Endoscopic treatment of GERD: Ready for primetime?

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The Problem

- GERD is a disease that remains a major burden to society despite medical therapy
- 10- 40% of GERD sufferers remain atleast partially symptomatic despite PPI use
- Medical therapy does not address the underlying pathophysiological defects leading to GERD

The Problem

- Long term PPI use may be associated with some risks
- Nissen Fundoplication has long been the only non-medical option for GERD, and has some disadvantages:
  - Invasive
  - Side Effects
  - Questionable Long term effectiveness
  - Permanent anatomical alteration of the GEJ

The Problem

- There has emerged a therapeutic gap between Medical and Surgical therapy
- Resulted in a hot bed of research in the Endoscopic therapy for GERD
- Devices:
  - Endoscopic Suturing Device (Cook Medical Inc.)
  - NDO Plicator (NDO Surgical Inc.)
  - Syntheon AntiReflux Device (Syntheon)
  - His-Wiz Device (Olympus)
  - Enteryx procedure (Boston Scientific)
  - Gatekeeper Reflux Repair System (Medtronic)
  - Durasphere GR (Carbon Medical Technologies)
  - Medigus MUSE


stretta

stretta®


MEDERI


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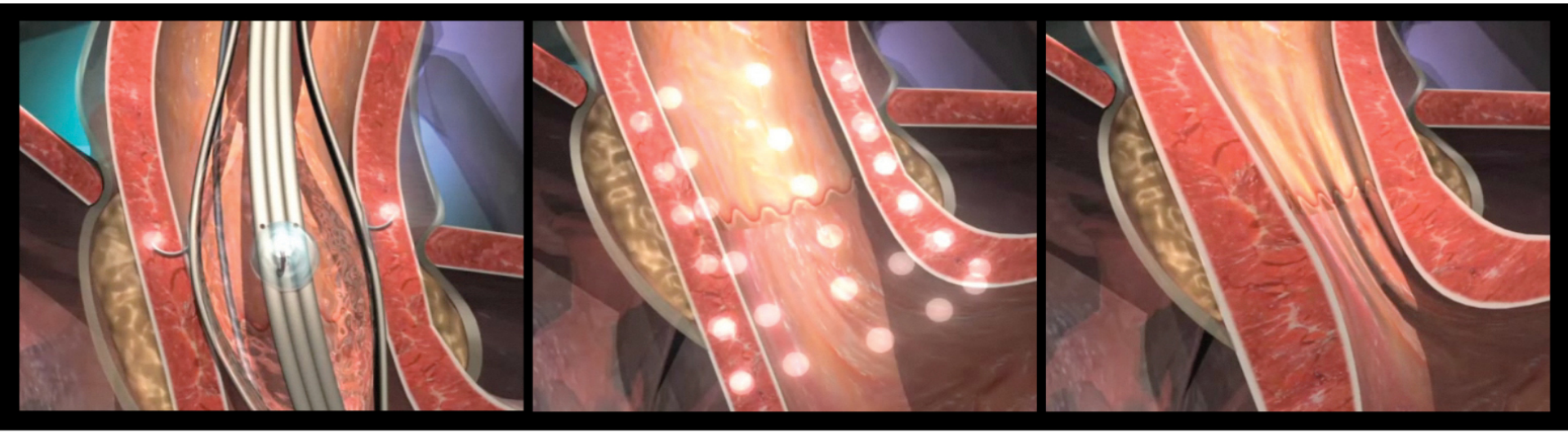
IRVINE

HOW STRETTA WORKS



- Concentrated RF energy delivered to tissue
- Multi-level thermal treatment remodels LES and Gastric Cardia
- Leads to objective :
  - Increased Wall thickness
  - Decreased Tissue Compliance
  - Increased LES Pressure
  - Decreased TLESRs

Stretta Patient Experience

- 45 minute procedure
- No overnight stay
- Post-op discomfort minimal
- Rapid recovery:
  - Most patients are back to work and most activities on the next day

Post Stretta Protocol

- Soft diet x 2-3 days, then resume normal diet
- Stay on PPI x 1 month to allow time for tissue remodeling
- Gradually wean off PPI over 1 month

4 Year STRETTA Efficacy

Sustained improvement in symptoms of GERD & antisecretory drug use: 4-year follow-up of the Stretta® procedure.

- 96 PATIENTS - 48 MONTHS
- 75% OFF ALL MEDICATION
- NO SERIOUS COMPLICATIONS

Noar MD, Lotfi-Emran S. *Gastrointest Endosc*. 2007 Mar; 65(3): 367-72.

Long-term results of RF energy delivery for treatment of GERD: sustained improvements in symptoms, quality of life, & drug use at 4-year follow-up.

- 83 PATIENTS - 48 MONTHS
- 86.4% OFF DAILY MEDICATIONS
- NO SERIOUS COMPLICATIONS

Reymunde A, Santiago N. *Gastrointest Endosc*. 2007 Mar;65(3):361-6

Long-term results of RF energy delivery for treatment of GERD. Results of a 48 month prospective study.

