Barrett’s esophagus: Ablate or just wait?

- Non-dysplastic BE
- Low grade dysplasia
- High grade dysplasia
- Early cancer
Who to treat?

- HGD: if the patient is properly selected.

Non-dysplastic BE  Low grade dysplasia  High grade dysplasia  Early cancer
Who to treat?

- **HGD**: if the patient is properly selected.
- **Early cancer**: only after endoscopic resection of the lesion.

| Non-dysplastic BE | Low grade dysplasia | High grade dysplasia | Early cancer |
What about low-grade dysplasia?

- Cancer risk is said to be low.

- Few clinical studies on treatment for LGD.

  *Small sized, complete removal of BE <50% of cases*
  
  *Significant side effects and deaths have been reported.*

- LGD patients: “less to gain and more to loose”?

- Should not be done outside clinical trials?
Is LGD an innocent disease?

- Depends on the pathologist making the diagnosis.
- If LGD is frequently diagnosed: the risk is low and vice versa.

<table>
<thead>
<tr>
<th>Study author(s) [ref. no.]</th>
<th>Year</th>
<th>Frequency of LGD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schnell et al. [4]</td>
<td>2001</td>
<td>67.2%</td>
</tr>
<tr>
<td>Sharma et al. [5]</td>
<td>2003</td>
<td>25.0%</td>
</tr>
<tr>
<td>Sharma et al. [6]</td>
<td>2006</td>
<td>21.4%</td>
</tr>
<tr>
<td>Egger et al. [7]</td>
<td>2003</td>
<td>20.2%</td>
</tr>
<tr>
<td>O’Connor et al. [8]</td>
<td>1999</td>
<td>17.6%</td>
</tr>
<tr>
<td>Csendes et al. [9]</td>
<td>2003</td>
<td>11.9%</td>
</tr>
<tr>
<td>Gopal et al. [10]</td>
<td>2003</td>
<td>9.7%</td>
</tr>
<tr>
<td>Conio et al. [11]</td>
<td>2003</td>
<td>9.6%</td>
</tr>
<tr>
<td>Vieth &amp; Stolte [12]</td>
<td>2002</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

1.4% in 7 yrs

40% in 28 mo
Correctly diagnosing LGD is tough

Consensus diagnosis: high risk of progression

Skacel et al. Am J Gastro 2000
146 LGD pts reviewed by 2 expert pathologists

- 110 pts NDBE (75%)
- 14 pts Indef (10%)
- 22 pts LGD (15%)

42% HGD/Ca 13.4% per pnt yr

0.49% per patient year

No HGD/Ca

Median FU of 51 months

Curvers et al. Am. J. Gastro. 2010
Radiofrequency Ablation in Barrett’s Esophagus with Dysplasia

Nicholas J. Shaheen, M.D., M.P.H., Prateek Sharma, M.D., Bergein F. Overholt, M.D., Herbert C. Wolfsen, M.D.,
Richard E. Sampliner, M.D., Kenneth K. Wang, M.D., Joseph A. Galanko, Ph.D., Mary P. Bronner, M.D.,
John R. Goldblum, M.D., Ana E. Bennett, M.D., Blair A. Jobe, M.D., Glenn M. Eisen, M.D., M.P.H.,
M. Brian Fennerty, M.D., John G. Hunter, M.D., David E. Fleischer, M.D., Virender K. Sharma, M.D.,
Robert H. Hawes, M.D., Brenda J. Hoffman, M.D., Richard I. Rothstein, M.D., Stuart R. Gordon, M.D.,
Hirosi Mashimo, M.D., Ph.D., Kenneth J. Chang, M.D., V. Raman Muthusamy, M.D.,
Steven A. Edmundowicz, M.D., Stuart J. Spechler, M.D., Ali A. Siddiqui, M.D., Rhonda F. Souza, M.D.,
Anthony Infantolino, M.D., Gary W. Falk, M.D., Michael B. Kimmey, M.D., Ryan D. Madanick, M.D.,
Amitabh Chak, M.D., and Charles J. Lightdale, M.D.
Radiofrequency Ablation in Barrett’s Esophagus with Dysplasia

- Complete removal of LGD: 95%.
- Complete removal of BE: 81%.
- Outpatient procedures, no severe complications.
Who to treat?

