effectiveness, patient preferences, and risk assessment.

Yadlapati and Kahrilas *BMC Medicine* (2017) 15:36

Medical treatment options:

- **Antacids and Alginic Acid:**
 - Temporarily relieve episodic heartburn
 - Useful add on therapy
- **Histamine H2-Receptor Blocking Agents:**
 - Safe and effective in mild esophagitis
 - Not useful in severe esophagitis
 - Useful for breakthrough symptoms
 - Concern for tachyphylaxis
- **Prokinetic Agents:**
 - Limited efficacy and side effects in up to 30%
- **TLESR Inhibitors:**
 - As add-on for non-acid reflux/post prandial reflux

Indications for anti-reflux surgery

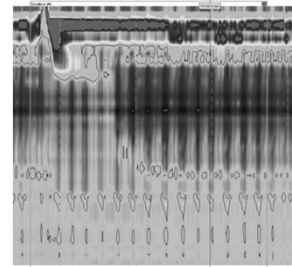
- Unwillingness to remain on medical therapy
- Intolerance of medical therapy
- Medically refractory symptoms with objective evidence of GERD
- GERD in the setting of a large hiatal hernia

Badillo R, Francis D. Diagnosis and treatment of gastroesophageal reflux disease. *World J Gastrointest Pharmacol Ther.* 2014;5(3):105-12.

Case Study 4:

42-year-old female with prior history of scleroderma is presenting with persistent reflux inspite of twice daily PPI, referred for fundoplication.

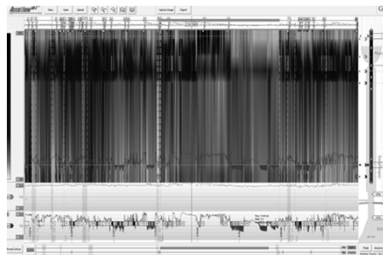
- Mean DCI: NA
- Mean LES IRP: 2mm Hg
- Mean DL: NA



Case Study 4:

- Acid exposure:
 - Total AET: 14.5%
 - Reflux events: 112
- Reflux symptom analysis:
 - SI: 54
 - SAP: 98

What would be the next step?

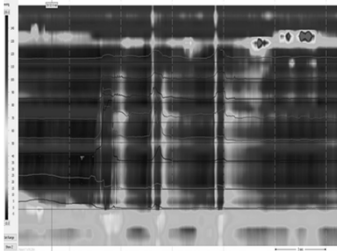


Case Study 4:

- Educated on lifestyle measures.
- Added H2B at bedtime.
- Was doing much better.

Case Study 5:

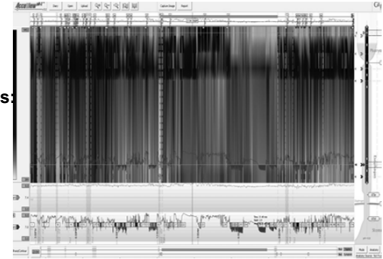
- 28 yr old female with anxiety presenting with persistent heartburn inspite of PPI twice daily
- EGD: normal esophagus with biopsy



Case Study 5:

- Acid exposure:
 - Total AET:10.5%
 - Reflux events:119
- Reflux symptom analysis:
 - SI:50
 - SAP: 96

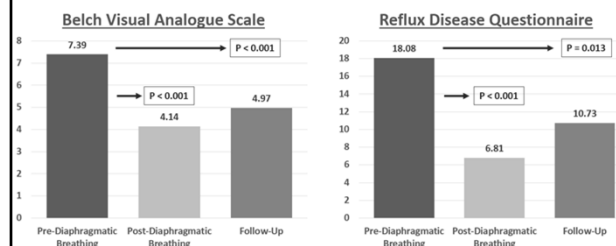
What would be the next step?



DDx to PPI-Refractory GERD

- | | |
|---|---|
| <ul style="list-style-type: none"> • Refractory reflux symptoms with esophagitis • Eosinophilic esophagitis • Pill induced esophagitis • Skin disorders like Lichen planus • Hypersecretory condition like ZES • Genotypic differences in CYP450 2C19 | <ul style="list-style-type: none"> • Refractory reflux symptoms with normal esophagus • Eosinophilic esophagitis • Achalasia • Gastroparesis • Aerophagia and Belching disorder • Rumination syndrome • Functional heartburn |
|---|---|

