Is there a role for screening gastric carcinoma or preneoplastic lesions?

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Faculty of Medicine, University of Porto, MEDCIDS/CINTESIS
Assumptions

- Frequent cancer with relevant **morbidity** and **mortality**
- **Effective** treatment
- **Screening test** with high sensitivity and specificity
- ... **acceptable**, safe and inexpensive
- Adequate **means for diagnosis, management and follow-up**

http://who.int/cancer/detection
Gastric cancer incidence is decreasing

WHO Database, 1950-1998
Gastric cancer
more relevant in Eastern countries
Gastric cancer in Europe: increasing number of cases and high mortality

Europe, European Union (EU-28)
Stomach
Number of new cancers in 2035 (all ages)

Europe, European Union (EU-28)
Stomach
Number of cancer deaths in 2035 (all ages)
Gastric cancer:
~14 millions years DALY lost in 2008
Gastric cancer survival: median survival = 1 year very high in early cases

“The surgery went well. I’m quite confident we got it all.”

Time (Months)

Dinis-Ribeiro M Eur J Oncolog 2001
Gastric cancer treatment: early cases can be managed endoscopically

R0 = 94% & S5 ≥ 90%
Endoscopic treatment preferred by patients

EORTC QLQ-C30 Dimensions

<table>
<thead>
<tr>
<th></th>
<th>Physical function</th>
<th>Role function</th>
<th>Emotional function</th>
<th>Cognitive function</th>
<th>Social function</th>
<th>Global health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrectomy 1 month</td>
<td>-11,7</td>
<td>-18,8</td>
<td>-1,8</td>
<td>-3,9</td>
<td>-5,3</td>
<td>-6</td>
</tr>
<tr>
<td>Gastrectomy 3-6 months</td>
<td>-9,3</td>
<td>-17,8</td>
<td>0,2</td>
<td>-4,6</td>
<td>-5,3</td>
<td>-2,5</td>
</tr>
<tr>
<td>Gastrectomy 1 year</td>
<td>-4,9</td>
<td>-9,7</td>
<td>3,6</td>
<td>-7,1</td>
<td>-5,9</td>
<td>-3,3</td>
</tr>
<tr>
<td>ESD 1 month</td>
<td>1,7</td>
<td>-1,5</td>
<td>6,1</td>
<td>2,5</td>
<td>0</td>
<td>6,4</td>
</tr>
<tr>
<td>ESD 3-6 months</td>
<td>0,9</td>
<td>-0,35</td>
<td>6,7</td>
<td>-1,4</td>
<td>0</td>
<td>3,8</td>
</tr>
<tr>
<td>ESD 1 year</td>
<td>-1,4</td>
<td>0,2</td>
<td>2,6</td>
<td>-4,4</td>
<td>0,3</td>
<td>5</td>
</tr>
</tbody>
</table>
Questions

• **To whom?** Population vs opportunistic

• **What?** Gastric cancer vs pre-neoplastic conditions

• **How?** Procedures and methods
Opportunistic screening during diagnostic upper GI endoscopy
Be aware!
(Improve) a priori probability
“setting”, older, known conditions, family

<table>
<thead>
<tr>
<th>Country</th>
<th>n</th>
<th>Prevalence (histology) (%)</th>
<th>Prevalence (endoscopy) (%)</th>
<th>Risk factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Netherlands (den Hoed, 2010)</td>
<td>383</td>
<td>1.4</td>
<td>?</td>
<td>Older</td>
</tr>
<tr>
<td>The Netherlands (de Vries A, 2010)</td>
<td>112</td>
<td>5</td>
<td>3</td>
<td>Precancerous cond/lesions</td>
</tr>
<tr>
<td>Finland (Varis K, 2000)</td>
<td>2332</td>
<td>2.4</td>
<td>2.4</td>
<td>Low pepsinogen</td>
</tr>
<tr>
<td>Portugal (Areia M, 2008)</td>
<td>45</td>
<td>2</td>
<td>2</td>
<td>Precancerous cond/lesions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chromoendoscopy</td>
</tr>
<tr>
<td>Romania (Alina B, 2011)</td>
<td>1651</td>
<td>9</td>
<td>4.8</td>
<td>Older patients</td>
</tr>
<tr>
<td>Turkey (Aygun C, 2010)</td>
<td>234</td>
<td>3.8</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Brazil (Motta CCA, 2007)</td>
<td>98 vs 116</td>
<td>4 (7.1% vs 0.8%)</td>
<td>3.5</td>
<td>Family history</td>
</tr>
</tbody>
</table>

