



Evidence-Based Endoscopy in GERD

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Objectives

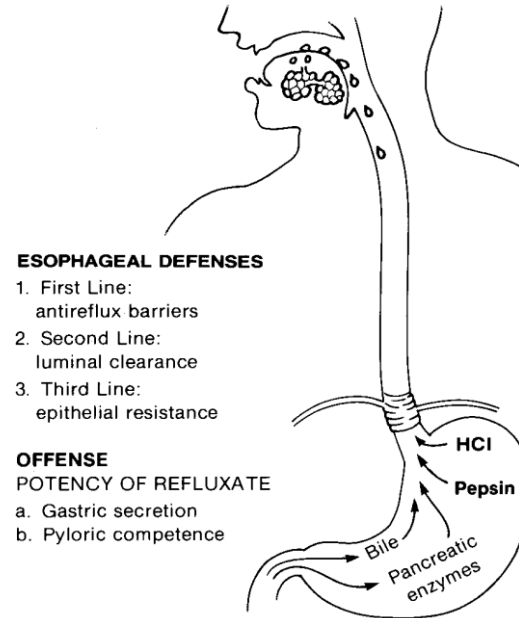
- Review the pathophysiology and typical symptoms of GERD
- Discuss the role of endoscopy among the typical diagnostic testing for GERD
- Enhance understanding of nuance of physiology testing for GERD
- Introduce and review endoscopic treatments for GERD

Definition

- the condition in which the reflux of gastric contents into the esophagus results in symptoms and/or complications
- the presence of characteristic mucosal injury seen at endoscopy and/or abnormal esophageal acid exposure demonstrated on a reflux monitoring study

Pathophysiology

- Barrier dysfunction
 - Transient LES relaxation (tLESR)
 - Hypotensive LES
 - Hiatal hernia
- Clearance mechanisms
 - Decreased salivation
 - Disorders of peristalsis
- Esophageal hypersensitivity
- Delayed gastric emptying



Orlando, R.C. *J Clin Gastroenterol*, 2008

Symptoms

- Typical
 - Heartburn
 - Regurgitation
- Atypical
 - Laryngitis
 - Hoarseness
 - Cough
 - Non-cardiac chest pain
 - Poor dentition
 - Aspiration
 - Asthma

Diagnosis

- No definitive test or gold standard
- Combination of:
 - Symptoms
 - Response to therapy
 - Endoscopy findings
 - Reflux testing

Diagnosis

- Symptoms
 - Typical (Heartburn and regurgitation)
 - Sensitivity for erosive esophagitis \implies 30-76%
 - Specificity \implies 62-96%
 - Atypical symptoms much worse

Numans, et al. *Ann Intern Med*, 2004. 140(7):518-27

Diagnosis

- Response to therapy with PPI
 - Pooled sensitivity of 78%
 - Pooled specificity of only 54%
 - EGD and pH monitoring used as standard of reference

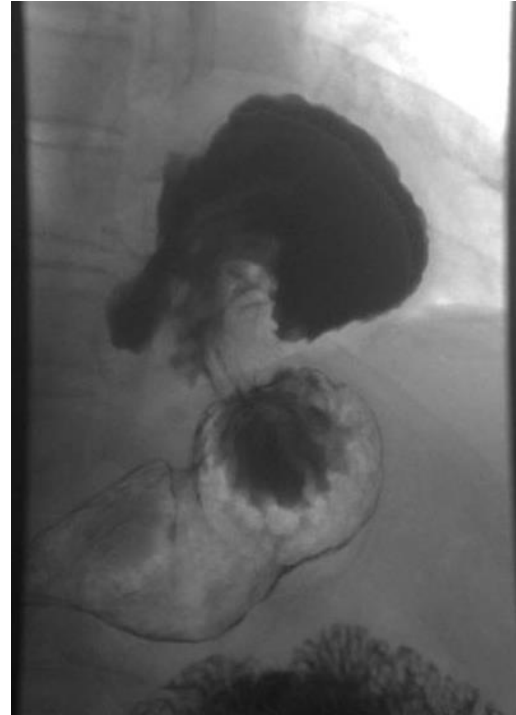
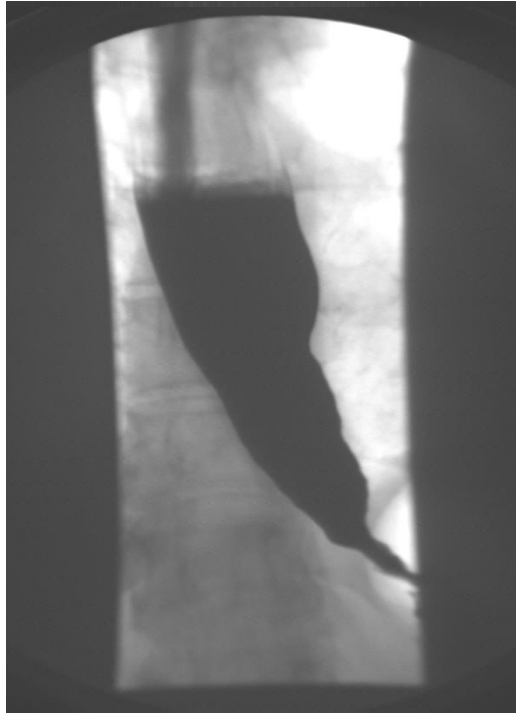
Cremonini, et al. *Am J Gastroenterol*, 2005. 100(6): 1226-32
Kahrilas, et al. *Gut*, 2011. 60(11):1473-8.

