Gastroesophageal Reflux Disorder & Barrett’s Esophagus

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August 14, 2014
“Your health insurance doesn’t cover heartburn. You need fire insurance for that.”
Learning Objectives

• Understand behavioral modifications as they relate to GERD symptoms

• Understand the definition and differential diagnosis of ‘refractory GERD symptoms’

• Understand management of Barrett’s esophagus

• What is the strongest known risk factor for esophageal adenocarcinoma?
GERD

• GER= normal physiologic process

• Disease= macroscopic damage or symptoms reducing QOL

• Classification: erosive esophagitis -vs- nonerosive reflux disease

• Montreal Classification
  • Symptoms ≥ 2 days/week, or moderate symptoms 1 x/week

• Prevalence 10-20% Western World, 5% Asia

• U.S.- 15% report heartburn weekly and 7% daily
Clinical Manifestations

- Heartburn
- Regurgitation
- Dysphagia
- Chest pain, globus sensation, odynophagia, nausea, water brash
- Extraesophageal manifestations
  - Bronchospasm, laryngitis, chronic cough
Diagnosis

- Clinical symptoms
- Response to anti-secretory therapy
  - 40-90% with symptoms consistent with GERD will have a response
  - Poor correlation with ambulatory pH monitoring
- Endoscopy
Differential Diagnosis

- Infectious esophagitis
- Pill esophagitis
- Eosinophilic esophagitis
- Peptic ulcer disease
- Non ulcer dyspepsia
- Biliary tract disease
- CAD
- Esophageal motor disorders
When to Conduct Endoscopy

- Heartburn + ‘Alarm Features’
  - Dysphagia, odynophagia, GI bleeding, anemia, weight loss, recurrent vomiting

- Severe erosive esophagitis on initial EGD (repeat two months later)

- Men older than 50 years with chronic GERD symptoms (> 5 years)

- Symptoms refractory to 8 weeks trial of PPI therapy
Treatment- Behavioral Modifications & GERD

- Weight loss
- Elevate head of bed
- Avoid late meals
- Dietary Modifications: fatty foods, caffeine, chocolate, spicy foods, peppermint
- Avoid tight fitting garments, chewing tobacco, smoking, alcohol
Treatment

- Initial therapy: step up -vs- step down
- Mild Sxs/no esophagitis: behavioral modification & H2 Antagonists PRN
Medications- Antacids, Histamine Receptor Blockers

- Antacids: provide relief within five minutes, but short duration of action
  - Alka Seltzer, Maalox, Mylanta, Pepto Bismol, Rolaids, Tums

- Surface agents: conflicting data

- Histamine receptor blockers
  - Zantac, Pepcid, Tagamet, Axicd
  - Decrease secretion of acid by inhibiting histamine receptor on gastric parietal cell
  - Tachyphylaxis in 2-6 weeks
Medications- Proton Pump Inhibitors

- Lansoprazole
- Omeprazole
- Zegerid
- Esomeprazole
- Pantoprazole
- Dexilant
- Nexium
- Aciphex
Severe/Frequent Symptoms or Erosive Esophagitis

- PPI once daily x eight weeks, lifestyle and dietary modification
- Goal: decrease to low dose PPI or H2 blocker except in those found to have erosive esophagitis or Barrett’s metaplasia
Proton Pump Inhibitors

• Indication: failed BID H2 receptor blocker, frequent symptoms (2 or more times per week), documented erosive esophagitis

• PPI at standard dose relieves symptoms and heal esophagitis in 86% of patients after eight weeks of treatment

• Meta-analysis: 34 trials, 1314 subjects. PPI significantly better than H2 receptor blockers at healing esophagitis, relieving heartburn (RR 0.66, 95% CI 0.60-0.73)
Definition of ‘Refractory Symptoms’

- Definition: failure to respond to once daily PPI
  - Refer to GI?
- Trial of BID PPI (expert opinion recommendation)
Refractory GERD Symptoms - Causes

- Improper dosing
- Compliance
- Functional heartburn
- Esophageal hypersensitivity
- Alkaline reflux (non-acid)
- Bile acid reflux
- Nocturnal breakthrough
- Reduced bioavailability of medication
- Psychological co-morbidity
Differential Diagnosis for Refractory GERD Symptoms

