



Approach to the Evaluation and Management of GERD

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Prevalence and Symptoms


30% of adults in the USA report weekly symptoms of GERD
- among the most common diseases seen by gastroenterologists, surgeons and primary care physicians

Typical: heartburn, regurgitation
- approximately 70% sensitive and specific for GERD

Atypical: non-cardiac chest pain

Extraesophageal: laryngeal and pulmonary
- hoarseness, throat clearing, chronic cough, laryngitis, pharyngitis, pulmonary fibrosis, asthma and dental erosions

Distinguish from dyspepsia (epigastric discomfort without heartburn or regurgitation) which may prompt more urgent endoscopic evaluation



Prevalence and Symptoms

Up to 50% of patients with GERD do not have adequate relief with empirical proton pump inhibitor (PPI) therapy – need further evaluation

Gastro-esophageal reflux is a physiologic process
- transient lower esophageal sphincter (LES) relaxation

Mediating factors
- anti-reflux barrier (LES and crural diaphragm)
- esophageal peristalsis
- salivation
- gastric motility


Patient Education

GERD mechanisms
– reflux problem, not acid problem

Weight management

Lifestyle and dietary behaviors

- quit smoking
- smaller, more frequent meals
- avoid fatty foods, alcohol, caffeine, chocolate, mint, spicy/acidic foods
- avoid lying down 3 hours after eating
- elevated head while sleeping
- loose-fitting clothes (no girdles)




Patient Education

Relaxation strategies

- deep, diaphragmatic breathing
- meditation

Brain-gut axis awareness


– bidirectional communication between the central and enteric nervous system, linking emotional and cognitive centers of the brain with peripheral intestinal functions

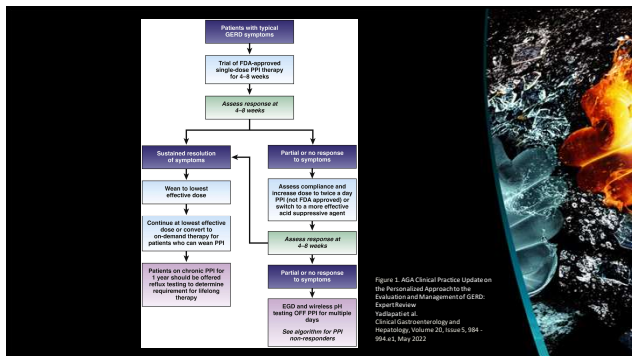


Patient Education

Alarm symptoms:
(may represent strictures, ulceration and/or malignancy)

- dysphagia (difficulty swallowing)
- odynophagia (painful swallowing)
- bleeding
- anemia
- weight loss
- vomiting





Indications for Objective Testing

Troublesome (>2x weekly) heartburn, regurgitation and/or non-cardiac chest pain that does not respond to PPI trial should be referred for endoscopy

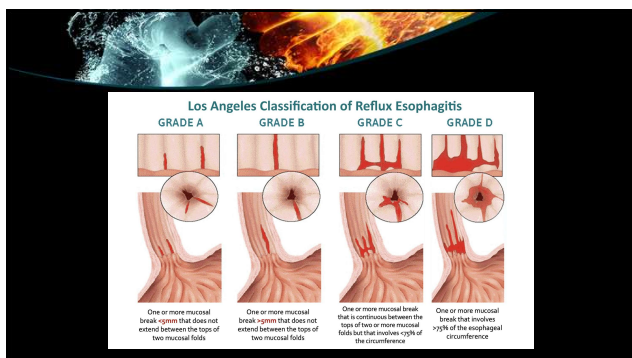
Isolated extra-esophageal symptoms with suspicion of reflux etiology

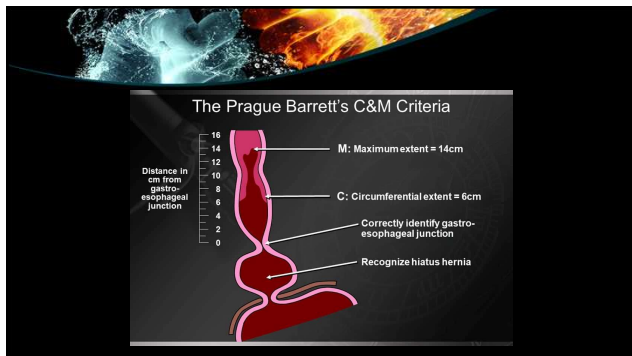
Endoscopy documentation should include:

