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REFRACTORY GERD PANEL DISCUSSION

1-DR MOZAFFARI

2-DR SHADKAM

3-DR FAKHARIAN

4-DR LATIFNIA

5-DR FARZANEHFAR

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GUIDELINES AND CONSENSUS STATEMENTS

Good clinical practice recommendations for the diagnosis and treatment of gastroesophageal reflux disease. An expert review from the *Asociación Mexicana de Gastroenterología*

M.A. Valdovinos Díaz[a,*], M. Amieva-Balmori[b], R. Carmona-Sánchez[c], E. Coss-Adame[d], O. Gómez-Escudero[e], M. González-Martínez[f], F. Huerta-Iga[g], E. Morel-Cerda[h], J.M. Remes-Troche[b], J.L. Tamayo-de la Cuesta[i], G. Torres-Villalobos[j], L.R. Valdovinos-García[a], G. Vázquez-Elizondo[k], A.S. Villar-Chávez[l], J.A. Arenas-Martínez[d]

[a] *Servicio de Gastroenterología, Hospital Médica Sur, Mexico City, Mexico*
[b] *Laboratorio de Fisiología Digestiva y Motilidad Intestinal, Instituto de Investigaciones Médico-Biológicas de la Universidad Veracruzana, Veracruz, Mexico*
[c] *Servicio de Gastroenterología, Práctica privada, San Luis Potosí, Mexico*
[d] *Departamento de Gastroenterología, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico*
[e] *Clínica de Gastroenterología, Endoscopia y Motilidad Gastrointestinal, Endoneurogastro, Hospital Ángeles Puebla, Puebla, Mexico*
[f] *Departamento de Endoscopia, Hospital de Especialidades del CMN Siglo XXI IMSS, Mexico City, Mexico*
[g] *Servicio de Gastroenterología, Hospital Ángeles Torreón, Torreón, Mexico*
[h] *Departamento de Gastroenterología, Hospital Civil de Guadalajara Fray Antonio Alcalde, Guadalajara, Mexico*
[i] *Servicio de Gastroenterología y Endoscopia Gastrointestinal, Centro de Investigación y Docencia en Ciencias de la Salud, Universidad Autónoma de Sinaloa, Culiacán, Sinaloa, Mexico*
[j] *Cirugía Experimental, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico*
[k] *Servicio de Gastroenterología, Centro de Enfermedades Digestivas ONCARE, Monterrey, Mexico*
[l] *Servicio de Gastroenterología, Hospital Ángeles Acoxpa, Mexico City, Mexico*

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KEYWORDS
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Abstract
Introduction: Gastroesophageal reflux disease (GERD) is very prevalent in the general population, with a broad spectrum of clinical manifestations, requiring accurate diagnosis and treatment.

* Corresponding author. Hospital Médica Sur Puente de Piedra 150-617. Colonia Toriello Guerra, Tlalpan, C.P. 14050, Mexico City, Mexico. Tel.: +52 55 56067987.
E-mail address: miguelvaldovinosd@gmail.com (M.A. Valdovinos Díaz).

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Review

Refractory Gastroesophageal Reflux Disease: Diagnosis and Management

Trevor A Davis[1] and C Prakash Gyawali[2]*

[1]Division of Pediatric Gastroenterology, Washington University School of Medicine, Saint Louis Children's Hospital, St. Louis, MO, USA; and [2]Division of Gastroenterology, Washington University School of Medicine, St. Louis, MO, USA

Gastroesophageal reflux disease (GERD) is common, with increasing worldwide disease prevalence and high economic burden. A significant number of patients will remain symptomatic following an empiric proton pump inhibitor (PPI) trial. Persistent symptoms despite PPI therapy are often mislabeled as refractory GERD. For patients with no prior GERD evidence (unproven GERD), testing is performed off antisecretory therapy to identify objective evidence of pathologic reflux using criteria outlined by the Lyon consensus. In proven GERD, differentiation between refractory symptoms (persisting symptoms despite optimized antisecretory therapy) and refractory GERD (abnormal reflux metrics on ambulatory pH impedance monitoring and/or persistent erosive esophagitis on endoscopy while on optimized PPI therapy) can direct subsequent management. While refractory symptoms may arise from esophageal hypersensitivity or functional heartburn, proven refractory GERD requires personalization of the management approach, tapping from an array of non-pharmacologic, pharmacologic, endoscopic, and surgical interventions. Proper diagnosis and management of refractory GERD is critical to mitigate undesirable long-term complications such as strictures, Barrett's esophagus, and esophageal adenocarcinoma. This review outlines the diagnostic workup of patients presenting with refractory GERD symptoms, describes the distinction between unproven and proven GERD, and provides a comprehensive review of the current treatment strategies available for the management of refractory GERD.
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Key Words
Endoscopy; Esophageal pH monitoring; Gastroesophageal reflux; Refractory GERD

Introduction

Gastroesophageal reflux disease (GERD) is a frequently encountered diagnosis in clinical practice, with an estimated prevalence ranging from 8-33% of the general population, and associated economic impact in the United States totaling as much as $10 billion on an annual basis.[1-4] Almost one-third of adults report typical GERD symptoms (ie, heartburn, regurgitation, and esophageal chest pain) on a weekly basis.[5,6] The mainstay of initial GERD management hinges on a proton pump inhibitor (PPI) trial to determine if symptoms improve with effective acid suppression.[7] While approximately two-thirds of patients with erosive esophagitis (EE) and one-half with non-erosive reflux disease (NERD) will achieve symptomatic response with an empiric PPI trial, patients presenting with atypical symptoms, especially laryngeal symptoms such as hoarseness, cough, throat clearing, and sore throat, are much less likely to improve.[3,6,7,8] Although PPI response is utilized

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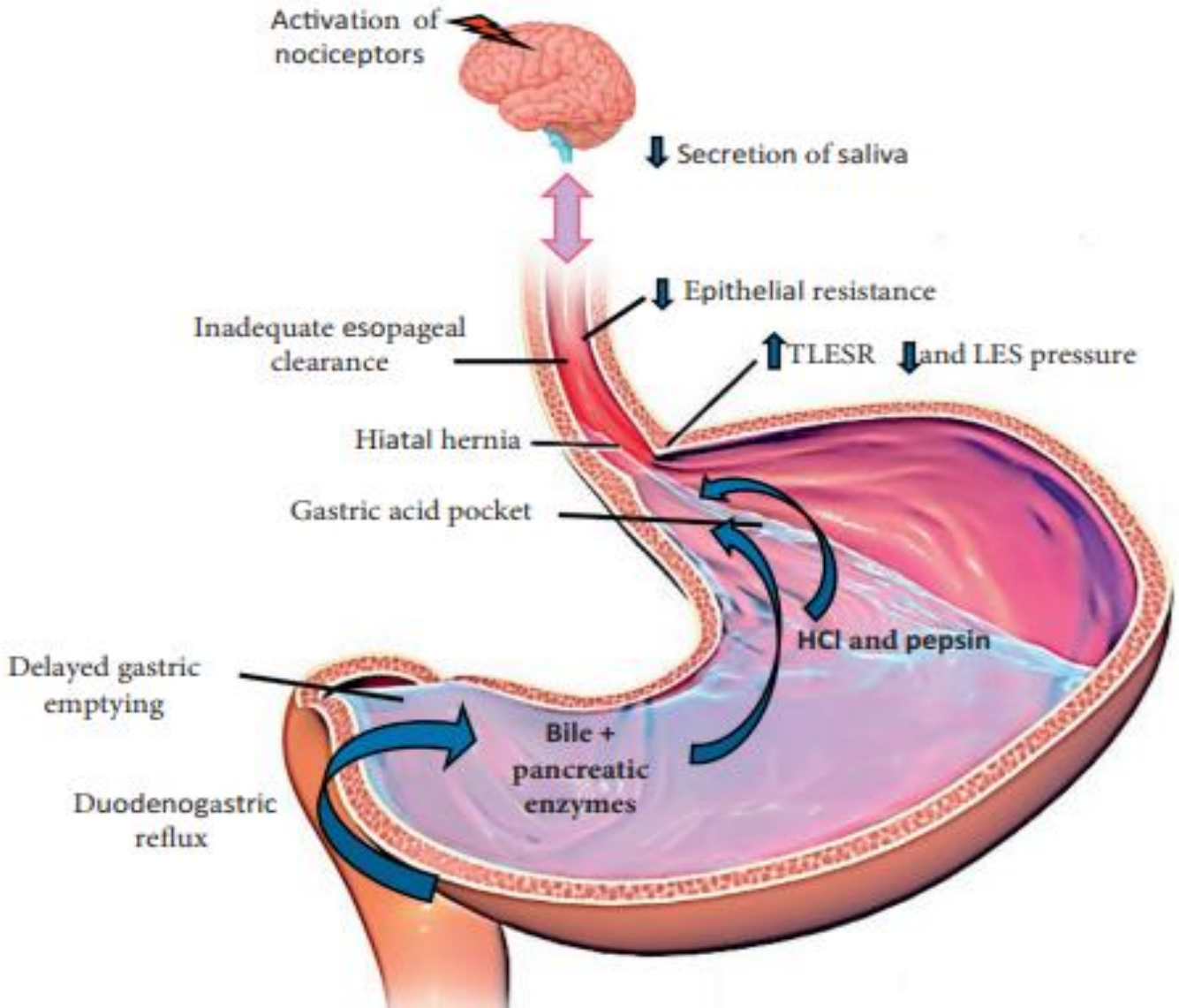
*Correspondence: C Prakash Gyawali, MD
Division of Gastroenterology, Washington University School of Medicine, 660 S. Euclid Ave, Campus Box 8124, St. Louis, MO 63110, USA
Tel: +1-314-454-8201, E-mail: cprakash@wustl.edu

Pathophysiologic mechanisms of gastroesophageal reflux disease:



Case presentation:

- I am a 30-year-old woman and currently 30 weeks pregnant.
- My gastroesophageal reflux disease (GERD) symptoms have become increasingly severe as my pregnancy progresses.
- I experience constant heartburn, acid reflux, and a burning sensation in my throat that makes eating, sleeping, and even concentrating on daily tasks difficult.
- The symptoms seem worse after meals and when I lie down.

Case Presentation:

- I am worried about whether these symptoms might harm my baby or lead to complications during pregnancy. Could the hormonal changes and increased abdominal pressure be contributing to this worsening GERD?
- What safe treatment options, including medications, dietary modifications, and lifestyle changes, would you recommend for pregnant women like me?

