Use of Esophageal pH and Impedance Testing in Your Practice

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What Kind of Patients Do We See

• Symptoms Suspected Due To GERD Partially Responsive to a PPI (often high dose)
• Complete heartburn relief with continued regurgitation
• Barretts/Complicated GERD
• Patients Considering Antireflux Surgery, Endoscopic Therapy
Options for the Work Up of A Patient with Suspect GERD Symptoms

- Perform EGD
- Ambulatory monitoring
  - pH
  - Impedance
- Esophageal function testing (manometry, impedance)


Prolonged pH (Reflux) Monitoring: When Do We Need It?

1. Documentation of abnormal esophageal acid exposure in endoscopy-negative patients
2. Evaluation for surgical or endoscopic intervention
3. After above if symptoms recur (BEFORE PPI)
4. Assess acid control in Barrett's/post ablation/complicated stricture

Symptoms Suspected Due to GERD Refractory to PPI (likely most common in GI practice)

What Question is Being Asked?

• Does the patient have GERD (baseline)?
• Is GERD the cause of continued symptom(s)?
• Is acid reflux controlled? (Barretts, post ablation, post surgery)
• Does the patient have non acid reflux?

What is the outcome (plan) for a negative study?
Ultimately No Real Evidence that One Monitoring Technique Best

Test Chosen Must Be Interpreted Using Combination of Traditional Scoring System, Symptom Correlation and Clinical Judgment

The “Easy” Patient

- Heartburn, typical
- Regurgitation
- Sleep disturbed
- On PPI twice a day, heartburn 85% better, still with regurgitation post prandial
- Never had a test
The Real Hard Patient

- Chronic Cough (5 years)
- Non smoker
- Normal Chest xray/CT
- Voice disturbance
- ENT says LPR, pulmonary says no asthma
- Dexlansoprazole once a day/H2 at bedtime no perceived improvement

Potential Causes of Continued Symptoms on PPI

The patient has GERD but:
- Acid is not controlled
- Healing/symptom relief not complete despite good antisecretory therapy
- The patient has weakly acidic or non-acid reflux

Potential Causes for Continued Symptoms on PPI

• The patient does not have GERD (medication, eosinophilic esophagitis, functional heartburn)

• The response to PPI is impacted by concurrent functional medical illness (IBS, migraine, anxiety, chest pain)

• Some people really have more than one problem

What Do We Need to Know

• Does the patient REALLY have GERD
• If so how do we “prove it.” What is a reasonable approach?
• If truly refractory what are the options?
• If not GERD what to do (if you keep the patient)
Options for the Work Up

- Perform EGD
- Ambulatory monitoring
  - pH
  - Impedance
- Esophageal function testing (manometry, impedance)


Optimize PPI Therapy

- Adjust dose therapy
- Consider switching PPI once (conditional rec, low quality evidence)
Patients Still Do Not Optimize PPI Therapy

- 27.8% > 60 minutes before meals
- 38.9% As needed
- 29.6% After meals
- 3.7% At bedtime


Why Proton Pump Inhibitors May Not Effectively Control Gastric Acidity

- Decreased bioavailability when given with food
- Dose timing related to food not optimal (not before a meal or taking PPI at bedtime)
- *Helicobacter pylori* negative
- Genetic variability in PPI metabolism
- Hypersecretion, PPI resistance

No response to PPI Optimization/Trial

- Exclude other etiologies
- Do NOT put on prokinetic, sucralfate
  – it does not work

Typical symptoms:

- EGD: Exclude non-GERD etiology
  (including esophageal eosinophilia; conditional recommendation low quality evidence)
Atypical symptoms:

- Refer for evaluation
  - ENT
  - Pulmonary
  - Allergy
- If above negative, EGD very low yield but hard not do to

If atypical symptoms persist and endoscopy is negative, perform ambulatory reflux monitoring (strong rec, low quality evidence)
Low probability of GERD

- Perform reflux monitoring OFF therapy
  - Telemetry capsule (choice for infrequent symptoms to increase yield)
  - Impedance/pH (choice if clearly post-prandial symptoms)

