Gastroesophageal Reflux Disease and Severe Asthma

Christopher Vélez, MD
Program Director, Advanced Fellowship in
Neurogastroenterology and Motility Disorders;
Massachusetts General Hospital Center for Neurointestinal Health;
Division of Gastroenterology, Hepatology, and Endoscopy;
Mass General Brigham Department of Medicine;
Harvard Medical School.

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Mass General Brigham

Disclosures and Conflicts of Interest

- I have received funding from the following sources:
  - Cystic Fibrosis Foundation
  - Ironwood
  - Ardelyx – investigator initiated trial of tenapanor in CF-related constipation
  - American College of Gastroenterology
  - Consultant Eli Lily
  - Internal MGH diversity, equity, and inclusion funding initiatives

Outline

- **Case introduction**
- Why is there an interloping gastroenterologist?
- The relationship between GERD and asthma
- How I approach GERD evaluation/refractory GERD
- Case wrap-up and clinical pearls

Case

- 54-year-old woman with a history of asthma with potential COPD overlap syndrome, complicated by recurrent exacerbations and hospitalizations (including ICU stays) presents to establish care with me in my community gastroenterology practice.
- She has a history of malformation of her subclavian artery, which compresses her esophagus and contributes to recurrent aspiration and pneumonia, never repaired (because of heavier smoking at the time of first evaluation).
- Her asthma/COPD exacerbations are quite frequent despite the use of triple therapy which includes inhaled steroids/long-acting beta agonists, long-acting muscarinic antagonist, as well as montelukast, with frequent need for steroids.
  - Possibly due to repeated insults from aspiration?

Case

- She was initiated on dupilumab. There was an initial period where dupilumab seemed to be making a difference.
  - There was another period of worsening symptoms and need for prednisone, leading us to transition to another agent, benralizumab, which has also not made a significant difference.
- I have been tasked to examine her since she has heartburn and regurgitation.
  - Also to determine if there is a component of her symptoms that could be related to GERD.
- Of note, body mass index is 35 kg/m^2, likely driven in part due to repetitive need for systemic glucocorticoids.
- Endoscopy done 10-years prior without concerning pathology.
- Patient is on omeprazole 40 mg twice daily and famotidine 40 mg nightly.
  - Omeprazole does not control typical GERD symptoms.
  - What is aspiration vs GERD?

Case

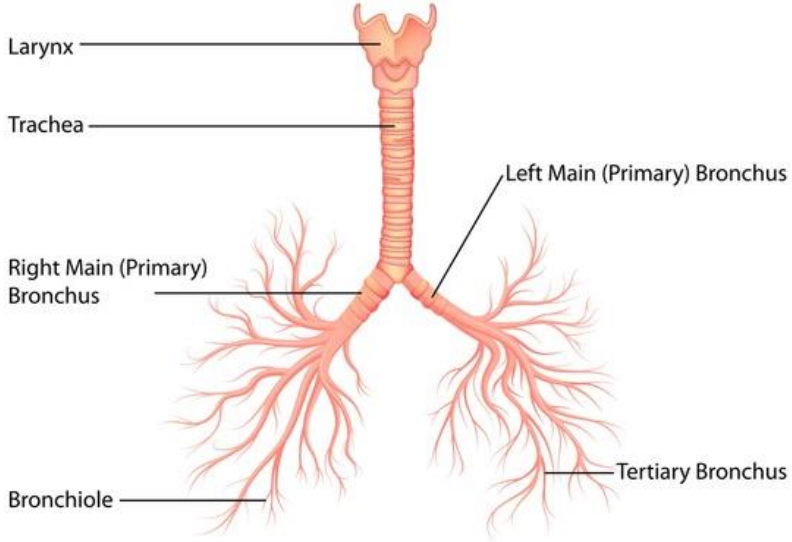
- As you listen to this talk, I would like for you to think of the following points:
  - What, if any additional gastroenterology testing is needed?
  - Is this severe asthma related to GERD, if she is maximally suppressed?

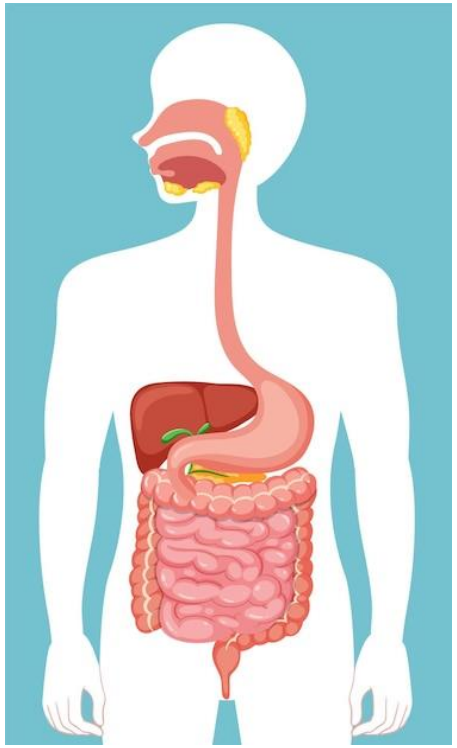
Outline

- Case introduction
- **Why is there an interloping gastroenterologist?**
- The relationship between GERD and asthma
- How I approach GERD evaluation/refractory GERD
- Case wrap-up and clinical pearls

Gastroenterologists and Pulmonologists

- Embryologically kindred organ systems.
- Both organs are a set of tubes.
- Similar disease processes (vascular, inflammatory, malignant, infectious) plague both organ tracts.
- Specialists within the specialty focus on procedural care, critical illness, preventive care, and addressing health inequity that can exist among different communities.

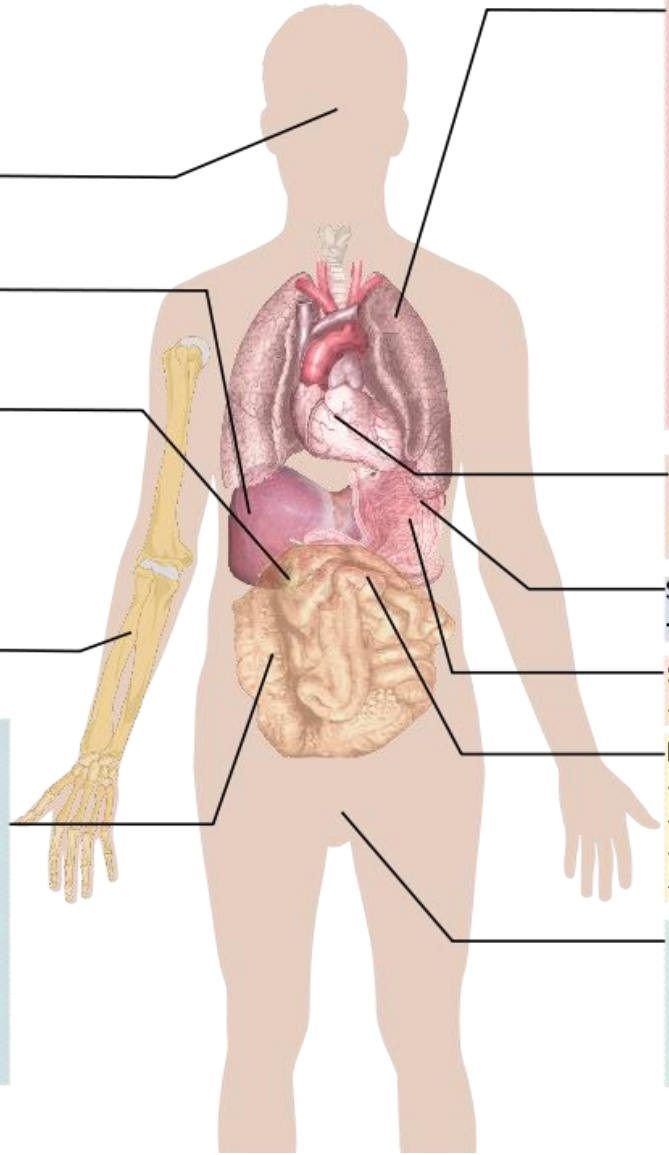




https://www.shutterstock.com/search/bronchial-branches
https://www.freepik.com/free-photos-vectors/digestive-system

Thinking about a combined aerodigestive system

Manifestations of Cystic Fibrosis



General
-Growth failure (malabsorption)
-Vitamin deficiency states
(vitamins A, D, E, K)

Nose and sinuses
-Nasal polyps
-Sinusitis

Liver
-Hepatic steatosis
-Portal hypertension

Gallbladder
-Biliary cirrhosis
-Neonatal obstructive jaundice
-Cholelithiasis

Bone
-Hypertrophic osteoarthropathy
-Clubbing
-Arthritis
-Osteoporosis

Intestines
-Meconium ileus
-Meconium peritonitis
-Rectal prolapse
-Intussusception
-Volvulus
-Fibrosing colonopathy (strictures)
-Appendicitis
-Intestinal atresia
-Distal intestinal obstruction syndrome
-Inguinal hernia

Lungs
-Bronchiectasis
-Bronchitis
-Bronchiolitis
-Pneumonia
-Atelectasis
-Hemoptysis
-Pneumothorax
-Reactive airway disease
-Cor pulmonale
-Respiratory failure
-Mucoid impaction of the bronchi
-Allergic bronchopulmonary aspergillosis

