A Practical Approach to the Refractory GERD Patient

Robert H. Lee, MD, MAS
Clinical Assistant Professor of Medicine
Director of GI Motility
H.H. Chao Comprehensive Digestive Disease Center
University of California Irvine

3/6/15: Gastroenterology and Hepatology Symposium
Case Presentation

- 36 yo F (BMI 28) presents with heartburn & regurg
  - 30% relief on omep 20 mg bid
  - Last egd 2/12 showed 2 cm HH, no erosive esophagitis
Next Step in Management?

a) Switch to esomeprazole 20 mg bid

b) ↑ Omep 40 mg bid

c) Repeat Egd
Definition of Refractory GERD Symptoms

- Heartburn and/or regurgitation
- < 50% response to double dose PPI Therapy
- 12 week Treatment Period

Sifrim et al. Gut 2012
Switching PPI Therapy

Efficacy of Esomeprazole 40 mg vs Lansoprazole 30 mg at 8 weeks

% of Patients with Symptom Relief

- Heartburn
- Regurg
- Dysphagia
- Epig Pain

Eso vs Lans

Kahrilas et al. Aliment Pharmacol & Ther 2005
Endoscopic Findings in Refractory GERD

Los Angeles Classification Esophagitis

- A: 14.3% (p=0.004), 2.9%
- B: 14.3% (p=0.01), 3.8%
- C: 1.1% (No Rx), 0.0%
- D: 1.1% (PPI Failure), 0.0%

OR for EE in PPI Tx: 0.11 (95% CI: 0.04-0.30)

0.9% with EoE

Poh et al. Gastrointest Endosc 2010
Case (Continued)

- Pt returns after 4 wks of Omep 40 mg bid w/o improvement

- Interested in anti-reflux surgery

“Indigestion is charged by God with enforcing morality on the stomach”
- Victor Hugo
What diagnostic test would have the highest yield?

a) 48-hr wireless pH test off of PPI

b) 24-hr pH/Impedance on PPI

c) 24-hr pH/Impedance off PPI
What is the Question?

• “Is GERD the cause of symptoms”
  - Pre-Surgical Evaluation
    ~ 24 or 48 hr pH Off PPI
    ~ pH/Impedance Off PPI

• “Why isn’t the patient responding to Treatment?”
  - pH/Impedance On PPI
Choices in Reflux Testing

Wireless pH

- Extended Recording Period up to 96 hrs
- ↓ Restrictive for Patient Activities
- Does not capture Non-Acid Reflux

Impedance

- May miss day-to-day variability
- Nasal catheter so ↑ Restrictive
- Captures Non-Acid Reflux
Impedance Testing Off vs On PPI

- 30 pts underwent pH-Imp Twice
  - On and Off PPI

- 50% pts who had (-) SAP On PPI had (+) SAP Off PPI

Hemmink et al. Am J Gastroenterol 2008
Case (Continued 2)

- Pt undergoes Impedance off PPI
  - 15.2% Total EAE
  - EAE abnl in Upright and Supine Positions
  - 89 Reflux Events
  - SAP Heartburn 98%

“I have never developed indigestion from eating my words” - Winston Churchill
Surgery or Medical Options?

• What would you recommend?
  
a) Lap Nissen
b) LINX
c) Trans-Oral Intraluminal Fundo?
d) Alternative Medical Therapies
## LNF vs H2-Blockers: VA Coop Study at 10 Years

<table>
<thead>
<tr>
<th></th>
<th>Surgical</th>
<th>Medical</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of Any Anti-Reflux Med</td>
<td>62%</td>
<td>92%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>GRACI Score Off Meds</td>
<td>82.6</td>
<td>92.7</td>
<td>0.003</td>
</tr>
<tr>
<td>GRACI Score On Meds</td>
<td>78.7</td>
<td>83.1</td>
<td>0.07</td>
</tr>
<tr>
<td>≥ 1 Anti-Reflux Surgery</td>
<td>10%</td>
<td>16%</td>
<td>0.38</td>
</tr>
<tr>
<td>Death</td>
<td>40%</td>
<td>28%</td>
<td>RR=1.89 (p=0.01)</td>
</tr>
</tbody>
</table>

VA Cooperative Study, Spechler et al. JAMA 2001
LNF vs PPI: SOPPRAN Trial

Neither Study Involved Pts with Medical Refractory GERD

Lundell et al. Clin Gastroenterol and Hepatol 2009
What happens if you don’t carefully select patients for LNF

- VA study of 3367 patients who had LNF (1990-2001)
  - 34.3% were back on PPI’s by 5-years
  - 23.8% on H2-blockers
  - 9.2% on prokinetics
  - 50% were on at least 3 anti-reflux agents

