Barrett’s Esophagus and Endoscopic Therapy

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Disclosures: Research support from CSA Medical Inc.
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Objectives

• Relationship of BE, acid reflux and esophageal cancer
• Screening and surveillance guidelines
• Management of dysplasia and early cancers
Esophagogastric Junction

Squamocolumnar junction

View on retroflexion
Esophagogastric Junction

• Definitions
  – **Squamocolumnar junction** (SCJ) = juxtaposition of the squamous and columnar mucosa
  – **Esophagogastric junction** (EGJ) = dynamic area including the distal esophagus and proximal stomach
  – **Hiatal hernia** = foreshortened esophagus with proximal stomach herniated into the chest
  – **Columnar lined esophagus** = SCJ displaced proximal to EGJ
Acid Reflux and EGJ

Ring during distention

Same ring during contraction
Hiatal Hernia and Esophagitis

Lax LES

Small erosions
Histology of the EGJ

- Junction-type epithelium
  - Tortuous, tubular mucus secreting glands without parietal cells
  - 1 to 4 mm in children autopsy study

Ormsby, Mod Path 2000
Kilgore, Am J Gastroenterol 1999
Histology of the EGJ

Alcian blue/PAS+

Squamocolumnar Junction
Hiatal Hernia and Erosive Esophagitis

LA Grade C: ≥1 mucosal breaks bridging the tops of folds but involving <75% of the circumference

LA Grade D: ≥1 mucosal breaks bridging the tops of folds and involving >75% of the circumference
Healing after Erosive Esophagitis

Hiatal hernia with short segment Barrett’s

Severe peptic stricture
Barrett’s and Esophageal Cancer

Long segment BE with mass lesion

Mass lesion is EUS stage T2N1
Barrett’s Esophagus

- Pathogenesis of Barrett’s
  - Repair of injured distal esophageal mucosa
  - Animal model of surgical hiatal hernia with increased acid secretion induces columnar epithelium
- Cell of origin candidates:
  - esophageal glandular cells
  - gastric cardia mucosa
  - primordial stem cell
Intestinal Metaplasia
### Endoscopic Screening for BE

<table>
<thead>
<tr>
<th>Criteria for Effective Screening Tool</th>
<th>BE Screening?</th>
</tr>
</thead>
<tbody>
<tr>
<td>High incidence disease</td>
<td>BE-yes Ca-no</td>
</tr>
<tr>
<td>High death/disability rate</td>
<td>BE-no Ca-yes</td>
</tr>
<tr>
<td>Early treatment decreases mortality</td>
<td>BE-no Ca-yes</td>
</tr>
<tr>
<td>Tool easy to apply and acceptable</td>
<td>No</td>
</tr>
<tr>
<td>Inexpensive</td>
<td>No</td>
</tr>
<tr>
<td>Accurate test</td>
<td>Yes</td>
</tr>
<tr>
<td>Subsequent f/u acceptable</td>
<td>?</td>
</tr>
</tbody>
</table>
Barrett’s Screening Rationale

1. Rising incidence of esophageal adenocarcinoma
Esophageal Cancer

• Distal esophageal and GEJ cancer mortality rate increased 4-fold over the last 20 years

• 5- to 6-fold increase from 1940 to 1989
  – Esophagus 3.6 / 100,000 (+3.6 APC)
  – Stomach 4.3 / 100,000 (-2.8 APC)
<table>
<thead>
<tr>
<th>Tissue</th>
<th>Both</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestive system</td>
<td>271,290</td>
<td>148,560</td>
<td>122,730</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>148,810</td>
<td>77,250</td>
<td>71,560</td>
</tr>
<tr>
<td>Pancreas</td>
<td>37,680</td>
<td>18,770</td>
<td>18,910</td>
</tr>
<tr>
<td>Stomach</td>
<td>21,500</td>
<td>13,190</td>
<td>8,310</td>
</tr>
<tr>
<td>Liver</td>
<td>21,370</td>
<td>15,190</td>
<td>6,180</td>
</tr>
<tr>
<td>Esophagus</td>
<td>16,470</td>
<td>12,970</td>
<td>3,500</td>
</tr>
<tr>
<td>Small intestine</td>
<td>6,110</td>
<td>3,200</td>
<td>2,910</td>
</tr>
</tbody>
</table>
## Estimated Cancer Deaths US 2008