Heart
-Right ventricular hypertrophy
-Pulmonary artery dilation

Spleen
-Hypersplenism

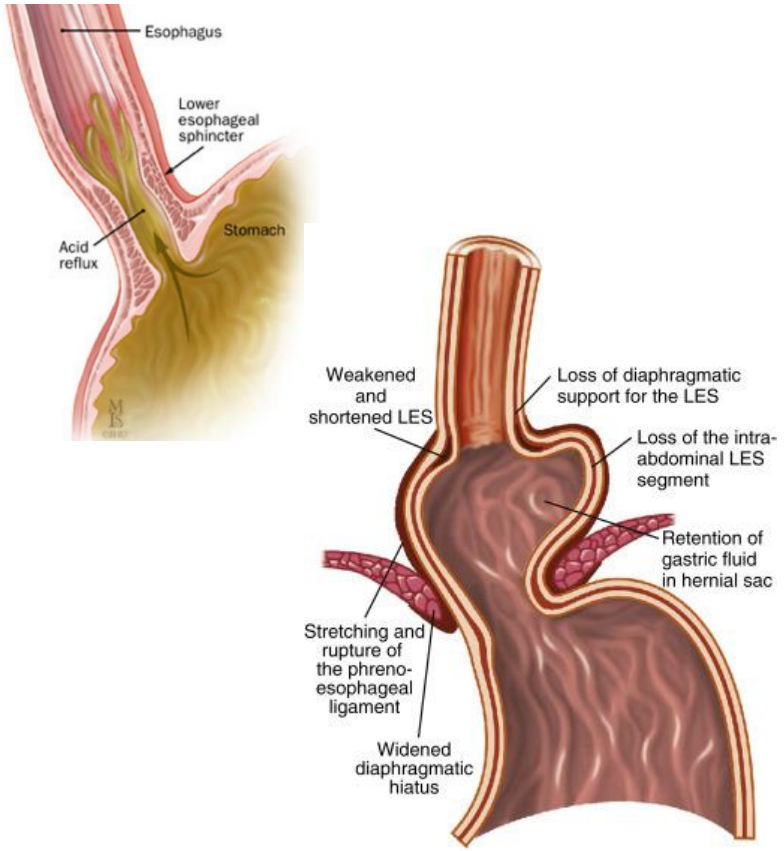
Stomach
-GERD

Pancreas
-Pancreatitis
-Insulin deficiency
-Symptomatic hyperglycemia
-Diabetes

Reproductive
-Infertility
(aspermia, Absence of vas deferens)
-Amenorrhea
-Delayed puberty

https://www.cancertherapyadvisor.com/home/decision-support-in-medicine/hospital-medicine/cystic-fibrosis-physician/

Heartburn and reflux: GERD



- Increased GER occurs when there is an imbalance between protective factors and aggravating factors
- Protective factors
  - Esophageal motility
  - Salivary bicarbonate
  - **Lower esophageal sphincter**
  - **Diaphragmatic crura**
  - **Gastric cardia**/ angle of His
- Aggravating factors
  - Increased intra-abdominal pressure
  - Excessive acid exposure
  - Impaired anti-reflux barriers (hiatal hernia, excessive transient lower esophageal sphincter relaxation)

Feldman M, et al. Sleisenger and Fordtran's gastrointestinal and liver disease E-book: pathophysiology, diagnosis, management. Elsevier; 2016.
Gastroesophageal Reflux Disease (GERD). Hopkinsmedicine.org. Accessed November 30, 2020

GI-related aspiration (GRASP)

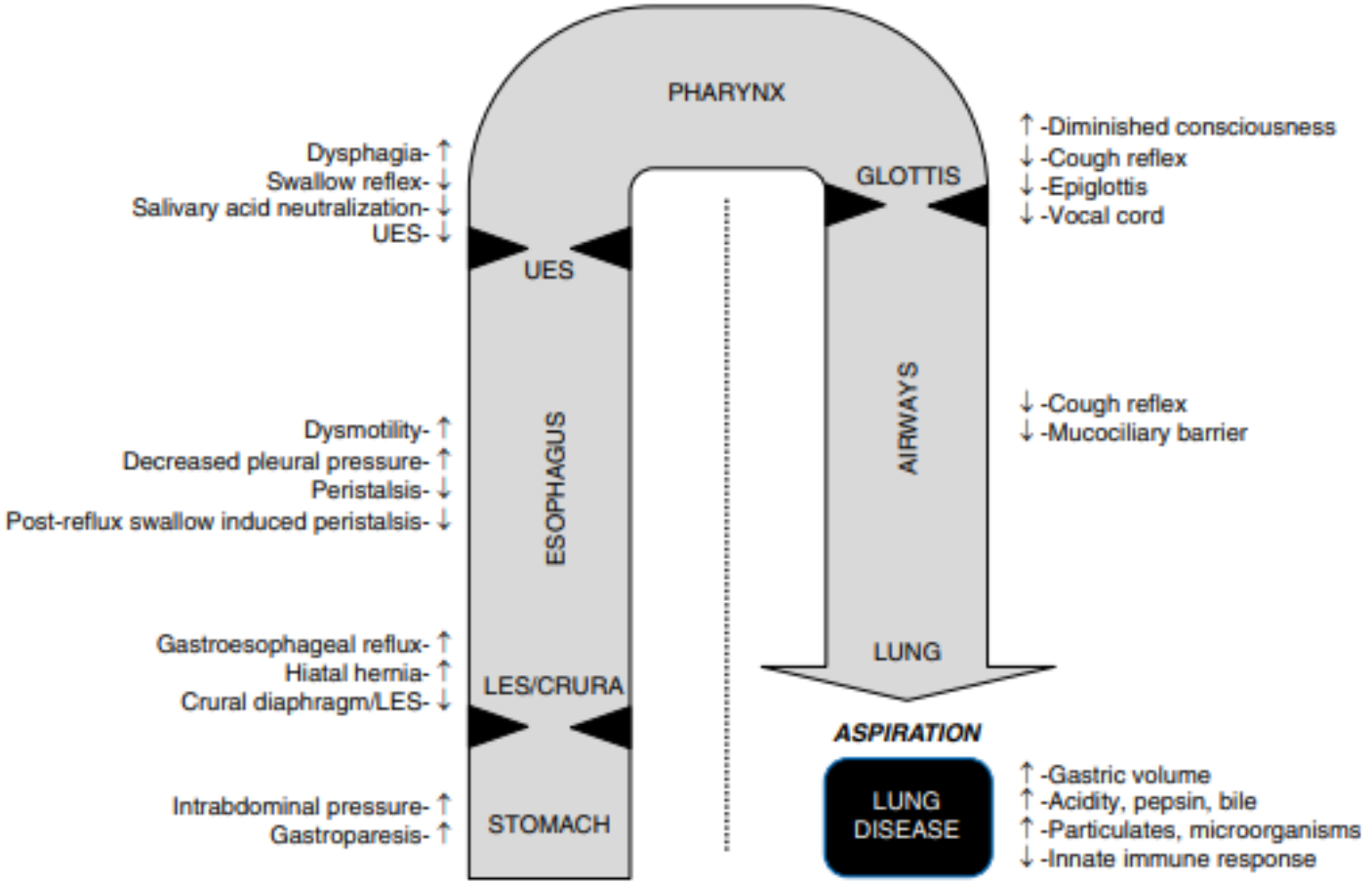
- Lung transplant outcomes are worse than all other solid organ transplant
- "Reflux" has been used as a short-hand for movement of foregut contents from the upper GI tract into the respiratory tree
  - Bile salts found in bronchoalveolar lavage

GRASPing for answers: The shortfalls of our current understanding of the effects of GI-related aspiration on the lungs in CF (GRASP-CF)[☆]

Vélez C, Neuringer I, King J. GRASPing for answers: The shortfalls of our current understanding of the effects of GI-related aspiration on the lungs in CF (GRASP-CF). J Cyst Fibros. 2024 Sep 27:S1569-1993(24)01779-X. doi: 10.1016/j.jcf.2024.09.014. Epub ahead of print. PMID: 39341689.

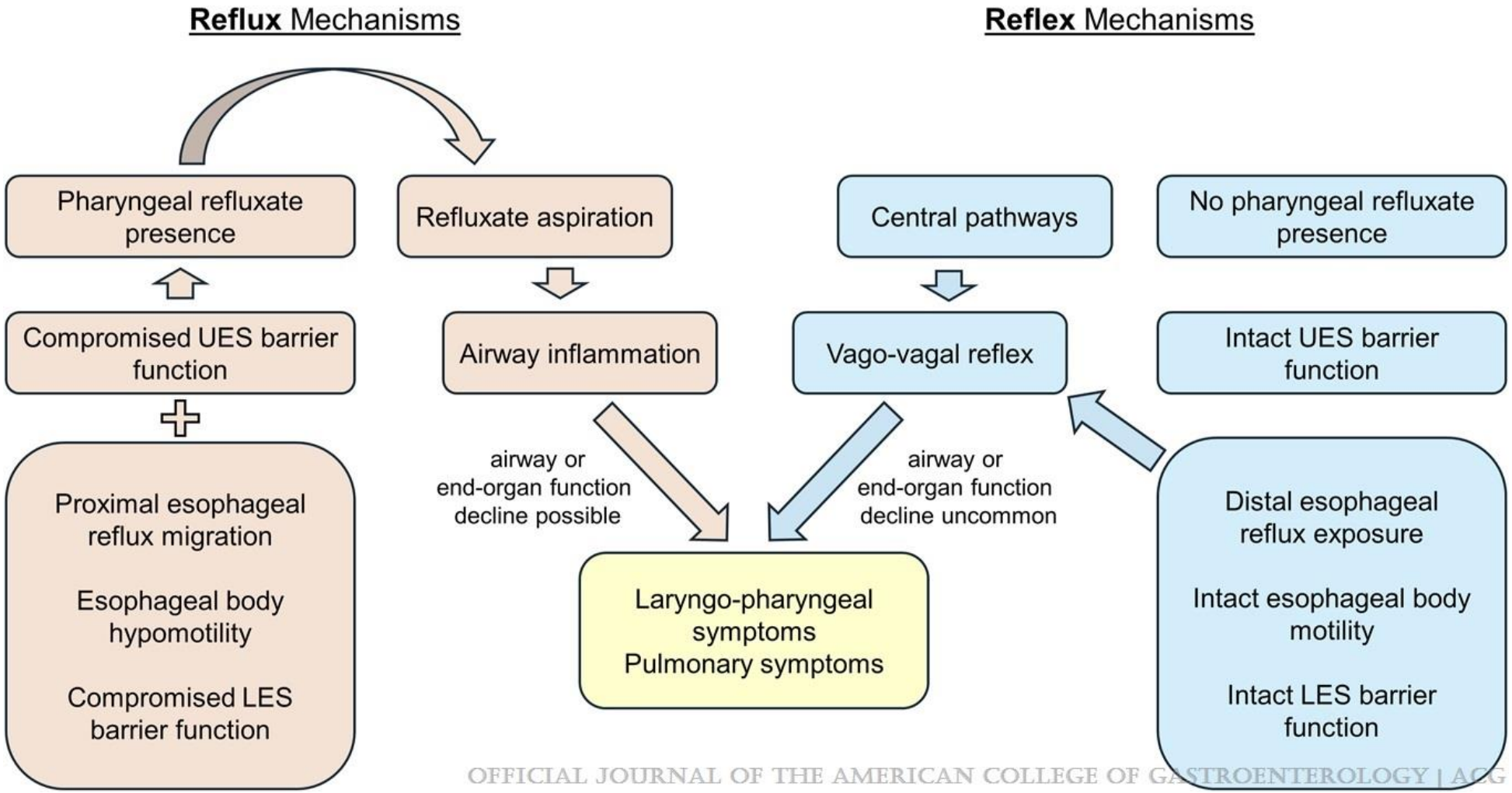
- Cystic Fibrosis Foundation has made a priority to study how GRASP impacts advanced lung disease and lung transplant survival
  - Standardization of motility testing protocol – is it needed? Does it change management? What tests should be used? Esophageal manometry vs wireless pH testing vs pH-mucosal intraluminal impedance, gastric emptying scan.
  - Should protocolized motility testing be offered irrespective of symptoms? Silent reflux? Lack of correlation between gastric emptying and gastroparesis symptoms?
  - Should motility testing be symptom-based?

