Personalizing the treatment of GERD

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Objectives

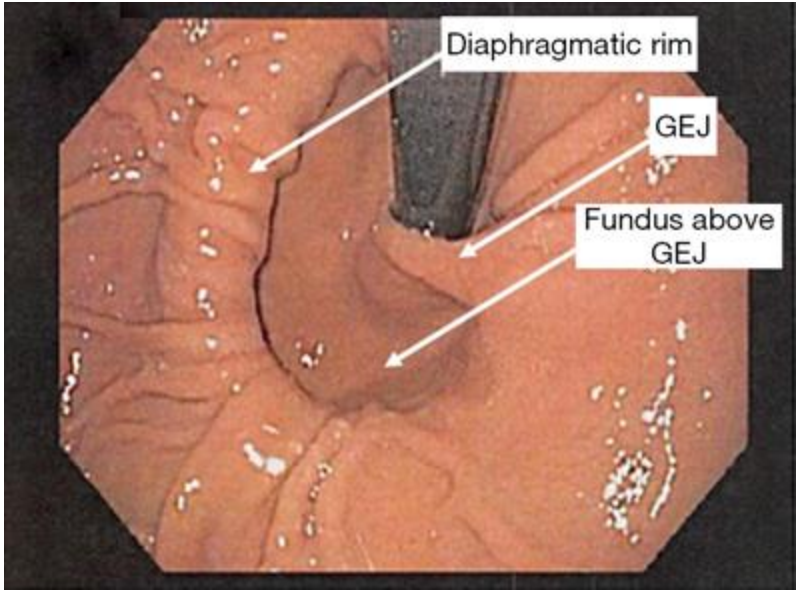
Define Gastroesophageal Reflux

Initial Treatment

Diagnostics/workup

How to manage refractory GERD

Minimally invasive antireflux procedures and hiatal hernia repair



Hennig A, Kurian AA. Flexible endoscopy and hiatal hernias. Ann Laparosc Endosc Surg 2021;6:45.

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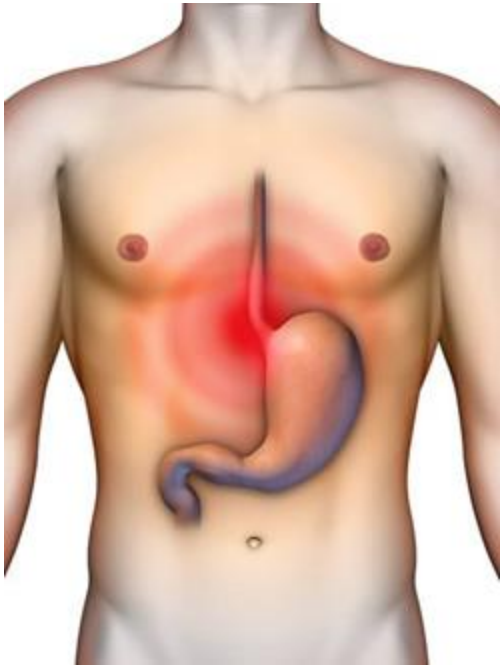
What is GERD?

- "A condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications."

- Estimated prevalence: 8-33% of all adults worldwide



El-Serag et al, Gut 2014

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The Anti-Reflux Barrier

- **LES Hypotension:** Transient lower esophageal sphincter relaxations (TLESRs) are the most common cause of reflux events.
- **Hiatal Hernia:** Displaces the LES into the chest, impairing the normal anatomic mechanisms to prevent reflux.
- **Impaired Clearance:** Ineffective esophageal motility prolongs acid exposure.

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Transient Lower Esophageal Sphincter Relaxations (TLESR's)

- Possibly the underlying cause of all physiologic reflux events, and two-thirds of reflux episodes in pathologic GERD.
- The majority of patients with reflux symptoms have a *normal* anatomy.

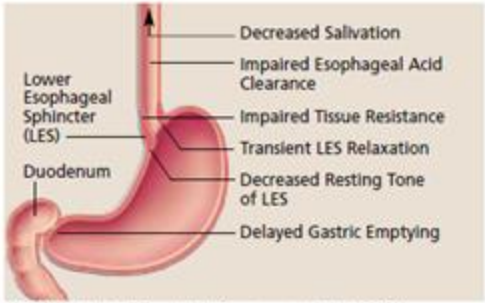

FIGURE 2. Possible etiologic factors involved in GERD.

TABLE 1
Mechanisms of gastroesophageal reflux in normal volunteers and in patients with GERD

Type	Normal volunteers	Patients with GERD
Transient lower esophageal sphincter relaxations (TLESRs)	94%	65%
Transient increase in intra-abdominal pressure	5%	17%
Spontaneous free reflux	1%	18%

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Kahrilas PJ 2003
https://www.health.harvard.edu/diseases-and-conditions/gastroesophageal-reflux-disease-gerd-a-to-z

Anatomy of Physiologic Reflux

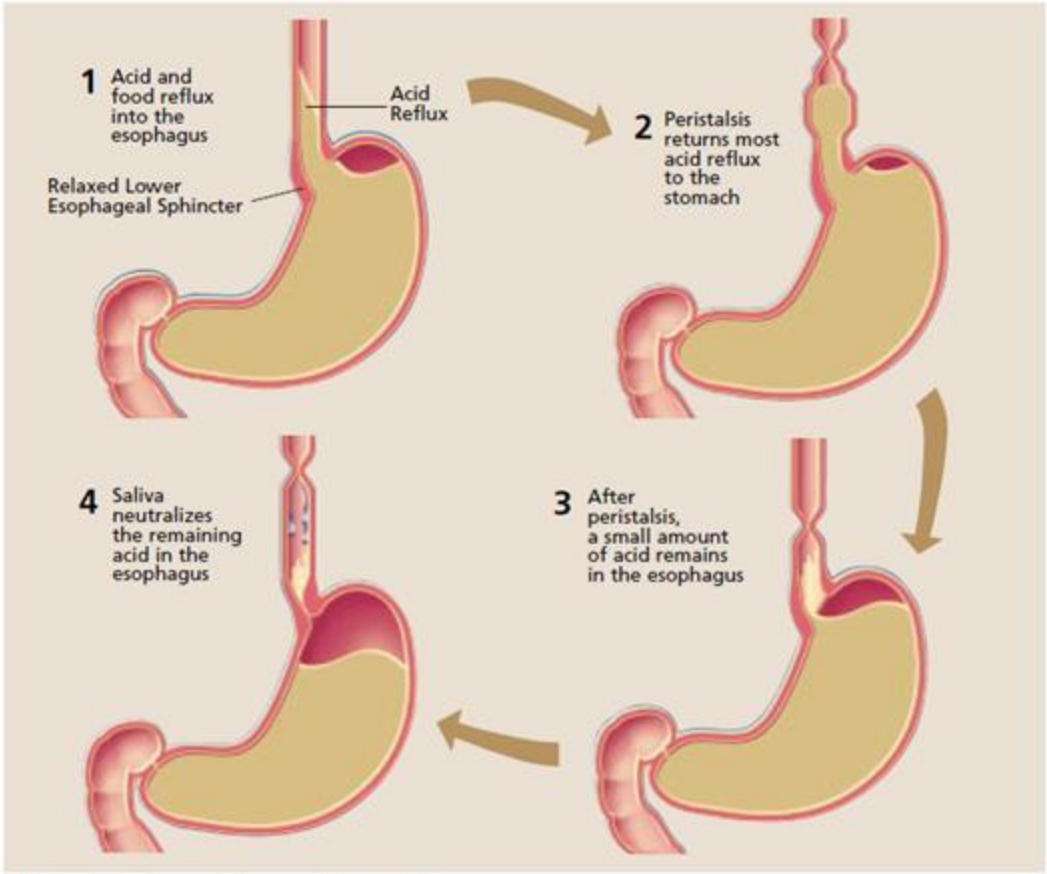

FIGURE 1. What happens during nonpathologic reflux.

