Clinician’s Perspective:
Upper GI Biopsies

Kunal Jajoo, MD
Assistant Professor of Medicine
Upper GI biopsies

Outline

• Barrett’s esophagus
• Eosinophilic esophagitis
• Gastric carcinoid
• Celiac disease
Barrett’s Esophagus

- Replacement of the normal squamous epithelium of the esophagus with metaplastic columnar epithelium
- Occurs as a result of chronic inflammation from gastroesophageal reflux disease
- Progression to carcinoma generally occurs in a step-wise fashion from no dysplasia, low-grade dysplasia and high-grade dysplasia
Barrett’s Esophagus

Screening

• AGA, ACG and ASGE have somewhat different guidelines for screening

• ACG and AGA’s most recent guidelines acknowledge the controversy in screening stating that the highest yield is in screening those with chronic GERD over age 50

• If Barrett’s is identified on screening, repeat in one year then every 3-5 years if no dysplasia
Barrett’s Esophagus
Screening – ACG 2015

• 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).

• In the presence of BE, the endoscopist should describe the extent of metaplastic change including circumferential and maximal segment length using the Prague classification (conditional recommendation, low level of evidence).

• The location of the diaphragmatic hiatus, GEJ, and squamocolumnar junction should be reported in the endoscopy report (conditional recommendation, low level of evidence).

• In patients with suspected BE, at least 8 random biopsies should be obtained to maximize the yield of IM on histology. In patients with short (1–2 cm) segments of suspected BE in whom 8 biopsies may be unobtainable, at least 4 biopsies per cm of circumferential BE, and one biopsy per cm in tongues of BE, should be obtained (conditional recommendation, low level of evidence).

• In patients with suspected BE and lack of IM on histology, a repeat endoscopy should be considered in 1–2 years of time to rule out BE (conditional recommendation, very low level of evidence).
Barrett’s esophagus

Endoscopic and pathologic diagnosis

Endoscopist

- Documents landmarks (SC junction / top of the gastric folds) and abnormalities (nodularity, ulceration, mass) and location of biopsies

Pathologist

- Presence of intestinal metaplasia
- ? junctional mucosa
- Grade of dysplasia
Barrett’s esophagus
**PRAGUE CRITERIA**
For Endoscopically Suspected Esophageal Columnar Metaplasia/Barrett’s Esophagus

Developed by the Barrett’s Oesophagus Subgroup of the International Working Group for the Classification of Reflux Oesophagitis (IWGCO)

1. Ensure Hiatus Hernia Is Recognised By Distinguishing Diaphragmatic Hiatal Impression From Gastroesophageal Junction

2. Locate Gastroesophageal Junction By Depth Of Endoscope Insertion* At Level Of:
   - tops of gastric mucosal folds
   - sphincter “pinch”
   - = 36 cm

3. Lock For Displacement Of Squamocolumnar Junction Above Gastroesophageal Junction

4. Measure Depth Of Endoscope Insertion* At The Most Proximal Circumferential Extent Of Suspected Columnar Metaplasia*
   - = 33 cm

5. Measure Depth Of Endoscope Insertion* At The Maximum Extent Of Suspected Columnar Metaplasia*
   - = 29 cm

6. Subtract the Depth of Insertion for Circumferential and Maximum Extents from the Depth of Endoscope Insertion at the Gastroesophageal Junction:
   - 29 cm - 33 cm = C3
   - 29 cm - 36 cm = M7
   - Prague C3 and M7

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* To the nearest centimeter
* Squamous and columnar islands do NOT contribute to measures of extent
* To the nearest centimeter, except when areas of columnar metaplasia are estimated to be less than 1 cm; report this as < 1 cm

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Barrett’s esophagus - Progression

- Prior data: 0.2 to 2.0% absolute risk per year with non-dysplastic BE

Sikkema 2010 (Meta-analysis)
  - 51 studies
  - Incidence: 6.3 / 1000p-y

Hvid-Jensen 2011 (Population-based cohort)
  - 11,028 patients
  - 0.12% absolute risk per year
  - Rises with dysplasia (5.0 / 1000 p-y for LGD)

Surveillance

- Endoscopic surveillance
  - White light, hi-definition endoscopy
  - Four-quadrant biopsies every 2 cm
    - Every 1 cm with history of or suspected dysplasia
  - Mucosal irregularities targeted, preferably by EMR
    - Greater than 50% of visible advanced neoplasia is seen in the 2 to 5 o’clock position

High-grade Dysplasia in Barrett’s

• Esophagectomy
  – High morbidity and mortality

• Ablation
  – Cryotherapy
  – Radiofrequency ablation

• Endoscopic mucosal resection (EMR)
• Endoscopic submucosal dissection (ESD)
Ablation of HGD in Barrett’s

• Cryotherapy
  – Cold Nitrogen gas applied by spray catheter to freeze tissue
  – 87% eradication of dysplasia
  – 5% complication rate (stricture, severe chest pain)
  – 3% buried glands

