

Minimally Invasive and Novel Therapeutics (M.I.N.T.) in Foregut Disease
September 29th -October 1st 2022

“My Cough is Uncontrolled Reflux”
*An Approach to Work-up and
Management*

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Stanford Health Care

Thursday, September 29, 2022

2:05 – 2:20 pm



Gastroesophageal Reflux Disease

Montreal Consensus

- “GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications.”¹

Lyon Consensus

- Presence of excess gastroesophageal reflux (acid exposure time >6)
- Evidence of LA Grade C or D esophagitis, long-segment Barrett’s mucosa, or peptic esophageal stricture²



Laryngopharyngeal Reflux

Definition

- The retrograde flow of gastroduodenal contents into the larynx and pharynx

Symptoms

- Hoarseness
- Sore throat
- Chronic cough
- Dysphonia
- Globus
- Throat clearing

Kamal et al. Dig Dis Sci. 2022 Aug 22. doi: 10.1007/s10620-022-07672-9.



Chronic Cough

Duration

- > 8 weeks

Cough attributed to reflux disease

- Historically thought to be due to reflux of gastric contents beyond the esophagus into the pharynx with microaspiration into the airways¹
- Likely a centrally mediated process, in which the cough reflex becomes 'hypersensitive' to stimuli such as esophageal reflux²

¹ Blondeau K et al. *Curr Gastroenterol Rep.* 2008;10(3):235-239.

² Gawron AJ, Kahrilas PJ, Pandolfino JE. *Curr Opin Otolaryngol Head Neck Surg.* 2013;21(6):523-529.



Case Study

55-year-old woman with PMH significant for hyperlipidemia, allergic rhinitis, and prior nasal septal surgery who presents for gastroenterology consultation regarding chronic cough and GERD.



She reports “stomach problems” for a long time that appear to be worsening. “The major problem I have is at night I am always coughing.” She feels acid reflux triggers her cough. She also reports regurgitation and occasionally throwing up at night. She cannot sleep. Describes vomitus is “not fully digested food.”

She is currently on omeprazole 20 mg bid “but I’m not sure if it works or not.” She has been on this for a year.

Case Study



She was previously evaluated by ENT. Laryngostroboscopy revealed post-cricoid erythema and edema. No mucosal lesions or masses seen. Advised by ENT to use nasal saline rinses and continue with allergy medications (loratadine & fluticasone).

The patient has followed these recommendations and feels her allergy symptoms are improved but cough is persistent.

Case Study



She had a prior endoscopy 5 years ago notable for LA Grade A esophagitis and a hiatal hernia. Doesn't think she has had a colonoscopy.

Prior CT of the abdomen and pelvis done this year showed a "moderate" hiatal hernia and was otherwise unremarkable.

Common Potential Etiologies for Chronic Cough

Environmental or
occupational
irritants

Primary or
secondary smoking

Use of angiotensin-
converting-enzyme
(ACE) inhibitors

Asthma

Upper airway
cough syndrome
due to rhinosinusus
conditions



2016 CHEST Guideline and Expert Panel Report: Chronic Cough Due to Gastroesophageal Reflux in Adults

Chronic cough suspected due to reflux-cough syndrome

Diet modification to promote weight loss in overweight or obese



Head of bed elevation and avoiding meals within 3 hours of bedtime



PPIs, H2-receptor antagonists, alginate, or antacid therapy if reporting heartburn and regurgitation



2016 CHEST Guideline and Expert Panel Report: Chronic Cough Due to Gastroesophageal Reflux in Adults

Chronic cough suspected due to reflux-cough syndrome,
but without heartburn or regurgitation

Recommend against
PPIs



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2016 CHEST Guideline and Expert Panel Report: Chronic Cough Due to Gastroesophageal Reflux in Adults

Chronic cough potentially due to reflux-cough syndrome
who are refractory to 3-month trial of antireflux therapy
and being evaluated for surgical management