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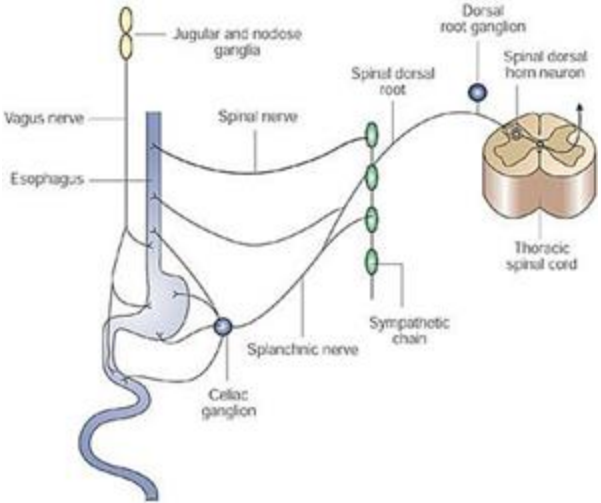
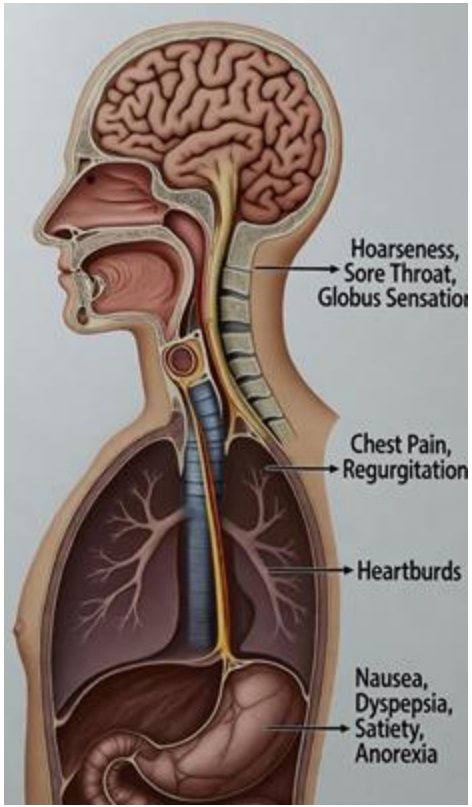
Kahrilas PJ, Clev Clin J Med 2003
Tack J, Pandolfino PJ, Gastroenterology 2018

Symptoms of GERD

Acid reflux is the most common cause of referred *pain* from the esophagus

- Classic Symptoms of GERD
  - Heartburn
  - Regurgitation
- Atypical GERD Symptoms
  - Chest pain
  - Water brash
  - Hoarseness
  - Globus Sensation
  - Cough
  - Wheezing/asthma





Sengupta et al, GI Motiliy Online 2006

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Initial Treatment Pathway

Patients with Typical Symptoms

- Presumptive Diagnosis of GERD
- ACG recommends 8 week trial of PPI therapy and re evaluation

Patients Presenting with alarm Symptoms

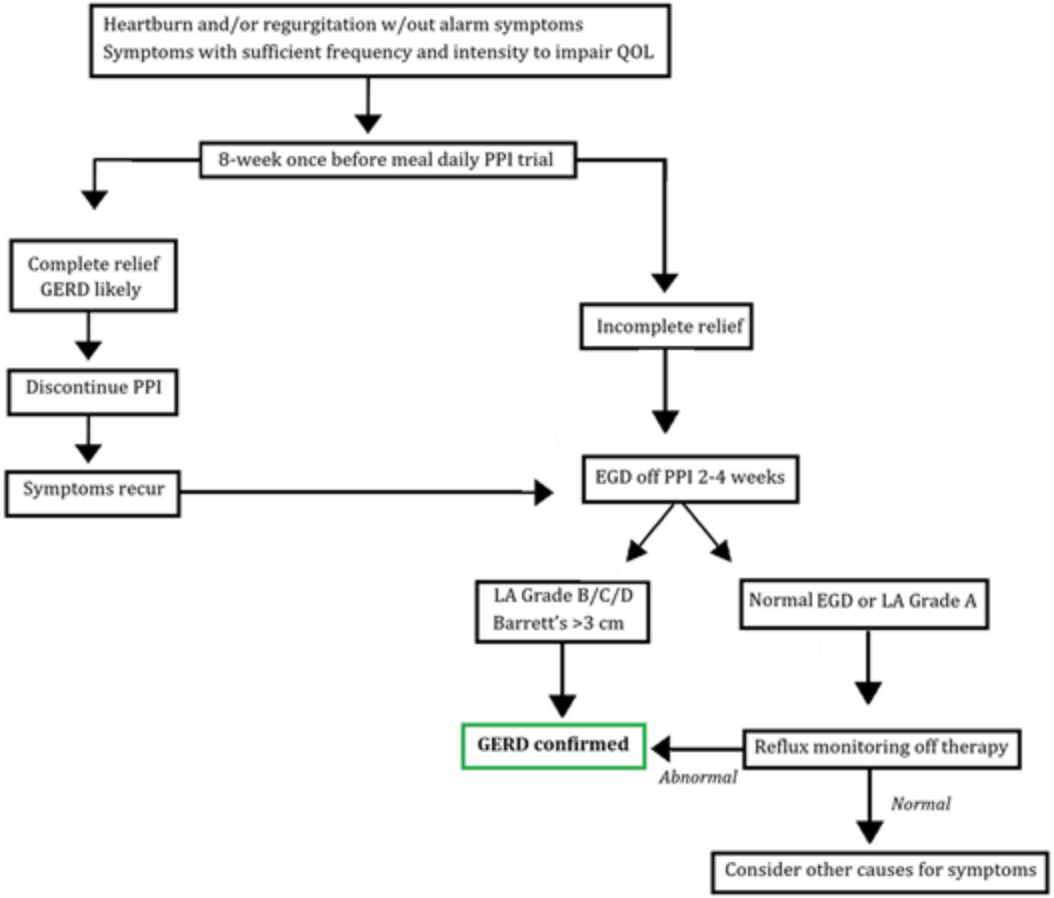
- Alarm symptoms: dysphagia, weight loss, gi bleeding, Hx of Barrett's, nausea and vomiting
- ACG recommends immediate referral for endoscopy

Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. Am J Gastroenterol. 2022 Jan 1;117(1):27-56.