GI-related aspiration (GRASP)



Ann Am Thorac Soc. 2020 Feb;17(2):155-164

GI-related aspiration (GRASP)



Chan, Walter W. MD, MPH, FACG[1]; Sharma, Nirmal MD[2]; Gyawali, C. Prakash MD, FRCP, FACG[3]. The Role of Gastroesophageal Reflux in Airway Inflammation. The American Journal of Gastroenterology 120(1):p 60-64, January 2025. | DOI: 10.14309/ajg.0000000000003205

Outline

- Case introduction
- Why is there an interloping gastroenterologist?
- **The relationship between GERD and asthma**
- How I approach GERD evaluation/refractory GERD
- Case wrap-up and clinical pearls

Relationship between GERD and asthma

- Asthma is heterogeneous, with incompletely characterized phenotypes.
- Multiple comorbidities (GERD, obstructive sleep apnea, obesity) are often present at higher incidence in those with asthma compared to those without asthma.
  - Are there shared pathophysiologic/inflammatory pathways?
- It has been estimated that GERD can occur in 30% and 80% of patients with asthma.
- Yet, the impact of acid suppression on asthma outcomes is unclear.
- Leads to a great degree of patient uncertainty and physician/patient frustration in more severe asthma cases.

Althoff MD, Ghincea A, Wood LG, Holguin F, Sharma S. Asthma and Three Colinear Comorbidities: Obesity, OSA, and GERD. J Allergy Clin Immunol Pract. 2021 Nov;9(11):3877-3884. doi: 10.1016/j.jaip.2021.09.003. Epub 2021 Sep 8. PMID: 34506967; PMCID: PMC8578370.

Relationship between GERD and asthma

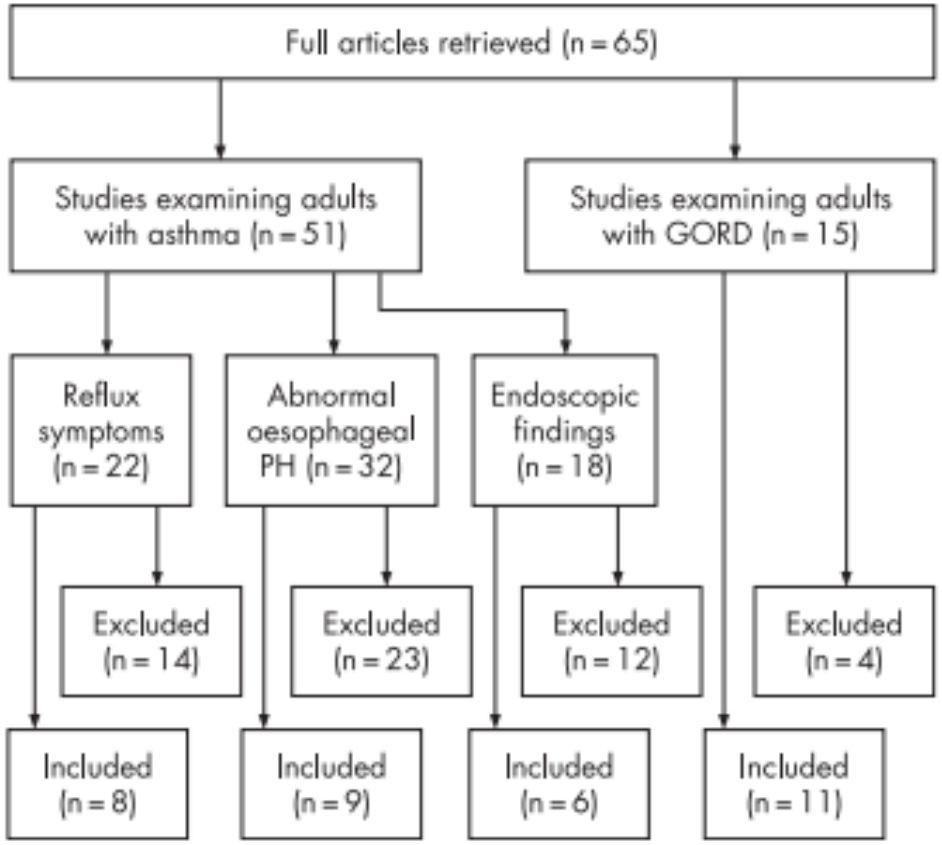
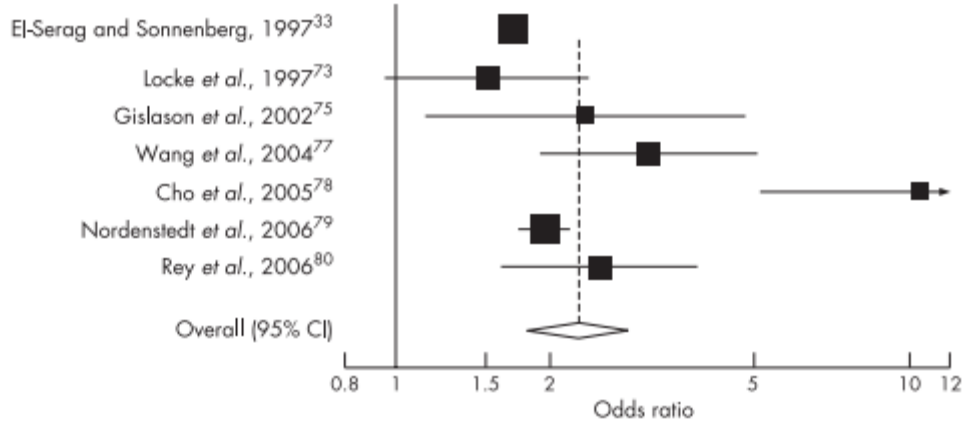


Figure 2 Organisation of articles retrieved from literature searches. GORD, gastro-oesophageal reflux disease.



Havemann BD, Henderson CA, El-Serag HB. The association between gastro-oesophageal reflux disease and asthma: a systematic review. Gut. 2007 Dec;56(12):1654-64. doi: 10.1136/gut.2007.122465. Epub 2007 Aug 6. PMID: 17682001; PMCID: PMC2095717.

Relationship between GERD and asthma

Effects of Asymptomatic Proximal and Distal Gastroesophageal Reflux on Asthma Severity

Emily DiMango[1], Janet T. Holbrook[2], Erin Simpson[1], Joan Reibman[3], Joel Richter[4], Surinder Narula[1], Nancy Prusakowski[2], John G. Mastronarde[5], and Robert A. Wise[2,6], for the American Lung Association Asthma Clinical Research Centers*

[1]Columbia University, College of Physicians and Surgeons, New York, New York; [2]Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland; [3]New York University School of Medicine, New York, New York; [4]Temple University School of Medicine, Philadelphia, Pennsylvania; [5]The Ohio State University Medical College, Columbus, Ohio; and [6]Johns Hopkins University School of Medicine, Baltimore, Maryland

- Rationale: Silent gastroesophageal reflux (GER) is common in patients with asthma, but it is unclear whether GER is associated with worse asthma symptoms or reduced lung function.
- Objectives: To determine in patients with poorly controlled asthma, whether proximal or distal esophageal reflux is associated with asthma severity, symptoms, physiology, or functional status.
- Methods: Baseline asthma characteristics were measured in patients with asthma enrolled in a multicenter trial assessing the effectiveness of esomeprazole on asthma control.
  - All participants underwent 24-hour esophageal pH probe monitoring.
  - Lung function, methacholine responsiveness, asthma symptoms, and quality-of-life scores were compared in subjects with and without GER.

DiMango E, Holbrook JT, Simpson E, Reibman J, Richter J, Narula S, Prusakowski N, Mastronarde JG, Wise RA; American Lung Association Asthma Clinical Research Centers. Effects of asymptomatic proximal and distal gastroesophageal reflux on asthma severity. Am J Respir Crit Care Med. 2009 Nov 1;180(9):809-16. doi: 10.1164/rccm.200904-0625OC. Epub 2009 Aug 6. PMID: 19661245; PMCID: PMC2773912.