Diagnosis

- Esophagram
 - Should not be used by itself as a diagnostic test for GERD
 - Poor specificity of reflux findings on esophagram
 - Only half with findings of reflux positive on pH monitor¹

1. Johnston, et al. *Am J Gastroenterol*, 1996. 91(6):1181-5

Esophagram

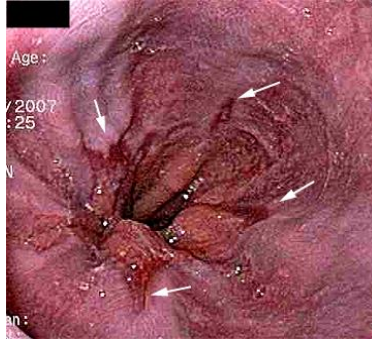


Endoscopy

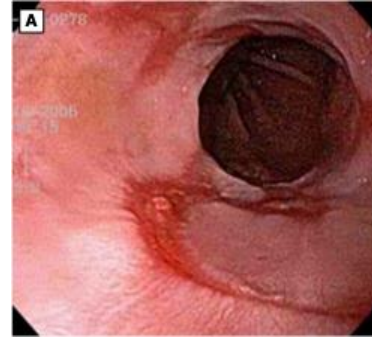
- When should we use it?
- How do we use it?
 - Diagnosis
 - Therapeutics

Endoscopy for Diagnosis

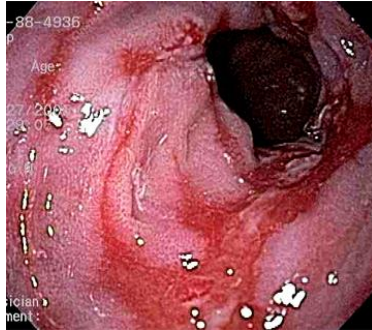
LA Classification



Grade A – 1 or more mucosal breaks \leq 5mm



Grade B – at least one mucosal break $>$ 5mm, non-contiguous



Grade C – at least one contiguous break, non-circumferential



Grade D – mucosal break that involves \geq 75% of circumference

Photos from UpToDate – courtesy of Andres Gelrud, M.D.

Endoscopy for Diagnosis

- The majority of patients will **NOT** have evidence of mucosal damage (30% or less of treatment-naïve patients).
 - NERD – **Non-Erosive Reflux Disease**
 - No esophagitis, abnormal pH testing with symptom correlation
 - Reflux hypersensitivity

Ambulatory pH Testing

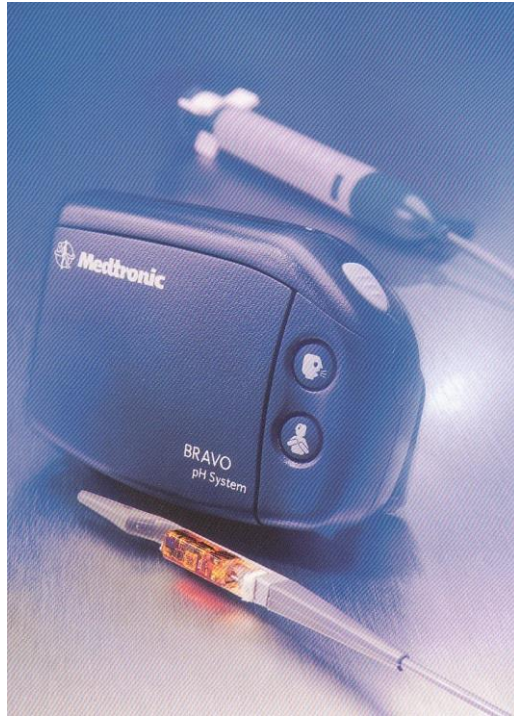
- What questions does it answer?
 - Do you have NERD (GERD without esophagitis)?
 - Testing OFF meds requires at least 1 week off PPI and at least 3 days off H2RB to account for rebound hypersecretion.
 - If your symptoms are atypical, are they caused by NERD?

1. Long, J.D. and Orlando, R.C. NERD: a pathophysiologic perspective. *Current Gastroenterology Reports*, 2008
2. *Best Practice & Research Clin Gastro* 2001; 15(3):487-495

Evaluation of GERD

- Ambulatory pH monitoring
 - Traditional
 - Transnasal catheter
 - 24 hr test
 - Bravo pH System
 - Wireless
 - 48 hr test

