GERD AND ITS COMPLICATIONS

Presentation, diagnosis and management of GERD
Importance of Barrett’s Esophagus
Diagnosis
Screening
Surveillance
Diagnosis and Management of Dysplasia
Endoscopic Therapy for Barrett’s Related Neoplasia
GERD and pregnancy
GASTROESOPHAGEAL REFLUX DISEASE

- Chronic, relapsing condition with associated morbidity and an adverse impact on quality of life
- Occurs when retrograde flow of stomach contents
- Can occur as non-erosive reflux disease (NERD) or erosive esophagitis
- Symptoms: Heartburn that occurs 30-60 minutes after meals or when laying flat
  - Often relieved with antacids or baking soda
  - Often triggered by spicy or acidic foods
- Endoscopy is not always necessary in patients with classic symptoms

PREVALENCE

- GERD is extremely common, with a prevalence of approximately 20% of adults in the western culture
- Most adults have mild disease, but mucosa damage can develop in 1/3 of patients
- Symptoms occur daily in approximately 7% of patients, weekly in 14% and monthly in 15% to 40% of all patients
- No difference in prevalence between men and women but men have increased risk of complications
- GERD increases in prevalence with age and obesity
  - A meta-analysis published in the Annals of Internal Medicine in 2005 concluded that obesity was associated with a statistically significant increase in the risk of GERD symptoms, erosive esophagitis, and esophageal carcinoma.
Impaired lower esophageal sphincter function
- LES functions as a barrier to reflux of gastric contents

Normally, a certain amount of physiologic gastroesophageal reflux occurs by means of transient relaxation of the LES, which increases after a meal to permit gas to be vented from the stomach

Risk factors for decreased LES pressures: pregnancy, diabetes, scleroderma, obesity, and medications such as calcium channel blockers, cholinergic antagonists, glucagon, nicotine from cigarette smoking and oral contraceptives.
Hiatal hernia
- Common and don’t always cause symptoms
- Associated with higher amounts of acid reflux and delayed esophageal acid clearance
- Hiatal hernias are found in a fourth of patients with non-erosive GERD, in three-fourths of patients with erosive GERD, and in over 90% of patients with Barrett Disease.

Irritant effects of Refluxate - gastric acid fluid (pH less than 4) is extremely caustic.

Abnormal esophageal clearance
- Acid that reaches the esophagus is normally cleared and neutralized by esophageal peristalsis and salivary bicarbonate
- During sleep, peristalsis is infrequent, prolonging acid exposure to the esophageal mucosa
- ETOH and sedatives delay clearance as well
- Also, conditions such as Sjögren disease that affect the quality or quantity of the saliva, anticholinergic medications, and oral radiation can further worsen the natural protective mechanisms and lead to higher exposure of the esophageal mucosa to damage
**HISTORY AND PHYSICAL**

- Typical symptoms include heartburn, regurgitation, dysphagia, globus sensation, odynophagia and nausea

- Retrosternal burning that starts in epigastrum and often radiates to the throat

- Postprandial - aggravated by ingestion of certain foods or beverages such as tomato sauce, chocolate, coffee, teas, and alcohol

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**EVALUATION**

- Initial diagnostic tests are not warranted with typical GERD symptoms

- Further workup is needed in patients with alarm features
  - Dysphagia
  - Odynophagia
  - Weight loss
  - Iron deficiency anemia
  - Persistent symptoms despite treatment
  - Family history of esophageal adenocarcinoma
  - Hematemesis
**EVALUATION**

- **Barium swallow- limited**
  - Can diagnose severe esophagitis, strictures, hiatal hernias and tumors
  - Often only utilized in areas where endoscopy is not available or if dysphagia is present

- **Esophagogastroduodenoscopy**
  - Also allows the diagnosis of other disease states
  - Allows grading of esophagitis and biopsy
**LOS ANGELES CLASSIFICATION**

Los Angeles Classification of reflux esophagitis:

- **LA grade A**: One (or more) mucosal break no longer than 4 mm, that does not extend between the tops of two mucosal folds.

- **LA grade B**: One (or more) mucosal breaks more than 4 mm long, that does not extend between the tops of two mucosal folds.

- **LA grade C**: One (or more) mucosal breaks that is continuous between the tops of two or more mucosal folds, but which does not extend between the tops of two mucosal folds.

- **LA grade D**: One (or more) mucosal breaks that is continuous at least 75% of the esophageal circumference.