Case presentation:

- Gastroesophageal reflux disease (GERD) tends to be worsened in pregnancy due to increased abdominal pressure and also hormonal changes cause reduced digestion, and the lower esophageal sphincter lax, thereby causing reflux of acid.
- The symptoms can not affect the baby. There is no sufficient data stating its effect on pregnancy.
- I advise you to follow certain lifestyle changes. These include:
  - Elevate the head of the bed with three pillows.
  - Eat three hours before bedtime.
  - Avoid coffee.
  - Avoid spicy foods.
  - Tablet Pantoperasole (proton pump inhibitor) is safe in pregnancy and can be used.

PPIs and pregnancy:

- PPIs are classified as category B drugs, according to the Food and Drug Administration (FDA), with the exception of omeprazole, which is classified as category C.
- Before starting any medication, the risks and benefits of antisecretory therapy should be carefully discussed.

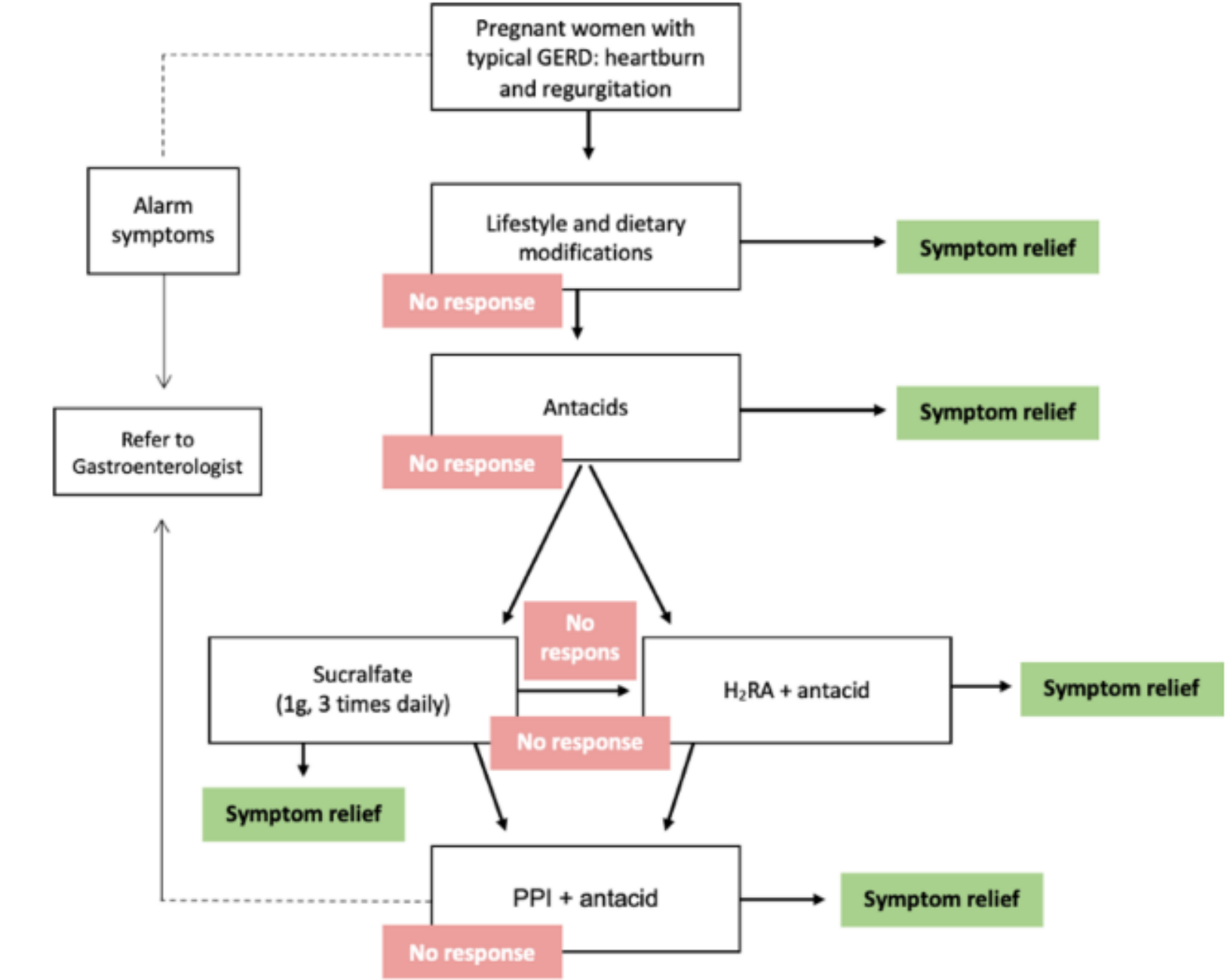


Figure 1. Step-up approach towards management of GERD during pregnancy. GERD = gastroesophageal reflux disease, H2RA = histamine-2 receptor antagonist, PPI = proton pump inhibitor.

Table 3

Summary of drugs used to treat typical reflux syndrome during pregnancy.

Drug	FDA classification		Comments
Antacids	None		• Magnesium-, aluminum-, or calcium-containing: most are safe, but calcium-containing drugs are recommended. • Magnesium trisilicates: avoid long-term, high dose. • Sodium bicarbonate: not safe, may cause fluid overload and alkalosis.
H2RAs	B		• A meta-analysis showed that there is no statistically significant difference in risk of spontaneous abortion, small size for gestational age, or preterm delivery in pregnant women exposed to H2RAs.
PPIs	*Esomeprazole* *Lansoprazole*	B	• A meta-analysis showed that there is no statistically significant difference in the odds ratios for spontaneous abortion or preterm delivery between pregnant women exposed to PPIs and unexposed pregnant women. • A large prospective cohort study found that exposure to PPIs during the first trimester of pregnancy was not associated with a significantly increased risk of major birth defects.
	Dexlansoprazole		
	Rabeprazole		
	Pantoprazole		
	Omeprazole	C	

FDA = Food and Drug Administration, H2RA = histamine-2 receptor antagonist, PPI = proton pump inhibitor.

Table 4

Summary of lifestyle modifications for GERD in pregnancy.

Lifestyle modifications for typical reflux syndrome
• Head of bed elevation (6–11 inches) and lying in the left lateral decubitus position.
• Avoidance or reduced intake of food that may precipitate reflux (fatty and spicy foods, citrus, carbonated beverages, and alcohol).
• Avoidance of lying down within 3 hr of eating.

GERD = gastroesophageal reflux disease.

Case Presentation:

- One month after giving birth, the patient complains of continuing the previous problems(Without alarming sign or symptom). What action or actions should be taken now?
  - Endoscopy
  - PH-metry
  - Manometry
  - High dose PPI
  - Change PPI
  - Added night H2-blocker
  - Psychiatric Consultation

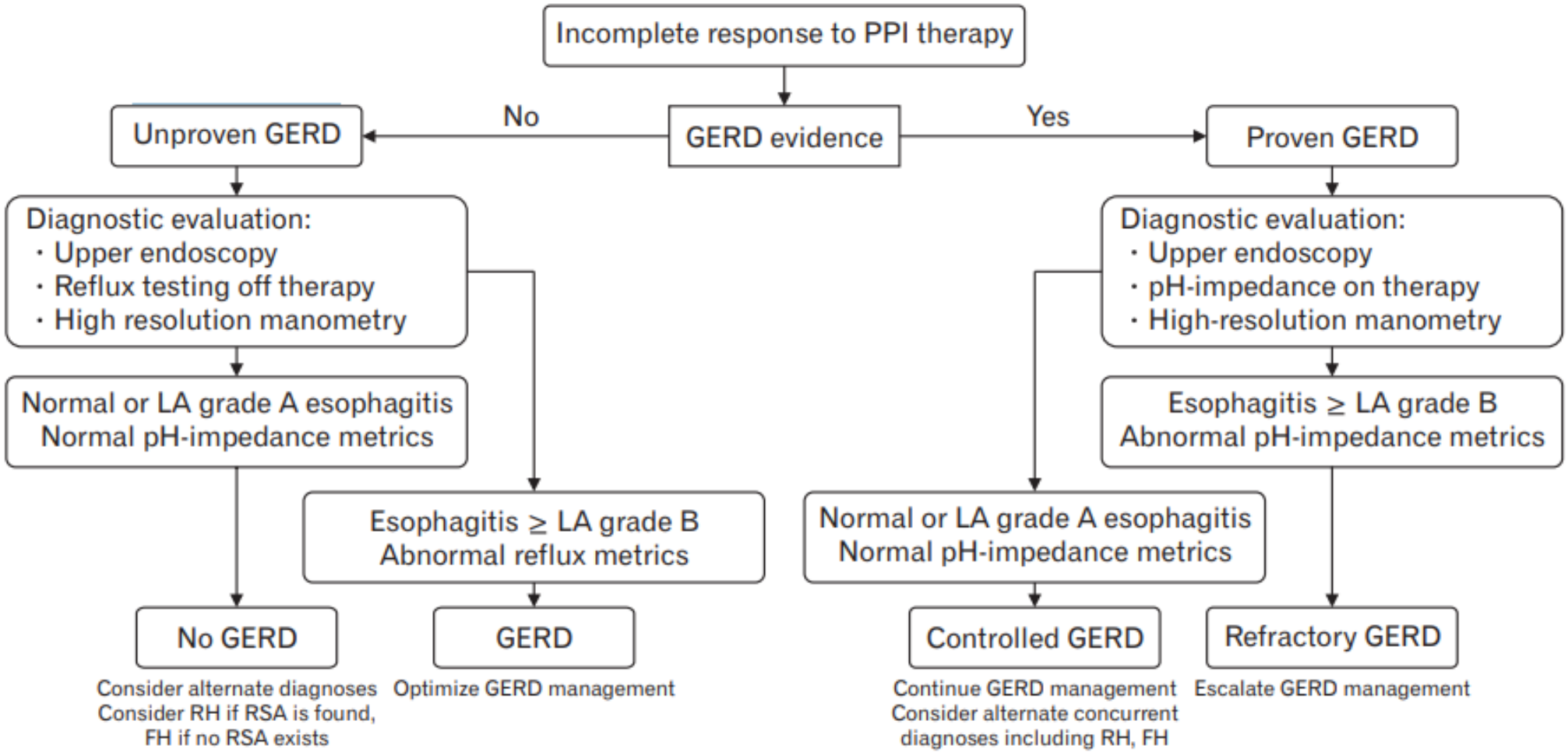


Figure 1. Algorithm for evaluation and management of esophageal symptoms suspicious for reflux disease. The concepts of proven gastroesophageal reflux disease (GERD) (prior objective evidence for GERD is present) and unproven GERD (no prior objective evidence for GERD) determine the optimal methodology of investigation of symptoms that persist despite proton pump inhibitor (PPI) therapy. The intent of evaluation of unproven GERD is to determine if GERD exists, while the intent in proven GERD is to determine if GERD persists despite therapy, which may need to be escalated if testing suggests persisting GERD evidence. LA, Los Angeles classification; RH, reflux hypersensitivity; RSA, reflux-symptom association; FH, functional heartburn.

