Gastroesophageal Reflux Disease

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Definition

• GERD
  – Symptoms or complications resulting from the reflux of gastric contents into the esophagus or beyond (oral cavity, larynx, or lung) occurring at least once per week.
  – Classified on endoscopic appearance
    • Non-erosive disease (NERD)
    • Erosive disease (ERD)
Heartburn

Normal EGD 65%

NERD 40%
Hypersensitive esophagus 35%
Functional heartburn 25%

Barrett's esophagus 3–5%

No dysplasia 83%
Low-grade dysplasia 7%
High-grade dysplasia/EAC 10%

LA class A/B 81%
LA class C/D 19%

Erosive esophagitis 20–30%
Symptoms of GERD

• Typical symptoms
  – Heartburn
  – Regurgitation
  – Water Brash

• Other symptoms
  • Chest pain
  • Dysphagia
  • Chronic cough
  • Asthma
  • Chronic laryngitis
  • Dyspepsia
  • Nausea
  • Bloating
  • Belching
  • Globus
The Pyramid of Diseases Associated with GERD

- Erosive esophagitis
- Non erosive reflux disease
- Chest pain
- ENT
- Asthma
- Misc
Aging, Gender and GERD

• Aging
  – Intensity of symptoms may decrease after age 50
  – Aging increases prevalence of erosive esophagitis LA grades C and D
  – Barrett’s esophagus increases in prevalence after age 50

• Gender
  – Men
    • More likely to have ERD
    • More likely to have esophageal cancer
    • More likely to have Barrett’s
  – Women
    • More likely to have NERD
Quality of Life, BMI and GERD

• Quality of Life
  – Nocturnal GERD has greater impact on QOL than daytime symptoms

• Body Mass Index
  – Higher degrees of ERD increases as BMI rose
  – Association between BMI and carcinoma of the esophagus and gastric cardia
Establishing the Diagnosis of GERD

• Presumptive diagnosis of GERD
  – Can be made in setting of typical symptoms
  – Empiric medical therapy with a PPI for 8 weeks
    • Counsel on take 30 minutes before breakfast
    • However PPI response does not reliably predict GERD
      – Several studies show that non GERD patients have a positive PPI response

• Upper endoscopy is not required in presence of typical GERD symptoms unless
  – Alarm symptoms
  – Greater than 50 years old

• Esophageal manometry is recommended for preoperative evaluation
  – but has no role in diagnosis of GERD
Establishing the Diagnosis of GERD

• Not recommended for diagnosis of GERD
  – Routine biopsies from the distal esophagus are not recommended specifically to diagnose GERD
  – Repeat endoscopy is not indicated in patients without Barrett's in the absence of new symptoms
  – Barium studies are not utilized for the diagnosis of GERD
  – H. pylori screening is not recommended
Establishing the Diagnosis of GERD

- Surrogate makers of GERD on endoscopy
  - Erosive esophagitis
    - Seen in 1/3 of patients with GERD
    - Repeat endoscopy after 8 weeks of therapy in severe erosive reflux disease to exclude underlying Barrett's
  - Barrett's
    - Seen in 5-15% of patients with GERD
  - Peptic stricture
    - Rare given PPI therapy
    - If tight, can cause false negative pH study
    - True peptic strictures generally occur at the squamocolumnar junction
      - If else where think of another etiology
The Los Angeles Classification System for Esophagitis

**Los Angeles Grade A**
One or more mucosal breaks no longer than 5 mm, not bridging the tops of mucosal folds

**Los Angeles Grade B**
One or more mucosal breaks longer than 5 mm, not bridging the tops of mucosal folds

**Los Angeles Grade C**
One or more mucosal breaks bridging the tops of mucosal folds involving <75% of the circumference

**Los Angeles Grade D**
One or more mucosal breaks bridging the tops of mucosal folds involving >75% of the circumference

Barrett's Esophagus

• Greatest risk factor for development Barrett’s
  – abnormal waist to hip ratio (>0.9)
• Most common reason for death is cardiovascular
• Regression of Barrett’s occurs more in short segment (1-3 cm) than long segment
  – Occurs both in PPI and surgical therapy
  – Surgical therapy may perform better than medical in regression
• Nissen does not lower risk of esophagical adenocarcinoma despite regression
  – Barrett’s Esophagus should not be the indication for Nissen
Establishing Diagnosis of GERD