Effect of DBT on belching and GERD



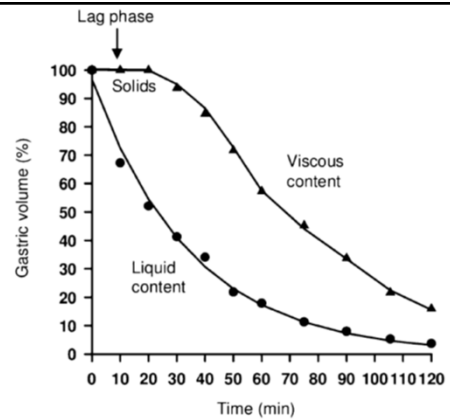
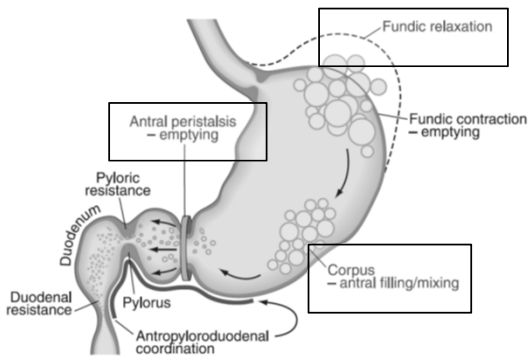
Ong et al. Diaphragmatic Breathing Reduces Belching and Proton Pump Inhibitor Refractory Gastroesophageal Reflux Symptoms. Clinical Gastroenterology and Hepatology 2018;16:407-416

Case Study 5:

- Continued PPI,
- Started on behavioral therapy and anti-anxiety medication,
- Educated on DBT

Gastroparesis-Case based approach

Physiology of stomach



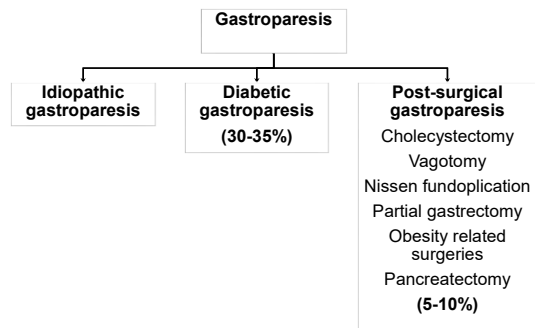
Normal Velocities of emptying of solid and liquid chyme.

Definition:

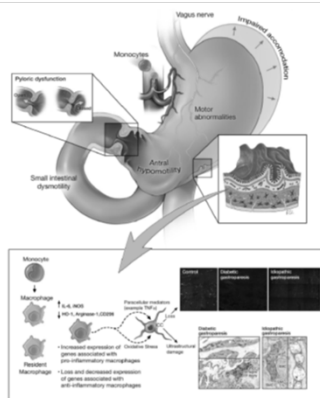
Gastroparesis is defined as a delay in the emptying of ingested food in the absence of mechanical obstruction of the stomach or duodenum.

Camilleri M, Parkman H, Shafi M, et al. Clinical guideline: management of gastroparesis. Am J Gastroenterol 2013;108:18–37.

Etiology of Gastroparesis



Pathophysiology



Grover, M et al. Gut. 2019 Dec;68(12):2238-2250.

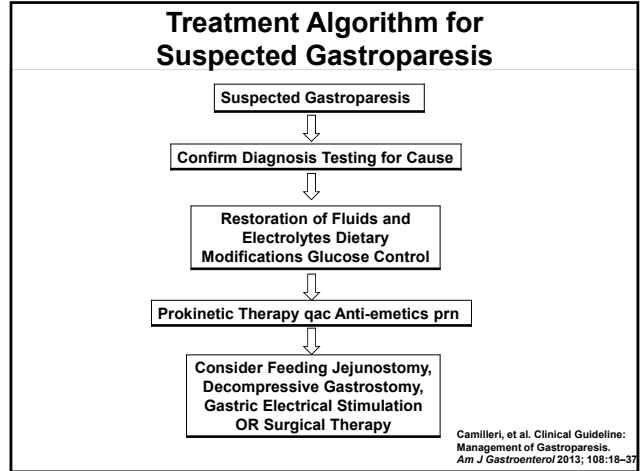
Clinical Presentation:

- Nausea
- Vomiting
- Early satiety
- Bloating
- Postprandial fullness
- Abdominal pain
- Weight loss/weight gain
- Constipation and/or diarrhea
- Wide glycemic fluctuations