- Los Angeles classification of erosive esophagitis (if present)
- Prague classification of Barrett's esophagus (if present)

Confirmatory findings of LA Class B or greater esophagitis and/or long-segment (>3cm) Barrett's esophagus – up to 80% of patients will not meet this criteria

Barium radiography (esophagram or upper GI series) has a poor sensitivity and specificity for GERD and not recommended as a diagnostic test





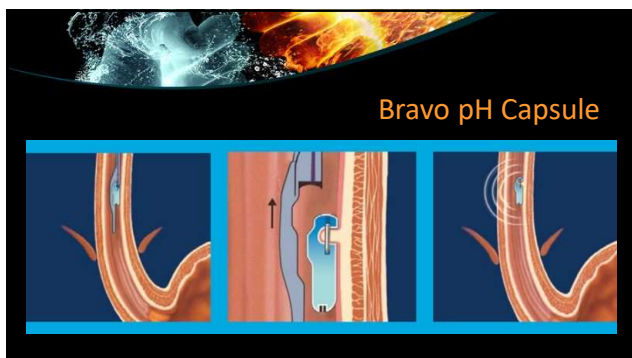
Ambulatory Reflux Monitoring

Catheter-based

- placed intranasally
- non-sedated
- 24 hours data

Wireless pH capsule (Bravo)

- placed endoscopically while sedated
- up to 96 hours data
- better tolerated




Reflux esophagitis vs hypersensitivity

LA grade A esophagitis and/or elevated acid exposure time (AET) >4% for ≥ 1 day is borderline for GERD diagnosis

LA grade B or greater esophagitis and/or AET >6% for ≥ 2 days supports GERD diagnosis


LA grade C or D esophagitis, bi-positional (both upright and supine) reflux and AET >12% or DeMeester score >50 and/or large hiatal hernia (>5cm) represents severe GERD



Reflux esophagitis vs hypersensitivity

Absence of erosive reflux on endoscopy and acid exposure time (AET) of <4% on wireless pH monitoring = high likelihood of reflux hypersensitivity (functional esophageal disorder)

- consider GI psychologist referral for Cognitive Behavioral Therapy (CBT), esophageal directed hypnotherapy and/or pharmacologic neuromodulation (TCA therapy – amitriptyline, nortriptyline)



Therapy Optimization


Aggressive lifestyle modifications

- smoking, weight, diet

Optimal PPI therapy

- Timing of dose (30-60 minutes before meal)
- Once daily dosing should be given before first meal of the day
- Escalation to BID dosing
- Switching to different PPI at daily dosing - once
- Weaning to lowest effective dose – except in:
 - LA Grade B esophagitis or greater
 - Biopsy proven Barrett's esophagus
 - Peptic stricture

Severe GERD requires indefinite PPI therapy and/or anti-reflux procedure




Are Proton Pump Inhibitors safe?

Kidney Disease?
 - Although evidence that patients who used PPIs for longer durations had higher risks for CKD, those who used PPIs for 2 years or more actually appeared protected against CKD

Dementia?
 - PPIs may block V-ATPases in mice leading to increased isoforms of amyloid-β (Alzheimer's protein)
 - Patients who initiate PPIs have more comorbidities and those who do not. In the human study, adults selected for PPIs also had strikingly higher rates of depression, stroke and polypharmacy

Bone Fracture?
 - Data is conflicting. Currently nothing to support routine use of bone mineral density monitoring in PPI users

Myocardial Infarction?
 - PPIs metabolized by cytochrome P450 isoenzyme CYP2C19, which activates clopidogrel. Concern that may decrease anti-platelet effect. 2010 COGENT study provided reassurance that PPIs do NOT meaningfully interact with clopidogrel




Are Proton Pump Inhibitors Safe?