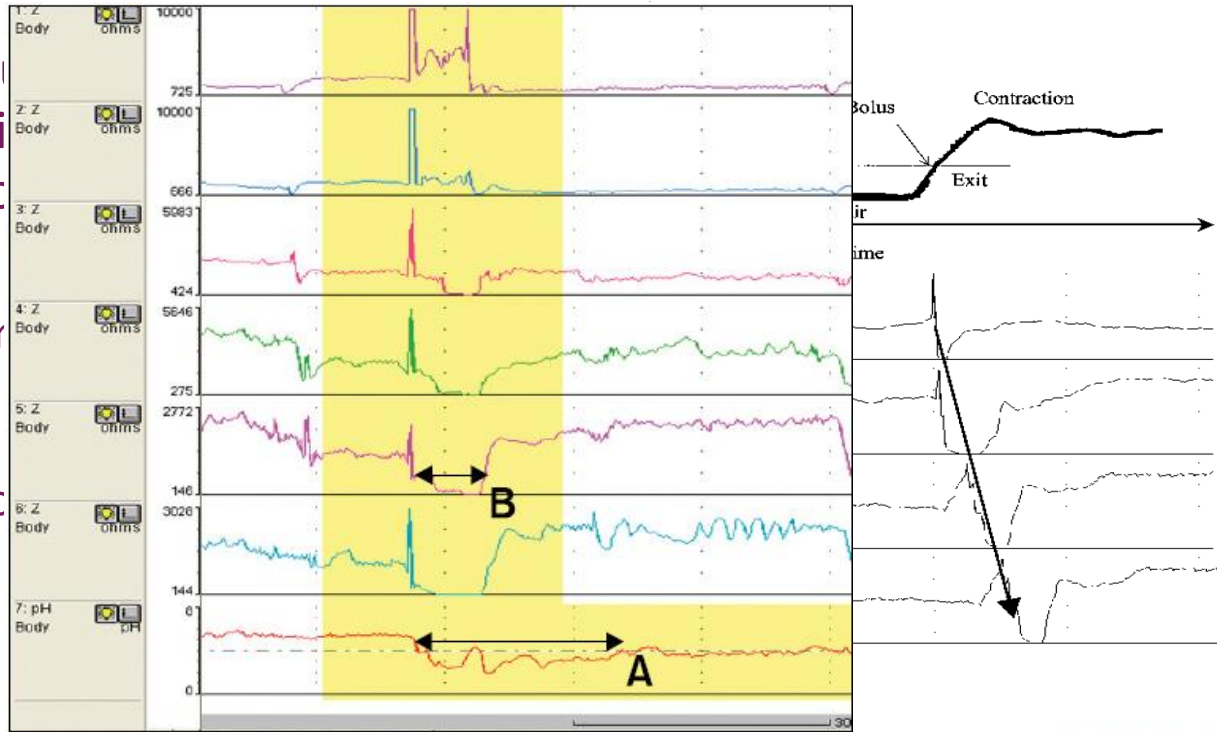
Bravo™ pH System



Impedance/pH testing

- Combined multi-channel intraluminal impedance and pH testing (MII-pH)

- Measures retrograde acidic fluid
- Advocated as standard for reflux testing



J Clin Gastroenterol. 2008

J Neurogastroenterol Motil 2010; 16:327-330

pH testing

- Testing should always be performed **OFF** acid suppression if GERD *has not* been proven
 - less than LA grade C when contemplating anti-reflux surgery
 - Less than LA grade B when planning long-term acid suppression
 - when prior pH testing has not been performed
- In patients who *have been* shown on prior testing to have GERD, testing should be performed **ON** twice daily PPI to evaluate refractory symptoms or exclude inadequate acid suppression.

pH testing

- Acid Exposure Time (AET) >6% is considered diagnostic
- <4% should be considered normal
- >80 reflux episodes per 24 hour considered abnormal
- <40 considered normal

pH testing

- Symptom index (SI) = $\frac{\text{reflux episodes assoc w/ symptoms}}{\text{total number symptom episodes}} * 100$
 - >50% is considered significant/positive

pH testing

- Symptom Association Probability (SAP) is calculated by dividing 24 hours in 720 two-minute periods.
 - Each 2 minute increment evaluated for occurrence of reflux/symptoms
 - Fisher's exact test performed to determine p-value for prob that reflux/symptom events randomly distributed
 - $SAP = 1 - p \text{ value} \times 100\%$. >95% considered positive

Wireless capsule vs. Impedance/pH

- Wireless capsule advantages:
 - Longer duration of recording - 48-96 hours
 - No transnasal catheter – patients more likely to perform usual daily activities
- Impedance/pH advantages:
 - Assessment of acidic or weakly acidic reflux
 - Assessment of bolus clearance
 - Extent of proximal reflux

Reflux testing

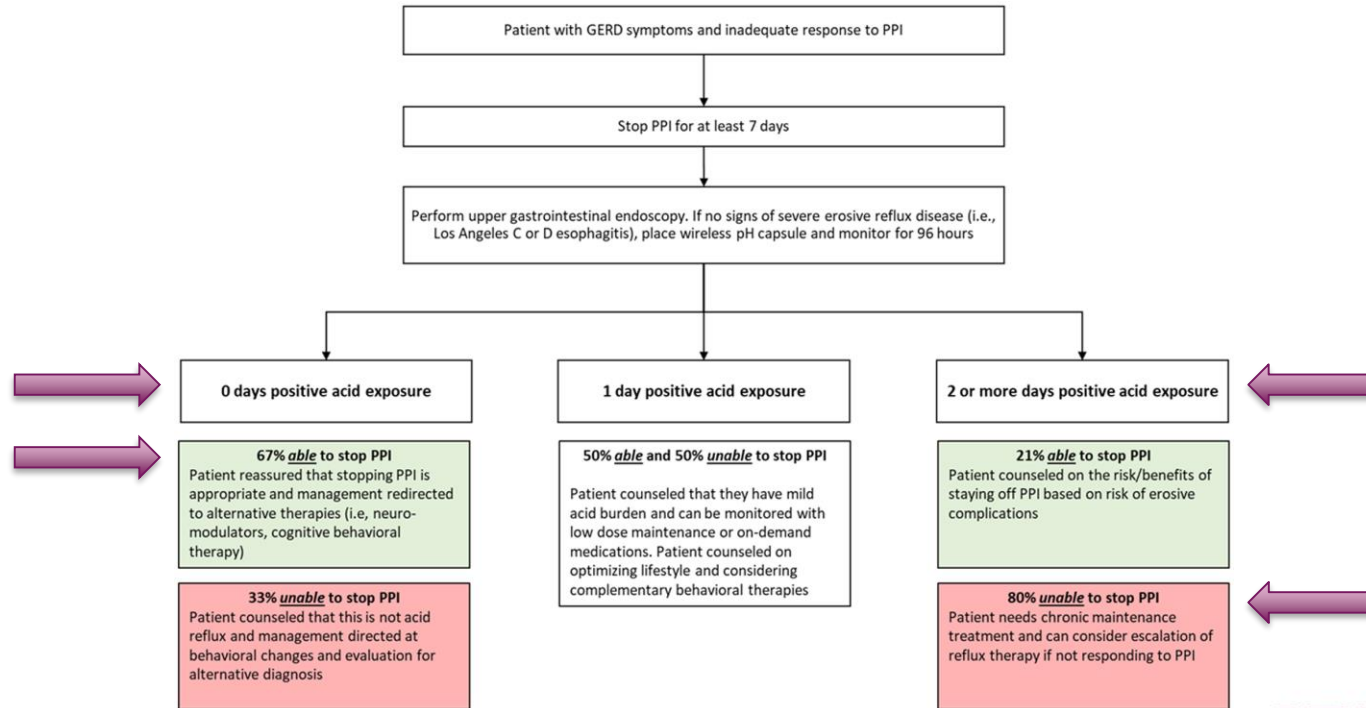
- Symptom association probability (SAP) on impedance/pH may help predict symptom response to therapy and to diagnose reflux hypersensitivity.
- With both study types, the most consistently reliable variables include total acid exposure time and composite DeMeester score.

