Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Gastroesophageal reflux disease (GERD).

Bibliographic Source(s)

University of Michigan Health System. Gastroesophageal reflux disease (GERD). Ann Arbor (MI): University of Michigan Health System; 2012 May. 12 p. [11 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Gastroesophageal reflux disease (GERD). Ann Arbor (MI): University of Michigan Health System; 2007 Jan. 10 p. [9 references]

Recommendations

Major Recommendations

Note from the University of Michigan Health System (UMHS) and the National Guideline Clearinghouse (NGC): The following guidance was current as of May 2012. Because UMHS occasionally releases minor revisions to its guidance based on new information, users may wish to consult the original guideline document for the most current version.

Note from NGC: The following key points summarize the content of the guideline. Refer to the full text for additional information, including detailed information on dosing, possible side effects, and cost of medications.

The strength of recommendation (I-III) and levels of evidence (A-D) are defined at the end of the "Major Recommendations" field.

Diagnosis

- *History*. If classic symptoms of heartburn and acid regurgitation dominate a patient's history, then they can help establish the diagnosis of gastroesophageal reflux disease (GERD) with sufficiently high specificity, although sensitivity remains low compared to 24-hour pH monitoring. The presence of atypical symptoms (see table below), although common, cannot sufficiently support the clinical diagnosis of GERD *[B]*.

Table. Atypical Signs of GERD

Chronic cough

Asthma
Recurrent sore throat
Recurrent laryngitis
Dental enamel loss
Subglottic stenosis
Globus sensation
Chest pain
Onset of symptoms at age >50

- *Testing*. No gold standard exists for the diagnosis of GERD *[A]*. Although pH probe is accepted as the standard with a sensitivity of 85% and specificity of 95%, false positives and false negatives still exist *[II B]*. Endoscopy lacks sensitivity in determining pathologic reflux but can identify complications (e.g., strictures, erosive esophagitis, Barrett's esophagus) *[I A]*. Barium radiography has limited usefulness in the diagnosis of GERD and is not recommended *[III B]*.
- *Therapeutic trial*. An empiric trial of anti-secretory therapy (AST) can identify patients with GERD who lack alarm/warning symptoms (see table below) *[I A]* and may be helpful in the evaluation of those with atypical manifestations of GERD, specifically non-cardiac chest pain (NCCP) *[II B]*.

Table. Alarm/Warning Signs Suggesting Complicated GERD

Dysphagia
Odynophagia
Gastrointestinal (GI) bleeding
Iron deficiency anemia
Weight loss
Early satiety
Vomiting

Treatment

- *Lifestyle modifications*. Lifestyle modifications (see table below) should be recommended throughout the treatment of GERD *[II B]*, yet there is evidence-based data to support only weight loss and avoiding recumbency several hours after meals *[II C]*.

Table. Lifestyle Modifications

Elevate head of bed 6-8 inches
Decrease fatty meals
Stop smoking
Avoid recumbency/sleeping for 3-4 hours postprandially
Avoid certain foods: chocolate, alcohol, peppermint, caffeinated coffee and other beverages, onions, garlic, fatty foods, citrus, tomato
Avoid large meals
Weight loss
Avoid medications that can potentiate symptoms: calcium channel blockers, β-agonists, α-adrenergic agonists, theophylline, nitrates, and some sedatives (benzodiazepines)

- *Pharmacologic treatment*. H2-receptor antagonists (H2RAs), proton pump inhibitors (PPIs), and prokinetics have proven efficacy in the treatment of GERD *[I A]*. Prokinetics are as effective as H2RAs but are currently unavailable *[III A]*. Carafate and antacids are ineffective *[III A]*, but may be used as supplemental acid-neutralizing agents for certain patients with GERD *[II D]*.
    - Non-erosive reflux disease (NERD): *Step-up* (H2RA then as followed by a PPI if no improvement) and *step-down* (PPI then followed by the lowest dose of acid suppression) therapy are equally effective for acute treatment and maintenance *[I B]*. *On demand* (patient-directed) therapy is the most cost-effective strategy *[I B]*.
    - Erosive esophagitis: Initial PPI therapy is the treatment of choice for acute and maintenance therapy for patients with documented erosive esophagitis *[I A]*.
    - Take PPI's 30-60 minutes prior to breakfast (and dinner if two times per day [BID]) to optimize effectiveness *[I B]*. Use generic and over-the-counter (OTC) formulations exclusively, eliminating need for prior authorizations.
    - Patients should not be left on AST without re-evaluation of symptoms to minimize cost and the potential adverse events from medications *[I B]*.
- *Surgery*. Anti-reflux surgery is an alternative modality in GERD treatment for patients with chronic reflux and recalcitrant symptoms *[II A]*, yet has a significant complication rate (10-20%). Resumption of pre-operative medication treatment is common (>50%) and may increase over time.
- *Other endoscopic modalities*. While less invasive and with fewer complications, they have lower response rates than anti-reflux surgery *[II C]*, and have not been shown to reduce acid exposure.