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Both</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestive system</td>
<td>135,130</td>
<td>74,850</td>
<td>60,280</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>49,960</td>
<td>24,260</td>
<td>25,700</td>
</tr>
<tr>
<td>Pancreas</td>
<td>34,290</td>
<td>17,500</td>
<td>16,790</td>
</tr>
<tr>
<td>Liver</td>
<td>18,410</td>
<td>12,570</td>
<td>5,840</td>
</tr>
<tr>
<td>Esophagus</td>
<td>14,280</td>
<td>11,250</td>
<td>3,030</td>
</tr>
<tr>
<td>Stomach</td>
<td>10,880</td>
<td>6,450</td>
<td>4,430</td>
</tr>
<tr>
<td>Small intestine</td>
<td>1,110</td>
<td>580</td>
<td>530</td>
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</tbody>
</table>

ACS www.cancer.org
**Male Cancer Deaths 2008**

<table>
<thead>
<tr>
<th></th>
<th>Cancer Type</th>
<th>Deaths</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Lung &amp; bronchus</td>
<td>90,810</td>
<td>31%</td>
</tr>
<tr>
<td>2.</td>
<td>Prostate</td>
<td>28,660</td>
<td>10%</td>
</tr>
<tr>
<td>3.</td>
<td>Colon &amp; rectum</td>
<td>24,260</td>
<td>8%</td>
</tr>
<tr>
<td>4.</td>
<td>Pancreas</td>
<td>17,500</td>
<td>6%</td>
</tr>
<tr>
<td>5.</td>
<td>Liver &amp; intrahep bile duct</td>
<td>12,570</td>
<td>4%</td>
</tr>
<tr>
<td>6.</td>
<td>Leukemia</td>
<td>12,460</td>
<td>4%</td>
</tr>
<tr>
<td>7.</td>
<td>Esophagus</td>
<td>11,250</td>
<td>4%</td>
</tr>
<tr>
<td>8.</td>
<td>Urinary bladder</td>
<td>9,950</td>
<td>3%</td>
</tr>
<tr>
<td>9.</td>
<td>Non-Hodgkin lymphoma</td>
<td>9,790</td>
<td>3%</td>
</tr>
<tr>
<td>10.</td>
<td>Kidney &amp; renal pelvis</td>
<td>8,100</td>
<td>3%</td>
</tr>
</tbody>
</table>
INCIDENCE OF ESOPHAGEAL ADENOCARCINOMA IN POPULATION BASED STUDIES

Esophageal Adenocarcinoma and Colon Cancer Screening

- Esophageal adenocarcinoma incidence
  - 3 per 100,000
- Colon cancer incidence
  - 58 per 100,000
Barrett’s Screening Rationale

1. Rising incidence of esophageal adenocarcinoma
2. Reflux symptoms are a risk factor for BE and esophageal cancer
Barrett’s Esophagus

How common is BE?

≤ 1% of unselected autopsies
≤ 1% of patients without GERD symptoms
6% - 12% of symptomatic GERD patients
## GERD Symptoms and BE

<table>
<thead>
<tr>
<th></th>
<th>Barrett’s (N=79)</th>
<th>GERD (N=94)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe symptoms</td>
<td>85%</td>
<td>59%</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Duration (yr)</td>
<td>16.36</td>
<td>11.81</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age of onset (yr)</td>
<td>35.3 ± 16</td>
<td>43.7 ± 13</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Eisen  Am J Gastroenterol 1997;92:27
Barrett’s Esophagus

• Who develops Barrett’s?
  – Clearly associated with severe GERD
  – Male:female ratio 9:1
  – Hiatal hernia
  – Low LES pressures
BE & Duration of GERD Symptoms