High probability of GERD

- Monitoring ON therapy with impedance-pH monitoring
  - Continued acid reflux (2%)
  - Weakly acidic reflux (↑ numbers)
  - Associate with symptoms (? reliability)
Impedance/pH Monitoring

- Impedance
  - Allows analysis of acid and non-acid events
  - Gastric monitoring
  - Assess reflux height
  - Data are from referral centers


Abnormal Reflux on Therapy by Impedance/pH

- Consider:
  - Surgery (laparoscopic fundoplication, limited data, no controls)
  - TLESR inhibitors (Baclofen – sound physiology, some data)

No one is happy with this approach but we have nothing better
Non Acid Reflux and Positive Symptom Index

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients with positive symptom index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regurgitation</td>
<td>72%</td>
</tr>
<tr>
<td>Heartburn</td>
<td>35%</td>
</tr>
<tr>
<td>Cough</td>
<td>32%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>16%</td>
</tr>
<tr>
<td>Abdominal Sx</td>
<td>14%</td>
</tr>
<tr>
<td>ENF symptoms</td>
<td>10%</td>
</tr>
<tr>
<td>Others</td>
<td>22%</td>
</tr>
</tbody>
</table>

Katz P., personal data from approx 1500 patients

Non Acid Reflux Options

- Baclofen
- Imipramine (functional)
- Surgery
Number of Reflux Episodes: Effect of Baclofen

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Baclofen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid</td>
<td>206</td>
<td>19</td>
</tr>
<tr>
<td>Nonacid</td>
<td>89</td>
<td>73</td>
</tr>
<tr>
<td>Rereflux</td>
<td>32</td>
<td>3</td>
</tr>
</tbody>
</table>


Effect Of Baclofen On Number Of Symptom Events

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<th>Baclofen</th>
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</thead>
<tbody>
<tr>
<td>Total</td>
<td>97</td>
<td>21</td>
</tr>
<tr>
<td>Acid-related</td>
<td>70</td>
<td>15</td>
</tr>
<tr>
<td>Nonacid-related</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Non-correlated</td>
<td>7</td>
<td>1</td>
</tr>
</tbody>
</table>

* p<0.05

(Vela et al. Al Pharm Ther 2003)
Symptom improvement and resolution after LARS among those presenting with the symptom

Heartburn: 67% Improved, 23% Resolution
Regurgitation: 70% Improved, 22% Resolution
Dysphagia: 57% Improved, 18% Resolution
Cough: 40% Improved, 29% Resolution
Hoarseness: 47% Improved, 22% Resolution


Reflex Monitoring Negative

- PPI therapy should be discontinued
- Consider treatment for functional symptoms (Imipramine or similar)
Refractory GERD

Optimize PPI therapy

No response

Exclude other etiologies

Typical Symptoms

EGD

Atypical Symptoms

Referral to ENT, pulmonary, allergy

Abnormal (eosinophilic esophagitis, erosive esophagitis, other)

Specific treatment

REFLUX MONITORING

Normal

Referral to ENT, pulmonary, allergy

Abnormal (ENT, pulmonary, or allergic disorder)

Specific treatment

Low pre-test Probability of GERD

Test off medication with pH or Impedance-pH

High pre-test Probability of GERD

Test on medication with pH or Impedance-pH

Abnormal (eosinophilic esophagitis, erosive esophagitis, other)
Esophageal Manometry

- Recommended by AGA technical review if GERD not present by above testing
- Especially helpful with dysphagia
- Rarely will find Achalasia/Spasm
- Upper sphincter abnormalities seen in >50% of ENT referrals. Significance unknown

AGA Technical Review. Gastroenterology 2008

Prolonged pH (Reflux) Monitoring

- Allows clinician to determine:
  - The amount and timing of acid reflux
  - The association between acid reflux and symptoms (does reflux precede symptom?)
  - The effect of therapy on acid reflux
  - Non-acid reflux (impedance)
  - Reflux Height

Should pH (Reflux) Monitoring Be Performed Off or On Therapy

- Low pre test probability of GERD at baseline/no diagnostic tests done
  - **OFF** Medication (7-10 days)
- GERD likely OR known. EGD done
  - **ON** Medication (impedance/pH)


