Barrett's Esophagus: Diagnosis
Surveillance and Therapy

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Barrett’s Esophagus

• Definition: intestinal
metaplasia/columnar-lined epithelium
in the tubular esophagus, proximal to
the squamo-columnar junction
The Keys to Barrett’s Management

• Make an accurate diagnosis
• Treat reflux
• Optimize surveillance
• Treat dysplasia when present
• Maintain long term success’s

What is the most important part of performing an EGD?

1. Take your time
2. Look twice (or 3 or 4 times) and biopsy once
3. Your first biopsy is the most important (everything after is affected by blood)
4. Remember: The concept of a ‘high quality’ exam is not reserved for the colon
The EGJ

There are 3 anatomical-endoscopic landmarks to be included in a complete examination

1. Squamocolumnar junction
2. The level of disappearance of the linear mucosal palisade vessels
3. Proximal margin of the gastric folds

Screening, diagnosis and staging:

- In patients who BE is being considered, the squamocolumnar junction, the gastro-esophageal junction (GEJ), and the location of the diaphragmatic hiatus (if there is a hiatal hernia present) should be recorded on each upper endoscopy.

  - Agreement: 20/23 = 87%
  - Grade of Recommendation: Weak
  - Quality of Evidence: Moderate
Prague Classification

Prague C&M Classification

• Most reliable and validated classification of Barrett’s
  – C = length of esophagus lined circumferentially
  – M = maximal length of esophagus involved at any point
Screening, diagnosis and staging:

- If BE is suspected on an endoscopy, the endoscopist should document the extent of suspected BE using Prague criteria.
  - Agreement: 19/23 = 82.6%
  - Grade of Recommendation: Weak
  - Quality of Evidence: Moderate

Biopsy Protocol

- Four quadrant biopsy every 2 cm of Barrett’s mucosa
- Samples from any visible abnormalities
- Biopsies from each segment should be submitted in separate containers
- Erosive esophagitis should be healed before biopsy to increase yield and avoid missing short segments of columnar lining
Improvements in Tissue Sampling

Wide Area Transepithelial Sampling With Computer Assisted Analysis (WATS\textsuperscript{3D})

Neural network-based computer system rank orders every cell on the submitted slide for:

- Abnormal cellular morphology
- Signature spectral abnormality of one or more molecular diagnostics
- Cytometric evaluation of nuclear DNA content (relative DNA ploidy)

The system can detect as few as two goblet or dysplastic cells out of the over 100,000 normal cells distributed on the specimen.
**WATS³D** Detects Residual or Recurrent IM and Dysplasia Missed on Forceps Biopsies

<table>
<thead>
<tr>
<th>IM/Dysplasia/Neoplasia</th>
<th>Forceps Biopsy Positive</th>
<th>Forceps Biopsy Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>WATS³D Positive</td>
<td>15</td>
<td>24</td>
<td>39</td>
</tr>
<tr>
<td>WATS³D Negative</td>
<td>24</td>
<td>145</td>
<td>169</td>
</tr>
<tr>
<td>Total</td>
<td>39 (18.8%)</td>
<td>169</td>
<td>208</td>
</tr>
</tbody>
</table>

Iorio et al. DDW 2015 abstract 345

**Kappa Values Among Pathologists in the Diagnosis of BE and Dysplasia Using WATS Technique**

<table>
<thead>
<tr>
<th>Overall (95% CI)</th>
<th>HGD/EAC (95% CI)</th>
<th>IND/LGD (95% CI)</th>
<th>NDBE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.86 (0.75-0.97)</td>
<td>0.95 (0.88-0.99)</td>
<td>0.74 (0.61-0.85)</td>
<td>0.88 (0.81-0.94)</td>
</tr>
</tbody>
</table>

BE, Barrett’s esophagus; CI, confidence interval; EAC, esophageal adenocarcinoma; HGD, high-grade dysplasia; IND, indeterminate for dysplasia; NDBE, non-dysplastic Barrett’s esophagus; WATS, wide-area transepithelial sampling.

Is this Barrett’s?

Screening, diagnosis and staging:

• The normal-appearing and normally located squamocolumnar junction should not be biopsied.

  – Agreement: 19/22 = 86.3%
  – Grade of Recommendation: Strong
  – Quality of Evidence: Moderate
Questions Regarding Therapy

• Do PPIs change natural history?
• Does high dose PPI matter?
• Does antireflux surgery alter natural history?
• Does ablation of non dysplastic Barrett’s alter the natural history?

• The answer to all these questions are debated HOWEVER NO THERAPY ELIMINATES THE RISK OF CANCER?

What do PPIs do to Acid Reflux?

What do PPIs do to Bile

Surveillance:

- If systematic surveillance biopsies performed in a patient known to have BE show no evidence of dysplasia, follow-up surveillance endoscopy should be recommended no sooner than in 3 to 5 years.

  - Agreement: 21/23 = 91.3%
  - Grade of Recommendation: Weak
  - Quality of Evidence: Low
Barrett’s Progression

Sharma, Clin Gastro Hep 2006;4:566

Non-Dysplastic BE Progression to Cancer in Several Recent Studies Averaged .29% per Year

de Jong, Gut, 2010
Desai, Gut, 2011
Wani, Clin Gastroenterol Hepatol, 2011
Bhat, J Nati Cancer Inst, 2011
Long Segment NDBE Progresses to HGD/EAC at a Significantly Elevated Rate

IM Progression to HGD/EAC by Length
(Anaparthy, Clin Gastroenterol Hepatol, 2013)

- Multi-center outcomes project
- 1175 NDBE pts were followed for a mean of 5.5 yrs
- 28% increase in risk of progression to HGD/EAC per 1 cm increase in length (p<0.001)
- Annual progression rate to HGD/EAC by length (p<0.0018):
  - 0.31%/year for length ≤3 cm
  - 0.97%/year for length 4-6 cm
  - 1.26%/year for length 7-9 cm
  - 1.64%/year for length 10-12 cm
  - 2.41%/year for length ≥13 cm

Surveillance:

- If a patient with known BE undergoes surveillance endoscopy, systematic biopsies should be taken from every 1 to 2 cm in 4 quadrants throughout the extent of the endoscopically involved segment.

