What to Do About Bizarre Esophageal Symptoms?

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Is GERD to Blame?

Yellow Tongue = Acid Reflux
Extra-Esophageal GERD

- **ENT**
  - Globus
  - Hoarseness
  - Laryngitis
  - Otitis
  - Pharyngitis
  - Sore Throat
  - Subglottic stenosis
  - Vocal Cord Granulomas

- **Pulmonary**
  - Chronic Cough
  - Asthma
  - Pulmonary fibrosis
  - Pneumonia

- **Miscellaneous**
  - Non-Cardiac Chest Pain
  - Dental erosions

Objectives

• Non-Cardiac Chest Pain (NCCP)

• Throat and Cough Symptoms

• Is there evidence that GERD is a cause?

• What are the best diagnostic tools?

• How effective are GERD treatments?

• If not GERD, then what?
Non-Cardiac Chest Pain

• Evidence for GERD as a cause

- NCCP reported in 37% with weekly heartburn vs 7.9% without GERD symptoms

- Heartburn is the only reliable risk factor for NCCP (OR=1.74, 95% CI: 1.08-2.79)

Diagnosis of NCCP

- **Upper Endoscopy**
  - 19.4% Erosive Esophagitis
  - 4.4% Barrett’s
  - 28.6% Hiatal Hernia
  - Findings were less common than in classic GERD

Dickman et al. Am J Gastroenterol 2007
Low Yield Esophageal Manometry

ESOPHAGEAL MANOMETRY FINDINGS

- Normal: 70%
- Abnormal: 30%

- Hypotensive LES: 61%
- Hypertensive LES: 10%
- Achalasia: 10%
- Nutcracker Esophagus: 5%
- Diffuse Esophageal Spasm: 10%
- Ineffective Peristalsis: 2%

Dekel et al. Aliment Pharmacol and Ther 2003
Empiric PPI Therapy

- Pooled Sensitivity 80%
- 74% Specificity for GERD as cause of NCCP

Cremonini et al. Am J Gastroenterol 2005
pH Testing predicts response to PPI Therapy

- Evidence of GERD

Kahrilas et al. Gut 2011
**pH Testing Predicts Response to Anti-Reflux Surgery**

- **Group A**
  - No episodes of chest pain during pH monitoring

- **Group B**
  - < 40% chest pain correlated with acid reflux

- **Group C**
  - > 40% chest pain correlated with reflux

**Response Rate to LARS for NCCP**

- Group A: 65%
- Group B: 79%
- Group C: 96%

Patti et al. Surg Endosc 2002
NCCP: Alternative Explanations

- Functional Chest Pain
  - Panic Disorder 15%
  - OCD 21%
  - Major Depression 28%

Evidence for GERD as Cause of Laryngopharyngeal Reflux Symptoms

El-Serag et al. Gastroenterology 1997
Diagnosis of GERD for LPR Symptoms: EGD

37% Prevalence of EE

Lin: 0.13 (0.04, 0.29)
Qua: 0.13 (0.04, 0.29)
Tauber: 0.43 (0.25, 0.63)
Ness: 0.55 (0.32, 0.76)
Batch: 0.63 (0.53, 0.73)
Wiener: 0.27 (0.13, 0.46)
Ossakow: 0.10 (0.04, 0.20)
Poeilmans: 0.52 (0.47, 0.57)
combined: 0.37 (0.26, 0.49)

Lee et al. Am J Gastroenterol 2008, (103) A994
Diagnosis: Laryngoscopy

Infraglottic Erythema

Obliteration of ventricles

Sensitive but Not Specific

Laryngeal Edema

Postma et al. GI Motility Online (2006) doi:10.1038/gimo46
Poor Inter-Observer Agreement of Laryngoscopy

<table>
<thead>
<tr>
<th>Finding</th>
<th>r</th>
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<tbody>
<tr>
<td>Anterior Edema</td>
<td>0.363</td>
</tr>
<tr>
<td>Membranous Fold Edema</td>
<td>0.461</td>
</tr>
<tr>
<td>Arytenoid Edema</td>
<td>0.161</td>
</tr>
<tr>
<td>Anterior Erythema</td>
<td>0.293</td>
</tr>
<tr>
<td>Membranous Fold Erythema</td>
<td>0.369</td>
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<tr>
<td>Arytenoid Erythema</td>
<td>0.181</td>
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<tr>
<td>Severity of GERD</td>
<td>0.265</td>
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<tr>
<td>Likelihood GERD</td>
<td>0.248</td>
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</table>

Branski et al. Laryngoscope 2002
## pH Testing for LPR Symptoms

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Abnormal Distal EAE</th>
<th>%</th>
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<tbody>
<tr>
<td>Havas</td>
<td>15</td>
<td>6</td>
<td>40%</td>
</tr>
<tr>
<td>Metz</td>
<td>10</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Little</td>
<td>222</td>
<td>90</td>
<td>40.5%</td>
</tr>
<tr>
<td>Chen</td>
<td>735</td>
<td>170</td>
<td>23.1%</td>
</tr>
<tr>
<td>Wiener</td>
<td>15</td>
<td>9</td>
<td>60%</td>
</tr>
<tr>
<td>Katz</td>
<td>10</td>
<td>7</td>
<td>70%</td>
</tr>
<tr>
<td>Ulualp</td>
<td>20</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>McNally</td>
<td>11</td>
<td>6</td>
<td>54.5%</td>
</tr>
<tr>
<td>Shaker</td>
<td>12</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ossakow</td>
<td>38</td>
<td>26</td>
<td>68.4%</td>
</tr>
<tr>
<td>Kouffman</td>
<td>32</td>
<td>24</td>
<td>75%</td>
</tr>
<tr>
<td>Wilson</td>
<td>97</td>
<td>17</td>
<td>17.5%</td>
</tr>
<tr>
<td><strong>Cumulative</strong></td>
<td><strong>1217</strong></td>
<td><strong>54%</strong></td>
<td></td>
</tr>
</tbody>
</table>
Oropharyngeal pH Testing and Salivary Pepsin