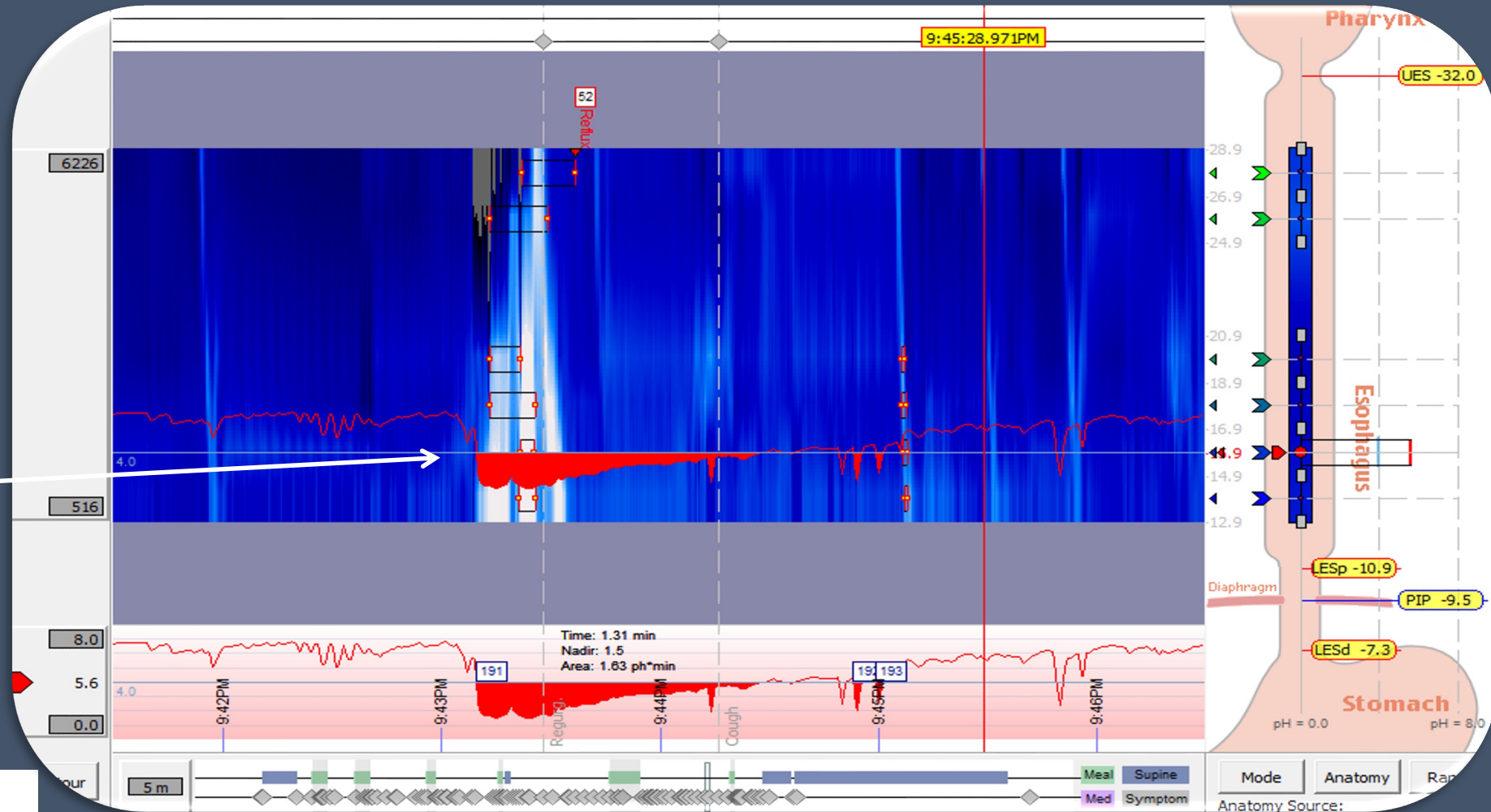


Recommend
esophageal manometry
and pH-metry (off
therapy)



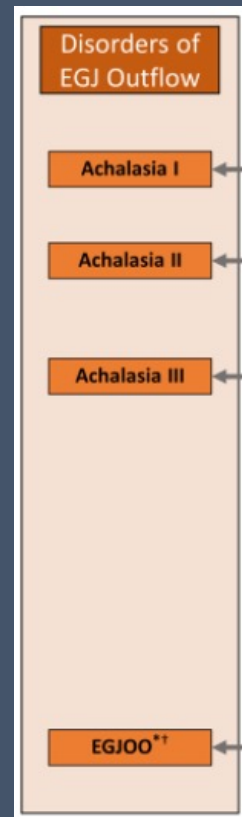
24-hour pH Impedance Testing

Below line =
pH < 4

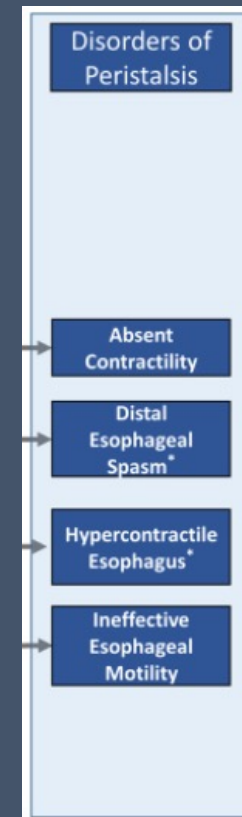


2016 CHEST Guideline and Expert Panel Report: Chronic Cough Due to Gastroesophageal Reflux in Adults

Chronic cough and a major motility disorder and/or normal acid exposure time in the distal esophagus