- Ambulatory esophageal reflux monitory is indicated
  - Before considering surgical therapy in patients with NERD
  - Evaluation of patients refractory to PPI therapy
  - NERD with inability to decrease to on demand PPI
  - Situation when the diagnosis of GERD is in question
  - Not necessary when Barrett’s or erosive esophagitis present to establish diagnosis of GERD
Chest pain & GERD

• Non-cardiac chest pain suspected due to GERD should have diagnostic evaluation
  – Presence of heartburn & chest pain
    • not predicative of PPI response of the chest pain component.
  – Cardiac cause should be excluded before commencement of a GI evaluation
  – Diagnostic evaluation
    • Endoscopy
      • If no objective signs of GERD on endoscopy then pH monitoring before PPI trial.
Management of GERD

• Weight loss
  – overweight
  – normal BMI with recent weight gain
• Head of bed elevation
  – 6-8 inches
• Avoidance of meals 2-3 hours before bed
• Global elimination of food that can trigger reflux is not recommended due to lack of data
  – Chocolate
  – Caffeine
  – Alcohol
  – Acidic or spicy foods
  – Tobacco
Management of GERD

• PPI Therapy
  – 8 week course of PPI is recommended for
    • symptom relief
    • Healing of erosive esophagitis
      – LA Grade B-C esophagitis
        » nearly 100% will relapse within 6 months if off therapy
      – NERD can be managed with on demand PPI therapy/H2 blocker
        » If they can’t then consider pH study to differentiate GERD from functional disorder
  – PPI should be taken 30-60 minutes before meal
    • Exception is omeprazole-sodium bicarbonate and dexlansoprazole
  – If partial response to PPI therap
    • increasing dose to twice daily therapy or switching to a different PPI may provide relief
  – PPIs are safe in pregnant patient
  – Omeprazole sodium bicarbonate has more effective control of nocturnal gastric PH in 1st 4 hours of sleep
Management of GERD

- H2 blockers use
  - can be used as maintenance option in those without erosive disease if relief
  - Bedtime H2 blocker can be used in addition to twice daily PPI in patients with night time reflux
  - May be associated with tachyphlaxis after 1 month of therapy
Management of GERD

• Miscellaneous Therapy
  – Prokinetic therapy or baclofen should not be used in GERD without diagnostic evaluation
    • Baclofen decreases number of post-prandial acid, non-acid reflux events, nocturnal reflux activity, and belching episodes
      – Dosage 5-10 mg TID
  – No role for sucralfate in non-pregnant GERD
Risks Associated with PPI

• Switching PPIs can be considered in the setting of side effects
  – Include headache, diarrhea, and dyspepsia <2% of users
  – Vitamin B12 deficiency in the elderly that are long term users
    • No data to support concern in other population
  – Iron deficiencies
    • No data demonstrating development of iron deficiency anemia in normal subjects on PPI therapy

• Short term PPI usage increases risk of community acquired pneumonia
  – Not elevated in long term users
  – H2 blockers associated with elevated risk of hospital acquired pneumonia

• PPI therapy does not need to be altered in concomitant clopidogrel users
Risks Associated with PPI

• Known osteoporosis can remain on PPI therapy.
  – Concern for hip fractures and osteoporosis should not affect decision to use long term PPI therapy
  – Excess hip fracture risk among PPI users was only present in persons with at least one other risk factor
  – Long term PPI users should not routinely raise their intake of calcium
  – No need to screen or monitor bone mineral density based of PPI use