Gyawali, et al, *Am J Gastroenterol*. 2020. 115(9):1412-28.

pH testing

- One study investigated use of 96 hour pH monitoring off PPI in patients with typical symptoms to predict if PPIs could be stopped.
 - Those with ≥ 2 days with esophageal acid exposure $>4\%$ unlikely to stop PPIs
 - Those with a normal study all four days = most likely able to stop PPIs

pH testing



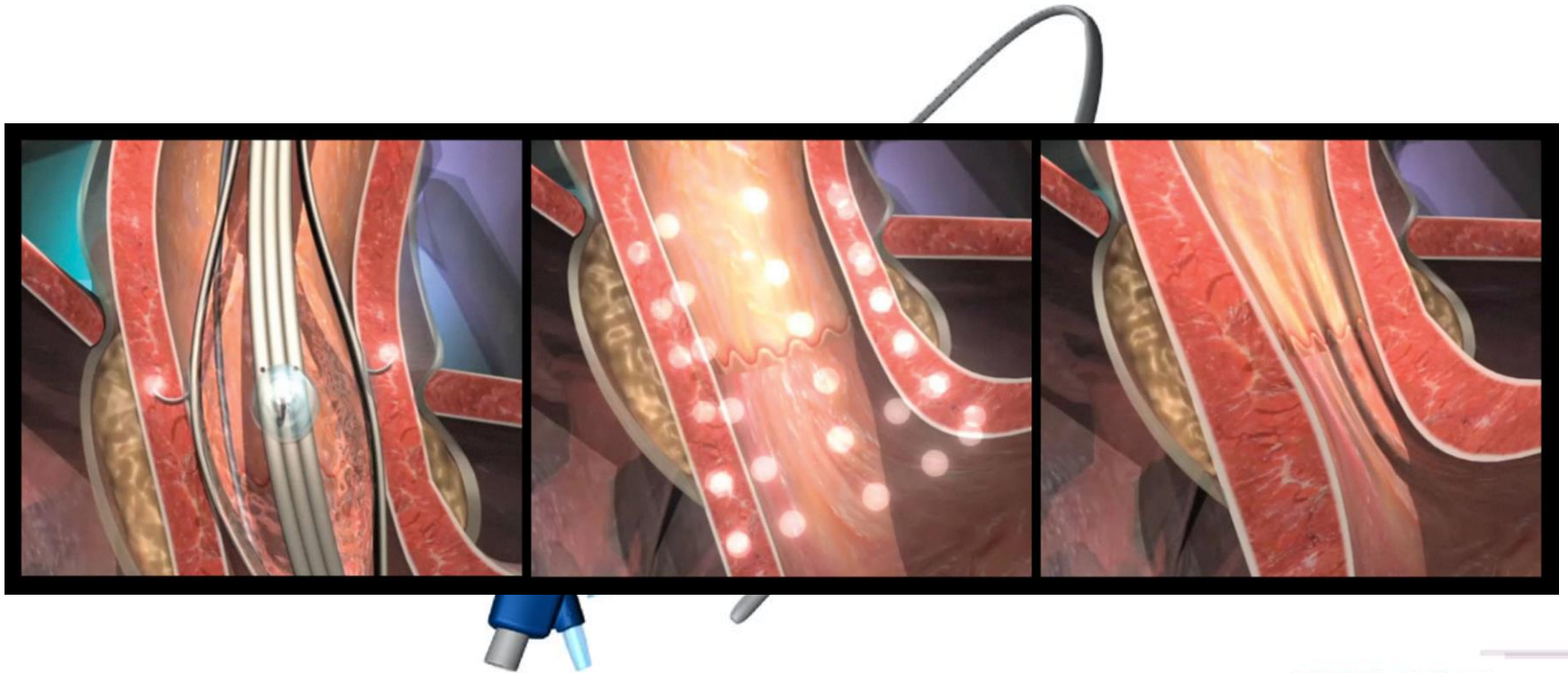
Endoscopic Therapy for GERD

- Radiofrequency ablation (Stretta)
- Transoral Incisionless Fundoplication (TIF)

Stretta

- This device uses radiofrequency ablation to create mild heat injury at multiple levels around the LES using a balloon/basket assembly with 4 retractable needles arranged radially around a balloon.
- It was initially thought to cause thickening and mechanical alteration at the GE junction.

Stretta



Stretta

- An early sham controlled trial found that 6 months after treatment, patients had improved symptoms and QOL but not acid exposure.
- This raised the question of whether it worked through alteration of sensory nerves.

Stretta

- After multiple conflicting studies were published, there have been further systematic reviews and meta-analyses which have contradictory results.