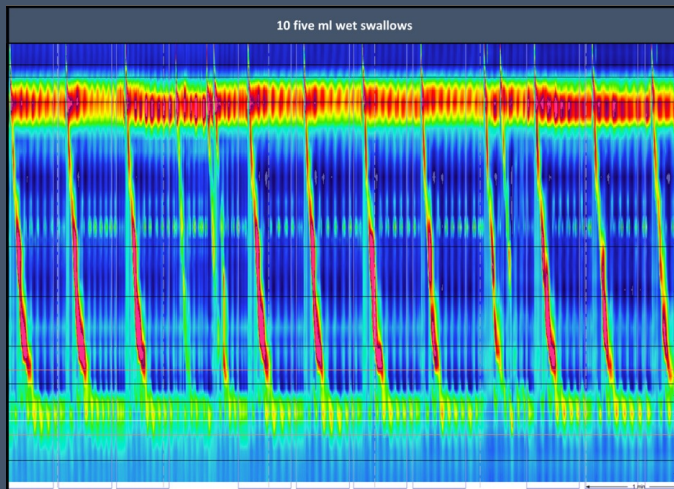
Suggest not advising antireflux surgery



2016 CHEST Guideline and Expert Panel Report: Chronic Cough Due to Gastroesophageal Reflux in Adults

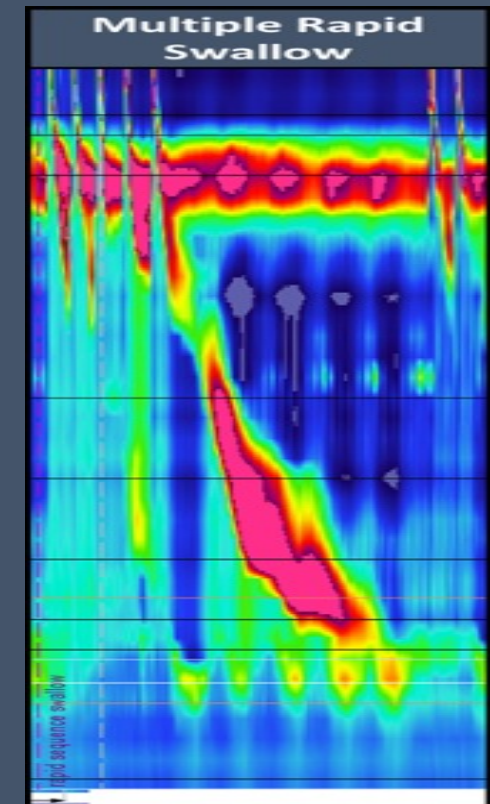
Chronic cough, adequate peristalsis, and abnormal esophageal acid exposure in whom medical therapy has failed

Suggest antireflux (or bariatric when appropriate) surgery for presumed reflux-cough syndrome



Kahrilas et al. *Chest*. 2016;150(6):1341-1360.

Yadlapati et al. *Neurogastroenterol Motil*. 2021;33(1):e14058.



Other Available Tests

Pharyngeal and oropharyngeal reflux monitoring

- Proposed as methods to better detect LPR
- Reliability has been questioned
- Systematic review found no significant differences in dual-channel pH testing results between normal controls and patients with laryngeal symptoms

Salivary pepsin testing

- Proposed as a noninvasive method of detecting LPR
- Meta-analysis of 11 observational studies examined the role of salivary pepsin testing in diagnosing LPR & significant heterogeneity was found (varying reference standards, differing assays, variable definitions of abnormal)
- Salivary pepsin levels can be elevated in control patients & may vary by time of day



2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux

Extraesophageal GERD symptoms

We recommend evaluation for non-GERD causes in patients with possible extraesophageal manifestations before ascribing symptoms to GERD.	Moderate	Strong
We recommend that patients who have extraesophageal manifestations of GERD without typical GERD symptoms (e.g., heartburn and regurgitation) undergo reflux testing for evaluation before PPI therapy.	Moderate	Strong
For patients who have both extraesophageal and typical GERD symptoms, we suggest considering a trial of twice-daily PPI therapy for 8–12 wk before additional testing.	Low	Conditional
We suggest that upper endoscopy should not be used as the method to establish a diagnosis of GERD-related asthma, chronic cough, or LPR.	Low	Conditional
We suggest against a diagnosis of LPR based on laryngoscopy findings alone and recommend additional testing should be considered.	Low	Conditional
In patients treated for extraesophageal reflux disease, surgical or endoscopic antireflux procedures are only recommended in patients with objective evidence of reflux.	Low	Conditional

Katz PO et al. *Am J Gastroenterol.* 2022;117(1):27-56.

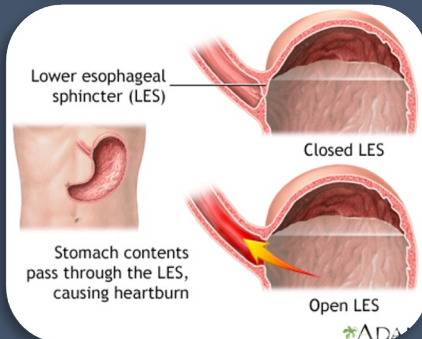
Other Therapeutic Options



Alginates



Neuromodulating agents



Baclofen



Case Study

Discussed further diagnostic testing options with patient.



Does not think she can tolerate any tests involving a 24-hour tube in her nose!