Characteristic	Pair-wise P value ^a					
	IG (n 254) N (% or mean) ^b	T1DM (n 78) N (% or mean) ^b	T2DM (n 59) N (% or mean) ^b	IG vs all DM	IG vs T1DM	IG vs T2DM
Symptoms prompting evaluation for gastroparesis						
Nausea	214 (84.3)	66 (84.6)	56 (94.9)	.19	.94	.03
Vomiting	152 (59.8)	69 (88.5)	54 (91.5)	<.001	<.001	<.001
Bloating	146 (57.5)	44 (56.4)	37 (62.7)	.75	.87	.46
Early satiety	146 (57.5)	37 (47.4)	44 (74.6)	.75	.12	.02
Postprandial fullness	136 (53.5)	44 (56.4)	39 (66.1)	.18	.66	.08
Abdominal pain	193 (76.0)	47 (60.3)	41 (69.5)	.01	.007	.30
Diarrhea	98 (38.6)	35 (44.9)	30 (50.9)	.09	.32	.08
Constipation	112 (44.1)	32 (41.0)	34 (57.6)	.44	.63	.06
Anorexia	32 (12.6)	12 (15.4)	17 (28.8)	.03	.53	.02
Weight loss	118 (46.5)	41 (52.6)	31 (52.5)	.25	.35	.40
Weight gain	45 (17.7)	14 (18.0)	14 (23.7)	.57	.96	.24
Gastroesophageal reflux	137 (53.9)	43 (55.1)	35 (59.3)	.57	.85	.45
Problems with diabetes control	0 (0.0)	39 (50.0)	27 (45.8)	<.001	<.001	<.001

In 416 patients from the NIH Gastroparesis Registry, symptoms prompting evaluation more often included vomiting for diabetic gastroparesis and abdominal pain for idiopathic gastroparesis.

Source: Parkman HP, Yates K, Haeler ML, et al. Similarities and differences between diabetic and idiopathic gastroparesis. Clin Gastroenterol Hepatol. 2011;9(12):1056–e134.



Diagnostic Testing for Gastroparesis:

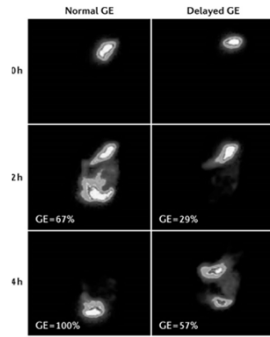
TABLE 2. Diagnostic Testing for Gastroparesis

Modality	Advantages	Disadvantages
Gastric scintigraphy		
4-hour solid phase	Widely available	Radiation exposure
	Considered the "gold standard" for diagnosis	False positives with liquid phase only studies
Wireless motility capsule		
Smart Pill, given imaging	Avoids radiation exposure	Less validated than scintigraphy
	FDA approved for diagnosis	Cannot be used in those with pacemaker or defibrillator
Radiolabeled carbon breath test		
¹³ C-labeled octanoic acid or Spirulina platensis	Low cost	Lack of standardization
		Has primarily been used as a research tool

Gastroparesis: A Review of Current Diagnosis and Treatment Options. Stein, Benjamin; Everhart, Kelly; Lacy, Brian. Journal of Clinical Gastroenterology. 49(7):550-558, August 2015.

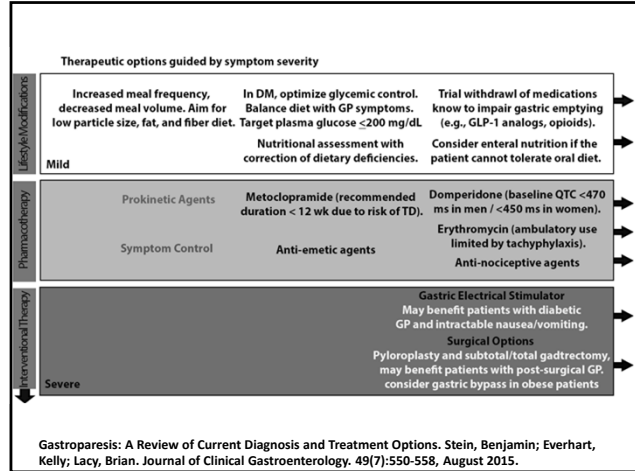
- ### Radionuclide Gastric Emptying Scintigraphy
- Best current test for measuring gastric emptying because it is sensitive, quantitative, and physiological.
 - ^{99m}Tc sulfur colloid-labeled low-fat egg white meal as a test meal.
 - Imaging is performed in the anterior and posterior projections at least at four time points (0, 1, 2, and 4 h).
 - The 1 h image is used to help detect rapid gastric emptying.
 - The 2 and 4 h images are used to evaluate for delayed gastric emptying.
 - *Hyperglycemia (glucose level > 270 mg/dL) delays gastric emptying in diabetic patients.*
- Parkman H.P. (2018) Gastric Emptying Studies. In: Bardan E., Shaker R. (eds) Gastrointestinal Motility Disorders. Springer, Cham

