What are “a normal esophagus” and “a normal z line”? Do we need biopsies?

Sergey Kashin
The main anatomic landmarks of the esophagogastric region

- **EGJ** (esophagogastric junction)
  - the distal extent of longitudinal palisade vessels
  - the proximal extent of the gastric folds

- **SCJ** (squamocolumnar junction, Z-line)
  - the pinch of the diaphragm and the dilated lumen of the stomach

Why the **Z-line** is an important area?

- The area where endoscopic signs of **reflux** may become apparent. Mucosal inflammation due to the reflux may lead to the development of **intestinal metaplasia** and finally to **neoplasia**
- The small area of the GI tract with the highest rate of **cancer** per cm. The incidence of GEJ adenocarcinoma has risen rapidly over the past decades

![Combined incidence of gastric and esophageal cancer](chart)

Combined incidence of gastric and esophageal (esophagus and EGJ) adenocarcinoma among Olmsted County, Minnesota residents, 1971–2000

Why would one want to biopsy a normal Z-line?

• to diagnose reflux esophagitis
• to detect IM
• to detect neoplasia
LA Classification: the standard grading system of reflux esophagitis

- Los Angeles classification is based on the extent of mucosal breaks
- It gives good inter-observer agreement based on endoscopic findings only

“Traditional” minimal changes (mucosal oedema, friability, erythema and increased vascularity) had unacceptably poor agreement with early 1990s endoscopes

Minimal changes:
High-resolution endoscopy

High resolution endoscopy criteria for non-erosive squamous mucosal injury by gastroesophageal reflux:

- Triangular indentations into the squamous mucosa
- Minute apical mucosal breaks at the vertex of a triangular
- Palisade blood vessels not visible
- Pinpoint blood vessels
- Branching blood vessels
- Serrated squamo–columnar junction
- Villiform mucosa

Interobserver study on high-resolution video images of patients with NERD and controls: none of the proposed criteria emerged as sufficiently valid to diagnose NERD endoscopically: all the criteria would have poor sensitivity and/or specificity and interobserver agreement

Further research into the vasculature patterns of the distal squamous epithelium in GERD is warranted

Edebo Aet al. Magnification endoscopy for diagnosis of nonerosive reflux disease Endoscopy 2007
PPI Test

of its availability, simplicity and the sensitivity of the PPI test in GERD diagnostics is excellent (ranging 95.5 -98.8%)

Test with PPI is commonly used globally, primarily because of high sensitivity

Pace F, Pace M The proton pump inhibitor test and the diagnosis of gastroesophageal reflux disease Expert Rev Gastroenterol Hepatol. 2010
Gasiorowska A, Fass R The proton pump inhibitor (PPI) test in GERD: does it still have a role? J Clin Gastroenterol. 2008
UMHS GERD Guideline, May 2012
Endoscopic biopsies are indicated to detect Barrett’s esophagus and eosinophilic esophagitis, but are not indicated when endoscopy is normal.

The value of taking routine biopsies from patients with NERD is controversial, current guidelines do not recommend this.
Detection of intestinal metaplasia in EGJ region

- Metaplastic columnar epithelium in the distal esophagus (short segment Barrett’s esophagus - SSBE): related to GERD
- Cardia intestinal metaplasia (CIM): related to H. pylori, IM in the cardia is however extremely prevalent and the risk for cancer is considered extremely low

**Risk of dysplasia/cancer is low**

Short segment Barrett’s esophagus
Do we need a biopsy for surveillance?

- The length of the BE was associated significantly with progression to adenocarcinoma (EAC < 6 cm, 0.09%/y vs EAC ≥ 6 cm, 0.65%/y; P = 0.001)
- SSBE do not appear to be as predisposed to malignancy as are long segments of intestinal metaplasia in the esophagus
- Surveillance intervals might be lengthened, especially for patients with shorter segments of BE

It is not recommended that endoscopists routinely obtain biopsy specimens from a healthy-appearing distal esophagus to look for specialized intestinal metaplasia

Tomas T. Meta analysis: cancer risk in Barrett's oesophagus, 2007
Spechler SJ Short and ultrashort Barrett's esophagus--what does it mean? Semin Gastrointest Dis. 1997
Detection of neoplasia at the level of Z-line

Main Tips & Tricks

• High-resolution scope
• Adequate air insufflation
• Retroflexed inspection
• Transparent distal attachment cap
Small transparent distal cap is useful for difficult cases

Courtesy of Professor Stefan Seewald (Hirslanden Klinik, Zurich)
Take home messages

• The accurate designation of the mucosal EGJ is of paramount importance and a prerequisite for any meaningful studies of diseases and classification of lesions spotted in the EGJ region.
• Endoscopic signs of reflux oesophagitis allow establishing the diagnosis of GERD but beyond the level of LA-abnormalities the specificity of minimal change oesophagitis does not allow clinical decision making.
• A test treatment with a PPI has better sensitivity/specificity than these features and the arguments for obtaining biopsies to diagnose reflux changes are even poorer.
• Inspection of the z-line is important since early neoplastic changes are subtle and easily overlooked but in the absence of abnormalities random biopsies should NOT be obtained.
• Tips and tricks such as applying high-resolution scopes, adequate air insufflation, retroflexed inspection, transparent distal attachment cap are useful in routine practice and for detection of suspicious lesions.
LOOK LONGER
THINK MORE
BIOPSY LESS
Minimal changes: Japanese perspective

Japanese endoscopists are generally convinced that they can recognize traditional minimal changes.

**Grade M (minimal changes)**
- Erythema without sharp demarcation ("red ones"): dilation of multiple intrapapillary vessels
- Whitish turbidity ("white ones"): acanthosis with or without keratinization of the epithelium

Takubo K et al. Arch Pathol Lab Med 2005

In two Japanese studies interobserver agreement for recognition grade M was poor (kappa-value was 0.094-0.26)

Amano Y et al. Interobserver agreement on classifying endoscopic diagnoses of nonerosive esophagitis. Endoscopy 2006

Why should endoscopy be done in the patient with GERD?

Endoscopy is recommended for patients who have symptoms suggesting complicated GERD or alarm symptoms for:

- Detecting and grading of reflux-esophagitis
- Detecting of Barrett’s esophagus
- Detecting neoplasia

Screening endoscopy is not a necessary precaution for individuals with GERD
PPI Test

• Endoscopic lesions are only present in a minority of GERD patients. Endoscopy has low sensitivity - less than 50% but specificity in 95%

• In clinical practice, presumptive diagnosis of GERD is reasonably assumed by the substantial reduction or elimination of reflux symptoms during the therapeutic trial of PPI, the so-called PPI test

• The sensitivity of the PPI test was excellent, ranging 95.5 - 98.8%, whereas the specificity was only 36.3%

• Test with PPI is commonly used globally, primarily because of its availability, simplicity, and high sensitivity.

Pace F, Pace M The proton pump inhibitor test and the diagnosis of gastroesophageal reflux disease Expert Rev Gastroenterol Hepatol. 2010
Gasiorowska A, Fass R The proton pump inhibitor (PPI) test in GERD: does it still have a role? J Clin Gastroenterol. 2008
UMHS GERD Guideline, May 2012
Main tips & tricks for detection of lesions at the level of Z-line

EXERA III Olympus high-resolution scope with optical magnification
Detection of intestinal metaplasia in EGJ region

Short segment Barrett’s esophagus

Cardia intestinal metaplasia