SYSTEMATIC REVIEWS AND META-ANALYSES

Fasiha Kanwal, Section Editor

No Evidence for Efficacy of Radiofrequency Ablation for Treatment of Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis

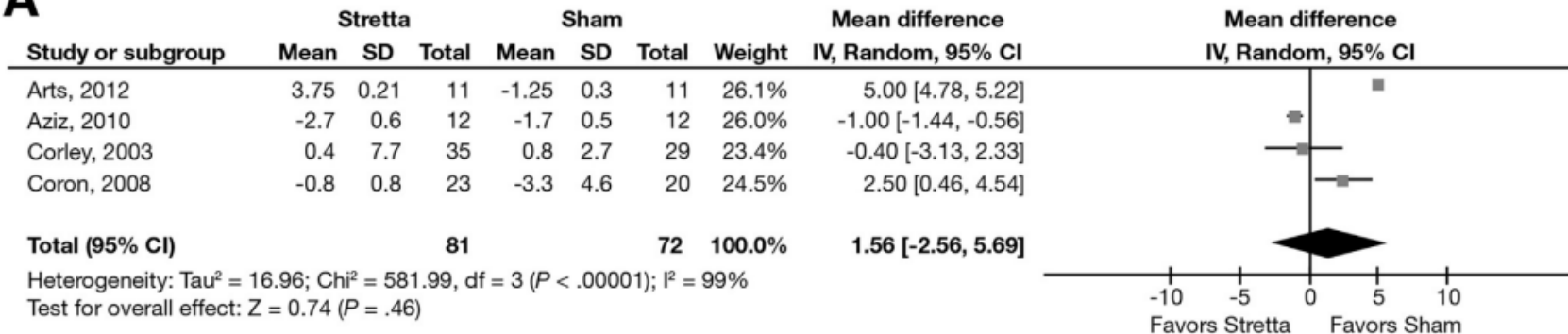


Seth Lipka,^{*} Ambuj Kumar,[‡] and Joel E. Richter[§]

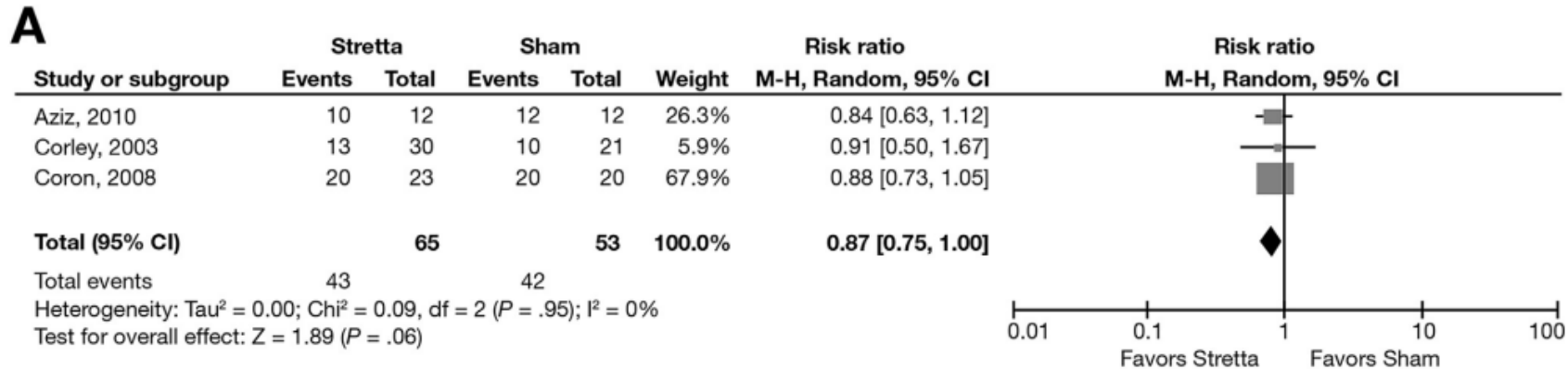
^{}Division of Digestive Diseases and Nutrition, [‡]Department of Medicine, Division of Evidence Based Medicine and Outcomes Research, [§]Department of Digestive Diseases and Nutrition, Joy McCann Culverhouse Center for Swallowing Disorders, University of South Florida Morsani College of Medicine, Tampa, Florida*

Stretta – % time pH < 4

A



Stretta – ability to stop PPI

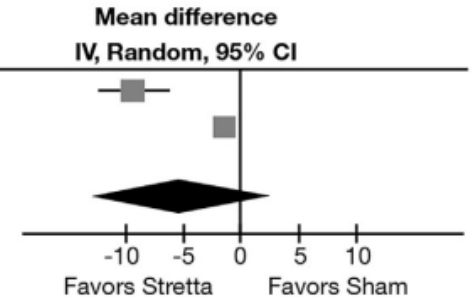


Stretta – HRQOL after being off meds

B

Study or subgroup	Stretta			Sham			Weight	Mean difference	
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI	IV, Random, 95% CI
Aziz, 2010	-15.2	0.9	12	-5.5	1.1	12	48.2%	-9.32	[-12.31, -6.33]
Corley, 2003	-12	4.1	35	-4	6.7	29	51.8%	-1.46	[-2.01, -0.90]
Total (95% CI)			47			41	100.0%	-5.24	[-12.95, 2.46]

Heterogeneity: Tau² = 29.71; Chi² = 25.64, df = 1 (P < .00001); I² = 96%
 Test for overall effect: Z = 1.33 (P = .18)



Surg Endosc (2017) 31:4865–4882
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REVIEW

Systematic review and meta-analysis of controlled and prospective cohort efficacy studies of endoscopic radiofrequency for treatment of gastroesophageal reflux disease