Non Pharmacologic Interventions

- **Weight Loss:** The strongest evidence-based lifestyle intervention. Central adiposity increases intragastric pressure.
- **Head Elevation:** Elevate the head of the bed 6-8 inches using blocks or a foam wedge. *Note: Simply using extra pillows is ineffective.*
- **Meal Timing:** Avoid meals 2-3 hours before recumbency (bedtime) to reduce nocturnal acid exposure.
- **Trigger Avoidance:** Tobacco, alcohol, chocolate, caffeine, and spicy/fatty foods (tailored to patient).

ACG 2022 GERD Diagnosis Pathway



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What about all the bad stuff out there about PPI's?

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Addressing the PPI Safety Concerns

Common Concerns

- Kidney Disease
- Dementia
- Bone Fractures
- Pneumonia
- Macronutrient deficiency (Mg, B12)

What about the evidence
ACG Guidelines 2022: High-quality evidence confirms that PPI's are safe for long term use in appropriate indications.

- Risks are low
- *C. difficile* risk of modest but real
- Benefit > risk for erosive esophagitis and Barrett's
- Goal is to use the lowest effective dose

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Evidence

- Maintains healing from erosive esophagitis (93%) — Gyawali et al, Gastroenterology 2018
  - Relieves heartburn in only 56-77%
- May induce regression of extent or incidence of Barrett's — Spechler SJ, Dig Dis. 2014
- Associated with reduced risk of dysplasia in Barrett's (RR 25%) — El-Serag et al, Am J Gastroenterol 2004
- Associated with reduced risk of esophageal adenocarcinoma in Barrett's (RR 29%) — Singh et al, Gut 2014
- Cost-effective as a first trial, "step down" approach in management of chronic heartburn — Habu et al, J Gastroenterol 2005

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What about patients who don’t respond or have refractory symptoms?

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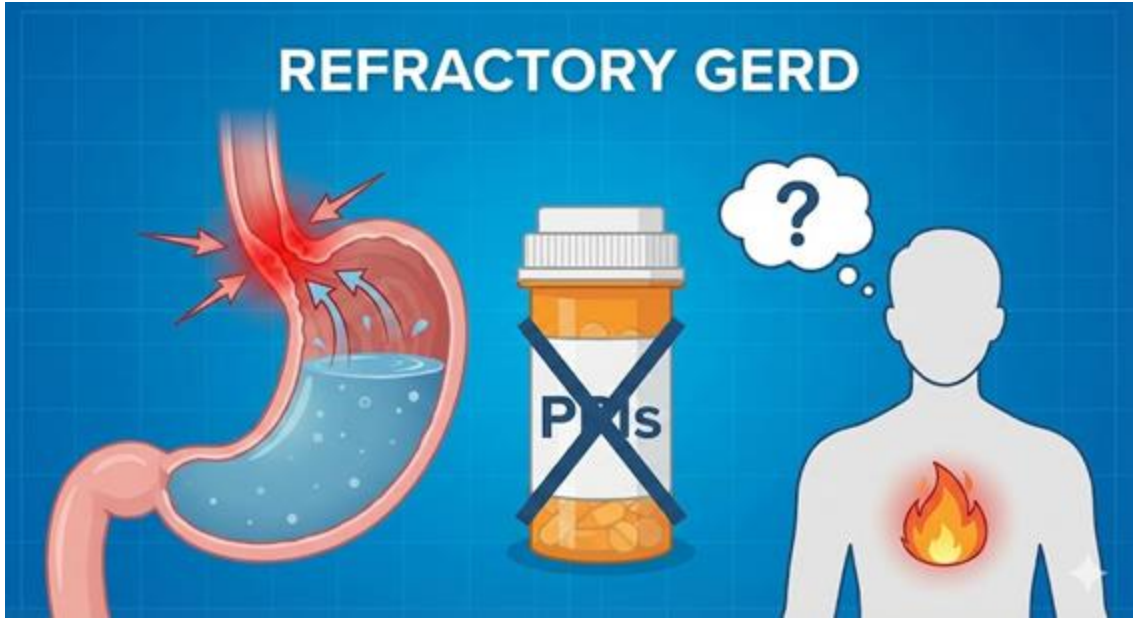
Refractory GERD

- Verify Adherence
  - Ensure PPI is being taken properly
- Optimize Therapy
  - Switch to different PPI
  - Twice daily dosing
- Refer and Test
  - Refer to GI for refractory symptoms despite twice daily therapy



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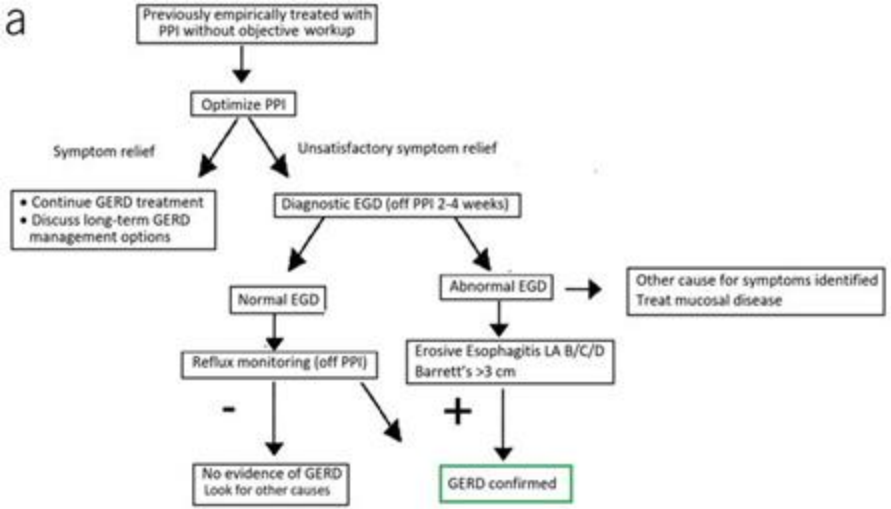
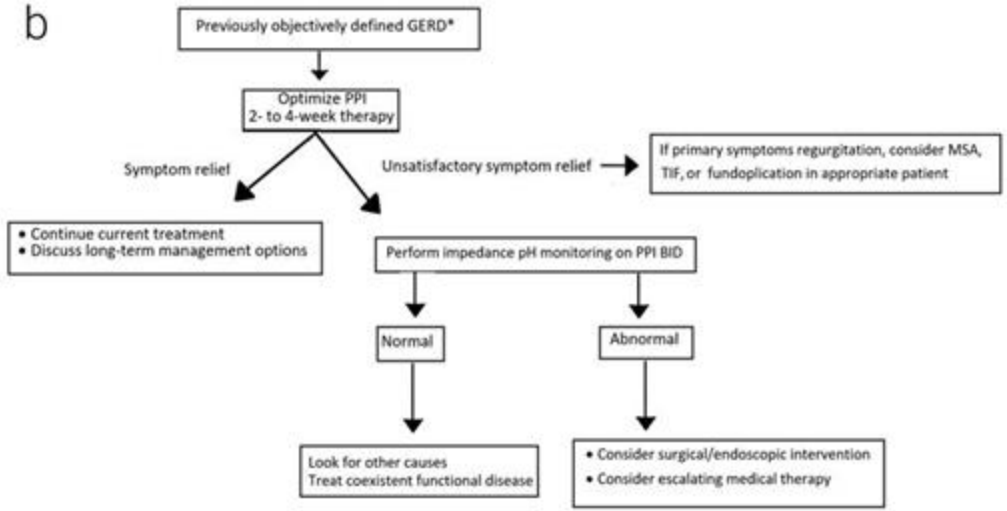
Gyawali et al, Gastroenterology 2018