*Lundell et al., Gut 40:172-180 (1999)*
ESOPHAGEAL ADENOCARCINOMA
EVALUATION

- **pH impedance/manometry**
  - Usually unnecessary for patients with classic GERD unless treatment is ineffective
  - Detects changes in the resistance of electrical current on a catheter placed within the esophagus
  - In addition to recording the esophageal pH, it can differentiate both antegrade and retrograde transit of liquid and gas

TREATMENT

- **Goals of treatment:**
  - Resolve symptoms
  - Heal esophagitis
  - Prevent complications

- **Lifestyle modifications**
  - Absolutely necessary - Without these medications are less effective
  - Weight loss - central obesity increases intrabdominal pressure
  - Elevate head of bed - not with extra pillows but 1-3 inch blocks
  - Tobacco cessation - nicotine relaxes LES
  - ETOH cessation
  - Avoid late night eating
  - Avoid trigger foods
TREATMENT

- Antacids - inexpensive and readily available
  - Sodium bicarbonate
  - Magnesium carbonate
  - Calcium carbonate
  - Aluminum hydroxide
- Histamine 2 receptor antagonists - inhibit secretion of gastric acid by blocking H-2 receptors in parietal cells
  - Inexpensive and readily available
  - 75% effective
  - Cimetidine
  - Famotidine
  - Nizatidine
  - Ranitidine

RANITIDINE RECALL

- The FDA recently released several safety alerts on ranitidine formulations, including the brand-name drug Zantac, which were found to contain a nitrosamine impurity called N-nitrosodimethylamine (NDMA) at low levels
- NDMA is a probable carcinogen
- For the latest list of effected manufacturers
- Nizatidine appears to be effected as well
TREATMENT- PROTON PUMP INHIBITORS

- Block the hydrogen-potassium ATPase on the apical surface of the parietal cells
- More effective than H2RA as well as longer acting
- omeprazole (Prilosec, Prilosec OTC, Zegerid)
- lansoprazole (Prevacid)
- pantoprazole (Protonix)
- rabeprazole (Aciphex)
- esomeprazole (Nexium)
- dexlansoprazole (Dexilant)

- PPIs long term effects have been extensively studied recently. Most recent study shows no increase in rate of dementia, ESRD, lung disease
  - There does seem to be increased osteoporosis due to decreased calcium and Vitamin D absorption
  - Increased risk of intestinal infections (C-dif)

TREATMENT- ANTIREFLUX PROCEDURES

- Nissen fundoplication
- ROUX- En-Y gastric bypass
- LYNX procedure
- Transoral incisionless fundoplication
- These patients are resistant to standard therapy or have side effects to medications
Acquired condition in response to Gastro-esophageal reflux leading to columnar lined epithelium in the distal esophagus

Intestinal metaplasia, characterized by goblet cells, is biologically unstable with greatest risk of neoplastic progression

Major risk factor in development of esophageal adenocarcinoma

Incidence of EAC rising rapidly in western countries


Change in the distal esophageal epithelium of any length that can be recognized as columnar type mucosa at endoscopy and is confirmed to have intestinal metaplasia by biopsy of the esophagus

Clearly visible endoscopically above the GEJ(>1cm) and confirmed histo-pathologically with distal esophageal biopsies of columnar lined epithelium only
BARRETT’S ESOPHAGUS

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[Image: Photomicrograph showing Barrett’s esophagus.]

[Text: This photomicrograph shows surface glandular epithelium with tall columnar cells punctuated by round to oval goblet cells (long arrow). The columnar epithelium resembles intestinal epithelium but is not identical in nature. It is unclear why this metaplasia occurs but long-standing gastro-esophageal reflux disease (GERD) is present in all patients. Barrett’s metaplasia is also characterized by universal presence of chronic inflammation (lower arrowhead)].

ENDOSCOPIC DIAGNOSIS OF BE

- Must distinguish BE from Irregular Z-line
- Where the squamo-columnar junction appears with tongues of columnar epithelium less than 1cm with no confluent columnar lined segments
- Biopsies are generally NOT RECOMMENDED for Irregular Z-line
- If done, then label as GEJ not esophageal biopsies
ENDOSCOPIC REPORTING OF BE

- Should be done using the Prague Criteria
- Which assesses the circumferential (C) and maximal (M) extent of endoscopically visualized Barrett’s Segment
- Diaphragmatic Pinch and Proximal End of the Gastric Folds
- The presence and location of visible lesions should be recorded according to Paris Classification

