بسم الله الرحمن الرحيم

Medical treatment in Refractory GERD

Up to date

- **Diagnostic evaluation and initial management** – The timing and extent of diagnostic evaluation in a patient with refractory GERD is based on the type of ongoing symptoms and the presence of alarm features (algorithm 1).
- •**Patients with alarm features** – We perform early upper endoscopy. Patients with alarm features in whom the early upper endoscopy is negative are subsequently managed similarly to patients without alarm features (algorithm 1). (See 'Patients with alarm features' above.)
- •**Patients without alarm features** – Initial management consists of reinforcement of lifestyle modification and compliance with PPI therapy. In patients with persistent symptoms despite once daily PPI therapy, we suggest twice daily PPI therapy (Grade 2B). Switching to a different PPI may be an equally effective alternative. In all patients who fail twice daily PPI therapy, we perform an upper endoscopy with biopsies of the esophagus, if not performed in the last one year. (See 'Residual acid reflux' above.)
- ●**Additional measures based on esophageal pH testing/symptoms** – Subsequent management in patients who have undergone esophageal pH testing are based on the pH of the refluxate. If pH testing cannot be performed, empiric management is based on the type of ongoing symptoms.
- •In patients with persistent acid reflux on esophageal impedance pH testing or when testing is unavailable and patients primarily report heartburn, we suggest adding a bedtime H2RA (Grade 2C). If clinical tolerance develops, H2RA can be used intermittently or on demand. (See 'Residual acid reflux' above.)
- •In patients with symptoms associated with non-acidic reflux on an esophageal impedance pH study or when testing is unavailable and patients primarily report regurgitation, we suggest a trial of baclofen (Grade 2C). (See 'Non-acid reflux' above and "Non-acid reflux: Clinical manifestations, diagnosis, and management".)
- •In patients with refractory GERD who have a normal esophageal impedance and pH study (esophageal hypersensitivity or functional heartburn), we suggest a trial of visceral analgesics (pain modulators), such as a tricyclic antidepressant, serotonin-norepinephrine reuptake inhibitor, selective serotonin uptake inhibitor, or trazodone (Grade 2C). (See 'Reflux hypersensitivity or functional heartburn' above.)
- •In patients with persistent GERD symptoms despite PPI therapy and delayed gastric emptying, we suggest treatment with prokinetics (Grade 2C). (See 'Other therapies' above.)

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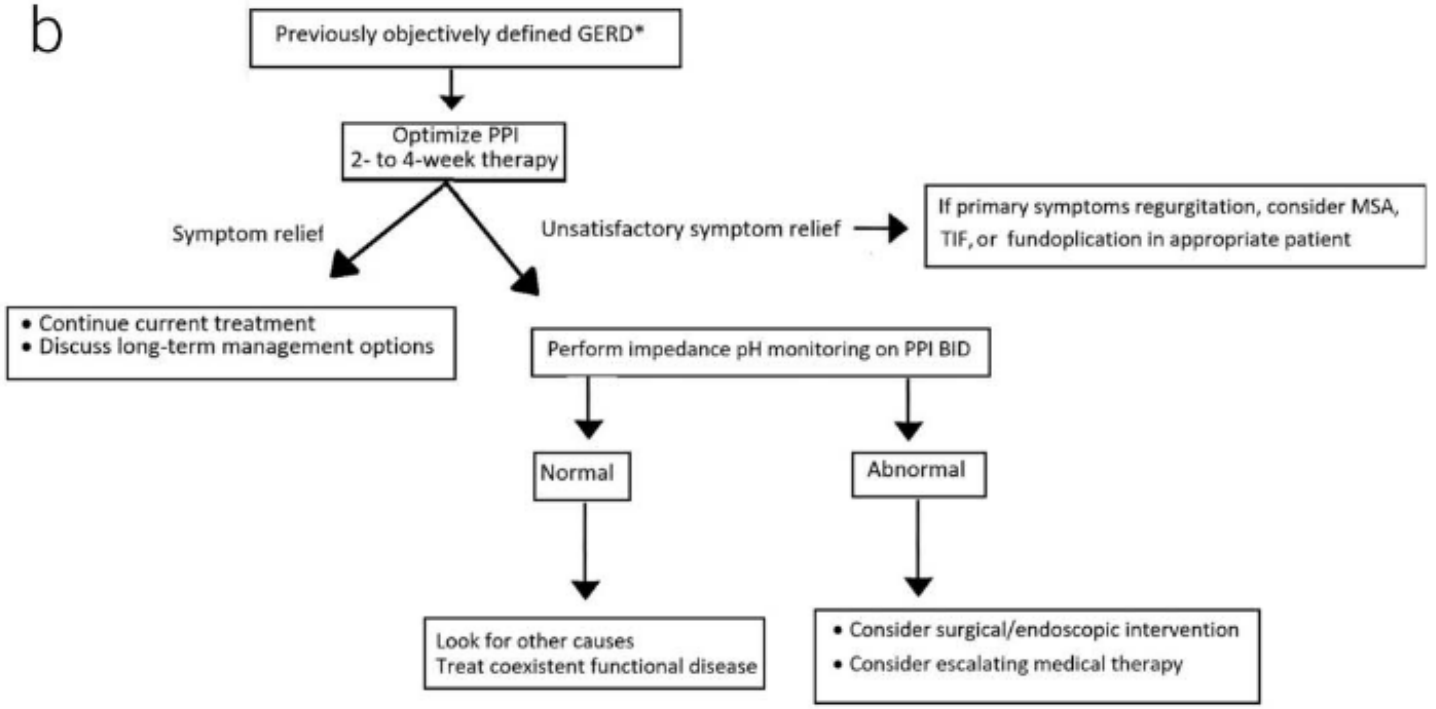

