Barrett’s Esophagus: Surveillance and Management

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Outline

- Introduction
- Medical Management
- Endoscopic Surveillance
- Endoscopic Therapies
- Surgical Management
- A word on Staging...
Introduction
Early History

- 1906 → Columnar lining of lower esophagus first described
  - Tileston’s review of 44 patients with peptic ulceration occurring in lower esophagus

- 1950 → Barrett’s article, “Chronic Peptic Ulcer of the Oesophagus and Oesophagitis
  - 1st detailed description
  - Interpreted condition as congenitally short esophagus with intrathoracic stomach
Early History

- **1953 → Allison and Johnstone**
  - Demonstrated that changes occurred in esophagus were (possibly) due to GERD
  - Mucosa transformed from squamous to columnar epithelium

- **1957 → Barrett accepted interpretation of Allison and Johnstone**
  - Proposed that condition simply be described as “the lower esophagus lined by columnar epithelium”
Barrett’s Esophagus

- Change in the lining of the distal esophagus (salmon colored)
- Long segment Barrett’s esophagus $\Rightarrow$ > 3 cm above the GE junction
- Short segment Barrett’s esophagus $\Rightarrow$ < 3 cm above the GE junction
Barrett’s Esophagus

- Intestinal metaplasia: (proven by biopsy)
  - Transition from squamous → columnar epithelium
  - Goblet cells

- Precursor lesion for adenocarcinoma of the esophagus
Barrett’s Esophagus

- Patients have very disturbed esophageal physiology

- LES pressures are lowest in these patients
  - Mean LES pressure $\rightarrow$ 5 mm Hg with Barrett’s
  - Mean LES pressure $\rightarrow$ 9 mm Hg with simple GERD
  - Mean LES pressure $\rightarrow$ 17 mm Hg in controls

- Patients can have low amplitude and nonperistaltic esophageal contractions (resulting from inflammation)
Barrett’s Esophagus

- Slower esophageal transit → poor clearance of refluxed gastric contents

- Acid and BILE reflux is most severe in these patients

- Reflux patterns are different:
  - Nocturnal reflux occurs more frequently in patient’s with Barrett’s esophagus
Barrett’s Esophagus

- Patients typically have aberrant anatomy at GE junction
  - Hiatal hernia of 2 cm or greater ➔ 96% of patients w/Barrett’s
  - Diaphragmatic hiatus is larger in patients with Barrett’s than with hiatal hernia alone
  - Peptic stricture and esophageal shortening ➔
    - Reflux also results in edema, spasm, and eventual fibrosis of the mucosa, submucosa, and muscularis propria
Medical Therapy
Proton Pump Inhibitors

- Eliminates reflux symptoms

- Usually results in resolution of erosive esophagitis

- Allows more accurate surveillance and biopsy of suspicious lesions
  - Interpretation can be difficult for the pathologist in the background of esophagitis
Proton Pump Inhibitors

- Control of symptoms does NOT mean normalization of inter-esophageal pH
  - Even high-dose, 2XD PPI therapy does not control esophageal acid exposure in 25% of patients with Barrett’s esophagus

- Volume reflux or regurgitation is not well controlled with PPIs
Proton Pump Inhibitors

- Does not reliably or completely restore normal squamous epithelium
- May not eliminate or prevent complications
- Does not do away with the need for continued endoscopic surveillance for cancer
Endoscopic Surveillance
Endoscopic Surveillance

- Current standard of practice in the United States

- Goal:
  - the prevention of cancer or early detection of esophageal adenocarcinoma
Endoscopic Surveillance

- Driven by the grade of dysplasia
- Esophagitis must be healed
  - to improve the interpretation of dysplasia
Endoscopic Surveillance

- Any mucosal irregularity is sampled

- For metaplasia and LGD:
  - Four-quadrant every 2 cm

- For HGD:
  - Four-quadrant biopsies every 1 cm
<table>
<thead>
<tr>
<th>Dysplasia</th>
<th>Documentation</th>
<th>Follow-up EGD</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>2 EGDs with biopsy</td>
<td>3-5 years</td>
</tr>
<tr>
<td>LGD</td>
<td>Highest grade on repeat endoscopy</td>
<td>1 year until no dysplasia</td>
</tr>
<tr>
<td>HGD</td>
<td>Repeat EGD with biopsy to rule out cancer/document HGD</td>
<td>Mucosal irregularity—endoscopic resection</td>
</tr>
<tr>
<td></td>
<td>Obtain expert pathologist's confirmation</td>
<td>Individualize intervention</td>
</tr>
</tbody>
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EGD, esophagogastroduodenoscopy; HGD, high-grade dysplasia; LGD, low-grade dysplasia.
Endoscopic Technology Research