Radionuclide Gastric Emptying Scintigraphy



Nature Reviews | Gastroenterology & Hepatology

Keller, J. et al. (2018) Advances in the diagnosis and classification of gastric and intestinal motility disorders. *Nat. Rev. Gastroenterol. Hepatol.*



Pro-kinetics:

Medications	Mechanism	Pros	Con
Metaclopramide	D2 Antagonist	Improves gastric emptying. Lowest possible dose (5 mg TID before meals). No long term study available. Efficacy:29-53%. Comparable to Domperidone	Black box warning:>12 weeks use of tardive dyskinesia Acute dystonias Parkinsonism type movements Associated with QTc interval
Domperidone	D2 Antagonist	Improvement in symptoms (54% to 79%). Drug interaction.	Less CNS effects Associated with QTc interval. Increases Prolactin levels. Requires IND for approval.
Erythromycin	Motilin agonist	Useful during acute exacerbation. IV better than PO.	Tachyphylaxis. Associated with QTc prolongation.
Cisapride	5-HT4 agonist	Significant improvement in symptoms.	cardiac arrhythmias and death Requires IND
Prucalopride	5-HT4 agonist	Improves gastric emptying and colon transit times. FDA approved for chronic constipation.	Diarrhea and suicidal ideations. Avoidance in ESRD. No cardiac toxicity document.

Anti-emetics:

Medications	MOA	Pros	Cons
Diphenhydramine	Antihistamines	Useful in mild nausea/vomiting.	• Sedative effect. • Anticholinergic S/E.
Hyoscine	Anti-cholinergics	Cheap and widely available. Useful in mild cases.	• Anti-cholinergic side effects(dry mouth, glaucoma,etc).
Phenothiazines/prochlorperazine	D1/D2 Antagonist	Useful in severe nausea and vomiting.	• EKG changes • Psychomotor issues in elderly • Dystonia/Parkinsonism
Ondansetron	5HT3 antagonists	Widely available. Useful in mild vomiting.	• QT prolongation. • Serotonin syndrome. • Constipation.
Transdermal granisetron	5HT3 antagonists	Not widely available/cost. Useful in those who cannot tolerate oral meds.	• QT prolongation. • Serotonin syndrome. • Constipation.
Aprepitant	NK1 receptor antagonists	Not widely available/cost. Useful in reducing N/V.	• Fatigue. • Neutropenia.
Dronabinol	Agonist of CB ₁ and CB ₂	Helpful for N/V when other therapies have failed.	• Delays gastric emptying.

Neuromodulators:

Medications	MOA	Pros	Con
Nortriptyline/ Amitriptyline	TCA	Modest improvement in N/V and abdominal pain	Worsens gastric emptying. Anti-cholinergic side effects. Constipation.
Mirtazapine/ Buspirone	SNRI/SSRI	Improves appetite. Improves fundic accommodation.	Suicidal thoughts. EKG changes. Serotonin syndrome.

Gastric electric stimulation

- **Patient Selection:** *Diabetic gastroparesis with refractory N/V even after 1 year of pro-kinetics.*
- **Response to therapy:**
 - Diabetics.
 - Not on narcotics.
 - Predominant nausea/vomiting.
- **Response was modest with 43% over a period of a year and half.**

Heckert, J., Sankinen, A., Hughes, W. B., Harblson, S., & Parkman, H. (2016). Gastric Electric Stimulation for Refractory Gastroparesis: A Prospective Analysis of 151 Patients at a Single Center. *Digestive Diseases and Sciences*, 61(1), 168-175.

Final Case Study

- **42-year-old gentleman with type 2 diabetes(HgbA1c:9) on exenatide presenting with recurrent vomiting and nausea for the last 6 months?**

What would be the next step?

Normal upper endoscopy with moderate food retention in the stomach. Bx: negative for H. pylori.

4-hour GES: 43%. What do we do next?

**Switch exenatide to insulin+CGM.
Nutrition consult for gastroparesis.**