## Who Gets Better With Surgery?

<table>
<thead>
<tr>
<th>Predictor of Response to LNF</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical GERD Symptoms</td>
<td>5.1</td>
<td>1.9-15.3</td>
</tr>
<tr>
<td>Abnormal 24-hour pH Score</td>
<td>5.1</td>
<td>1.9-13.7</td>
</tr>
<tr>
<td>Complete or Partial Response to PPI</td>
<td>3.3</td>
<td>1.3-8.7</td>
</tr>
</tbody>
</table>

Campos et al. J Gastrointest Surg. 1999
## Impedance Parameters and Response to Surgery

### Predictors of Response to GERD Therapies (Reported as p-values on Univariate Analysis)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Surgical</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal Acid Exposure %</td>
<td>0.048</td>
<td>0.936</td>
</tr>
<tr>
<td>Reflux Events &gt; 48</td>
<td>0.48</td>
<td>0.373</td>
</tr>
<tr>
<td>Reflux Events &gt; 73</td>
<td>0.080</td>
<td>0.414</td>
</tr>
<tr>
<td>SAP</td>
<td>0.160</td>
<td>0.340</td>
</tr>
</tbody>
</table>

Patel et al. Clin Gastroenterol and Hepatol 2014
Long-Term Efficacy Depends Upon Pre-Operative Reflux Pattern

Outcomes 5 Years After LNF

- Abnl pH After Surgery
- Need for Re-Operation

Broeders et al. Am J Gastroenterol 2004
Transoral Incisionless Fundoplication (TIF)

- Fasteners create circumferential serosal-serosal plications
- Does not preclude future LNF
TIF Outcomes

- TIF vs Sham for Regurgitation
- Post-Op Period
  - Sham → PPI
  - TIF → Placebo
- Correction of pH seen with TIF and not sham

Complete Relief of Symptoms

% of Patients

Hunter et al. Gastroenterology 2015

p=0.023
Esophageal Sphincter Augmentation (LINX)

- Self-Expandable Bracelet of Magnetic Beads
- Can self-adjust to external forces
- Use limited to $\leq 2$ cm Hiatal Hernia

Ganz et al New Eng J Med 2013
LINX Outcomes Data

- 64% achieved normalization of acid exposure

**GERD Related Quality of Life Before and After LINX**

- **Without PPI at Baseline**: Median QOL Score
- **With PPI at Baseline**: Median QOL Score
- **3 Yrs After LINX**: Median QOL Score

- **p < 0.005**

**LNF vs LINX**

- No Head-to-Head RCTs
- Similar QOL Scores
- LNF had better correction of pH Scores

**Baclofen for NAR**

- **GABA-B Agonist**
  - Decreases TLESR’s
  - Decreased HB Severity Score (10.3-5.8)
  - Decreased # of HB Episodes by 65%

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**Impedance Findings on Baclofen vs Placebo**

- **Acid No Reflux Episodes**
  - Placebo: 151
  - Baclofen: 59

- **Non-Acid No Reflux Episodes**
  - Placebo: 72
  - Baclofen: 15

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1) Vela et al. Aliment Pharmacol Ther. 2003  
2) Koek et al. Gut 2002  
Targeting Acid Pocket

- **Acid Pocket**
  - Un-buffered acid pool floating at top of meal
  - Location of the pocket above the diaphragm associated with acid reflux with TLESRs

1) Kahrilas et al. Am J Gastroenterol 2013
2) Beaumont et al. Gut 2010
Raft-Forming Alginates

- Floats to top of Acid Pocket
- ↓ Reflux Events
- Shifts Pocket to below diaphragm
Pain Modulators for Refractory GERD

• Reserved for Patients with Negative Testing:
  - Acid-Sensitive Esophagus
    ~ (+) SAP but normal reflux
  - Functional Heartburn
    ~ (-) SAP and normal reflux
Citalopram for Acid-Sensitive Esophagus

Citalopram 20 mg vs. Placebo for 6 months

% Pts with Persistent Sx's

- Citalopram 20 mg
- Placebo

p=0.021

Viazis et al. Am J Gastroenterol 2012
Conclusions

• Refractory GERD Initial Management:
  - Low diagnostic yield to repeat egd
  - Qday → bid of existing PPI is same as switching to alternative agent
Conclusions (2)

- Off PPI Reflux Testing
  - Highest diagnostic yield
  - Is reflux the cause of symptoms?
  - Pre-surgical evaluation
  - BRAVO vs Imp has pros/cons
Conclusions (3)

• Surgical/Endoscopic Therapies:
  - PPI response and abnormal Reflux Testing predict response
  - No well done trials comparing medical vs LNF for REFRACTORY GERD
  - LINX and TIF for younger patients
Conclusions (4)

- Alternative Medical Therapies:
  - Baclofen for TLESRs
  - Alginates target acid pocket
  - Pain modulators for FH and Acid-Sensitive Esophagus