of GERD incompletely responsive to PPIs, previously empirically treated with PPI
esophagogastroduodenoscopy; LA, Los Angeles; PPI, proton pump inhibitor. (**b**)
pletely responsive to PPIs in patients previously objectively defined as GERD. *LA
denoscopy; LA, Los Angeles; MSA, magnetic sphincter augmentation; PPI, proton

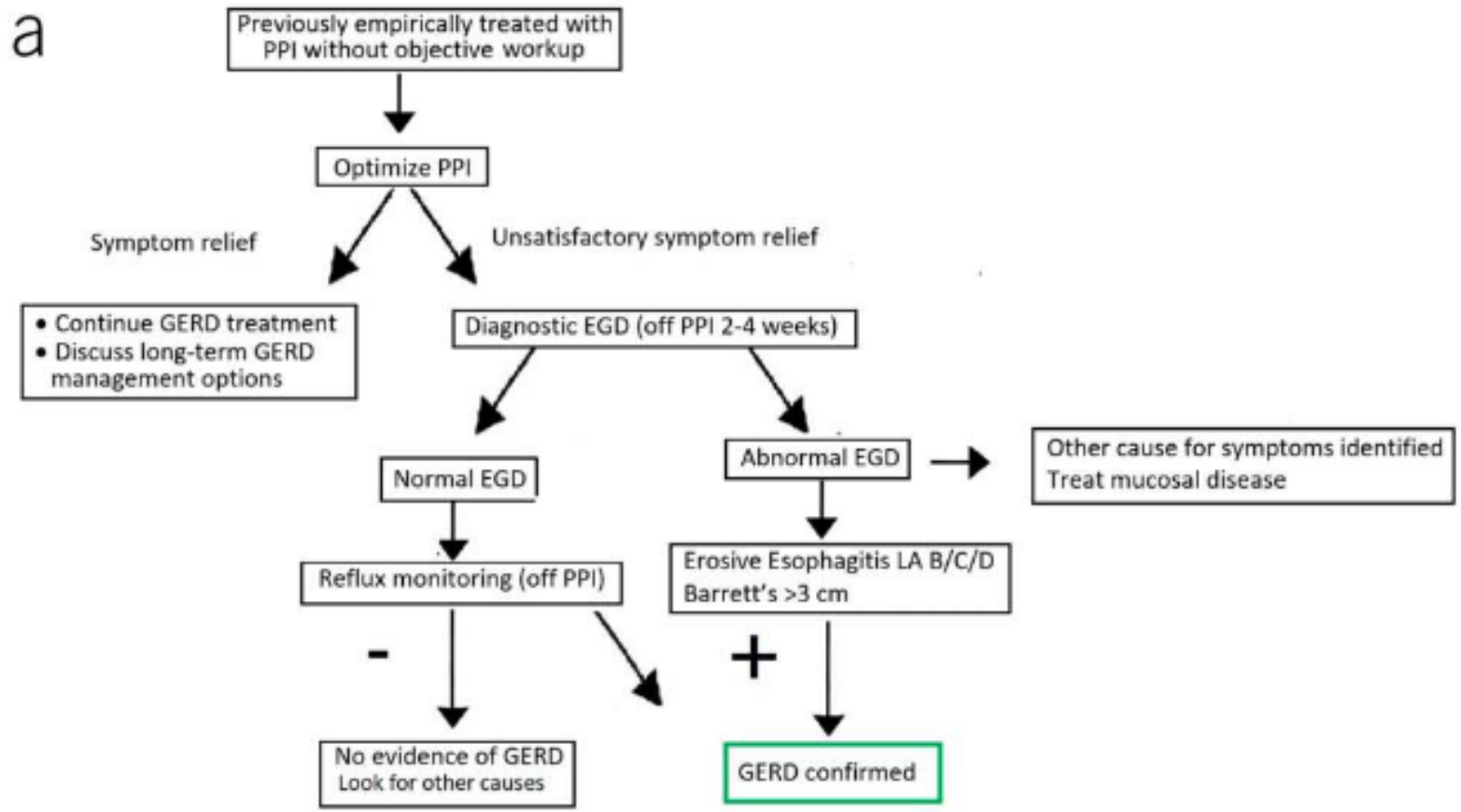

Figure 3. (**a**) Management algorithm of symptoms suspected because of without objective workup. GERD, gastroesophageal reflux disease; EGD, e Management algorithm of symptoms suspected because of GERD incomp B/C/D GERD, gastroesophageal reflux disease; EGD, esophagogastroduod pump inhibitor; TIF, transoral incisionless fundoplication.

Recommendations

1. We recommend optimization of PPI therapy as the first step in management of refractory GERD (strong recommendation, moderate level of evidence).
2. We suggest esophageal pH monitoring (Bravo, catheter-based, or combined impedance-pH monitoring) performed OFF PPIs if the diagnosis of GERD has not been established by a previous pH monitoring study or an endoscopy showing long-segment Barrett's esophagus or severe reflux esophagitis (LA grade C or D) (conditional recommendation, low level of evidence).
3. We suggest esophageal impedance-pH monitoring performed ON PPIs for patients with an established diagnosis of GERD whose symptoms have not responded adequately to twice-daily PPI therapy (conditional recommendation, low level of evidence).
4. For patients who have regurgitation as their primary PPI-refractory symptom and who have had abnormal gastroesophageal reflux documented by objective testing, we suggest consideration of antireflux surgery or TIF (conditional recommendation, low level of evidence).