Refractory GERD Definition?

- Refractory GERD is defined as the objective evidence of GERD (EE or abnormal exposure to esophageal acid and/or elevated numbers of reflux episodes in MII-pH), despite medical therapy utilizing a double-dose PPI for eight weeks.
- Even though the majority of patients with persistent symptoms of GERD, despite medical treatment, are taking the standard-dose PPI, the strict diagnosis of refractory GERD means that the patient has taken a double-dose PPI for at least eight weeks.

Cause of refractory gastroesophageal reflux disease :

- The persistence of symptoms of GERD despite medical treatment does not necessarily imply the diagnosis of refractory GERD.
- Symptom persistence, despite medical treatment, occurs in 30-40% of patients with GERD.
- There are multiple possible causes of treatment failure, especially with PPIs, and they include lack of treatment adherence, inadequate PPI use or administration, pharmacogenetic differences (polymorphisms associated with CYP 450), and incorrect diagnosis, among others .

Table 1 Causes of persistent symptoms in gastroesophageal reflux disease (GERD).

Causes of persistent symptoms of GERD
Lack of treatment adherence
Inadequate drug prescription or administration
Genetic polymorphisms (PPI metabolism)
Poor drug quality
Esophageal hypersensitivity
Hypervigilance, anxiety, somatization
Functional heartburn
Other esophageal diseases
• Eosinophilic esophagitis
• Pill-induced esophagitis (NSAID, potassium, bisphosphonates)
• Infectious esophagitis
Esophageal motility disorders
• Achalasia
• Diffuse esophageal spasm
• Jackhammer esophagus
Gastroduodenal disorders
• Excessive supragastric burping
• Rumination syndrome
Others
• Zollinger-Ellison syndrome
• Gastroparesis

NSAID: nonsteroidal anti-inflammatory drug; PPI: proton pump inhibitor.

Case presentation?

- The patient states that she stopped the medication out of fear that it would be harmful to the child, even though she did not experience any improvement while taking the medication?
- I started for patient Lansoprazole 30 bid .

Proven or Unproven GERD?

- It is important to recognize these causes and classify patients with ‘‘therapeutic failure’’ into two large groups:
  - Symptoms of persistent GERD in patients without a previous diagnosis. These are patients who assume they have GERD and have experienced treatment failure, but they are patients that have had no objective evidence of GERD (through endoscopic or physiologic studies).
  - Performing the necessary studies for evidence of GERD, before resuming treatment of these patients, is recommended.
  - Symptoms of persistent GERD in patients with a previous diagnosis. These patients have objective evidence of GERD (BE, EE, abnormal AET) and are receiving treatment, but their symptoms continue. In such cases, it is important to first review adherence to PPI use and rule out other causes.

Refractory Symptoms' rather than Refractory GERD.

- Given that symptoms do not necessarily correlate with pathologic reflux, further evaluation can define whether the patient truly has refractory GERD versus esophageal hypersensitivity and/or functional heart-burn
- The core difference between esophageal hypersensitivity (reflux hypersensitivity) and functional heartburn is determined by presence or absence of reflux symptom association, which is best assessed using pH-impedance monitoring.
- Without proper investigation for ongoing symptoms, however, pathologic reflux is difficult to differentiate from esophageal disorders of gut-brain interaction (DGBI).

Refractory Symptoms' rather than Refractory GERD.

- The reasons for symptom persistence are complex and heterogeneous.
- Two-thirds of the subjects with symptom persistence and GERD also presented with criteria for functional heartburn, and the remaining subjects had reflux hypersensitivity.
- Therefore, patients with symptom persistence, despite medical treatment, should be studied, to corroborate the presence of GERD as the cause of symptom persistence or to opportunely detect sensitive-sensory disorders as an explanation for the symptoms in those patients.

Endoscopy in GERD:

- We recommend diagnostic endoscopy in patients :
  - With alarm symptoms or at risk for BE
  - Patients that do not respond to a PPI test,
  - Patients that present with symptom recurrence upon suspending the PPI or potassium-competitive acid blockers (P-CABs).

Case presentation:

- The patient returned with recurring symptoms and no improvement and underwent endoscopy.
- Endoscopy with PPI or after D/C PPI?

GERD A



Ambulatory Reflux Monitoring:

- Patients with persistent or treatment-refractory symptoms of GERD should be studied through ambulatory reflux monitoring to identify overlap with esophageal functional disorders.
- In patients with no previous signs of GERD at endoscopy and with refractory symptoms to anti secretory therapy, we recommend carrying out wireless capsule pH monitoring or pH-impedance testing **without treatment.**
- In patients with previous signs of GERD at endoscopy and refractory symptoms, we recommend evaluation through pH-impedance testing **with treatment.**

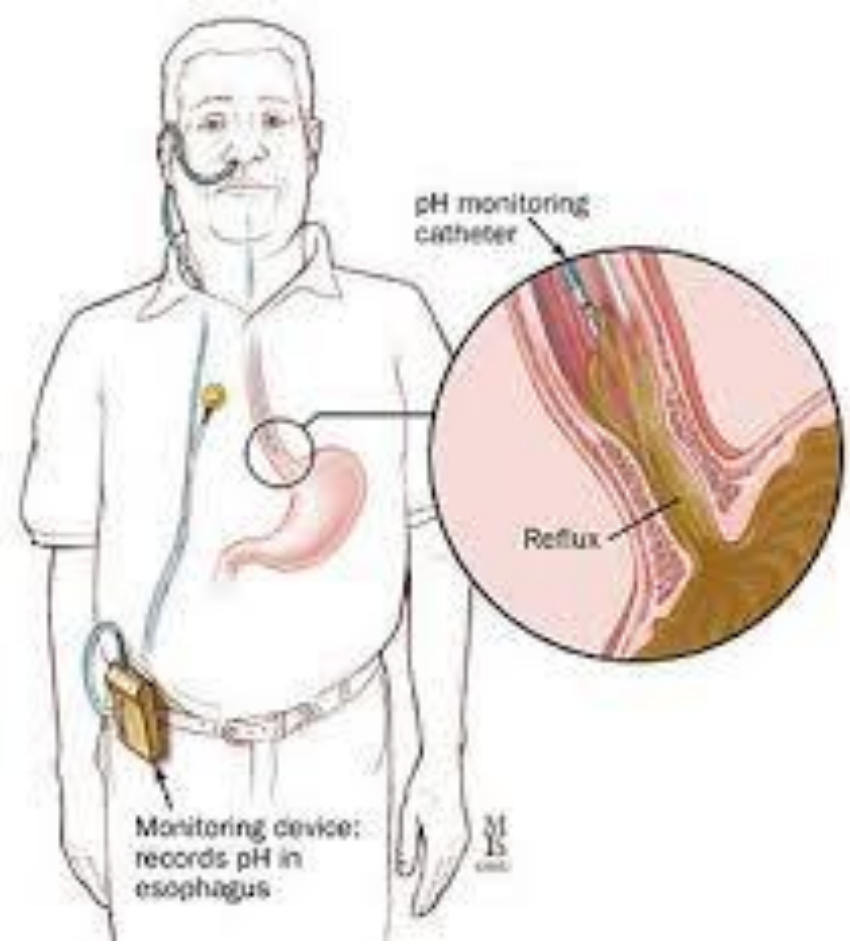
Gastroesophageal reflux measurement: pH-impedance, wireless capsule, mucosal impedance

- Ambulatory reflux measurement has two configurations: with a catheter or with a wireless capsule.
- The Bravo® wireless capsule (MedtronicTM, Minneapolis, MN, USA) is placed during endoscopy in the distal esophagus (6 cm proximal to the squamocolumnar junction), utilizing a suction and clipping mechanism.
- Exposure to acid can be measured with this technique for up to 96 hours and the relation between the symptoms reported by the patient and reflux episodes can be evaluated.
- It is better tolerated but more costly.



Gastroesophageal reflux measurement: pH-impedance, wireless capsule, mucosal impedanc

- In catheter-based pH monitoring, a pH probe is introduced transnasally and placed 5 cm above the upper edge of the LES, identified through manometry.
- This technique measures AET in the distal esophagus for 24 hours and establishes the association between symptoms and reflux episodes.
- The pH catheters can also be combined with multichannel intraluminal impedance (MII-pH), **utilizing impedance rings, to evaluate the movement of air and fluids through the esophagus (anterograde-retrograde), regardless of the pH, and classify them into acid, weakly acid, weakly alkaline, gas, liquid, or mixed.**



Gastroesophageal reflux measurement: pH-impedance, wireless capsule, mucosal impedance