ACG 2022 Refractory GERD Pathway





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Esophageal Testing

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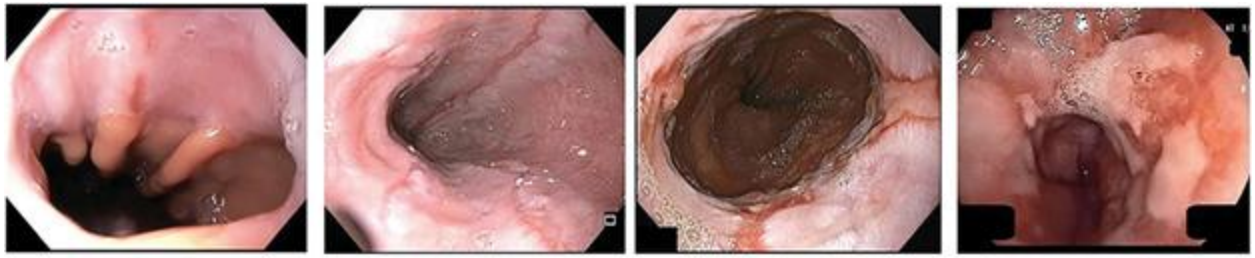
Esophagogastroduodenoscopy

- First test in patients with alarm symptoms
- Can objectively identify GERD related damage to the esophagus
  - LA Grade C and D Erosive Esophagitis
  - Barrett's Esophagus >3 cm with intestinal metaplasia on biopsy



LA-A
≥1 mucosal break, ≤5 mm, does not extend between mucosal folds

LA-B
≥1 mucosal break, >5 mm, does not extend between mucosal folds

LA-C
≥1 mucosal break, extends between mucosal folds, involves <75% of circumference

LA-D
≥1 mucosal break, involves >75% of circumference

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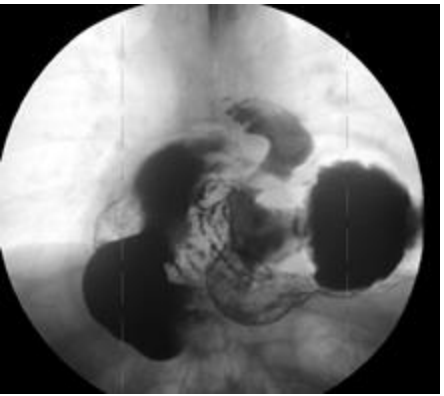
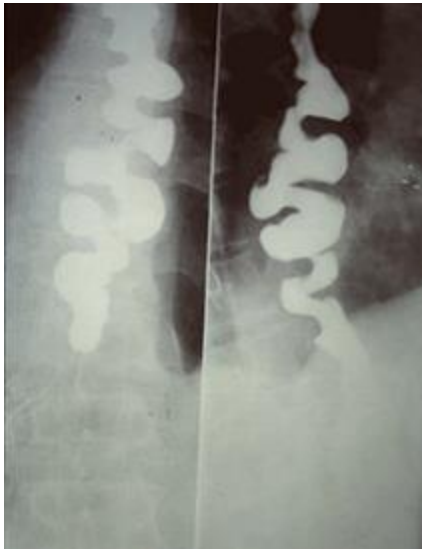
Spechler, Stuart J. Laine, Loren DeVault, Kenneth R. Nabulsi, Azmi Katz, Philip et al. Comparison of Los Angeles Grades of Erosive Esophagitis Scored by Local Investigators vs Central Adjudicators in a Clinical Trial. Clinical Gastroenterology and Hepatology, Volume 22, Issue 12, 2526 - 2528

Esophagram





- Quick Easy minimally invasive Test
- ACG 2022 does not recommend as the sole test for GERD
  - Poor sensitivity and specificity for GERD
- Useful for patients pre and post surgery, potentially identifying anatomic abnormalities, strictures
- Reflux up to the thoracic inlet increases sensitivity but not enough to be the sole test for GERD

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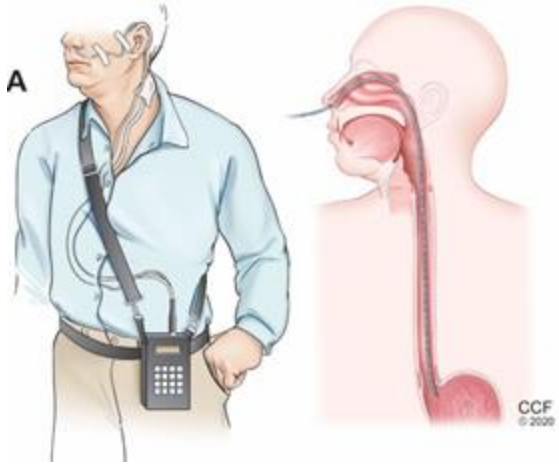
Esophageal pH Testing

- 24hrs, catheter based probe with two pH sensors and six impedance sensors
- Require either an EGD or manometry for optimal placement of the catheter from the nares
- Patient wears a recorder on a belt and pushes buttons to report symptoms, meal times, and supine positioning



- Considered gold standard for GERD diagnosis:
  Acid exposure time (AET) >6%, equivocal if 4-6%, DeMeester score tiebreaker

https://www.ccjm.org/content/87/4/223

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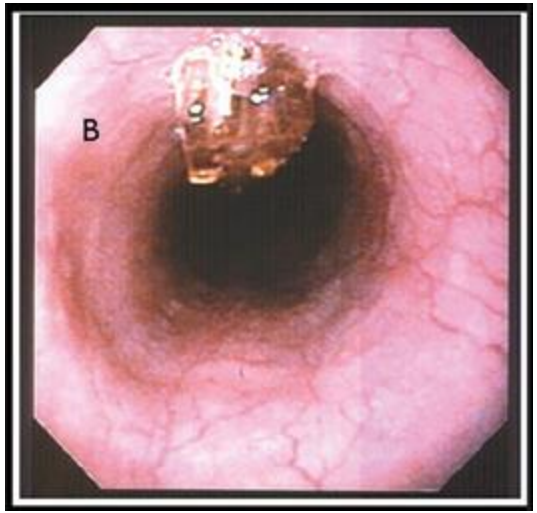
Bravo pH Monitoring

