Clinical Considerations in GERD & Barretts Esophagus

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How is GERD Classified?

GERD is a condition which develops when the reflux of stomach content causes troublesome symptoms and/or complications.

**Esophageal syndromes**
- Symptomatic syndromes
  - Typical reflux syndrome
  - Reflux chest pain syndrome
- Syndromes with esophageal injury
  - Reflux esophagitis
  - Reflux stricture
  - Barrett's esophagus
  - Adenocarcinoma

**Extra-esophageal syndromes**
- Established association
  - Reflux cough
  - Reflux laryngitis
  - Reflux asthma
  - Reflux dental erosions
- Proposed association
  - Sinusitis
  - Pulmonary fibrosis
  - Pharyngitis
  - Recurrent otitis media
What Can We Expect Epidemiologically?

GERD

- Erosive esophagitis 20 – 30%
- Non-erosive reflux disease 60 – 70%
- Barrett’s esophagus 6 – 12%

pH testing

- NERD-pH positive 50%
- Functional heartburn 50%

Symptoms associated with pH changes?

- Yes
  - Hypersensitive Esophagus 40%
- No
  - Functional heartburn - reflux negative 60%

Fass R Dickman R. GI Motility online (May 2006) | doi:10.1038/gimo42
Healing of Esophagitis: $H_2$ RA vs PPI
Highly Effective

But They Gotta Take Them Right!
Compliance With Medications

Coping With GERD Internet Survey (N = 587)

Regularly, as directed by their physician 55%
As needed 22%
Do not take medication 17%
Fairly regularly but sometimes forget 6%

Esomeprazole should be taken at least 1 hour before meals.
GERD Is a Chronic Condition That Is Likely to Relapse

Pretreatment endoscopic grades:
- No mucosal breaks (normal)
- LA Grade A
- LA Grade B
- LA Grade C

\[ P = .04 \] for normal vs. grade A.
\[ P = .002 \] for normal vs. grade A + B + C.
\[ P = .003 \] for normal + grade A + B vs. grade C.

Who Might be Good Candidates for Anti-Reflux Surgery?

- Inadequate acid control on PPI
- Volume refluxers
- Intolerant of PPIs
- Poor compliance with PPIs
- Very large hiatal hernias
- Para-esophageal hernias
- Aspirators
What are the Longterm Outcomes with Anti-Reflux Surgery?

Spechler SJ et al, JAMA, 2001
So an Anti-Reflux Surgery is Certainly not Forever
Survival Rate Was Diminished in the Surgical Group…

![Graphs showing survival rates compared between medical and surgical treatment groups.](image-url)
Like Any Surgery, There are Risks and SE’s…

- Bleeding
- Infection
- Perforation
- Gas-Bloat
- Persistent Dysphagia
- Diarrhea
• Weight loss should be advised for overweight or obese patients with esophageal GERD syndromes
What is the effect of weight gain on GERD symptoms?

• Twice daily PPI therapy for esophageal syndrome patients with an inadequate symptom response to once daily PPI therapy
• Endoscopy with biopsy for esophageal GERD syndrome patients with troublesome dysphagia. Biopsies should target any areas of suspected metaplasia, dysplasia, or in the absence of visual abnormalities, normal mucosa (at least 5 samples to evaluate for eosinophilic esophagitis)
Other Tips for GERD Management

• Metoclopramide (Reglan) should not be used in GERD management
  – Efficacy is too poor
  – Side Effect profile too severe

• Night-time H2 blockers should not be used every night due to tachyphylaxis

• Can try baclofen to augment LES pressures
  – Usually given 10 mg TID
  – Side effects (CNS) usually limit use

• Most patients still symptomatic on BID PPI do not have acid reflux
  – Consider centrally-acting agent for functional CP
Esophageal Symptom Generation

Chemo-stimulation
*Acid mediated*

Reflux

Mechano-stimulation
*Volume mediated*

Heartburn

Regurgitation
Chest pain

Cough

Kahrilas PJ 2007
But What About Barrett’s?
Barrett’s Esophagus - Through the ‘Scope
Barrett’s is Thought to Be the Precursor of Adenocarcinoma

Non-Dysplastic BE

Low-Grade Dysplasia

Adenocarcinoma

High-Grade Dysplasia
Adenocarcinoma – A Disease with a Rapidly Increasing Incidence

Not Much Progress Being Made…

Incidence

Mortality

What About the Epidemiology of BE?


So BE is Going Up, and Esophageal Adenocarcinoma is Going Up.

How Come?
Some Postulate that the Increasing Cancer Incidence Could Be Secondary to the Epidemic of Obesity in the U.S.
Obesity is Strongly Associated with the Risk of AdenoCa of the Esophagus

189 Cases, 820 Controls
Adjusted for age, sex, tobacco smoking, alcohol use, socioeconomic status, reflux symptoms, intake of fruit and vegetables, energy intake, and physical activity.

