Reflux Monitoring: Current recommendations and a look to the future

Pr Frank ZERBIB

Bordeaux - France

Disclosures
Medtronic
Reckitt-Benckiser
Allergan
Gastro-esophageal reflux disease

GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications

**Esophageal Syndromes**
- Symptomatic Syndromes
  - 1. Typical Reflux Syndrome
  - 2. Reflux Chest Pain Syndrome
- Syndromes with Esophageal injury
  - 1. Reflux Esophagitis
  - 2. Reflux Stricture
  - 3. Barrett’s Esophagus
  - 4. Esophageal Adenocarcinoma

**Extraesophageal Syndromes**
- Established Associations
  - 1. Reflux Cough Syndrome
  - 2. Reflux Laryngitis Syndrome
  - 3. Reflux Asthma Syndrome
  - 4. Reflux Dental Erosion Syndrome
- Proposed Associations
  - 1. Pharyngitis
  - 2. Sinusitis
  - 3. Idiopathic Pulmonary Fibrosis
  - 4. Recurrent Otitis Media

*The Montreal definition and classification, Am J Gastro 2006*
Diagnosis of gastro-esophageal reflux disease

Symptoms
- Typical
- Atypical/Extra-esophageal

Endoscopy
- Esophagitis
- Complications
- Rule out differential diagnosis (EoE)

Ambulatory reflux monitoring
Diagnosis of gastro-esophageal reflux disease

• An adequate clinical evaluation is crucial
  Heartburn ?
  Rumination ?

• Virtually all patients receive PPIs before being referred

• 30 to 40% of patients don’t achieve adequate symptom relief
  Normal endoscopy
  Extra-esophageal symptoms

• Refractory symptoms ≠ refractory GERD

• Endoscopy is mandatory despite a low diagnostic yield
The roles of ambulatory reflux testing

-> Make a definite diagnosis of GERD
   - refractory symptoms
   - extra-esophageal symptoms

-> Select patients suitable for surgery
Functional esophageal disorders – Rome IV

The reflux symptoms spectrum

The GERD spectrum

Acid exposure

- Erosive esophagitis
- NERD
- Reflux hypersensitivity
- Functional heartburn

PPIs efficacy

IBS

Functional Dyspepsia

+++
Types of Reflux Monitoring

1) pH only:
   A) Catheter-based
      • Single channel pH-catheter
      • Proximal and distal (multi channel) pH-catheter
   B) Wireless
      • Bravo pH capsule

2) Catheter-based pH-Impedance
   - esophageal
   - pharyngeal and esophageal
Ambulatory reflux monitoring for diagnosis of gastro-esophageal reflux disease: Update of the Porto consensus and recommendations from an international consensus group

Sabine Roman (1), C. Prakash Gyawali (2), Edoardo Savarino (3), Rena Yadlapati (4), Frank Zerbib (5), Justin Wu (6), Marcelo Vela (7), Radu Tutuian (8), Roger Tatum (9), Daniel Sifrim (10), Jutta Keller (11), Mark Fox (12), John E Pandolfino (4), Albert J Bredenoord (13) and the GERD consensus group

Neurogastroenterol Motil 2017, in press

GERD consensus group
Fernando Azpiroz, Arash Babaei, Shobna Bhatia, Guy Boeckxstaens, Serhat Bor, Dustin Carlson, Donald Castell, Michele Cicala, John Clarke, Nicola De Bortoli, Vasile Drug, Marzio Frazzoni, Richard Holloway, Peter Kahrilas, Arne Kandulski, Phil Katz, David Katzka, Ravinder Mittal, Francois Mion, Luis Novais, Amit Patel, Roberto Penagini, Mentore Ribolsi, Joel Richter, Renato Salvador, Vincenzo Savarino, Jordi Serra, Felice Schnoll-Sussman, Andre Smout, Edy Soffer, Rami Sweis, Jan Tack, Salvatore Tolone, Michael Vaezi, Philip Woodland, Yinglian Xiao
Ambulatory reflux monitoring for diagnosis of gastro-esophageal reflux disease: Update of the Porto consensus and recommendations from an international consensus group

Sabine Roman (1), C. Prakash Gyawali (2), Edoardo Savarino (3), Rena Yadlapati (4), Frank Zerbib (5), Justin Wu (6), Marcelo Vela (7), Radu Tutuian (8), Roger Tatum (9), Daniel Sifrim (10), Jutta Keller (11), Mark Fox (12), John E Pandolfino (4), Albert J Bredenoord (13) and the GERD consensus group

Neurogastroenterol Motil 2017, in press

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High quality</strong></td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td><strong>Moderate quality</strong></td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td><strong>Low quality</strong></td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td><strong>Very low quality</strong></td>
<td>Any estimate of effect is very uncertain.</td>
</tr>
</tbody>
</table>
Indications and choice of GERD Testing

Esophageal pH impedance monitoring is the gold standard but availability, cost and patients preference may drive the choice between catheter based pH, impedance or wireless pH.

- Esophageal pH impedance monitoring may be indicated for refractory symptoms despite PPI therapy prior to and/or following anti-reflux surgery, for symptoms of cough, frequent belching and rumination syndrome.

- Wireless pH:
  - Patients intolerant of a pH or pH impedance catheter
  - Patients with a negative catheter based pH study to elicit day to day variation in acid exposure and symptom association.
The Wireless pH monitoring (Bravo°)

Improved diagnostic yield related to prolonged recording duration

Prakash et al 2005
Indications and choice of GERD Testing « off » or « on » PPIs?