Infections?
 - SIBO, Salmonella, Campylobacter, SBP, C. Diff, Pneumonia
 - quality of evidence is low to very low

Micronutrient Deficiencies?
 - Calcium – acid suppression only affects water insoluble calcium
 - water soluble calcium, milk, cheese unaffected
 - Iron - conflicting data, In Zollinger-Ellison Syndrome no, in Hemochromatosis maybe
 - Magnesium – rare reaction
 - Vitamin B12 – most studies report 2-4 fold risk of deficiency

Gastrointestinal Malignancy?
 - low to no increased risk for gastric or colorectal cancers




Are Proton Pump Inhibitors Safe?

Overall, studies suggesting risk were mostly observational studies with low to very low quality of evidence
 - Absolute excess risk in these studies was low, typically less than 1%

Benefit of PPI therapy for GERD, Barrett's esophagus and NSAID bleeding prophylaxis is demonstrated by both observational and randomized controlled trials with moderate to high quality of evidence in most studies

In summary:
 Correlation does not equal causation
 If a patient has a definite indication for PPI therapy, there is little compelling evidence to withhold treatment



Adjunctive Pharmacotherapy


Alginate antacids for occasional breakthrough symptoms (Gaviscon)
- interact with acid in the stomach to form a gel-like substance called a raft that acts as a physical barrier

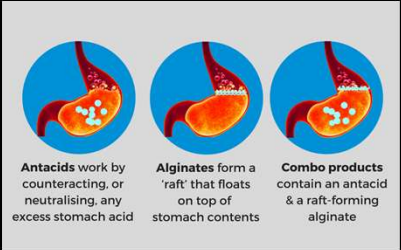
H2RA (famotidine) at bedtime, for nocturnal symptoms – use limited by tachyphylaxis

Baclofen for regurgitation/belching – inhibits transient LES relaxation

Prokinetics for coexistent gastroparesis
- metoclopramide, erythromycin, prucalopride
- not indicated for GERD without gastroparesis
- limited by tachyphylaxis

Sucralfate – not recommended outside of pregnancy, may be useful for bile reflux





Antacids work by counteracting, or neutralising, any excess stomach acid

Alginates form a 'raft' that floats on top of stomach contents


Combo products contain an antacid & a raft-forming alginate

Other functional esophageal disorders

Esophageal hypersensitivity
- perception of non-painful esophageal stimuli as being painful and of painful stimuli being even more painful
- PPI therapy does not prevent reflux

Hypervigilance
- increased awareness and amplification of esophageal symptoms and sensations

Behavioral disorders
- Supragastric belching – fast and frequent (hundreds to thousands of times daily), does not vent stomach
- Rumination – food is brought up, rechewed, reswallowed or spit out



Management of extraesophageal reflux

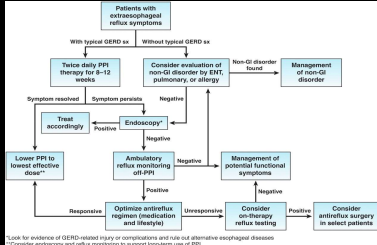


Figure 1. AGA Clinical Practice Update on the Diagnosis and Management of Extraesophageal Gastroesophageal Reflux Disease: Expert Review. Chan, Juan W, et al. Clinical Gastroenterology and Hepatology, Volume 21, Issue 6, 1414 - 1421.e3, June 2023

Anti-reflux Procedures

Laparoscopic fundoplication (Nissen)

- non-obese patient (BMI < 35)
- partial fundoplication reduces risk of hiatal hernia recurrence, dysphagia, gas/bloat and inability to vomit, but more reflux

Magnetic sphincter augmentation (LINX)

Endoscopic procedures:

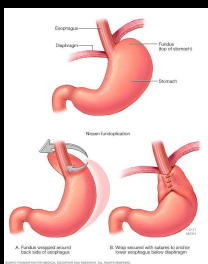
- Transoral incisionless fundoplication (TIF)
- Stretta – radiofrequency balloon to reshape the LES

