Screening and Surveillance of Barrett’s Esophagus

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Outline

• What is the epidemiology of Barrett’s esophagus?
• What are current guidelines for screening and surveillance?
• What advances have been made in screening and surveillance?
• Recommendations for current practice
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...

What About the Epidemiology of BE?


Barrett’s Classification and Management

- **Non-dysplastic IM**
  - Surveillance every 3 years
  - Detect progression to dysplasia or cancer

- **LGD (low-grade dysplasia)**
  - Surveillance every 6-12 months
  - Detect progression to HGD or cancer

- **HGD (high-grade dysplasia)**
  - Surveillance every 3 months
  - Esophagectomy
  - EMR and ablation: options at select institutions

Endoscopists try to lower the risk of cancer death in those with chronic reflux by performing screening and surveillance endoscopy.

We scope those with chronic heartburn (screening), then periodically re-scope those with Barrett’s (surveillance).
Can EAC Death be Averted by Screening Endoscopy?

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.”

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

Practice Parameters Committee, 2002

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).
Lots of Problems Inherent in Current Practices

- Variability in path readings
  - Get histology re-read in cases of dysplasia, esp LGD!
- Inadequate numbers of biopsies taken
- Noncompliance with scheduled exams
- Sampling error
- Poor prognostic ability of dysplasia as a marker
- Expense
Too few Needles, Too Big a Haystack

Population (Millions)

7,600
10,000

US Pop >50
>50, weekly GERD
US CA's, 2002
Endo Complications

The Risk of Progression in BE is Low

- Meta-analyses suggest rate of progression to cancer of app 0.5% per pt-yr\(^1\)

GI’s Endorse Endoscopic Screening and Surveillance!

Survey of 1,000 GI’s

- Academic and PP
- Asked about endoscopic surveillance for BE
- 45% response rate
- Most commonly used interval for surveillance is 2 yrs

But We Are Screening Indiscriminately…

224 GI’s attending Board Review Courses

We have Met the Enemy, and He is Us.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall n=235</th>
<th>Mayo n=79</th>
<th>SAVAMC n=75</th>
<th>UNC n=81</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years with BE (mean ± SD)</td>
<td>6.5 ± 5.9</td>
<td>5.2 ± 5.4</td>
<td>9.3 ± 6.2</td>
<td>5.2 ± 5.2</td>
</tr>
<tr>
<td>Endoscopy after BE diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n (%))</td>
<td>211 (92.1)</td>
<td>68 (87.2)</td>
<td>69 (94.5)</td>
<td>74 (94.9)</td>
</tr>
<tr>
<td>No (n (%))</td>
<td>18 (7.9)</td>
<td>10 (12.8)</td>
<td>4 (5.5)</td>
<td>4 (5.1)</td>
</tr>
<tr>
<td>Total surveillance endoscopies (mean ± SD)</td>
<td>4.0 ± 4.0</td>
<td>3.1 ± 2.8</td>
<td>5.3 ± 5.1</td>
<td>3.8 ± 3.7</td>
</tr>
<tr>
<td>Months per endoscopy (mean ± SD)</td>
<td>20.2 ± 16.8</td>
<td>20.9 ± 18.6</td>
<td>25.4 ± 14.2</td>
<td>14.3 ± 15.5</td>
</tr>
<tr>
<td>Surveillance endoscopies per 2 year period† (mean ± SD)</td>
<td>1.8 ± 1.7</td>
<td>1.5 ± 1.0</td>
<td>1.1 ± 0.7</td>
<td>2.8 ± 2.5</td>
</tr>
<tr>
<td>Surveillance endoscopies per 3 year period† (mean ± SD)</td>
<td>2.7 ± 2.6</td>
<td>2.2 ± 1.5</td>
<td>1.7 ± 1.0</td>
<td>4.2 ± 3.7</td>
</tr>
<tr>
<td>&gt;1 endoscopic surveillance per 2 year period†‡ (n (%))</td>
<td>70 (44.9)</td>
<td>20 (37.7)</td>
<td>16 (29.6)</td>
<td>34 (69.4)</td>
</tr>
<tr>
<td>&gt;1 endoscopic surveillance per 3 year period†‡ (n (%))</td>
<td>102 (65.4)</td>
<td>30 (56.6)</td>
<td>31 (57.4)</td>
<td>41 (83.7)</td>
</tr>
</tbody>
</table>

Crockett SD et al. G/E, epub ahead of print.
A Perfect Storm

ACG campaign

New drug class

DTC Ads

Cancer phobia
So Where are We in 2012?

