REFRACTORY GERD: MEDICAL TREATMENT

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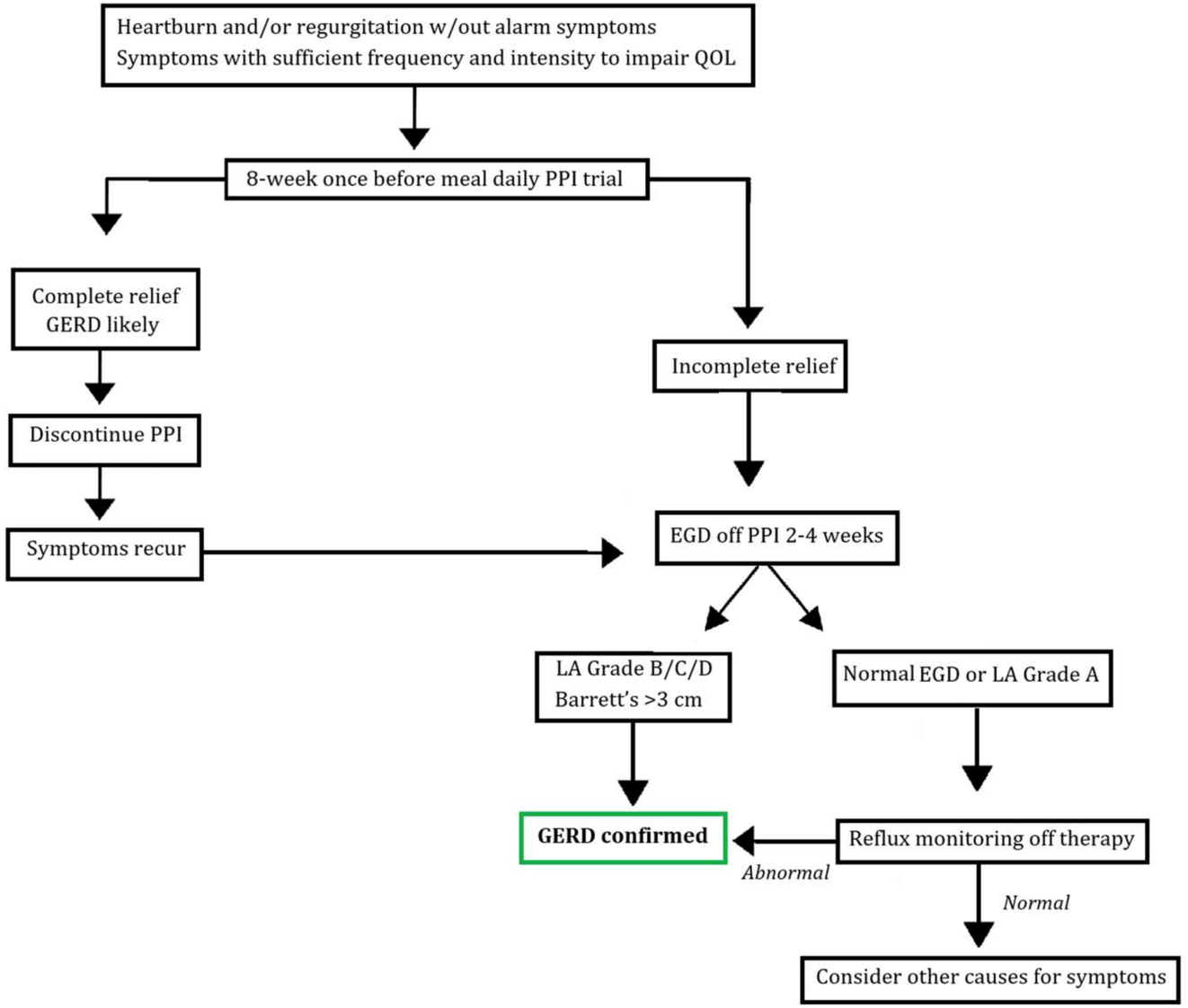
REFRACTORY GERD

Definition

- PPI is not controlling symptoms

➞ GERD has been documented by EGD (erosive esophagitis or Barrett's) or by PH monitoring but symptoms remain despite a PPI

➞ Symptoms suspected due to GERD have been treated empirically with PPI, but symptoms have not been relieved



Philip O Katz, AJG, 2021

REFRACTORY GERD

EGD AND H. PYLORI

- In patients with refractory reflux-like symptoms, we suggest performing endoscopy to identify patients with erosive esophagitis or other reflux-related injury

GRADE: Conditional recommendation, low quality of evidence

- In patients with refractory reflux-like symptoms, we recommend against treatment of confirmed Helicobacter pylori infection solely for the purpose of improving reflux symptoms

GRADE: Strong recommendation, moderate quality of evidence

Alimentary Pharmacology & Therapeutics, 2025

REFRACTORY GERD

PH testing

- In patients with refractory reflux-like symptoms, we suggest that oesophageal pH testing should be performed off PPI therapy to determine whether the patient has excess acid gastro-oesophageal reflux as a cause for symptoms.