- Focused on optical recognition of dysplasia for better biopsy targeting and endoscopic resection/ablation
  - High-resolution endoscopy, narrow band imaging, confocal microscopy, autofluorescence, Raman spectroscopy, optical coherence tomography

Autofluorescence endoscopy: area of HGD seen in purple
Endoscopic Therapy
Endoscopic Therapy

- Radiofrequency ablation
- Cryospray ablation
- Photodynamic therapy
- Argon beam coagulation
- Endoscopic mucosal resection

RISKS: Progression, inability to provide histologic material, possible buried Barrett’s segment
Endoscopic Therapy

- Radiofrequency ablation
Multicenter, sham-controlled trial

127 pts w/Barrett’s were assigned 2:1 to receive RFA or sham procedure

Eradication of dysplasia in 90.5% of ablation group vs. 22.7% of control group (P<0.001)

Overall eradication in 77.4% of ablation group vs. 2.3% of control group

Less disease progression (3.6% vs. 16.3%, P=0.03) in ablation group

Fewer cancers (1.2% vs. 9.3%, P=0.0045) in ablation group

COMPLICATIONS: One patient had upper GI bleeding and 5 patients had esophageal strictures

Shaheen NJ et al. NEJM. 2009;360(22):2277-88
Endoscopic Therapy

- Cryospray ablation
Endoscopic Therapy

- **Photodynamic therapy**

  - Nd:YAG laser activation of light-sensitive drugs that concentrate in pre-neoplastic tissue

  - **Porfimer sodium** (Photofrin) is injected intravenously

  - Causes it to release damaging oxygen free radicals
Endoscopic Therapy

- Photodynamic therapy (PDT)
  - Overhold and Panjehpour:
    - 103 patients with low grade, high grade dysplasia, or early cancer
    - Mean follow up of 58.5 months in 82 patients
    - 65 pts with HGD $\rightarrow$ 94% cure rate
    - 3 pts developed subsquamous carcinoma
Endoscopic Therapy

- Photodynamic therapy (PDT)

  - Overhold and Panjehpour:
    - Subsquamous metaplastic (but not nondysplastic) epithelium was found in 4.9%
    - Strictures occurred in 18% after one session, and 50% after two sessions
    - Success rates: 92.9%, 77.5%, and 44.4% for LGD, HGD, and early cancer
Endoscopic Therapy

- Photodynamic therapy (PDT)

  - Multicenter randomized trial of 208 patients with Barrett’s esophagus and HGD:
    - PDT eliminated HGD in 77% of patients versus 35% without PDT (P<0.001).
    - In 2 years, esophageal adenocarcinoma developed in 13% of the PDT arm vs. 28% of the control arm (P=0.006)
    - 30% of patients developed strictures, and photosensitivity reactions were common
Endoscopic Therapy

- Argon beam coagulator
  - Noncontact electrocoagulation device
  - Provides high-frequency monopolar current to the tissue via a flow of ionized argon gas
  - Requires several successive sessions especially with circumferential Barrett’s esophagus
Endoscopic Therapy

- **Argon beam coagulator**
  - **Van Laethem et al.**
    - 10 patients (7 with HGD, 3 with adenocarcinomas)
    - 8 showed complete regression
    - 1 progressed to cancer
    - 1 had persistent HGD
  - **Attwood et al.**
    - 29 patients with HGD
    - 22 had complete regression
    - 4 developed cancer at mean follow-up of 37 months
Endoscopic Therapy

- **Endoscopic Mucosal Resection (EMR)**
  - Can be used to sample an area of 20mm diameter
  - Submucosa is expanded by normal saline injection
  - Hot snare device is used for mucosal resection
Endoscopic Therapy

- Endoscopic Mucosal Resection
  - Lesions are removed piecemeal or as single piece
  - Removal as one single specimen is preferable to improve completeness of resection and to assess depth and resection margins
    - Risk of missing invasive cancer (T1b → invading the submucosa) decreases substantially in patients with HGD or T1a carcinoma
Endoscopic Therapy

- **EMR: Vieth and coworkers**
  - 742 EMR specimens from 326 patients
  - Complete resection in 74.5% of patients
    - 26.8% after one attempt
    - 47.8% after repeated sessions
  - 84% of lesions contained LGD, HGD, or T1a tumor
  - 16% had tumor infiltrating submucosa