Relationship between GERD and asthma

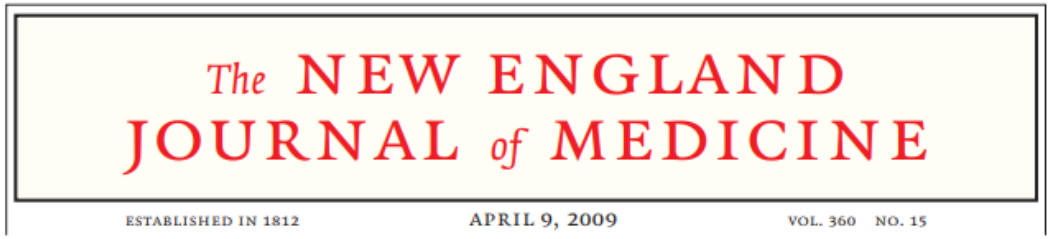
TABLE 2. BASELINE ASTHMA CHARACTERISTICS FOR SUBJECTS WITH AND WITHOUT GASTROESOPHAGEAL REFLUX

Asthma characteristics	pH Probe Result: Distal or Proximal Positive	pH Probe Result: Distal Negative and Proximal Negative or Missing	*P* Value*
N (%)	160 (53)	144 (47)	
Mean age of asthma onset, yr ± SD	16 ± 17	17 ± 17	0.14
Use of inhaled short-acting β-agonist (MDI/Neb) ⩾ 2 times/wk, % of group	81	78	0.55
⩾2 Unscheduled health care visit in past yr, %	64	57	0.54
ACQ ⩾ 1.5, %	92	91	0.78
Oral corticosteroids for asthma in past yr, %	56	43	0.03
Night awakenings due to asthma in past 2 wk, %	18	10	0.08
Daily use of ICS, %	100	100	
Daily dose of ICS, μg	663 ± 23.4	647 ± 21.7	0.31
Mean ACS (↓) (score range: 0–6) ± SD	1.9 ± 0.9	1.8 ± 0.8	0.25
Mean ASUI (↑) (score range: 0–1) ± SD	0.73 ± 0.18	0.77 ± 0.15	0.08
Mean AQL (↑) (score range: 1–7) ± SD	4.4 ± 1.3	4.8 ± 1.2	0.01
SF-36 quality of life (↑) (score range: 0–100), N	160	143	
Mean physical score ± SD	41 ± 10	43 ± 10	0.06
Mean emotional score ± SD	48 ± 11	49 ± 11	0.56
Mean pulmonary function measures, N	160	144	
Pre-BD FEV_1, % predicted ± SD†	76 ± 15	77 ± 14	0.84
Pre-BD FVC, % predicted ± SD†	87 ± 15	88 ± 13	0.56
FEV_1, % change post-BD ± SD	10 ± 9	11 ± 11	0.15
FVC, % change post-BD ± SD	5 ± 8	6 ± 8	0.37
Peak expiratory flow rate (% predicted ± SD)	79 ± 18	80 ± 17	0.40
Methacholine contraindicated (% of group)	60	55	0.39
PC_{20}, mg/ml, N, mean ± SD	61, 3.4 ± 4.0	64, 4.3 ± 5.1	0.94

- Results: Of 304 participants with probe recordings, 53% had reflux.
  - Of 242 participants with recordings of proximal pH, 38% had proximal reflux.
  - There was no difference in need for short-acting bronchodilators, nocturnal awakenings, dose of inhaled corticosteroid, use of long-acting b-agonists, lung function, or methacholine reactivity between individuals with and without proximal or distal GER.
  - Participants with GER reported more use of oral corticosteroids and had worse asthma quality of life and subjects with proximal GER had significantly worse asthma quality of life and health-related quality of life compared with participants without GER.
- Conclusions: Asymptomatic GER is not associated with distinguishing asthma symptoms or lower lung function in individuals with suboptimal asthma control who are using inhaled corticosteroids.
  - Patients with proximal reflux report significantly worse asthma and health-related quality of life despite lack of physiologic impairment or increase in asthma symptoms.

DiMango E, Holbrook JT, Simpson E, Reibman J, Richter J, Narula S, Prusakowski N, Mastronarde JG, Wise RA; American Lung Association Asthma Clinical Research Centers. Effects of asymptomatic proximal and distal gastroesophageal reflux on asthma severity. Am J Respir Crit Care Med. 2009 Nov 1;180(9):809-16. doi: 10.1164/rccm.200904-0625OC. Epub 2009 Aug 6. PMID: 19661245; PMCID: PMC2773912.

Relationship between GERD and asthma



- Methods
  - 402 people with asthma with inadequate asthma control despite inhaled corticosteroids and absent or minimal GER symptoms were randomly assigned to either esomeprazole 40mg b.i.d. or matching placebo in a parallel-group double-masked clinical trial.
  - Participants were followed for 24 weeks with daily asthma diaries, every 4-week spirometry, and asthma symptom questionnaires.
  - Participants were classified with respect to GER status with ambulatory pH probe monitoring.
  - The primary outcome was the rate of episodes of poor asthma control (EPACs) based on asthma diaries.

American Lung Association Asthma Clinical Research Centers; Mastronarde JG, Anthonisen NR, Castro M, Holbrook JT, Leone FT, Teague WG, Wise RA. Efficacy of esomeprazole for treatment of poorly controlled asthma. N Engl J Med. 2009 Apr 9;360(15):1487-99. doi: 10.1056/NEJMoa0806290. PMID: 19357404; PMCID: PMC2974569.

Relationship between GERD and asthma

Table 3. Episodes of Poor Asthma Control and Component Events.*

Variable	Placebo (N=193)	Esomeprazole (N=200)	Incidence-Rate Ratio, Esomeprazole vs. Placebo (95% CI)	P Value: Esomeprazole vs. Placebo†	P Value: Gastroesophageal-Reflux Interaction‡
Asthma episodes, according to definition that did not include use of beta-agonists as a criterion					
No. of events	201	224			
No. of events/person-yr	2.3	2.5	1.1 (0.8–1.5)	0.66	0.93
Patients with ≥1 event (%)	42	42			
Exacerbation components					
≥30% drop in peak expiratory flow on 2 consecutive days					
No. of events	141	180			
No. of events/person-yr	1.7	2.1	1.2 (0.8–2.0)	0.35	0.99
Patients with ≥1 event (%)	26	28			
Urgent care visit					
No. of events	53	51			
No. of events/person-yr	0.6	0.6	0.9 (0.6–1.5)	0.79	0.44
Patients with ≥1 event (%)	17	18			
New use of oral corticosteroids					
No. of events	50	48			
No. of events/person-yr	0.6	0.5	0.9 (0.6–1.3)	0.62	0.85
Patients with ≥1 event (%)	24	21			

- Episodes of poor asthma control occurred with similar frequency in the placebo and esomeprazole treatment groups (2.3 vs 2.5 events/person-year, respectively, P=0.66).
- There was no treatment effect with respect to components of the EPACs, or secondary outcomes including pulmonary function, airways reactivity, asthma control, symptom scores, nocturnal awakenings, or quality of life.
- GER documented by pH probe studies in 40% of participants with absent or minimal symptoms did not identify a subgroup benefitting from PPI treatment.
- Conclusion—Despite a high prevalence of asymptomatic GER in patients with poorly controlled asthma, treatment with proton pump inhibitors does not improve control. Silent GER is not a likely cause of poorly controlled asthma

American Lung Association Asthma Clinical Research Centers; Mastronarde JG, Anthonisen NR, Castro M, Holbrook JT, Leone FT, Teague WG, Wise RA. Efficacy of esomeprazole for treatment of poorly controlled asthma. N Engl J Med. 2009 Apr 9;360(15):1487-99. doi: 10.1056/NEJMoa0806290. PMID: 19357404; PMCID: PMC2974569.

Relationship between GERD and asthma

CHEST

Volume 128, Issue 3, September 2005, Pages 1128-1135

Clinical Investigations

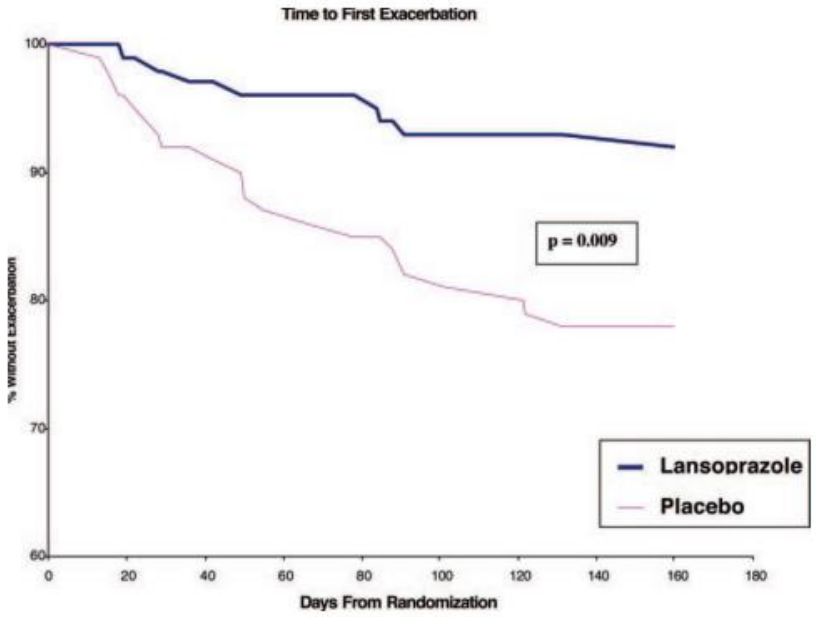
Effects of 24 Weeks of Lansoprazole Therapy on Asthma Symptoms, Exacerbations, Quality of Life, and Pulmonary Function in Adult Asthmatic Patients With Acid Reflux Symptoms

Littner Michael R. MD [a], Leung Felix W. MD [a], Ballard E. David II MD [b], Huang Bidan PhD [c], Samra Nina K. MS [b]

- **Background:** Difficult-to-control asthma has been associated with gastroesophageal acid reflux. Acid-suppressive treatment has been inconsistent in improving asthma control.
- **Objective:** To determine whether a proton-pump inhibitor improves asthma control in adult asthmatic patients with acid reflux symptoms.
- **Design:** Multicenter, double-blind, randomized, placebo-controlled trial.
- **Setting:** Twenty-nine private practices and 3 academic practices in the United States.
- **Patients:** Two hundred seven patients receiving usual asthma care including an inhaled corticosteroid (ICS). Patients had acid reflux symptoms and moderate-to-severe persistent asthma.
- **Intervention:** Lansoprazole, 30 mg bid, or placebo, bid, for 24 weeks.
- **Measurements:** The primary outcome measure was daily asthma symptoms by diary. Secondary asthma outcomes included rescue albuterol use, daily morning and evening peak expiratory flow, FEV1, FVC, asthma quality of life with standardized activities (AQLQS) questionnaire score, investigator-assessed symptoms, exacerbations, and oral corticosteroid-treated exacerbations.

