Management of Barrett’s Esophagus

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Disclosure

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The Most Important Thing Stayed the Same
Adenocarcinoma – A Disease with a Rapidly Increasing Incidence


Not Much Progress Being Made...

Trends in EAC


Most Presentation is Late-Stage

We are Losing the Battle Against Esophageal Adenocarcinoma

So What Changed?
Who With GERD Needs Scoped?

• OLD
  – The utility of screening is unclear
  – Risk factors may help pick who should get scoped

• NEW
  – Screening for BE may be considered in men with chronic (>5 yrs) and/or frequent (weekly or more) GERD symptoms PLUS 2 or more of the following: age >50, Caucasian race, central obesity, tobacco, first degree relative with BE or cancer

Why Exclude Women?

Many of those developing cancer have no or trivial reflux symptoms.

- Series of esophageal carcinoma demonstrate 20-51% of subjects have no or infrequent reflux symptoms.
- Removal of those subjects from our endoscopy pool cuts the number of “findable” cancer by 40%.


GERD symptom presence and frequency are poor predictors of the presence of BE.
How Should They Be Scoped?

- OLD
  - Standard Per Oral Upper Endoscopy

- NEW
  - Standard Per Oral Upper Endoscopy OR
    Unsedated Transnasal Endoscopy
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

OK. They Found My Patient Has Barrett’s. How Often Do They Need Scoped?

- **OLD**
  - Repeat within one year to confirm diagnosis and exclude dysplasia
  - Then every 3 years with standard per oral endoscopy

- **NEW**
  - Make sure the patient understands risks and benefits of surveillance, then
  - Every 3-5 years with high resolution endoscopy
Case-control study in the KP Bay Area population

- Cases: Pts with known BE who died of EAC, 1995-2009
- Controls: Pts from the pop with BE who did not die of EAC
- Matched for age, sex, and duration of f/u
- Exposure: Surveillance endoscopy in 3 yrs prior to index date
- Basic idea is that those dying of CA should be less likely to have surveillance exam than those who did not die

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**CLINICAL—ALIMENTARY TRACT**

**Impact of Endoscopic Surveillance on Mortality From Barrett's Esophagus–Associated Esophageal Adenocarcinomas**

**Table 4. Associations Between Surveillance Endoscopy and Fatal Adenocarcinomas**

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In surveillance</td>
<td>In surveillance</td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surveillance examina</td>
<td>21 (55.3)</td>
<td>61 (60.4)</td>
<td>0.82 (0.35-2.00)</td>
</tr>
<tr>
<td>Controlling factors</td>
<td></td>
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<tr>
<td>Dysplasia status</td>
<td></td>
<td></td>
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<tr>
<td>Barrett's esophagus</td>
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<td></td>
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<tr>
<td>Excluding cases with</td>
<td></td>
<td></td>
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<tr>
<td>7-12 months</td>
<td>19 (52.8)</td>
<td>57 (60.0)</td>
<td>0.95 (0.32-2.70)</td>
</tr>
<tr>
<td>Excluding cases</td>
<td></td>
<td></td>
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<tr>
<td>with high-grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dysplasia before</td>
<td>16 (55.2)</td>
<td>38 (52.8)</td>
<td>1.00 (0.34-2.94)</td>
</tr>
<tr>
<td>3-year surveillance</td>
<td></td>
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<tr>
<td>Excluding cases with</td>
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<td>Excluding cases</td>
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<tr>
<td>with high-grade</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>dysplasia before</td>
<td>19 (61.3)</td>
<td>57 (67.1)</td>
<td>0.88 (0.29-2.67)</td>
</tr>
<tr>
<td>3-year surveillance</td>
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<td>Excluding cases with</td>
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<tr>
<td>Excluding cases</td>
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<tr>
<td>with high-grade</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>dysplasia before</td>
<td>18 (56.3)</td>
<td>54 (64.3)</td>
<td>0.80 (0.27-2.34)</td>
</tr>
<tr>
<td>3-year surveillance</td>
<td></td>
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<tr>
<td>Excluding cases with</td>
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<td>Barrett's esophagus</td>
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<tr>
<td>Excluding cases</td>
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<tr>
<td>with treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>related mortality</td>
<td>14 (51.9)</td>
<td>47 (65.3)</td>
<td>0.46 (0.13-1.64)</td>
</tr>
<tr>
<td>Total</td>
<td>38 (100)</td>
<td>101 (100)</td>
<td></td>
</tr>
</tbody>
</table>

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Yikes! My Patient Has Dysplasia! What Should Be Done?

• OLD
  – Low-Grade Dysplasia: Repeat endoscopy in 6 months, then annually
  – High-Grade Dysplasia: Repeat every 3 months, or intervention with either esophagectomy or photodynamic therapy

• NEW
  – Confirm Diagnosis, then
    • Low-Grade Dysplasia: Radiofrequency Ablation
    • High-Grade Dysplasia: Radiofrequency Ablation

RFA

The AIM-D Trial
RCT of 127 Subjects with LGD & HGD

• Intervention: RFA+PPI or Sham+PPI (2:1)
• Follow-up: 12 mos
• Assessment: Bx’s q3 mos (HGD)/ 6 mos (LGD)
• 1° Outcomes:
  – Ablation of all dysplasia:
    • 81% of HGD
    • 91% of LGD
    • app 20% of controls
  – Complete eradication of IM (77% of Rx, 2% Sham)
• SE’s: Strictures in 6% of subjects

3 year Durability

Shaheen NJ et al, Gastroenterology 2011.

LGD is an Indication for Endoscopic Intervention

SURF study

RCT, n=140, surveillance EGD vs. ablation with RFA

Primary outcome: occurrence of HGD/EAC

Phoa KN et al, JAMA 2014
My Patient Has a Mucosal Cancer! What Should Be Done?

• OLD
  – Esophagectomy

• NEW
  – Confirm Diagnosis, then
    • Endoscopic Mucosal Resection of the Cancer
    • Followed by Radiofrequency Ablation

Ell C et al. GIE, 2007
What’s Next?

We are not getting to the people we need

Dulai GS, Gastroenterology 2002.
Cooper GS, GIE, 2009.
It is not for lack of trying...

Can We Prevent Cancer in Barrett’s Esophagus?

YES!!!
But probably not by doing what we have been doing...

The Way Forward...
Making the Needle Bigger...

The Pitchforks of the Future?
How Good in the Sponge?

• 501 subjects screened in a general medicine population, EGD used as gold standard
• For BE of ≥ 1 cm:
  – Sensitivity – 73.3% (44.9-92.2%)
  – Specificity – 93.8% (91.3-95.8%)
• For BE of ≥ 2 cm:
  – Sensitivity – 90.0% (55.5-99.7%)
  – Specificity – 93.5% (90.9-95.5%)

Conclusions

- The epidemiology of both BE and EAC is unfavorable and worrisome
- Current screening and surveillance practices in BE are limited by poor risk stratification
- Self-congratulation for improved care in subjects with known BE is largely unwarranted
- Doing we have been doing, but harder, is unlikely to result in success
- Relatively small changes in our current paradigm would result in incremental improvements
- A “disruptive technology” is needed to improve our approach to preventing esophageal adenocarcinoma

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
  - Look for a low-cost, widely available (?non-endoscopic?) screening test to open the top of the funnel
  - 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