- Placed 6 cm proximal to lower esophageal sphincter
- Still requires EGD for placement
- Better tolerated, no catheter
- 48hr study vs 24hrs
- No gastric pH monitoring or impedance monitoring
- Heavily reliant on patient report



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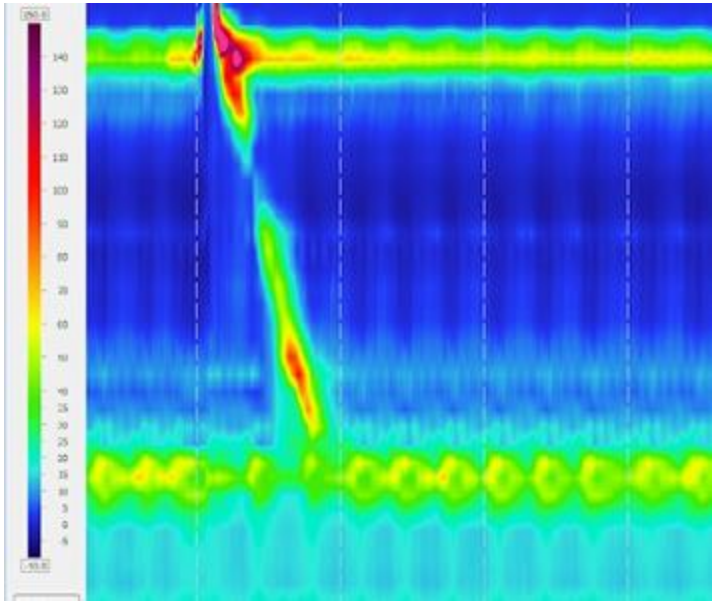
https://www.ccjm.org/content/87/4/223

High Resolution Esophageal Manometry

- Used to identify esophageal motility disorders that may present as GERD symptoms
- Poorly tolerated by patients
- Only 1-3% of patients with refractory GERD are found to have achalasia or a peristalsis
- HRM is helpful in assessing esophageal function prior to surgery
  - Absent contractility is a contraindication to fundoplication



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“Functional Reflux Disease”

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What is functional Reflux

Rome IV Functional Heartburn

- Burning retrosternal discomfort
- No symptom relief on optimal antisecretory therapy
- No evidence of GERD or EoE
- No esophageal motility disorders

Rome IV Reflux Hypersensitivity

- Burning retrosternal discomfort
- Normal endoscopy and absence of EoE
- No esophageal motility disorders
- Evidence of triggering symptom by reflux events despite normal acid exposure by pH impedance monitoring

https://theromefoundation.org/rome-iv/rome-iv-criteria/

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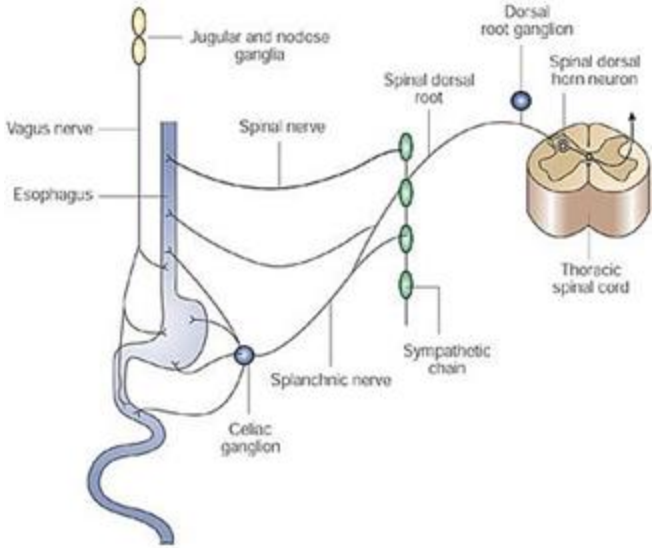
Visceral Afferent Signaling Pathways

- Just because acid reflux has been excluded in certain conditions of esophageal *pain*, that does not mean that there is no neuropathology that would be amenable to pharmacotherapy



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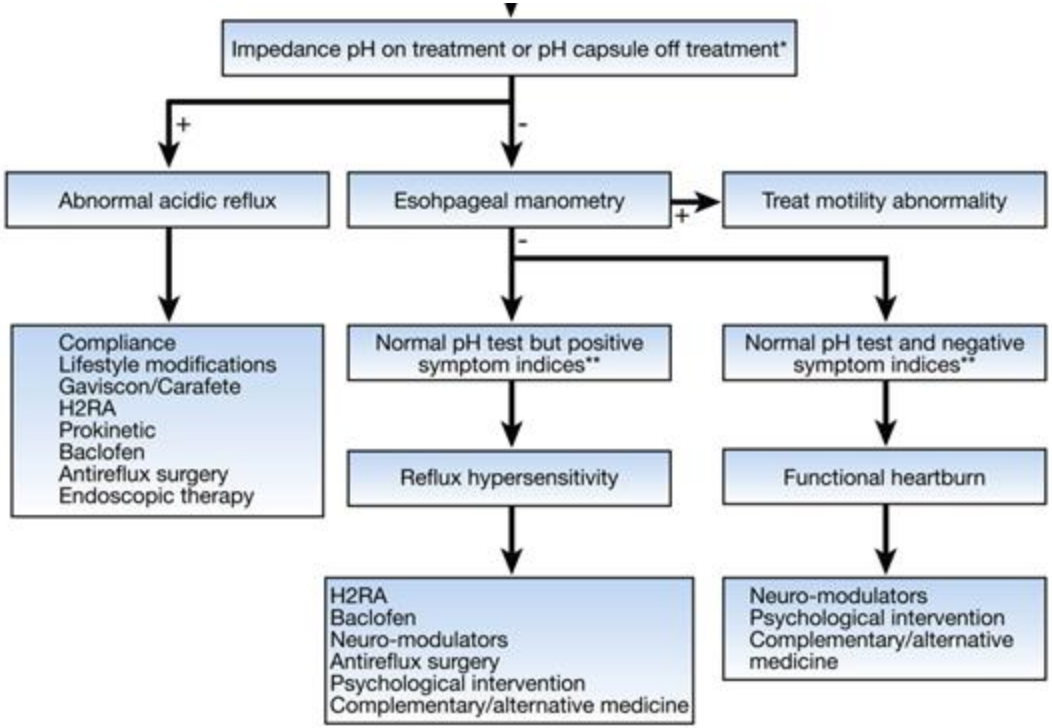
Sengupta et al, GI Motility Online 2006

Functional Heartburn



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Gyawali et al, Gastroenterology 2018

Pharmacotherapy for Functional Reflux

- AGA best-practice recommendations support neuromodulators as first-line pharmacologic therapy in functional heartburn and as add-on therapy when it overlaps with proven GERD
- Alternative therapies such as behavioral interventions, hypnotherapy, and acupuncture are also recommended.