- Recurrence rate of 25-30% during first 3 years after EMR for HGD or T1a cancer is expected
Indications for Surgery
Indications for Surgery
Indications for Surgery

- Laparoscopic antireflux surgery
  - For symptom control
  - Complications
    - Ulceration
    - Strictures (following use of medical Tx & dilation, and complete workup)
  - Metaplasia $\rightarrow$ Dysplasia $\rightarrow$ Carcinoma sequence
Laparoscopic Antireflux Surgery

- Results for typical symptoms
  - Parilla et al: At 5 years follow up…
    - Excellent or good symptoms control with antireflux surgery in 91%
  - Oelschlager et al: At 40 months follow up…
    - Heartburn: resolution 70%, improvement 26%, no improvement 4%
    - Regurgitation: resolution 75%, improvement 9%, no improvement 16%
    - Dysphagia: resolution 64%, improvement 18%, no improvement 18%
Laparoscopic Antireflux Surgery

- Results for atypical symptoms
  - Chest pain, chronic cough, asthma, hoarseness, globus sensation, halitosis, laryngitis, sore throat, enamel loss
  - Cannot be predicted
  - 50% chance of relief
Laparoscopic Antireflux Surgery

- Rarely produces significant regression of Barrett’s metaplasia

- (Several limited reports exist suggesting regression from low-grade dysplasia to metaplasia)
Indications for Esophagectomy

- Non-malignant Barrett’s Esophagus
  - Non-dilatable strictures
  - Penetrating ulcers
  - End-stage, nonfunctioning esophagus

- NOT indicated in cases of need for long-term surveillance in the young patient
Indications for Esophagectomy

- High grade dysplasia
  - Considered intraepithelial carcinoma
  - Difficulty in differentiating high-grade dysplasia from intramucosal carcinoma
  - In 50% of resected specimens from esophagectomy for HGD, intramucosal carcinoma or more invasive cancers can exist
  - Overall risk for developing esophageal adenocarcinoma is estimated to be 50-350 times higher.
Indications for Esophagectomy

- For cancer
  - 5-year cancer-free survival with esophagectomy for HGD and T1a > 90%
  - For T1b, dependent on nodal involvement
    - No nodes, 5-year survival > 90%
    - With nodal involvement, 5-year survival 40-60%
    - Morbidity rate 20-45%
    - Mortality rate 1-5%

[Figure 30.2: Early (T1) adenocarcinoma in Barrett’s esophagus. Cancer specific survival in T1a and T1b. (Data from the LEVY database 1990-2000)]
Tumor Depth and Lymph Node Status

TUMOR DEPTH IS EXTREMELY IMPORTANT!

<table>
<thead>
<tr>
<th>Tumor Depth</th>
<th>Prevalence of Node Metastases[†]</th>
<th>No. of Involved Nodes (median [IQR][‡])</th>
<th>No. With 1-4 Involved Nodes[#]</th>
<th>No. With &gt;4 Involved Nodes[$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intramucosal</td>
<td>1/16 (6.25%)</td>
<td>2 (n/a)</td>
<td>1/16 (6.25%)</td>
<td>0/16 (0)</td>
</tr>
<tr>
<td>Submucosal</td>
<td>5/16 (31.25%)</td>
<td>1 (n/a)</td>
<td>4/16 (25%)</td>
<td>1/16 (6.25%)</td>
</tr>
<tr>
<td>Intramuscular</td>
<td>10/13 (76.92%)</td>
<td>2 (1-4)</td>
<td>9/13 (69.1%)</td>
<td>1/13 (7.69%)</td>
</tr>
<tr>
<td>Transmural</td>
<td>47/55 (85.45%)</td>
<td>5 (3-13.5)</td>
<td>22/55 (40%)</td>
<td>25/55 (45.45%)</td>
</tr>
</tbody>
</table>

* $X^2 = 42.0$, $P < .0001$ (Chi square test for trend).
† $X^2 = 11.02$, $P = .0116$ (Kruskal-Wallis) includes only patients with involved nodes.
‡ $X^2 = 13.64$, $P = .0035$ (Chi square test for trend).
§ $X^2 = 21.38$, $P < .0001$ (Chi square test for trend).
A word on Staging...
Staging

- Accurate staging is ESSENTIAL!
  - Determine if lesion is appropriate for endoscopic therapy (HGD…)
  - Superficial and without regional LNs

- Endoscopic resection for depth of wall invasion (T classification)

- Endoscopic ultrasonography with FNA for lymph node involvement

Lymph node biopsy (FNA) through the tumor would lead to a false positive result.
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