Barrett’s Esophagus: An Update

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Disclosures

- Grants/Research Support: Sandhill Scientific
Case

A 62 year-old male presents with recent diagnosis of Barrett’s esophagus.
He has had mild heartburn, which is controlled on antacids.
Denies any dysphagia or regurgitation.
Last endoscopy was 6-months ago showing a 2-cm columnar mucosa which on biopsy showed intestinal metaplasia without dysplasia.
What is the next step in care of this patient?

1. Continue current tx and endoscopy with bx’s in 3-years
2. Change to BID PPI and repeat endoscopy with bx’s in one year
3. Endoscopy with repeat bx’s now
4. Change to once daily PPI tx and repeat biopsies in 3-years
5. pH monitoring on PPI therapy to ensure normalized esophageal acid exposure
Regarding the statements below, which is the correct option?

- PPI therapy will reduce the length of columnar mucosa in patients with Barrett’s esophagus
- Prospective randomized trials have shown reduced incidence of dysplasia and cancer with PPI use in this group of patients
- Randomized trials and society guidelines favor the use of ASA and NSAIDS as chemoprevention in patients with Barrett’s esophagus
- There is adequate evidence to support the use of PPI therapy for symptom control and reducing risk of dysplasia in Barrett’s esophagus
- Antacid and H2RA’s are reasonable alternative in patients with Barrett’s esophagus as long as patients’ symptoms are controlled
GERD Severity

Symptoms

Esophagitis

Barrett’s
GERD Severity

Symptoms

Esophagitis

Barrett’s
Barrett’s Esophagus

Columnar distal esophagus

Intestinal Metaplasia
Rising Incidence of Esophageal Adenocarcinoma

Rising Incidence of Esophageal Adenocarcinoma

Barrett’s Esophagus: 
*The Prague Classification*

Barrett’s Esophagus: The Prague Classification

Distance (cm) from GEJ

Maximal extent of metaplasia: M = 5.0 cm

Circumferential extent of metaplasia: C = 2.0 cm

True position of GEJ: Origin = 0.0 cm

Approximately Half of Patients With Reflux Symptoms Have Esophagitis

Endoscopic findings in 97 patients presenting with reflux symptoms

- Esophagitis (45.3%)
- Barrett’s Esophagus (12.3%)
- No Esophagitis (42.3%)

Abdominal Obesity - Risk Factors

Common Symptoms of Barrett’s

• Similar to GERD
  – Heartburn
  – Regurgitation

• Less common
  – Dysphagia
  – Odynophagia
Less Symptoms in Barrett’s Age Related
Importance of Barrett’s
Symptomatic GERD as a Risk Factor For Esophageal Adenocarcinoma

Absence of heartburn, regurgitation or both ≥ once weekly

Non-dysplastic Barrett’s: Cancer Risk

- Hameeteman 1989 (n=50)
- Streitz 1998 (n=149)
- Bani Hani 2000 (n=307)
- Sharma 2006 (n=618)
- Wani 2010 (n=1204)
- De Jonge 2008 (n=14,231)
Non-dysplastic Barrett’s: Cancer Risk

1989 (n=50) 1998 (n=149) 2000 (n=307) 2006 (n=618) 2008 (n=14,231) 2010 (n=1204)
What is the Real Risk?

- Nationwide, population-based, cohort study of all Barrett’s patients in Denmark

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Non dysplastic BE: 0.1%
Low grade dysplasia: 0.5%

Endoscopic Surveillance of Barrett’s and Outcome

<table>
<thead>
<tr>
<th>Author</th>
<th>Surveillance</th>
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*Exclude 4 high grade dysplasia \( p=0.09 \)

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Do Patients With Barrett’s Die From Esophageal Cancer?

- 166 patients with BE
- Mean follow up: 9.3 years
- Only 2.5% died from esophageal cancer
- Raises doubts if surveillance would help patients with BE

AGA Medical Position Statement

• Endoscopic surveillance be performed in patients with BE
AGA Medical Position Statement

- Endoscopic surveillance be performed in patients with BE
- Weak recommendation
AGA Medical Position Statement

- Endoscopic surveillance be performed in patients with BE
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- **Surveillance intervals:**
  - No dysplasia: 3-5 years
  - LGD: 6-12 months
  - HGD: 3 months (if no therapy)
AGA Medical Position Statement

- Endoscopic surveillance be performed in patients with BE
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  - Surveillance intervals:
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Decreasing Cancer Risk With Increasing Number of Consecutive EGDs Showing No Dysplasia

- 1401 BE patients, no dysplasia
- Average age: 59 years; 87% men

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- 1401 BE patients, no dysplasia
- Average age: 59 years; 87% men

Treatment Options for Barrett’s

- Medication
- Chemoprevention
- Surgery
- Ablation
Why Treat Barrett’s?

