Screening and Surveillance for Gastric and Esophageal Cancer

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Surveillance ???
Crowd Thinking

Goals

• Challenge audience to re-think screening for upper tract disease
• Discuss new methods to perform screening
• Understand the new evidence regarding surveillance for esophageal and gastric cancers
Case

- 54 yo WM smoker with 25 pack year history
- BMI = 35
- PMH
  - MI age 51
  - HTN, High lipids
- Heartburn symptoms for 5 years, worse over last year
- Past FH of esophageal cancer in father and brother

Question

- Would you screen this patient?
  1. Yes
  2. No
Today

- There are no guidelines that recommend mass screening for Barrett’s esophagus nor esophageal adenocarcinoma.
- The vast majority of esophageal cancers are only detected at late stage symptomatic presentation.
- Large amount of resources are being spent on practices that are of little benefit.
Why Consider Screening for Barrett’s Esophagus?

- 90% of patients with esophageal cancer never were known to have BE (Hvid-Jensen New England Journal of Medicine 365(15): 1375-1383, 2011)
- Over half of patients with BE do not have a history of reflux symptoms (Ronkainen, Gastroenterology 129(6): 1825-1831, 2005)
- Most patients with BE related cancer present with late stage symptoms of dysphagia (Gibbs Journal of the National Medical Association 99(6): 620-626, 2007)

2011 AGA Barrett’s Guideline

- Screening
  - Age > 50
  - Male (OR=1.5 to 3.0)
  - White (OR=4 to 6)
  - Chronic GERD (OR=6 to 10, dose response)
  - Hiatal hernia (OR= 2.1)
  - ↑ BMI (OR=1.4 for BMI > 25 or 30)
  - intra-abdominal distribution of body fat (OR=2.8 for all BE, 4.3 for LSBE)
**GERD and Columnar Lined Esophagus**

<table>
<thead>
<tr>
<th>CLE Length</th>
<th>Prevalence of CLE, n=1058, n (%)</th>
<th>Prevalence of CLE with intestinal metaplasia, n=1058, n (%)</th>
<th>Proportion of patients with intestinal metaplasia in all CLE, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 cm</td>
<td>31 (2.9)</td>
<td>9 (0.8)</td>
<td>29</td>
</tr>
<tr>
<td>1–3 cm</td>
<td>167 (15.9)</td>
<td>98 (9.3)</td>
<td>58.7</td>
</tr>
<tr>
<td>≥3 cm</td>
<td>49 (9.5)</td>
<td>43 (4.0)</td>
<td>87.8</td>
</tr>
</tbody>
</table>

- 1058 pts with symptomatic GERD
  - Columnar lined esophagus in 23%
  - SIM in 14%
- Family history of GERD nor BE predictive of BE
- Heartburn >5 years predictive of BE, but not regurgitation or daily heartburn

Balasubramanian, Am J Gastroenterol 2012; 107:1655–1661

**Screening : EGD**

- Screening tools: Sedated EGD
  - Costs
  - Modeling studies: assumptions (?) limited real data¹,²
  - Performance characteristics
    » Sensitivity and specificity not optimal³
    » Reproducibility of findings ?
  - Negative predictive value of normal endoscopy is unclear

¹Inadomi, Ann Int Med 2003,
²Barbiere Gastroenterology 2009
³Kim Gastroenterology 1994
uTNE

- Accurate\(^1\)
- Well tolerated
- ? Preferred over sEGD\(^2\)
- Lower direct and indirect costs
- Cost effective in modelling studies in GER subjects\(^3\)
- ? Patient reluctance
  - Acceptance in population
- ? MD reluctance\(^4\)
- Comparative yield and accuracy ?

\(^1\)Jobe Am J Gastro 2006,
\(^2\)Saien Am J Gastro 2002,
\(^3\)Nietert Gastrointest Endo 2003
\(^4\)Atkinson Am J Gastro 2008

CytoSponge

- Studied in UK Primary Care Setting
  - 504 pts from 12 practices
  - Acceptability: 19% of pts asked participated
    - 3 could not swallow capsule
  - Total cases of BE n=15 (3%)
  - Sensitivity 73% (BE > 1 cm length)
    - Increased to 90% for BE > 2 cm
  - Specificity 94%
  - Low anxiety in 84%

Kadri BMJ 2010
Screening with the Sponge

Benaglia, Gastroenterology 2013;144:62–73

Who Should Undergo Surveillance?

