Advances in the Diagnosis and Management of Barrett’s Esophagus

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Barrett’s Esophagus

Condition in which any extent of metaplastic columnar epithelium that predisposes to cancer development replaces stratified squamous epithelium that normally lines distal esophagus

Shaheen NJ et al. ACG Guidelines Am J Gastroenterol. November 2015; doi: 10.1038/ajg.2015.322
Correct definition of OGJ allows detection of short segment Barrett’s esophagus

SCJ=squamocolumnar junction

OGJ=oesophagogastric junction

Evolution of Barrett’s

Squamous esophagus

Chronic inflammation

Barrett’s metaplasia

Low-grade dysplasia

High-grade dysplasia

Adenocarcinoma

Injury: Acid & bile reflux

Genetics: Gender, race, other factors (cox-2)

Accumulate Genetic Changes
Endoscopic diagnosis

- Diagnosis of Barrett’s esophagus
- Surveillance
- Detection of dysplasia
- Staging of the disease

Technologies for endoscopic imaging

- High definition white light endoscopy
- Narrow band imaging
- Confocal Endomicroscopy
- Optical coherence tomography
Endoscopic Diagnosis of BE
ACG Practice Guidelines

- BE should be diagnosed when there is extension of salmon colored mucosa into the tubular esophagus extending ≥1 cm proximal to the gastroesophageal junction (GEJ) with biopsy confirmation of IM (strong recommendation, low level of evidence).

- Endoscopic biopsy should not be performed in the presence of a normal Z line or a Z line with <1 cm of variability (strong recommendation, low level of evidence).

Shaheen NJ et al. ACG Guidelines Am J Gastroenterol. 2015

Reporting Barrett’s esophagus-
Prague Classification
Surveillance of BE

Observational studies suggest that patients with BE in whom EAC was detected in a surveillance program have their cancers detected at an earlier stage with markedly improved survival compared with similar patients not undergoing routine endoscopic surveillance.

Corley DA. Gastroenterology 2013;145:312-9

HD White light Endoscopy

- High definition superior to standard-definition white light endoscopy for dysplasia detection.
- Careful examination of retroflexed view of the GEJ.
- Direct correlation between inspection time of the Barrett’s segment and detection of patients with HGD/EAC.
- Inspection of the Barrett’s segment should also involve careful attention to the right hemisphere, extending from the 12 o’clock to 6 o’clock location where early cancer appears to have a predilection to develop.

Shaheen NJ et al. ACG Guidelines Am J Gastroenterol. 2015

Careful attention to the right hemisphere
Narrow Band Imaging - NBI

Conventional Filter

NBI Filter

Superficial imaging

NBI evaluation in Barretts

Improves visualization and identification of:

- Pit pattern
- Microvasculature pattern
Normal and dysplastic mucosal patterns in Barretts

- **circular**
- **Tubular/ linear/villous**

“distorted” mucosal pattern in Barretts indicating Dysplasia

Anagnostopoulos et al. High resolution magnification endoscopy with narrow band imaging in patients with Barretts esophagus. Gastrointest Endosc 2006;63(5):AB130
Evidence for NBI

- Randomized clinical trial of NBI vs. HD-WLE demonstrated that NBI targeted biopsies can have the same IM detection rate as an HD-WLE examination with the Seattle protocol while requiring fewer biopsies. (3.6 vs. 7.6, p<0.0001)
- NBI detected a higher proportion of areas with dysplasia (30% vs. 21%, p=0.01)

Optical coherence tomography

- OCT is an optical analog of ultrasound B mode imaging, which is performed by measuring the echo time delay and intensity of back-reflected or backscattered light.
- Balloon based application in the diagnosis and surveillance of BE.
Abnormal Irregular Glands

Loss of layering

Highly Septated Cribiformed Glands

Histopathologic diagnosis: EAC

Confocal endomicroscopy
CLE comparison to HD-WLE

Endoscopic Diagnosis of BE
ACG Practice Guidelines

- Surveillance should be performed with high-definition white light endoscopy (strong recommendation, low level of evidence).
- Routine use of advanced imaging techniques other than electronic chromoendoscopy is not recommended for endoscopic surveillance at this time (conditional recommendation, very low level of evidence).
- Endoscopic surveillance should employ four-quadrant biopsies at 2 cm intervals in patients without dysplasia and 1 cm intervals in patients with prior dysplasia (strong recommendation, low level of evidence).
Endoscopic Management of BE
ACG Practice Guidelines

Know what you are treating

- Take time
- Look carefully with white light
- Invest in HD endoscopes
- Use optical enhancement functions – NBI
Candidates for Endoscopic therapy

- Patients with flat HGD
- Patients with nodular HGD
- Patients with IMC
- Patients with LGD
- No role of treatment of non-dysplastic BE