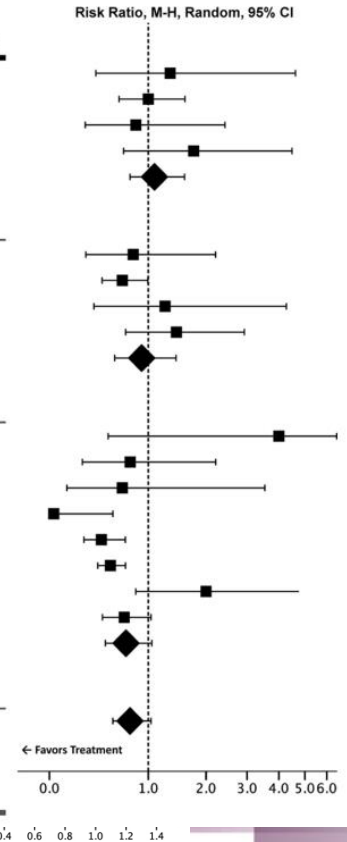
Ronnie Fass¹ · Frederick Cahn² · Dennis J. Scotti³ · David A. Gregory⁴

Stretta



- Change in reliance on PPI
- Change in HRQL
- Change in heartburn symptom score
- Change in erosive esophagitis

A

Study	Study Type	Treatment	Baseline		Follow-up		Risk Ratio, M-H, Random, 95% CI	Weight (Random)
			N	Esophagitis	N	Esophagitis		
Arts et al., 2012	RCT	Sham	11	3	11	4	1.33 [0.39, 4.62]	8.8%
Aziz et al., 2010	RCT	Sham	12	9	12	9	1.00 [0.63, 1.59]	63.9%
Corley et al., 2003	RCT	Sham	29	6	29	5	0.83 [0.29, 2.43]	11.9%
Coron et al., 2008	RCT	PPI	20	5	16	7	1.75 [0.68, 4.48]	15.4%
Control Subgroup	RCT	Sham	72	23	68	25	1.09 [0.76, 1.58]	100.0%
Heterogeneity: Tau ² = 0.00; Chi ² = 1.52, df = 3 (P = 0.68); I ² = 0%								
Test for overall effect: Z = 0.48 (P = 0.63)								
Arts et al., 2012	RCT	Stretta	11	5	11	4	0.80 [0.29, 2.21]	6.4%
Aziz et al., 2010	RCT	Stretta	12	12	12	8	0.68 [0.45, 1.02]	14.7%
Corley et al., 2003	RCT	Stretta	35	4	35	5	1.25 [0.37, 4.27]	4.8%
Coron et al., 2008	RCT	Stretta	23	8	20	10	1.44 [0.71, 2.93]	9.7%
Stretta RCT Subgroup	RCT	Stretta	81	29	78	27	0.91 [0.58, 1.43]	35.6%
Heterogeneity: Tau ² = 0.07; Chi ² = 4.41, df = 3 (P = 0.22); I ² = 32%								
Test for overall effect: Z = 0.41 (P = 0.68)								
Arts et al., 2007	Cohort	Stretta	13	1	13	4	4.00 [0.51, 31.13]	2.1%
Cipolletta et al., 2005	Cohort	Stretta	32	8	21	4	0.76 [0.26, 2.21]	5.9%
DiBaise et al., 2002	Cohort	Stretta	18	3	18	2	0.67 [0.13, 3.53]	3.0%
Dughera et al., 2011	Cohort	Stretta	56	14	56	0	0.03 [0.00, 0.56]	1.2%
Liu et al., 2011	Cohort	Stretta	90	41	90	18	0.44 [0.27, 0.70]	13.6%
Reymunde and Santiago, 2007	Cohort	Stretta	72	60	72	32	0.53 [0.40, 0.70]	17.0%
Tam et al., 2003	Cohort	Stretta	20	5	20	10	2.00 [0.83, 4.81]	7.7%
Triadafilopoulos et al., 2002	Cohort	Stretta	118	35	118	25	0.71 [0.46, 1.11]	14.0%
Mean Stretta (Cohort)	Cohort	Stretta	419	167	408	95	0.69 [0.45, 1.04]	64.4%
Heterogeneity: Tau ² = 0.17; Chi ² = 17.78, df = 7 (P = 0.01); I ² = 61%								
Test for overall effect: Z = 1.76 (P = 0.08)								
Mean Stretta (All)	Total	Stretta	500	196	486	122	0.76 [0.56, 1.04]	100.0%
Heterogeneity: Tau ² = 0.13; Chi ² = 24.60, df = 11 (P = 0.01); I ² = 55%								
Test for overall effect: Z = 1.74 (P = 0.08)								
Test for subgroup differences: Chi ² = 0.81, df = 1 (P = 0.37), I ² = 0%								



Systematic review and meta-analysis of cohort efficacy studies of gastroesophageal reflux