- Achalasia
- Esophageal Cancer
- Esophageal Stricture
- Gastroparesis
- Untreated Esophagitis
- Eosinophilic Esophagitis?
Evaluation of Refractory GERD Symptoms

- Esophagogastroduodenoscopy (EGD)
- Esophageal pH testing
- Impedence testing
- Esophageal manometry testing
- Gastric emptying study- order the ‘Tougas Protocol’
Treatment of Refractory GERD

- Optimize current therapy
- Lifestyle modifications
- Bedtime H2 receptor blocker
- Treat for esophageal hypersensitivity
- Treat delayed gastric emptying
- Surgery
- No approved endoscopic treatment
Maintenance Therapy of GERD

- 2/3 those with non-erosive GERD and nearly all with erosive will relapse when therapy stopped
- Recommend using the dose and medication that originally achieved symptoms control
- Pulse dosing for eight weeks?
  - Better healing and quality of life with continuous
- Tapering - consider if on PPI > 8 weeks
  - Rebound hyperacidity
  - Half the dose weekly until at the lowest possible dose
Safety of PPIs

- *Clostridium* difficile infection
- Aspiration pneumonia
- Malabsorption
  - Magnesium
  - Vitamin B12
  - Calcium
  - Iron
- Interaction with clopidogrel
  - Use pantoprazole (*Protonix*) if possible?
  - COGENT trial showed no difference in events
Side Effects of PPIs

- Diarrhea
- Nausea
- Vomiting
- Abdominal pain
- Indigestion
- Headache
Barrett’s Esophagus

- Metaplastic columnar epithelium replaces stratified squamous epithelium
  - Consequence of chronic acid exposure
  - Predisposes to development of esophageal adenocarcinoma

- Prevalence: 0.4% to 20% depending on the study
  - U.S. study: 6.8%
    - 5.6% without heartburn, 8.3% with heartburn
    - 10-15% of those getting screening EGD for heartburn
      - Screening for Barrett’s esophagus in colonoscopy patients with and without heartburn, Rex DK, Cummings OW, Shaw M, Cumings MD, Wong RK, Vasudeva RS, Dunne D, Rahmani EY, Helper DJ, Gastroenterology. 2003;125(6):1670
Barrett’s Esophagus

- Squamous lined
- Squamocolumnar junction (Z-line)
- Barrett’s mucosa
- Lower esophageal sphincter
- Hiatus hernia
- Diaphragm
Risk Factors for Barrett’s Esophagus

- GERD
- Male gender (2:1 male:female)
- Caucasian ethnicity
- Obesity
- Aspirin and/or NSAIDS use might be protective but studies show only weak correlation
- Genetics?
Short Segment -VS- Long Segment Barrett’s Esophagus

- Study: 889 pts underwent protocol biopsies
  - 13.2% with Barrett’s
  - Long segment 1.6%
  - Short segment 6.4%
  - Intestinal metaplasia at GEJ 5.6%
Barrett’s Esophagus and Esophageal Adenocarcinoma

• Barrett’s esophagus (BE) is the primary risk factor for the development of esophageal adenocarcinoma (EAC)

• Incidence of EAC has increased by 500-600% since 1970; it remains one of the fastest growing cancers in the US

  • 17% 5-year survival
    Pohl, J Natl Cancer Inst, 2005
    de Jonge, Gut, 2010

Surveillance, Epidemiology and End Results (SEER)
Esophageal Adenocarcinoma Is One of the Fastest Growing Cancers of the Past Four Decades

Pohl, J Natl Cancer Inst, 2005
Well-Studied & Commonly Accepted Clinical Factors May Further Elevate This Progression Risk

- Caucasian
- Male
- Smoker
- Obese
- Young Age
- Long Segment
- Large Hiatal Hernia
- Family History of BE & EAC

