Core Lecture: GERD

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Core Lecture: GERD

- Epidemiology
- Pathophysiology
- General Concepts
- Typical vs. Atypical
- Treatment

Prevalence of GERD Symptoms: The Olmsted County Study*



*Data collected by self-report questionnaire.

Locke et al. Gastroenterology. 1997;112:1448-1456.

GERD Symptoms are Associated with Obesity in Meta-Analysis Study



Hampel H, et al. Ann Intern Med. 2005;143:199-211.



Significance of Intragastric pH >4 in GERD

- Pepsin is inactive at pH >4
- Most bile acids and pancreatic enzymes inactive at pH >4
- Esophageal mucosa injury is rare at pH >4

Hunt. Arch Intern Med. 1999;159:649-657. Smith et al. Gastroenterology 1989:96:683-689

Three Mechanisms Causing Pathologic Acid Reflux



Van Herwaarden et al. *Gastroenterology*. 2000;119:1439-1446.

Transient LES Relaxation



Hiatal Hernia

Wo JM et al. Am J Gastroenterol 1996;91:914-916.

Increased Intragastric Pressure and BMI

Higher intragastric pressure may increase the chance that gastric contents will ascend into the esophagus

Pandolfino JE, et al. Gastroenterol 2006:130:639-649.

Acid Pocket After Meals Below the GEJ

GERD—A Spectrum of Disease?

Pro-GERD Epidemiological Study from Germany, Austria, and Switzerland

Kulig M et al. Clin Epidemiol 2004;57:580-9

New Conceptual Model for GERD

Fass R et AL. Am J Gastroenterol 2002:97:1901-9.

Heartburn Severity Does Not Correlation with Erosive Esophagitis

undell et al Gut 1999:45:172-180

Heartburn Severity May Not Correlate with Disease Severity in GERD

No hiatal hernia Transient LES relaxation

Large hiatal hernia Low LES pressure

"Hypersensitive" esophagus NERD Functional heartburn

Barrett's esophagus Peptic stricture

No Esophagitis

Severe Esophagitis

GERD Severity —

Brain-Gut Axis for Non-Erosive Reflux Disease

Fass 2004. J Clin Gastroenterol 2004;38:628.

Typical vs. Atypical GERD			
	Typical	<u>Atypical</u>	
Symptoms	consistent	variable	
Esophagitis/Barrett's	common	uncommon	
Causes	reflux	reflux + multifactorial	
Treatment response	rapid	variable	
Therapy	step-therapy	more aggressive + longer duration	

Typical GERD

Empiric Therapy is Appropriate in Patients with Typical Heartburn

When is Upper Endoscopy Indicated?

- 1. Alarm symptoms of GERD
 - Dysphagia, odynophagia, GI bleed, weight loss
- 2. Refractory heartburn
- 3. Recurrent disease
- 4. At risk for Barrett's esophagus

DeVault, Castell. Guidelines for the Diagnosis and Treatment of GERD. Arch Intern Med 1995;155:2165-73

GERD Complications

- Esophagitis
- Esophageal stricture
- Barrett's esophagus
- Adenocarcinoma

Los Angeles Grading System

Los Angeles A

Los Angeles C

One or more mucosal breaks <u>no</u> <u>longer than</u> 5 mm, not bridging the tops of mucosal folds

Los Angeles B

One or more mucosal breaks <u>longer than</u> 5 mm, not bridging the tops of mucosal folds

Los Angeles D

One or more mucosal breaks <u>bridging</u> the tops of mucosal folds <u>involving <75% of</u> <u>the circumference</u>

One or more mucosal breaks bridging the tops of mucosal folds involving >75% of the circumference

Esophageal Peptic Stricture

Barrett's Esophagus

EGD Improves the Management of Patients with Alarm Symptoms of GERD

Wo et al. Am J Gastroenterol 2004:99; 2304-10.

Healing of Erosive Esophagitis

Meta-analysis from 23 placebo-controlled trials with grade II to grade IV EE. Chiba et al. *Gastroenterology*. 1997:112:1798-1810.

Erosive Esophagitis is a Chronic Condition that is Likely to Relapse

Lundell LR, et al. *Gut.* 1999;45:172-180.

Long-Term PPI for Reflux Esophagitis

Healed

Esophagitis Relapses

Omeprazole ≥20 mg.

Klinkenberg-Knol et al. Gastroenterology. 2000;118:661-669.

Laryngopharyngeal Reflux (LPR)

Symptoms of LPR are not Specific

- Hoarseness
- Globus
- Sore throat
- Throat clearing
- Excessive throat mucus
- Cough
- Throat burning/pain
- Voice weakness
- Cervical dysphagia

• Heartburn (6-50%)

Dog Model of LPR

Adhami et al. Am J Gastroenterol 2004;99:2098

Laryngeal Signs of LPR

Normal Laryngeal Tissue

True Vocal Fold Erythema

Bilateral True Vocal Fold Nodules

Reinke's Edema

Arytenoid Medial Wall Edema

Posterior Pharyngeal Wall Cobble Stoning

aezi et al. Clin Gastroenterol Hepatol 2003:1:333-344

Laryngeal Findings of LPR are Common in Normal Volunteers

ENT Findings

Interarytenoid bar Arytenoid medial wall erythema Posterior pharyngeal wall cobblestoning Arytenoid medial wall granularity True vocal cord erythema Prevalence 35/50 (70%) 20/50 (40%) 10/50 (20%) 7/50 (14%) 5/50 (10%)

Hicks et al. J of Voice 2002;16:564.