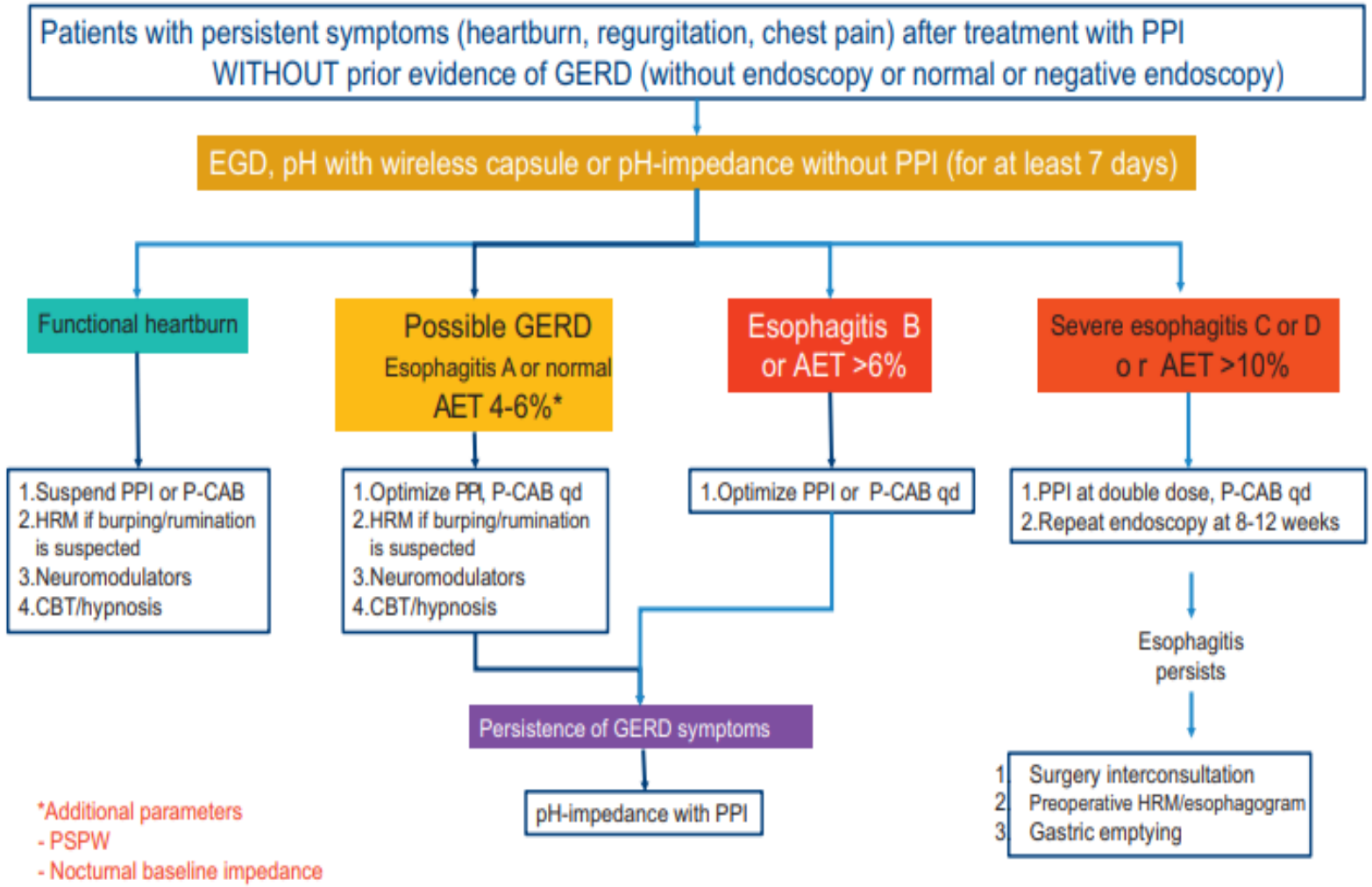
- **The combination of an AET > 4% and > 80 reflux episodes/day, with optimum antisecretory treatment, is evidence of refractory GERD.**
- MII-pH with PPIs in this group of patients aids in determining which patient has refractory GERD and would benefit from treatment scaling, as well as identifying whether there is overlapping with an esophageal functional disorder.

High-resolution esophageal manometry:

- High-resolution esophageal manometry is not recommended for diagnosing GERD.
- It is indispensable for the preoperative evaluation of the candidate for antireflux surgery.
- In patients with GERD that do not respond to lifestyle changes or PPI therapy and have no relevant endoscopic findings, HRM is recommended to make the differential diagnosis, as well as to evaluate other factors that could be conditioning GERD.
- Achalasia is an esophageal motility disorder, characterized by aperistalsis and a lack of relaxation of the EGJ. Patients clinically present with progressive dysphagia, heartburn from the acidification of retained food, regurgitation, and occasional chest pain, with or without weight loss, and so can clinically be confused with GERD, and in the majority of cases, the diagnosis is delayed.
- In patients with achalasia, HRM has 93-98% sensitivity and 96- 98% specificity.

Esophagogram :

- We do not recommend esophagogram for diagnosing GERD.
- This test can be useful in the complementary evaluation of esophageal strictures and is mandatory in cases of suspected short esophagus.


Patients with persistent symptoms (heartburn, regurgitation, chest pain) after treatment with PPI
WITHOUT prior evidence of GERD (without endoscopy or normal or negative endoscopy)
EGD, pH with wireless capsule or pH-impedance without PPI (for at least 7 days)
Functional heartburn
Possible GERD
Esophagitis A or normal
AET 4-6%*
Esophagitis B
or AET >6%
Severe esophagitis C or D
o r AET >10%
1.Suspend PPI or P-CAB
2.HRM if burping/rumination is suspected
3.Neuromodulators
4.CBT/hypnosis
1.Optimize PPI, P-CAB qd
2.HRM if burping/rumination is suspected
3.Neuromodulators
4.CBT/hypnosis
1.Optimize PPI or P-CAB qd
1.PPI at double dose, P-CAB qd
2.Repeat endoscopy at 8-12 weeks
Esophagitis persists
Persistence of GERD symptoms
pH-impedance with PPI
1. Surgery interconsultation
2. Preoperative HRM/esophagogram
3. Gastric emptying
*Additional parameters
- PSPW
- Nocturnal baseline impedance

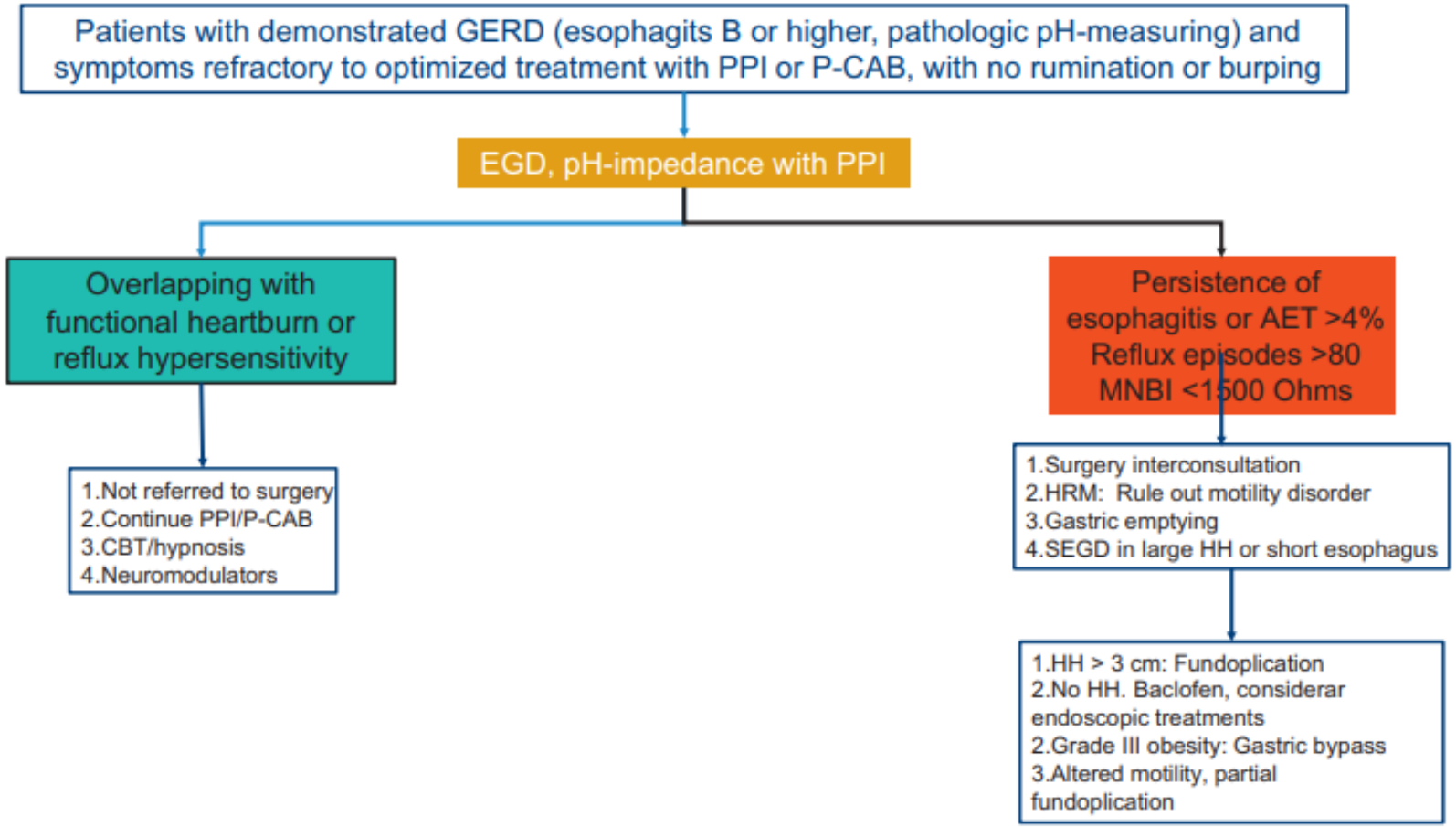


Figure 4 Diagnostic and therapeutic algorithm in refractory gastroesophageal reflux disease (GERD). Patients with esophagitis B or higher or a pathologic acid exposure time (AET) and persistent symptoms after an optimized treatment with a proton pump inhibitor (PPI) or potassium-competitive acid blocker (P-CAB) for eight weeks, should be studied through a new endoscopy (EGD) and/or pH impedance testing with treatment with a PPI. Patients with esophageal cicatrization failure, an AET > 4%, a number of reflux episodes > 80, or a mean nocturnal baseline impedance (MNBI) < 1,500 Ohms should be evaluated for antireflux treatment. Patients with GERD and functional disorder (functional heartburn or reflux hypersensitivity) overlapping should be treated with neuromodulators or psychologic therapies, in addition to continuing antisecretory treatment.

