Refractory GERD and pH Testing: Indications and Applications

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Bani Chander Roland, M.D
Assistant Professor of Medicine
Director, Neurogastroenterology and Motility Program
Columbia University Medical Center/NY Presbyterian Hospital
Objectives & disclosures

- Overview of current knowledge about Gastroesophageal Reflux Disease (GERD)
- Review the clinical indications and available pH testing options
- Review existing and novel GERD therapies

Disclosures:
- Covidien/Medtronic: Consultant
Outline

• Definition
• Epidemiology
• Symptoms
• Diagnostic Options
• Treatment modalities
What is GERD?

• A condition that develops when reflux of stomach content causes troublesome symptoms (e.g. heartburn, regurgitation) and/or complications (*Montreal Classification*)

• **Symptoms considered troublesome if:**
  - Mild symptoms occur ≥2 days/week
  - Moderate to severe sx >1 day/week

• **Reflux esophagitis:** Subset of pts with Sx of GERD with endoscopic/histologic evidence of esophageal inflammation
GERD is a condition which develops when the reflux of stomach content causes troublesome symptoms and/or complications.

**Esophageal syndromes**
- Symptomatic syndromes
  - Typical reflux syndrome
  - Reflux chest pain syndrome
- Syndromes with esophageal injury
  - Reflux esophagitis
  - Reflux stricture
  - Barrett’s esophagus
  - Adenocarcinoma

**Extra-esophageal syndromes**
- Established association
  - Reflux cough
  - Reflux laryngitis
  - Reflux asthma
  - Reflux dental erosions
- Proposed association
  - Sinusitis
  - Pulmonary fibrosis
  - Pharyngitis
  - Recurrent otitis media

*Am J Gastroenterol 2006 Montreal Classification*
How common is GERD?

- **Most common** diagnosis among outpatient clinic visits in the US

- **Prevalence:**
  - 20-28% in the Western world
  - <10% in east Asia

- **Prevalence of complications:**
  - Barrett’s esophagus: 10-15% (vs 1.6% general population)
  - Esophagitis: 15.5%
  - *Only 30-40% had reflux symptoms!*

Paradox of GERD

- Poor correspondence between symptoms and endoscopic features
- 2/3 of patients with “typical” reflux symptoms have no evidence of esophagitis
- Majority (60-70%) with evidence of damage due to GERD (e.g. Barrett’s, esophagitis) are asymptomatic
- Although GERD most common cause of heartburn (HB), other disorders also cause/contribute to HB (e.g. Achalasia, Eosinophilic Esophagitis)
**Typical Symptoms**

- **Most common:**
  - Heartburn (Pyrosis)
  - Regurgitation
  - Dysphagia (Difficulty Swallowing)

- **Extra-esophageal manifestations**
  - Cough
  - Asthma/bronchospasm
  - Laryngitis
  - Globus
Diagnostic Testing

• **No diagnostic testing needed:**
  – Typical symptoms present
  – Response to acid-suppressive therapy (e.g. PPI)

• **Diagnostic testing:**
  – Avoid misdiagnosis
  – Identify complications
  – Evaluate refractory sx/treatment failure and prior to anti-reflux techniques

• **Testing modalities:**
  – EGD: evaluate for complications, r/o alternative diagnoses
  – Esophageal manometry (r/o subtle motility disorder)
  – Ambulatory pH monitoring (wireless or impedance): Quantifies acid exposure + identifies reflux events
Indications for pH Testing

- Typical symptoms of GERD despite PPI
- Atypical symptoms of GERD despite PPI
- Prior to undergoing anti-reflux intervention
- Prior anti-reflux intervention and still with ongoing symptoms
Diagnostic Testing Modalities

• **24 hr pH/Impedance Testing**
  – To evaluate both non-acid and acidic reflux episodes
  – Identify symptom correlation
  – Performed on and off PPI therapy
  – Advantage: Can evaluate both acidic & non-acidic reflux episodes
  – Disadvantage: Catheter based, patient discomfort

• **Bravo wireless pH capsule testing**
  – To evaluate acid reflux episodes
  – Identify symptom correlation
  – Typically performed on PPI therapy
  – Advantage: Wireless technology, can evaluate up to 96 hours,
  – Disadvantage: Only evaluates acid reflux episodes
24 hr pH/Impedance testing

- Catheter based pH monitoring
- Detects changes in resistance (impedance) to passage of a low electrical current

**Impedance:**
- Low: Water
- Mid: Food
- High: Air
pH Impedance Testing

• Can record and classify pH into 3 zones:
  – Acid reflux: pH 1-4
  – Weakly acid reflux: pH 4-7
  – Non-acid reflux: pH >=7

• Can detect reflux traveling to proximal esophagus
High Resolution 24-hour pH & Impedance
Bravo wireless pH testing