- 56 PATIENTS - 48 MONTHS
- 72% OFF ALL MEDICATION
- 1 TRANSIENT COMPLICATION

Dughera et al, *Diagnostic and Therapeutic Endoscopy*, August 2011

Surg Endosc (2014) 28:2323–2333
DOI 10.1007/s00464-014-3461-6

Long-term maintenance effect of radiofrequency energy delivery for refractory GERD: a decade later

Mark Noar · Patrick Squires · Emmanuelle Noar · Martin Lee

Received: 29 September 2013 / Accepted: 21 January 2014 / Published online: 22 February 2014

Abstract
Background Patients with gastroesophageal reflux disease (GERD) often seek alternative therapy for inadequate symptom control, with over 40 % not responding to medical treatment. We evaluated the long-term safety, efficacy, and durability of response to radiofrequency treatment of the lower esophageal sphincter (Stretta).
Methods Using an intent-to-treat analysis, we prospectively assessed 217 patients with medically refractory GERD before and after Stretta. There was no concurrent control group in the study. Primary outcome measure was normalization of GERD-health-related quality of life (GERD-HRQL) in 70 % or greater of patients at 10 years. Secondary outcomes were 50 % reduction or elimination of proton pump inhibitors (PPIs) and 60 % or greater improvement in satisfaction at 10 years. Successful treatment was defined as achievement of secondary outcomes in a minimum of 50 % of patients. Complications and effect on existing comorbidities were evaluated. The results of a 10-year study are reported.
Results The primary outcome was achieved in 72 % of patients (95 % confidence interval 65–79). For secondary outcomes, a 50 % or greater reduction in PPI use occurred in 64 % of patients, (41 % eliminating PPIs entirely), and a 60 % or greater increase in satisfaction occurred in 54 % of patients. Both secondary endpoints were achieved. The most common side effect was short-term chest pain (50 %). Pre-existing Barrett's metaplasia regressed in 85 % of biopsied patients. No cases of esophageal cancer occurred.
Conclusions In this single-group evaluation of 217 patients before and after Stretta, GERD-HRQL scores, satisfaction, and PPI use significantly improved and results were immediate and durable at 10 years.

Keywords Stretta · GERD · Medication use · GERD-HRQL · Reflux · Radiofrequency energy · Barrett's

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Gastroesophageal reflux disease (GERD) is the most common principal gastroenterological diagnosis in the US, associated with a wide range of symptoms, typically heartburn, acid regurgitation, and dysphagia, while severely impairing health-related quality of life (HRQL) [1, 2]. Until recently, it was thought that the predominant disease-causing mechanism of action was acid and/or bile penetration of the esophageal mucosa as the sole cause of heartburn manifestations [3, 4]. However, in recent years, research into mucosal receptors and their molecular response to stimulation, demonstrated both a direct and an indirect mechanism of action of acid and other caustic-sensing receptors causing release and activation of both neural and non-neural chemokine pathways leading directly to a decline in cell integrity, and the development of inflammation, pain, and compromised motility [5–9].

10 Year Stretta Efficacy Study
Noar et al.
Surgical Endoscopy 2014 28: 2323-33

- Prospective single center analysis
- 217 Patients underwent Stretta
- Followed for > 4 years
- 99 patients analyzed at 10 years

- Complications:
  2 patients with minor gastric bleeding (self limited) with no other adverse events

- 10 year Results:
  72 % had normalization of GERD-HRQL
  64% had reduction in PPI dose
  41% had elimination of PPI

- Limitations: 50 Lost to follow up

- Conclusion:

After Stretta GERD-HRQL scores, satisfaction, and PPI use significantly improved and results were immediate and durable at 10 years

STRETTA Efficacy

META-Analysis - 18 Studies – 1,441 Patients

Outcome Variable	Studies (n)	Patients (n)	Mean Follow-up (mo)	Pre-Stretta	Post-Stretta	P-value
SUBJECTIVE MEASUREMENTS						
GERD-HRQL	9	433	19.8	26.11	9.25	0.0001
QOLRAD	4	250	25.2	3.30	9.25	0.0010
SF-36 Physical	6	299	9.5	36.45	46.12	0.0001
SF-36 Mental	5	264	10.0	46.79	55.16	0.0015
Heartburn Score	9	525	24.1	3.55	1.19	0.0001
Satisfaction Score	5	366	21.9	1..43	4.07	0.0006
OBJECTIVE MEASUREMENTS						
Esophageal Acid Exposure (%Ph<4)	11	364	11.9	10.29	6.51	0.0003
DeMeester score	7	267	13.1	44.37	28.53	0.0074
LES pressure	7	263	8.7	16.54	20.24	0.0302

Radiofrequency Energy Delivery to the Lower Esophageal Sphincter Reduces Esophageal Acid Exposure and Improves GERD Symptoms: A Systematic Review and Meta-analysis. Kyle A. Perry, MD, Ambar Banerjee, MD, and William Scott Melvin, MD. *Surg Laparosc Endosc Percutan Tech* 2012;22:283–288