Table 3. Neuromodulators Studied in Randomized-Controlled Trials of Patients With Functional or Nonfunctional Esophageal Disorders

Name	Class of drugs	Disorder	Dose	Response rate	Side effects
Imipramine[161]	TCAs	NCCP	50 mg/d	52%	QT prolongation
Imipramine[162]	TCAs	NCCP	50 mg/d	Significant	Dry mouth, dizziness
Imipramine[163]	TCAs	FH, RH	25 mg/d	37.2%	Constipation
Amitriptyline[164,165]	TCAs	NCCP, globus	10,25 mg/d	52%, significant	Excessive sleeping, dizziness
Sertraline[166]	SSRIs	NCCP	50–200 mg/d	57%	Nausea, restlessness
Sertraline[167]	SSRIs	NCCP	50–200 mg/d	Modest	Dry mouth, diarrhea
Paroxetine[168]	SSRIs	NCCP	10–50 mg/d	Modest	Fatigue, dizziness
Paroxetine[169]	SSRIs	NCCP	10–50 mg/d	21.7%	None
Citalopram[170]	SSRIs	RH	20 mg/d	Significant	None
Fluoxetine[171]	SSRIs	FH/RH	20 mg/d	Significant	Headache, dry mouth
Trazodone[160]	SRIs	Dysmotility	100–150 mg/d	29%–41%	Dry mouth, dizziness
Venlafaxine[172]	SNRIs	NCCP	75 mg/d	52%	Sleep disturbances
Ranitidine[176]	H2RAs	FH	300 mg/d	Significant	None
Theophylline[173]	Adenosine antagonists	NCCP	200 mg twice per d	58%	Nausea, insomnia, tremor
Gabapentin[174]	GABA analog	Globus	300 mg 3 times per d	66%	None

FH, functional heartburn; GABA, gamma-aminobutyric acid; NCCP, noncardiac chest pain; RH, reflux hypersensitivity; SNRIs, serotonin-norepinephrine reuptake inhibitors; SRIs, serotonin reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants.

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Fass R, Zerbib F, Gyawali CP. AGA Clinical Practice Update on Functional Heartburn: Expert Review. Gastroenterology. 2020 Jun;158(8):2286-2293.

What about anatomic causes of reflux?

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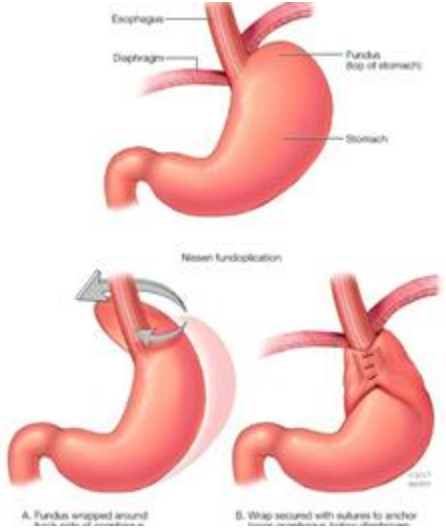
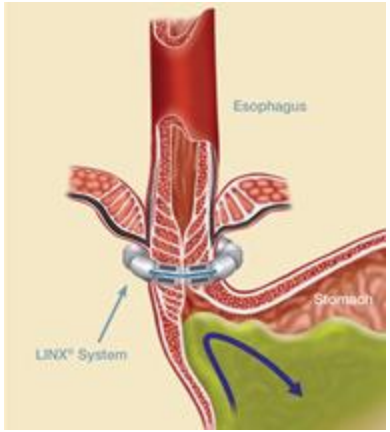


Surgery for Refractory Reflux

ACG 2022 Recommendations for Surgical or Endoscopic Therapies for GERD

- Used in patients with objective findings of GERD, large hiatal hernias, and/or persistent troublesome GERD symptoms
- Transoral incisionless fundoplication (TIF) useful in patients without hiatal hernia and reflux esophagitis but have troublesome regurgitation or GERD
- Magnetic Sphincter Augmentation (LINX) useful in patients with regurgitation who fail medical management



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https://www.oregonclinic.com/resource/laparoscopic-magnetic-sphincter-augmentation-linx/

PPI Cessation Rates 3-5 years post procedure

LNF remains the most effective for absolute acid control, though MSA demonstrates non-inferiority in many matched cohorts. TIF offers significant improvement but has a higher rate of partial PPI resumption.

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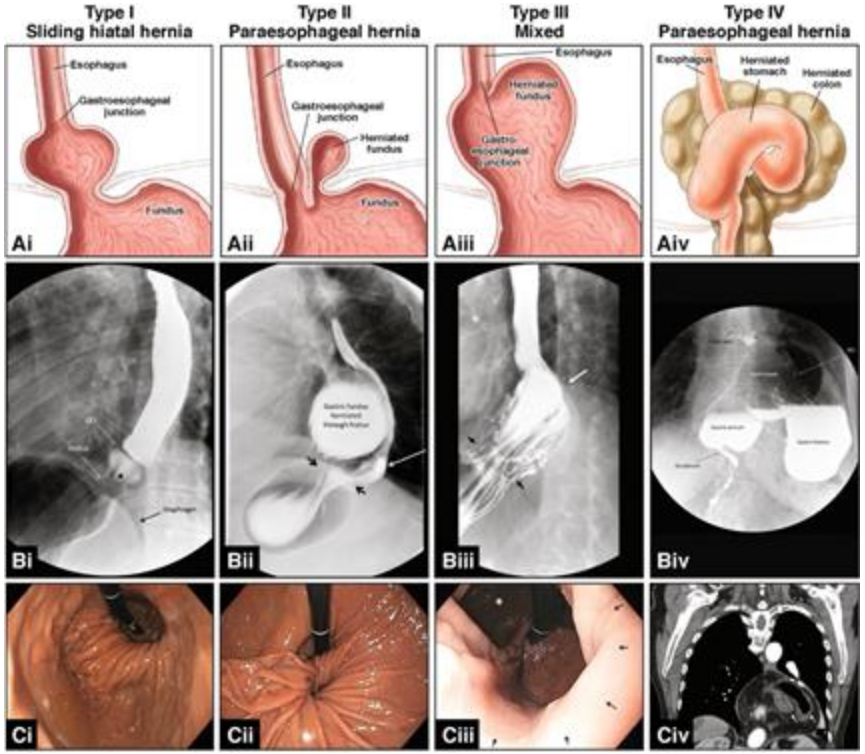

Types of Hiatal Hernias

- **Type I:** Sliding type hernia with the gastroesophageal junction and part of the stomach moving into the chest.
- **Type II:** Herniation of the gastric fundus while the gastroesophageal junction remains normal.
- **Type III:** Combination of sliding and paraesophageal components, with both the junction and fundus herniated.
- **Type IV:** Herniation of other abdominal organs, like the colon or spleen, into the thoracic cavity.