Follow up

- *Symptoms unchanged*. If symptoms remain unchanged in a patient with a prior normal endoscopy, repeating endoscopy has no benefit and is not recommended *[III C]*.
- *Warning signs*. Patients with warning/alarm signs and symptoms suggesting complications from GERD (see table above) should be referred to a GERD specialist.
- *Risk for complications*. Further diagnostic testing (e.g., EGD [esophagogastroduodenoscopy], pH monitoring) should be considered in patients who do not respond to acid suppression therapy *[I C]* and in patients with a chronic history of GERD who are at risk for complications. Chronic reflux has been suspected to play a major role in the development of Barrett's esophagus, yet it is unknown if outcomes can be improved through surveillance and medical treatment *[D]*.

Definitions:

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

Strength of Recommendation

I. Generally should be performed
II. May be reasonable to perform
III. Generally should not be performed

Clinical Algorithm(s)

An algorithm for diagnosis and treatment of gastroesophageal reflux disease (GERD) is provided in the original guideline document.

Scope

Disease/Condition(s)

Gastroesophageal reflux disease (GERD)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Gastroenterology

Internal Medicine

Pharmacology

Intended Users

Advanced Practice Nurses

Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

To implement a cost-effective and evidence-based strategy for the diagnosis and treatment of gastroesophageal reflux disease (GERD)

Target Population

Adults with suspected or confirmed gastroesophageal reflux disease (GERD)

Interventions and Practices Considered

Diagnosis/Evaluation

1. History (signs, symptoms)
2. Testing
    - Esophageal pH monitoring
    - Endoscopy
    - Barium radiology (considered but not recommended)
    - Esophageal manometry
3. Empiric/therapeutic trials of anti-secretory therapy

Treatment/Management

1. Lifestyle modifications
2. Pharmacologic treatment

    - Histamine type-2 receptor antagonists (H2RAs)
    - Proton pump inhibitors (PPIs)
    - Supplemental acid-neutralizing agents
    - Over-the-counter (OTC) remedies
3. Anti-reflux surgery
4. Alternative endoscopic treatments (radiofrequency heating of the gastroesophageal junction, endoscopic gastroplasty, polymer injections and full thickness gastroplication)
5. Maintenance regimens
    - Step-up therapy
    - Step-down therapy
    - On-demand therapy
6. Follow-up
    - Referral to gastroesophageal reflux disease (GERD) specialists
    - Further diagnostic testing (e.g., esophagogastroduodenoscopy (EGD), pH monitoring) for those non-responsive to acid suppression therapy or at risk for complications
7. Special considerations for older adults, pregnant patients, and atypical manifestations of GERD
8. Screening and treatment for Barrett's esophagus
9. Treatment of *Helicobacter pylori* infection (not recommended as treatment for GERD)

Major Outcomes Considered

- Sensitivity and specificity of diagnostic tests
- Rate of symptomatic relief
- Esophagitis healing rates
- Medication and treatment side effects
- Cost-effectiveness of treatment

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The literature search began with the results of the literature searches performed through May 2006 for the previous versions of this guideline. The results of three more recent literature searches were initially reviewed and accepted as adequate through the time they were performed:

- American Gastroenterological Association (AGA): Position statement on the management of gastroesophageal reflux disease, 2008, literature search through early 2007.
- American Society for Gastrointestinal Endoscopy (ASGE): Role of endoscopy in the management of GERD, 2007, literature search through March 2008.
- Society of American Gastrointestinal and Endoscopic Surgeons: Guidelines for surgical treatment of gastroesophageal reflux disease, 2010, literature search through early 2006.

A search of more recent literature was conducted prospectively on Medline from January 2007 (end of AGA search) through March 2011, except January 2006 was the start date for endoscopy (since ASGE search) and January 2008 was the start date for surgical treatment (since SAGES search). The major keywords were: *gastroesophageal reflux disease (or GERD, NERD [non-erosive reflux disease], NEED [non-erosive esophageal disease]), human adults, English language, guidelines, clinical trials, and cohort studies*. Terms used for specific topic searches within the major key words included: *symptoms and classification (atypical symptoms, heartburn, retrosternal burning sensation*

precipitated by meals or a recumbent position, hoarseness, laryngitis, sore throat, chronic cough, chest pain, bronchospasm/asthma, dental erosions), eosinophile, lymphocytic esophagitis, non acid reflux and weekly acid reflux, nocturnal (or nocturnal breakthrough, night time), endoscopy, pH recording, manometry, provocative testing (Bernstein's), video esophagography, empiric/therapeutic trial to acid suppression, lifestyle measures/treatment (avoiding fatty foods, chocolate, peppermints, ethanol-containing beverages; recumbency for 3 hours after a meal; elevating head of bed; weight loss), antacids, alginic acid (gaviscon), carafate, prokinetic agents (cisapride, metoclopramide, bethanechol, dromperidone), H2 receptor antagonists (nizatidine, ranitidine, famotidine, cimetidine), proton pump inhibitors (omeprazole, lansoprazole, rabeprazole, pantoprazole, esomeprazole) – toxicity and adverse reactions/events, proton pump inhibitors – other references, baclofen, fundoplication (open vs. laparoscopy; endoscopic antireflux procedures), Barrett's esophagus (screening, surveillance). Detailed search terms and strategy available upon request.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent information available to expert members of the panel, including abstracts from recent meetings and results of clinical trials. Negative trials were specifically sought. The search was a single cycle.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Level of Evidence Supporting a Diagnostic Method or an Intervention