Plan:

- 1) Upper endoscopy with wireless pH probe (off acid suppressive therapy)
- 2) Colonoscopy
- 3) Further recommendations to follow pending above



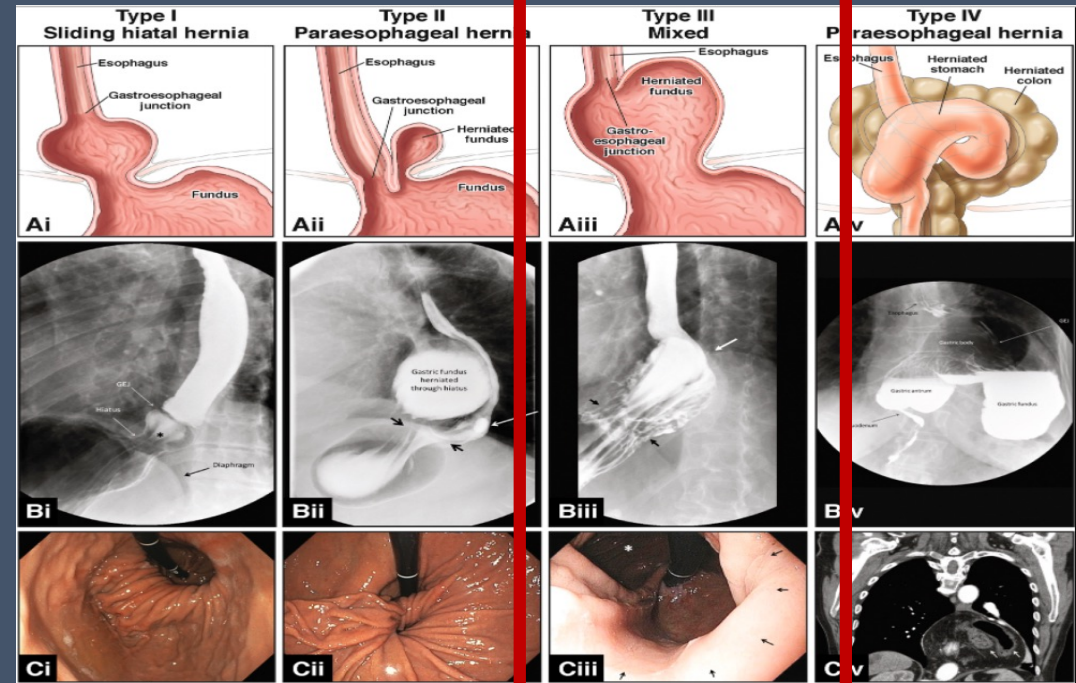
Case Study

EGD:

- 1) Large (7 cm) hiatal hernia (mixed type)
- 2) Los Angeles Grade B esophagitis
- 3) Otherwise, unremarkable

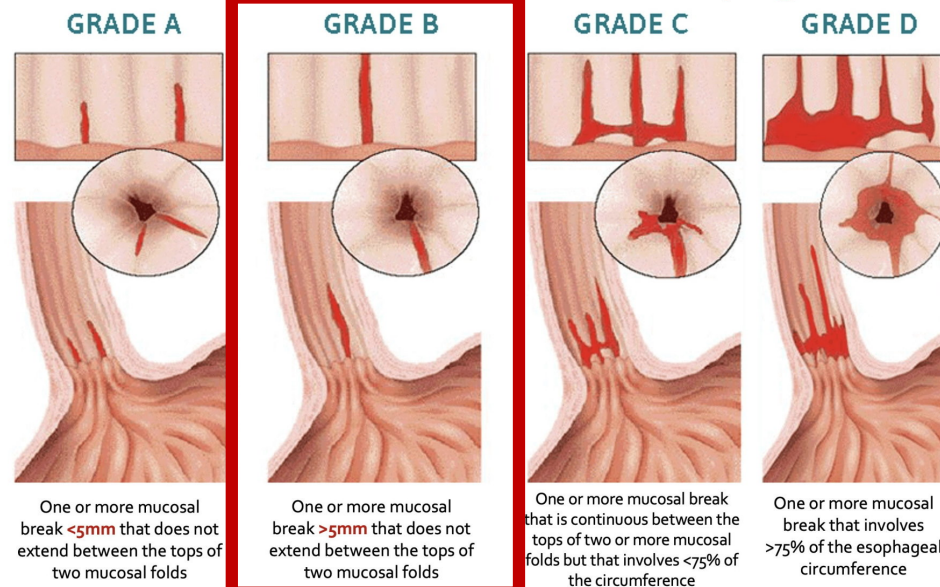
Colonoscopy:

- 1) < 5 mm polyp in sigmoid colon
- 2) Otherwise, unremarkable



Callaway JP, Vaezi MF. *Clin Gastroenterol Hepatol.* 2018;16(6):810-813

Los Angeles Classification of Reflux Esophagitis





Case Study

Wireless pH Study Results



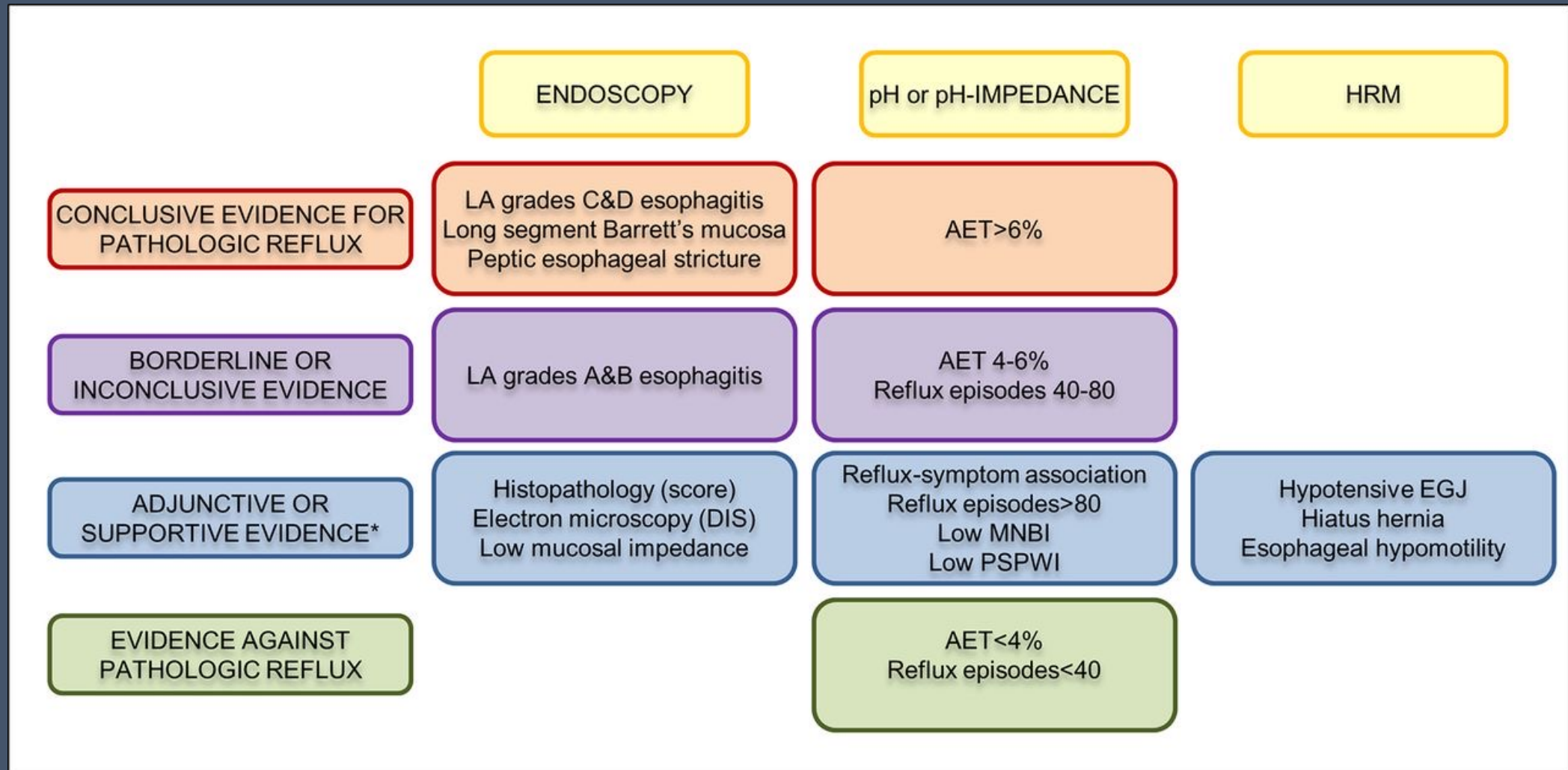
Day	Acid Exposure Time (AET)
1	12.0
2	9.8
3	14.2
4	13.5

Symptom Analysis	Regurg.	Cough
Number of occurrences	2	5
Symptoms related to reflux	1	2
Symptoms not related to reflux	1	3
Reflux periods	36	36
Symptom Index (SI)	50.0	40.0
Symptom Association Prob. (SAP)*	70.4	96.1

* Probability that symptom and reflux are not associated solely by chance, (>95% is significant)



The Lyon Consensus





Case Study Next Steps?

- 1) Stop omeprazole. Start dexlansoprazole 30 mg once daily.
- 2) Continue lifestyle & diet measures for reflux.
- 3) Discussed barium esophagram to better characterize hernia with clinic follow-up after.
- 4) Discussed pros/cons of hernia repair.



Case Study



Esophagram Results

- Moderately sized hiatal hernia with gastroesophageal reflux
- Moderate esophageal dysmotility