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)
Step 4: determine C

CIRCUMFERENTIAL EXTENT OF SUSPECTED BARRETT'S

http://www.quality-in-endoscopy.org/assets/download/pdf/reports/qine30/04_1_LT_Blebs.pdf
**Step 5: Determine M**

MAXIMAL EXTENT OF SUSPECTED BARRETT’S

http://www.quality-endoscopy.org/assets/downloads/pdf/reports/qine30/04_1_LT_Bliss Hopkins.pdf

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**PRAHCE CRITERIA**

For Endoscopically Suspected Esophageal Columnar Metaplasia/Barrett’s Esophagus

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

- Minimum of 8 biopsies provides adequate assessment of Intestinal Metaplasia
- Starting distally 1-2cm above GEJ, 4 quadrant random biopsies should be done every 2cm while advancing proximally
- Targeted biopsies of visible lesions (should be done before random biopsies)
- Ideally, erosive esophagitis should be healed prior to biopsies for BE to avoid missing short segments of columnar epithelium


SCREENING FOR BE

- Screening for BE in unselected population of patients with gastro esophageal reflux symptoms is not recommended
- Screening should be considered in patients with chronic GERD (> 5-13 years) and multiple risk factors including at least 3 of the following
  - Age 50 or older
  - White race
  - Male sex
  - Obesity
  - Family history of esophageal adenocarcinoma
- Threshold of multiple risk factors should be lowered in those with a first degree relative with Barrett’s or esophageal adenocarcinoma
**SURVEILLANCE**

- Aim of surveillance is to detect cancer or pre-cancer at a stage when intervention may be curative
- Surveillance correlates with earlier staging and improved survival from cancer
- Endoscopic monitoring with histo-pathologic assessment of dysplasia is the only current method of surveillance
- High resolution Endoscopy should be used for surveillance

**PATHOLOGIC FEATURES AND REPORTING OF DYSPLASIA**

- Dysplasia should be reported as low or high grade (controversy over indefinite)
- Any grade of dysplasia should be confirmed by an expert or two independent pathologist
- Revised Vienna Classification for GI mucosal neoplasia standardizes diagnostic terminology into biologically similar groupings with scores of 1-5 depending on presence/absence of dysplasia or malignancy
  - 1. Negative for Dysplasia
  - 2. Indefinite for Dysplasia
  - 3. Low Grade Dysplasia
  - 4. High Grade Dysplasia
  - 5. Submucosal Invasion of Adenocarcinoma
**INTESTINAL METAPLASIA**

[BARRETT’S METAPLASIA]. Barrett’s metaplasia of esophagus is defined as replacement of the normal squamous epithelium of distal esophagus by metaplastic glandular epithelium containing intestinal-type goblet cells. Note the squamous epithelium on the left (arrowhead) is continuous with the metaplastic epithelium containing goblet cells (long thin arrow) on the right. The transition is shown by downward arrow on the top.

**HIGHER POWER**

[BARRETT’S METAPLASIA]. This photomicrograph shows surface glandular epithelium with tall columnar cells punctuated by round to oval goblet cells (long arrow). The columnar epithelium resembles intestinal epithelium but is not identical in nature. It is unclear why this metaplasia occurs but long-standing gastro-esophageal reflux disease (GERD) is present in all patients. Barrett’s metaplasia is also characterized by universal presence of chronic inflammation (lower arrowhead).
INDEFINITE FOR DYSPLASIA

Barrett’s metaplasia. Inflammation present in Barrett’s metaplasia may lead to nuclear atypia of varying degrees. In some cases the nuclear atypia simulates dysplasia but histologic features diagnostic of dysplasia are not seen. Also, this is one area in diagnostic histopathology where consensus among pathologists to what is a low grade dysplasia in a given case is lacking. To address this issue of reactive atypia versus low-grade dysplasia a diagnosis of “indefinite for dysplasia” may be used. This case with inflammation in glands (bottom long arrow) shows loss of polarity, pseudo-stratification, mild nuclear enlargement and hyperchromasia, and distinct nucleoli may be called "nuclear atypia indefinite for dysplasia."

LOW GRADE DYSPLASIA

Barrett’s esophagus (metaplasia). A low-grade dysplasia in Barrett’s esophagus, at a minimum, requires nuclear enlargement (right arrow), nuclear hyperchromasia, and nuclear contour irregularity. Prominent nucleoli and mitoses are common but reactive epithelium may also show mitoses and prominent nucleoli. Generally, dysplasia reaches the surface epithelium but not all biopsy specimens show surface epithelium involvement. The dysplastic epithelium in this case can be contrasted to normal glandular epithelium on the right (arrowhead).
Controversy exists for management of indefinite for dysplasia.