• PPI therapy can be a risk factor for Clostridium difficile
<table>
<thead>
<tr>
<th>Potential adverse effect</th>
<th>Types of studies</th>
<th>Threats to validity</th>
<th>Overall quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney disease</td>
<td>Observational only</td>
<td>Modest effect size; Residual confounding would bias towards harm; Absence of dose-response effect</td>
<td>Very low</td>
</tr>
<tr>
<td>Dementia</td>
<td>Observational only</td>
<td>Modest effect size; Residual confounding would bias towards harm</td>
<td>Very low</td>
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<tr>
<td>Bone fracture</td>
<td>Observational only</td>
<td>Inconsistent results; Modest effect size; Residual confounding would bias towards harm</td>
<td>Low or very low</td>
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<tr>
<td>Myocardial infarction</td>
<td>Observational • RCT</td>
<td>Results differ between RCTs and observational studies; Secondary analysis of RCT data; Modest effect size; Residual confounding would bias towards harm</td>
<td>Very low</td>
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<tr>
<td>Small intestinal bacterial overgrowth</td>
<td>Observational • Crossover</td>
<td>Sparse data; Residual confounding would bias towards harm; Protopathic bias</td>
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<td>Spontaneous bacterial peritonitis</td>
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<td>Modest effect size; Residual confounding would bias towards harm</td>
<td>Very low</td>
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<tr>
<td><em>Clostridium difficile</em> infection</td>
<td>Observational only</td>
<td>Modest effect size; Residual confounding would bias towards harm</td>
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<td>Pneumonia</td>
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<tr>
<td>Micronutrient deficiencies</td>
<td>Observational only</td>
<td>Inconsistent results; Modest effect size; Absence of dose-response effect; Residual confounding would bias towards harm</td>
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</tr>
<tr>
<td>Gastrointestinal malignancies</td>
<td>Observational • RCT</td>
<td>Results differ between RCTs and observational studies; RCTs use surrogate outcomes; Modest effect size; Residual confounding would bias towards harm; Confounding by indication and protopathic bias</td>
<td>Very low</td>
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</table>
Poor Control of GERD

• Risk factors for lack of symptoms control include:
  – Longer duration of disease
  – Presence of hiatal hernia
  – Extraesophageal symptoms
  – Lack of compliance
  – Increased BMI (>25 kg/m²)
Surgical Options for GERD

• Reasons to refer for surgery
  – Desire to discontinue medical therapy
  – Non compliance
  – Side effects associated with medical therapy
  – Presence of a large hiatal hernia
  – Esophagitis refractory to medical therapy
  – Persistent symptoms documented to be caused by refractory GERD
Surgical Options for GERD

• Surgical therapy is a treatment option for long-term therapy in GERD patients
  – Generally not recommended in patients who do not respond to PPI therapy
  – Pre-operative pH monitory is mandatory in patients without evidence of erosive esophagitis.
  – Pre-operative manometry is required
  – Surgical therapy is as effective as medical therapy for carefully selected patients
  – Obese patients with GERD should consider Roux-en-y
Surgical Options for GERD

• Outcomes in patients with extra-esophageal symptoms undergoing Nissen have been less encouraging
  – A response to PPI is critical
  – In the absence of PPI response, surgery is unlikely to be effective even with an abnormal pH study.
Surgical Options for GERD

- 10 year follow up of a randomized controlled trial comparing medical to surgical therapy
  - 92% of patients in medical arm were using medical therapy
  - 62% of patients in surgical arm were using medical therapy
- 12 year follow up of patients randomized to fundoplication compared with omeprazole
  - 53% of surgery cohort were in remission
    - Although more had gas-bloat symptoms in 15-20% patients
  - 45% of medically treated patients were in remission
- A community study demonstrated that 30% of Nissen patients will resume medical therapy in 5 years.
Surgical Options for GERD

- LINX Reflux system
  - Not for patients with large hiatal hernia or abnormal peristalsis
  - Made of titanium beads with magnetic link
  - Approved by the FDA
  - Performance of Linx resulted in consistent symptom relief and pH control with markedly fewer side effects than traditional laparoscopic fundoplication
Endoscopic Therapy for GERD

• The use of endoscopic therapy or transoral incisionless fundoplication (TIF) cannot be recommended as an alternative to medical or traditional surgical therapy.
Extra-esophageal GERD

The Pyramid of Diseases Associated with GERD

- Erosive esophagitis
- Nonerosive reflux disease
- Chest pain
- ENT
- Asthma
- Misc.