Stretta Meta-Analysis 2017

Surg Endosc (2017) 31:4865–4882
DOI 10.1007/s00464-017-5431-2

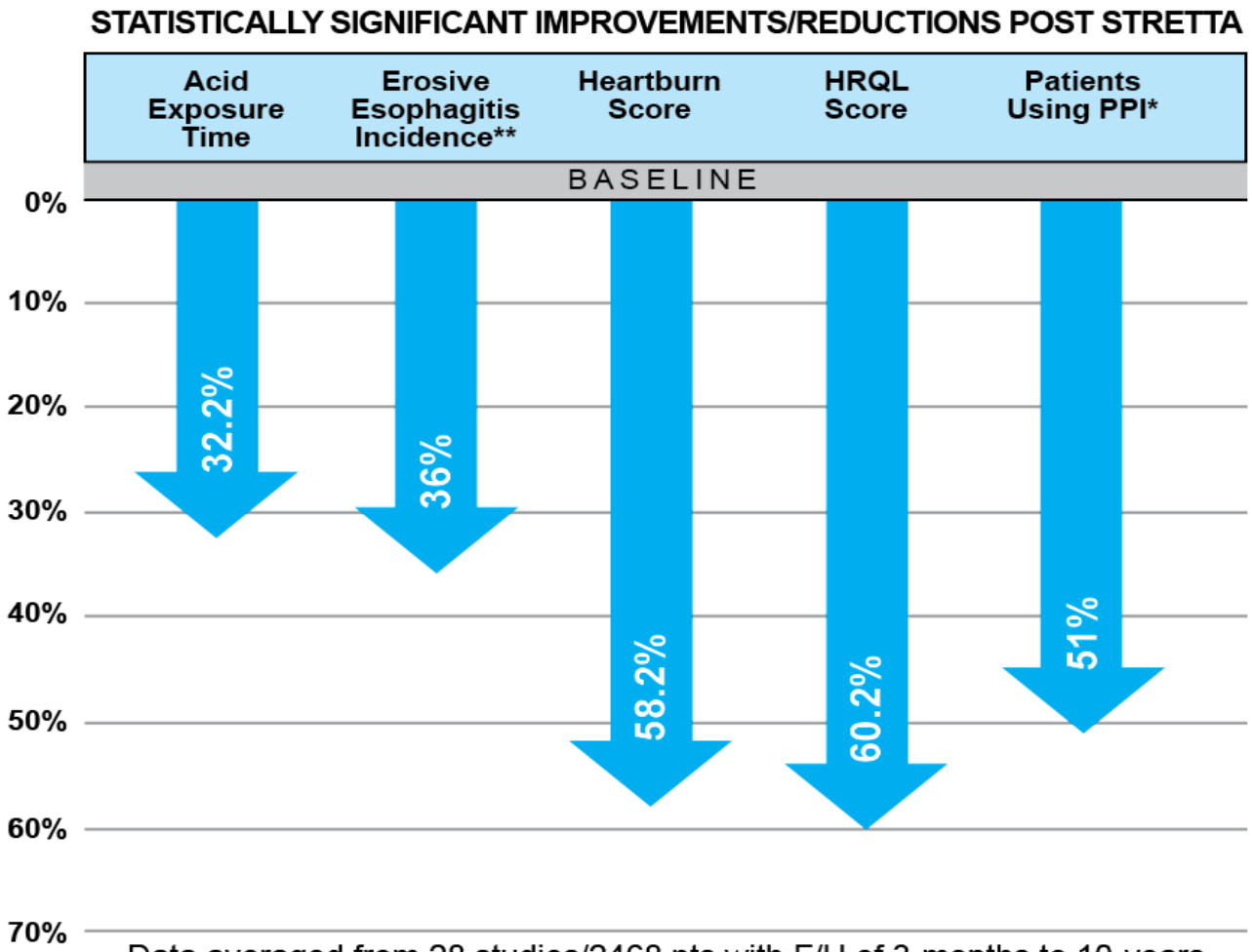
REVIEW

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

Ronnie Fass[1] · Frederick Cahn[2] · Dennis J. Scotti[3] · David A. Gregory[4]

- 28 Studies, 2468 Patients, up to 10-yrs follow-up (avg 25 months)