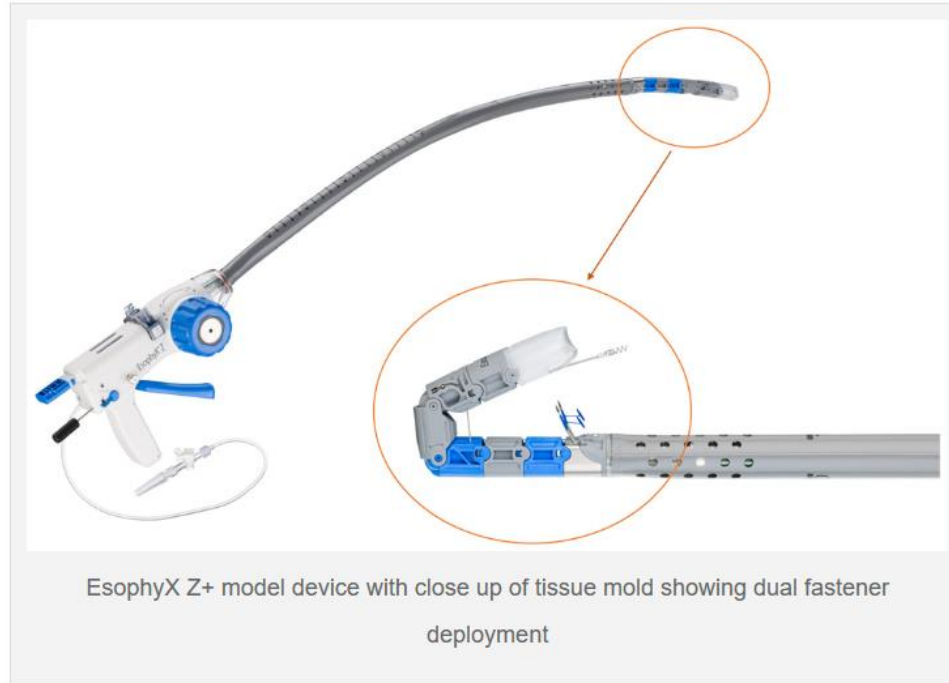
Disclosures Dennis J. Scotti is a Part-time Consultant with Baker Tilly Virchow Krause, LLC. Baker Tilly Virchow Krause, LLC is a Business Advisor to Mederi Therapeutics, Inc. David A. Gregory is a principal with Baker Tilly, a Business Advisor to Mederi Therapeutics. Frederick Cahn is a principal with BioMedical Strategies, a Business Advisor to Baker Tilly. Ronnie Fass is an Advisor to Ironwood and Mederi Therapeutics, Speaker for AstraZeneca, Dr. Reddy, Mederi Therapeutics and Takeda and receives Research Grant from Ironwood.

Ronnie Fass¹ · Frederick Cahn² · Dennis J. Scotti³ · David A. Gregory⁴

Stretta

- Despite the controversy, in 2013 the Society of American Gastrointestinal and Endoscopy Surgeons (SAGES) gave Stretta a strong recommendation for use in patients who refuse laparoscopic Nissen fundoplication.

Transoral Incisionless Fundoplication (TIF)

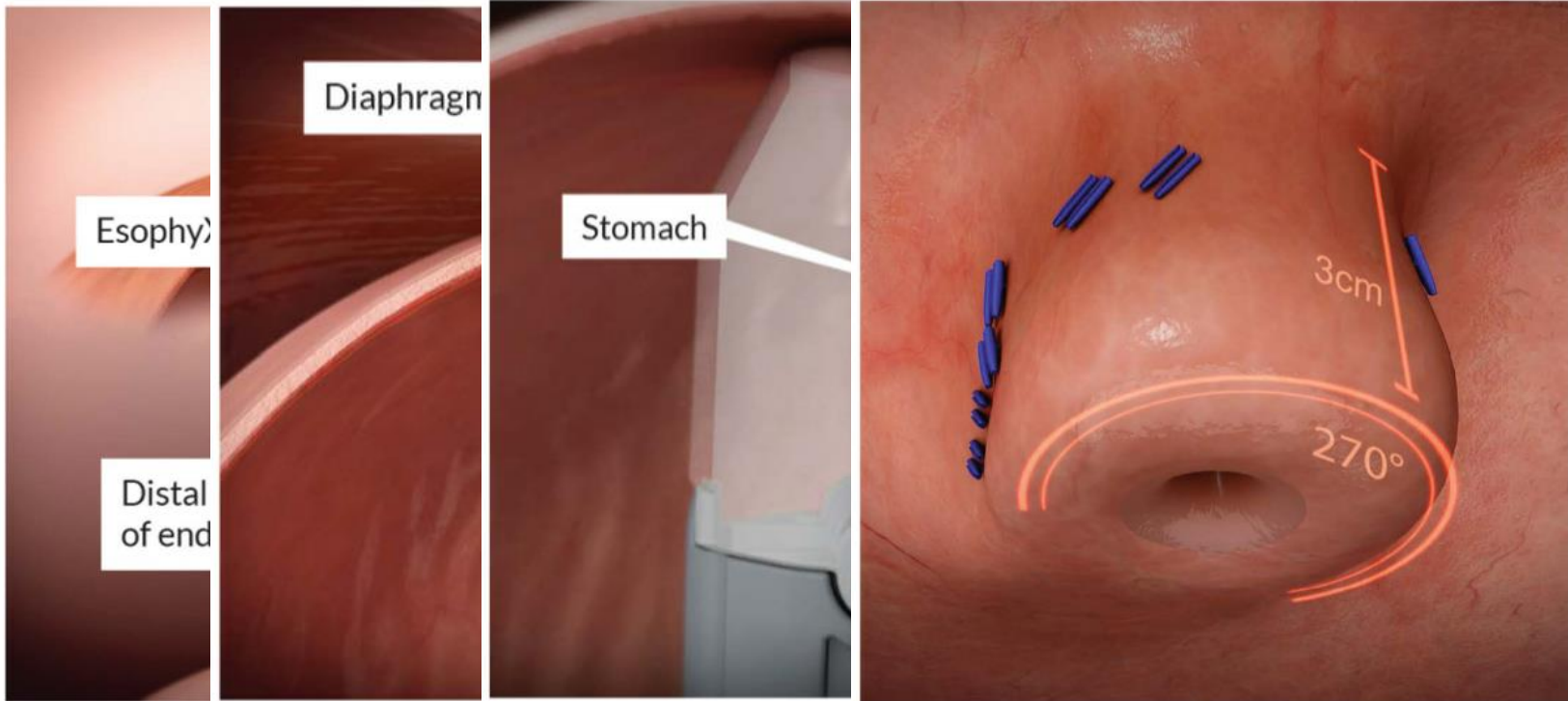


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TIF

- Attempts to create a 270 degree valve about 3 cm in length
- Plicates a portion of proximal stomach with H fasteners