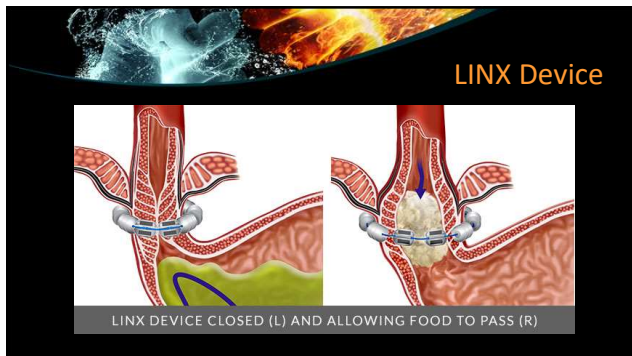
Roux-en-Y gastric bypass

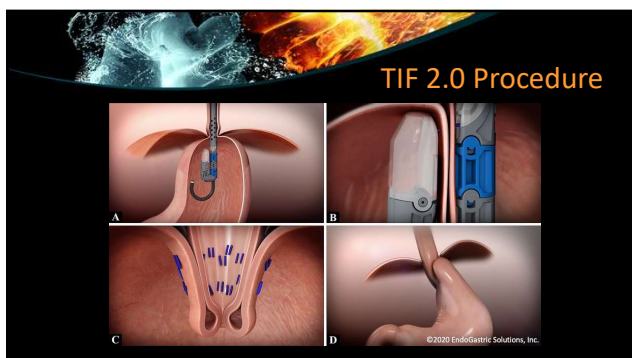
- effective in obese patient or salvage in non-obese patients

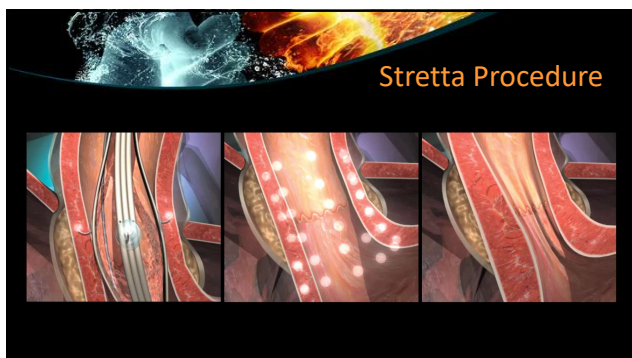
Sleeve gastrectomy – not recommended as can worsen GERD

Nissen Fundoplication












Endoscopic, surgical, or medical treatment for adults with GERD

Multi-Society Consensus Conference and Guideline



<p>OPERATIVE</p> <p>Either Magnetic Sphincter Augmentation (MSA) or Nissen fundoplication</p> 	<p>NON-OPERATIVE MANAGEMENT</p> <p>Transoral Incisionless Fundoplication (TIF) 2.0 & Stretta may be superior to Proton Pump Inhibitors</p> 	<p>ENDOSCOPY</p> <p>Endoscopic treatments may be inferior to Nissen</p> 
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Slater BJ, et al. *Surgical Endoscopy* 2022. Visual Abstract by Rodriguez-Luna MR.

SAGES MULTI-SOCIETY CONSENSUS CONFERENCE AND GUIDELINE ON THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) (2022)
Slater, Behary, et al. <https://www.sages.org/publications/guidelines/multi-society-consensus-conference-and-guideline-on-the-treatment-of-gerd>

Preoperative evaluation of adults with GERD

Multi-Society Consensus Conference and Guideline




<p>Typical symptoms</p> <p>Endoscopy Los Angeles Grade C or D esophagitis pH monitoring No more testing required</p> 	<p>EXTRA-ESOPHAGEAL</p> <p>symptoms and pts with equivocal initial testing need more diligent workup</p> 	<p>Research Recommendations:</p> <ul style="list-style-type: none"> Standardization of terminology Written documentation of endoscopic findings <ul style="list-style-type: none"> Photo documentation Newer technologies <ul style="list-style-type: none"> High resolution esophageal manometry Endo-FLIP
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Slater BJ, et al. *Surgical Endoscopy* 2022. Visual Abstract by Gallings, AT.