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| ACG (2008) | • Potential to prolong life expectancy with therapeutic intervention for Ca  
           • Weigh age/comorbidities |
| AGA (2011) | • Patients with reasonable life expectancy  
           • Tolerate treatment of dysplasia/cancer |
Describing Barrett’s Esophagus

1. Locate gastro-esophageal junction
2. Recognise the squamocolumnar junction
3. Describe extent of metaplasia consistently

Current Status

- Diagnosis
  - Endoscopy
  - EMR for visible lesions
- Surveillance biopsies
  - Four quadrant biopsies
  - Every cm for HGD
  - Every two cm for LGD

• Diagnosis
  • Endoscopy
  • EMR for visible lesions
• Surveillance biopsies
  • Four quadrant biopsies
  • Every cm for HGD
  • Every two cm for LGD
Updated ACG guidelines for Barrett’s esophagus: Surveillance intervals according to dysplasia grade

Chronic GERD Symptoms

Screening Endoscopy with Biopsies

Negative for dysplasia

Repeat x 1

Low-grade dysplasia

Repeat x 1

Annual surveillance until no dysplasia

High-grade dysplasia

Repeat endoscopy with biopsy

Expert pathologist opinion

Wang and Sampliner AJG 2008

Limitations of Endoscopic Biopsy Surveillance of Barrett’s Esophagus

• Interobserver variability in dysplasia interpretation

• *Most patients never develop cancer*
  – Incidence 0.5%/year
The Case for Barrett’s Surveillance
5-year Survival of Surveyed and Non-Surveyed Cases

![Bar chart showing 5-year survival rates for surveyed and non-surveyed cases.]

- Surveyed cases: 73.3%, 52.9%, 90.0%
- Non-surveyed cases: 0.0%, 20.0%, 20.0%

Corley et al, Gastroenterology 2002; 122:633

Lack of Efficacy of Surveillance

- Case control study from Northern California Kaiser program
- 38 cases of individuals diagnosed with esophageal and GE junctional cancer
- 101 controls
- Surveillance within 3 years not associated with a decreased risk of death from esophageal adenocarcinoma (adjusted odds ratio, 0.99; 95% confidence interval, 0.36–2.75)

Corley, Gastroenterology, 2013
Non-dysplastic Barrett’s oesophagus

- Regular mucosal pattern
- Regular vascular pattern

Dysplastic Barrett’s oesophagus

- Irregular mucosal pattern
- Irregular vascular pattern
- Abnormal blood vessels

Kara et al. Gastrointest. Endosc, 2006

Meta-Analysis NBI for HGD

- Pooled sensitivity and specificity
- Per patient analysis

Endoscopy 2010; 42: 351 – 359
Narrow Band Imaging for Dysplasia

<table>
<thead>
<tr>
<th>Study</th>
<th>Pt # (HGD/Total)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharma 2006</td>
<td>7 / 51</td>
<td>100%</td>
<td>98.7%</td>
</tr>
<tr>
<td>Kara (AFI+NBI) 2006</td>
<td>14 / 20</td>
<td>96%</td>
<td>93%</td>
</tr>
<tr>
<td>Wolfsen 2008</td>
<td>28 / 66</td>
<td>100%</td>
<td>SR no increased dysplasia</td>
</tr>
<tr>
<td>Singh 2009</td>
<td>3/21</td>
<td>89%</td>
<td>75%</td>
</tr>
<tr>
<td>Curver AFI-NBI 2010</td>
<td>55/87</td>
<td>65%</td>
<td></td>
</tr>
<tr>
<td>Sharma 2013</td>
<td>14/113</td>
<td>53%*</td>
<td>100%</td>
</tr>
<tr>
<td>Giachino (AFI+NBI) 2013</td>
<td>14/42</td>
<td>71%</td>
<td>46%</td>
</tr>
</tbody>
</table>

Probe Laser Confocal Endomicroscopy

- 2 mm probe passes through biopsy channel
- 12 frames per second near real time
- IV fluorescein
**Miami Classification**

**Non dysplastic BE**
- Uniform villiform architecture
- Columnar cells (block arrow)
- Dark “goblet” cells (thin arrow)

**Dysplastic BE**
- Villiform structures
- Dark, irregularly thickened epithelial borders (arrow)
- Dilated irregular vessels (block arrow)

*Wallace MB et al Endoscopy 2011*

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**Accuracy of pCLE for Dysplasia**

- Multicenter, prospective RCT
- Comparison of HD-WLE alone to HD-WLE + pCLE
- 101 pts in 5 centers
- HD WLE + pCLE
  - Sensitivity 68%
  - Specificity 88%
- HD WLE
  - Sensitivity 34%
  - Specificity 92%

*Sharma, Gastrointestinal Endoscopy 74(3): 465-472, 2011*
Gastric Cancer

- Male predominant disease 1.6:1
- 21,320 will be diagnosed in 2012 in US
  - 10,540 will die (49%)
- Decreasing over last decades (1.5% per decade)

