The diagnosis and reporting of Barrett’s esophagus

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McMaster – 6 month ago
Three month later
Three month later
Thank you for bringing us to warm weather
OUTLINE

• Definitions
• GERD
• Dysplasia
• Markers
DEFINITIONS

• What is the GE junction?
• What is Barrett’s?
What is the definition of the distal end of the esophagus (gastro-esophageal junction GEJ)?

Looking from outside

It’s where esophagus stops and stomach begins
What is the definition of the distal end of the esophagus (gastro-esophageal junction GEJ)?

Looking from inside

GEJ is where squamous epithelium stops and columnar starts
What is the **definition** of the distal end of the esophagus (gastro-esophageal junction GEJ)?

**Normal**: GEJ (squamo-columnar) are the same looking from outside and inside.
What is the definition of the distal end of the esophagus (gastro-esophageal junction GEJ)?

In Western countries, the landmark is the upper end of the gastric longitudinal folds.
Squamous-columnar is in the esophagus
What is the definition of the distal end of the esophagus (gastro-esophageal junction GEJ)?

In Prague’s C&M Barrett’s criteria: “C” for circumferential extent “M” for maximal extent

Aliment Pharmacol Ther
2004;20(Suppl 5):40-7
DEFINITIONS

Columnar Lined Esophagus CLE

If you don’t see goblets call it Columnar Lined Esophagus CLE

Replacement by glandular mucosa of any type. Need to state whether goblet cells are present or not.

No goblets = implies no cancer risk)
Intestinal Metaplasia at the GEJ

6-37%  
<3cm

20-60%  
短 segment
columnar lined oesophagus

50-100%  
>3cm

long segment
columnar lined oesophagus

CANCER RISK POST BARRETT’S

Non-erosive Reflux disease → Limited progression → Erosive Reflux disease

Cancer → ? → Barrett’s with dysplasia → ? 3 yrs → Barrett’s esophagus With Goblet cells

No data
PATHOLOGY ROLE

Non-erosive Reflux disease

1. Diagnose GERD

Erosive Reflux disease

Limited progression

2. Diagnose Barrett’s
   "C&M" w/without goblets

3. Diagnose and grade dysplasia

? 3 yrs

4. Diagnose cancer
   Cancer

? No data
CRITERIA USED TO DIAGNOSE GERD

- Elevated rete ridges (reach upper 1/3)
- Basal cell hyperplasia
- Intraepithelial eosinophils & neutrophils
ADDITIONAL CRITERIA USED TO DIAGNOSE GERD

Differential is *H. pylori* gastritis in gastric cardia
Look for amount of acute and chronic inflammation
Best look in other gastric biopsies

Foveolar hyperplasia - cardia
ADDITIONAL CRITERIA USED TO DIAGNOSE GERD

Dilated intercellular spaces

Look for extent (C & M)
Intra epithelial EOSINOPHILs
(GERD vs. Eosinophilic Esophagitis)

- Eos abscess
  - Not at top except next to ulcer
  - Reach superficial layer

- Eos found in proximal biopsies
  - Numerous

- Eos absent in proximal biopsies
  - Few (if found)

- Eosinophilic eosophagitis
- GERD
Eosinophilic Eosophagitis

Furrows
The sensitivity of histologic changes in reflux esophagitis is only 50% to 65%.

The objective diagnosis of GERD should be based on pH monitoring & endoscopic changes (not histology) specially in non-erosive disease.

Histology is only needed to exclude Barrett’s esophagus and related malignancy.
Problems in the biopsy diagnosis of Barrett’s Esophagus

1. Definition
2. Is the diagnosis of BE/CLE endoscopic or pathologic?
3. Can we distinguish SSBE from IM in native cardia?
Types of epithelium in Columnar Lined Esophagus (CLE)
(No goblet cells- implies no malignant risk)

Implied: no cancer risk
DEFINITIONS: Barrett’s Esophagus

Replacement by glandular mucosa with goblet cells/intestinalized mucosa with an appropriate endoscopic appearance

Goblets = implies a cancer risk

You need histology (goblet cells) and an appropriate endoscopic appearance for a diagnosis of Barrett’s esophagus
(implies a cancer risk)

Barrett’s

Multilayered epithelium with goblet cells
Intestinal Metaplasia: is it cardia?
Or is it Barrett’s
CYTOKERATIN 7/20 PROFILE IN BARRETT’S

Not true
Don’t use it
No body uses them (including the authors)

CK 7 Diffuse
CK 20 Superficial band like

Ormsby et al Hum Pathol 1999; 30:288-294
Intestinal Metaplasia: is it cardia? Or is it Barrett’s
What are your options?

Issue a diagnosis of:
Columnar Lined epithelium with no goblet cells
Columnar Lined Epithelium with goblet cells

Let the gastroenterologist decide whether it is metaplasia of the
gastric cardia or distal end of
esophagus (Barrett’s)
What are the Possible Sources of GEJ Cancer?

Carcinoma at the Cardia

- Half are gastric
  - Need gastric surveillance
  - 53% according to El-Zimaity et al. 2005

- Half are esophageal
  - Need esophageal surveillance
  - 47%
Either way you need to screen

- If intestinal metaplasia is from SS or LS Barrett’s patients needs to be screened for dysplasia and cancer post Barrett’s.
- If intestinal metaplasia is from the gastric cardia patient need to be screened for gastric atrophy and possible development of gastric dysplasia and cancer.
Is it intestinal metaplasia of the gastric cardia or Barrett’s metaplasia?