Prolonged pH (Reflux) Monitoring – Indications

- In general, pH or reflux monitoring is most useful in patients with refractory symptoms suspected due to GERD on antisecretory therapy
  - Endoscopy-negative
  - Prior to antireflux surgery

Prolonged pH (Reflux) Monitoring: Options

- Telemetry capsule: Off therapy choice
- Transnasal pH: Use if all you have
- Transnasal impedance/pH monitoring: On therapy choice

Non Acid or Weakly Acidic Reflux

- Is predominantly post prandial
- May be symptomatic, particularly proximal propagation
- +SI variable: most common with regurgitation, heartburn and possibly cough
- Most have normal number of reflux episodes
Symptoms with Postprandial Reflux

- ANY Sx: P = 0.0005
- HB: P < 0.0001
- AT: P = 0.003
- RE: P = ns

MII-pH in Patients on PPI BID

- 200 patients
- Symptoms: 172 (86%)
  - +SI Non-acid: 61 (35%)
    - Possible GERD
  - +SI Acid Reflux: 13 (8%)
    - Likely GERD
- No symptoms: 28 (14%)
- Test Not Helpful
- Symptoms with -SI: 98 (57%)
  - NOT GERD
Reflux on PPI with Positive Symptom Index: Surgery Outcome

19 Patients

NAR
- Heartburn-2
- Regurgitation-3

Acid
- Cough-7
- Throat Clearing-1
- Hoarseness-1
- Heartburn-3
- Nausea-1

Symptoms not associated with reflux
- Heartburn-1

Improving the Diagnosis of GERD: Prolonged and Dual Probe pH Studies

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Day One/Two Bravo Validation: Control Criteria

<table>
<thead>
<tr>
<th>Strong Clinical Evidence of GERD</th>
<th>Minimal Clinical Evidence of GERD</th>
<th>Indeterminate Clinical Evidence of GERD</th>
</tr>
</thead>
</table>
| • Primary symptoms of heartburn and/or regurgitation  
  • Response to PPI therapy > 50%  
  • Hiatal hernia > 2 cm on barium esophagram  
  • Esophageal mucosal injury (endoscopic esophagitis, microscopic inflammatory infiltrate or intestinal metaplasia) | • Primary symptoms other than heartburn and/or regurgitation  
  • Response to PPI therapy < 50%  
  • No hiatal hernia  
  • No esophageal mucosal injury | • Patients with mixed characteristics who did not fit clearly into either of the previous two groups |


Diagnostic Precision of the Composite pH Score Using the Bravo pH Capsule

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal first 24 hrs</td>
<td>86%</td>
<td>100%</td>
<td>100%</td>
<td>71%</td>
<td>89%</td>
</tr>
<tr>
<td>Abnormal second 24 hrs</td>
<td>79%</td>
<td>100%</td>
<td>100%</td>
<td>63%</td>
<td>84%</td>
</tr>
<tr>
<td>Abnormal combined 48 hrs</td>
<td>82%</td>
<td>100%</td>
<td>100%</td>
<td>67%</td>
<td>87%</td>
</tr>
<tr>
<td>Abnormal either first or second 24 hrs</td>
<td>93%</td>
<td>100%</td>
<td>100%</td>
<td>83%</td>
<td>95%</td>
</tr>
</tbody>
</table>

Telemetry Capsule

Is traditional placement best?

Placement 1 cm above SCJ:
More sensitive for diagnosis of GERD?
Optimal position for Barretts monitoring?
### Sensitivity of 48-h Wireless pH Monitoring in GERD Patients Measured Immediately Above the SCJ and at the Standard pH Electrode Position 6 cm Above the SCJ at a Predefined Test Specificity of 90%

<table>
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<tr>
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<th>Esophagus</th>
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<tr>
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<td>Sensitivity (95% CI)</td>
<td>Patients Correctly Classified w/ GERD</td>
</tr>
<tr>
<td>All pts (N=62)</td>
<td>0.85 (0.71-1.0)</td>
<td>53/62</td>
</tr>
<tr>
<td>No esophagitis (N=30)</td>
<td>0.73 (0.51-0.96)</td>
<td>22/30</td>
</tr>
<tr>
<td>Esophagitis (N=32)</td>
<td>0.97 (0.90-1.0)</td>
<td>31/32</td>
</tr>
</tbody>
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Wenner J. et al. AM J Gastroenterol 2008; 103:2977-2985