1/100 – 1/10
Be aware!
locations of lesions / missed 9.4%

Missed

“known locations”
Quality procedures:
blind spots & adequate insufflation
Quality procedures: Time

• High risk lesions:
  – 14% vs. 6%; OR 2.5 (1.5-4.1)

• Dysplasia/Cancer:
  – 3.4% vs. 1%; OR 3.4 (1.3-10.4)

“Slow” endoscopists (>7 min) vs. “fast” endoscopists (<7 min)

"Slow" endoscopists (>7 min) vs. “fast” endoscopists (<7 min)
Adequate scopes

Ezoe Y Gastro 2011

Pimentel-Nunes Endoscopy 2016
Performance measures for upper gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative

### Authors
Raf Bisschops, Miguel Areia, Emmanuel Coron, Daniela Dobru, Bernd Kaskas, Roman Kuvaev, Oliver Pech, Krish Ragunath, Bas Weusten, Pietro Familiari, Dirk Domagk, Roland Valori, Michal F. Kaminski, Cristiano Spada, Michael Brethauer, Cathy Bennett, Carlo Senore, Mário Dinis-Ribeiro, Matthew D. Rutter

### Domains
- Pre-procedure
- Completeness of procedure
- Identification of pathology
- Management of pathology
- Complications
- Number of procedures
- Patient experience
- Post-procedure

### Key performance measures
- Proportion of patients with proper instructions for fasting (≥ 95%)
- Proportion of reports stating procedure time (≥ 90%)
- Proportion of reports with standardized terminology (≥ 95%)
- Proportion of patients with registration of complications after therapeutic procedures (≥ 95%)
- No current standard defined
- No current standard defined
- No key performance measure defined

### Minor performance measures
- Inspection time in the stomach (≥ 90%)
- Inspection time in Barrett’s esophagus (≥ 90%)
- Lugol staining in the esophagus for patients at risk of SCC (≥ 90%)
- Proportion of Barrett’s patients entered into a registry to monitor the incidence of dysplasia (≥ 85%)
Gastric carcinogenesis
premalignant stomach = “extension”
MAPS Guidelines
MAnagement of Precancerous conditions and lesions in Stomach

MAAnagement of Precancerous Lesions in the Stomach (MAPS)
JUNE 27, 2011
PORTO, PORTUGAL

Patients with atrophic gastritis and/or intestinal metaplasia without dysplasia

- Extension
- Magnification chroendoendoscopy and/or
  - Several biopsies should be obtained (≥2 in antrum and
    ≥2 in corpus; lesser and greater curvature)

Spread of lesions

Mild/moderate atrophic gastritis or intestinal metaplasia only in antrum

- H. pylori eradication

Atrophic gastritis or intestinal metaplasia both in antrum and corpus

Follow-up

Every 3 years
Narrow Band Imaging
“Simple” Mucosal, vascular pattern

<table>
<thead>
<tr>
<th>Proposed classification</th>
<th>Kikuste I Scand J Gastro 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Mucosal pattern</td>
<td>Regular circular</td>
</tr>
<tr>
<td>Vascular pattern</td>
<td>Regular Thin/periheric (body (b) or thick/central (a) vessels)</td>
</tr>
<tr>
<td>Expected outcome</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Images:
(a) Regular circular mucosal pattern
(b) Light blue crest
(c) Irregular/absent White opaque substance
(d) Regular vascular pattern
(e) Irregular
Narrow Band Imaging
Easy to learn and effective in real time use

Dias-da-Silva GIE 2013

Pimentel-Nunes Endoscopy 2016
Premalignant stomach endoscopy only?
NBI vs WLE versus mapping biopsy for GIM: a prospective blinded trial

- Per patient:
  - WLE + Mapping: 82
  - NBI + WLE: 71
  - NBI + Mapping: 100

- Per site:
  - WLE + Mapping: 75
  - NBI + WLE: 60
  - NBI + Mapping: 95
Atrophic mucosa and intestinal metaplasia can be accurately detected by image-enhanced endoscopy, after appropriate training.
Surveillance pre-malignant:
CE 3y OLGIM III/IV 50-75a

