New Advances in GERD: Diagnostics & Therapeutics

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Objectives & Disclosures

- Objectives (in 20 minutes)
  1) To discuss key updates in the past 12 months
  2) To present the current diagnostic options for GERD
  3) To review available therapies for GERD – lifestyle, complementary, medical, endoscopic & surgical
- Disclosures
  - Consultant: Alnylam, Isothrive, Medtronic, Pfizer, Regeneron, Sanofi
  - Grant support: Aluvra, Ironwood

Key updates in GERD over the past year

1) Randomized trial of medical versus surgical treatment of GERD (Spechler et al, NEJM, VA)
2) FDA approval of Mucosal Integrity (aka mucosal impedance)
3) Updates on recently-concluded GERD clinical trials
4) Other key papers regarding treatment (rapid fire)

The NEW ENGLAND JOURNAL of MEDICINE

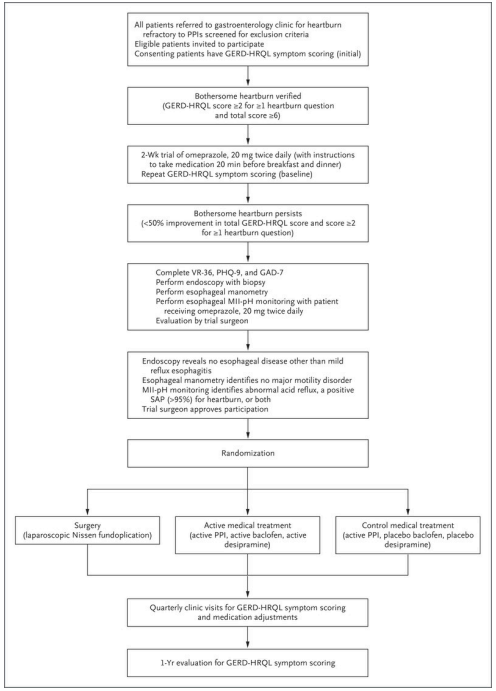
ESTABLISHED IN 1812 OCTOBER 17, 2019 VOL. 381 NO. 16

Randomized Trial of Medical versus Surgical Treatment for Refractory Heartburn

S.J. Spechler, J.G. Hunter, K.M. Jones, R. Lee, B.R. Smith, H. Mashimo, V.M. Sanchez, K.B. Dunbar, T.H. Pham, U.K. Murthy, T. Kim, C.S. Jackson, J.M. Wallen, E.C. von Rosenvinge, J.P. Pearl, L. Laine, A.W. Kim, A.M. Kaz, R.P. Tatum, Z.F. Gellad, S. Lagoo-Deenadayalan, J.H. Rubenstein, A.A. Ghaferi, W.-K. Lo, R.S. Fernando, B.S. Chan, S.C. Paski, D. Provenzale, D.O. Castell, D. Lieberman, R.F. Souza, W.D. Chey, S.R. Warren, A. Davis-Karim, S.D. Melton, R.M. Genta, T. Serpi,* K. Biswas, and G.D. Huang

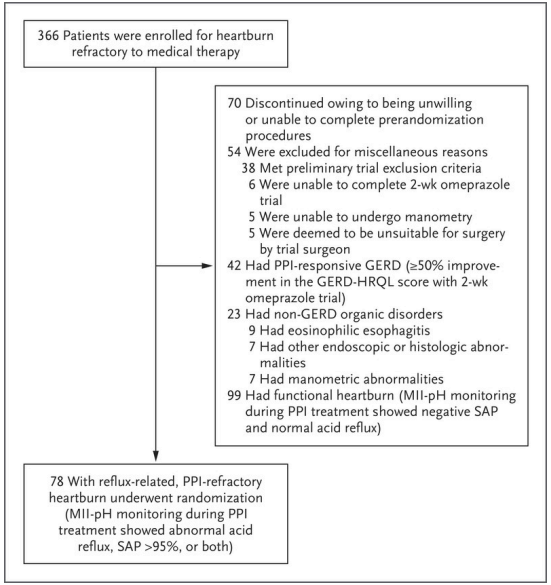
Spechler et al. NEJM VA GERD RCT: Study Design

- RCT of refractory GERD patients at VA
- PPI-refractory patients with symptoms despite omeprazole 20 mg BID
- Evaluation: endoscopy, biopsies, manometry, pH/impedance
- Confirmed GERD randomized:
  - Surgery (laparoscopic fundoplication)
  - Medical (omeprazole, baclofen, desipramine)
- Primary outcome: > 50% decrease in GERD-HRQL at 1 year