Lieberman  Am J Gastroenterol 1997;92:1293
<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent reflux</td>
<td>(1 / wk)</td>
<td>7</td>
</tr>
<tr>
<td>Frequent reflux</td>
<td>(&gt;3 / wk)</td>
<td>16</td>
</tr>
<tr>
<td>Severity &amp; duration</td>
<td>(&gt;20 yr.)</td>
<td>43</td>
</tr>
</tbody>
</table>

Lagergeren NEJM 1999
Barrett’s Screening Rationale

1. Rising incidence of esophageal adenocarcinoma
2. Reflux symptoms are a risk factor for BE and esophageal cancer
3. Barrett’s esophagus is the only known intermediate stage
Rising Incidence of BE in Olmstead County

Conio Gut 2001
North America Estimates of Barrett’s and Esophageal Cancer

Barrett’s Esophagus Disease State

- SIM: 4,290,000
- LGD: 1,980,000
- HGD: 330,000
- CA: 20,513
Barrett’s and Esophageal Cancer

- Mean annual incidence of cancer in long- and short- segment BE is ~0.5%
  - 30-fold increase over the general population

Short segment BE Elevated lesion < 20mm diameter
Short-Segment Barrett’s

- Dilemmas of the expanded definition of BE
  - Differentiation from gastric metaplasia
  - Differentiation from cardia intestinal metaplasia
  - Natural history of ultra-short segment BE
REPORTED CANCER RISK IN BARRETT'S ESOPHAGUS VERSUS SIZE OF STUDY

Barrett’s Screening Rationale

1. Rising incidence of esophageal adenocarcinoma
2. Reflux symptoms are a risk factor for BE and esophageal cancer
3. Barrett’s esophagus is the only known intermediate stage
4. Early detection provides better survival
Barrett’s Screening Rationale

• Only 5% of esophageal adenocarcinoma cases occur in patients with known Barrett’s esophagus
### Five-Year Relative Survival Rates by Stage at Diagnosis 1996-2003

<table>
<thead>
<tr>
<th>Tumor Site</th>
<th>Local</th>
<th>Regional</th>
<th>Distant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>33.7</td>
<td>16.9</td>
<td>2.9</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>89.8</td>
<td>67.7</td>
<td>10.3</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>98.0</td>
<td>83.5</td>
<td>26.7</td>
</tr>
<tr>
<td>Pancreas</td>
<td>20.3</td>
<td>8.0</td>
<td>1.7</td>
</tr>
<tr>
<td>Stomach</td>
<td>61.1</td>
<td>23.7</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Ries SEER Cancer Statistics Review, 1975-2004
Impact of Surveillance in Barrett’s Associated Cancers
Impact of Surveillance in Barrett’s Associated Cancers

Corley Gastroenterol 2002
SURVIVAL AFTER ESOPHAGECTOMY FOR CARCINOMA AT THE CLEVELAND CLINIC: NO NEOADJUVANT THERAPY

IMPACT OF ENDOSCOPIC BIOPSY SURVEILLANCE OF BARRETT'S ESOPHAGUS ON CANCER SURVIVAL

Survival (%)

Time after resection (months)

Survveillance (●; n=16)  15 11  6  2  0
Non-Surveillance (○; n=54)  36 15  5  0  0

p = 0.0029

Screening for BE

- GERD symptoms for > 10 years
- Endoscopic biopsy:
  - Columnar epithelium
  - Intestinal metaplasia
  - Any length
Endoscopic Surveillance of Barrett’s
Endoscopic Surveillance of Barrett’s
Distribution of Dysplasia and Cancer in Resection Specimens

Cameron Am J Gastroenterol 1997;92:586
## Endoscopic Surveillance of Barrett’s

<table>
<thead>
<tr>
<th>Dysplasia</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>3 years*</td>
</tr>
<tr>
<td>Indefinite</td>
<td>3 to 6 months after PPI</td>
</tr>
<tr>
<td>Low-grade</td>
<td>12 months</td>
</tr>
<tr>
<td>High-grade</td>
<td></td>
</tr>
<tr>
<td>Focal</td>
<td>3 months</td>
</tr>
<tr>
<td>Multi-focal</td>
<td>Intervention or observation?</td>
</tr>
</tbody>
</table>