Littner MR, Leung FW, Ballard ED 2nd, Huang B, Samra NK; Lansoprazole Asthma Study Group. Effects of 24 weeks of lansoprazole therapy on asthma symptoms, exacerbations, quality of life, and pulmonary function in adult asthmatic patients with acid reflux symptoms. Chest. 2005 Sep;128(3):1128-35. doi: 10.1378/chest.128.3.1128. PMID: 16162697.

Relationship between GERD and asthma



- **Results:**
  - Daily asthma symptoms, albuterol use, peak expiratory flow, FEV1, FVC, and investigator-assessed asthma symptoms at 24 weeks did not improve significantly with lansoprazole treatment compared to placebo.
  - Fewer patients receiving lansoprazole (8.1% vs 20.4%, respectively; p = 0.017) had exacerbations and oral corticosteroid-treated (ie, moderate-to-severe) exacerbations (4% vs 13.9%, respectively; p = 0.016) of asthma.
  - A post hoc subgroup analysis revealed that fewer patients receiving one or more long-term asthma-control medications in addition to an ICS experienced exacerbations (6.5% vs 24.6%, respectively; p = 0.016) and moderate-to-severe exacerbations (2.2% vs 17.5%, respectively; p = 0.021) with lansoprazole therapy.

Conclusion:

- Treatment with 30 mg of lansoprazole bid for 24 weeks did not improve asthma symptoms or pulmonary function or reduce albuterol use.
- However, this dose significantly reduced asthma exacerbations and improved asthma quality of life, particularly in those patients receiving more than one asthma-control medication.

Littner MR, Leung FW, Ballard ED 2nd, Huang B, Samra NK; Lansoprazole Asthma Study Group. Effects of 24 weeks of lansoprazole therapy on asthma symptoms, exacerbations, quality of life, and pulmonary function in adult asthmatic patients with acid reflux symptoms. Chest. 2005 Sep;128(3):1128-35. doi: 10.1378/chest.128.3.1128. PMID: 16162697.

Relationship between GERD and asthma

- Possible future research directions:
  - Efficacy of GERD treatment in patients with asthma with manometry- and pH-proven pathologic gastro-esophageal reflux disease with or without traditional GERD symptoms.
  - Examining whether a distinction needs to be drawn between proximal vs distal esophageal reflux.
  - Examining asthma outcomes as it relates to medical, endoluminal, and surgical GERD treatments.

Althoff MD, Ghincea A, Wood LG, Holguin F, Sharma S. Asthma and Three Colinear Comorbidities: Obesity, OSA, and GERD. J Allergy Clin Immunol Pract. 2021 Nov;9(11):3877-3884. doi: 10.1016/j.jaip.2021.09.003. Epub 2021 Sep 8. PMID: 34506967; PMCID: PMC8578370.

Outline

- Case introduction
- Why is there an interloping gastroenterologist?
- The relationship between GERD and asthma
- **How I approach GERD evaluation/refractory GERD**
- Case wrap-up and clinical pearls

TL, DR: Please do not rely on esophagrams to diagnose clinically significant reflux

CME

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

Philip O. Katz, MD, MACG[1], Kerry B. Dunbar, MD, PhD[2,3], Felice H. Schnoll-Sussman, MD, FACG[1], Katarina B. Greer, MD, MS, FACG[4], Rena Yadlapati, MD, MSHS[5] and Stuart Jon Spechler, MD, FACG[6,7]

- Barium radiographs should not be used solely as a diagnostic test for GERD.
- The presence of reflux on a barium esophagram or upper GI series has poor sensitivity and specificity for GERD when compared with pH testing.
- In one study, only about one-half of patients with abnormal reflux on a barium study were found to have abnormal pH monitoring.
- The finding of barium reflux above the thoracic inlet with or without provocative maneuvers (including the water siphon test) somewhat increases the sensitivity for reflux, but not sufficiently for barium esophagram to be recommended as a diagnostic test for GERD

Testing for foregut conditions potentially impacting respiratory tree

Disease	Definition	Symptoms	Diagnosis	Treatment (selected)
Gastro-esophageal reflux disease (GERD), possibly with laryngopha- ryngeal reflux (LPR)	Endoscopic findings: Peptic stricture, erosive esophagitis, Barrett's esophagus Ambulatory reflux monitoring: • Elevated acid exposure time in the esophagus • Excessive reflux episodes • Nascent consensus as to LPR definitions and diagnosis, but not widely employed	Esophageal: heartburn, regurgitation Extra-esophageal: cough, sinusitis, voice change, exacerbation of chronic lung disease	GERD symptom improvement • Favorable symptom response to acid suppression Ambulatory reflux monitoring • Elevated acid exposure time in the esophagus (*Conclusive*: >6 % over 24-hours; *Inconclusive*: 4–6 % over 24-hours); • Excessive reflux episodes (*Conclusive*: >80 episodes over 24-hour period; *Inconclusive*: 40–80 episodes over 24-hour period) Esophagogastroduodenoscopy (EGD) demonstrating: • Barrett's esophagus – esophageal intestinal metaplasia, • Erosive esophagitis – LA Grades B, C, and D • Peptic stricture	Medical: • Histamine 2 antagonism (famotidine) • Proton pump inhibition • Potassium competitive acid blockers (vonoprazan) Endoluminal: • Transoral incisionless fundoplication • Radiofrequency (Stretta) Surgical: • Surgical fundoplication (e.g. Nissen, Toupet, Dor etc.)

Vélez C, Neuringer I, King J. GRASPing for answers: The shortfalls of our current understanding of the effects of GI-related aspiration on the lungs in CF (GRASP-CF). J Cyst Fibros. 2024 Sep 27:S1569-1993(24)01779-X. doi: 10.1016/j.jcf.2024.09.014. Epub ahead of print. PMID: 39341689.

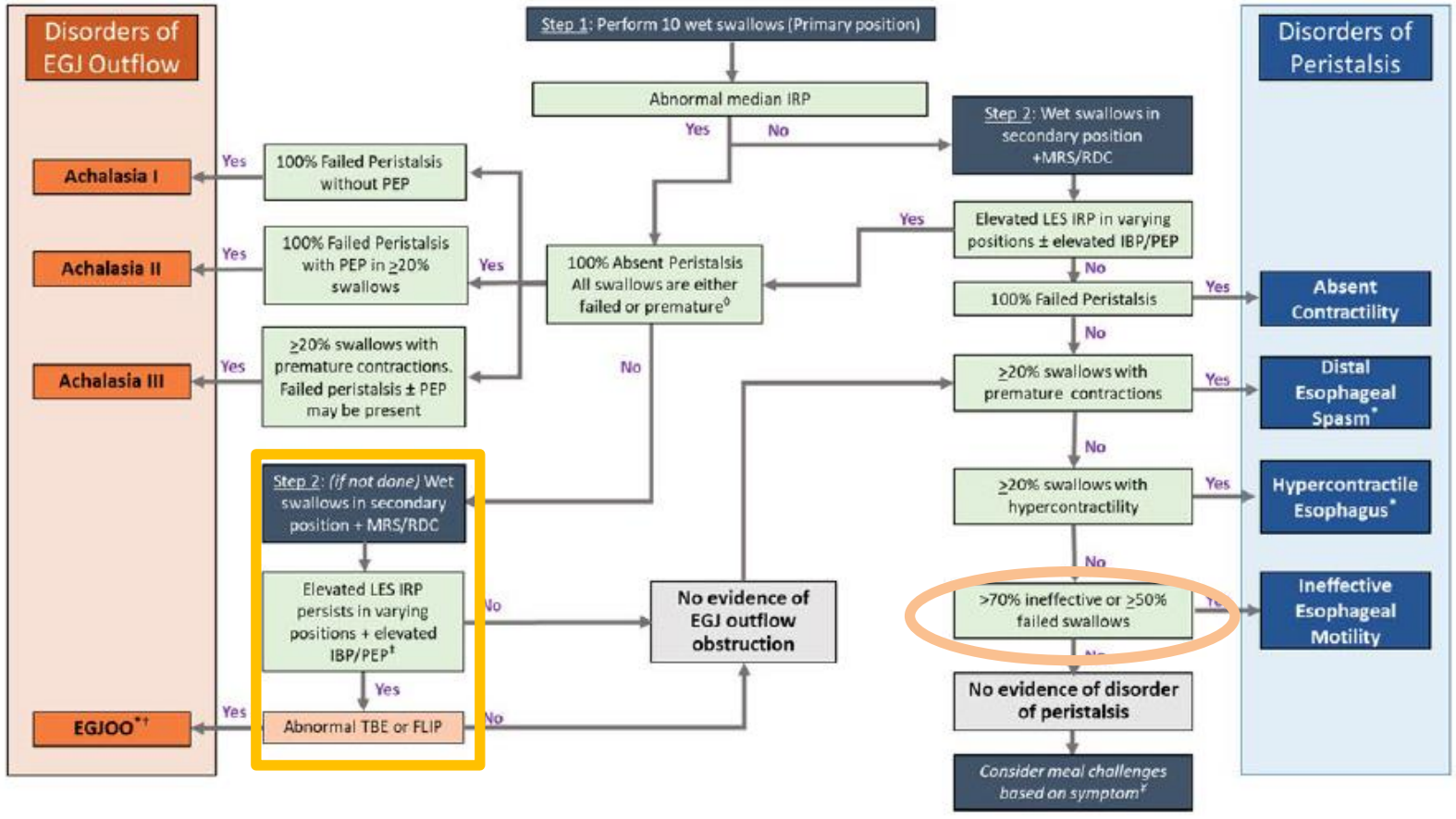
Testing for foregut conditions potentially impacting respiratory tree