TIF



CLINICAL—ALIMENTARY TRACT

Efficacy of Transoral Fundoplication vs Omeprazole for Treatment of Regurgitation in a Randomized Controlled Trial



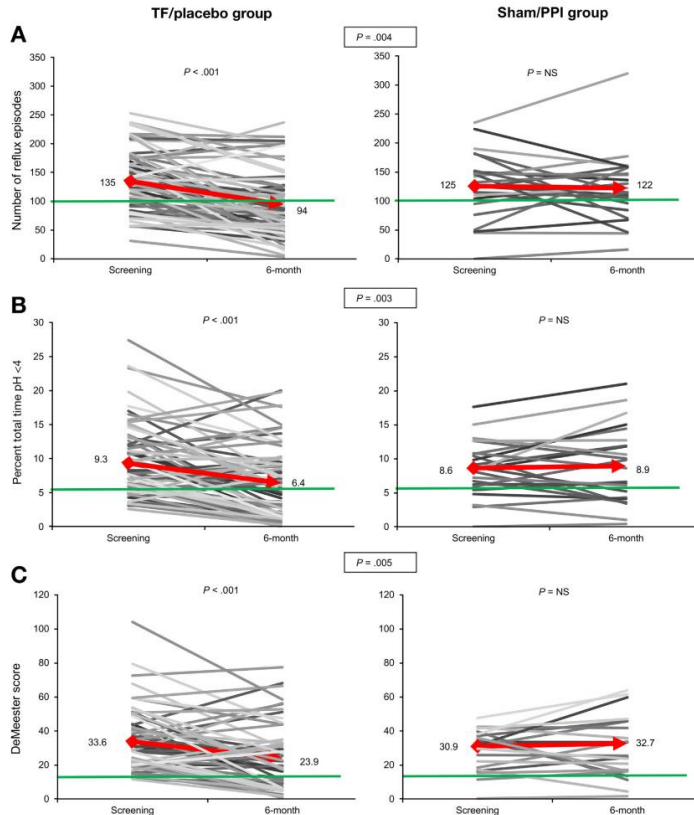
John G. Hunter,^{1,*} **Peter J. Kahrilas**,^{2,*} Reginald C. W. Bell,³ Erik B. Wilson,⁴ Karim S. Trad,^{5,6} James P. Dolan,¹ Kyle A. Perry,⁷ Brant K. Oelschlager,⁸ Nathaniel J. Soper,² Brad E. Snyder,⁴ Miguel A. Burch,⁹ William Scott Melvin,⁷ Kevin M. Reavis,^{1,10} Daniel G. Turgeon,^{5,6} Eric S. Hungness,² and Brian S. Diggs¹

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TIF

- 129 patients with troublesome GERD despite daily PPI
- ≤ 2 cm hiatal hernia
- Randomly assigned (2:1) to TIF+placebo vs Sham+PPI
- Patients blinded
- Assessed at 2, 12 and 26 weeks

TIF



- ITT at 6 mo
 - 67% of TIF/placebo pts reported elim of troublesome regurg
 - Only 45% in the Sham/PPI arm ($p=0.023$)
- PP analysis no different
- No difference in median improvement on Reflux Disease Questionnaire

TIF

- Another study performed at multiple centers with 63 patients randomized 2:1 had similar, though more impressive results.
- However, outcomes beyond 6 months not established.

TIF

Review

 Thieme

Long-term outcomes of transoral incisionless fundoplication for gastro-esophageal reflux disease: systematic-review and meta-analysis

**OPEN
ACCESS**



Authors

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TIF

- Systematic review and meta-analysis of 8 studies
- 418 patients
- Mean f/u of 5.3 years
- Long-term patient satisfaction 74-86%
- Interruption/reduction in PPI in about 54 & 76%
- Significant/persistent improvement in GERD-related symptoms and QOL (80% at 4-5 years, 67% at 10 years)

TIF

- Based on this, in carefully selected patients (Hill grade 1&2 LES, hiatal hernia \leq 2 cm, with documented GERD and normal motility) TIF is a reasonable option to consider for patients who want an alternative to surgery or medical therapy.

Summary

- GERD is characterized by reflux resulting in symptoms or complications
- NERD is characterized by GERD which is non-erosive
- Both result from breakdown in defense mechanisms including compromise in either barriers against reflux or clearance mechanisms
- Symptoms may be *typical*, or *atypical*

Summary

- Diagnosis based on typical symptoms and response to acid suppression have reasonable ROC characteristics, but generally are not considered definitive enough to commit to surgical or endoscopic interventions
- Surgical candidacy based on endoscopy alone is adequate for LA grade C or D esophagitis findings
- Only 30% of patients will have esophagitis

Summary

- Ambulatory pH testing may be used to diagnose GERD or NERD
- Baseline testing for presence of GERD should be performed OFF acid suppression
- Testing to determine cause of refractory symptoms after established diagnosis should include impedance/pH testing

Summary

- Two endoscopic methods for GERD treatment include Stretta (RFA) and Transoral Incisionless Fundoplication (TIF).
- Stretta, while recommended by thoracic surgery societies, has controversial data and is not endorsed by GI societies based on available data
- TIF does have some promising data, and appears to be a reasonable option for milder cases of reflux without large hiatal hernias or esophageal dysmotility, but availability is still regional.

Endoscopy and GERD



Like Microsoft AI Image generator....

Promising, but...

We still have a ways to go!

Thank you!