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Conclusions were based on prospective randomized controlled trials (RCTs) if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

I. Generally should be performed
II. May be reasonable to perform
III. Generally should not be performed

Cost Analysis

Several studies have demonstrated that on-demand therapy with Proton pump inhibitors (PPIs) is the most cost-effective method for non-erosive reflux disease (NERD).

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Family Medicine, General Medicine, and Gastroenterology.

The Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers endorsed the final version.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Conclusions were based on prospective randomized controlled trials (RCTs) if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Accurate diagnosis and appropriate, cost-effective treatment of gastroesophageal reflux disease (GERD)

Potential Harms

- H2 receptor antagonists (H2RAs) have been associated with rare cytopenias, gynecomastia, liver function test abnormalities, and hypersensitivity reactions. In the long-term, there have been no controlled trials with follow-up on the safety of chronic use of H2RAs. Cimetidine may cause gynecomastia or androgenic side effects, and may interact with medications metabolized by cytochrome P450.
- The potential benefit of chronic proton pump inhibitor (PPI) therapy in patients with chronic or complicated gastroesophageal reflux disease (GERD) generally outweighs any theoretical risk of adverse events. Risks associated with chronic PPI therapy include *Clostridium-difficile*-associated diarrhea (adjusted odds ratio [AOR] = 2.1 – 2.6); community-acquired pneumonia (AOR = 1.5 – 1.9); bone fracture (AOR = 1.4 – 1.6); vitamin B12 deficiency (AOR = 1.0 – 4.46); antiplatelet interactions (AOR = 1.25). Data regarding risks of bone fracture and antiplatelet interactions are controversial. A recent U. S. Food and Drug Administration (FDA) warning recommends periodic

surveillance of serum magnesium levels due to potential hypomagnesiumia. Since all data were collected retrospectively, a definitive cause-and-effect relationship cannot be proven. All patients on long-term PPI therapy should be re-evaluated periodically to determine need and to weigh potential risks versus benefits of therapy.

- Controlled trials comparing open and laparoscopic approaches have shown similar efficacy and complications with lower morbidity and shorter hospital stays in the laparoscopic repair group. Post-surgical complications are common, but typically short term and manageable in most instances. Short-term solid food dysphagia occurs in 10% of patients (2% to 3% have permanent symptoms) and gas bloating occurs in 7% to 10% of patients. Diarrhea, nausea and early satiety occur more rarely. While some complication occurs in up to 20% of patients, major complications occur in only 3% to 4% of patients.

Qualifying Statements

Qualifying Statements

These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Patient Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

University of Michigan Health System. Gastroesophageal reflux disease (GERD). Ann Arbor (MI): University of Michigan Health System; 2012 May. 12 p. [11 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2002 Mar (revised 2012 May)

Guideline Developer(s)

University of Michigan Health System - Academic Institution

Source(s) of Funding

University of Michigan Health System

Guideline Committee

Gastroesophageal Reflux Disease (GERD) Guideline Team

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Financial Disclosures/Conflicts of Interest

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Team Member	Relationship	Company
Joel J Heidelbaugh, MD	None	
Mark A McQuillan, MD	Speakers Bureau	Tadeka, Pfizer, Astra Zeneca
R Van Harrison, PhD	None	

Team Member	Relationship	Company
Timothy T Nostrant, MD	None	

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Gastroesophageal reflux disease (GERD). Ann Arbor (MI): University of Michigan Health System; 2007 Jan. 10 p. [9 references]

Guideline Availability

Electronic copies: Available from the University of Michigan Health System Web site .

Availability of Companion Documents

Continuing Medical Education (CME) credit is available from the University of Michigan Health System Web site .

Patient Resources

The following are available:

- Gastroesophageal reflux disease (GERD). University of Michigan Health System; 2012 May. 3 p. Electronic copies: Available in Portable Document Format (PDF) from the University of Michigan Health System (UMHS) Web site .
- Gastroesophageal reflux disease (GERD) - patient instructions. University of Michigan Health System; 2012 May. 2 p. Electronic copies: Available in PDF from the UMHS Web site .
- Understanding GERD. A consumer education brochure about gastroesophageal reflux disease. University of Michigan Health System; 10 p. Electronic copies: Available in PDF from the UMHS Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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