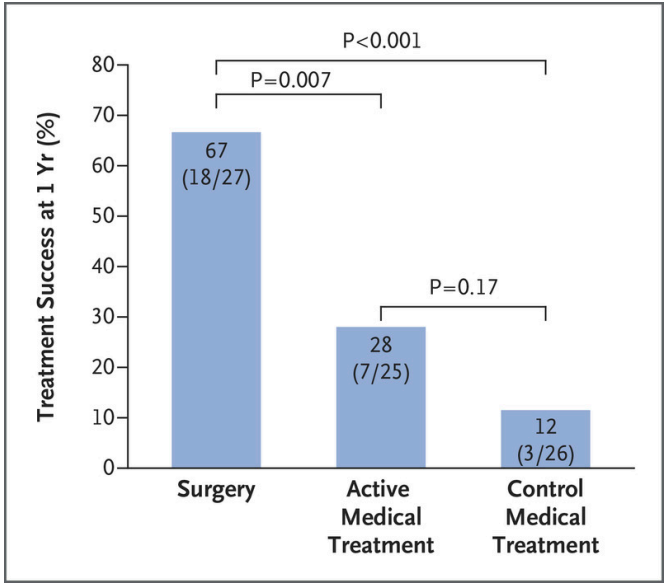


Spechler et al. NEJM VA GERD RCT: Conclusions

Conclusion 1: Most patients with refractory GERD symptoms do not have truly refractory GERD

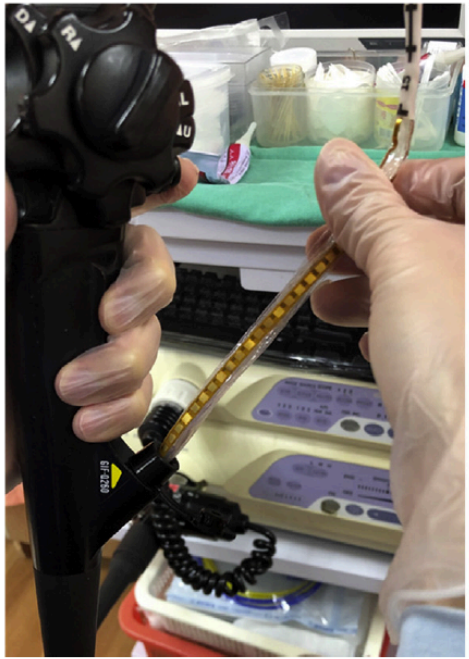


Conclusion 2: Those patients that do have truly refactory GERD after evaluation do better with surgery then medical therapy

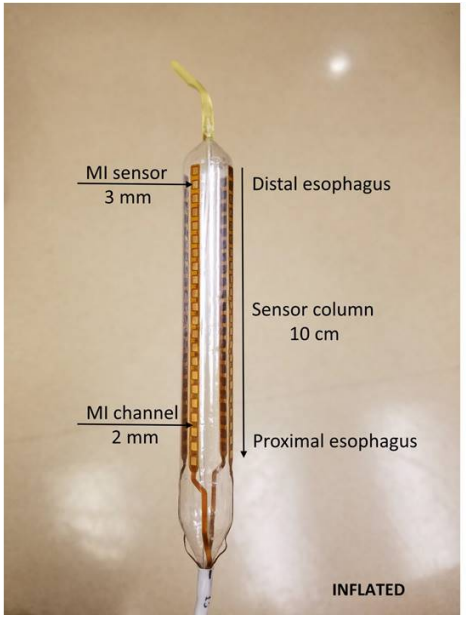


Mucosal Integrity (aka Mucosal Impedance)

- Background
  - Mucosal impedance can be measured directly
  - Marker of dilated intercellular spaces, or spongiosis, which affects permeability
  - Can be measured in real-time during endoscopy
  - May predict GERD and EoE – and separate the two
  - Developed by Michael Vaezi & Vanderbilt team in conjunction with Diversatek
  - FDA-approved in December 2019



Mucosal Integrity (aka Mucosal Impedance)