*After 2 exams are negative for dysplasia 1 yr apart

*Requires 4-quadrant biopsies every 1 to 2 cm
Why adenocarcinoma of the esophagus is so malignant

- Epithelium
- Adenocarcinoma
- Basement membrane
- Lamina propria
- Muscularis mucosa
- Submucosa
- Muscularis propria
- Lymphatic vessels
- Thoracic duct

CCF ©2001
Staging Esophageal Cancer
SURVIVAL AFTER ESOPHAGECTOMY FOR CARCINOMA AT THE CLEVELAND CLINIC: NO NEOADJUVANT THERAPY

EGJ Cancer

- Extrinsic compression from infiltrative gastric cardia mass
- Prosthetic stent required to maintain lumen
Screening for Barrett’s

• Barriers to screening
  – Cost
  – Screening tool not universally accepted
  – Compliance with follow-up

• Future plans for screening
  – Small bore endoscopes
  – Capsule endoscopy
  – Genetic testing
Capsule Endoscopy Screening for BE

Capsule
Recorder
Lower Sphincter with Short Segment BE
Endoscopic Therapy for BE with Dysplasia?

ASSUMPTIONS

• Esophagectomy may not be in the best interest of all patients
• Observation without intervention may not be the best option in some patients
• Successful eradication of dysplasia and early cancers is possible in some patients
Endoscopic Therapy
Ablation vs. Mucosectomy

Ablation

Pain  Strictures  Cancer cover-up

EMR

Pathologic Staging

Strictures  Bleeding
Photodynamic Therapy (PDT)

Red Light

[Diagram showing the interaction between light, oxygen, and cell death]

Cell Death
PDT for Barrett’s and Early Cancer

Barrett’s segment with IMCa

Cylindrical laser fiber and light
PDT for Barrett’s and Early Cancer

Severe esophagitis – 48 hrs

Follow up surveillance – 1 yr
Two year follow-up reveals ongoing esophagitis due to unremitting reflux.
PDT for Barrett’s and Early Cancer

- Photofrin® only FDA approved therapy
  - 70% - 80% effective
  - Up to 3 treatment sessions required
- Complications
  - Photosensitivity for 30 – 40 days per session
  - Universal chest pain
  - 30% patients stricture
PDT for Barrett’s and Early Cancer

- 100 patients (13 with T1 lesions)
- Light dose 100 to 250 J/cm
- Treatment failures
  – 3 of 13 cancers progressed
- Complications
  – strictures in 34%
  – pain
- Follow up 19 months (4 to 84)

Overholt Gastrointest Endosc 1999

Centering balloons
PDT for Barrett’s HGD

• Multicenter trial
  – 208 patients (2:1) PDT vs. omeprazole
  – Complete ablation HGD 77% (106/138) PDT compared to 39% (27/70) omeprazole group
  – Multiple treatments
    • 68% PDT patients required 2 treatments
    • 47% PDT patients required 3 treatments

Overholt Gastrointest Endosc 2005;62:488
PDT for Barrett’s HGD

• Multicenter trial – 5 year follow up
  – 208 patients (2:1) PDT vs. omeprazole
  – Progression to cancer 15% PDT compared to 29% omeprazole group

Overholt Gastrointest Endosc 2007;66:460
PDT Stricture

Short inflammatory 5 mm stricture

Balloon dilation to 16 mm
Barrett’s Esophagus after PDT

Residual islands of dysplasia

BICAP ablation
Cleveland Clinic Experience with PDT

- 17 patients (12 IMCA / 5 HGD)
  - Follow up 2.3 (±1.7) years
  - Age 78.9 (±5.1)
  - BE length 5.8 (±2.2) cm

![Pie chart showing distribution of treatments: 42% PDT alone, 29% PDT + other endoscopic treatments, 29% Non-responders]
RFA - HALO\textsuperscript{360} System