Surgery may provide good results in refractory patients with

- Abnormal esophageal acid exposure (true NERD)
- Hypersensitive esophagus


At 5 Year follow-up

Indications and choice of GERD Testing

« off » or « on » PPIs?

Abnormal oesophageal acid exposure and Symptom index

Charbel et al, AJG 2005
Indications and choice of GERD Testing
« off » or « on » PPIs?

Off PPI (n = 79)  On PPI (n = 71)

% of patients

SAP (+) SI (+)  SAP (+) SI (+)

pH-Impedance  pH alone

SAP: Symptom Association Probability
SI: Symptom Index

Zerbib et al, Am J Gastro 2006
Reflux monitoring ON therapy
Combined pH-impedance

- Acid not controlled 10%
- Symptoms due to “non-acid” reflux 30-40%
- Symptoms not due to reflux 50-60%
Indications and choice of GERD Testing
« off » or « on » PPIs?

Reflex monitoring (catheter based pH, wireless pH, or pH impedance) should be performed off of PPI to demonstrate abnormal reflux prior to antireflux surgery.

Reflex monitoring (catheter based pH, wireless pH, or pH impedance) should be performed off of PPI to demonstrate abnormal reflux in the setting of PPI non response.

Reflex monitoring in the form of pH impedance should be performed on PPI in settings with prior evidence for reflux.
Persistent symptoms suggestive of GERD

- Upper GI endoscopy without esophagitis grade C or D, Barrett’s mucosa or peptic stricture
- Esophagitis grade C or D, Barrett’s mucosa or peptic stricture
  - Atypical symptoms
  - Prior to anti-reflux surgery
  - Recurrent/persistent symptom on PPI and/or after surgery
  - Catheter based or wireless pH monitoring or 24-h pH-impedance monitoring off PPI

- Prior positive pH testing

- 24-h pH-impedance monitoring on double dose PPI
Interpretation of pH and pH-impedance monitoring

A total AET value of <4% is consistently normal  
Moderate

A total AET value of >6 % is consistently abnormal  
High

Automated analysis of pH impedance studies is adequate for acid RE  
Automated analysis of pH impedance overestimates non-acidic RE  
Manual review of the 2 minutes preceding each symptom event in pH impedance studies is necessary  
Very low
Grade C or D esophagitis and/or Peptic stricture and/or Barrett’s esophagus or

24-h esophageal pH ±impedance monitoring (off or on therapy)

AET > 6% or

AET 4-6 %

Considering additional testing: total number of reflux, baseline impedance, evaluation of microscopic esophagitis

Pathological GERD

Normal Grade A or B esophagitis

No pathological GERD

Upper gastrointestinal endoscopy
# Interpretation of pH and pH-impedance monitoring

## Symptom reflux association

<table>
<thead>
<tr>
<th>Statement</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>The only <strong>time window</strong> for symptoms following a reflux event is <strong>2 minutes</strong></td>
<td>Moderate</td>
</tr>
<tr>
<td>All reflux events detected by impedance are used in calculation of <strong>RE</strong></td>
<td>High</td>
</tr>
<tr>
<td>Symptom index (SI) and Symptom Association Probability (SAP) have <strong>value</strong> in pH and pH-impedance monitoring</td>
<td>High</td>
</tr>
<tr>
<td>SI and SAP are complementary and cannot be directly compared to each other</td>
<td>Very low</td>
</tr>
<tr>
<td>The <strong>2 minute period prior</strong> to each symptom event and <strong>2 minute period following each reflux episode</strong> should be evaluated prior to calculating the <strong>SI</strong></td>
<td>Moderate</td>
</tr>
<tr>
<td>Abnormal <strong>AET</strong> with both <strong>SAP</strong> and <strong>SI</strong> positive represents the strongest evidence for reflux</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
The GER phenotypes

**Study off medication**
Catheter based or wireless pH monitoring or 24-h pH-impedance monitoring (all adequate)

- Abnormal reflux burden
  - GERD (non erosive reflux disease)
  - Reflux hypersensitivity
  - Functional symptoms*
    - Functional heartburn
      - Functional symptoms
  - Alternate diagnosis¥
    - Rumination
    - Supragastric belching
    - Eosinophilic esophagitis

- Normal reflux burden, but positive symptom association
  - No GERD
  - Alternate diagnosis¥

- Normal reflux burden, and negative symptom association

**Study on medication**
24-h pH-impedance monitoring

- Abnormal reflux burden
  - Persistent GERD despite PPI or poor adherence to PPI
  - Reflux hypersensitivity
  - Alternate diagnosis¥

- Normal reflux burden, but positive symptom association
  - Symptom not due to reflux
  - Functional symptoms*

**Overlap with GERD**
Stratification of Patients with Typical Reflux Symptoms

What is not in the consensus
What could have been in
What may be in the future

Pharyngeal reflux /Dual probe pH monitoring have no value to guide clinical management

The total number of reflux episodes alone, baseline impedance, histological assessment

- not sufficient to confirm the diagnosis of GERD
- should be considered as an exploratory tool.
What is not in the consensus
What could have been in
What may be in the future

Validation of additional parameters
- Number of reflux events
- Bolus exposure
- Baseline impedance

Validation of new tools
- Microscopic esophagitis
- Salivary pepsin
- Direct measurements of MI
- Combined HRM-impedance studies
- Automatic analysis of impedance recordings

Outcome prospective studies +++