Gastroparesis (GP)	Endoscopic findings: Retained food/food bezoar Motility testing • Gastric emptying scan/ scintigraphy (GES) • Wireless motility capsule (WMC) • Gastric emptying breath test (GEBT)	Motor symptoms: Nausea, vomiting, early satiety Sensory symptoms: Nausea, abdominal pain	Motor abnormalities: • GES: >10 % solid food retained at 4-hours • WMC: Failure of capsule to progress in less than 5-hours • GEBT: Variation of carbon isotopes over time Sensory abnormalities: • Symptom reporting • Patient reported outcome measures	Medical: • Macrolide antibiotics (azithromycin, erythromycin) • Dopaminergic (metoclopramide, domperidone*) • Serotonergic (prucalopride*) Endoluminal: • Per oral pyloromyotomy (POP) • Botulinum toxin injection (pylorus) Surgical: • Gastric stimulator (Enterra) • Surgical pyloroplasty *depending on jurisdiction

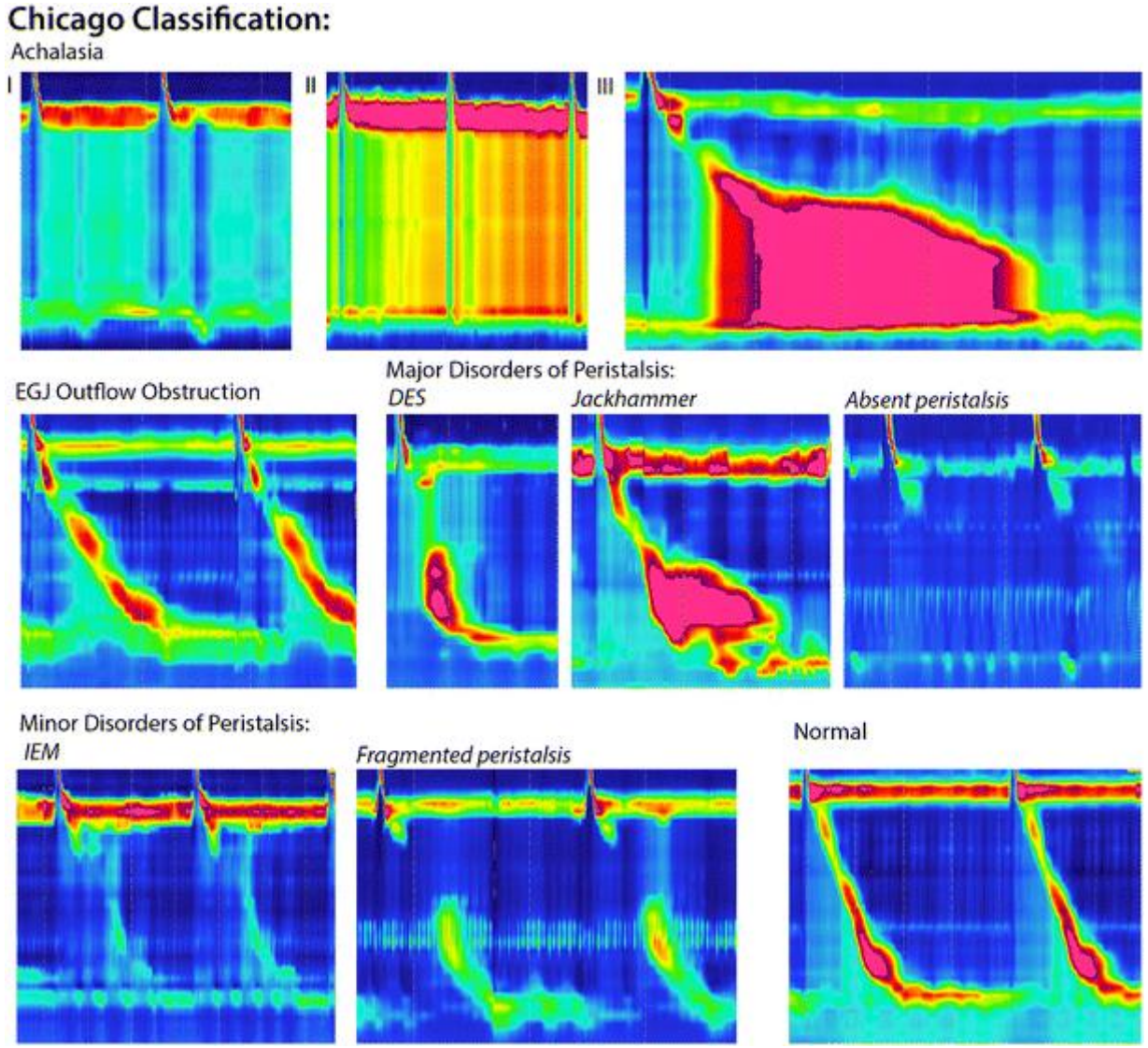
Vélez C, Neuringer I, King J. GRASPing for answers: The shortfalls of our current understanding of the effects of GI-related aspiration on the lungs in CF (GRASP-CF). J Cyst Fibros. 2024 Sep 27:S1569-1993(24)01779-X. doi: 10.1016/j.jcf.2024.09.014. Epub ahead of print. PMID: 39341689.