### Telemetry Capsule for Barrett’s

- 25 patients on Esomeprazole 40mg BID
- All with 3 cm or greater columnar lined esophagus (all non dysplastic IM)
- Capsule placed 2cm above top of gastric folds in columnar mucosa
- 24/25 successful 48 hour monitoring
- 22/25 “normalized” using traditional normals” (Katz DDW 06)
Chest Pain Response: No GERD by pH or EGD


Chest Pain Response: GERD by pH or EGD

Chest Pain GERD +/-GERD-

A

Chest Pain GERD +/-GERD-


4 Day Bravo Study

96 Hour Bravo pH

4 Day Bravo (Two on Two Off)

4 Day Bravo: Two on Two Off


4 Day Bravo: Two on Two Off

4 Day Bravo: Symptom Association


Hypopharyngeal Monitoring: Normals

Should pH (Reflux) Monitoring Be Performed Off or On Therapy

- Low pre test probability of GERD at baseline/no diagnostic tests done
  - **OFF** Medication (7-10 days)
- GERD likely OR known. EGD done
  - **ON** Medication (impedance/pH)


Symptom Generation: Impedance/pH

- Clearance time (s)
- Age (yr)
- Change in pH
- Acidity
- Gender
- Esophageal extent
- Position
- Composition

Imp/pH On and Off PPI


Reflux Height: On or Off PPI

Median (Interquartile Range) Acid Exposure Time (% of Time With pH < 4) off and on PPI Therapy in Total and in Upright and Supine Position

<table>
<thead>
<tr>
<th>Acid Exposure Time</th>
<th>Off PPI</th>
<th>On PPI</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td>Total (%)</td>
<td>5.0 (2.0–14.2)</td>
<td>1.1 (0.2–6.3)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Upright (%)</td>
<td>7.5 (2.6–13.8)</td>
<td>1.5 (0.3–8.9)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Supine (%)</td>
<td>0.5 (0.0–6.8)</td>
<td>0.0 (0.0–1.3)</td>
<td>0.12</td>
</tr>
</tbody>
</table>


Reproducibility of Reflux Episodes Detected With 24-hour pH-Impedance Monitoring

<table>
<thead>
<tr>
<th>Reflux Events (Nr/24 h)</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Kendall’s W</th>
<th>P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>All reflux</td>
<td>63.8 (47.1–80.6)</td>
<td>53.9 (41.1–66.7)</td>
<td>0.92</td>
<td>0.01</td>
</tr>
<tr>
<td>Gas reflux</td>
<td>24.2 (11.5–36.8)</td>
<td>22.6 (10.3–34.6)</td>
<td>0.78</td>
<td>0.05</td>
</tr>
<tr>
<td>Acidic reflux</td>
<td>23.6 (13.1–34.0)</td>
<td>17.8 (11.6–24.0)</td>
<td>0.90</td>
<td>0.01</td>
</tr>
<tr>
<td>Weakly acidic reflux</td>
<td>40.3 (28.6–51.9)</td>
<td>36.1 (24.9–47.3)</td>
<td>0.90</td>
<td>0.01</td>
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Aanen MC, Et al. Am J Gastroenterol 2008; 103:2200-2208
Reproducibility of Symptom-Reflux Association Indices

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<th>P Values</th>
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<tbody>
<tr>
<td>SAP</td>
<td>69.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>84.5</td>
<td>0.90</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(50.9-88.8)</td>
<td></td>
<td></td>
<td>(7.35-</td>
<td></td>
</tr>
<tr>
<td>95.5)</td>
<td></td>
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Aanen MC, Et al. Am J Gastroenterol 2008; 103:2200-2208

Acid Only v Adding Impedance

Savarino E, et al. Am J Gastroenterol 2008; 103:2685-2693
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| Esophagitis (N=32)    | 0.97 (0.90-1.0)      | 31/32                                   | 0.78 (0.58-0.99)     | 25/32                                   | 0.014      

Wenner J, et al. AM J Gastroenterol 2008; 103:2977-2985