We are using an insensitive predictor of risk (GERD symptoms) to decide who gets an expensive, insensitive test (endoscopy w/ bx), to diagnose a condition with a low risk of progression (BE), so we can perform an unproven, expensive maneuver (endoscopic surveillance) to try to prevent a rare cancer (EAC).

So How Do We Improve Care In This Disease?
1) Stratify risk!

2) Intervene instead of charting rates of decay
Dr. Sharma will tell you about interventions in BE.
How Can We Better Stratify Risk?
Stratifying Risk:
Taking screening out of the Endo Unit
How Well Does Cytosponge Work?

- 504 patients in general medical clinics with a prescription for acid suppressant therapy in the last 5 yrs
- Underwent both EGD and Cytosponge
- 3% (15) had BE of ≥1 cm in length
- Sensitivity/Specificity of sponge for BE of ≥1 cm: 73%/94%
- Sensitivity/Specificity of sponge for BE of ≥2 cm: 90%/94%

Is It Feasible in Clinical Practice?

<table>
<thead>
<tr>
<th>Findings</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td>Erosive 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 Requiring Subsequent Endoscopic Resection</td>
<td>12 (3)</td>
</tr>
<tr>
<td>Gastritis</td>
<td>15 (4)</td>
</tr>
</tbody>
</table>

Peery AF et al, *GIE*, pub pending.
What About Biomarkers?
Characteristics of a Good Biomarker

- Economically viable
- Sensitive
- Specific
- Minimally invasive sampling
- Predates the development of disease sufficiently to allow intervention

“Bonus:”
- Correlates with disease progression
- Biologically plausible
Proposed BE Biomarkers

<table>
<thead>
<tr>
<th>Biomarker</th>
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<tbody>
<tr>
<td>Cyclin D1</td>
<td>K-ras</td>
</tr>
<tr>
<td>APC</td>
<td>Ki-67</td>
</tr>
<tr>
<td>Bcl-2</td>
<td>P16</td>
</tr>
<tr>
<td>VEG-F</td>
<td>p53</td>
</tr>
<tr>
<td>ECAD</td>
<td>NF-KB</td>
</tr>
<tr>
<td>MUC2</td>
<td>COX-2</td>
</tr>
<tr>
<td>Rab 11</td>
<td>Cdx-2</td>
</tr>
<tr>
<td>CEA</td>
<td>Flow cytometry</td>
</tr>
<tr>
<td>Promoter Methylation</td>
<td>Etc, etc, etc</td>
</tr>
<tr>
<td>Question</td>
<td>Answer</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>Economically Viable?</td>
<td>Not clear</td>
</tr>
<tr>
<td>Sensitive?</td>
<td>Varies – some promising</td>
</tr>
<tr>
<td>Specific?</td>
<td>Data mixed - often unknown</td>
</tr>
<tr>
<td>Min. Invasive Sampling?</td>
<td>Most off of biopsy samples</td>
</tr>
<tr>
<td>Predates dev of disease?</td>
<td>Very limited data. Most X-sectional</td>
</tr>
<tr>
<td>Correlates w/ disease prog?</td>
<td>Often, yes</td>
</tr>
<tr>
<td>Biologically plausible?</td>
<td>Yes</td>
</tr>
</tbody>
</table>
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 active intervention
What is Logical?

• Don’t screen women
• Don’t screen anyone under age 50
• Don’t screen more than once
• If you want to screen, pay attention to the epidemiology of the disease

Conclusions

• Our current approach to BE is illogical and has not improved outcomes
• Little is understood about pathogenesis or risk stratification for progression
• For now, concentrate screening effort on those who get the cancers
  • Elderly, Obese, Caucasian males with GERD symptoms
• Better screening methods and newer biomarkers holds promise
“The Best Day in the Life of any Barrett’s Patient is the Day their Endoscopist Dies.”

-Steve Sontag, MD