New Stretta Meta-Analysis 2017



30%
Normalized pH

-14
Demeester Score Reduction

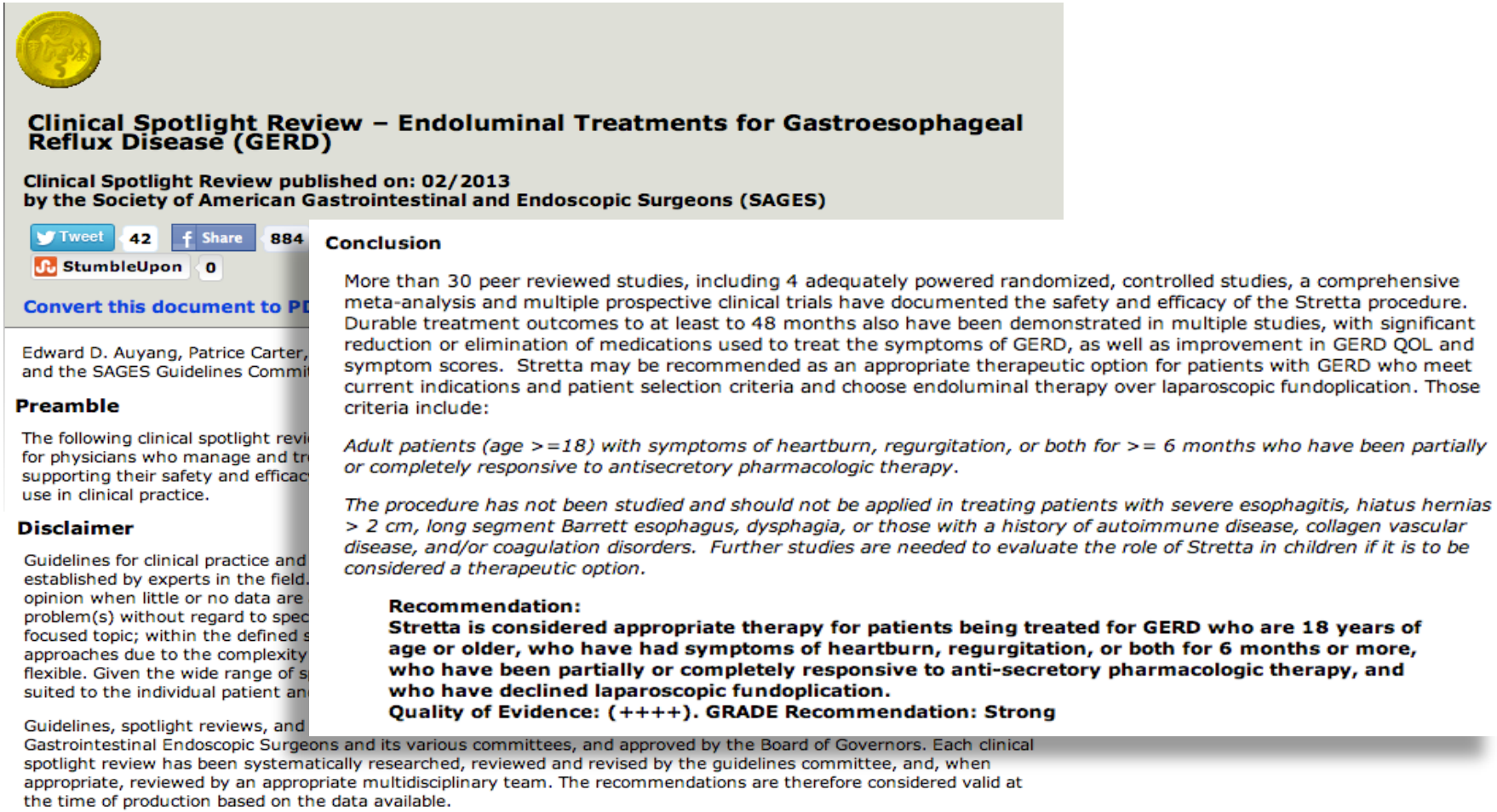
86%
4-yr off PPI

72%
8-yr off PPI

64%
10-yr off daily PPI
(41% eliminated)

Data averaged from 28 studies/2468 pts with F/U of 3-months to 10-years
*51% is OFF all reflux medication (partial reduction not included)
**Measured presence of EE (partial reduction not included)

SAGES GUIDELINES



Clinical Spotlight Review – Endoluminal Treatments for Gastroesophageal Reflux Disease (GERD)

Clinical Spotlight Review published on: 02/2013
by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)

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Edward D. Auyang, Patrice Carter,
and the SAGES Guidelines Commi

Preamble

The following clinical spotlight revi
for physicians who manage and tr
supporting their safety and efficac
use in clinical practice.

Disclaimer

Guidelines for clinical practice and
established by experts in the field.
opinion when little or no data are
problem(s) without regard to spec
focused topic; within the defined s
approaches due to the complexity
flexible. Given the wide range of s
suited to the individual patient an

Guidelines, spotlight reviews, and
Gastrointestinal Endoscopic Surgeons and its various committees, and approved by the Board of Governors. Each clinical spotlight review has been systematically researched, reviewed and revised by the guidelines committee, and, when appropriate, reviewed by an appropriate multidisciplinary team. The recommendations are therefore considered valid at the time of production based on the data available.

Conclusion

More than 30 peer reviewed studies, including 4 adequately powered randomized, controlled studies, a comprehensive meta-analysis and multiple prospective clinical trials have documented the safety and efficacy of the Stretta procedure. Durable treatment outcomes to at least to 48 months also have been demonstrated in multiple studies, with significant reduction or elimination of medications used to treat the symptoms of GERD, as well as improvement in GERD QOL and symptom scores. Stretta may be recommended as an appropriate therapeutic option for patients with GERD who meet current indications and patient selection criteria and choose endoluminal therapy over laparoscopic fundoplication. Those criteria include:

Adult patients (age >=18) with symptoms of heartburn, regurgitation, or both for >= 6 months who have been partially or completely responsive to antisecretory pharmacologic therapy.

The procedure has not been studied and should not be applied in treating patients with severe esophagitis, hiatus hernias > 2 cm, long segment Barrett esophagus, dysphagia, or those with a history of autoimmune disease, collagen vascular disease, and/or coagulation disorders. Further studies are needed to evaluate the role of Stretta in children if it is to be considered a therapeutic option.

Recommendation:
Stretta is considered appropriate therapy for patients being treated for GERD who are 18 years of age or older, who have had symptoms of heartburn, regurgitation, or both for 6 months or more, who have been partially or completely responsive to anti-secretory pharmacologic therapy, and who have declined laparoscopic fundoplication.
Quality of Evidence: (++++). GRADE Recommendation: Strong

STRETTA PATIENT SELECTION

Stretta can be considered in :

- Patients who don't respond to, or are intolerant of PPIs
- Patients with a <2cm hiatal hernia
- Patients who don't wish to have surgery or an implant
- Non-erosive reflux (NERD) patients
- Laryngopharyngeal reflux (LPR) patients, and those with other extra-esophageal symptoms of GERD
- Post-Nissen patients with recurring reflux
- Post-gastric bypass/sleeve patients