Esophageal motility testing: Chicago

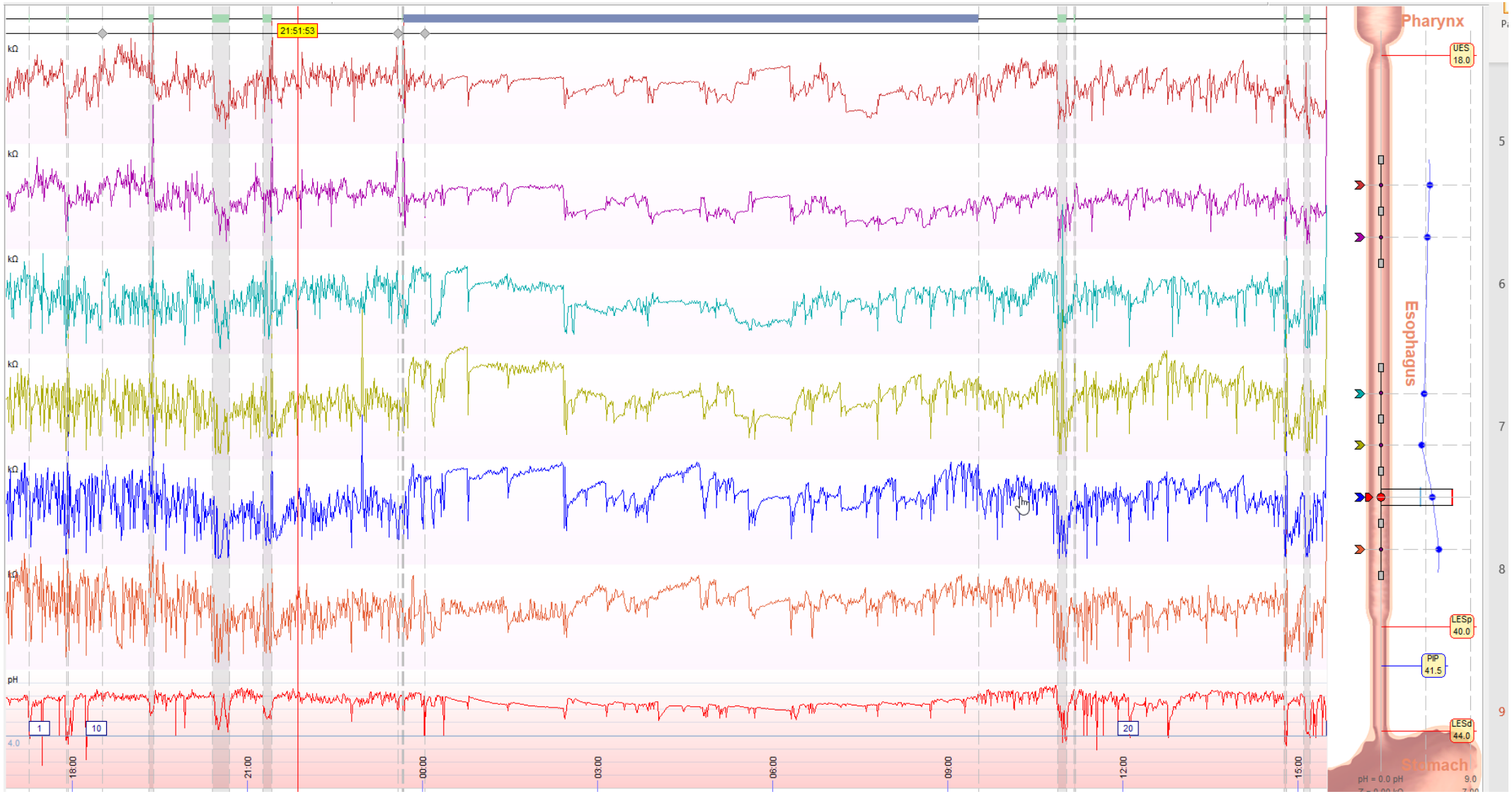
CC v. 4.0



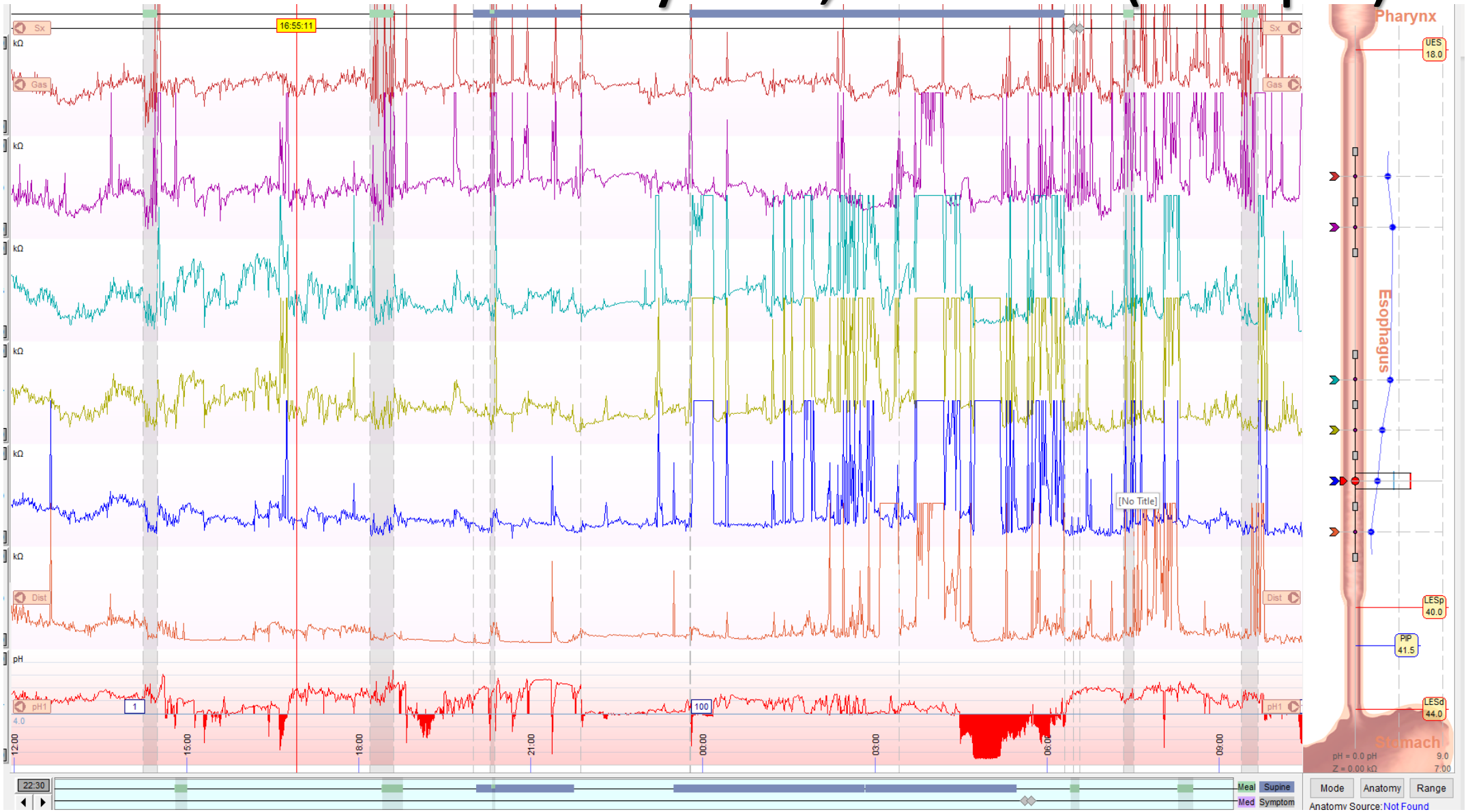
Esophageal manometry output



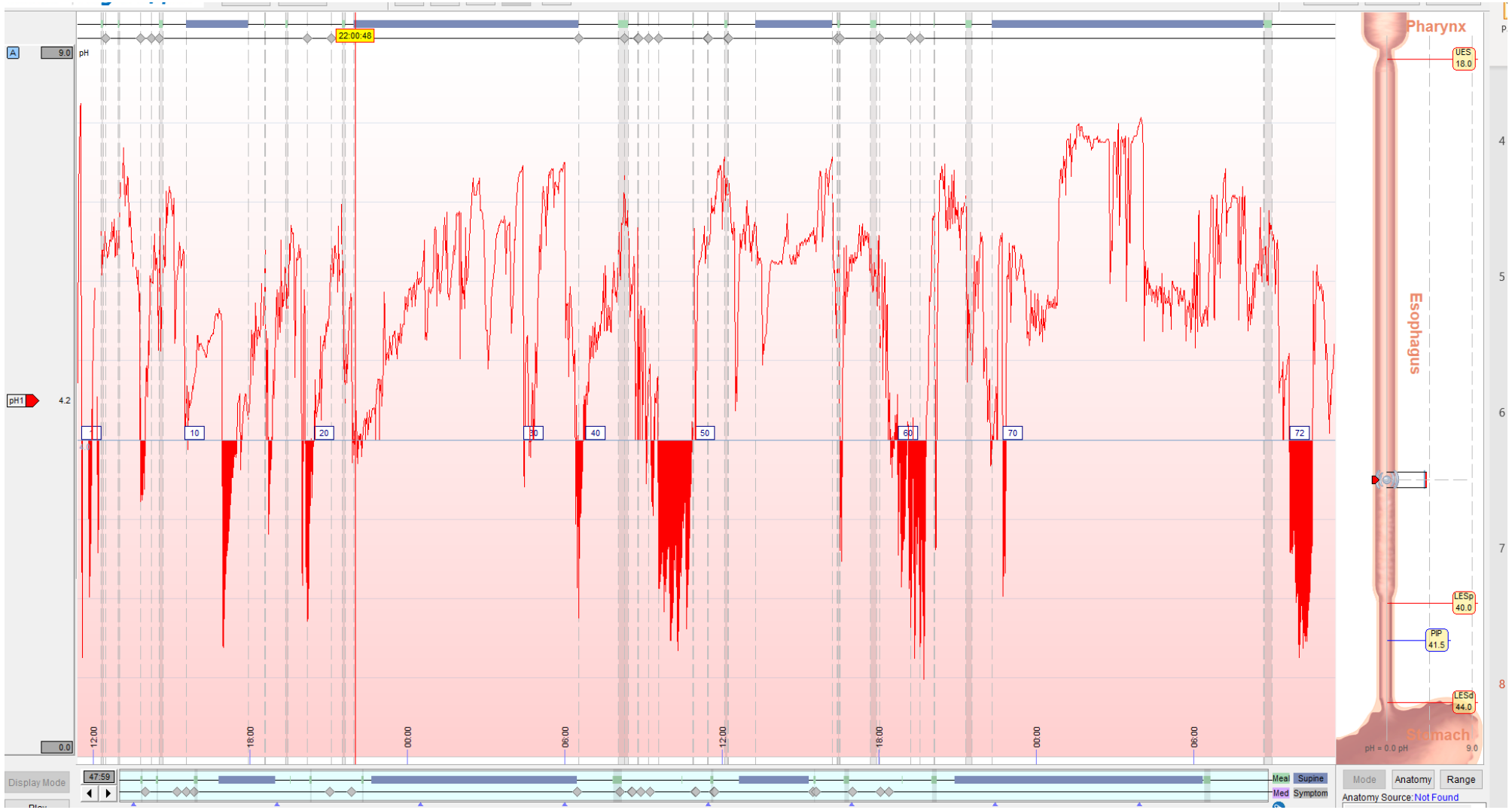
Absent GERD by AET, reflux # (MII-pH)



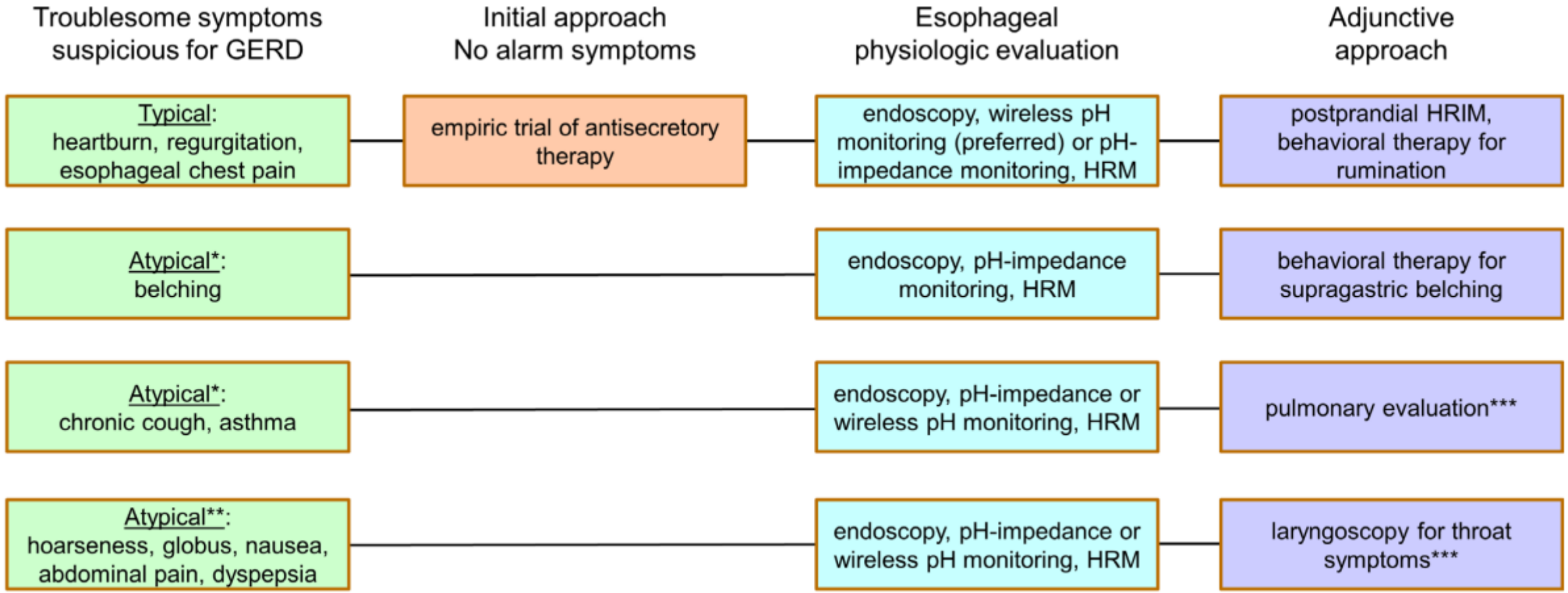
Definitive GERD by AET, reflux # (MII-pH)



Definitive GERD by AET, reflux # (Bravo)