  - Agreement: 22/23 = 95.7%
  - Grade of Recommendation: Strong
  - Quality of Evidence: Moderate
Surveillance:

- If a patient with known BE undergoes surveillance endoscopy, biopsies from any visible raised or depressed lesions should be obtained and processed separately from the systematic biopsies.
  
  - Agreement: 22/23 = 95.7%
  - Grade of Recommendation: Strong
  - Quality of Evidence: Moderate

Confirmed LGD Will Likely Progress

LGD Progression to HGD/EAC

(Skacel, Am J Gastroenterol, 2000)

- A retrospective review of 25 pts diagnosed with LGD by 3 independent pathologists
- If 2 – 3 pathologists agreed on a LGD diagnosis then 41 – 80% progressed to HGD or cancer in a median time of 11 mos
Confirmed LGD Carries a Substantial Annual Cancer Progression Risk

**LGD Progression to EAC**
*(Curvers, Am J Gastroenterol, 2010)*

- Population-based study (Amsterdam Gastroenterological Association Barrett’s Registry)
- 147 LGD pts from community hospitals were reviewed by two expert GI pathologists
- Confirmed LGD pts had a 13.4% annual HGD+EAC progression risk, 3.4% for EAC alone

Treatment and management of Barrett’s and early cancer:

- In patients with dysplastic BE or early EAC, a diagnostic endoscopic resection should be performed on any raised or suspicious areas.
  - Agreement: 22/23 = 95.6%
  - Grade of Recommendation: Strong
  - Quality of Evidence: Moderate
Treatment and management of Barrett’s and early cancer:

- In patients with BE-associated neoplasia, the goal of the endoscopic treatment should be complete eradication of the BE segment in addition to any dysplastic lesions.

  - Agreement: 23/23 = 100%
  - Grade of Recommendation: Strong
  - Quality of Evidence: Moderate

RFA Effectively Ablates Barrett’s/Dysplasia

RFA Significantly Decreases Progression of Barrett’s Esophagus


RFA Has Infrequent Recurrence

**UNC Recurrence Study** *(Orman, Am J Gastroenterol, 2013)*

- A retrospective review of 119 BE patients
- The majority of recurrences were similar or lower grade than pre-treatment
- In pts with baseline LGD, HGD, and IMC, annual recurrence rates were 2.4%, 5.5% and 9.4%, respectively
- “In general, these results should serve to reassure patients and their physicians that, in most cases, RFA induces a durable complete eradication of dysplasia and intestinal metaplasia.”
High Remission at 5 Years After RFA for HGD/IMC

Remission 5 Years After RFA± EMR
(Phoa, Gastroenterology, 2013)

- Prospective trial of 54 patients with HGD/IMC treated with RFA±EMR
- 90% of pts IM free 5 years after CR-IM; only pts with entry diagnosis of IMC recurred
- 0.7% annual development of EAC (only in pts with IMC entry diagnosis) vs. ~10% expected, all managed endoscopically
- Gastric cardia IM found in 35% of patients: “The clinical relevance of focal IM of the cardia after RFA is unknown, but our long-term data do not suggest that this is related to residual BE or recurrent disease”

Relative Effectiveness of Ablation to Prevent Progression of LGD to HGD or Cancer

<table>
<thead>
<tr>
<th>Risk of progression after RFA</th>
<th>HR (95% CI)</th>
<th>P value</th>
<th>Adjusted HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity analysis, variable tested on effect of RFA</td>
<td>0.06 (0.01–0.61)</td>
<td>.02</td>
<td>0.06 (0.02–0.48)</td>
<td>.009</td>
</tr>
<tr>
<td>Only patients with LGD diagnosed from 2006 to end of study period (excluded all cases diagnosed before 2006)</td>
<td>0.09 (0.01–0.73)</td>
<td>.02</td>
<td>0.09 (0.01–0.73)</td>
<td>.02</td>
</tr>
<tr>
<td>Flat LGD excluded all patients with nodularity</td>
<td>0.10 (0.01–0.91)</td>
<td>.03</td>
<td>0.10 (0.01–0.91)</td>
<td>.03</td>
</tr>
<tr>
<td>Progressions after &gt;1 year (excluded all patients who progressed within the first year in surveillance group)</td>
<td>0.13 (0.02–0.96)</td>
<td>.04</td>
<td>0.13 (0.02–0.96)</td>
<td>.04</td>
</tr>
</tbody>
</table>

Progression to HGD or Adenocarcinoma from First RFA or Surveillance Endoscopy

Proportion of Patients without EAC After Ablation


Wolf WA, et al. Gastroenterology 2015; epub
Probability of Developing EAC

Survival

Wolf WA, et al. Gastroenterology 2015; epub
IF YOU'RE DOING YOUR BEST, YOU WON'T HAVE TIME TO WORRY ABOUT FAILURE.

thingsweforget.blogspot.com

THE END