Pathway to Gastric Cancer

Chronic Gastritis

Gastric Intestinal Metaplasia
NBI Classification Mucosa of Gastric Polyps

Omori et al. BMC Gastroenterology 2012, 12:17

NBI Classification of Capillary Pattern Gastric Polyps
Classification of Gastric Polyps

<table>
<thead>
<tr>
<th>Polyp Classification</th>
<th>Fundic gland</th>
<th>Hyperplastic</th>
<th>Adenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small round pattern</td>
<td>++++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Prolonged pattern</td>
<td>-</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Villous or ridged</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Honeycomb</td>
<td>++++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Dense vascular</td>
<td>-</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Core vascular</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Fine network, unclear</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Effects of H. Pylori Eradication

- Effect on gastric histology 1 yr after HP eradication
- RCT of treatment (n=295) versus no treatment (n=292)
- Decreased inflammation
- No change in IM, atrophy

Sung et al, Gastroenterology 119:7–14, 2000
Risk of Cancer Developing in Gastric Mucosa (Netherlands)

Annual incidence of gastric cancer

- 0.1% for patients with atrophic gastritis
- 0.25% for intestinal metaplasia
- 0.6% for mild-moderate dysplasia
- 6% for severe dysplasia within 5 years

Sampling Protocols

- Devries et al 2010: 12 non-targeted biopsies and additional biopsies of any lesions
  - Primarily found in incisura
  - Second most common antrum
  - Third was less curve
- A protocol of 7 biopsies found 97% of IM/dysplasia
  - 3 antrum
  - 1 incisura
  - 3 body (1 greater, 2 lesser curve)
Survival Benefit of Gastric Cancer Screening

<table>
<thead>
<tr>
<th>Case-control studies</th>
<th>Number of participants</th>
<th>Age (year)</th>
<th>Follow-up (years)</th>
<th>Effect measure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kakoski et al. (2008)</td>
<td>154 cases+58 controls</td>
<td>50–60</td>
<td>3–5</td>
<td>HR 0.88 (0.56–1.20)</td>
</tr>
<tr>
<td>Kohira et al. (1989)</td>
<td>51 cases+178 controls</td>
<td>70–80</td>
<td>5</td>
<td>HR 1.02 (0.68–1.53)</td>
</tr>
<tr>
<td>Fukao et al. (1993)</td>
<td>151 cases+97 controls</td>
<td>50–60</td>
<td>10</td>
<td>HR 1.26 (0.80–1.98)</td>
</tr>
<tr>
<td>Abe et al. (1995)</td>
<td>820 cases+2413 controls</td>
<td>40–60</td>
<td>5</td>
<td>HR 1.22 (0.86–1.74)</td>
</tr>
</tbody>
</table>

Prospective studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Number of cases</th>
<th>Age (year)</th>
<th>Follow-up (years)</th>
<th>Effect measure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obihiro et al. (1973)</td>
<td>12789 cases</td>
<td>40–70</td>
<td>10</td>
<td>RR 1.10 (0.95–1.28)</td>
</tr>
<tr>
<td>Muisse et al. (1964)</td>
<td>7008 cases</td>
<td>40–60</td>
<td>10</td>
<td>RR 1.02 (0.83–1.27)</td>
</tr>
<tr>
<td>Inaba et al. (1999)</td>
<td>24336 cases</td>
<td>40–70</td>
<td>10</td>
<td>RR 1.26 (0.95–1.68)</td>
</tr>
<tr>
<td>Miase et al. (2003)</td>
<td>87152 cases</td>
<td>40–70</td>
<td>10</td>
<td>RR 1.15 (0.95–1.27)</td>
</tr>
<tr>
<td>Lee et al. (2006)</td>
<td>42569 cases</td>
<td>40–70</td>
<td>10</td>
<td>RR 1.10 (0.90–1.35)</td>
</tr>
</tbody>
</table>

Table 2: Japanese data for reduction in death from gastric cancer by screening

ESGE Recommendations

- Intestinal Metaplasia or Atrophy
- NBI or Chromoendoscopy
- Atrophy or IM
- Treatment of H. pylori
- Surveillance every 3 years
- Dysplasia
  - Visible lesion resect
  - High grade lesion follow-up 6–12 months
- Low grade lesion follow-up 12 months

ASGE Recommendations

• Gastric polyps
  – Adenomatous: 1 year after removal, Repeat surveillance 3-5 years
  – Hyperplastic: No follow-up

• Intestinal metaplasia/atrophy
  – Surveillance if increased risk due to ethnicity or family history
  – Topographically mapping indicated
  – High grade dysplasia should be resected

Gastrointestinal Endoscopy 63: 570, 2006

Mayo Rochester Barrett’s Research Group