• Relief Symptoms
• Regress Barrett’s Epithelium
• Prevent Cancer
GERD Severity

Symptoms

Esophagitis

Barrett’s
Acid Reflux In GERD Spectrum
Barrett’s Length Correlates With Acid Reflux

- Barrett’s Length (cm)
- % Total Time pH < 4

$r = 0.62$
$p = 0.0005$
Meta-Analysis

ENDOSCOPIC HEALING WITH PPI'S

- **PPI**
- **H₂RA**
- **Placebo**

7635 patients

Grade II-IV

85% 52% 28%

% Total healed

Weeks

PPIs Are More Effective Than H2RAs


% Time pH < 4

<table>
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<th>Upright</th>
<th>Supine</th>
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<tr>
<td>PPIs</td>
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<tr>
<td>H2RAs</td>
<td>n=31</td>
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40 mg BID

150 mg BID
Effects of Treatment with Omeprazole 20mg BID

**Acid Reflux**
- pH < 4 (% Total time)
- NoMeds vs Omeprazole: p < .001

**Billirubin Absorbance**
- Billirubin Absorbance (% Total time)
- NoMeds vs Omeprazole: p < .003
Endoscopic Regression with PPIs

<table>
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<th>% Patients</th>
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Aggressive Acid Control: % time pH < 1.6%
Rate of Change in Barrett’s Length

Rate of Change in Barrett’s Length

Rate of Change in Barrett’s Length

Patient Number

Centimeter / year

0.94

N = 67

Continued Acid Reflux
Asymptomatic Patients

% Patients

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<tr>
<th></th>
<th>O 20-60</th>
<th>L 60</th>
<th>L 15-30</th>
<th>O 20-60</th>
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GALA
## Hypothetical Model

### Effect of Acid on Barrett’s

<table>
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<tr>
<th></th>
<th>No Acid</th>
<th>Prolonged Acid</th>
<th>Acid Pulses</th>
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<td><strong>Proliferation</strong></td>
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Reduced Incidence of Dysplasia
PPIs

Reduced Incidence of Dysplasia
PPIs - Australian Study

Chemoprevention Celecoxib (200mg bid) Randomized Trial

Changes in grade / extent of dysplasia after 48 wks

<table>
<thead>
<tr>
<th></th>
<th>Low-grade</th>
<th></th>
<th>High-grade</th>
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<tr>
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<td>Celecoxib</td>
<td>Placebo</td>
<td>$P$</td>
<td>Celecoxib</td>
<td>Placebo</td>
<td>$P$</td>
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<tr>
<td>Median (IQR)</td>
<td>-0.09 (-0.32-0.14)</td>
<td>-0.07 (-0.27-0.13)</td>
<td>.64</td>
<td>0.12 (-0.31-0.55)</td>
<td>0.02 (-0.24-0.28)</td>
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<td>Change Dysplasia</td>
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<td>-0.08 (-0.39-0.23)</td>
<td>-0.06 (-0.35-0.23)</td>
<td>.84</td>
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2008 ACG Barrett’s Esophagus Guidelines: Chemoprevention

• Sufficient evidence that any treatment prevents cancer or cancer-related deaths is lacking

• Chemoprevention represents a promising future strategy
2011 AGA Barrett’s Esophagus Guidelines: Chemoprevention

• Suggest against the use of ASA solely to prevent esophageal cancer in the absence of other indications

• Definitive studies are lacking
EAC Treatment Trends

Year of diagnosis

Percentage of patients

Esophagectomy
Endoscopic therapy

HALO$^{90}$ Device
PDT Before/After
Radiofrequency Ablation

AIM-Dysplasia Trial: Complete response dysplasia, HGD cohort

Radiofrequency Ablation

AIM-Dysplasia Trial: Complete response IM (N=101)

Barrett’s Esophagus

• Education about cancer risk
  – 0.2%/year
  – Most patients die of other causes
  – Survival no different than general population

• Control reflux symptoms
### Current Guidelines

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<tr>
<th></th>
<th>Year</th>
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<th>Surveillance</th>
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<tr>
<td><strong>American College of Gastroenterology</strong></td>
<td>2008</td>
<td>• No recommendation for or against</td>
<td>• No dysplasia: 3 years</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• LGD: 1 year</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• HGD without endoscopic therapy: 3 months</td>
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<tr>
<td><strong>American Gastroenterological Association</strong></td>
<td>2011</td>
<td>• Recommended for patients with multiple risk factors for EAC</td>
<td>• No dysplasia: 3-5 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Recommended against for general population with GERD</td>
<td>• LGD: 6-12 months</td>
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<td>• HGD without endoscopic therapy: 3 months</td>
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<tr>
<td><strong>British Society of Gastroenterology</strong></td>
<td>2013</td>
<td>• Consider in patients with chronic GERD symptoms and multiple risk factors for EAC</td>
<td>• No dysplasia and BE length &lt;3 cm: 3-5 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not justified for general population with GERD</td>
<td>• No dysplasia and BE length ≥3 cm: 2-3 years</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• LGD: 6 months</td>
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