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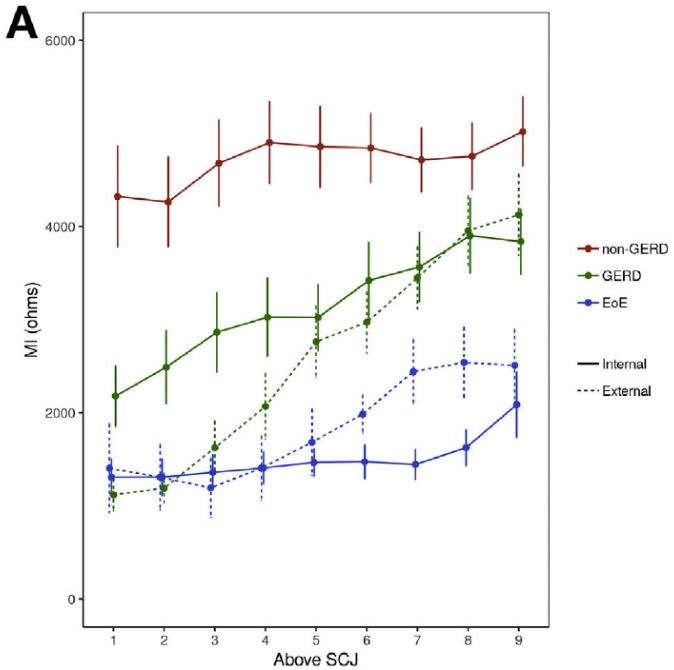

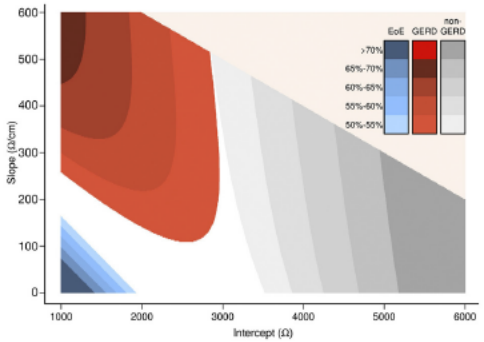

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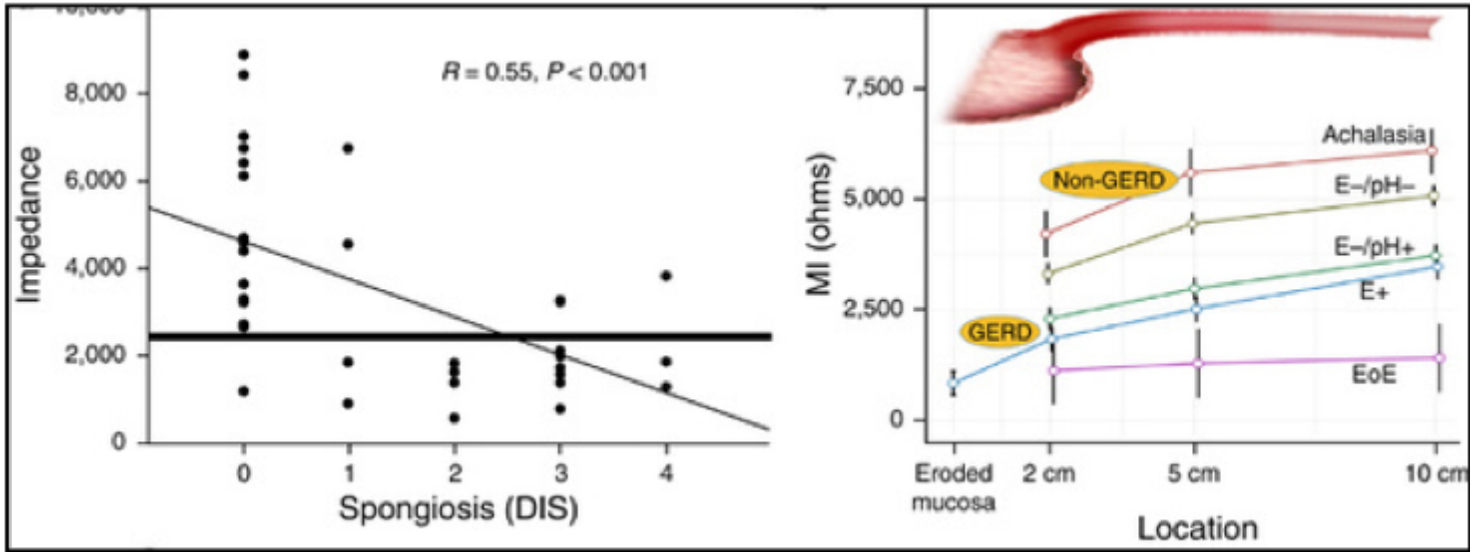
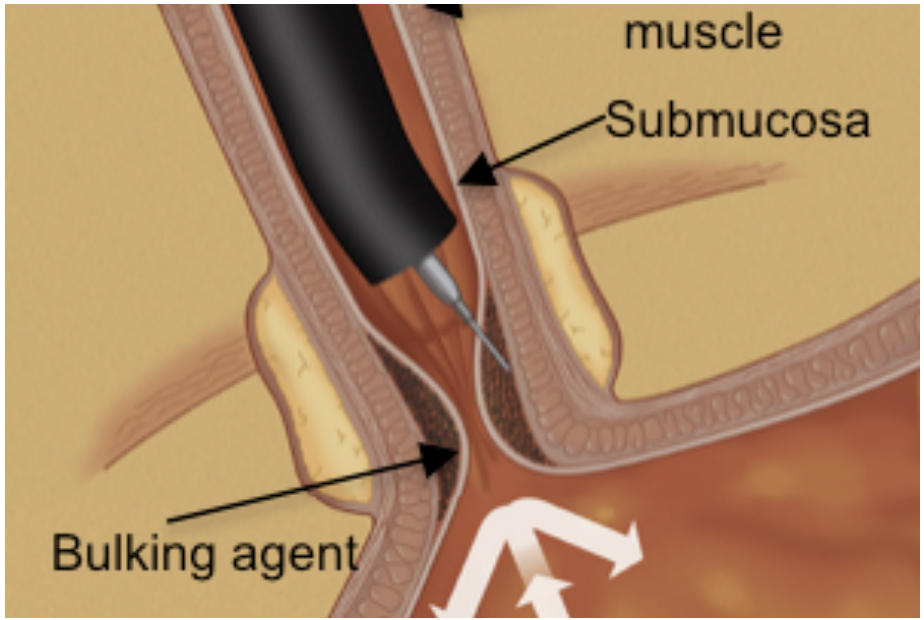