Shaheen NJ, et al. GIE 2010; 71
Ablation of HGD in Barrett’s

- Radiofrequency (BARRX)
  - Bipolar electrode array generates heat to “burn” < 600 micron depth
Ablation of Barrett’s

• Video
Ablation of BE with Dysplasia

- Ablative therapies (cryo-ablation and RFA) are highly effective in eliminating dysplasia (79 – 100%) and effective in eliminating IM (67 - 81%)
- These therapies are relatively safe with a complication rate of 6-7% (primarily strictures)
- Multiple procedures are often needed (mean 2.5)

Shaheen NJ, et al. Gastro 2011; 141
EMR of BE with Dysplasia

Fig. 1. EMR-ML technique (A to D): ML uses the single rubber-band ligator to create a pseudopolyp and enable snare polypectomy (Picture: courtesy of Cook®).
EMR Barrett’s with IMC
ESD of Neoplastic Barrett’s

- Technique pioneered in Japan, primarily for early gastric neoplasms and now being utilized in the esophagus and colon
- Allows for en bloc resection and assessment of margins
- Superior $R_0$ resection rates compared to EMR at the cost of increased perforation and bleeding risk

Y Cao, et al *Endoscopy*. 2009;41
A Repici, et al. *Gastrointest Endosc*. 2010;71
Images courtesy of Hiroyuki Aihara, M.D., Ph.D.
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Images courtesy of Hiroyuki Aihara, M.D., Ph.D.
**Combination Therapy**

- EMR for focal raised lesions and RFA / cryoablation for flat dysplasia.
- Equivalent to RFA alone for flat Barrett’s with HGD or IMC
  - 76-94% vs. 71-83% eradication of dysplasia
  - 43-88% vs. 74-78% eradication of Barrett’s

HP Kim, et al. *Gastrointest Endosc.* 2012;76
Combination Therapy

• Highly effective in more routine use as well
  – NHS registry
  – HGD eradication in 86% of patients
  – Dysplasia eradication 81%
  – BE eradication 62%

Eosinophilic esophagitis

- Chronic immune/antigen mediated disease characterized clinically by symptoms of esophageal dysfunction and histologically by eosinophil predominant inflammation (> 15 Eos per hpf)
- Thought to be an allergic response to a variety of foods and aeroallergens
- Primary symptom – dysphagia / food impaction
- Requires biopsies from mid and distal esophagus required
Eosinophilic esophagitis
Eosinophilic esophagitis

Treatment
- Swallowed topical steroids (budesonide, fluticasone)
- PPI
- IL-5 inhibitors
- Elimination diet +/- food allergy testing

MA Ali, D Lam-Himlin, L Voltaggio. GJE 2012
Gastric carcinoid

Type I

- Chronic atrophic gastritis, hypergastrinemia and hyperplasia of enterochromaffin-like cells
- Accounting for about 70-80% of gastric carcinoid
- Endoscopically: small (<10 mm), polypoid lesions or smooth, rounded submucosal lesions.
Gastric carcinoid

Mapping biopsies

• biopsy samples from the antrum, corpus, incisura angularis, and any endoscopically visible lesion

• to assess for intestinal metaplasia / dysplasia
Gastric carcinoid

Treatment

• Endoscopic resection appropriate for lesions \( \leq 1 \text{ cm} \) (potentially 1.5 cm) and less than 5 in total number

• Surgical resection with antrectomy to remove the trophic stimulus for larger / multiple lesions
Intestinal metaplasia

Pathology report with IM in a gastric mucosa biopsy sample

Assess for *H. pylori* infection (test with serology if biopsy is negative) and treat
Assess extension and type of IM in original biopsies

Extensive IM* or incomplete type

Yes/unknown

Endoscopic surveillance with mapping or serum PG levels at 1 year
Repeat every 3 years if extensive IM/atrophy** or incomplete-type IM persists

No

No surveillance required

P Correya, et al. Am J Gastroenterol 2010
Celiac disease

- Allergy to wheat gluten causing mucosal inflammation (intra-epithelial lymphocytosis), villous atrophy, and crypt hyperplasia and resultant malabsorption
- Diagnosis is currently made with serology (anti-TTG) and confirmed by duodenal biopsy
- Diagnostic yield is dependent upon biopsy quality
Celiac - Endoscopy
Celiac disease

• Biopsy
  – Guidelines advocate for > 4 biopsies from the duodenum, at least 2 of which should be from the bulb if serology is positive
  – Recent studies have demonstrated better biopsy orientation when the biopsies are taken one at a time

Summary

Barrett’s

- Imperative to adequately biopsy to assess for dysplasia
- Ablative therapies and EMR/ESD have supplanted esophagectomy for HGD +/- T1a

EoE

- Biopsies from both mid and distal esophagus

Carcinoid

- Often endoscopically resectable
- Mapping biopsies for IM

Celiac

- Multiple biopsies needed, taken individually