Chak, Gut, 2002  
Gopal, Dig Dis Sci, 2003  
Weston, Am J Gastroenterol, 2004  
Hage, Scand J Gastroenterol, 2004  
Iftikhar, Gut, 1992  
Bani-Hani, World J Gastroenterol, 2005  
de Jonge, Gut, 2010  
Prasad, Am J Gastroenterol, 2010  
Anaparthy, Clin Gastroenterol Hepatol, 2013

Anandasabapathy, Cancer, 2007  
Pohl, Am J Gastroenterol, 2013  
Sikkema, Am J Gastroenterol, 2011  
Sappati Biyyani, Dis Esophagus, 2007  
Munitiz, J Clin Gastroenterol, 2008  
Abnet, Eur J Cancer, 2008  
de Jonge, Am J Gastroenterol, 2006  
Jung, Am J Gastroenterol, 2011  
Coleman, Gastroenterology, 2012
Screening for Barrett’s

- Chronic GERD
- Age > 50 years
- Male
- Caucasian
- Increased BMI
Surveillance of Barrett’s Esophagus

- Same for short or long segment Barrett’s

- No dysplasia - repeat EGD in one year, and if stable at 3-5 year intervals

- Low grade dysplasia - high dose acid suppression and repeat in three months. If stable, repeat annually

- High grade dysplasia - every three months, verses surgery, verses ablation (RFA)
Genetic Alterations Can Occur in Early BE (IM & LGD) Preceding Histologic Changes of Disease Progression

Ong, World J Gastroenterol, 2010
Radiofrequency Ablation for Barrett’s Esophagus

- Endoscopic treatment modality
- Balloon-based bipolar electrode
- Replacing APC and PDT

Indications:
- Visible lesions containing HGD or IMC (after endoscopic mucosal resection)
- Flat Barrett’s containing HGD
- LGD
Surveillance Is Hampered by Sampling Error & Pathologic Discordance

A Multicenter Study Found 50% of Those Who Developed HGD or Cancer While Undergoing Surveillance Did Not Have Prior Findings of Dysplasia

Falk, Tech Gastrointest Endosc, 2000
Sharma, Clin Gastroenterol Hepatol, 2006
Non-Dysplastic BE Progression to Cancer in Several Large 2010-2012 Studies Averaged .29% per Year

de Jonge, Gut, 2010
Wani, Clin Gastroenterol Hepatol, 2011
Bhat, J Natl Cancer Inst, 2011
Desai, Gut, 2012
CLE/IM Progression to HGD/EAC
(Bhat, J Natl Cancer Inst, 2011)

- Population-based study (Northern Ireland Barrett’s Register or NIBR) from 1993 to 2005
- 8522 IM pts were followed for a mean of 7 yrs
- “Results from the NIBR demonstrate a constant risk of progression to cancer over time.”
IM Progression to HGD/EAC

(Wani, Clin Gastroenterol Hepatol, 2011)

- Multi-center outcomes project
- 1204 pts were followed for a mean of 5.5 yrs
- 2.9% of IM pts developed cancer in 10 yrs
- 7.3% of IM pts developed HGD or cancer in 10 yrs

For Many Physicians, a 10 Year Cancer Risk of ~ 3% for Non-Risk Stratified IM Is of Concern
Long Segment NDBE Progresses to HGD/EAC at a Significantly Elevated Rate

IM Progression to HGD/EAC by Length

(Anaparthy, Clin Gastroenterol Hepatol, 2013)

• Multi-center outcomes project
• 1175 NDBE pts were followed for a mean of 5.5 yrs
• 28% increase in risk of progression to HGD/EAC per 1 cm increase in length (p<0.001)
• Annual progression rate to HGD/EAC by length (p<0.0018):
  • 0.31%/year for length ≤3 cm
  • 0.97%/year for length 4-6 cm
  • 1.26%/year for length 7-9 cm
  • 1.64%/year for length 10-12 cm
  • 2.41%/year for length ≥13 cm
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Experts Agree on High Annual Cancer Progression Risk for HGD Patients

BADCAT Consensus Statement

*Bennett, Gastroenterology, 2012*

- An int’l, multidisciplinary, evidence-based review of BE management strategies using 80% agreement as a threshold for all consensus statements

- “Risk of progression from HGD to cancer is approximately 10% per year.”
Thank you!