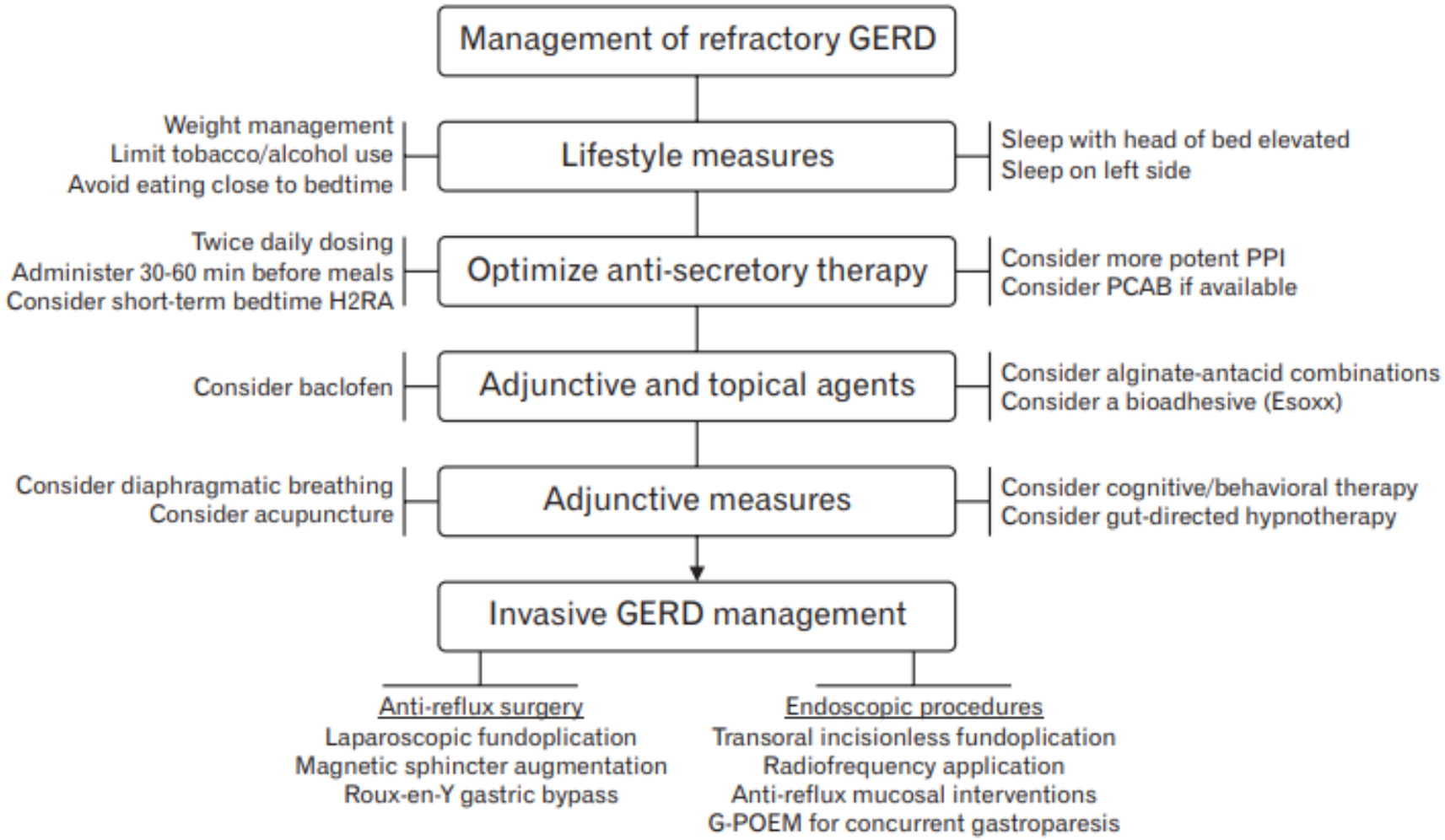


Figure 2. Management of refractory gastroesophageal reflux disease (GERD). Lifestyle adjustments are useful in any patient with reflux symptoms. Antisecretory therapy should be optimized and escalated if indicated. Adjunctive and topical agents, as well as adjunctive measures can be employed to improve symptoms. In patients with objective evidence of refractory GERD, escalation of management to anti-reflux surgery or other invasive interventions may be appropriate. H2RA, histamine H2 receptor antagonist; PPI, proton pump inhibitor; PCAB, potassium competitive acid blocker; G-POEM, gastric peroral endoscopic myotomy.

Lifestyle Measures:

- No matter the clinical presentation, lifestyle modifications should be incorporated into the management strategy of all patients with refractory GERD.
- Weight management is an important consideration for overall health, and is beneficial in improving both symptoms and acid burden.
- Although weight loss may be achieved by the patient independently, a structured weight loss program may be more impactful in improving reflux symptoms, as demonstrated using validated reflux questionnaires following a 6-month weight loss program in overweight and obese individuals.
- Although a graded response has been demonstrated between degree of body mass index decline and improvement of reflux symptoms, benefits specific to refractory GERD have not explicitly been reported.

Lifestyle Measures:

- Tobacco use has finite associations with GERD pathophysiology
- Although alcohol can potentially trigger esophageal symptoms in some patients and use should be limited accordingly, most studies suggest no significant cause and-effect association.
- Avoidance of triggering foods and drinks should be individualized.
- However, separating the last meal of the day from bedtime by several hours can reduce supine acid exposure, with available evidence demonstrating significant decrease in night-time acid burden with an earlier evening meal.
- Additionally, supine acid exposure is lower with elevation of the head of the bed and sleeping in the left lateral decubitus position.

Treatment of refractory GERD:

- We recommend antisecretory treatment optimization in patients with refractory symptoms of GERD, through the following strategies:
  - a)Treatment adherence and appropriate PPI dose in relation to foods
  - b)Double-dose PPI
  - c)Different PPI
  - d)Switch from PPI to P-CAB
  - e)Adjuvant treatment
- Multiple pharmacokinetic studies have shown that foods reduce their potency between 50 and 70%.

Treatment of refractory GERD:

- The standard dose is used for four weeks in NERD and for eight weeks in EE.
- In severe esophagitis (Los Angeles classification C or D), double-dose PPI for eight weeks is recommended.
- They have 70 to 80% efficacy in EE and 50 to 60% efficacy in nonerosive disease.
- Delayed-release PPIs (omeprazole, lansoprazole, rabeprazole, pantoprazole, esomeprazole, ilaprazole), dual delayed-release PPIs (dexlansoprazole), and immediate-release PPIs (omeprazole-sodium bicarbonate) are recommended at the standard dose for four weeks in NERD and eight weeks in erosive disease.

Treatment of refractory GERD:

- In cases of severe esophagitis (LA classification C and D), a double-dose delayed-release PPI should be used for eight weeks.
- The symptom relief and esophageal cicatrization rate is similar among the PPIs.
- They should be administered 30 to 60 minutes before breakfast at the standard dose regimen once a day and 30 to 60 minutes before breakfast and dinner at the double-dose regimen.
- Several studies suggest that genetic differences in the CYP2C19 isoenzyme metabolism can affect the response to PPIs.
- However, the usefulness of a genetic test for identifying rapid or slow metabolizers is not recommended in daily practice.
- When this condition is suspected, switching to **rabeprazole or ilaprazole**, PPIs that do not rely on CYP2C19 for their primary metabolism, is suggested.

PPI Agent	Defined Daily Dose Equivalent, mg
Omeprazole	20
Pantoprazole	40
Esomeprazole	30
Lansoprazole	30
Rabeprazole	20

Abbreviation: PPI, proton pump inhibitor.

Histamine H2 receptor antagonists (H2RAs):

- Alternative classes of antisecretory medications may have benefit as adjunctive therapy in refractory GERD.
- Nocturnal acid breakthrough, defined as at least 1 overnight hour of intragastric pH < 4.0 despite optimal PPI therapy, can manifest as nighttime symptoms.
- Histamine H2 receptor antagonists (H2RAs) are sometimes utilized at bedtime, since histamine release can be a mechanism underlying nocturnal acid secretion, and histamine blockade can provide symptom relief from reduced nocturnal acid breakthrough in the short term.
- When effective, tachyphylaxis and medication tolerance can return nocturnal acid production to baseline levels within 1 week to 1 month despite continued use of the medication, limiting H2RA efficacy.
- **Patients with H2RA tachyphylaxis may ultimately benefit from as needed use rather than adherence to a fixed regimen.**

Potassium-competitive acid blockers:

- P-CABs,are a new therapeutic class of antisecretory drugs with pharmacokinetic and pharmacodynamic advantages over PPIs.
- They:
  - Do not require activation
  - Are super-concentrated in the acid space of the parietal cell
  - They bind competitively and reversibly to the potassium (K+) binding site of the proton pump,
  - They have a half-life in plasma up to four-times higher than that of PPIs
  - They produce complete acid inhibition from the first dose.
- Thus:
  - They are faster-acting
  - Stronger drugs
  - Whose dose is food-independent
  - They raise the intragastric pH above four from the first dose, lasting for 24 hours.
- Revaprazan, vonoprazan, tegoprazan, and fexuprazan have been tested and approved for clinical use in Asian countries.

Potassium-competitive acid blockers:

- This drugs have been shown to be faster and more effective than placebo in controlling heartburn in NERD.
- P-CABs have been shown to effectively control nocturnal symptoms in GERD.
- In maintenance treatment in erosive GERD, half-dose P-CABs have been superior to PPIs.
- P-CABs have also been shown to be effective in on-demand treatment in nonerosive GERD.
- Therefore, in countries where they are available, P-CABs can be considered first-line drugs in the treatment of GERD.
- The standard dose (tegoprazan 50 mg daily) for four weeks is recommended in NERD and for eight weeks in mild or severe EE.
- Half of the standard dose is recommended in both on-demand and continuous maintenance therapy.
- In clinical trials and post-market clinical follow-up, P-CABs have shown a safety profile similar to that of PPIs, reporting no severe adverse effects attributable to them.

Reflux Inhibitors and Mucosal Protective Agents

- Baclofen, a gamma aminobutyric acid-B (GABA-B) receptor agonist, can reduce frequency of transient LES relaxations (TLESRs).
- Since TLESRs are the primary mechanism of gastroesophageal reflux, baclofen has proven useful by reducing number and duration of reflux episodes that could be contributing to refractory symptoms.
- Baclofen has been shown to be effective in reducing symptoms both with and without large hiatal hernias.
- However, its use is limited by side effects including sedation, lightheadedness, central nervous system depression, and short half-life necessitating multiple daily doses for results.

Mucosal protective agents:

- Mucosal protective agents, on the other hand, are useful adjuncts for managing breakthrough heartburn and regurgitation despite PPI therapy.
- These agents can form a raft or mechanical barrier at the interface between meal-stimulated gastric acid (the postprandial acid pocket) and the esophageal mucosa to provide symptomatic benefit in patients with refractory GERD, with a favorable side effect profile.
- Specifically, antacid preparations combined with alginate (Gaviscon Advance), as well as a hyaluronic acid-chondroitin sulfate based bioadhesive formulation (Esoxx) demonstrated benefit when used as an adjunct to PPI therapy compared to placebo with or without PPI in multicenter randomizedcontrolled trials.
- Although **relief of persistent GERD symptoms** has been demonstrated with the addition of mucosal protective agents, there is a paucity of literature detailing effect on **objective reflux metrics** through pH-impedance monitoring.