- HGD: if the patient is properly selected.
- Early cancer: only after endoscopic resection of the lesion.
- LGD: not outside clinical trials?
Who to treat?

- HGD: if the patient is properly selected.
- Early cancer: only after endoscopic resection of the lesion.
- LGD: if the diagnosis is confirmed by an expert pathologist.
Total patients in database n=2264

Exclusions n=628:
Prevalent HGD/EAC (249)
No IM (266)
Missing Data (113)

NDBE at inception n=1415
LGD at inception n=221

Remained NDBE n=1263

Developed LGD n=152

< 1 yr FU n=108

Mean FU of 75 months

LGD ≥ 1 yr FU n=97 INCIDENT
LGD ≥ 1 yr FU n=113 PREVALENT

Wani et al. Gastro. 2011
Results

• Incidence rates of HGD/EAC:
  – All LGD: 1.83 %/year
  – Incident LGD: 2.33 %/year
  – Prevalent LGD: 2.69 %/year

• Extent of LGD:
  – Unifocal (n=73): 1.39
  – Multifocal (n=50): 3.51
  \[\text{Non-significant}\]

• Pathology review (n=88):
  – Consensus (n=41): 0.84 (95% CI: 0.21–3.35)

Wani et al. Gastro. 2011
Discussion points

• FU interval calculated from 1st BE diagnosis
• “Indefinite for dysplasia” mixed with LGD
• Path review in only subgroup of cases
  – 23% upgraded to HGD
  – $\kappa$ value between expert pathologists only 0.14

• There is “good” and “bad” pathology review.
• Need for easy access to good quality expert pathology panels.
Ablating non-dysplastic Barrett’s?

• **No**, given the low risk of progression to cancer (0.5%/yr) or HGD (0.9%/yr).

• **Maybe**, if we find ways of identifying those cases at risk.

• **Yes**, if we find “the Holy Grail” for ablating BE.
Ablation is the dominant strategy if complete removal of BE is achieved >40% and the effect is maintained over time.
Is the effect of ablation maintained over time?

**Fleischer et al. *Endoscopy* 2010**
- 50 NDBE pts (median length 6 cm)
- Balloon-based RFA supplemented with focal RFA.
- At 60-mo: 92% persisting eradication of BE.

**Shaheen et al. *Gastroenterology* 2011**
- 2-year FU data of RCT (HGD and LGD cases)
- Balloon-based RFA supplemented with focal RFA.
- Complete removal of BE persisted in 95%.
AMC 5 year FU study in 54 patients

- High-resolution endoscopy + NBI.
- Endoscopic ultrasound (+/-FNA).
- Endoscopic resection neosquamous mucosa.
- Bx < 5-mm of the neo-Z-line.
- 4Q/2cm biopsies taken.
- All histology reviewed by expert pathologist.
5-year follow-up in 54 patients

• Median FU: 60 mo, 6 FU endoscopies, median 73 Bx.
• Sustained CR-NEO/CR-IM in 52/54 patients (96%).
• 3,351 neosquamous Bx: buried Barrett’s in 3 (0.09%)
• ER specimens: no buried Barrett’s.
Ablating non-dysplastic Barrett’s?

• Complete removal of BE
• No significant side-effects
• Easy, well tolerated
• Remains functional integrity of the esophagus
• Normal squamous mucosa free of oncogenetic abnormalities.
• Persistent effect during follow-up
Endoscopic ablation of NDBE?

• Ablation of NDBE spreading into the field rapidly (not good).
• Antagonized by unjustified conservatism (not good either).
• Large-scale RCT is not likely to be performed.
• Personal perspective: ablation of NDBE justified for selected cases (e.g. < 50 years, family history of BE-ca).
• Near future: risk stratification with panel of biomarkers.
• HGD: if the patient is properly selected.
• Early cancer: only after endoscopic resection of the lesion.
• LGD: if the patient is properly selected (path review!).
• NDBE: selected cases (e.g. <50 years, family history BE-cancer).