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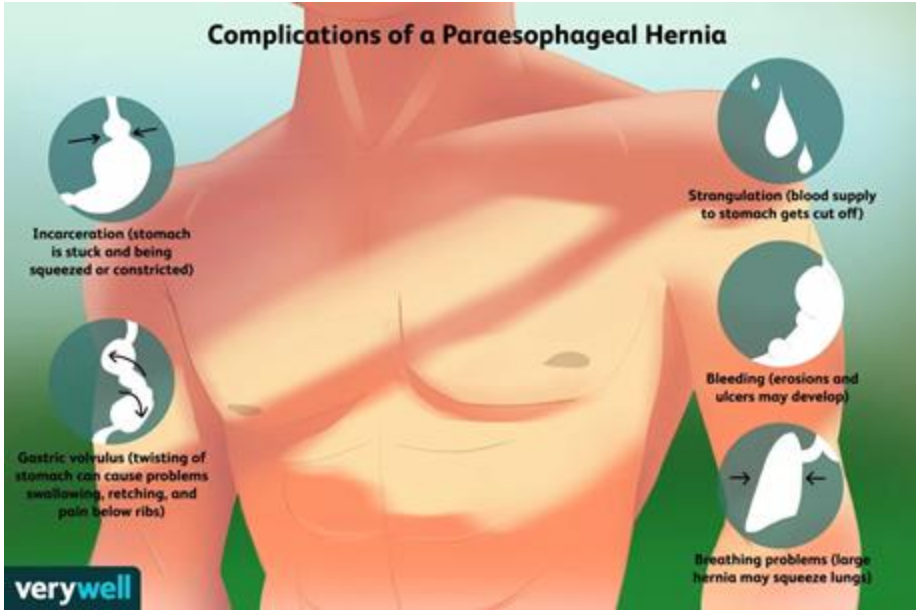
Callaway, James P. et al. Hiatal and Paraesophageal Hernias. Clinical Gastroenterology and Hepatology, Volume 16, Issue 6, 810 - 813

Symptoms of Paraesophageal Hernia

- Pain after eating: chest or upper abdominal discomfort, especially after meals.
- Difficulty swallowing: hernia pressure can cause dysphagia.
- Heartburn and regurgitation: stomach contents flow back into the esophagus.
- Shortness of breath: hernia may affect lung or stomach function.
- Iron deficiency anemia: from Cameron's erosions due to ischemic gastric mucosa at the hiatus.



Verywell / Laura Porter

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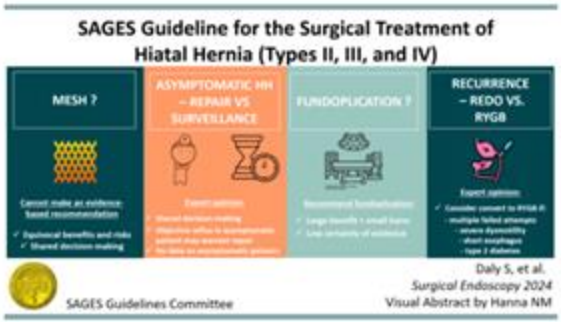
Guidelines for Paraesophageal Hernia Repair


RICHARD E. CLARK MEMORIAL PAPER FOR GENERAL THORACIC SURGERY

The Impact of Age and Need for Emergent Surgery in Paraesophageal Hernia Repair Outcomes

Lyn-Yeng Wong, MD,[1] Niharika Parsons, PhD,[2] Elizabeth A. David, MD, MAS,[3] William Burfeind, MD,[3] and Mark F. Berry, MD[3]

ABSTRACT



Symptomatic Patients

- Surgery for symptoms like chest pain, dysphagia, or reflux.
- Urgent surgery for obstruction, strangulation, or perforation carries higher risks; elective surgery is preferred post-stabilization.

Asymptomatic Patients

- Surgery considered to reduce sudden complication risk.

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Watchful Waiting vs Elective Surgery

- **Watchful Waiting**
  - The 2017 article by Jung et al. found that watchful waiting is better than elective surgery until the mortality rate for elective repair reaches 0.5%.
- **Progress in Minimally Invasive Surgery**
  - Damani et al. (2022) analyzed the ACS-NSQIP database and found a mortality rate of 0.5% for elective paraesophageal hernia repair in patients over 65.
  - Findings indicate minimally invasive surgery may be preferable to watchful waiting.

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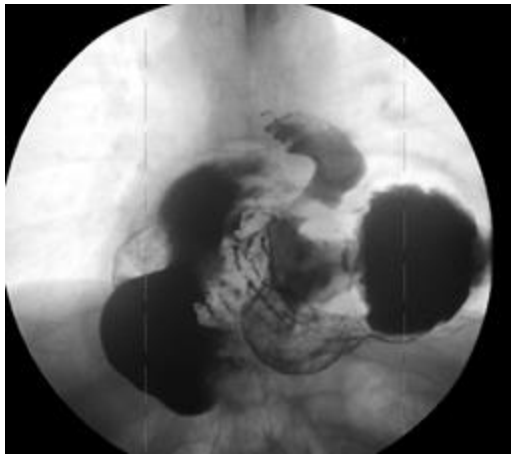
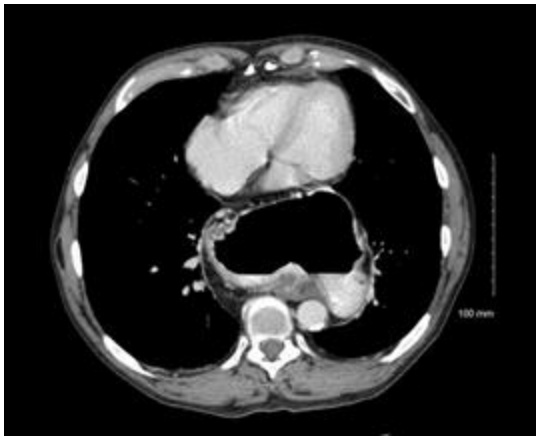
Damani, T., Ray, J.J., Farag, M. *et al.* Elective paraesophageal hernia repair in elderly patients: an analysis of ACS-NSQIP database for contemporary morbidity and mortality. *Surg Endosc* **36**, 1407–1413 (2022).

Jung, J.J., Naimark, D.M., Behman, R. *et al.* Approach to asymptomatic paraesophageal hernia: watchful waiting or elective laparoscopic hernia repair?. *Surg Endosc* **32**, 864–871 (2018).





Paraesophageal Hernia: Diagnostics

- **Barium Swallow:** Visualizes anatomical details and hernia type, guiding surgical planning.
- **Upper Endoscopy:** Detects mucosal injury or Barrett's esophagus for crucial management information.
- **Esophageal Manometry:** Measures motility to identify functional issues impacting surgical decisions.
- **Additional Imaging:** CT scans or other imaging for complex hernias to provide comprehensive anatomical overview.