Mucosal protective agents:



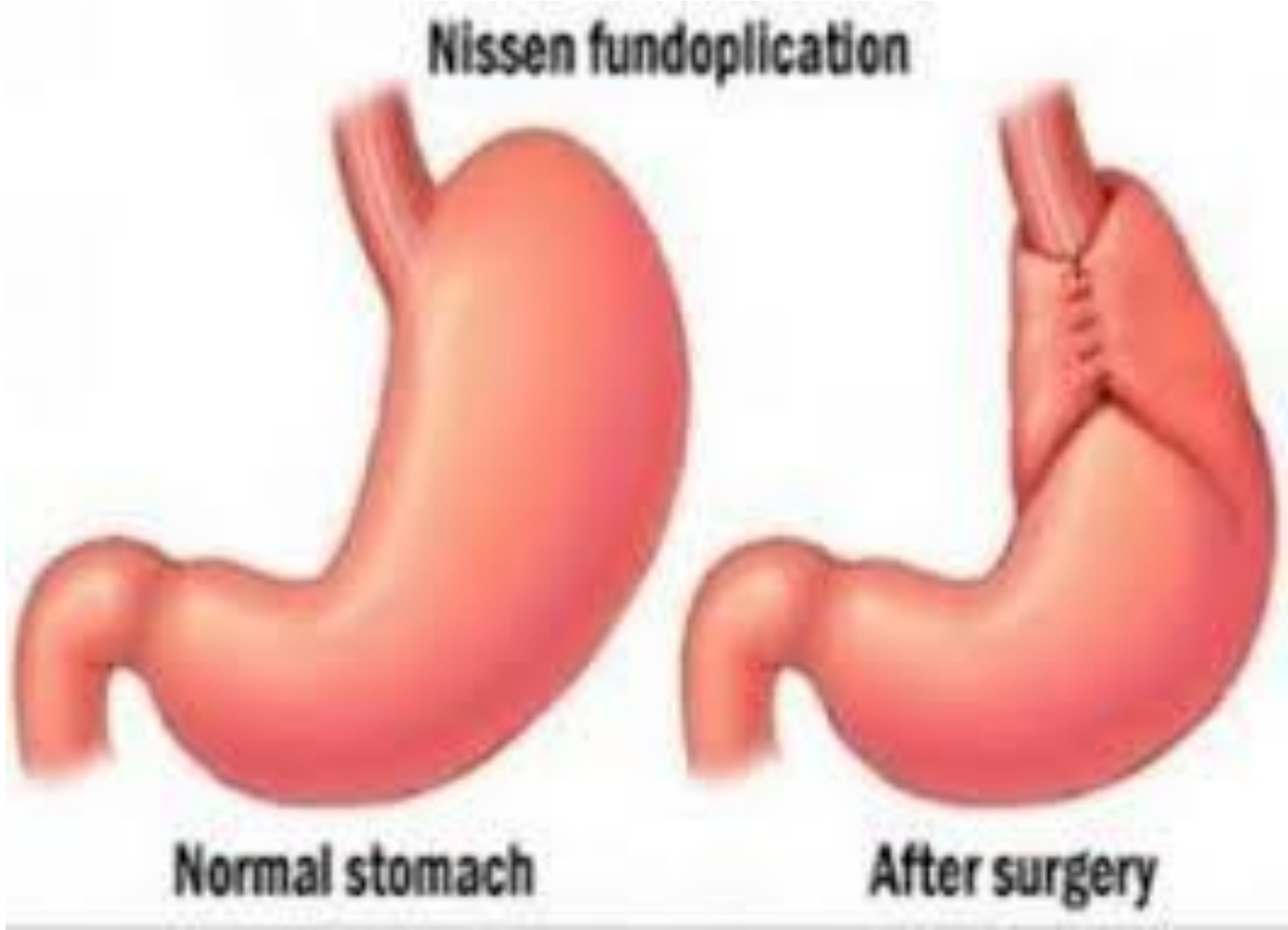


Endoscopic treatment and surgical treatment:

- We recommend antireflux surgery in patients:
  - With objective evidence of GERD
  - Regurgitation as the predominant symptom
  - Large HH
  - No severe esophageal motility disorder
  - No important symptoms of dyspepsia or IBS
  - Performed by an experienced surgeon
  - In patients that reject long-term medical treatment
- Surgical treatment in patients objectively diagnosed with GERD is as effective as medical treatment with PPIs.
- **The best predictors of a favorable response to surgical treatment are positive pH-monitoring and adequate symptom response to a PPI.**
- Patients with refractory GERD, i.e., those with the persistent EE and abnormal AET after optimum treatment with PPIs or P-CABs, are candidates for fundoplication.

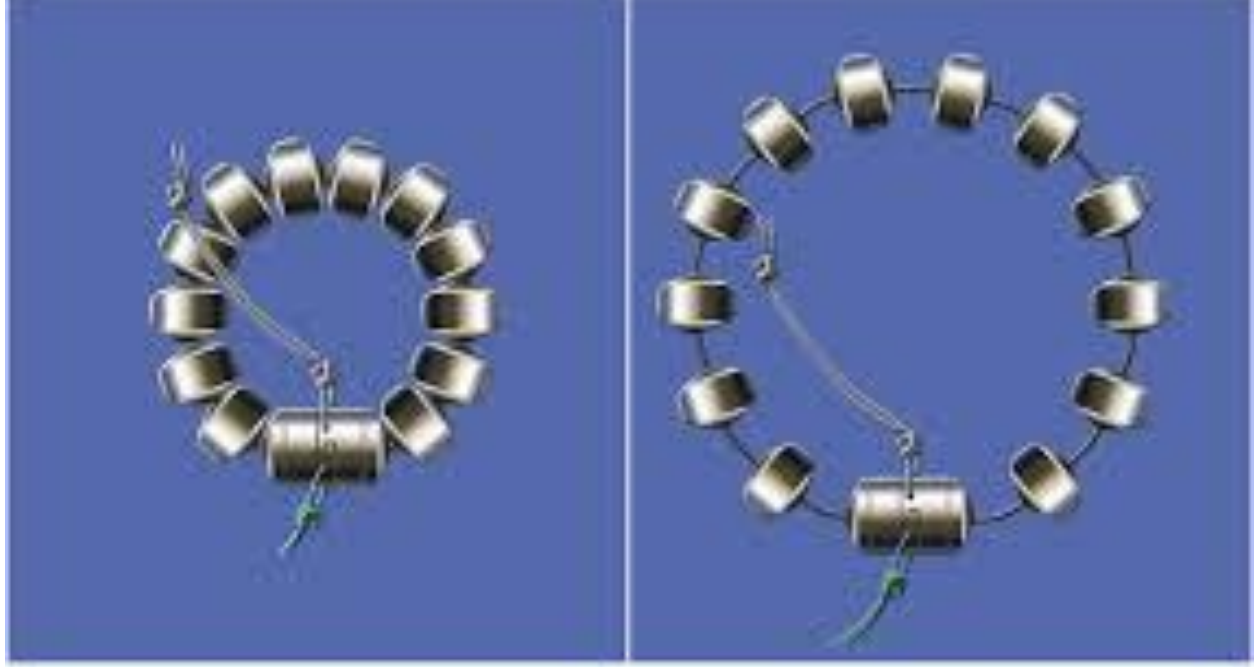
Endoscopic treatment and surgical treatment:

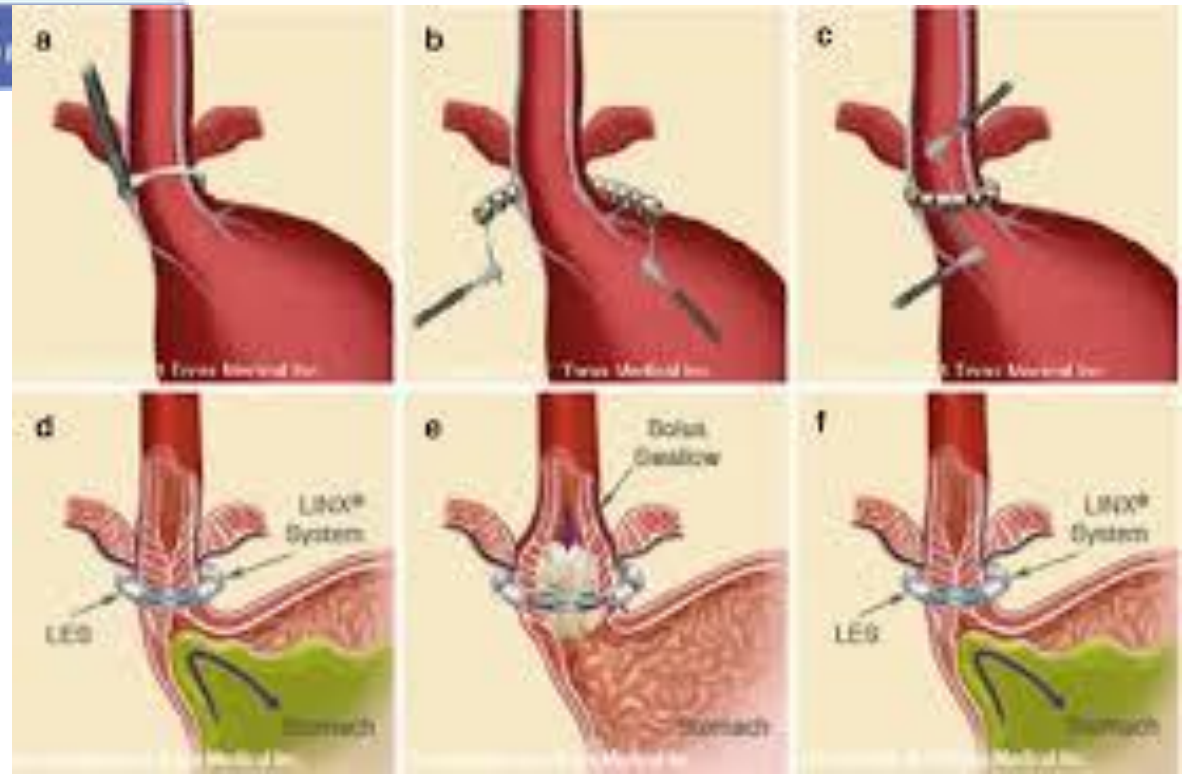
- Every patient that is going to have a fundoplication should undergo HRM to rule out esophageal motility alterations.
- Partial fundoplication is advisable when there is a decrease in the peristaltic reserve.
- Surgery is not recommended in patients with extraesophageal manifestations with no typical GERD symptoms.
- Fundoplication can be useful in a small group of patients, in whom there is objective evidence of reflux as the cause of those manifestations.
- In patients with BE, fundoplication is indicated to control symptoms, even though a recent meta-analysis showed a lower risk of progression to high-grade dysplasia or EAC.
- With respect to the type of surgery, no differences have been found between partial or complete fundoplication, in GERD symptom control.