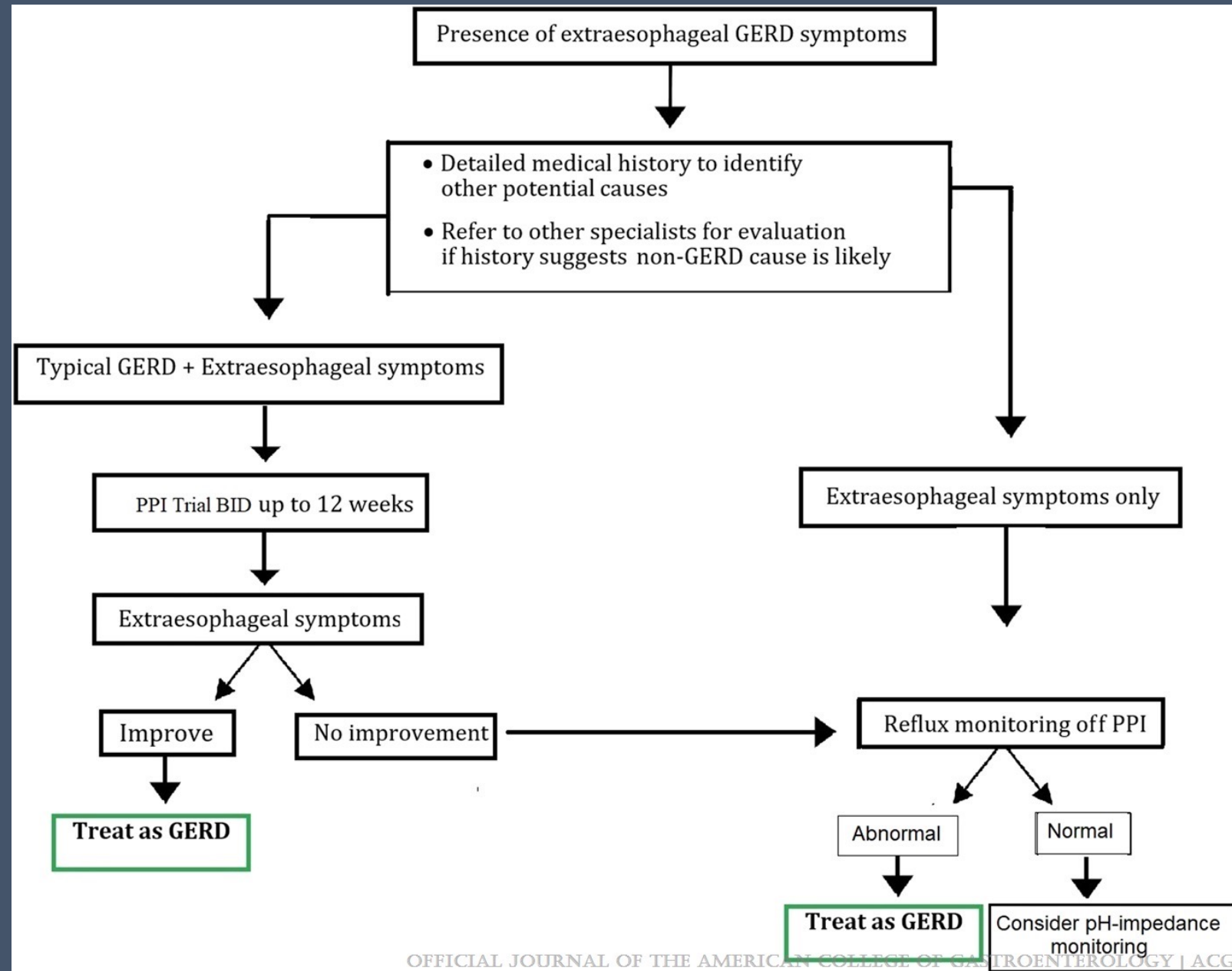


Case Study Next Steps?