GRADE: Conditional, very low.

- In patients with refractory reflux-like symptoms for whom testing is performed on PPI therapy, we suggest oesophageal pH-impedance rather than oesophageal pH testing to identify reflux as a cause for symptoms.

GRADE: Conditional, very low.

Alimentary Pharmacology & Therapeutics, 2025

REFRACTORY GERD

Manometry

- In patients with refractory reflux-like symptoms, we suggest oesophageal manometry to identify other causes for the symptoms.
  GRADE: Conditional, very low.

Alimentary Pharmacology & Therapeutics, 2025

REFRACTORY GERD

Medical Treatment

- In patients with refractory reflux-like symptoms after 8 weeks of twice-daily PPI therapy, we suggest against using higher dose PPI therapy compared to continuing twice-daily PPI therapy to improve symptoms.

GRADE: Conditional, very low.

- No consensus D. In patients with refractory reflux-like symptoms after 8 weeks of twice-daily PPI therapy, we do not make a recommendation (for or against) adding a prokinetic to twice-daily PPI therapy to improve symptoms.

GRADE: NO recommendation, low

Alimentary Pharmacology & Therapeutics, 2025

REFRACTORY GERD

Medical Treatment

- In patients with refractory reflux-like symptoms after 8 weeks of twice-daily PPI therapy, we suggest against adding a bile acid sequestrant to twice-daily PPI therapy to improve symptoms.

GRADE: Conditional, very low.

- In patients with refractory reflux-like symptoms after 8 weeks of twice-daily PPI therapy without objective evidence of GERD, we suggest against adding a TLESR inhibitor to twice-daily PPI therapy to improve symptoms.

GRADE: Conditional, low.

Alimentary Pharmacology & Therapeutics, 2025

REFRACTORY GERD

Surgery or Endoscopic procedures

In patients with refractory reflux-like symptoms after 8 weeks of twice-daily PPI therapy, without objective evidence of GERD, we suggest against performing an endoscopic anti-reflux procedure to improve symptoms.

GRADE: Conditional, low.

- In patients with refractory reflux-like symptoms after 8 weeks of twice-daily PPI therapy without objective evidence of GERD, we recommend against performing surgical fundoplication to improve symptoms.

GRADE: Strong, very low.

Alimentary Pharmacology & Therapeutics, 2025

REFRACTORY GERD

Vonoprazan Versus Lansoprazole

- Vonoprazan was noninferior and superior to the PPI lansoprazole in healing and maintenance of healing of erosive esophagitis. This benefit was seen predominantly in more severe erosive esophagitis.

  (Laine, gastroenterology, 2023)

Vonoprazan, a potassium-channel acid blocker, advantages over PPIs
1- Acid stable, no need for an enteric coating >>> more rapid onset of action,
2- Longer serum t1/2 compared to PPI: 9h v 1-2 h
3- PPIs bind only to activated proton pumps, PCABs reversibly binds to the HK-ATPase to compete with potassium binding, No need for preprandial dosing

GERD

H2 Receptor Antagonist

- Bedtime for nocturnal symptoms

Drawback: Loss of PH control after one month because of tachyphylaxis

- Beneficial if:

1- Dose on as-needed basis on nocturnal symptoms

2- Objective evidence of nocturnal acid reflux on PH monitoring

Katz et al, AJG, 2021

REFRACTORY GERD

Why PPIs may not control gastric Acid?

- Timing related to food
- Insufficient dose
- Variability in PPI metabolism
- Acid hypersecretion (rare)
- PPI Resistance (not documented)
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Refractory gerd

What determines symptoms?

- The refluxate (perhaps bile)
- Timing of reflux (post prandial, upright, nocturnal)
- Anatomic (hiatal hernia)
- Volume
- Gastric factors (gastroparesis)

REFRACTORY GERD

DO NOT HAVE GERD

★Patient with primary diagnosis of GERD:

➡GERD 65%

➡Functional heartburn 30%

➡Functional chest pain 2%

➡Achalasia 2%

➡Rumination 1%

➡ Herregods T et al, Neurogastro Mobil, 2015

Refractory GERD

Home Message

- GERD non-responsive to PPI >> EGD should be performed 2-4 weeks off drug
- Non-responsive with normal EGD or LA A >> PH monitoring
- Relux-like symptoms with normal EGD and PH monitoring >> consider other cause especially functional
- Without objective evidence of GERD, the patient should not be referred for endoscopic anti-reflux procedures or surgery
- Timing and dosage of PPI must be corrected before considering the patient as refractory GERD