Nissen fundoplication
Normal stomach
After surgery

Magnetic Sphincter Augmentation(MSA):

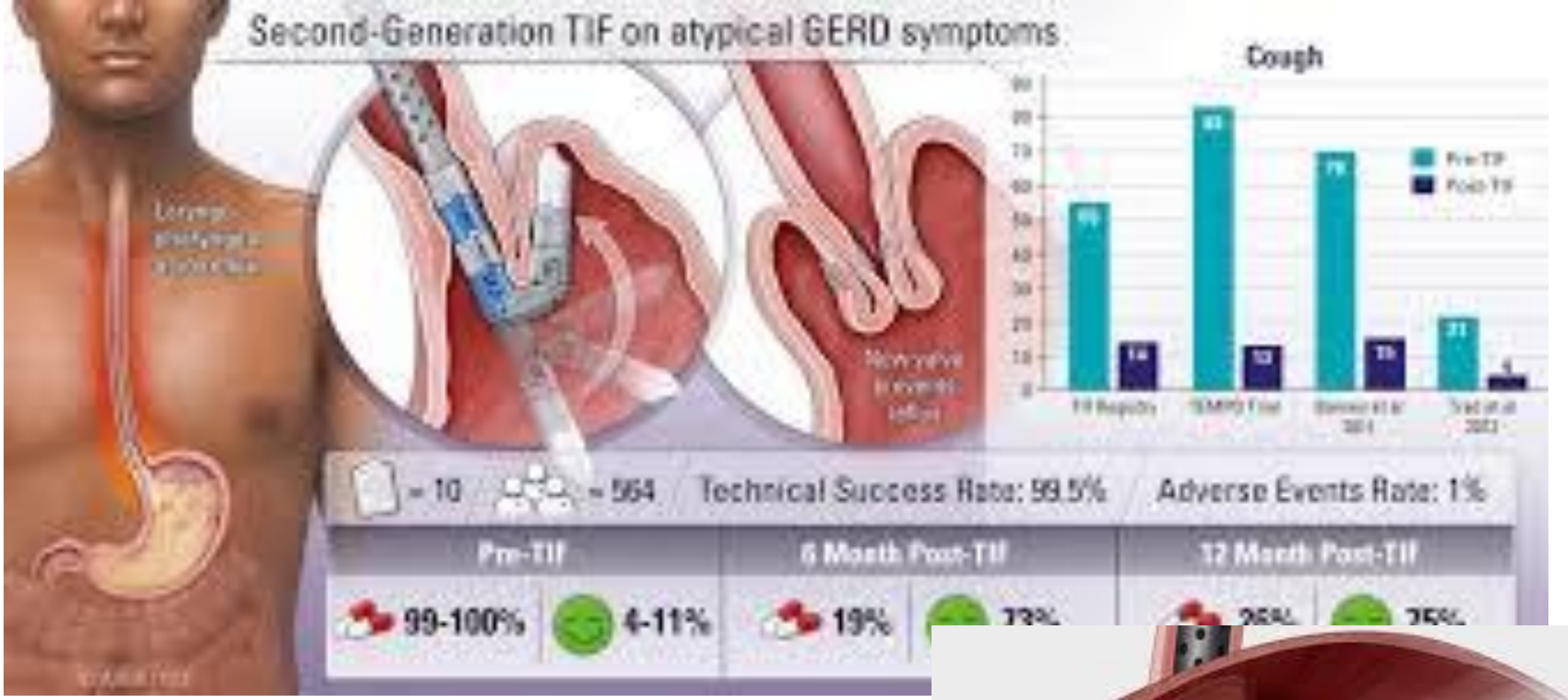
- An alternative minimally invasive surgical option is magnetic sphincter augmentation (MSA) where a bracelet of magnets encased in titanium is implanted around the EGJ.
- As many as 58% normalize esophageal AET within 1 year after MSA, and > 90% are able to halve their use of antisecretory therapy.
- Although MSA appears beneficial in all PPI-refractory GERD, regurgitation-predominant symptoms achieve particularly favorable results.
- Number of total reflux episodes > 80 on preoperative pH-impedance monitoring despite optimized medical therapy predicts patient satisfaction and improved symptom scores following MSA.
- Sustained symptom improvement has been demonstrated 5 years from implantation, with reduction in PPI use from 100% to 15.3%, and moderate-to-severe regurgitation symptoms from 57% to 1.2%.
- Dysphagia post-MSA was typically mild, with resolution in most patients (89% at 1 year and 96% at 3 years), and the need for device explant was infrequent.


A
Clasp closure device in closed position
B
Clasp closure device in open


a
b
c
d
LINX® System
LES
Stomach
e
Bolus Swallow
f

Transoral Incisionless Fundoplication (TIF):

- Among endoscopic approaches, transoral incisionless fundoplication (TIF) 2.0 creates a 3 cm valve with a 270° circumferential wrap without need for laparoscopic surgery.
- Although TIF has reported success despite presence of < 2 cm hiatal hernia, laparoscopic crural repair can be performed in conjunction with TIF when necessary.
- Short-term benefits are well demonstrated over PPI therapy in randomized trials, particularly for regurgitation predominant symptoms.
- Even refractory atypical GERD symptoms may improve, with nearly three-fourths of patients off PPI therapy at 12-month follow-up.
- Long-term efficacy data are mixed; one 10-year study reported > 90% of patients off PPI or on doses 50% lower than baseline, yet others have reported decreased effectiveness over time.


Second-Generation TIF on atypical GERD symptoms
Cough
Pre-TIF
Post-TIF
= 10
= 564
Technical Success Rate: 98.5%
Adverse Events Rate: 1%
Pre-TIF
6 Month Post-TIF
12 Month Post-TIF
99-100%
4-11%
19%

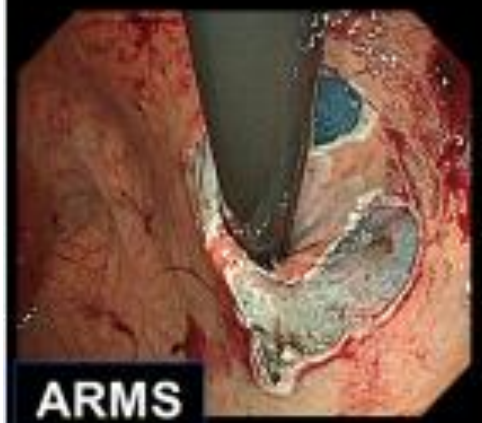


Radiofrequency application:

- Radiofrequency application (RFA, also termed Stretta) to the EGJ attempts to improve EGJ barrier function while reducing TLESR frequency through altering esophageal nerve and muscle function, and potentially through reduction in sensation perception.
- While generally safe, efficacy of RFA remains under debate.
- Separate meta-analyses have reported unchanged LES pressures and inconsistent outcomes in regards to PPI discontinuation, improvement in quality of life, and esophageal AET normalization.

Antireflux Mucosectomy:

- A newer endoscopic technique termed **antireflux mucosectomy** creates scarring around the EGJ using crescentic or circumferential mucosal resection to reduce reflux burden.
- In observational **antireflux mucosectomy** studies, improvement in reflux-related quality of life has been demonstrated.
- Other antireflux mucosal interventions reduce reflux in a similar fashion, including antireflux **band mucosectomy** (ARBM) and **antireflux mucosal ablation (ARMA)** using argon plasma coagulation.
- A pooled success rate of 73.8% has been reported over short-term follow up with antireflux mucosal interventions in a meta-analysis of uncontrolled trials.
- Post-procedure dysphagia requiring dilation was reported by 10%, while perforation occurred in 2.2%.



ARMS

- mucosectomy without closure
- Require over 3/4 to 4/5 of the mucosal resection



ARMA

- ablation without closure
- Require over 3/4 to 4/5 of the mucosal ablation



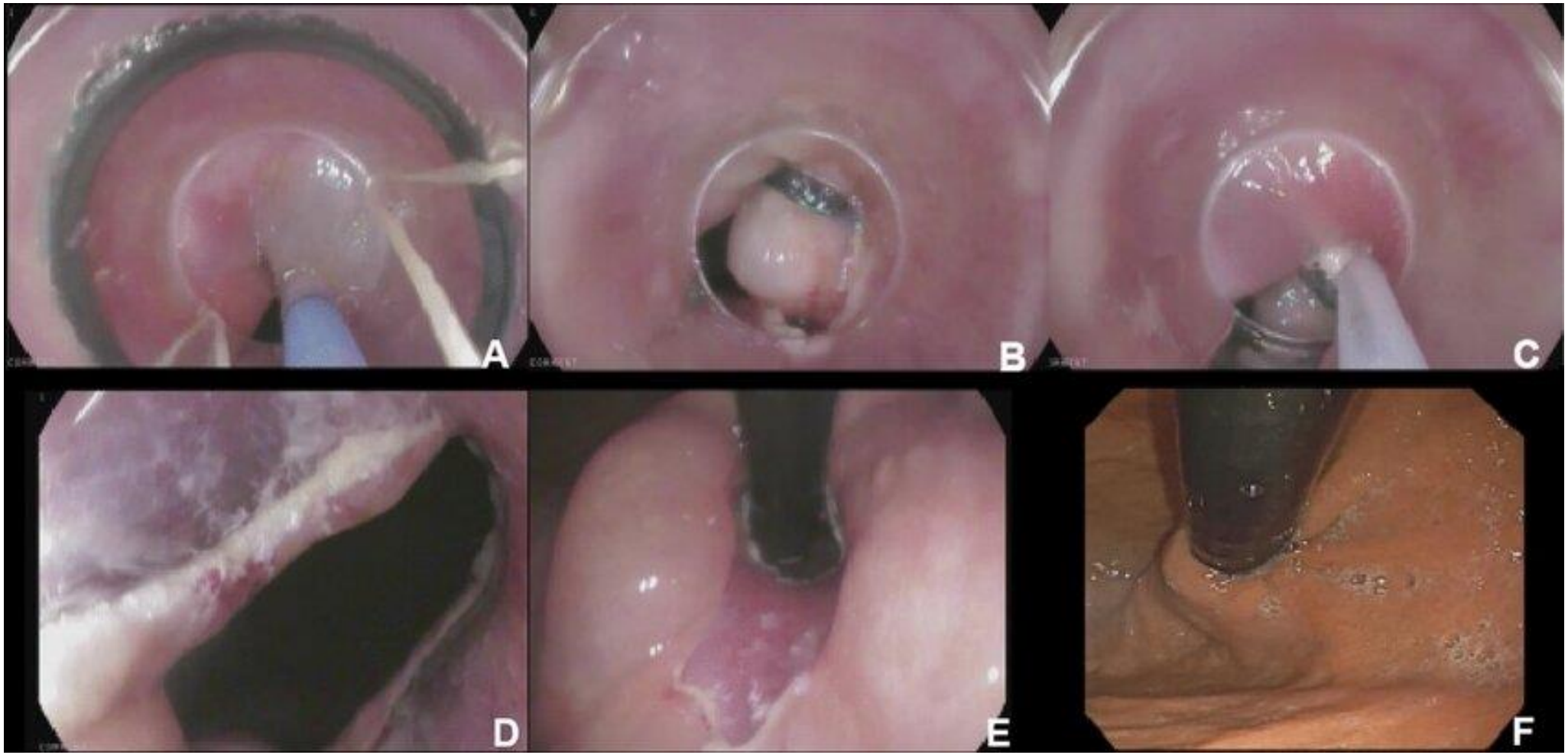
ARM-P

- mucosectomy with closure
- Require only less than 1/3 of the mucosal resection



ARM-P/V

- valvuloplasty with preservation of the mucosa, fortified by closure
- Require only less than 1/3 of the mucosal resection


A
B
C
D
E
F



Gastric per-oral endoscopic myotomy(POEM):

- For the subset of refractory GERD patients where gastroparesis co-exists, improving gastric emptying can improve reflux symptoms.
- Medical management with prokinetics is typically utilized at the outset.
- Gastric per-oral endoscopic myotomy can be an option for persistent delay in gastric emptying, especially when this is believed to contribute to refractory GERD symptoms.
- A recent multicenter retrospective study of 20 lung transplant patients with concomitant GERD and gastroparesis demonstrated normalization of pH testing in 90% with improvement in gastric emptying and ability to wean off PPI therapy in 75%.