SAGES MULTI-SOCIETY CONSENSUS CONFERENCE AND GUIDELINE ON THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) (2022)
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Partial vs. complete fundoplication for adults with GERD

Multi-Society Consensus Conference and Guideline

<p>Partial</p> <p>In adult patients with GERD + esophageal dysmotility</p> 	<p>Benefits of Partial over Complete</p> <ul style="list-style-type: none"> Fewer Heartburn Recurrences Fewer Postop dysphagia Fewer Gas, bloating, inability to vomit >1 year 	<p>Downfalls of Partial over Complete</p> <ul style="list-style-type: none"> More objective reflux >1 year More subjective reflux >1 year 
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SAGES MULTI-SOCIETY CONSENSUS CONFERENCE AND GUIDELINE ON THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) (2022)
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Future Therapies

Potassium Competitive Acid Blockers (PCAB)
- Vonoprazan
- FDA approved as of November 1, 2023
- First approved in Japan December 2014

PPIs	P-CABs
Prodrug and unstable in acid	No need for conversion and stable in acid
Irreversible binding to the external surface of proton pump	Reversible binding to K ⁺ binding domain of proton pump
Need to stimulate proton pump	No food effect
Inhibit activated proton pump only	Block both resting and stimulated proton pump
Take 4-5 days to maximal effect	On demand control due to Fast onset

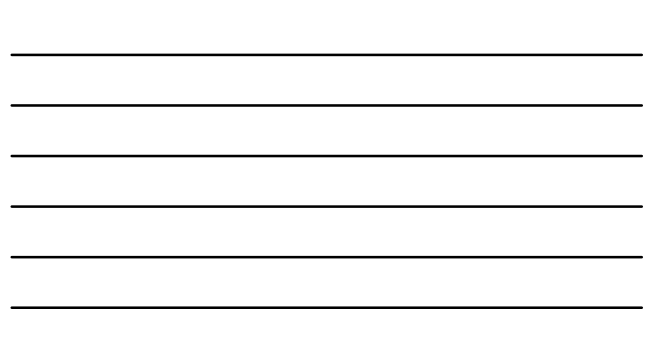


Patients with esophageal symptoms with unproven GERD and incomplete response to PPI trial for 4-8 weeks
(All patients should undergo pH monitoring without slow-wave disease)

EDD off PPI for 7 days
If EGD without Los Angeles BGD esophagitis or 80% segment to 3rd Barrett's esophagus → concurrent prolonged wireless pH monitoring off PPI

EGD: No esophageal disease and Physiologic acid exposure (pHi < 4.2%, on at least 2 days)	EGD: Los Angeles A esophagitis and Borderline acid exposure (> 1 day A/E 2-4 GHz, not meeting GERD criteria)	EGD: Los Angeles BGD esophagitis and Borderline acid exposure (> 2 days with A/E 2-4 GHz)
No GERD, likely functional esophageal disorder	Borderline GERD	GERD
1. Stop PPI 2. HRA if reversion or esophageal cancer disease suspected 3. Evaluate nutritional status, get correct bodyweight, or malabsorption	1. Discontinue proton pump inhibitors 2. Aggressive therapy with antacids/alginate if symptomatic 3. Evaluate nutritional status, get correct bodyweight, or malabsorption as indicated	1. Continue PPI to control symptoms 2. Aggressive therapy with antacids/alginate if symptomatic 3. Evaluate nutritional status, get correct bodyweight, or malabsorption as indicated
Controlled symptoms after optimization (HRA to be done off PPI for 4 weeks and done if therapy with PPI discontinued) Unprovoked symptoms after optimization (HRA to be done on PPI for 4 weeks and done if therapy with PPI discontinued) Unprovoked symptoms after optimization (HRA to be done off PPI for 4 weeks and done if therapy with PPI discontinued)	Controlled symptoms after optimization (HRA to be done off PPI for 4 weeks and done if therapy with PPI discontinued) Unprovoked symptoms after optimization (HRA to be done on PPI for 4 weeks and done if therapy with PPI discontinued)	Controlled symptoms after optimization (HRA to be done off PPI for 4 weeks and done if therapy with PPI discontinued) Unprovoked symptoms after optimization (HRA to be done on PPI for 4 weeks and done if therapy with PPI discontinued)

Figure 3. AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD. *Gastroenterology*, Volume 152, Issue 5, 954-964.e4, May 2017





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