• Circumferential balloon-ablation
• Controlled depth
  – energy density, electrode geometry
RFA - HALO$^{90}$ System

- Scope-mounted ablation
- Primary therapy
  - short segment Barrett’s
  - touch-up residual disease
AIM II Complete Response

Complete response to SIM in 98% patients (n = 70)
2.5-year follow-up after stepwise circumferential and focal ablation

Fleischer Gastrointest Endosc 2008
RFA Advantages

• Limited depth of injury
  – Limits strictures
• Immediate effect
• No restrictions on surgical anatomy or complex hiatal hernias
RFA Limitations

- Limited depth of injury
  - Inadequate for nodular areas
- Requires contact with mucosa
- Skip areas and residual disease
RFA Limitations

- EGJ most like area for failure
RFA Summary

• 85-98% Complete response IM and dysplasia
  – Elimination of abnormal genetic markers
  – Preservation of esophageal function
  – Safety profile high with low incidence strictures
  – Pain significant and requires management

• Requires contact with the mucosa
  – Difficult to treat in strictures or angulated lumen
  – Inadequate response with nodular mucosa
LN Cryotherapy
Mechanism of Injury

The freeze-thaw cycle

- Ice crystals disrupt lipids and cytoskeleton
- Ischemia and vascular stasis
- Reperfusion injury with cellular leakage and submucosal hemorrhage
- Inflammatory response
- Immune stimulation
LN Cryotherapy Depth of Injury

1 hour: minimal inflammation

48 hours: marked inflammation

Johnston Gastrointest Endosc 2001 A3448
LN Cryotherapy Advantages

• High patient tolerance
  – Minimal chest pain
  – Familiarity with concept

• Able to treat uneven surfaces

• Possible to treat submucosal lesions

Greenwald DDW 2007
LN Cryotherapy

• Dosimetry
  – Spray duration
    (10 – 20 seconds)
  – Spray cycles
    (2 – 4)
LN Cryotherapy Risks

• Liquid nitrogen conversion to gas
  – 20 second spray releases 7 – 8 liters
  – Perforation 3 of 116 patients; 365 cases
    • 2 Gastric rents from over distention
    • 1 Pneumoperitoneum
LN Cryotherapy Risks

- Strictures 4%
  - Appears limited to those with prior narrowing or therapy
- Lip ulcer
- Pain usually mild – 0 to 5 days
### TABLE 1. Cryoablation results

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (y)</th>
<th>Precryo BE length (cm)</th>
<th>Postcryo BE length (cm)</th>
<th>BE length 6 mo after cryo</th>
<th>No. cryo sessions</th>
<th>Reversal</th>
<th>Histologic reversal at 6 mo</th>
<th>Dysplasia before cryo</th>
<th>Dysplasia after cryo</th>
<th>Subsquamous SIM (no. Bxs) at 1 mo after cryo</th>
<th>Subsquamous SIM (no. Bxs) at 6 mo after cryo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>Yes</td>
<td>No</td>
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<td>None (12)</td>
<td>None (12)</td>
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<tr>
<td>2</td>
<td>51</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6</td>
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<td>Yes</td>
<td>LGD</td>
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<td>None (4)</td>
<td>None (4)</td>
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<tr>
<td>3</td>
<td>72</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>8</td>
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<td>No</td>
<td>LGD</td>
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<td>None (20)</td>
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<tr>
<td>4</td>
<td>74</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
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<td>Yes</td>
<td>LGD</td>
<td>None</td>
<td>None (12)</td>
<td>None (12)</td>
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<tr>
<td>5</td>
<td>57</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>5</td>
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<td>Yes</td>
<td>IFD</td>
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<td>None (16)</td>
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<tr>
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<td>Yes</td>
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<td>4</td>
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<td>0</td>
<td>4</td>
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<td>Yes</td>
<td>LGD</td>
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<tr>
<td>8</td>
<td>53</td>
<td>3</td>
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<td>0</td>
<td>4</td>
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<td>No</td>
<td>None</td>
<td>None</td>
<td>None (12)</td>
<td>None (8)</td>
</tr>
<tr>
<td>9</td>
<td>53</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>Yes</td>
<td>No</td>
<td>LGD</td>
<td>None</td>
<td>None (12)</td>
<td>None (12)</td>
</tr>
<tr>
<td>10</td>
<td>50</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
<td>None</td>
<td>1 Bx “+” of 12</td>
<td>None (12)</td>
<td>None (12)</td>
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<tr>
<td>11</td>
<td>64</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>HGD</td>
<td>1 Bx “+” of 24</td>
<td>None (20)</td>
<td>None (20)</td>
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<tr>
<td>Mean</td>
<td>59</td>
<td>4.6</td>
<td>0.27</td>
<td>46</td>
<td>64%</td>
<td></td>
<td>2/160 (1.25%)</td>
<td>0/148 (0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*BE*, Barrett’s esophagus; *SIM*, specialized intestinal metaplasia; *Bx*, biopsy; *LGD*, low-grade dysplasia; *IFD*, indefinite for dysplasia; “+”, positive for subsquamous SIM; *HGD*, high-grade dysplasia.
LN Cryotherapy with EMR

