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- Colon
- Colorectal Cancer Prevention
- Endoscopy Video Forum
- Esophagus
- Functional Bowel Disease
- General Endoscopy
- GI Bleeding
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All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.
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ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2022 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2023 for this activity.

MOC QUESTION
If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.
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**Week 23 – June 9, 2022**
*Overcoming the Challenges & Mitigating the Disparities in Our LGBTQI+ Patients: A Digestive Diseases Health Perspective*
Sonali Paul, MD, MS
June 9, 2022 at Noon Eastern and **NEW! 8pm Eastern!**

**Week 24 – June 16, 2022**
*Hereditary Pancreatic Cancers: What Should We Screen and How?*
Yasmin G. Hernandez-Barco, MD
June 16, 2022 at Noon Eastern and **NEW! 8pm Eastern!**

Visit [gi.org/ACGVGR](http://gi.org/ACGVGR) to Register
Disclosures

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Sebela Pharmaceuticals: Consultant
Phathom Pharmaceuticals: Consultant
AstraZeneca: Advisory Board Member

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Medscape: Consultant
Phathom Pharmaceuticals: Consultant
RJS Mediagnostix: Advisory Board
Ironwood Pharmaceuticals: Consultant, Research Grant (institution)
Medtronic: Consultant (institution)
StatLink MD: Consultant (institution)

*All of the relevant financial relationships listed for these individuals have been mitigated

ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease

Philip O. Katz, MD, MACG
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Jay Monahan Center for Gastrointestinal Health
Weill Cornell Medicine
New York, New York
Co Authors

- Kerry Dunbar MD
- Felice Schnoll-Sussman MD
- Katarina Greer MD (Grade methodologist)
- Rena Yadlapati MD (Grade methodologist)
- Stuart Jon Spechler MD

Questions are guaranteed in life; Answers aren't.
Today’s Talk will address key features of ACG GERD Guidelines 2022

- Definition of GERD
- Diagnostic Approach including Extraesophageal and Refractory GERD
- Therapy
- PPI Adverse Events

What has changed since the 2013 ACG Guidelines?

- New data on pathogenesis of erosive esophagitis
- Increased acceptance of prolonged telemetry capsule monitoring for GERD
- Improved imaging technology
- Widespread availability and use of HRM and impedance/pH monitoring
- Lyon Consensus

- HRM, high resolution manometry
What has changed since the 2013 ACG Guidelines? (continued)

- Clearer understanding and definition of “refractory GERD”
- Level 1 evidence for laparoscopic fundoplication, magnetic sphincter augmentation and TIF success.
- Major change in approach to PPI use
- Wealth of data on PPI adverse events

- TIF, transoral incisionless fundoplication

GERD Defined

GERD is a condition in which the reflux of gastric contents into the esophagus results in symptoms and/or complications.

GERD is objectively defined by the presence of characteristic mucosal injury seen at endoscopy and/or abnormal esophageal acid exposure demonstrated on a reflux monitoring study.

Katz, Dunbar, Schnoll, Spechler AJG 2022
Pathophysiology of GERD

• Poorly functioning esophagogastric junction: antireflux barrier composed of the lower esophageal sphincter and crural diaphragm
• Impaired esophageal clearance and alterations in esophageal mucosal integrity.
• Decreased salivary production
• Delayed gastric emptying, and
• Esophageal hypersensitivity
• Reflux esophagitis develops when refluxed gastric juice is sufficient to trigger the release of cytokines and chemokines that attract inflammatory cells

GERD Symptoms: Typical/Classic

• Heartburn
• Regurgitation
• Chest Pain
• No symptom is exclusive to GERD
Extraesophageal: Symptoms/Associations

- Hoarseness, Throat Clearing: ENT symptoms
- Cough
- Asthma symptoms
- Dyspepsia
- Nausea
- Pneumonia, Bronchitis, Interstitial Lung Disease