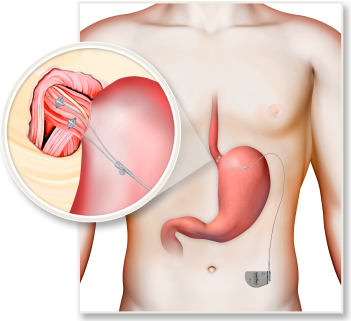
Vaezi MF. Amer J Gastroenterol 2017

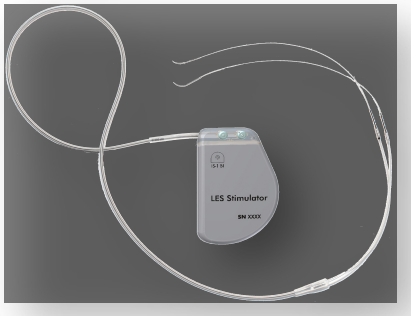
Updates on recently-completed clinical trials

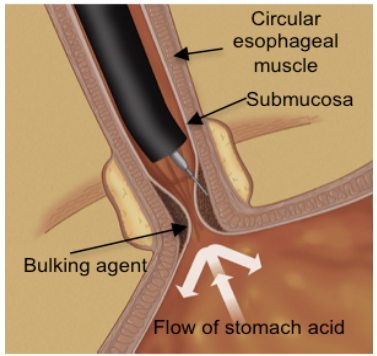


Updates on recently-completed clinical trials

1) Endostim: did not meet endpoint
2) NECTAR: closed due to safety concerns
3) Ironwood: did not meet endpoint







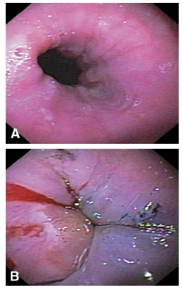
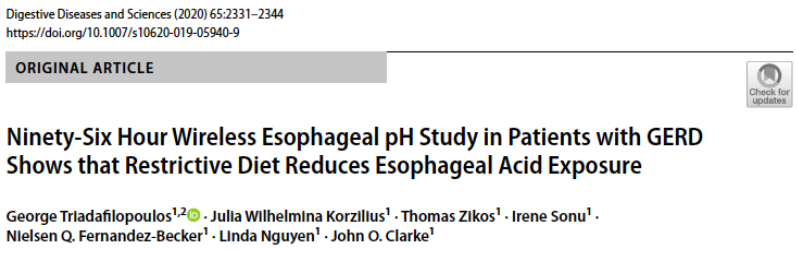


Figure 2. A, Region of the GEJ before Durasphere injection. **B,** After injection, note the tissue bulking effect and closure of the GEJ lumen.