Probability of Cancer Free Survival

- Proportion cancer free

- Months Post-CSA

- N At Risk

- N at Risk: 31, 28, 23, 22, 14, 10

Dumot Gastrointest Endosc 2009
LN Cryotherapy and Squamous Cell Cancer

- SSC case series (n = 6)
  - 74 years median age (IQR 65 – 82)
    - 2 Tsm1 and 4 Tm
    - 20 mm median size (IQR 14-26)
    - Cricopharyngeus (3), diverticulum (1), stricture (3), varices (1) and prior radiation therapy (3)
  - Uniform response
    - 5 of 6 local complete response
LN Cryotherapy and Squamous Cell Cancer

Invasive SCC
PET positive
3rd head / neck ca
Future Goals

• Improve decompression
  – Safety
  – Increase dosimetry (depth of injury)
  – Reduce treatment times

• Improve visibility
LN Cryotherapy Summary

• Unique mechanism
  – Noncontact technique effective for lesions in difficult topography
  – Depth of injury capable of treating early cancers

• High patient acceptance
  – Low incidence of pain and strictures
  – Patient familiarity
Cap-fitted Technique

- Crescent-type snare
- Friction fit caps
- Disposable injection needle
Cap-fitted EMR Technique

- Submucosal injection is made in standard fashion
- Crescent-shaped snare is “pre-looped” into the cap rim
- Cap sucks lesion into cap and strangulates lesion
- Snare is closed and suction is released then cut tissue
- Cap is used to aspirate the resected lesion
Band-Ligation Technique

- Standard E.V.L. device or Duette®
- Deploy rubber band around lesion
- Hexagon-type snare

Suzuki et al. GE 1999;49:192-9
Ell et al. Gastro 2000;119:670-7
EMR-Ligation vs. EMR-Cap: Early Esophageal CA

- 100 endoscopic resections (72 patients)
  - 50 EMR-L (w/o SM lift)
  - 50 EMR-C (w/ SM lift: diluted epinephrine and saline)

- Specimen (max. dia. / mm) (max. area / mm$^2$)
  - EMR-L  16.4 x 11  185
  - EMR-C  15.5 x 10.7  168

- Site at 24 hr
  - EMR-L  20.6 x 14.3  314
  - EMR-C  18.9 x 12.9  260

Failure rate:
  - 1/50 (2%) EMR-L (due to scarring from prior procedures)
  - 6/50 (12%) EMR-C (technical difficulties)

May Gastrointest Endosc 2003;57:167
Short Segment Barrett’s and Esophageal Cancer

- Short segment BE with TisN0 mass
- 1 month after EMR
- Surveillance at 6 years
# Endoscopic Therapy for Early Cancers in BE: Mayo Clinic Experience

