Non-cardiac Chest Pain: Beyond GERD

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Esophageal Symptom Generation

Chemo-stimulation
Acid mediated

Reflux

Mechano-stimulation
Volume mediated

Heartburn
Regurgitation
Chest pain
Cough
Do Patients with NCCP Have Reflux?

Angina-type pain with normal coronaries
46% had abnormal 24 hour pH studies

100 patients referred by cardiologist for NCCP
48% had abnormal 24 hour pH studies
Does Treating Reflux Improve NCCP?

Achem 97
Fass 96
Xia 03
Pandak 02
Bautista 04
Squillace 93
Fass

Overall (95% CI)

Risk Ratio

Do Patients with NCCP Have Motility Abnormalities?

910 patients with NCCP

- Normal Motility (72%)
- Abnormal Motility (28%)
- Nutcracker (48%)
- NEMD (36%)
- DES (10%)
- Achalasia <1%
- Hypertensive LES (4%)

*DES 2.8%

Temporal Correlation Between Motor Abnormality and NCCP?

24-hr Ambulatory Esophageal Manometry

Peters (Gastro 94: 898, 1988)
16% of chest pain episodes with motor abnormality

Soffer (DDS 34: 1651, 1989)
9% of chest pain episodes with motor abnormality

Brumelhoft (Gastro 99: 1237, 1990)
13.8% of chest pain episodes with motor abnormality

Hawson (DDS 35: 302, 1990)
10% of chest pain episodes with motor abnormality
Chest Pain Associated with Sustained Muscle Contraction

- **pH**
- **Intraluminal Pressure (mmHg)**
- **Wall Thickness (mm)**

60 sec
Does Treating Motility Abnormality Improve NCCP?

**Anticholinergic Agents**
- Decrease amplitudes of abnormal contractions
- Decrease pain produced by balloon distention
- No trials for noncardiac chest pain

**Nitrates**
- Decrease amplitudes of abnormal contractions
- Only anecdotal reports of success

**Calcium Channel Antagonists**
- Decrease amplitudes of abnormal contractions
- Only anecdotal reports of success
- Nutcracker Esophagus - No benefit vs placebo
Does Treating Motility Abnormality Improve NCCP?

*cGMP Phosphodiesterase Inhibitors*
Decrease amplitudes of abnormal contractions and LES tone
No studies of symptoms

*Botulinum Toxin (BoTox)*
Open Label Trial
50% reduction in pain, 72% of patients
Mean duration 7.3 months

**Pain Hypersensitivity from Injury/Inflammation**

**Primary Allodynia/Hyperalgesia**
- Occurs in field of injury
- Sensitization of peripheral primary nociceptive afferents.

**Secondary Allodynia/Hyperalgesia**
- Occurs in healthy tissue around injury
- Increased excitability of spinal neurons activated by peripheral nociceptive afferents in the field of injury.
Do Patients with NCCP have Esophageal Hypersensitivity?

Barish (DDS 31: 1292, 1986)

- Balloon inflation
  - 28/50 (56%) patients had typical chest pain
    - 24 at \( \leq 8 \text{cc} \)
  - 6/30 (20%) controls had chest pain
    - All >8cc


- Impedance Planimetry
  - 20/24 (83%) patients, typical chest pain at
    - \(<50 \text{ cm H}_2\text{O}\)
  - 0 controls with chest pain at \(<50 \text{ cm H}_2\text{O}\)
Hypersensitivity to Balloon

(Barish et al: Gastroenterology 1986)
**NCCP Hypersensitivity or Motor Dysfunction**

**Balloons Pressure (cm H$_2$O)**

- **Normal**
- **NCCP**
- **NCCP post-atropine**

**Sensory Perception**
- Sensory Perception

**Moderate Discomfort**
- Moderate Discomfort

**Pain**
- Pain

Relation Between Additional Acid Exposure for 30 Minutes Preceding (GER-25) and Reflux Immediately for 5 Minutes Preceding (+SRA) Individual Chest Pain Episodes

<table>
<thead>
<tr>
<th>SI Level</th>
<th>Chest pain Episodes with +GER-25</th>
<th>Chest pain Episodes with –GER-25</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>High SI (≥50%)</td>
<td>23</td>
<td>2</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>+SRA</td>
<td>23</td>
<td>2</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>-SRA</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Low SI (&lt;50%)</td>
<td>7</td>
<td>2</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>+SRA</td>
<td>7</td>
<td>2</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>-SRA</td>
<td>16</td>
<td>72</td>
<td></td>
</tr>
</tbody>
</table>


Treatment of Esophageal Visceral Hyperalgesia with Pain Modulators

**Imipramine**

- 75 mg/day, increased pain threshold to balloon distention.
- 50 mg/day, 52% reduction in frequency of CP (RPCT).

**Trazodone**

- 100-150 mg/day, improved CP frequency and intensity.
  - no Δ in motor fxn (RPCT)

**Sertaline**

- 50-200 mg/day, improved CP regardless of psych Δ (RPCT).

**Theophylline**
Imipramine (75 Mg) Increases Esophageal Pain Threshold

Studies in normal subjects

Vascular Hyperalgesia Adenosine Receptors?

**Placebo**

- Before: 
- After: 

**Theophylline**

- Before: 
- After: 

\[ P = 0.027 \]

\[ P = 0.028 \]

Visceral Hyperalgesia Adenosine Receptors?

**Placebo**

Before: $P = 0.9$

After: $P = 0.9$

**Theophylline**

Before: $P = 0.014$

After: $P = 0.03$

Noncardiac Chest Pain

Off the Wall
Do Psychiatric Abnormalities Cause NCCP%
**Does Psychiatric Treatment Improve with NCCP?**

**Effect of Cognitive-Behavioral Therapy on Noncardiac Chest Pain**

<table>
<thead>
<tr>
<th></th>
<th>Time</th>
<th>Therapy</th>
<th>No Therapy</th>
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</thead>
<tbody>
<tr>
<td><strong>CP Frequency (per wk)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>6.0±2.8</td>
<td>5.6±3.2</td>
<td></td>
</tr>
<tr>
<td>6 Months</td>
<td>1.1±1.8</td>
<td>5.1±4.3</td>
<td></td>
</tr>
<tr>
<td>12 Months</td>
<td>1.4±2.5*</td>
<td>5.5±6.5</td>
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</tr>
<tr>
<td><strong>CP Intensity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>3.7±1.9</td>
<td>3.5±2.0</td>
<td></td>
</tr>
<tr>
<td>6 Months</td>
<td>2.0±2.6</td>
<td>3.4±2.2</td>
<td></td>
</tr>
<tr>
<td>12 Months</td>
<td>1.7±2.2*</td>
<td>3.1±2.1</td>
<td></td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
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<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>10.3±4.5</td>
<td>7.9±3.9</td>
<td></td>
</tr>
<tr>
<td>6 Months</td>
<td>6.6±3.3</td>
<td>7.1±3.6</td>
<td></td>
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<tr>
<td>12 Months</td>
<td>6.9±3.1</td>
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No effect on physical, social, or emotional limitations or problems at work