Limited Data

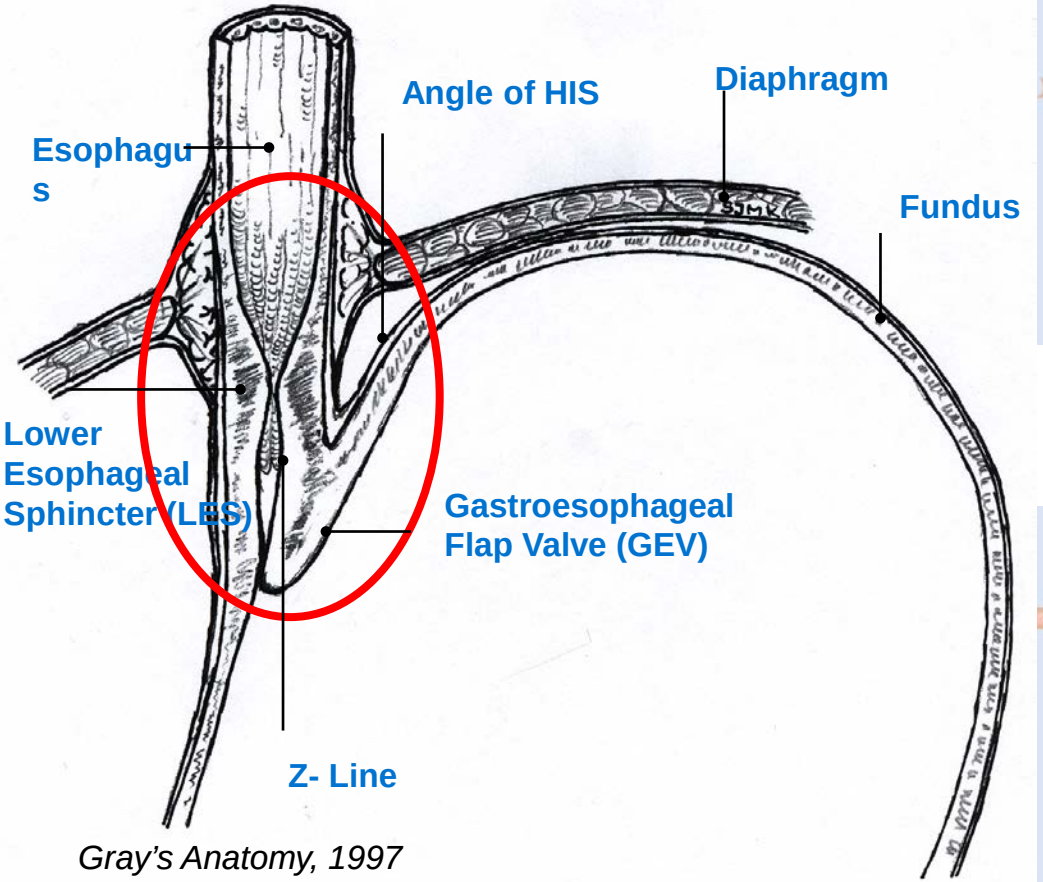
Stretta Summary

- Easy procedure to learn and perform
- Well tolerated by patients
- Low risk of complications
- Large amount of evidence supporting its efficacy
- Does not preclude further endoscopic therapy
- The true benefit may be with the upright refluxers

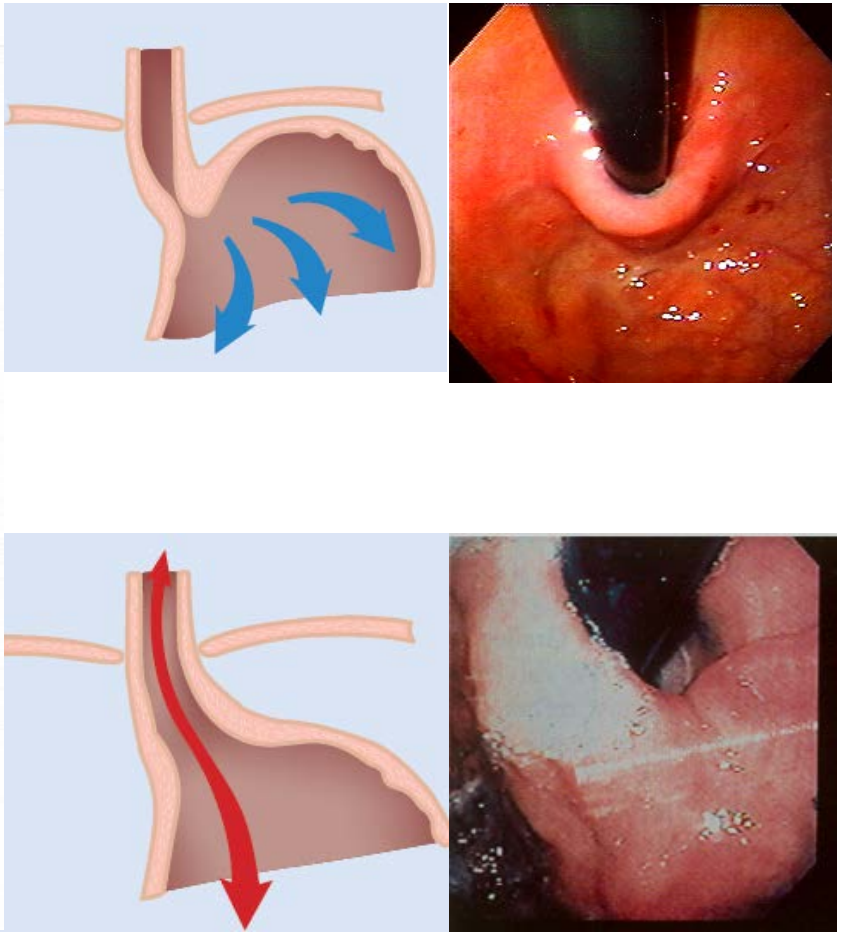
Transoral Incisionless Fundoplication (TIF)