<table>
<thead>
<tr>
<th></th>
<th>Surgery (n=64)</th>
<th>EMR/PDT (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex (M/F)</strong></td>
<td>58 / 6</td>
<td>21 / 3</td>
</tr>
<tr>
<td><strong>Age (mean±SE)</strong></td>
<td>67 ± 1</td>
<td>68 ± 2</td>
</tr>
<tr>
<td><strong>BE length (cm±SE)</strong></td>
<td>6.5 ± .5</td>
<td>5.6 ± .8</td>
</tr>
<tr>
<td><strong>Follow up (mo.±SE)</strong></td>
<td>19 ± 3</td>
<td>12 ± 2</td>
</tr>
</tbody>
</table>

Pacifico Clin Gastroenterol 2003
**Endoscopic Therapy for Early Cancers in BE: Mayo Clinic Experience**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Surgery (n=64)</th>
<th>EMR/PDT (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photosensitivity</td>
<td>0 (0%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Strictures</td>
<td>10 (16%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>5 (8%)</td>
<td>0</td>
</tr>
<tr>
<td>Wound infections</td>
<td>5 (8%)</td>
<td>0</td>
</tr>
<tr>
<td>Dumping syndrome</td>
<td>3 (5%)</td>
<td>0</td>
</tr>
<tr>
<td>Other*</td>
<td>8 (13%)</td>
<td>0</td>
</tr>
</tbody>
</table>

(*Empyema, blood transfusions, atrial fib., aspiration, chylothorax)
## Endoscopic Therapy for Early Cancers in BE: Mayo Clinic Experience

<table>
<thead>
<tr>
<th></th>
<th>Surgery (n=64) (%)</th>
<th>EMR/PDT (n=24) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death due to therapy</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Unrelated death</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Failed therapy</td>
<td>0</td>
<td>4*</td>
</tr>
<tr>
<td>- Ca on 1st F/U Bx</td>
<td></td>
<td>1 - surgery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 - CRT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 - died</td>
</tr>
</tbody>
</table>
Ablation Risks – All methods

• Failure to continue surveillance
  – Remember squamous overgrowth occurs in treatment naïve patients
Endoscopic Mucosal Resection

- Provides pathological specimen
  - Margins
    - Peripheral and deep
  - Tumor grade
  - Lymphatic and vascular involvement
- Immediate effect
- Most complications readily apparent
- Well tolerated
EGJ Cancer Staging with EMR

Thick proximal gastric fold

Submucosal saline injection

Cap-fitted EMR site
EMR Specimen of EGJ Adenocarcinoma

Polypoid specimen with invasive cancer into the deep submucosal layer
Barrett’s and Esophageal Cancer

- 100 patients
- 36.7 month mean follow up

**TABLE 1. Low-risk criteria**

Lesion diameter < 20 mm; and macroscopically type I, IIa, IIb, or IIc lesions < 10 mm; and
Well-differentiated or moderately differentiated adenocarcinoma (grading G1/G2); and
Lesions limited to the mucosa (m type) on the basis of staging procedures and proved by histology of the resected specimen
No invasion of lymph vessels or veins proved by histology of the resected specimen

<table>
<thead>
<tr>
<th>FU [months]</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
<th>72</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pts at risk</td>
<td>99</td>
<td>80</td>
<td>43</td>
<td>21</td>
<td>11</td>
<td>3</td>
</tr>
</tbody>
</table>
Squamous Cell Cancer Esophagus

- EMR 5-year survival data for early lesions
  - 84 vs. 77%

Shimizu Gastrointest Endosc 2002;56:387
Late Failures

- Long term follow up imperative
- Direct surveillance yourself
- Treat recurrences aggressively
Conclusions

• Endoscopic therapy is effective for dysplasia and some early cancers
  – Well and moderately differentiated cancer
  – Limited to the mucosal layer

• Mucosectomy provides accurate pathologic staging and therapy in some cases
  – Ablation is appropriate for treating large areas of high-grade dysplasia

• Surgical resection provides the only durable cure
  – Endoscopic therapy requires intense life-long surveillance