Key Papers of Interest: Rapid Fire



Digestive Diseases and Sciences (2020) 65:2331–2344
https://doi.org/10.1007/s10620-019-05940-9

ORIGINAL ARTICLE

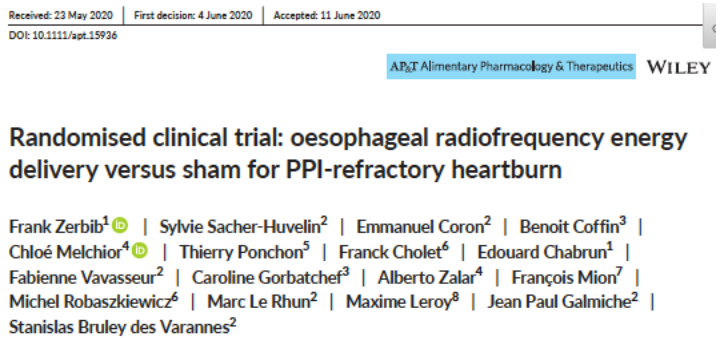
Check for updates

Ninety-Six Hour Wireless Esophageal pH Study in Patients with GERD Shows that Restrictive Diet Reduces Esophageal Acid Exposure

George Triadafilopoulos[1,2] · Julia Wilhelmina Korzilius[1] · Thomas Zikos[1] · Irene Sonu[1] · Nielsen Q. Fernandez-Becker[1] · Linda Nguyen[1] · John O. Clarke[1]

- Prospective study of 66 patients undergoing 96-hour wireless pH study
- All patients placed on regular diet for the first 48 hours, restricted diet for the last 48 hours
- Restricted diet decreased GERD significantly & normalized acid exposure in 2/3 of patients

Key Papers of Interest: Rapid Fire



Received: 23 May 2020 | First decision: 4 June 2020 | Accepted: 11 June 2020
DOI: 10.1111/apt.15936

APT Alimentary Pharmacology & Therapeutics WILEY

Randomised clinical trial: oesophageal radiofrequency energy delivery versus sham for PPI-refractory heartburn

Frank Zerbib[1] | Sylvie Sacher-Huvelin[2] | Emmanuel Coron[2] | Benoit Coffin[3] | Chloé Melchior[4] | Thierry Ponchon[5] | Franck Cholet[6] | Edouard Chabrun[1] | Fabienne Vavasseur[2] | Caroline Gorbatchef[3] | Alberto Zalar[4] | François Mion[7] | Michel Robaszkiewicz[6] | Marc Le Rhun[2] | Maxime Leroy[8] | Jean Paul Galmiche[2] | Stanislas Bruley des Varannes[2]

- Esophageal radiofrequency ablation (Stretta) versus sham
- Double-blind study
- 62 patients: 29 Stretta, 33 sham
- Response rate:
  - Sham: 15% (5/33 patients)
  - Stretta: 3% (1/29 patients)
- No change in PPI use, heartburn frequency
- No predictors of response on pH/impedance

Key Papers of Interest: Rapid Fire

Digestive Endoscopy 2020; ••: ••–••

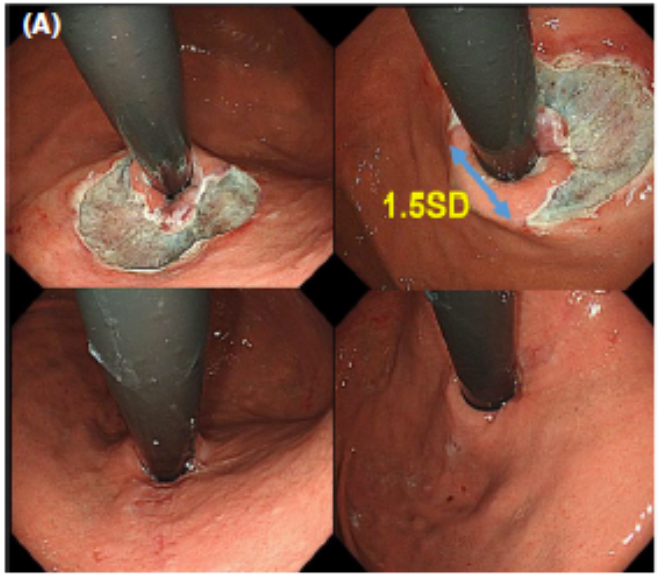
doi: 10.1111/den.13727

Original Article

Endoscopic treatment of proton pump inhibitor-refractory gastroesophageal reflux disease with anti-reflux mucosectomy: Experience of 109 cases

Kazuya Sumi, Haruhiro Inoue, Yasutoshi Kobayashi, Yugo Iwaya, Mary Raina Angeli Abad, Yusuke Fujiyoshi, Yuto Shimamura, Haruo Ikeda and Manabu Onimaru

Digestive Diseases Center, Showa University Koto-Toyosu Hospital, Tokyo, Japan



Key Papers of Interest: Rapid Fire

Clinical Gastroenterology and Hepatology 2020;18:1736–1743

Magnetic Sphincter Augmentation Superior to Proton Pump Inhibitors for Regurgitation in a 1-Year Randomized Trial

