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Evaluation and management of gastroesophageal reflux disease: A brief look at the updated guidelines

ABSTRACT

Gastroesophageal reflux disease (GERD) is the most common gastrointestinal disorder seen in primary care offices and is usually managed with proton pump inhibitors (PPIs). The authors present an overview of the updated guidelines from the American College of Gastroenterology, which address the evaluation and management of GERD, including the consequences of long-term PPI therapy and emerging therapies.

KEY POINTS

If GERD symptoms have resolved with PPIs and the patient has no erosive esophagitis or Barrett esophagus, tapering to the lowest effective dose, intermittent PPI therapy or replacement with a histamine 2 receptor antagonist, and discontinuation when possible should be considered.

Endoscopy is indicated in patients with alarm symptoms such as dysphagia, weight loss, bleeding, vomiting, anemia, chest pain, or refractory symptoms after optimization of PPI therapy.

Surgical options are recommended for patients with objective evidence of GERD and severe reflux esophagitis, large hiatal hernias, or persistent, troublesome GERD symptoms such as regurgitation.

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In response to advances in the diagnostic evaluation and management of gastroesophageal reflux disease (GERD) since previous guidelines were published in 2013,[1] the American College of Gastroenterology (ACG) updated the guidelines in 2022.[2] Here, we offer a brief overview of changes in the outpatient management of GERD outlined in the latest guidelines.

DIAGNOSTIC AND TREATMENT CHALLENGES

GERD, the result of the reflux of gastric contents into the esophagus,[2] is a diagnosis based on the presence of typical clinical symptoms, characteristic mucosal injury seen on endoscopy, or abnormal esophageal acid exposure demonstrated on a reflux monitoring study. The diagnosis can be challenging because symptoms may overlap with other disorders such as achalasia, eosinophilic esophagitis, or cardiac or pulmonary disease.

Proton pump inhibitors (PPIs) are still the medical treatment of choice for GERD. Although a PPI trial is used as a diagnostic "test" in patients with the typical symptoms of heartburn and regurgitation, the sensitivity of this approach is only 80% and the specificity 74%.[3] Also, up to 45% of patients treated with PPIs may continue to have symptoms.[4] These patients are designated as having refractory GERD, defined as persistent symptoms despite 8 weeks of twice-daily PPI therapy. In these patients, continued reflux is the cause of the

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symptoms in only 21%, with the rest having reflux hypersensitivity or functional heartburn.[5]

Extraesophageal symptoms such as cough, asthma, laryngitis, and throat-clearing have been attributed to GERD. Laryngopharyngeal reflux is defined as the retrograde flow of stomach content to the larynx and pharynx that comes into contact with the upper aerodigestive tract. Evaluation by an ear, nose, and throat, allergy, or pulmonary specialist can be considered to rule out non-GERD causes of the symptoms. Finally, antireflux surgery can be considered in severe cases of erosive esophagitis or large hiatal hernia.[2]

WHO WROTE THE GUIDELINES?

The original ACG guidelines for the evaluation and management of GERD, published in 1995, were updated in 1999, 2005, and 2013. The 2022 guidelines provide updated evidence-based recommendations. They are structured in the format of statements that are clinically relevant in GERD. The authors developed PICO (patient-population, intervention, comparison, and outcomes) questions and performed an extensive literature search for each question with assistance from a research librarian. The GRADE system (Grading of Recommendations, Assessment, Development, and Evaluation)[6] was used to assess the quality of evidence for each statement.

WHAT ARE THE MAIN RECOMMENDATIONS?

The updated ACG guidelines include the following recommendations:

- Adult patients with classic GERD symptoms of heartburn and regurgitation without alarm symptoms such as dysphagia, weight loss, bleeding, vomiting, anemia, and chest pain can be treated with an 8-week empiric trial of a PPI taken once daily before meals. An upper age limit is not specified.
- Endoscopy is indicated in patients with alarm symptoms or refractory symptoms after optimization of PPI therapy.
- Reflux testing with a wireless telemetry capsule attached to the esophageal mucosa during endoscopy or transnasal catheter is considered in patients with suspected GERD and normal endoscopy, extraesophageal GERD symptoms, or refractory GERD.
- PPIs continue to be the mainstay of medical treatment. For patients with GERD whose symptoms have resolved and who do not have erosive esophagitis or Barrett esophagus, tapering the PPI to the lowest effective dose, replacement with intermittent PPI therapy or a histamine 2 receptor antagonist, and, when possible, discontinuation should be considered.
- Long-term PPI therapy or antireflux surgery is recommended for patients with Los Angeles classification grade C esophagitis (erosions extending over mucosal folds, but over less than three-quarters of the circumference) or grade D esophagitis (confluent erosions extending over more than three-quarters of the circumference).[7]
- Surgical options are recommended for patients with objective evidence of GERD who have severe reflux esophagitis (Los Angeles grade C or D), large hiatal hernias, or persistent, troublesome GERD symptoms such as regurgitation.[7] The treatment is fundoplication, in which the lower esophageal sphincter is strengthened by wrapping the fundus of the stomach around the esophagus in the abdomen. Roux-en-Y gastric bypass is an option to treat GERD in patients with obesity who are candidates for this procedure.
- Transoral incisionless fundoplication (TIF), the endoscopic creation of a gastric fundal wrap with plication, and magnetic sphincter augmentation (MSA), the laparoscopic insertion of a flexible ring of interlinked magnetic beads to augment the weak lower esophageal sphincter, can be alternatives in patients with troublesome regurgitation or heartburn who do not wish to undergo fundoplication and who do not have severe reflux esophagitis or large hiatal hernia.

WHAT IS THE EXPECTED CLINICAL IMPACT?

The updated ACG guidelines provide a streamlined approach to the management of the myriad presentations of GERD and the indications for use of emerging nonmedical therapies such as TIF and MSA.

Prior guidelines were ambiguous regarding the step-up approach vs the step-down approach in the medical treatment of GERD. The current recommendation is to start PPI therapy when a clinical diagnosis of GERD is made, then to proceed with diagnostic testing if there is no response, or to cut down to the lowest effective dose if there is a complete response.

As discussed in the updated guidelines, another issue in the past was concern about adverse effects with long-term PPI use as reported in observational studies.[2] However, 2 randomized clinical trials published since the last guidelines provide reassuring evidence about the safety of chronic PPI use.[8,9]

AspECT (A Phase III, Randomized, Study of Aspirin and Esomeprazole Chemoprevention in Barrett's

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Metaplasia)[8] randomized 2,557 patients with Barrett esophagus to low- or high-dose esomeprazole (20 mg vs 80 mg), with or without aspirin (300 mg or 325 mg), in a 2 × 2 factorial design with a median follow-up period of 8.9 years.[8] Treatment-related serious adverse events were reported in 1% of patients, with no differences between low-dose and high-dose PPI therapy.

In the COMPASS trial (Cardiovascular Outcomes for People Using Anticoagulation Strategies),[9] 17,598 patients being treated with rivaroxaban and aspirin, rivaroxaban alone, or aspirin alone were randomized to receive pantoprazole 40 mg daily or placebo and were followed for 3 years.[9] No significant differences in side effects were noted between PPI and the placebo group except for a trend toward increased risk of enteric infections. However, it is difficult to exclude if PPIs confer any increased risk of these adverse events because they are infrequent, and the study duration may not have been long enough for some adverse events to develop.

Therefore, based on these studies, PPIs are safe for long-term use, especially in patients with erosive esophagitis, Barrett esophagus, esophageal stricture, eosinophilic esophagitis, and PPI-dependent GERD. In addition, potassium-competitive acid blockers are exciting potential new agents for pharmacologic treatment of GERD as they are not purported to have PPI-associated adverse events.

WHAT IS DIFFERENT FROM PRIOR GUIDELINES?

The updated guidelines differ from previous versions on the following points:

- In the evaluation of GERD refractory to PPI therapy, endoscopy should be performed off PPI therapy for 2 to 4 weeks. Prior guidelines did not recommend cessation of PPI therapy before endoscopy.
- In patients with partial or no relief from PPI therapy with no previous evaluation or in those with extraesophageal symptoms and normal endoscopy, pH testing to detect acid reflux should be performed off PPI therapy.
- In patients with objective evidence of GERD who have refractory symptoms, pH impedance on PPI should be performed to detect the amount of reflux (acidic, weakly acidic, or nonacidic).
- Salivary pepsin testing or oropharyngeal or pharyngeal pH testing is not recommended for the evaluation of laryngopharyngeal reflux symptoms.
- If patients do not respond to a PPI, they can be switched to a different PPI. For patients who have not responded to the new PPI, more than one switch to a different PPI cannot be supported.
- Regarding possible patient concerns about long-term PPI therapy, the current guidelines suggest advising patients that high-quality studies have found that PPIs do not significantly increase the risk of pneumonia, stomach cancer, osteoporosis-related bone fractures, chronic kidney disease, nutritional deficiencies, heart attacks, strokes, dementia, and early death, and that he benefits of PPI therapy far outweigh the risks.
- TIF and MSA may be considered as alternative therapies for refractory GERD.