- Typical symptoms may or may not be present: if not do not treat empirically

Alarm Symptoms: Mandates Work up prior to therapeutic trial

- Dysphagia
- Weight loss
- Bleeding
Case

- 44 yr old male/Caucasian female 3 years now daily substernal burning, mostly post prandial. Notes daily regurgitation of undigested food 10-15 minutes after eating, rarely in between meals, never has nausea, rare belching presents for evaluation. Halitosis for 20 years. Rare OTC, no longer helpful does not want to take PPI because of seizure medicine (Lamotrigine). Wakes from sleep once or twice a month. No dysphagia, weight loss or bleeding.
- Has attempted to avoid acidic trigger foods, late night eating
- BMI 33
- Family history of esophageal cancer in grandfather
- No other medical problems

ACG GERD Guidelines: Diagnostic Algorithm

Heartburn and/or regurgitation without alarm symptoms
Symptoms with sufficient frequency and intensity to impair QOL

8-week once daily before meal PPI trial

Complete relief
GERD likely
Discontinue PPI
Symptoms recur

Incomplete relief

EGD off PPI 2-4 weeks

LA Grade B/C/D
Barrett > 3 cm

GERD confirmed

Abnormal
Reflex monitoring off therapy

Normal EGD or LA Grade A

Normal
Consider other causes for symptoms

Office Based Clinical Diagnosis: How often do you want to be right?

**Gold Standard**
- Esophagitis on endoscopy
- Acid exposure time (AET) > 6%
- Symptom association probability > 95%
- AET 4-6% & symptom improvement

**Gold Standard**
- Acid exposure time (AET) > 4.2%
- Symptom association probability > 95%

---

PPI trial as a diagnostic test

- Practical, simple but has danger of giving and continuing a medicine for the wrong disease
- Pooled sensitivity of 78% and specificity of only 54% (using endoscopy and pH monitoring as the reference standard)
- As such its use should be limited to classic symptoms, the absence of warning signs
- Step up therapy offers no long-term advantage over a PPI trial
- Continuing an unsuccessful PPI trial beyond 8-12 weeks cannot be justified. Adjustment or ideally a workup is strongly recommended.
Case

- Patient agrees to try PPI as she prefers to not have EGD (sedation) after discussion of potential interactions with her seizure medications
- PPI once daily, taken 30 minutes before breakfast for 8 weeks, misses next appointment.
- Returns for video visit 2 months later, reports PPI was helpful with heartburn (90% gone), not as good for regurgitation and no help with halitosis.
- Stopped PPI on her own, symptoms returned slowly and returned to baseline.

Guidelines 2022: Endoscopy

- Diagnostic endoscopy if classic GERD symptoms do not respond adequately to 8-week empiric trial of PPIs or symptoms return when PPIs are discontinued
- Performed off PPI, ideally for 2-4 weeks
- 1 week minimum for intended pH testing if endoscopy is negative
- Mandatory off therapy ≥ 1 week if biopsy planned for normal mucosa (EoE cannot be ruled out if biopsy on PPI)

- EoE, eosinophilic esophagitis
Endoscopy

- For diagnosis if PPI trial unsuccessful or patient relapses
- For any patient with dysphagia, anemia, weight loss
- Should be performed off PPI for at least a week, ideally 2-4 weeks
- Mucosal abnormality <50% of patients with heartburn, lower when extraesophageal symptoms are reason for exam
- Normal endoscopy mandates a reflux monitoring study for diagnosis

Endoscopy/Biopsy

- Biopsy should NOT be performed to make a diagnosis of GERD
- Biopsy of the gastroesophageal junction is not recommended
- Biopsy of a reflux erosion is not necessary
- Eosinophilic Esophagitis cannot be ruled out if the patient is on a PPI
Recommended

- Should be performed off therapy for all patients who do not have a clear endoscopic diagnosis (Grade B, C or D, Barrett, clear peptic stricture)
- On therapy with impedance/pH if GERD previously objectively documented and optimized PPI not effective

Reflux Monitoring

- Only test to evaluate for reflux over time
- Can be 24-96 hours, catheter or telemetry capsule
- Weakly or non-acidic contents can be assessed
- Can evaluate belching
- Should be done in all patients who do not have EE or Barrett’s and those who fail PPI before an operation

A Normal EGD and Reflux Monitor Makes it Highly Unlikely GERD is Responsible for Symptoms

The best way to make decisions on long term PPI use
ACG Guidelines 2022: Management of Refractory GERD