Reginald Bell, MD,[*] John Lipham, MD,[‡] Brian E. Louie, MD,[§] Valerie Williams, MD,[‖] James Luketich, MD,[¶] Michael Hill, MD,[#] William Richards, MD,[**] Christy Dunst, MD,[‡‡] Dan Lister, MD,[§§] Lauren McDowell-Jacobs, MD,[‖‖] Patrick Reardon, MD,[¶¶] Karen Woods, MD,[‖‖‖] Jon Gould, MD,[##] F. Paul Buckley III, MD,[***] Shanu Kothari, MD,[‡‡‡] Leena Khaitan, MD,[§§§] C. Daniel Smith, MD,[‖‖‖] Adrian Park, MD,[¶¶¶] Christopher Smith, MD,[###] Garth Jacobsen, MD,[****] Ghulam Abbas, MD,[‡‡‡‡] and Philip Katz, MD[§§§§]

- Compared reflux patients with regurgitation despite once-daily PPI
- Randomized to Magnetic Sphincter Augmentation (Linx) versus twice daily PPI
- 152 patients at 20 sites
- Response rates:
  - MSA (96%)
  - PPI (19%)
- Esophageal acid exposure in MSA decreased from 10.7% to 1.3%
- Dysphagia 7%, bloating 25%

Diagnosis of GERD in 2020

Mechanisms of GERD

- Reflux is a physiologic process
  - Esophageal acid exposure < 4%
  - Reflux episodes < 40/day
  - Required to gas-vent
- Normal defense mechanisms for reflux
  - Lower esophageal sphincter
  - Fundic compliance
  - Diaphragmatic pinch
  - Secondary peristalsis
  - Salivary production
  - Frequent swallowing
  - Epithelial barrier function

Roman S. Neurogastroenterol Motil 2017

Diagnostic options: tests available

- Response to antisecretory therapy
- Endoscopy
- Esophageal capsule endoscopy
- Wireless pH testing
- Combined pH/impedance testing
- Mucosal impedance testing

Which test to choose?

- Wireless pH monitoring
  - Benefits
    - Can be combined with endoscopy
    - No need for a catheter
    - Allows recording of multiple days
    - Maybe more physiologic activities
    - Patient preference
  - Downsides
    - Does not look at non-acid reflux
    - May confuse swallows/reflux
    - Forced to choose on/off therapy
    - More expensive
    - Not as widely available
    - Requires endoscopy
- Combined pH/impedance
  - Benefits
    - Measures both acid and non-acid
    - Can separate swallows and reflux
    - Can measure proximal extent of reflux
    - Can measure air movement
    - No need for endoscopy/sedation
    - Cheaper
  - Downsides
    - Requires a transnasal catheter
    - Limited to 24 hours
    - Interpretation more complicated

How to interpret the results?

Received: 22 December 2016 | Accepted: 20 February 2017
DOI: 10.1111/nmo.13067

REVIEW ARTICLE

WILEY

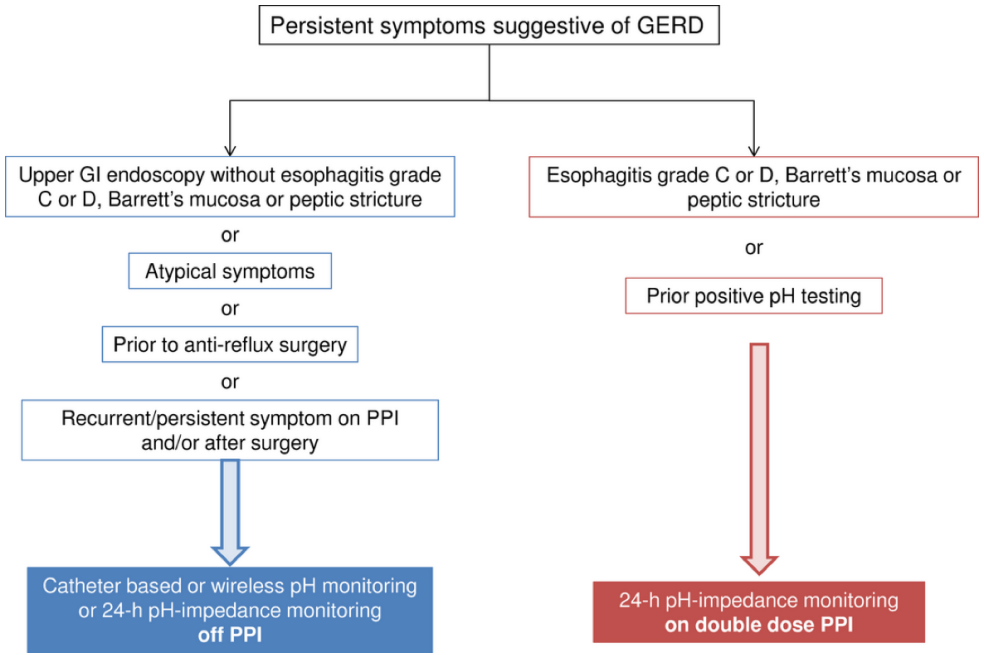
Ambulatory reflux monitoring for diagnosis of gastro-esophageal reflux disease: Update of the Porto consensus and recommendations from an international consensus group