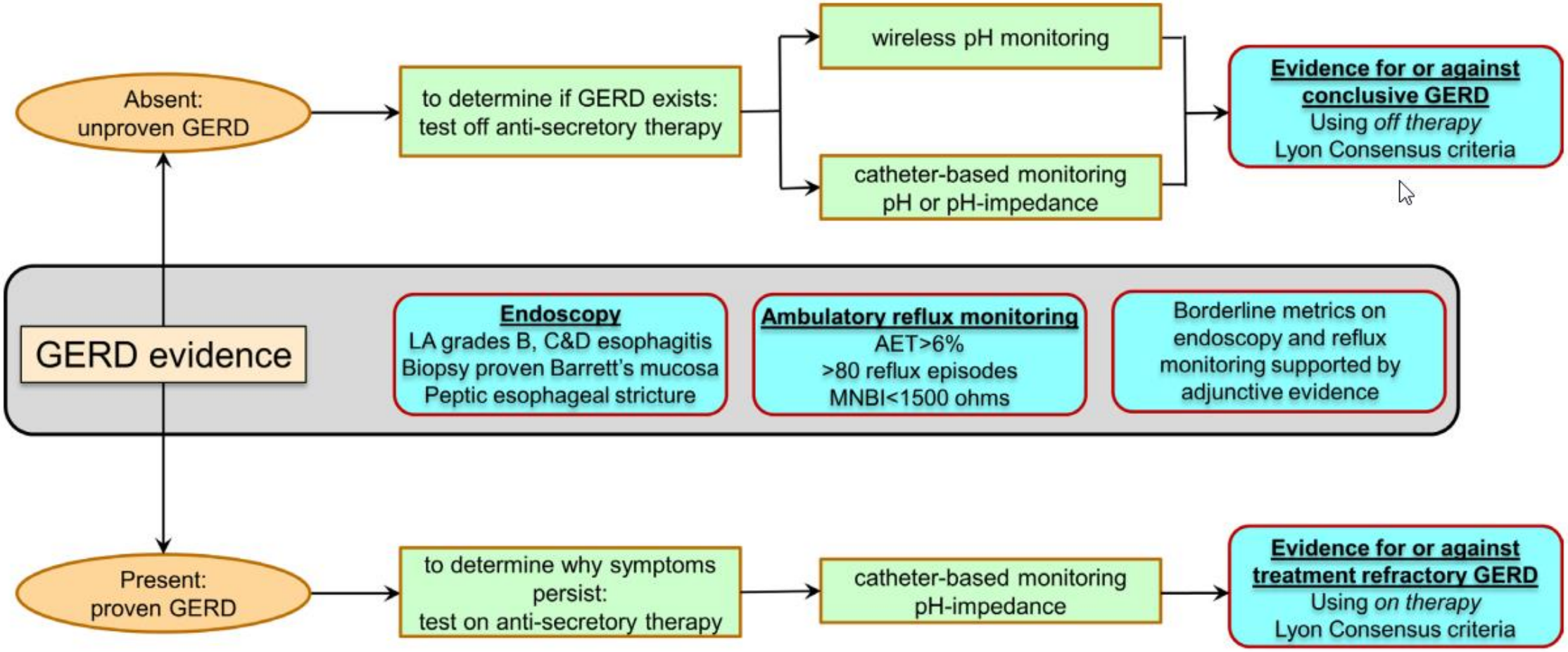


Lyon Consensus: Reflux



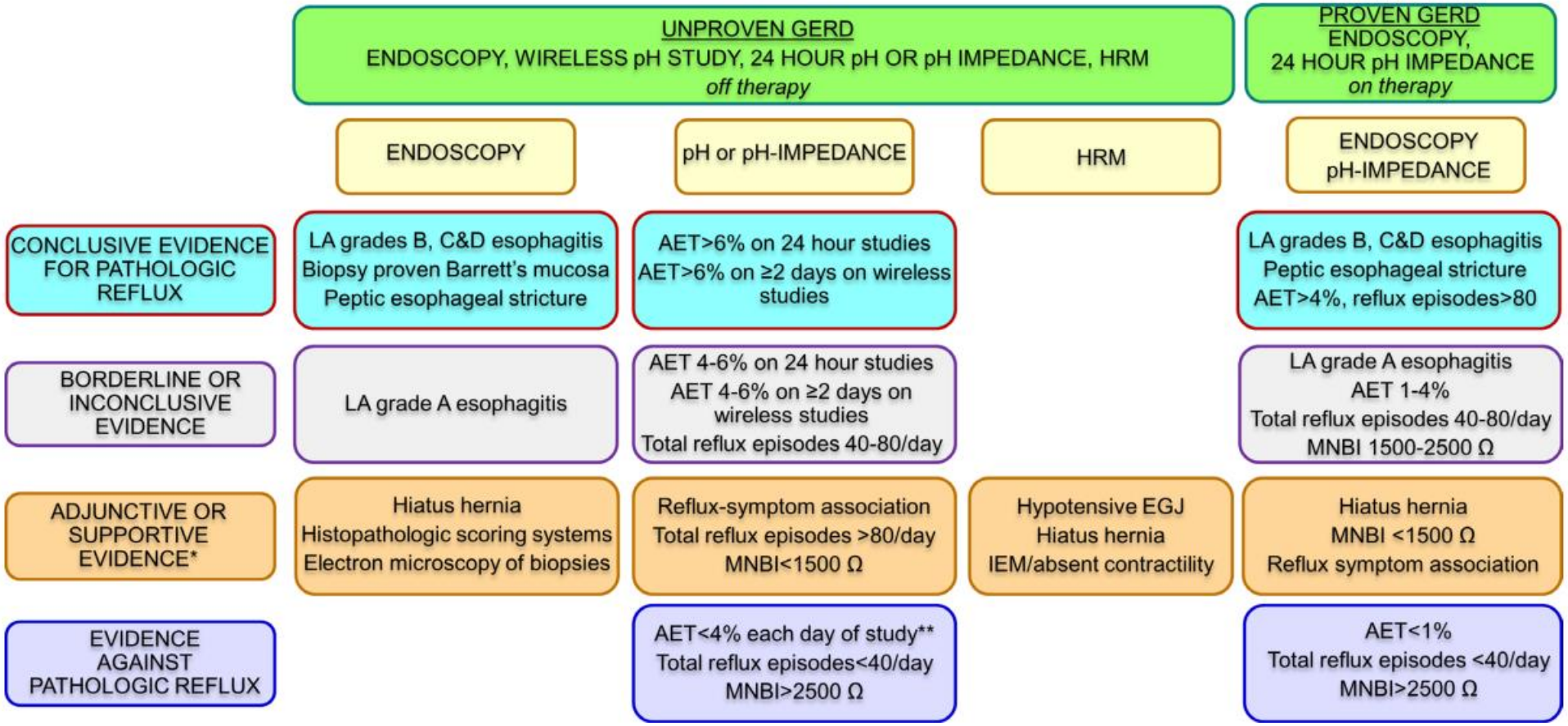
Gyawali CP, Yadlapati R, Fass R, Katzka D, Pandolfino J, Savarino E, Sifrim D, Spechler S, Zerbib F, Fox MR, Bhatia S, de Bortoli N, Cho YK, Cisternas D, Chen CL, Cock C, Hani A, Remes Troche JM, Xiao Y, Vaezi MF, Roman S. Updates to the modern diagnosis of GERD: Lyon consensus 2.0. Gut. 2024 Jan 5;73(2):361-371. doi: 10.1136/gutjnl-2023-330616. PMID: 37734911; PMCID: PMC10846564.

Lyon Consensus: Reflux



Gyawali CP, Yadlapati R, Fass R, Katzka D, Pandolfino J, Savarino E, Sifrim D, Spechler S, Zerbib F, Fox MR, Bhatia S, de Bortoli N, Cho YK, Cisternas D, Chen CL, Cock C, Hani A, Remes Troche JM, Xiao Y, Vaezi MF, Roman S. Updates to the modern diagnosis of GERD: Lyon consensus 2.0. Gut. 2024 Jan 5;73(2):361-371. doi: 10.1136/gutjnl-2023-330616. PMID: 37734911; PMCID: PMC10846564.

Lyon Consensus: Reflux



Gyawali CP, Yadlapati R, Fass R, Katzka D, Pandolfino J, Savarino E, Sifrim D, Spechler S, Zerbib F, Fox MR, Bhatia S, de Bortoli N, Cho YK, Cisternas D, Chen CL, Cock C, Hani A, Remes Troche JM, Xiao Y, Vaezi MF, Roman S. Updates to the modern diagnosis of GERD: Lyon consensus 2.0. Gut. 2024 Jan 5;73(2):361-371. doi: 10.1136/gutjnl-2023-330616. PMID: 37734911; PMCID: PMC10846564.

Outline

- Case introduction
- Why is there an interloping gastroenterologist?
- The relationship between GERD and asthma
- How I approach GERD evaluation/refractory GERD
- **Case wrap-up and clinical pearls**

Case wrap-up

- She is on the maximum daily dose of omeprazole, among the more potent proton pump inhibitors.
  - Consider switch to rabeprazole?
  - Consider potassium competitive acid blocker (vonoprazan)?
- Fortunately, with no recent endoscopy, the decision to exclude erosive esophagitis is an easy one (as the next clinical step).
  - Could pair this with a wireless 96-hour BRAVO test (off of PPI since we do not have established GERD).
  - Or, could consider 2 pH probe catheter-based multichannel intraluminal impedance 24-hour test.
- Emphasis on weight loss, as this contributes to refluxate.
- Readdressing possible surgical intervention of aberrant subclavian artery.

Clinical pearls: Severe asthma and GERD

- While asthma and GERD are frequently comorbid conditions, and causality to some degree is likely, we cannot predict well which patients with severe asthma will improve with more aggressive GERD treatment.
- In refractory/severe asthma cases, it is reasonable to pursue ambulatory reflux monitoring (ideally off acid suppression) to determine if there is intervenable GI disease.
- Know the limitations of the different diagnostic modalities and treatments, prior to invoking GERD in the management of patients with severe asthma.
  - Do not rely on esophagrams.