Previously objectively defined GERD*

- Optimize PPI
- 2-4 week therapy

Symptom relief

 Unsatisfactory symptom relief

If primary symptoms regurgitation, consider MSA, TIF or fundoplication in appropriate patient

- Continue current treatment
- Discuss long-term management options

Perform impedance pH monitoring on PPI BID

Normal

- Look for other causes
- Treat coexistent functional disease

Abnormal

- Consider surgical/endoscopic intervention
- Consider escalating medical therapy

* LA B/C/D GERD


Treatment
Food: Diet

- Weight loss in overweight and obese patients for improvement of GERD symptoms
- Suggest avoiding meals within 2–3 hours of bedtime
- Suggest avoidance of “trigger foods” for GERD symptom control (conditional recommendation, low level of evidence).
- Suggest elevating head of bed for nighttime GERD symptoms

Lifestyle Changes: The Evidence is Generally Weak

<table>
<thead>
<tr>
<th>Lifestyle modification</th>
<th>Strength of scientific evidence</th>
<th>Pathophysiologically conclusive?</th>
<th>Recommendable?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid fatty meals</td>
<td>Equivocal</td>
<td>Equivocal</td>
<td>Yes</td>
</tr>
<tr>
<td>Avoid carbonated beverages</td>
<td>Moderate</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Select decaffeinated beverages</td>
<td>Equivocal</td>
<td>Equivocal</td>
<td>Not generally</td>
</tr>
<tr>
<td>Avoid citrus</td>
<td>Weak</td>
<td>Yes</td>
<td>Yes, if citrus triggers symptoms</td>
</tr>
<tr>
<td>Eat smaller meals</td>
<td>Weak</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Lose weight</td>
<td>Equivocal</td>
<td>Equivocal</td>
<td>Yes*</td>
</tr>
<tr>
<td>Avoid alcoholic beverages</td>
<td>Weak</td>
<td>Mechanisms not understood; different alcoholic beverages have different effects</td>
<td>Not generally</td>
</tr>
<tr>
<td>Stop smoking</td>
<td>Weak</td>
<td>Yes</td>
<td>Yes*</td>
</tr>
<tr>
<td>Avoid excessive exercise</td>
<td>Weak</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sleep with head elevated</td>
<td>Equivocal</td>
<td>Equivocal</td>
<td>Yes</td>
</tr>
<tr>
<td>Sleep on the left side</td>
<td>Unequivocal</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Obesity and smoking seem to be risk factors for cancer of the distal esophagus.
General Principle: Healing (Symptom improvement) Related to Acid Control

Katz P et al, APT 2007

Acid Control Reduces Relapse

Johnson DA, Katz P
J Clin Gastro 2010
PPIs are the BEST drugs currently available

- Block terminal step of acid secretion
- Require active proton pump to be effective
- Block 70% of active pumps
- Half-life short, half-life of pump long so 5-7 days to reach steady state
- Pumps regenerate so MUST take drug daily
- PUMPS ACTIVATED by FOOD
- PPI absorption may be diminished by FOOD

Intragastric pH control with once daily PPI

* \( p = 0.0010 \) vs. esomeprazole
† \( p \leq 0.0001 \) vs. esomeprazole

2022 Guidelines: Surgery/Endoscopic Treatment

Recommended

- PPI indefinitely or surgery in patients with C or D erosive esophagitis (or clear Barrett esophagus)
- Consider early intervention for patients with regurgitation as primary symptom, objective evidence for GERD
- Surgery: option for long term management of objectively proven GERD
- Refractory regurgitation: MSA, laparoscopic hernia repair plus fundoplication or TIF
- If patient does not wish to have surgery: TIF if non-erosive, A, B, Hill 1 or 2 and axial HH 2 cm or less

- MSA, magnetic sphincter augmentation; TIF, transoral incisionless fundoplication

A second dose increases time pH>4 by 5 hours

Pantoprazole is the weakest PPI and used the most as it is on most formulary due to cost
Adverse Events Associated with PPIs

The longest running Risks of “Concern”