- pH capsule measures esophageal pH with antimony pH sensor
- Uses radio-telemetry to send data to receiver
- Dimensions:
  - 6 x 6.3 x 26 mm
Benefits of Bravo wireless pH Monitoring

• Improved patient comfort and acceptance
• Continued normal work, activities, diet during the study
• Longer reporting periods possible (96-hours)
• Maintain constant probe position relative to SCJ
Endoscopic placement of Bravo
Therapies

Goals of Therapy

1. Reduce reflux symptoms
2. Prevent damage to the esophagus

Treatment Options

- Dietary/Lifestyle Modifications
- Medical Therapies
- Endoscopic Therapies
- Surgical Options
Lifestyle Modifications

- Smoking Cessation
- Weight Reduction
- Dietary modifications
- Consumption of smaller and more frequent meals
- Avoidance of eating 3 hours prior to bedtime
- Elevating the head of the bed
- Reduction in alcohol consumption
Treatment – Medical Therapy

-Most common & effective treatment of GERD are medications to reduce gastric acid secretion
-These therapies *do not* prevent reflux, but reduce acidity of refluxate

1. **H2RBs**
   - Blocks action of histamine on parietal cells, decreasing acid production in the stomach (Ex. Zantac, Pepcid)

2. **Proton Pump Inhibitors (PPIs)**
   - Mainstay of treatment
   - Irreversibly blocks proton pump in the stomach → decreasing gastric acid output (Ex. Prilosec, Nexium, Protonix)
Adjunctive Medical Therapies

• Bethanechol
  – Esophageal prokinetic, increases LES pressure, promotes gastric emptying
  – Side Effects: Diarrhea, N/V, abdominal cramps, increased HR, salivation, urinary urgency

• Baclofen
  – GABA$_B$ receptor agonist
  – Inhibits transient lower esophageal sphincter relaxation (TLESR)
  – Side Effects: Sedation and Dizziness
Refractory GERD?

• Several therapeutic options among patients with refractory symptoms and proven GERD
• Problem becomes challenging among patients with chronic symptoms but no proven reflux on pH monitoring
• Anti-reflux procedures (surgical or endoscopic) are risky if you can’t prove reflux is the cause of symptoms
  – Majority of patients who do not respond to PPI therapy will not respond to surgical therapies
Surgical Fundoplication

- Refractory symptom despite PPI therapy
- Esophagitis refractory to medical therapy
- Patient doesn’t wish to take medications
- Patient unable to tolerate medical therapy
- Presence of large hiatal hernia
Types of Fundoplication, Laparoscopic View

TIF PROCEDURE
Transoral fundoplication
270° anterior wrap

TOUPET
Transabdominal fundoplication
270° posterior wrap

NISSEN
Transabdominal fundoplication
total posterior wrap
Long-term Outcomes (10 year follow-up) of GERD in medical and surgical treatment groups

Table 3. Long-term Outcomes of GERD in the Medical and Surgical Treatment Groups*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Medical Treatment Group</th>
<th>Surgical Treatment Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRACI score while taking medication, mean (SD)</td>
<td>83.1 (13.7) [n = 74]</td>
<td>78.7 (9.5) [n = 29]</td>
<td>.07</td>
</tr>
<tr>
<td>GRACI score while not taking medication, mean (SD)</td>
<td>96.7 (21.4) [n = 68]</td>
<td>82.6 (17.5) [n = 27]</td>
<td>.003</td>
</tr>
<tr>
<td>Endoscopic grade of esophagus, mean (SD)</td>
<td>1.89 (1.15) [n = 63]</td>
<td>1.80 (0.95) [n = 20]</td>
<td>.76</td>
</tr>
<tr>
<td>24-h esophageal pH &lt; 4, mean (SD) %</td>
<td>31.0 (61.6) [n = 38]</td>
<td>17.1 (41.1) [n = 10]</td>
<td>.50</td>
</tr>
<tr>
<td>Using antireflux medications regularly, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any antireflux medication</td>
<td>92 [n = 90]</td>
<td>62 [n = 37]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>64 [n = 89]</td>
<td>32 [n = 37]</td>
<td>.002</td>
</tr>
<tr>
<td>Histamine2 receptor blockers</td>
<td>65 [n = 88]</td>
<td>41 [n = 37]</td>
<td>.02</td>
</tr>
<tr>
<td>Prokinetics</td>
<td>15 [n = 86]</td>
<td>8 [n = 36]</td>
<td>.39</td>
</tr>
<tr>
<td>≥1 Antireflux operation since end of original study, %</td>
<td>10 [n = 90]</td>
<td>16 [n = 38]</td>
<td>.38</td>
</tr>
<tr>
<td>Treatment for esophageal stricture since end of original study, %</td>
<td>8 [n = 90]</td>
<td>14 [n = 37]</td>
<td>.46</td>
</tr>
</tbody>
</table>

*GERD indicates gastroesophageal reflux disease; GRACI, Gastroesophageal Reflux Disease Activity Index. Numbers in brackets are the sample sizes for each outcome.

