Barrett’s esophagus (BE) is a metaplastic change from squamous epithelium to columnar epithelium in the distal esophagus due to GERD. It is the only known precursor lesion to esophageal adenocarcinoma (EAC). The diagnosis of EAC after symptom onset has poor survival (<20% at 5 years). Screening and surveillance to identify early and treat endoscopically is key.

### Background

**Candidates for Screening**
- Chronic GERD + ≥3 additional risk factors
  - Male
  - Age >50 years old
  - White race
  - Tobacco smoking
  - Obesity
  - 1st degree male relative with BE or EAC

**Screening Modalities**
- **Endoscopy** = gold standard but invasive & expensive
- Alternative: Swallowable Capsule Device + Biomarker
- Other developing screening modalities:
  - Unsedated transnasal endoscopy
  - Exhaled volatile organic compounds
  - Risk prediction scores

### Diagnosis

- Diagnosis = ≥1 cm length of columnar mucosa with **intestinal metaplasia (IM)**
- Do not biopsy:
  - Normal-appearing Z line
  - < 1 cm displaced irregular Z line
  - < 1 cm = low reliability of Prague criteria & low risk of progression
- Yield of IM ↑ with ↑ # of biopsies & ↑ length of the BE segment
- All IM with dysplasia confirmed by 2nd pathologist with GI expertise

**Classify using Prague Criteria**

### Screening

**Candidates for Screening**

- Chronic GERD + ≥3 additional risk factors
  - Male
  - Age >50 years old
  - White race
  - Tobacco smoking
  - Obesity
  - 1st degree male relative with BE or EAC

**Screening Modalities**

- **Endoscopy** = gold standard
- Alternative: Swallowable Capsule Device + Biomarker
- Other developing screening modalities:
  - Unsedated transnasal endoscopy
  - Exhaled volatile organic compounds
  - Risk prediction scores

### Surveillance

- White light endoscopy + chromoendoscopy (electronic OR vital dyes) to better identify irregular mucosa or vascular pattern
- Structured biopsy protocol to ↓ detection bias
- Length + degree of dysplasia = determines surveillance intervals

### Cannot recommend (insufficient evidence):
- Wide-area transepithelial sampling with computer-assisted 3-dimensional analysis (WATS-3D) or predictive tools/biomarkers

---

Salmon-colored mucosa extending proximally from the GEJ on endoscopy

- <1 cm salmon-colored mucosa OR
  - Irregular Z-line OR
  - Regular Z-line
  - No biopsy

- ≥1 cm salmon-colored mucosa
  - Biopsy
    - ≥8 endoscopic biopsies should be obtained
    - If only 1-2 cm segment or tongues and 8 biopsies not possible:
      - ≥4 biopsies per cm of circumferential BE
      - ≥1 biopsy per cm of tongue
    - If >4 cm segment, then follow Seattle protocol = biopsy visible lesions + 4 quadrant biopsies of every 2 cm starting 1 cm above the gastroesophageal junction (GEJ)

Intestinal Metaplasia

- Negative for IM
  - Repeat endoscopy with biopsy in 1-2 years

- <3 cm BE segment
  - Repeat surveillance EGD in 5 years
- ≥3 cm BE segment
  - Repeat surveillance EGD in 3 years

Non-dysplastic BE (NDBE)

- Confirm by 2nd pathologist with GI expertise

Indefinite for Dysplasia (IND)

- Confirm by 2nd pathologist with GI expertise

LGD

- For LGD, can consider surveillance
  - At 6 months & 12 months after diagnosis, then annually

HGD

- Follow that algorithm

Early EAC

- EGD annually

Treatment

Quality indicators for screening and surveillance

1. Documentation of landmarks + extent of BE
2. Not obtaining biopsies in the setting of normal-appearing junction
3. Sampling using Seattle protocol
4. Performing surveillance endoscopy in patients with NDBE no sooner than 3-5 years