S. Roman[1] | C. P. Gyawali[2] | E. Savarino[3] | R. Yadlapati[4] | F. Zerbib[5] | J. Wu[6] | M. Vela[7] | R. Tutuian[8] | R. Tatum[9] | D. Sifrim[10] | J. Keller[11] | M. Fox[12] | J. E. Pandolfino[4] | A. J. Bredenoord[13] | the GERD consensus group[a]

Modern diagnosis of GERD: the Lyon Consensus

C Prakash Gyawali,[1] Peter J Kahrilas,[2] Edoardo Savarino,[3] Frank Zerbib,[4] Francois Mion,[5,6,7] André J P M Smout,[8] Michael Vaezi,[9] Daniel Sifrim,[10] Mark R Fox,[11,12] Marcelo F Vela,[13] Radu Tutuian,[14] Jan Tack,[15] Albert J Bredenoord,[8] John Pandolfino,[2] Sabine Roman[5,6,7]

To Test On or Off Therapy?



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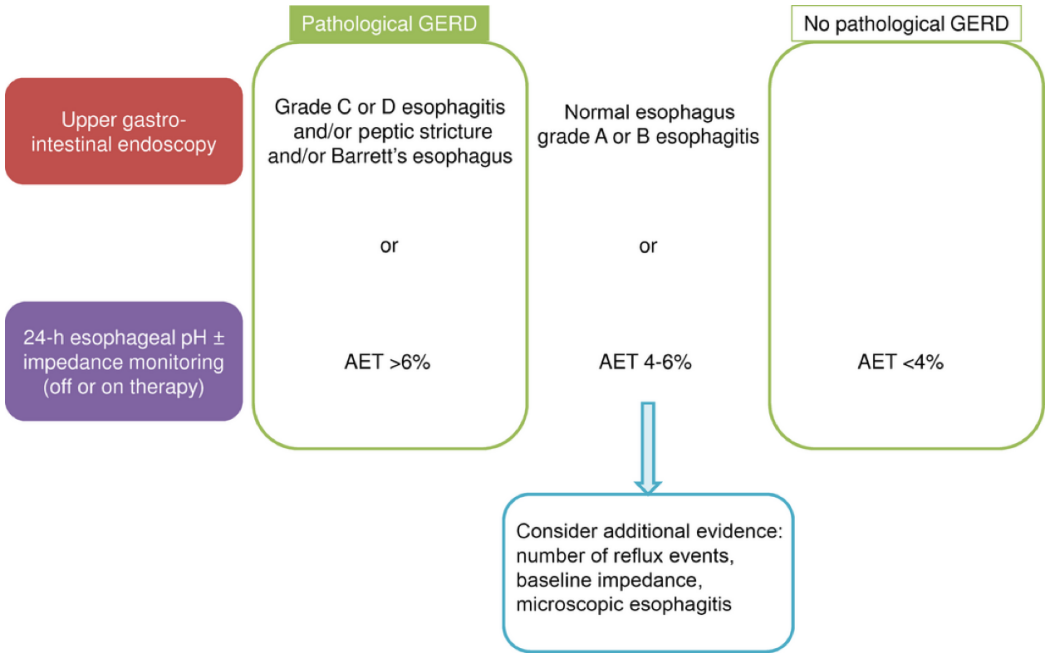
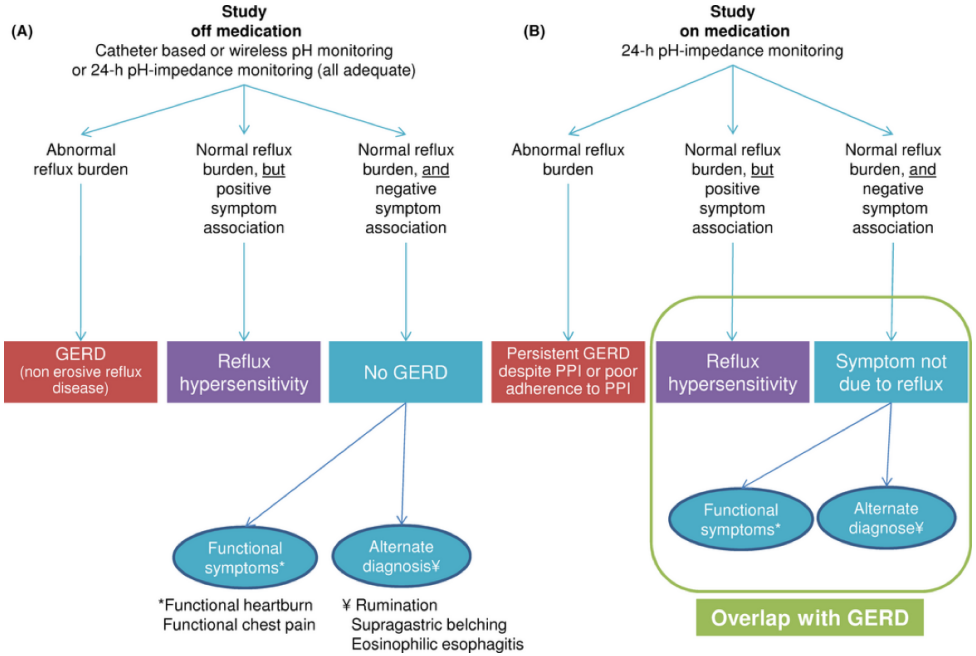
Interpretation