Too few Needles, Too Big a Haystack

Rate of Progression of Non-Dysplastic BE may be Lower than Appreciated!

- Meta-analyses suggest rate of progression to cancer of app 0.5% per pt-yr

What to Do?

Depends on who you ask…
“Screening EGD for Barrett’s esophagus should be considered in selected patients with chronic, longstanding GERD. After a negative screening examination, further screening endoscopy is not indicated.”

American College of Gastroenterology

“Patients with chronic GERD symptoms are most likely to have Barrett’s esophagus and should undergo upper endoscopy.”

Practice Parameters Committee, 2002

PRACTICE GUIDELINES

Updated Guidelines 2008 for the Diagnosis, Surveillance and Therapy of Barrett’s Esophagus

Kenneth K. Wang, M.D. and Richard E. Sampliner, M.D.  
The Practice Parameters Committee of the American College of Gastroenterology

“In summary, screening for Barrett’s esophagus in the general population cannot be recommended at this time. (Grade B recommendation) The use of screening in selective populations at higher risk remains to be established (Grade D recommendation) and therefore should be individualized.”
American Gastroenterological Association Medical Position Statement on the Management of Barrett’s Esophagus

In patients with multiple risk factors associated with esophageal adenocarcinoma (age 50 years or older, male sex, white race, chronic GERD, hiatal hernia, elevated body mass index, and intra-abdominal distribution of body fat), we suggest screening for Barrett’s esophagus (weak recommendation, moderate-quality evidence).

We recommend against screening the general population with GERD for Barrett’s esophagus (strong recommendation, low-quality evidence).
Women don’t get much EAC!

Figure 1. Cancer incidence as a function of age.
How Can We Better Stratify Risk?
Stratifying Risk: Taking screening out of the Endo Unit
What is the Yield of TNE in a Primary Care Population?

<table>
<thead>
<tr>
<th>Characteristics (n = 426)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagitis</td>
<td>143 (34)</td>
</tr>
<tr>
<td>LA Grade A</td>
<td>73 (51)</td>
</tr>
<tr>
<td>LA Grade B</td>
<td>46 (32)</td>
</tr>
<tr>
<td>LA Grade C</td>
<td>18 (13)</td>
</tr>
<tr>
<td>LA Grade D</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Hiatal Hernia</td>
<td>180 (43)</td>
</tr>
<tr>
<td>Barrett’s Esophagus</td>
<td>18 (4)</td>
</tr>
<tr>
<td>Esophageal Mass/Nodularity</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Gastritis</td>
<td>15 (4)</td>
</tr>
</tbody>
</table>

Peery AF, Shaheen NJ. Jobe B. Gastrointest Endosc 2012.
What About Biomarkers?
Proposed BE Biomarkers

- Cyclin D1
- APC
- Bcl-2
- VEG-F
- ECAD
- MUC2
- Rab 11
- CEA
- Promoter Methylation

- K-ras
- Ki-67
- P16
- p53
- NF-KB
- COX-2
- Cdx-2
- Flow cytometry
- Etc, etc, etc
What is Current State?

- Economically Viable? Not clear
- Sensitive? Varies – some promising
- Specific? Data mixed - often unknown
- Min. Invasive Sampling? Most off of biopsy samples
- Predates dev of disease? Very limited data. Most X-sectional
- Correlates w/ disease prog? Often, yes
- Biologically plausible? Yes
Other Tips for Managing BE in Primary Care

• All BE patients should be on daily PPI unless they can’t tolerate or have had antireflux surgery
  – More than daily dosing not needed unless symptomatic on daily dosing

• Don’t give daily aspirin unless they need it for another reason

• In general, endoscopy for non-dysplastic BE is only needed every 3 yrs

• Endoscopic therapy for BE is generally only performed in patients with dysplasia

• There is some heritability in BE
  – Probably worthwhile to screen 1st degree relatives with reflux symptoms
Conclusions

• Most subjects with GERD can be well-controlled with medical therapy
  – Some residual symptoms are common
• PPI dosing at more than twice daily rarely necessary
• Anti-reflux surgery has a role in a defined subset of GERD patients
• The epidemiology of both BE and EAC is unfavorable and worrisome
• Current screening and surveillance practices in BE are limited by poor risk stratification
• Demographic and health history data are inadequate to markedly improve these practices
How Might This Impact My Practice?

• For Now…
  – Obey Sutton’s Law
    • If you are going to do screening, pay attention to GERD complaints in old white males with truncal obesity

• In the Future…
  – Stay tuned for a “risk stratification panel,” which may include anthropometric measurements, demographics, genetic markers, and genotyping of important determinants of phenotypic expression
    • The biggest benefit of such a panel might be telling us who we don’t need to worry about
  – Surveillance will be supplanted by more active intervention
“The Best Day in the Life of any Barrett’s Patient is the Day their Endoscopist Dies.”

-Steve Sontag, MD