- Biopsy the stomach.
- In Barrett’s: stomach is healthy
- In metaplasia post gastritis (cardia), the stomach has a lot of *H. pylori* associated changes.
Is there Dysplasia?

1. Architectural pattern
2. Nuclear Pattern
3. Surface maturation
LOW GRADE DYSPLASIA

- Preserved crypt architecture
- Nuclei are enlarged, but don’t reach apical surface
- Loss of surface maturation
• Architectural distortion (with branching, lateral budding or cribriform pattern)
• Nuclear abnormalities as in low-grade dysplasia but there is bigger variation among the nuclei; stratified nuclei reaches luminal surface; loss of polarity.
• Loss of surface maturation.

High grade dysplasia
1. Architectural pattern = normal
2. Nuclear Pattern = basal ? Nuclear maturation
3. Surface maturation = present
no dysplasia – tangential sectioning
Surface maturation implies it is benign
1. Architectural pattern = mild distortion
2. Nuclear Pattern = basal
3. Surface maturation = present/?

Indefinite for dysplasia
1. Architectural pattern = mild distortion
2. Nuclear Pattern = basal
3. Surface maturation = ????
Low-Grade Dysplasia (lack of surface maturation)
1. Architectural pattern = distorted
2. Nuclear Pattern = ? adenoma
3. Surface maturation = no

Low-Grade Dysplasia (resembles tubular adenoma)
Low-Grade Dysplasia (resembles tubular adenoma)
1. Architectural pattern = complex
2. Nuclear Pattern = prominent atypia
3. Surface maturation = negative

High-Grade Dysplasia

HUM PATHOL 32:368-378
Intramucosal Carcinoma: syncytial arrangements of cells and complex glandular budding is believed to reflect early invasion (before desmoplasia becomes well-developed).
ADENOCARCINOMA IN BARRETT’S ESOPHAGUS

Invasive (deep lesions) are usually easy to diagnose
AdenoCa
What is the Interobserver variation between pathologists?

substantial

There is considerable interobserver variation in interpretation even among experts. This is most marked in the differential between no dysplasia, indefinite vs. low grade dysplasia.

Less subjective makers are needed.
Role of Biomarkers in Diagnosing Dysplasia in Barrett’s

1. P53
2. Racemase
p53 in Diagnosing Dysplasia in Barrett’s

Though controversial, alterations in p53 expression can facilitate the interpretation of an epithelial abnormality.
What is a positive stain for p53

Sporadic nuclear staining should be considered negative (-).

Nuclear staining in continuity indicates clonal expansion of mutated cells (+).
p53 Role in Diagnosing Barrett’s

<table>
<thead>
<tr>
<th></th>
<th>Non dysplastic</th>
<th>Low grade dysplasia</th>
<th>High grade dysplasia</th>
<th>Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.4 %</td>
<td>30%</td>
<td>68%</td>
<td>72%</td>
</tr>
<tr>
<td>(0-10%)</td>
<td>(0-60%)</td>
<td>(50-100%)</td>
<td>(45-100%)</td>
<td></td>
</tr>
</tbody>
</table>

Table shows gradual increase in p53 expression as dysplasia increases.

Why is p53 use controversial?

Because of the considerable overlap in expression between and within categories.
If histopathology suggests dysplasia, and is p53 (+) specimen is more likely to be dysplastic; if it is dysplastic it is more likely to progress to cancer if p53 (+).
Is AMACR expression a marker for neoplastic progression?

- AMACR stands for alpha-methylacyl-coenzyme A racemase. A racemase is an enzyme that catalyzes the reversible interconversion of two enantiomeric forms of a racemic compound.
- Two studies demonstrated high specificity for Barrett’s neoplasia.
- Third study indicates lack of reliability.

The jury is still out. More studies are needed.

Observer variation in the diagnosis of superficial oesophageal adenocarcinoma

Even experienced gastrointestinal pathologists frequently disagree on a diagnosis of high grade dysplasia versus intramucosal adenocarcinoma.
CANCER RISK POST BARRETT’S

Non-erosive Reflux disease

Limited progression

Erosive Reflux disease

Patients bounce back and forth between categories

Cancer

risk following Barrett’s is 0.5%/year

MOST AdCa GEJ arise in patients with NO prior endoscopy - ? SSBE ?IM in native

No data
# Proposed Classification of Intestinal Metaplasia at GEJ

<table>
<thead>
<tr>
<th>Term</th>
<th>Length</th>
<th>Cancer Risk</th>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSBE</td>
<td>&gt; 3 cm</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>SSBE</td>
<td>&lt; 3 cm</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Gastric cardia IM</td>
<td></td>
<td>Unclear</td>
<td>has gastric cancer risk? No risk for GEJ</td>
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</table>
Main differential with GERD is Eosinophilic esophagitis. History, endoscopic appearance and proximal biopsies will help differential.

Barrett’s is columnar lined esophagus. Call it columnar lined in absence of goblets. Call it Barrett’s metaplasia if you see goblets.

Use architecture, nuclear features, and surface maturation to diagnose low grade dysplasia and high grade dysplasia.

In doubt, P53 expression can facilitate interpretation but can only be used in conjunction with histopathology.
Considering the mortality with esophagectomy and substantial interobserver variability in diagnosing dysplasia and intra-mucosal carcinoma, endoscopic mucosal resection should be the preferred treatment.