DO OTHER SOCIETIES AGREE OR DISAGREE?

The latest recommendations made by the American Gastroenterological Association (AGA) in its 2022 AGA Clinical Practice Update,[10] though almost entirely in concordance with the 2022 ACG guideline, includes the following additional recommendations:

For patients with functional heartburn or reflux hypersensitivity, pharmacologic neuromodulation, referral to a behavioral therapist for hypnotherapy, cognitive behavioral therapy, diaphragmatic breathing, and relaxation strategies, or both, should be offered.

The AGA Clinical Practice Update also recommends Roux-en-Y gastric bypass as an effective primary antireflux intervention in patients with obesity and as a salvage option in nonobese patients, whereas the 2022 ACG guidelines recommend Roux-en-Y gastric bypass only for patients with obesity.[10]

Regarding the role of endoscopy in the management of GERD, the 2015 guidelines of the American Society for Gastrointestinal Endoscopy[11] are largely in concordance with the 2022 ACG guidelines, except that they list the antireflux Stretta procedure (delivery of radiofrequency energy to lower esophageal sphincter) alongside TIF as a potential endoluminal GERD therapy for select patients. The 2022 ACG guidelines do not recommend it in view of cumulative evidence suggesting lack of efficacy.[2]

HOW WILL THIS CHANGE DAILY PRACTICE?

Even though PPIs are the preferred initial therapy for GERD, a sizable proportion of patients continue to have symptoms. For these patients, it is common practice to try different PPIs without investigating for objective evidence of GERD. Also, PPIs are often prescribed in patients with cough, asthma, or laryngitis on the presumption that it represents extraesophageal GERD, even in the absence of typical GERD symptoms. In these patients, reflux testing should be performed before starting PPI therapy, and esophageal

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manometry should be done to rule out motility disorders such as achalasia. If the evaluation shows no evidence of abnormal reflux, PPIs should be stopped. For patients found to have reflux hypersensitivity or functional heartburn, a pain modulator such as a tricyclic antidepressant or selective serotonin reuptake inhibitor may be considered.

If a patient with no alarm symptoms and a good response to a PPI stops the drug after several months and has a relapse of symptoms, PPI therapy is often resumed without further evaluation. For such patients, the updated guidelines recommend endoscopy to identify severe disease necessitating indefinite PPI therapy (eg, erosive esophagitis, Barrett esophagus) and alternative diagnoses (eg, eosinophilic esophagitis).

WHEN WOULD THE GUIDELINES NOT APPLY?

The 2022 ACG guidelines recommend endoscopic evaluation in patients who have symptoms refractory to PPI therapy or who have a relapse of symptoms after cessation of PPI therapy. This may not apply in certain conditions such as pregnancy or severe cardiopulmonary disease, where endoscopic evaluation may be associated with unacceptable risk. Conversely, endoscopy is indicated even in patients with well-controlled GERD symptoms if they have multiple risk factors for Barrett esophagus such as age over 50, White ethnicity, male sex, smoking, obesity, or a positive family history.[12]

Also, diagnostic testing for GERD such as endoscopy and reflux monitoring is sometimes indicated in asymptomatic patients.[13,14] For example, before lung transplant, a routine evaluation with reflux monitoring and esophageal manometry is indicated, as untreated GERD may contribute to graft failure.[13] Another group of asymptomatic patients who may benefit from diagnostic testing for GERD are those awaiting bariatric surgery such as sleeve gastrectomy, as this procedure may be associated with worsening of GERD postoperatively.[14]

It is also worthwhile to note that manometry and reflux evaluation are not available in all healthcare settings, and patients may need referral to a tertiary care center for evaluation.

Lastly, the 2022 ACG guidelines also do not mention the on-demand use of histamine-2 receptor antagonists as solo therapy in patients with intermittent symptoms. Randomized controlled trials have demonstrated that standard-dose histamine-2 receptor antagonists are more effective than placebo at relieving heartburn in cases of GERD, with symptomatic relief reported in 60% of cases.[15]

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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