- Pepsin could not discriminate between controls and LPR+ subjects

- Oropharyngeal pH scores similar between all groups

Yadlapati et al. Clin Gastroenterol and Hepatol 2015
pH Impedance and Response to Surgery

- Only abnormal pH predicted response
- No impedance parameter was predictive
- Abnormal pH+Heartburn ➤ 90% probability of improvement

Response Rate of LPR Symptoms After Lap Nissen

<table>
<thead>
<tr>
<th>Time</th>
<th>Improvement Rate</th>
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<tr>
<td>1 month</td>
<td>81%</td>
</tr>
<tr>
<td>12 months</td>
<td>59%</td>
</tr>
<tr>
<td>33 months</td>
<td>56%</td>
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</table>

Francis et al. Laryngoscope 2011
Diagnostic Approach to LPR

- ACG Guidelines
  - Empiric PPI trial in pts who have both LPR and GI GERD Symptoms
  - Ambulatory Reflux Testing in pts with LPR Symptoms Alone

ACG Guidelines on Gastroesophageal Reflux Disease 2013
Effectiveness of PPI Therapy for LPR Symptoms

Favors Placebo  Favors PPI

Wo  Vaezi  Steward  Havas  Noordzij  Eherer  El-Serag  Langevin  Combined

RR=1.28 (95% CI: 0.94-1.74)

Qadeer et al. Am J Gastroenterol 2006
High Dose PPI Therapy for LPR Symptoms

Symptom Response on PPI Therapy at 8 Weeks

- BID PPI
- BID PPI + H2RA
- QD PPI
- QD-> BID

% With >50% Improvement

p=0.03

Park et al. Laryngoscope 2005
Prolonged Course of PPI Therapy

<table>
<thead>
<tr>
<th>Improvement Rate</th>
<th>30 days</th>
<th>60 days</th>
<th>90 days</th>
<th>120 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPR</td>
<td>30%</td>
<td>49.8%</td>
<td>62.7%</td>
<td>71.1%</td>
</tr>
<tr>
<td>Esophageal</td>
<td>45.5%</td>
<td>78.3%</td>
<td>89%</td>
<td>91.7%</td>
</tr>
</tbody>
</table>

Raft-Forming Alginates

- Floats to the Top of the Fundus
- Mechanical barrier to both acid and non-acid reflux
- In vitro inhibits pepsin diffusion and enzymatic activity

Strugala et al. J Pharm Pharmacol 2009
Gaviscon Advance

Gaviscon Advance vs Usual Care

McGlashan et al. Eur Arch Otorhinolaryngol 2009
LPR Symptoms and Response to LNF for GERD

Presence of Airway Symptoms were a negative predictor of overall response

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Improved (%)</th>
<th>Resolution (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td>67%</td>
<td>23%</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>70%</td>
<td>22%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>57%</td>
<td>18%</td>
</tr>
<tr>
<td>Cough</td>
<td>49%</td>
<td>29%</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>47%</td>
<td>22%</td>
</tr>
</tbody>
</table>

Oelschalger et al. Am J Gastroenterol 2008
LNF Not Effective for PPI Non-Responders

LPR Pts (n=72) → High Dose PPI x 4 mo's → Non-Responders (n=25) → 24-hr pH on PPI → Normalized EAE (n=25) → Lap Nissen

Symptom Improvement At 1 Year

- LNF
- Continued PPI Tx

Swoger et al. Clin Gastroenterol and Hep 2006
Alternative Explanation for Cough

- **Chronic Cough Patients**
  - 24-hr pH/Impedance Testing
  - Acoustic recording of cough
  - Calculation of symptom correlation (SAP) for Cough

- **48% had + SAP for cough preceded by reflux**
  - Normal levels of EAE (3.6%)
  - High level of airway sensitivity to citric acid

Smith et al. Gastroenterology 2010
Cough May Lead to GERD

Cough → Intra-abd Pressure Gradient → TLESR → Esophagus

Cough Related Reflux Events

- After Cough: 69%
- Before Cough: 31%

p<0.05

Conclusions

• Non-Cardiac Chest Pain
  - GERD statistically is most common cause
  - pH testing prior to initiation of PPI therapy
  - Abnormal pH predicts response to PPI and LNF
  - Visceral Hypersensivity may be alternative cause
Conclusions (2)

- **Cough and Throat Symptoms**
  - Epidemiologic link with GERD
  - GI GERD + LPR symptoms warrant trial of empiric PPI Therapy
  - LPR symptoms alone ➤ pH testing
  - Abnormal pH and response to PPI predict LNF outcomes
  - Airway hypersensitivity may be an alternative cause