Key concepts

1. It is important to stop PPI therapy in patients whose off-therapy reflux testing is negative, unless another indication for continuing PPIs is present.
2. Esophageal manometry should be considered as part of the evaluation for refractory GERD in patients with a normal endoscopy and pH monitoring study and for patients being considered for surgical or endoscopic treatment.
3. If not already performed off PPIs, we recommend diagnostic upper endoscopy after discontinuing PPI therapy, ideally for 2 to 4 weeks. Esophageal biopsies should be performed even if endoscopy reveals normal mucosa.
4. We recommend performing high-resolution esophageal manometry in patients with refractory GERD if reflux monitoring and endoscopy are unrevealing.

Table 4. Potential mechanisms underlying symptoms suspected due to GERD but refractory to PPI therapy

Despite PPI therapy, abnormal acid reflux persists and is causing symptoms
There is reflux hypersensitivity, a condition in which PPIs have normalized esophageal acid exposure, but "physiologic" reflux episodes (acidic or nonacidic) nevertheless are strongly associated with and evoke symptoms
The symptoms are not due to GERD, but are caused by esophageal disorders other than GERD (e.g., EoE and achalasia)
The symptoms are not due to GERD, but are caused by nonesophageal disorders (e.g., gastroparesis, rumination, and heart disease)
The symptoms are functional (i.e., not because of GERD or any other identifiable histopathologic, motility, or structural abnormality).

EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; PPI, proton pump inhibitor.

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