Original Article

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Efficacy of abdominal breathing on sleep and quality of life among patients with non-erosive gastroesophageal reflux

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Hassnaa Eid Shaban Mosa[1,2], Hanan G. El- Bready[3], Abeer El- Said Hassan El-Sol[1], Hanaa E. Bayomy[4,5], Rehab Omar Taman[1] and Hanady Sh. Shehata[3]

Abstract

Aim: Abdominal breathing recently has demonstrated an important role in managing symptoms of Gastroesophageal Reflux Disease (GERD), improving quality of life, medication adherence, and sleep quality. This study aimed to evaluate the effectiveness of abdominal breathing on sleep and quality of life in patients with non-erosive gastroesophageal reflux.

Subject and methods: A Quasi-experimental design was used. A purposive sample of 100 patients was selected from the medical outpatient clinics of Menoufia University Hospital and the outpatient clinics of the National Liver Institute in Menoufia Governorate, Egypt. A Structured interview questionnaire was used to collect data on patients' sociodemographic characteristics, belly breathing exercise performance and self-reported compliance, GERD symptoms severity and frequency, Pittsburgh Sleep Quality Index, and GERD Health-Related Quality of Life.

Results: The frequency of GERD symptoms decreased from 26.64 pre-intervention to 17.61 and 9.58, respectively, at two- and four-months post-intervention. Antacid consumption among patients taking it 7 days/week was reduced from 34% pre-intervention to 2% and 0% post-intervention by two and four months, respectively. Good sleepers were 24% pre-intervention then increased to 62% and 90% post-intervention by 2 and 4 months, respectively. Regarding GERD related quality of life, only 1% was satisfied pre-intervention, which increased to 32% and 72% post-intervention by 2 and 4 months, respectively.

Conclusion: Abdominal breathing offers better therapeutic improvements in all patients' outcomes such as reduced severity and frequency of GERD symptoms, reduced antacid consumption, increased sleep quality, and increased satisfaction with life quality. Healthcare professionals are encouraged to incorporate abdominal breathing into treatment protocols for patients with non-erosive GERD.

Keywords

Abdominal breathing, non-erosive gastroesophageal reflux, GERD, sleep and life quality

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[1]Department of Medical Surgical Nursing, Faculty of Nursing, Menoufia University, Shebin El Kom, Egypt
[2]Department of Medical Surgical Nursing, Nursing Faculty, Jouf University, Sakakah, Saudi Arabia
[3]Department of Family and Community Health Nursing, Faculty of Nursing, Menoufia University, Shebin El Kom, Egypt
[4]Department of Public Health and Community Medicine, Faculty of Medicine, Benha University, Benha, Egypt
[5]Department of Family and Community Medicine, Faculty of Medicine, Northern Border University, Arar, Saudi Arabia

Corresponding author:
Hanaa E. Bayomy, Department of Public Health and Community Medicine, Faculty of Medicine, Benha University, Benha, Egypt and Department of Family and Community Medicine, Faculty of Medicine, Northern Border University, 7012 Alkasabah, Almosadiah Alsharkiah, Arar, 350673311, Saudi Arabia.
Emails: hana.bayuomi@fmed.bu.edu.eg; Hanaa.Sayed@nbu.edu.sa

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Other Measures

- **Complementary approaches** benefit some refractory GERD patients.
- **Diaphragmatic breathing** can increase LES pressure and reduce postprandial reflux episodes.
- In a randomized trial of patients with NERD or healed esophagitis, diaphragmatic breathing reduced abnormal AET with improvement in quality of life scores.
- Benefits may last for as long as 9 months, with sustained improvement in quality of life as well as PPI discontinuation.
- **Both acupuncture and hypnotherapy** can improve symptom intensity, especially chest pain, in refractory GERD.
- Heightened psychological stress, anxiety, and/or depression exacerbate refractory GERD symptoms in population-based studies, which may benefit from **targeted therapy administered by a behavioral psychologist.**

Conclusions:

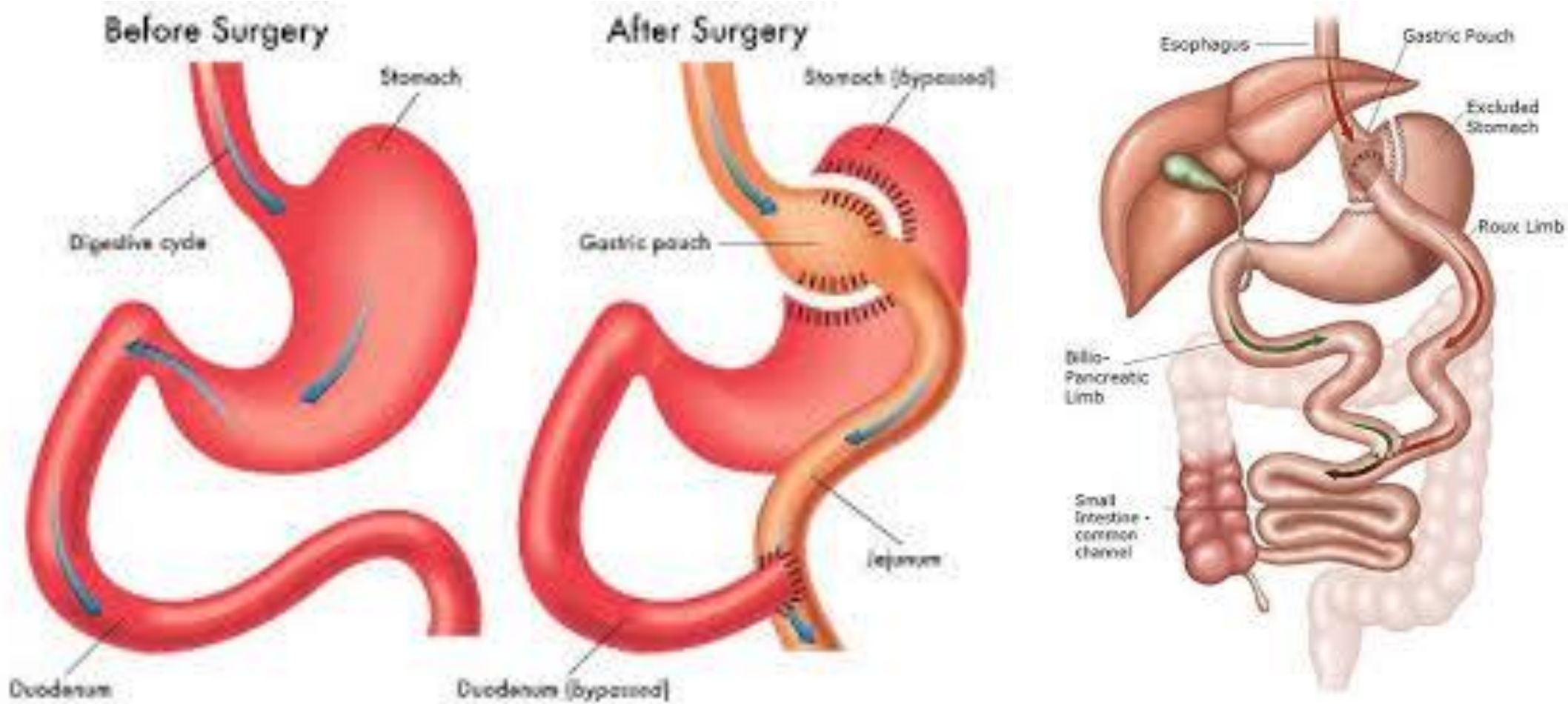
- Persistent esophageal symptoms despite seemingly adequate acid suppressive therapy is the starting point for evaluation to determine if GERD evidence exists.
- Refractory GERD is diagnosed when abnormal reflux metrics persist on endoscopy and/or pH impedance monitoring performed on optimized GERD therapy in patients with previously proven GERD.
- While several non-pharmacologic, pharmacologic, endoscopic, and surgical interventions are available at the disposal of the clinician for effective treatment of refractory GERD, the management strategy should be personalized to each patient, taking into account underlying comorbidities, risk-benefit profile, and patient preference.

Older adults and GERD

- We recommend the performance of **endoscopy** in older adults with symptoms of GERD due to the **elevated prevalence of more serious disease.**
- GERD tends to be **more severe in older adults due to a lower perception of heartburn.**
- When diagnostic studies are performed on older adults, **severe EE** is often found, making an **early diagnostic approach, regardless of symptom severity,** mandatory.
- **Xerostomia** has been described to reduce protective factors of the esophagus, such as bicarbonate in the saliva, in the older adult.
- In addition, **motility disorders and HH** are frequently found in this group of patients.
- Treatment of GERD in the older adult should follow the same guidelines used for younger patients.

GERD and obesity:

- In the patient with GERD and obesity, who is a candidate for bariatric surgery, we recommend **gastrojejunal bypass** as the surgery of choice.
- **Sleeve gastrectomy and adjustable gastric banding** are not recommended because they are procedures that can worsen GERD by causing reflux.


Before Surgery
Stomach
Digestive cycle
Duodenum
After Surgery
Stomach (bypassed)
Gastric pouch
Jejunum
Duodenum (bypassed)
Esophagus
Gastric Pouch
Excluded Stomach
Roux Limb
Bilio-Pancreatic Limb
Small Intestine - common channel


Thanks for your attention