Screening & Surveillance

10 step approach to endoscopic exam of BE

- Identify esophageal landmarks: diaphragmatic hiatus, GEJ, squamocolumnar junction
  - Critical for further examinations
- Consider distal attachment cap (especially if prior dysplasia)
  - Facilitate visualization
- Clean mucosa well (water jet and careful suction)
  - Remove mucus or debris and limit mucosal trauma
- Use insufflation & deflation
  - Fine adjustments can help detect subtle changes
- Spend adequate time inspecting the Barrett’s segment & gastric cardia on retroflexion
  - Increases dysplasia detection
- Examine with chromoendoscopy
  - Enhances mucosa pattern and surface vasculature
- Use Prague classification- circumferential and maximal length
  - Standardized reporting system
- Use Paris classification- describe superficial neoplasia
  - Standardized reporting system
- Use Seattle protocol with partially deflated esophagus to sample Barrett’s segment
  - Increases dysplasia detection

**Consider cessation of surveillance if no longer a candidate for EET (Endoscopic Eradication Therapy) or life expectancy <5 years
**Medical Treatment**

- **PPI therapy** (at least once daily) if no allergy or contraindication
- No evidence for aspirin (ASA) with PPI therapy → no significant difference in cancer related outcomes
- Patients with BE also likely on ASA for cardio protection due to risk factors
- **DO NOT use antireflux surgery** as antineoplastic measure in BE → no change in progression to neoplasia risk compared to standard PPI therapy

**Endoscopic Eradication Therapy (EET)**

- Esophagectomy has 2% mortality & ↑ morbidity compared to EET
- **Goal of EET** = complete eradication of IM (CEIM) → defined as 1-2 surveillance endoscopies w/o visible BE or IM on biopsies
- Endoscopic resection of any visible lesions, THEN ablative therapy

**Step 1: Endoscopic resection (ER) of any visible lesions**
- Cap-assisted vs multiband endomucosal resection (EMR)
- Bigger sample for accurate tumor staging & prognostication
- Endoscopic submucosal dissection (ESD)
- Reserved for en bloc resection of larger lesions, submucosal invasion or post-ablation lesions

**Step 2: Ablative therapy**
- **Radiofrequency ablation (RFA)** → thermal ablation
  - Achieve CEIM in 3 sessions
  - Adverse events (AEs): esophageal stricture (4.2-7%) & perforation (0.4-0.9%)
- **Endoscopic cryotherapy** (spray vs balloon) → rapid freeze + slow thaw
  - Alternative modality in patients unresponsive to RFA
  - Adverse events: esophageal stricture (9-12%)

**Post EET Surveillance Keys:**
1) Examine with white light + virtual chromoendoscopy
2) Biopsies from GEJ + distal 2-5 cm

**Quality indicators for EET in dysplastic BE**
- The rate of confirmation by GI pathologist prior to EET
- Rate at which CEN (complete eradication of neoplasia) and CEIM is achieved by 18 mo in patients with dysplasia or IMC
- The rate at which AEs are being tracked and documented post EET

- **Patients with BE-related neoplasia referred for EET**
  - Expert pathology review

  **NDBE**
  - **Surveillance**
    - BE ≥ 3 cm → EGD q3 years
    - BE < 3 cm → EGD q5 years
  - Discuss risks/benefits of surveillance vs EET (↓ risk of progression to HGD or EAC)

  **LGD**
  - **EET**
    - Resection of visible lesions then ablation of remaining BE epithelium. Goal: CEIM

  **HGD or IMC (T1a)**
  - **Surveillance**
    - EGD q6 months x 1 year, then annually
  - Resection of visible lesions then ablation of remaining BE epithelium. Goal: CEIM

  **Submucosal cancer (T1b)**
  - **Surgical referral** for esophagectomy
  - Consider EET if sm1 (invasion into the upper 1/3 of submucosa) with low-risk features
    - Well differentiated
    - <2 cm
    - No lymphovascular invasion

  After achieving CEIM, enroll in surveillance program (annual incidence of recurrent IM is 8.6-10% & dysplasia is 2%) & optimize reflux control

- **Baseline LGD**
  - EGD at 1 year, 3 years, then every 2 years

- **Baseline HGD or T1a**
  - EGD at 3, 6, and 12 months, then annually