Diagnosis Associated with LPR

Harrell et al. DDW 2004 (N=167, confirmed by pH monitoring)

Randomized, Placebo-Controlled Trial in Patients with Suspected LPR

Vaezi et al. Laryngosc 2006;116:254.

Randomized, Placebo-Controlled Trial in Patients with LPR with +pH Test

Wo et al. Am J Gastroenterol 2006; accepted for publication.

Meta-Analysis of RCT for LPR

Qadeer et al. Clin Gastroenterol Hepatol 2006; submitted for publication.

Treatment Response Do Not Correlate with Acid Suppression

Wo et al. Am J Gastroenterol 2006; accepted for publication.

Causes of LPR are Multifactorial

- GI
 - Gastroesophageal reflux, impaired esophageal peristalsis, gastroparesis
- ENT
 - Voice abuse, vocal dysfunction, vocal granuloma, laryngeal carcinoma, sinusitis, post nasal drip
 - Others
 - Impaired reflex, impaired sensation, irritants, allergy, psychological

Management Algorithm for LPR

Signs and Symptoms of LPR

PPI (Qd vs. Bid) x 3-4 months or ??

Sx improve

Consider other diagnoses Come off therapy

Pulmonary Manifestations

How GERD May Cause Pulmonary Symptoms

Esophageal-Bronchial Reflex via Vagus Nerve

rwin and Richter Am I Gastroenterol 2000.95(suppl 8).S9-S14

Prevalence of GERD in Adult Patients With Asthma

Sontag. J Clin Gastroenterol. 2000;30(suppl):9-30.

When to Suspect GER-Related Asthma?

- Nocturnal symptoms
- Difficult to control asthma
- Non-allergic asthma
- Presence of heartburn

Irwin et al. Chest 1993;6:1662-69.

Acid Suppression by Proton Pump Inhibitors Based on 24-hour pH Monitoring

Harding et al. Am J Med. 1996;100:395-405.

Randomized Controlled Trial for GERD-Related Asthma

Kiljander et al. Am J Resp Crit Med 2005.

Why PPI is not Working?

Six Most Common Reasons for Why PPI Is Not Working

- 1. Inadequate acid suppression
- 2. Not taking the medication correctly
- 3. Large hiatal hernia
- 4. Impaired esophageal motility
- 5. Gastroparesis
- 6. Wrong diagnosis

Inadequate Acid Suppression by PPI

Adapted from Tutuian et al. Med Gen Med 6(4), 2004. ¹ Hammer et al. Aliment Pharmacol Ther. 2004 15;

Not Taking the PPT before Meals

Reprinted with permission from Hatlebakk JG, et al. Aliment Pharmacol Ther. 2000:14;1267-1272.

PPI Oral Formulation

- Delayed-release PPI
 - Tablet
 - Capsule
 - Powder
 - Dissolvable
- Immediate-release PPI
 Tablet
 - Powder

Median Gastric pH During Night PPI Dosing q.h.s. (Day 7)

Katz PO et al. Gastroenterol 2006;130(2):A175.

Qhs "Before Bed" Dosing is Not Appropriate with Delayed-Release PPI*

(n=49) Zegerid vs. lansoprazole p-value <0.001 Zegerid vs. esomeprazole p-value <0.001

*Nighttime Interval (2200-0600) on day 7

Katz PO et al. Gastroenterol 2006:130(2):A175.

Pharmacokinetics of Immediate-release and Delayed-release Omeprazole

N=31, open label cross-over, after 7 days of study drug

Diagnostic Testing for GERD*

	Sensitivity	Specificity
	(%)	(%)
Empiric Trial With a PPI	70-80	60-85
Endoscopy	40-70	90-95
Esophageal pH Monitoring	70-90	80-95
Barium Swallow	30-35	60-75
Esophageal Manometry	15-30	20-40

*Depends on clinical suspicion

Presentation of Gastroparesis

Bizer et al. Gastroenterol 2005; 128 (suppl 2): abstract.

Indigestible Food Bezoars in Patients with Gastroparesis

Transnasal pH monitoring

- Strength
 - Most sensitive and specific test for GERD
 - Useful for atypical GERD
- Weakness
 - Patient discomfort
 - Costly

Bravo Wireless pH Telemetry

- Strength

 Patient friendly
 48-hr test

 Weakness
 - Single sensor

Activation plunger and plastic keeper

Conclusion

- All GERD patients are not the same
 NERD vs. EE vs. BE
- Causes of atypical GERD are multifactorial
- Acid suppression is the first-line of therapy
- Reflux complications require maintenance therapy
- Six most common reason for refractory typical or atypical GERD are