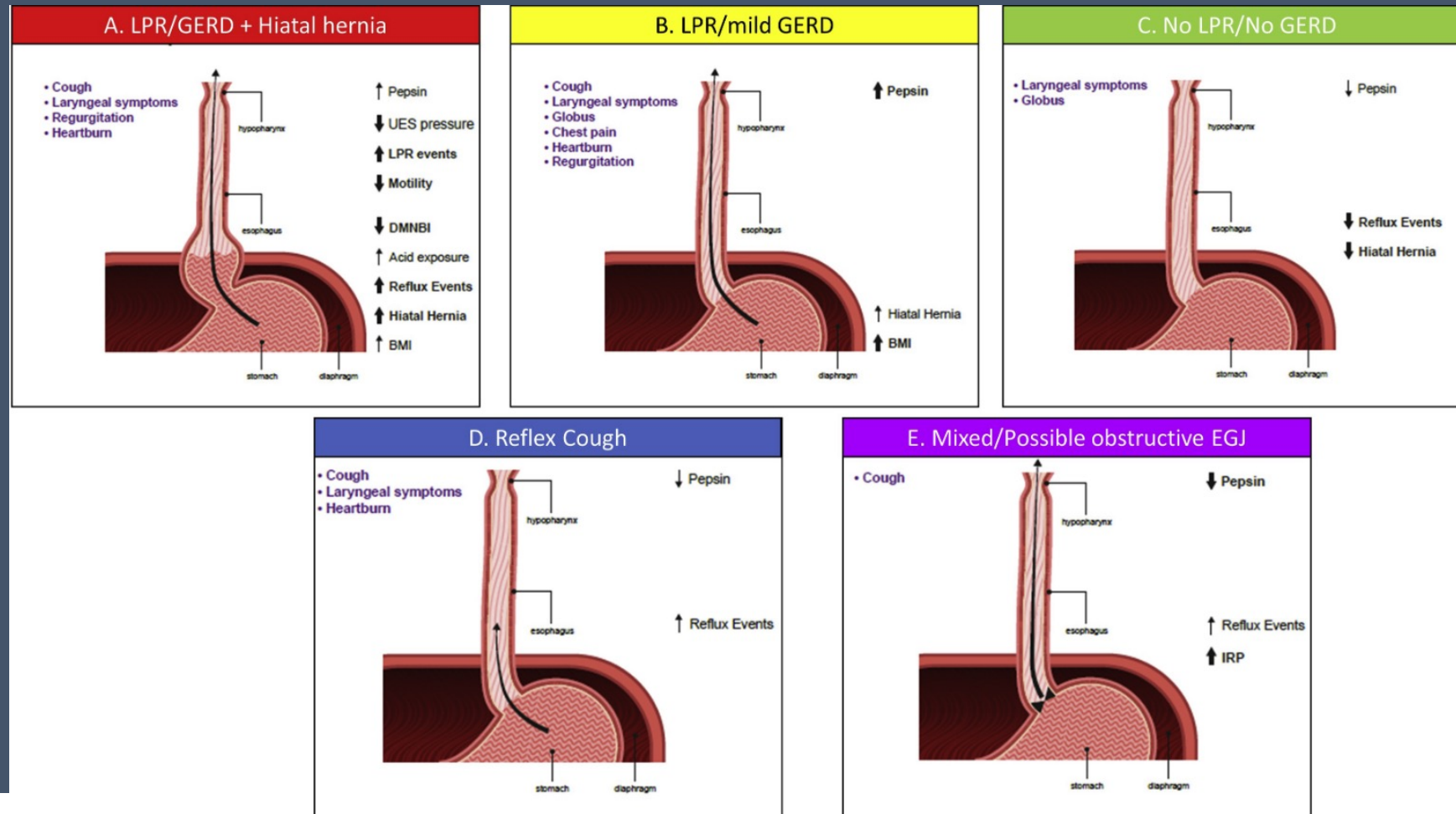
- 1) High-resolution esophageal manometry.
- 2) Consider Gastric emptying study.
- 3) Referral for surgical consultation.



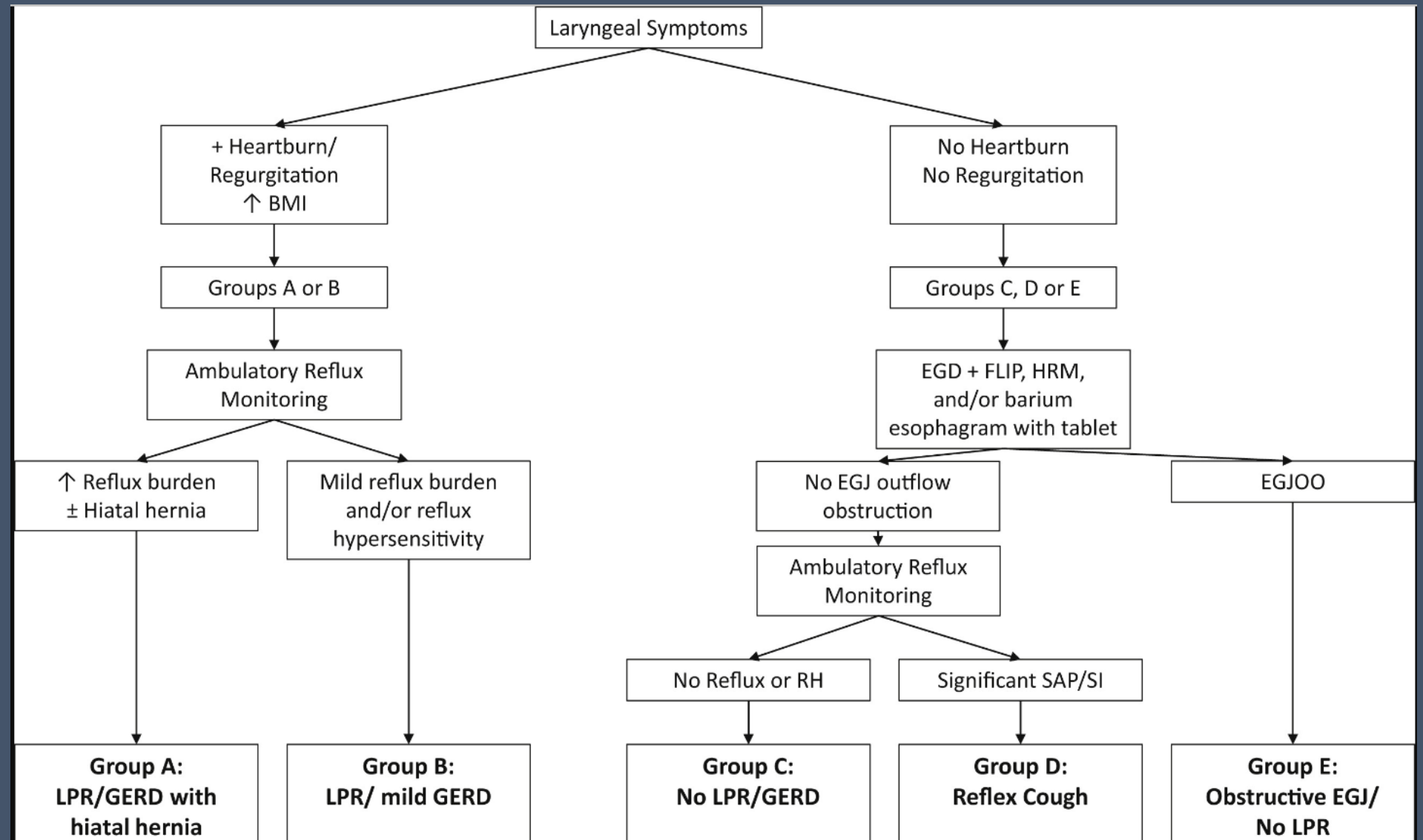
2022 ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux



Distinct Clinical Physiologic Phenotypes of Patients With Laryngeal Symptoms



Clinical Approach to Identifying Phenotypes of Patients with Suspected LPR



Yadlapati et al. Clin Gastroenterol Hepatol. 2022 Apr;20(4):776-786.e1

Table 2 Questions reaching agreement on importance, scientific acceptability, usability and feasibility

Statement categories

<i>Lifestyle modification</i>	1. If a patient has suspected, presumed, or demonstrated LPR, then recommending dietary and lifestyle modifications can be an effective part of an overall treatment approach 2. If a patient has suspected LPR with mild complaints, then dietary and lifestyle modifications may be considered as an initial step in care without additional medication
<i>Laryngoscopy</i>	3. If a patient has LPR symptoms without classic GERD complaints, then work-up should include laryngopharyngoscopy 4. If a patient with suspected or presumed LPR has concomitant voice complaints that do not improve with reflux treatment, then referral for laryngoscopy and/or laryngeal videostroboscopy is indicated
<i>Proton pump inhibitor (PPI)</i>	5. If a patient with presumed LPR whose symptoms respond to initial acid suppression treatments cannot later be weaned from medication without symptom recurrence, then titrate to lowest dose of PPI or H2 antagonist needed for long-term symptom control or consider other options for long-term reflux control 6. If a patient with presumed or demonstrated LPR is taking PPI with improvement in symptoms, then inform patient of reported risks of long-term PPI use and offer alternative treatments if the patient does not want to be on PPIs long-term 7. If PPIs are chosen for use in LPR treatment, then they should be dosed 30–60 min before meals 8. If a patient is prescribed PPIs for LPR empiric treatment, then risks and benefits of PPI use should be reviewed with the patient carefully prior to use
<i>Endoscopic treatment and surgery</i>	9. If a patient is being considered for endoscopic or surgical reflux treatment, then a thorough pre-procedure evaluation should be performed to assess esophageal function as part of treatment planning 10. If a surgeon is considering fundoplication for a patient with LPR symptoms in the absence of GERD, then otolaryngologic evaluation is warranted prior to any surgery in order to assess for non-reflux etiologies contributing to patient symptoms 11. If a patient is being considered for endoscopic treatment of LPR, then they should be counseled that its efficacy in LPR patients is not completely understood 12. If a patient with LPR demonstrates good symptom control with medications, then with supportive objective reflux and motility testing, a surgical anti-reflux procedure may be considered as an alternative to continued medication
<i>Philosophy and/or empiric treatment</i>	13. If a patient with presumed LPR responds to initial treatment but has persistent complaints even when titration/addition of medication has reached a plateau, then objective testing such as pH-impedance reflux testing can be pursued to help identify refractory reflux or suggest, if reflux is adequately controlled, that non-reflux etiologies for patient complaints need to be considered 14. If a patient with presumed LPR has reached therapeutic plateau with reflux treatment and still has persistent symptoms, then consider evaluation of non-reflux etiologies for common complaints such as globus pharyngeus, cough, throat clearing, hoarseness, etc., that had previously been attributed to LPR 15. If a patient is sent for objective reflux testing, then the referring physician should think critically about testing on therapy vs off therapy relative to interpretation of results 16. If a patient with suspected LPR does not have any response to an adequate empiric trial of antacid medication, then objective testing such as pH-impedance and high-resolution esophageal manometry testing can be pursued to help identify refractory non-acidic or weakly acidic reflux or to suggest that etiologies other than reflux for patient complaints need to be considered 17. If a patient is being treated for LPR, then approaches to evaluation and management should take into account factors such as symptom severity and patient-related factors such as age, health status, and comorbid conditions

Best Practices in Treatment of Laryngopharyngeal Reflux Disease

Kamal et al. Dig Dis Sci. 2022 Aug 22. doi: 10.1007/s10620-022-07672-9.



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In summary:

Cough can be an extraesophageal manifestation of GERD

Evaluate for other causes of chronic cough

If GERD is considered as a possible culprit, reflux monitoring should be considered

A negative diagnostic test can provide reassurance and avoidance of long-term PPI use

A multidisciplinary approach is valuable, and care should be individualized

“Chronic cough remains a vexing problem for many...”



Thank you!



References

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