ACG Practice Guidelines

- Patients with confirmed LGD and without life-limiting comorbidity, endoscopic therapy is considered as the preferred treatment modality, although endoscopic surveillance every 12 months is an acceptable alternative (strong recommendation, moderate level of evidence).
- Patients with BE and confirmed HGD should be managed with endoscopic therapy unless they have life-limiting comorbidity (strong recommendation, high level of evidence).
Intervention for dysplastic Barrett’s

Options for endoscopic treatment of Barrett’s

- Ablate
- Resect

Nodularity in Barrett’s esophagus

Endoscopically visible nodularity in BE

Endoscopic mucosal resection

Low-grade dysplasia → Endoscopic ablative therapy
High-grade dysplasia → Endoscopic ablative therapy
T1a EAC → Favorable histology?
  Yes → Endoscopic ablative therapy
  No → Discussion at multidisciplinary oncology group
T1b EAC
Cap-Band EMR system

Esophageal EMR-Nodular disease Must be Removed
Efficacy of EMR

**CLINICAL—ALIMENTARY TRACT**

Long-term Efficacy and Safety of Endoscopic Resection for Patients With Mucosal Adenocarcinoma of the Esophagus

Oliver Pech,1 Andrea May,2 Hendrik Manner,2 Angelika Behrens,2 Jürgen Pohl,2 Maren Weferling,2 Urs Hartmann,2 Nicola Manner,2 Josephus Huijsmans,2 Liebwin Gossner,3 Thomas Rabenstein,4 Michael Vieth,5 Manfred Stolte,6 and Christian Elf7

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**Efficacy**

- 1000 consecutive patients with IMC and BE
- Mean follow-up period of 56 ± 33 months
- 96.3%-complete remission
- Recurrence noted in 140 patients (14.5%)
- Endoscopic treatment successful in 115 patients resulting in 93.8%
- Endoscopic treatment should be standard of care in IMC
Efficacy of EMR

![Image of Kaplan-Meier plot for estimating freedom from tumor]

Figure 2. Kaplan-Meier plot for estimating freedom from tumor.

**Human Esophagus**

- Epithelium
- Lamina Propria
- Muscularis Mucosae
- Submucosa
- Muscularis Propria

**Keys to Endotherapy:**
1. Uniform mucosal removal
2. Controlled depth of ablation

- RFA Depth
- PDT/MPEC/APC/Cryo Depth?
- EMR Depth
- Surgical Depth

**Time (months):** 12 24 36 48 60 72 84 96 108 120
**Patients at risk:** 991 818 668 474 349 280 212 192 75 39

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Circumferential Ablation

Focal Ablation

Radiofrequency ablation of Barretts
RFA reduces progression in confirmed low-grade dysplasia

Summary of SURF RCT Results

- European multicenter RCT of 136 confirmed LGD patients
- Patients randomized to treatment (RFA) and control (surveillance) arms
- Per-protocol analysis at 12 month f/u

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<th>RFA</th>
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<td>CE-D</td>
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<tr>
<td>CE-IM</td>
<td>98%</td>
<td>0%</td>
<td>&lt;0.01</td>
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- Primary Outcome (Median 21 months follow-up)

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<th>RFA</th>
<th>Control</th>
<th>p value</th>
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<tr>
<td>Progression to HGD/EAC</td>
<td>1.5%</td>
<td>20.6%</td>
<td>&lt;0.01</td>
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Phoa KN et al. JAMA 2014;311(12):1209-17

RFA Disease Eradication

Disease Progression

• Extension of the AIM Dysplasia Trial for patients with complete BE eradication after 1 year of treatment (n=106)

Durability of RFA in Barrett’s esophagus with dysplasia (AIM dysplasia trial)

• Extension of the AIM Dysplasia Trial for patients with complete BE eradication after 1 year of treatment (n=106)
• 91 to 98% dysplasia & IM eradication rate at 2 & 3 years
• 0.55% per year cancer progression rate (vs. 9.3% annual cancer progression in the sham group)

• Conclusion:
  • RFA has acceptable safety profile
  • RFA is durable
  • RFA is associated with a low rate of disease progression for up to 3 years

Shaheen NJ et al. Gastroenterology 2011;141(2):460-8
Cryotherapy in Barrett’s esophagus

Shaheen NJ et al. GIE 2010

Schölvinck DW et al. Endoscopy 2015
Surveillance after treatment of Barrett’s esophagus

• Endoscopic surveillance following CEIM, for patients with HGD or intramucosal carcinoma before ablation, is recommended every 3 months for the first year following CEIM, every 6 months in the second year, and annually thereafter (conditional recommendation, low level of evidence).

• In patients with LGD before ablation, endoscopic surveillance is recommended every 6 months in the first year following CEIM, and annually thereafter (conditional recommendation, low level of evidence).

Conclusions

• Careful examination is required to detect nodular disease
• Use both HD-WLE and NBI evaluation
• Nodular disease must be removed first
• Ablative therapy is highly effective (Both RFA and cryotherapy)
• Rigorous acid suppression and close endoscopic surveillance is important to improve outcomes