Esophyx Procedure

Objective of Surgical Treatment



Gray's Anatomy, 1997

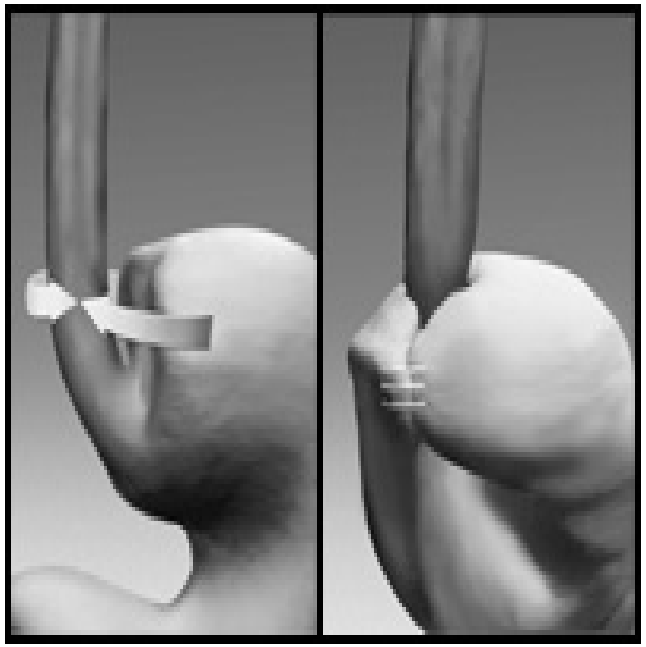


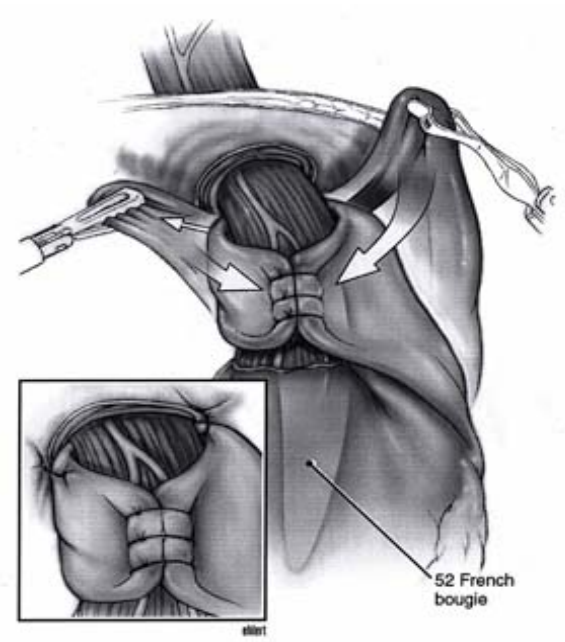
Surgical Treatment

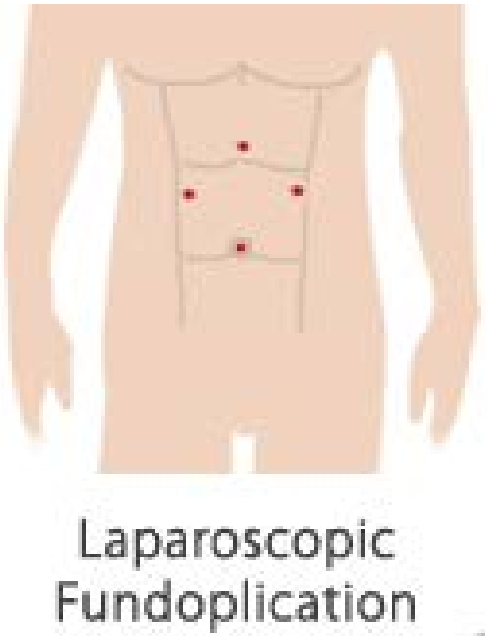
Surgical Objectives of Treatment

Requirement	Nissen	TIF
Recreates Angle of HIS	Yes	Yes
Tightens greater curve side of cardia to lesser curve	Yes	Yes
Submerges distal esophagus into proximal stomach	Yes	Yes
Restores intraabdominal esophageal length	Yes	Yes
Reduces hiatal hernia	Yes	≤2cm
Creates a valve the length of the fundoplication	Yes	Yes
Tightens phrenoesophageal membrane	Yes	Yes

