Endoscopic Treatment and Surveillance of Esophageal Cancer: GI Perspective

Charles J. Lightdale, MD
Columbia University
New York, NY
Evolution of Barrett’s esophagus

- Squamous esophagus
- Chronic inflammation
- Barrett's metaplasia
- Low-grade dysplasia
- High-grade dysplasia
- Adenocarcinoma

Accumulate Genetic Changes

Injury
- Acid & bile reflux

Genetics
- Gender, race

1.0%/yr
<0.5%/yr

Barrett’s Prevalence Estimates

• 1.6% of general adult population (3.3 M)

• 6.8% of persons over age 40 (8.7 M)

• Majority without GERD
Accuracy and Acceptability of Cytology Sponge with IHC for TFF3

- 501/504 patients swallowed sponge capsule
- Compared to endoscopy and biopsy:
  
<table>
<thead>
<tr>
<th>BE Diameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
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<tbody>
<tr>
<td>&gt;1 cm</td>
<td>73.3%</td>
<td>93.8%</td>
</tr>
<tr>
<td>&gt;2 cm</td>
<td>90.0%</td>
<td>93.5%</td>
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</tbody>
</table>

Barrett’s Esophagus

Technique of Biopsy in Endoscopic Surveillance

Falk GW, Techniques in GI Endoscopy 2000; 2:186
BE With and Without Dysplasia: Confounding Factors

- **Endoscopic Biopsy Sampling Error**
  - Persists even with "Seattle Protocol"

- **Pathology Interpretation**
  - LGD: $K = 0.32$ (fair)
  - HGD/IMC: $K = 0.65$ (substantial)
  - HGD vs IMC: $K = 0.42$ (fair)

Montgomery, Canto. CG & H 2006;4:1434-39
Adherence to Surveillance Biopsy Guidelines by Year

Optical Contrast Endoscopy

WLE

NBI
Mucosal Patterns: Regular/Irregular
Confocal Probe BE

IM

HGD
Wide Area Transepithelial Sample (WATS)
Flat HGD and IMCA can occur in a mosaic pattern missed by 4-Q biopsy. WATS method is designed to decrease biopsy sampling error.
Early Esophageal Adenocarcinoma

Risk of lymph node metastases:

- $Tis$ (intraepithelial) 0%
- $T1a$ (intramucosal) 2%
- $T1b$ (submucosal) 25%

EMR Techniques

- **INJECTION ASSISTED:**
  - Inject and snare (saline-assisted polypectomy)
  - Inject, lift, and cut with snare (2-channel scope)

- **CAP ASSISTED:**
  - Inject, endoscopic suction, and snare

- **LIGATION ASSISTED:**
  - Band and snare

- **ENDOSCOPIC SUBMUCOSAL DISSECTION) (ESD)**
  - Inject and cut with free-hand knife for en-bloc resection
EMR for HGD/Early Carcinoma in Barrett’s Esophagus

- Outpatient procedure
- Major risk is bleeding, usually mild, < 5%
- Perforation is rare, < 1%
- Pathology specimen for evaluation of tumor depth and margins.

Good Risk Lesions For EMR in Early Esophageal Adenocarcinoma

- Non-ulcerated lesions, < 2.0 cm in diameter
- Invasion limited to mucosa
- No lympho-vascular invasion
- No poorly differentiated histology

Ell et al. Gastrointest Endosc 2007;65:3-10.
EMR in HGD/T1a complicating Barrett’s esophagus

• 100 patients, 144 resections
• No major complications; 11 mild bleeding
• Complete local remission in 99% after a maximum of 3 resections
• 11% recurred in 36.7 months, all successfully retreated with EMR

Ell. Gastrointest Endosc 2007;65:3-10
Complete Removal of BE with EMR: Radical Sequential EMR

- Length of Barrett’s segment is a major factor
- SSBE < 3 cm has best results
- Strictures >50% if >3.0 cm length or > ¾ circumference of lumen
- Longer segments: focal EMR + ablation

Currently Available Endoscopic Ablation Techniques for BE

- Argon Plasma Coagulation (APC)
- Multipolar Electrocoagulation (MPEC)
- Heat Probe
- Lasers (Nd:YAG, KTP, Argon)
- Photodynamic Therapy (PDT)
- Cryotherapy
- Radiofrequency Ablation (RFA)
Focal Radiofrequency Ablation Device
RFA versus Surveillance at 1-Year

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>RFA</th>
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</thead>
<tbody>
<tr>
<td>Complete Eradication</td>
<td>2.3%</td>
<td>77.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>(All patients, n=127)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete Eradication</td>
<td>22.7%</td>
<td>90.5%</td>
</tr>
<tr>
<td>(LGD patients, n=64)</td>
<td></td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Complete Eradication</td>
<td>19.0%</td>
<td>81.0%</td>
</tr>
<tr>
<td>(HGD patients, n=63)</td>
<td></td>
<td>P&lt;0.001</td>
</tr>
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Intention-to-Treat Comparison Groups
RFA Complications

**Serious Adverse Events:**
3/84 (3.6%). 1 UGI bleed, 2 chest pain

**Strictures:**
5/84 patients (6%) resolved: mean 2.6 dilations

**Subsquamous intestinal metaplasia:**

<table>
<thead>
<tr>
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<th>RFA</th>
<th>Surveillance</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>25%</td>
<td>26%</td>
</tr>
<tr>
<td>1-year</td>
<td>5%</td>
<td>40%</td>
</tr>
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</table>
Longterm Durability of Ablation

- Complete Eradication of IM (All)
- Complete Eradication of Dysplasia (HGD)
- Complete Eradication of Dysplasia (LGD)

EMR+RFA vs. Esophagectomy in BE with HGD/IMC

- All patients treated at USC 2001-2010

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Survival (3 yr)</th>
<th>Morbidity</th>
</tr>
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<tbody>
<tr>
<td>EMR+RFA (40)</td>
<td>94%</td>
<td>0%</td>
</tr>
<tr>
<td>Esophagectomy (61)</td>
<td>94% ns</td>
<td>39% p &lt; 0.0001</td>
</tr>
</tbody>
</table>

Conclusions

- Low-cost screening for BE may become feasible.
- New methods may improve surveillance.
- Need for better risk stratification in BE.
- EMR for staging of all focal dysplastic lesions.*
- HGD/IMCA: Endoscopic Therapy (EMR, Ablation) preferred in most patients to esophagectomy.*