ICER € 18,336
Pepsinogen
1/50 endoscopies

<table>
<thead>
<tr>
<th>PG Method &amp; cutoff</th>
<th>Pos rate (%)</th>
<th>S (95%CI)</th>
<th>p*</th>
<th>Sp (95%CI)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGI ≤70 &amp; PGI/II ≤3 (n=7)</td>
<td>23%</td>
<td>77.3 (69.8–83.8)</td>
<td>0.942</td>
<td>73.2 (72.8–73.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PGI ≤50 &amp; PGI/II ≤3 (n=4)</td>
<td>22%</td>
<td>68.4 (59.1–76.8)</td>
<td>0.259</td>
<td>69.3 (68.6–70.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PGI ≤30 &amp; PGI/II ≤2 (n=3)</td>
<td>18%</td>
<td>51.9 (40.3–63.5)</td>
<td>0.001</td>
<td>84.4 (83.7–85.0)</td>
<td>0.016</td>
</tr>
</tbody>
</table>


Gastric cancer screening in population based studies

Lomba-Viana R EJGH 2014
**Pepsinogen**

**Good LR - but repeat at 3 years!**

<table>
<thead>
<tr>
<th></th>
<th>Follow-up*</th>
<th>Disease Present</th>
<th>Risk of cancer (%)**</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 year</td>
<td>3 years</td>
<td>5 years</td>
<td></td>
</tr>
<tr>
<td>PG +</td>
<td>2</td>
<td>7</td>
<td>8</td>
<td>225</td>
</tr>
<tr>
<td>PG -</td>
<td>2</td>
<td>5</td>
<td>10</td>
<td>5688</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>12</td>
<td>18</td>
<td>5913</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>1 year</th>
<th>3 years</th>
<th>5 years</th>
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<tr>
<td>PG +</td>
<td>0.9</td>
<td>3.1</td>
<td>3.6</td>
</tr>
<tr>
<td>PG -</td>
<td>0</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Total</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
</tr>
</tbody>
</table>

*Lomba-Viana R under review*
Population screening

<table>
<thead>
<tr>
<th>Intervention</th>
<th>ICER, $</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammograms every 2 years</td>
<td>35,500</td>
<td>(118)</td>
</tr>
<tr>
<td>Hepatocellular cancer screening in cirrhosis*</td>
<td>73,500</td>
<td>(119)</td>
</tr>
<tr>
<td>Upper endoscopy at time of screening colonoscopy</td>
<td>95,559</td>
<td></td>
</tr>
<tr>
<td>Screening colonoscopy every 2 years in ulcerative colitis</td>
<td>147,500</td>
<td>(120)</td>
</tr>
<tr>
<td>Human papilloma virus vaccination for girls</td>
<td>152,700</td>
<td>(121)</td>
</tr>
</tbody>
</table>

ICER, Incremental cost-effectiveness ratio.
*Using semiannual US and alpha-fetoprotein level testing.
Cost-effective stand alone vs together with CRC screening

![Graph showing cost-effectiveness]

**Table 2. Deterministic one-way sensitivity analysis results of the endoscopic screening strategies versus no screening.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base case value</th>
<th>Range</th>
<th>Threshold to change the cost-effective strategy</th>
<th>Explanation for screening to be cost-effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario: endoscopic screening combined with screening colonoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric cancer risk (age standardised rate)</td>
<td>13.1 per 100,000 (rate in Portugal)</td>
<td>3.9−29.9 per 100,000</td>
<td>10 per 100,000</td>
<td>An age standardised rate ≥10</td>
</tr>
<tr>
<td>Scenario: stand-alone endoscopic screening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endoscopic cost (from a societal point of view)</td>
<td>€137 (considering fees, hospital costs, anaesthesia, transportation and work lost)</td>
<td>€60−€398</td>
<td>€75</td>
<td>Endoscopic cost between €60 and €75</td>
</tr>
<tr>
<td>Number of screening exams (between 50 and 75 years old)</td>
<td>6 (one screening exam every five years)</td>
<td>3−6</td>
<td>3</td>
<td>Only three screening exams per patient (1 every 10 years)</td>
</tr>
<tr>
<td>Gastric cancer risk (age standardised rate)</td>
<td>13.1 per 100,000 (rate in Portugal)</td>
<td>3.9−29.9 per 100,000</td>
<td>25 per 100,000</td>
<td>An age standardised rate ≥25</td>
</tr>
</tbody>
</table>

€: euros.
Cost-effective
> 10 ASR
# Take home messages

<table>
<thead>
<tr>
<th>Population</th>
<th>Opportunistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric cancer</td>
<td>Europe CE w/ CRC if ASR &gt; 10</td>
</tr>
<tr>
<td>Pre-malignant conditions</td>
<td>No</td>
</tr>
</tbody>
</table>
ESGE Days 2018
Budapest Congress Center, Budapest, Hungary
April 19 - 21, 2018
www.esgedays.org
www.esge.com