True prevalence of GERD

0%

100%
Extra-esophageal GERD

• Careful evaluation for non-GERD causes should be undertaken in all of these patients
• GERD can be considered as a potential co-factor in
  – Asthma
  – Chronic cough
  – Laryngitis
    • A diagnosis of reflux laryngitis should not be made based solely upon laryngoscopic findings
      – 80% of healthy controls had one or more signs of laryngeal irritation
      – High intra-observer variability describing edema, erythema and severity
        » Non-GERD etiologies allergy, smoking, or voice abuse
• A PPI trial is recommended to treat extra-esophageal symptoms in those with typical symptoms of GERD twice daily for 3 months
  – Reflux monitoring should be considered before a PPI trial in patient with extra-esophageal symptoms who have atypical symptoms of GERD
Extra-esophageal GERD

- EGD is not recommended as a means to establish a diagnosis of GERD related asthma, chronic cough, or laryngitis
- Extra-esophageal symptoms that were refractory to PPI therapy
  - Presence of heartburn or abnormal acid exposure on pH monitoring predicted response to escalation of therapy
    - SI, SAP, or impedance variable did not predict PPI response
- Currently available diagnostic tools to establish GERD as causes of extra-esophageal symptom have serious limitations
GERD Refractory to Treatment

• 1\textsuperscript{st} step in management of refractory GERD is optimization of PPI therapy
  – Confirming compliance
    • Associated with a lack of response
    • Adherence to PPI therapy was found in on 60%
  – Ensuring appropriate dosing
GERD Refractory to Treatment

• Upper endoscopy
  – should be performed in refractory patients with typical or dyspeptic symptoms to exclude non-GERD etiologies such as excluding EoE.

• pH monitoring
  – If diagnosis of GERD is in question (i.e. not responding to PPI therapy and no objective signs on endoscopy) then perform pH monitoring off PPI therapy
    – Make sure biopsies were taken to rule out eosinophillic esophagitis
    – Functional heartburn
      » Typical GERD symptoms but no correlation with reflux on pH study
    – Hypersensitive esophagus
      » Typical GERD symptoms with correlation of reflux but less than 5% of the total time
  – If diagnosis of GERD established and still with refractory symptoms consider pH-impedance monitoring on PPI therapy
    – Only 10% will be ongoing acid reflux on PPI twice daily

• Manometry
  – Also consider manometry for achalasia or esophageal spasm if above are all negative
GERD Refractory to Treatment

- Acid exposure
- Erosive esophagitis
- NERD
- Reflux hypersensitivity
- Functional heartburn

Esophageal hypersensitivity
GERD Refractory to Treatment

• Functional heartburn
  – Defined as burning retrosternal discomfort or pain without evidence of GERD for at least 3 of the last 6 months
  – stepwise evaluation supports the absence of GERD, EoE, and a major esophageal motor disorder.
  – No correlation of symptoms with objective pH testing
  – More commonly affects women after age 40
  – High rates of anxiety with fewer social support structures
  – 2/3 of these patients will have other GI symptoms such as belching, bloating, and postprandial fullness
    • On average report >6 upper GI symptoms

• Esophageal hypersensitivity
  – Normal esophageal acid exposures but positive correlation between reflux events and symptoms

• Treatment
  – TCA and SSRIs
  – Melatonin 6 mg for 3 months
  – Psychological therapies, ie cognitive behavioral therapy.
GERD Refractory to Treatment

- Other causes of heartburn not responding to acid suppression should be considered:

Table 1. Differential diagnosis for heartburn not responding to acid suppression

<table>
<thead>
<tr>
<th>Condition</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Ongoing acid reflux due to insufficient acid suppression</td>
<td>Peptic ulcer disease</td>
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<tr>
<td>Esophageal hypersensitivity</td>
<td>Esophageal motility disorders</td>
</tr>
<tr>
<td>FH</td>
<td>Esophagitis of any etiology</td>
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<tr>
<td>Non-acidic or weakly acidic reflux</td>
<td>Esophageal cancer</td>
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<tr>
<td>Eosinophilic esophagitis</td>
<td>Cardiac etiologies</td>
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<tr>
<td>Gastroparesis</td>
<td>Biliary pathology</td>
</tr>
<tr>
<td></td>
<td>Pulmonary pathology</td>
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</tbody>
</table>

FH, functional heartburn.
References


• Patti MG. 2016. An Evidence-Based Approach to the Treatment of Gastroesophageal Reflux Disease. JAMA Surgery, 151 (1), 73-78.


Thank you for your attention