Options for endoscopic treatment of Barrett’s esophagus

Barrett’s neoplasia treatment trends

• Endoscopic treatments with acceptable efficacy & safety

• Patients with HGD/T1 cancer who previously may have undergone surgery are now undergoing endoscopic therapy

• Patients with pathology less advanced than HGD are now undergoing endoscopic therapy
Barrett’s neoplasia treatment trends

Ngamruengphong et al, Clin Gastroenterol Hepatol 2013

Photodynamic therapy 5-year data

Overholt et al, Gastrointest Endosc 2003
Radiofrequency ablation (AIM-Dysplasia)

Complete response—dysplasia (HGD cohort)

- ITT: 80% RFA, 11% sham
- Per protocol: 91% RFA, 12% sham


Endoscopic treatment goals

- Eradicate dysplasia
- Eliminate intestinal metaplasia
- Provide durable remission of intestinal metaplasia
Endoscopic treatment goals

- Eradicate dysplasia
- Eliminate intestinal metaplasia
- Provide durable remission of intestinal metaplasia
- Prevent progression to esophageal cancer
- Provide durable cancer-free survival

Photodynamic therapy 5-year data

Progression from HGD to cancer

<table>
<thead>
<tr>
<th></th>
<th>PDT (N=138)</th>
<th>PPI (N=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15%</td>
<td>29%</td>
<td></td>
</tr>
</tbody>
</table>

Overholt et al, Gastrointest Endosc 2003
AIM-Dysplasia: 12-month progression to cancer

**All patients:**
- Sham group: 9.3%
- RFA group: 1.2%

**HGD patients:**
- Sham group: 19%
- RFA group: 2.4%


HGD: post-treatment survival

Figure 1. Overall survival in the PDT and surgical groups.

Prasad et al, Gastroenterology 2007
Advances in endoscopic staging

- High-definition white light endoscopy
- Narrow band imaging
- Endoscopic ultrasound
- Endoscopic mucosal resection

Directional distribution of neoplasia

Cassani et al, Gastrointest Endosc 2013
Endoscopic treatment strategy (HGD)

1) Staging and induction therapy: EMR

Barrett’s high-grade dysplasia?
Barrett’s high-grade dysplasia?

Expert path review and EMR change diagnosis

Ayers et al, Surg Endosc 2013
Disease Progression in Barrett’s

- BE
- LGD
- HGD
- T1a cancer
- T1b cancer

INTERVENTION

Safety of EMR

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Patients</td>
<td>681</td>
</tr>
<tr>
<td>Procedures</td>
<td>1388</td>
</tr>
<tr>
<td>Bleeding</td>
<td>8 (1%)</td>
</tr>
<tr>
<td>Stricture</td>
<td>7 (1%)</td>
</tr>
<tr>
<td>Perforation</td>
<td>0</td>
</tr>
</tbody>
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Tomizawa et al, Am J Gastro 2013
ACG position statement

Any mucosal irregularity, such as nodularity or ulcer, is best assessed with mucosal resection for a more extensive histologic evaluation and exclusion of cancer

Wang and Sampliner, Am J Gastro 2008

International consensus statement

For patients with high grade dysplasia in an endoscopically visible abnormality, endoscopic resection is essential for proper diagnosis and staging

Bennett et al, Gastroenterology 2012
Endoscopic treatment strategy (HGD)

1) Staging and induction therapy: EMR

2) Consolidation therapy: RFA
Endoscopic treatment strategy (HGD)

1) Staging and induction therapy: EMR
2) Consolidation therapy: RFA
3) Endoscopic surveillance

RFA cohort studies

<table>
<thead>
<tr>
<th>Study</th>
<th>N=</th>
<th>≥HGD</th>
<th>EMR</th>
<th>Treatment duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gupta et al (USA)</td>
<td>448</td>
<td>71%</td>
<td>55%</td>
<td>22 months</td>
</tr>
<tr>
<td>Haidry et al (UK)</td>
<td>335</td>
<td>72%</td>
<td>49%</td>
<td>12 months</td>
</tr>
<tr>
<td>Phoa et al (Netherlands)</td>
<td>54</td>
<td>100%</td>
<td>72%</td>
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</table>

Gastroenterology 2013
Points to consider

- Ablation is a commitment
- Disease remission is achievable for many patients
- What is the estimated durability of the treatment response?
- What does the patient want?
Clinical case

- 42 year old male long segment BE (12 cm) and multifocal HGD
- Was counseled re: surgical and endoscopic options
- Pursued endoscopic therapy at a different institution
- After 4 ablation sessions, BE-HGD persisted

Clinical case

- Was counseled re: surgical and endoscopic options
- Underwent 3 additional EMR sessions, HGD detected each time
- T1a adenocarcinoma detected at 4th EMR session
- Underwent esophagectomy 2 years after initial consultation
Clinical case

- The decision to pursue surgery vs endoscopic therapy is often patient-driven
- Surgery remains a strategy for some patients with HGD
- Endoscopic therapy does not preclude future surgery
- Adherence to a strict therapy/surveillance protocol is critical for those patients who choose endoscopic therapy

Registry data

- N=3724 with CE-IM following RFA
- N=2285 (61%) underwent surveillance after CE-IM
- Pre-treatment diagnosis HGD: Mean 7.8 months to first surveillance EGD after CE-IM

Li et al, DDW 2013
Subsquamous intestinal metaplasia

- Neoplasia arising from SSIM has been described
- Forceps biopsies may not be sufficient depth to detect SSIM
- SSIM exists in a significant portion of treatment naïve patients
- Endoscopic therapy does not increase the prevalence of SSIM
- Concern re: SSIM should not alter current endoscopic practice

Yachimski and Falk, Clin Gastroenterol Hepatol 2012
Disease Progression in Barrett’s

BE → LGD → HGD → T1a cancer → T1b cancer

**INTERVENTION**

<table>
<thead>
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<tbody>
<tr>
<td>High-grade dysplasia</td>
<td>Yes (vs surgery)</td>
<td>• Recommend RFA, PDT, or EMR</td>
</tr>
<tr>
<td>Low-grade dysplasia</td>
<td>No comment</td>
<td>• RFA an option</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Shared decision making</td>
</tr>
<tr>
<td>Nondysplastic</td>
<td>No comment</td>
<td>• Not suggested</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Option for select individuals at high risk of progression</td>
</tr>
</tbody>
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Wang and Sampliner, Am J Gastro 2008
Gastroenterology, 2011
Summary

- Endoscopic mucosal resection and ablation techniques have expanded treatment options for Barrett’s neoplasia
- Accurate pre-treatment staging is critical
- Endoscopic remission vs cure
- Post-treatment surveillance is mandatory