Nissen Fundoplication







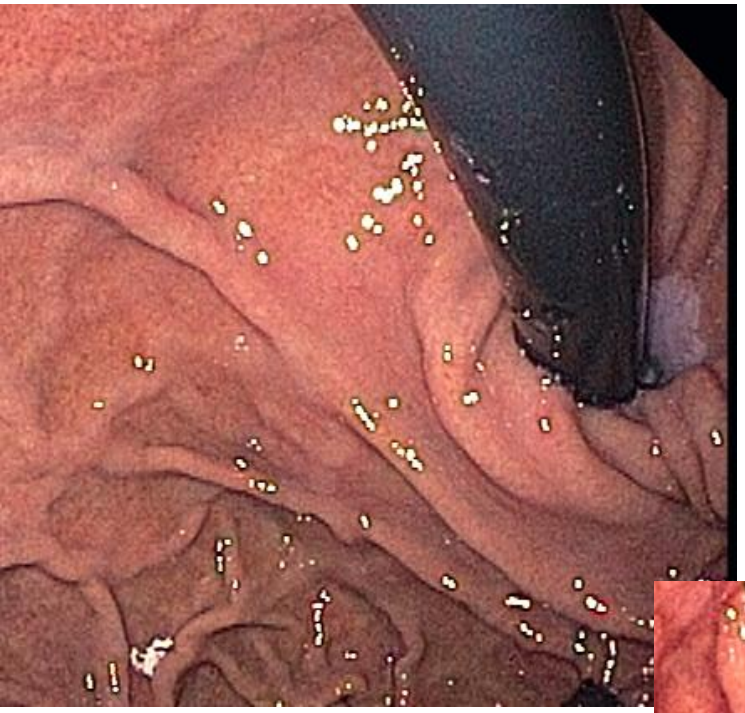
Lap Nissen Fundoplication

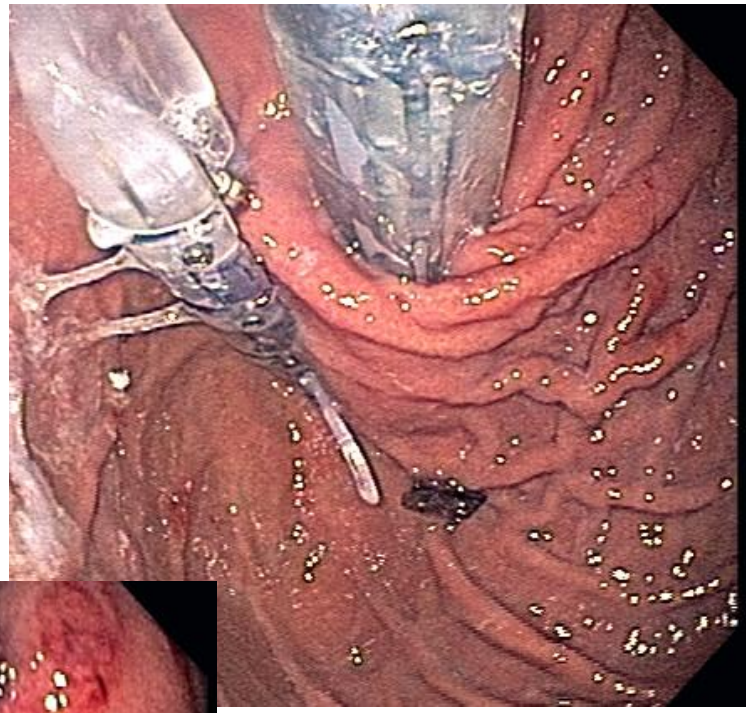
1,000 cases

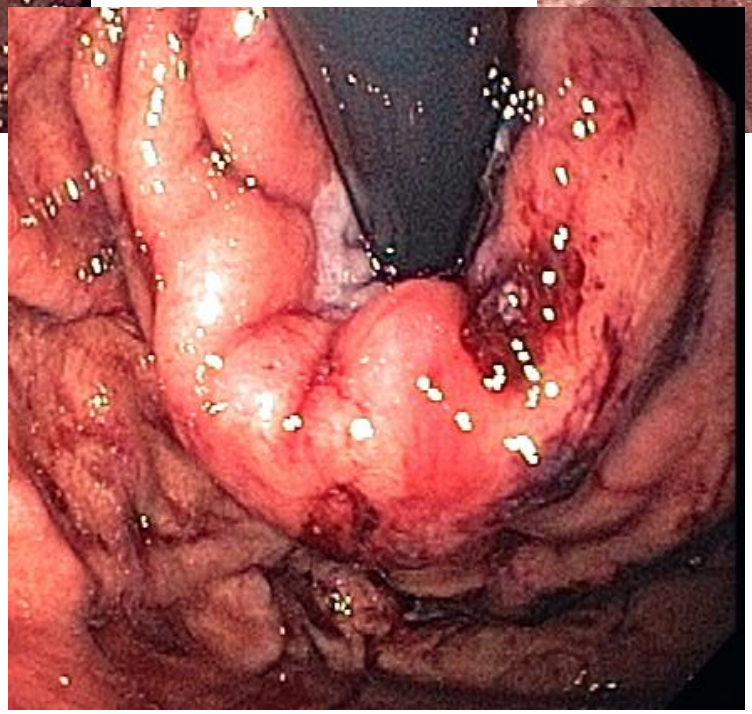
- Average hospital stay 1.2 days
- Resolution of symptoms at 1 year: 94%
- Major complications: 2%
- Long term complications: 2-62%
  - Gas and bloating
  - Dysphagia

Hunter JG, et al. Surgical Endoscopy 2001

Esophyx
(Endogastric Solutions®)







TIF Patient Experience

- 45 - 60 minute procedure
- Overnight stay
- Post-op discomfort usually minimal
- Rapid recovery:
  - Most patients are back to work and most activities on Post Procedure Day 3-5
- 12 weeks of soft diet recommended
- Limit lifting > 25lbs for 2 weeks

TIF Outcomes Data

- Almost all published studies are prospective case series with Pre-TIF baseline studies and Post-TIF evaluation
- Most Follow up ranges from 6 – 12 months
- Patient numbers range from 8 -124
- TEMPO Trial
  - RCT TIF vs PPI underway
- RESPECT Trial
  - RCT TIF vs Sham + PPI