- Fractures (FDA Class warning 2010, revised 2011)
- Clopidogrel interaction (FDA warning 2009, different PPI labels)
- Clostridium difficile (FDA Class warning 2012)
- Pneumonia (No class Warning)
- Magnesium Deficiency (Class Warning)
Other Potential PPI “Risks”

- Interstitial Nephritis
- Cardiac Disease (adjudicated by FDA in past)
- Small Intestinal Bacterial Overgrowth
- Bacterial Peritonitis
- Traveller’s Diarrhea
- Iron Deficiency Anemia
- Rhabdomyolysis
- Cardiac Defects when used in pregnancy

The Latest most talked about “Worries”

- Myocardial Infarction
- Chronic Kidney Disease
- Dementia
- Ischemic stroke
- Early death
What are the possible mechanisms of PPI adverse events

1. Infectious consequences of hypochlorhydria
2. Non-infectious consequences of hypochlorhydria
3. Dysbiosis
4. Consequences of hypochlorhydria on electrolyte and nutrition absorption

Proposed Effects/
Concerns of Long-Term PPI Therapy

1. Bone consequences (Ca absorption)
2. Dementia (Amyloid in mice, B12)
3. Renal Disease (AIN, idiosyncratic)
Results of Studies

• Results expressed as Hazard Ratios or Odds Ratios rather than NNT or NNH
• Increased likelihood of an unlikely event still unlikely
• Relative Risk increased
• Absolute Risk Variable
• Prospective studies though smaller all show no harms or reported events

Examining the Data: Methodology of studies

• Retrospective Cohort
• Database Reviews using ICD-9/10 codes
• Meta analysis
• Few RCT’s or prospective cohort studies
Criteria for Judging a Study of Association

- **Strength of the Association**: Is the association of high magnitude
- **Consistency**: Is the association reproducible
- **Specificity**: Is the effect directly attributed to (in this case) PPIs
- **Temporality**: Does the use of the PPI precede the outcome
- **Biologic gradient**: Direct relationship between dose and or duration
- **Biologic plausibility**: Any logical reason for the outcome
- **Coherence**: Conflict with what is known about the disease in question
- **Experiment**: Are the results based on an experiment
- **Analogy**: Any similarity to associations that are deemed causal

*Hill, 1965*
Randomized Trial: Panto v placebo: 53K patient years of follow-up

17,598 randomised to PPI or placebo

8791 assigned to pantoprazole 40 mg od
- 8740 vital status known
  - 41 withdrew consent
  - 10 lost to follow-up
- 8791 included in the analysis
  - 0 excluded

8807 assigned to placebo
- 8743 vital status known
  - 48 withdrew consent
  - 16 lost to follow-up
- 8807 included in the analysis
  - 0 excluded

Moayyedi, 2019

MI/Stroke

A  Myocardial Infarction

HR (95% CI): 0.94 (0.79-1.12); P-value:.51

B  Stroke

HR (95% CI): 1.16 (0.94-1.44); P-value:.16

Moayyedi, 2019
Other Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Incident events, n (%)</th>
<th>Pantoprazole, 40 mg od (n = 8791)</th>
<th>Placebo (n = 8807)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric atrophy</td>
<td>19 (0.2)</td>
<td>26 (0.3)</td>
<td></td>
<td>0.73 (0.40–1.32)</td>
<td>.30</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>9 (0.1)</td>
<td>4 (&lt;0.1)</td>
<td></td>
<td>2.26 (0.70–7.34)</td>
<td>.18</td>
</tr>
<tr>
<td>Other enteric infection</td>
<td>119 (1.4)</td>
<td>90 (1.0)</td>
<td></td>
<td>1.33 (1.01–1.75)</td>
<td>.04</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>184 (2.1)</td>
<td>158 (1.8)</td>
<td></td>
<td>1.17 (0.94–1.45)</td>
<td>.15</td>
</tr>
<tr>
<td>Dementia</td>
<td>55 (0.6)</td>
<td>46 (0.5)</td>
<td></td>
<td>1.20 (0.81–1.78)</td>
<td>.36</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>318 (3.6)</td>
<td>313 (3.6)</td>
<td></td>
<td>1.02 (0.67–1.59)</td>
<td>.82</td>
</tr>
<tr>
<td>Fracture</td>
<td>203 (2.3)</td>
<td>211 (2.4)</td>
<td></td>
<td>0.96 (0.79–1.17)</td>
<td>.71</td>
</tr>
<tr>
<td>COPD</td>
<td>146 (1.7)</td>
<td>124 (1.4)</td>
<td></td>
<td>1.18 (0.93–1.51)</td>
<td>.17</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>513 (5.8)</td>
<td>532 (6.0)</td>
<td></td>
<td>0.96 (0.85–1.09)</td>
<td>.56</td>
</tr>
</tbody>
</table>