Roman S. Neurogastroenterol Motil 2017

Diagnostics & Definitions: Putting it all together



Roman S. Neurogastroenterol Motil 2017

Treatment of GERD in 2020

Treatment options: a tailored approach

- GERD occurs from multiple causes & mechanisms
- Patients with GERD symptoms are not a monolith
- Treatment should be tailored to the specific problems involved

Treatment of GERD: a brief summary

- Lifestyle modification
- Medications
- Alternative therapy
- Endoscopic therapy
- Surgical therapy

Lifestyle Modification

- Dietary measures (avoidance)
  - Chocolate
  - Citrus fruits/fruit juices
  - Tomatoes
  - Peppermint
  - Onions/garlic
  - High-fat meals
  - Carbonation
- Small meal size
- Weight loss
- Smoking cessation
- Avoidance of alcohol
- Elevation of the head of the bed
- Sleeping in the left decubitus position
- No meals within 3 hours of sleeping
- Exercise

Kaltenbach T. Arch Intern Med 2006; 166: 965-71.

Medications

	Onset	Duration	Efficacy (v placebo)	U.S. cost per year
Antacids	seconds	60 mins	11 %	$350 million
H2 Blockers	< 20 mins	6-10 hours	41 %	$200 million
PPI	90-300 mins	24-72 hours	62 – 94 %	> $14 billion

Medications

- Alginates
- Baclofen
- Bile acid binders
- Buspirone
- Neuromodulators
- Prokinetics

Alternative therapies

Alimentary Pharmacology & Therapeutics

Clinical trial: acupuncture vs. doubling the proton pump inhibitor dose in refractory heartburn

R. DICKMAN*,†, E. SCHIFF‡,§, A. HOLLAND‡,¶, C. WRIGHT¶, S. R. SARELA*, B. HAN* & R. FASS*

Mechanical therapies

- Endoscopic therapies
- Stretta procedure
- Transoral incisionless fundoplication (TIF)
- Anti-reflux Mucosectomy (ARM)

- Surgical therapies
- Fundoplication
  - Nissen
  - Toupet
  - Dor
- Linx procedure
- Roux-en-Y gastric bypass

Stanford Esophageal Center

- GI (esophagus & motility)
  - Laren Becker
  - John Clarke
  - Nielsen Fernandez-Becker
  - Patricia Garcia
  - Houssan Halawi
  - Afrin Kamal
  - Monica Nandwani
  - Linda Nguyen
  - Irene Sonu
  - George Triadafilopoulos
  - Thomas Zikos
- GI (therapeutics)
  - Shai Friedland
  - Joo Ha Hwang
- Nutrition
  - Elaine Hon
  - Sandy Sun
- Surgery (Minimally-invasive)
  - Dan Azagury
  - Micaela Esquivel
  - Mary Hawn
  - Jim Korndorffer
  - Yulia Zak
- Surgery (Thoracic)
  - Mark Berry
  - Natalie Lui
  - Joe Shrager
- ENT
  - Ed Damrose
  - Karuna Dewan
  - Heather Starmer
  - Kwang Sung
- Research Coordinator
  - Divya Pathak

Thank you

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