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Minimally Invasive Repair

Benefits of Minimally Invasive Repair

- Lower perioperative morbidity and mortality
- Shorter recovery time and hospital stay
- Similar long-term outcomes to open repair

Laparoscopic Paraesophageal Hernia Repair

- Preferred procedure in SAGES 2024 Guidelines

Robotic Paraesophageal Hernia Repair

- Increasingly preferred

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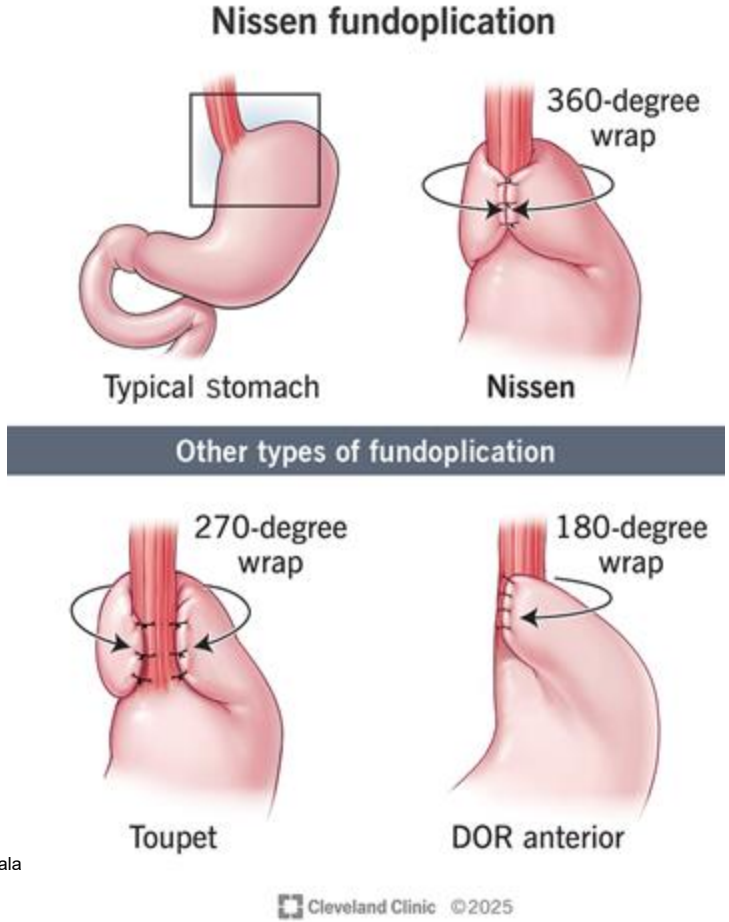
Fundoplication

- Complete vs partial
- Address GERD symptoms
- SAGE 2024 guidelines found patients undergoing PEH may benefit from fundoplication
  - Partial fundoplication may be a better option based on GERD studies



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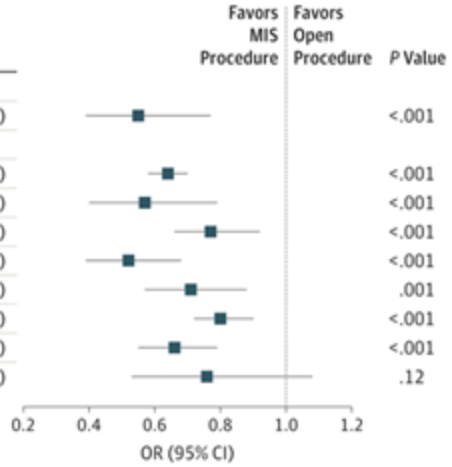
Daly S, Kumar SS, Collings AT, Hanna NM, Pandya YK, Kurtz J, Kooragayala K, Barber MW, Paranyak M, Kurian M, Chiu J, Ansari MT, Slater BJ, Kohn GP. SAGES guidelines for the surgical treatment of hiatal hernias. Surg Endosc. 2024 Sep;38(9):4765-4775.

Long-Term Outcomes:
Minimally Invasive Paraesophageal Hernia Repair

Source	MIS vs Open, %	OR (95% CI)	P Value
Mortality classification			
In-hospital mortality	0.6 vs 3.0	0.55 (0.39-0.77)	<.001
Morbidity classifications			
Wound complications	0.4 vs 2.9	0.64 (0.58-0.70)	<.001
Bleeding complications	0.6 vs 1.8	0.57 (0.40-0.79)	<.001
Urinary complications	2.6 vs 6.6	0.77 (0.66-0.92)	<.001
Septic complications	0.9 vs 3.9	0.52 (0.39-0.68)	<.001
Respiratory complications	1.8 vs 3.6	0.71 (0.57-0.88)	.001
Cardiac complications	7.7 vs 16.6	0.80 (0.72-0.90)	<.001
Intraoperative injury	2.5 vs 6.1	0.66 (0.55-0.79)	<.001
Thromboembolic complications	0.6 vs 1.5	0.76 (0.53-1.08)	.12



- Durable Symptom Relief
  - Most patients experience lasting symptom relief, significantly improving their overall quality of life after surgery.
  - Lazar et al (2017) reported dysphagia, reflux, and regurgitation symptoms improved in 95% of patients, 90% pleased with surgery
- Low Complication Rate
  - Complications following surgery are infrequent, making this technique safe and preferred for suitable patients. (McLaren et al., 2017)

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Lazar DJ, Birkett DH, Brams DM, Ford HA, Williamson C, Nepomnayshy D. Long-Term Patient-Reported Outcomes of Paraesophageal Hernia Repair. JSLS. 2017 Oct-Dec;21(4)

McLaren PJ, Hart KD, Hunter JG, Dolan JP. Paraesophageal Hernia Repair Outcomes Using Minimally Invasive Approaches. JAMA Surg. 2017;152(12):1176–1178.

Paraesophageal Recurrence

- Recurrence:
  - Defined as a 2 cm fundus measurement or 10% stomach size increase above the hiatus.
  - Rates vary (25-50%), but most are well tolerated.
  - Lazar et al. (2017) found 54% of patients needed medication for symptoms after 6.6 years.
- Reoperation:
  - Though recurrence is high, reoperation rates are low, decided case-by-case, often for younger patients.

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Bhargava A, Andrade R. Giant paraesophageal hernia: What do we really know? JTCVS Tech. 2020 Aug 13;3:367-372

Lazar DJ, Birkett DH, Brams DM, Ford HA, Williamson C, Nepomnayshy D. Long-Term Patient-Reported Outcomes of Paraesophageal Hernia Repair. JSLS. 2017 Oct-Dec;21(4)

Key Takeaways

- Empiric PPI therapy at a low dose is the best initial treatment in patients with typical GERD or without alarm symptoms
- Promptly refer all patients with alarm symptoms to GI or Surgery
  - nausea, vomiting, dysphagia, pain after meals
- Re-evaluate after 8 weeks
  - Ensure compliance and lifestyle modifications
- Refer to GI for refractory GERD
- PPIs are safe and effective
- Refer all symptomatic hiatal or paraesophageal hernias to discuss surgery
  - Surgery in the minimally invasive era is safe and better tolerated leading to improved QOL

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Thank You

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