Spechler et al. JAMA 2001; 285(18):2331-2338
12 year follow up of Patients Randomized to Fundoplication vs Omeprazole

Endoscopic therapies
TIF: Transoral Incisionless Fundoplication

- Device wraps the fundus around distal esophagus to reconstruct the valve
  - FDA approved in 2007
  - Full thickness polypropylene fasteners create a serosa to serosa fundoplication
  - 2 year follow up:
    - 85% HB free & 79% remain off PPIs

- Advantages:
  - Non-invasive with shorter recovery
  - Low complication rate and can be repeated

- Contraindications: Hiatal hernia >2-3 cm
**STEP 1**
The EsophyX® device is inserted into the esophagus through the mouth and is positioned at the junction of the stomach and esophagus. A small hiatal hernia is reduced by engaging suction (invaginator) and positioning the esophagus below the diaphragm.

**STEP 2**
A full thickness tissue fold at the gastroesophageal junction is retracted, wrapped and anchored using SerosaFuse® implantable fasteners—equivalent to 3.0 sutures—which are delivered across the tissue to complete the plication.

**STEP 3**
The valve is extended and multiple fasteners (12-20) are delivered with a single device insertion. The TIF procedure reconstructs the primary components of the antireflux barrier, creating a tight 3-5 cm valve enveloping the distal esophagus below the diaphragm.
TIF
Systematic review of TIF

• Systematic review of TIF included 15 studies and 550 procedures
• Found improved GERD health-related quality of life scores (21.9 vs 5.9, p<0.0001)
• Long-term PPI use discontinued in 67% of patients

Does TIF Work?

• 3 randomized control trials
• All minimum of 6 months follow-up
• TIF more effective than high dose PPI in eliminating troublesome regurgitation (67% vs 45%) or extra-esophageal symptoms of GERD

Trad et al. BMC Gastroenterol 2014;14:174
MUSE: Trans-oral Anterior Fundoplication

- A transoral anterior fundoplication
- Endoscopic flap valve reconstruction; increases angle of HIS
- Creates “high pressure zone” above GE junction
- Standard 4.8 mm titanium surgical staples

- 5 staples per firing
- 3 firings per patient (typically)
Anterior fundoplication

- As effective as Nissen (Level 1a evidence)\(^1\)
- Low incidence of dysphagia and gas bloat
  - Most common anti-reflux operation in children
  - Standard anti-reflux addition to Heller’s myotomy for achalasia (best Rx by SAGES and AGA guidelines)
- Can be performed as:
  - Open or laparoscopic surgery
  - Endoscopically with MUSE

MUSE: Procedure Overview

- Overtube placed
- Stapler inserted and retroflexed
- Tissue clamped and staples fired
Stretta

- FDA approved in 2000
- Uses radiofrequency energy delivery to the distal esophagus
- Reduces reflux by decreasing tissue compliance and reducing transient lower esophageal relaxations

Auyang et al. Surg Endoc 2012;27:2658-72
Does Stretta Work?

- Meta-analysis of 18 studies, 1441 patients
- Reported significant improvement in heartburn and quality of life scores after Stretta
- Esophageal acid exposure as assessed by the DeMeester score was reduced after treatment (44.4 vs 28.5, p=0.007)
- Normalization of esophageal acid exposure not observed

Long-term Follow up with Stretta?

- Appears to durably relieve GERD symptoms up to 10 years in the majority of patients
- 80% patients off PPI at 4 years
- 76.9% patient off PPI at 8 years

LINX: Magnetic Device for Augmentation of the Lower Esophageal Sphincter

LINX Reflux System

- Magnetic device to augment the lower esophageal sphincter
- Consists of small, flexible band of beads
- Prospective study of 100 patients with GERD before and after LINX
- Primary outcome: Normalization of esophageal acid exposure (or >50% reduction at 1 year) achieved in 64%
- Secondary outcome: Reduction of 50% or more in PPI use in 92%
- Adverse events: Dysphagia (68% post-op, 11% at 1 year, and 4% at 3 years)

Summary

• GERD is an increasingly common disease
• The consequences of GERD are significant
• 24-hour pH impedance and Bravo wireless pH testing aid in the diagnosis and clinical management of GERD
• PPI therapy remains standard of care but does not prevent refluxate
• Endoscopic therapies emerging but further prospective trials are needed to evaluate the long term efficacy in clinical practice
Thank you