Rate of cancer progression in patients with indefinite for dysplasia was similar to non-dysplastic patients; however, if the indefinite for dysplasia was multifocal, the rate of progression was as high as in patients with LGD.

DYSPLASTIC BARRETT’S ESOPHAGUS

- Always needs confirmed by expert pathologist
- Obtain every 1 cm in patients with known dysplasia
- Consider radiofrequency ablation

Endoscopic ablative therapy is a superior management strategy to endoscopic surveillance in patients with Barrett’s esophagus and confirmed low-grade dysplasia

Ablation treatment was generally safe with esophageal stricture being the most common complication (11.8%), requiring a median of 1 dilation

Patients with LGD should have a repeat endoscopy in 6 months time

If LGD is found in any of the follow up EGDs and is confirmed by an expert GI pathologist, the patient should be offered endoscopic ablation therapy.

If the possibility of high grade dysplasia has been raised, it is critical that a high-quality baseline endoscopy is done to map out any visible lesions and extent of dysplasia.

Endoscopic assessment will usually identify the area with the most advanced neoplasia. EMR should aim to resect all visible abnormalities.

HGD and Barrett’s-related adenocarcinoma confined to the mucosa, endoscopic therapy is preferred over esophagectomy or endoscopic surveillance.
Table 8 Subclassification of T1a and T1b oesophageal adenocarcinoma

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1a</td>
<td></td>
</tr>
<tr>
<td>m1</td>
<td>Carcinoma in situ or with questionable invasion beyond the basement membrane</td>
</tr>
<tr>
<td>m2</td>
<td>Invasion into the lamina propria</td>
</tr>
<tr>
<td>m3</td>
<td>Invasion into the muscularis mucosa</td>
</tr>
<tr>
<td>T1b</td>
<td></td>
</tr>
<tr>
<td>sm1</td>
<td>Invasion into the upper third of the submucosa within 500 μm</td>
</tr>
<tr>
<td>sm2</td>
<td>Invasion into the middle third of the submucosa</td>
</tr>
<tr>
<td>sm3</td>
<td>Invasion into the lower third of the submucosa</td>
</tr>
</tbody>
</table>

ESOPHAGEAL ADENOCARCINOMA

Endoscopic ultrasonography (EUS)

Unlike CT, EUS allows visualization of the distinct layers within the esophageal wall. Alternating circumferential layers define:

- the mucosal interface (hyperechoic),
- the mucosa (hypoechoic),
- the submucosa (hyperechoic),
- the muscularis propria (hyperechoic),
- and the adventitial interface (hyperechoic).
Endoscopic ultrasonography (EUS)

**Esophageal carcinoma stage T1.**
EUS revealed a small hypoechoic irregular tumor that was infiltrating into echogenic submucosa but had not breached underlying muscularis.

**Esophageal carcinoma stage T2.**
The tumor (TU) invades muscle layer but does not penetrate through wall. L1-lymph node.
Endoscopic therapy for Barrett’s neoplasia has been developed on the evidence that HGD and T1a EAC is associated with a low rate of lymph node metastasis: endoscopic and surgical series indicate a 0–10% risk in T1a cancer, while submucosal invasion carries a higher risk (up to 46%).

ER should be considered the therapy of choice for dysplasia associated with visible lesions and T1a adenocarcinoma (Recommendation grade B).
ESOPHAGEAL ADENOCARCINOMA

- For patients at high surgical risk, endoscopic therapy can be offered as an alternative to surgery for treatment of good prognosis T1b adenocarcinomas (T1b sm1, well differentiated and without lymph vascular invasion).

- For T1b adenocarcinomas with involvement of the second sub-mucosal layer or beyond (T1b sm2–sm3), endoscopic therapy should not be considered curative.

ESOPHAGEAL ADENOCARCINOMA

- In the presence of HGD or intramucosal cancer without visible lesions (flat HGD/intramucosal cancer), these should be managed with an endoscopic ablative technique. RFA currently has a better safety and side-effect profile and comparable efficacy.

- Eradication of residual Barrett’s esophagus after focal ER reduces the risk of metachronous neoplasia and is recommended.
In patients treated for HGD, endoscopic follow-up is recommended every 3 months for 1 year and yearly thereafter.

This should include biopsies at the GEJ and within the previous extent of the Barrett’s epithelium.
QUESTIONS?