Moayyedi, 2019

Association Never Proves Casualty
Guideline Statement Regarding PPI Safety

Regarding the safety of long-term PPI usage for GERD, we suggest that patients should be advised as follows: “PPIs are the most effective medical treatment for GERD. Some medical studies have identified an association between the long-term use of PPIs and the development of numerous adverse conditions including intestinal infections, pneumonia, stomach cancer, osteoporosis-related bone fractures, chronic kidney disease, deficiencies of certain vitamins and minerals, heart attacks, strokes, dementia, and early death. Those studies have flaws, are not considered definitive, and do not establish a cause-and-effect relationship between PPIs and the adverse conditions. High-quality studies have found that PPIs do not significantly increase the risk of any of these conditions except intestinal infections. Nevertheless, we cannot exclude the possibility that PPIs might confer a small increase in the risk of developing these adverse conditions. For the treatment of GERD, gastroenterologists generally agree that the well-established benefits of PPIs far outweigh their theoretical risks.”

Katz, et al. AJG 2022

ACG GERD Guidelines: Diagnostic Algorithm

Heartburn and/or regurgitation without alarm symptoms
Symptoms with sufficient frequency and intensity to impair QOL

8-week once daily before meal PPI trial

Complete relief
GERD likely
Discontinue PPI
Symptoms recur

Incomplete relief
EGD off PPI 2-4 weeks

LA Grade B/C/D
Barrett > 3 cm

GERD confirmed

Abnormal

Normal EGD or LA Grade A
Reflux monitoring off therapy
Normal
Consider other causes for symptoms

ACG Guidelines 2022: Management of Extraesophageal GERD

Presence of extraesophageal GERD symptoms

- Detailed medical history to identify other potential causes
- Refer to other specialists for evaluation if history suggests non-GERD cause is likely

Typical GERD + extraesophageal symptoms

- PPI trial BID up to 12 weeks
- Extraesophageal symptoms

- Improve
- No improvement

  - Treat as GERD

Extraesophageal symptoms only

- Reflux monitoring off PPI

  - Abnormal
  - Treat as GERD

  - Normal
  - Consider pH-impedance monitoring

ACG Guidelines: Management of Refractory GERD

Previously empirically treated with PPI without objective workup

- Symptom relief
- Unsymptomatic symptom relief

  - Continue GERD treatment
  - Discuss long-term GERD management options

- Optimize PPI

Diagnostic EGD (off PPI 2-4 weeks)

- Normal EGD
  - Reflux monitoring (off PPI)

- Abnormal EGD
  - Erosive Esophagitis LA B/C/D
  - Barrett > 3 cm

  - Other cause for symptoms identified
  - Treat mucosal disease

- No evidence of GERD
  - Look for other causes

- GERD confirmed

ACG Guidelines 2022: Management of Refractory GERD

Previously objectively defined GERD*

Optimize PPI 2-4 week therapy

If primary symptoms regurgitation, consider MSA, TIF or fundoplication in appropriate patient

Symptom relief

Unsatisfactory symptom relief

Perform impedance pH monitoring on PPI BID

Normal

Abnormal

• Continue current treatment
• Discuss long-term management options

• Look for other causes
• Treat coexistent functional disease

• Consider surgical/endoscopic intervention
• Consider escalating medical therapy

• * LA B/C/D GERD


Truth

It is more important for a philosophy to be interesting, than true.

A.N. Whitehead
Truth

I didn’t say everything that I said.

Yogi Berra
Questions and Answers

Philip O. Katz, MD, MACG, AGAF

Rena Yadlapati, MD, MSHS, FACG