GERD Related Quality of Life

Table 1 The Gastroesophageal Reflux Disease-Health Related Quality of Life instrument

• **Scale**: No symptoms = **0**; Symptoms noticeable, but not bothersome = **1**; Symptoms noticeable and bothersome, but not every day = **2**; Symptoms bothersome every day = **3**; Symptoms affect daily activities = **4**; Symptoms are incapacitating, unable to do daily activities = **5**

• **Questions**

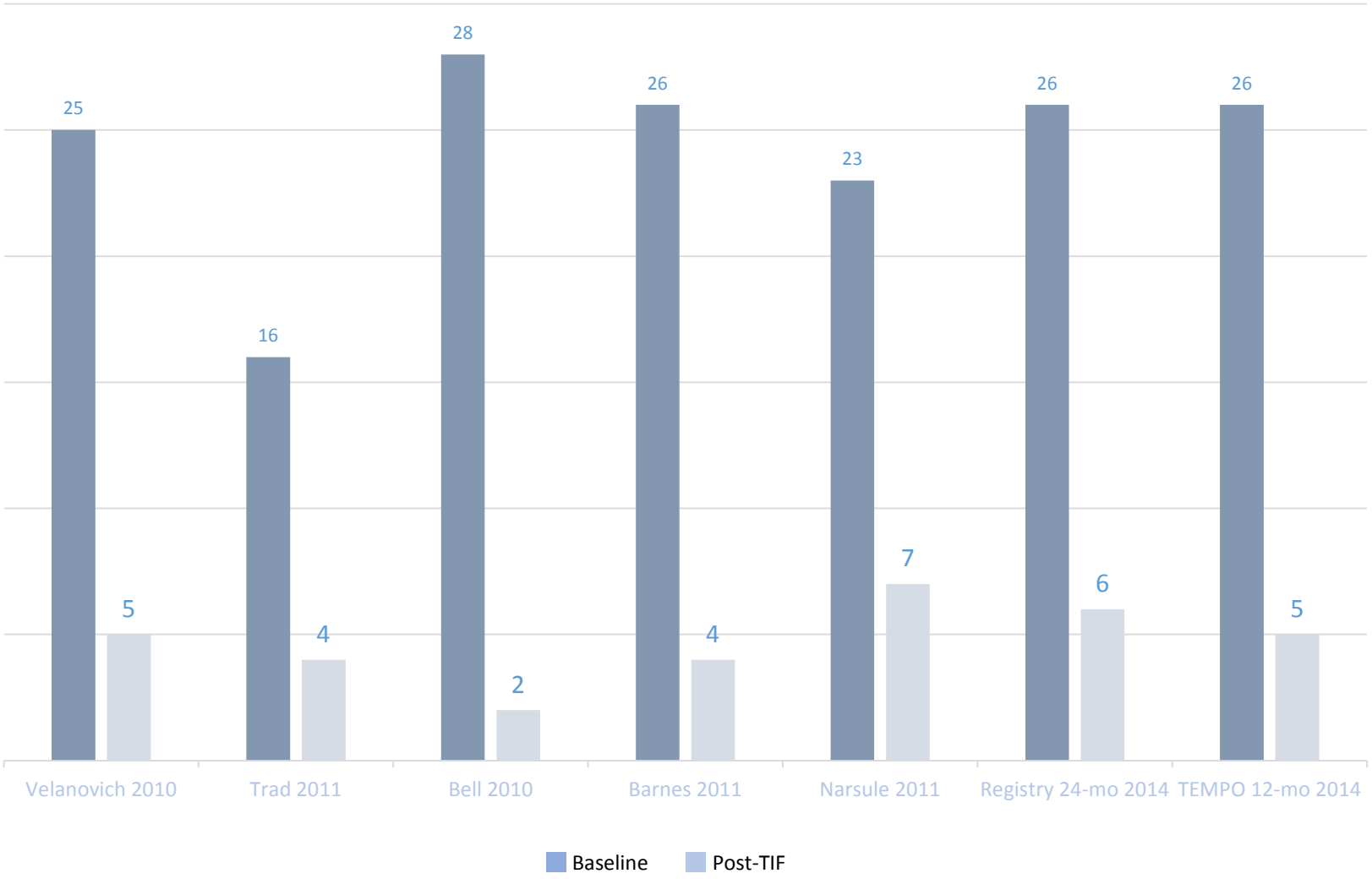
__ 1. How bad is your heartburn?	0 1 2 3 4 5
__ 2. Heartburn when lying down?	0 1 2 3 4 5
__ 3. Heartburn when standing up?	0 1 2 3 4 5
__ 4. Heartburn after meals?	0 1 2 3 4 5
__ 5. Does heartburn change your diet?	0 1 2 3 4 5
__ 6. Does heartburn wake you from sleep?	0 1 2 3 4 5
__ 7. Do you have difficulty swallowing?	0 1 2 3 4 5
__ 8. Do you have pain with swallowing?	0 1 2 3 4 5
__ 9. Do you have bloating or gassy feelings?	0 1 2 3 4 5
__ 10. If you take medication, does this affect your daily life?	0 1 2 3 4 5

__ How satisfied are you with your present condition? Satisfied __ Neutral __ Dissatisfied __

Velanovich V. Dis Esophagus. 2007;20(2):130-4

GERD Health Related Quality of Life (HRQL)

(Median GERD-HRQL in 7 US experience studies)



$p < 0.01$ in all studies

n= 387 (wt. avg. f/u at 12 mos.)

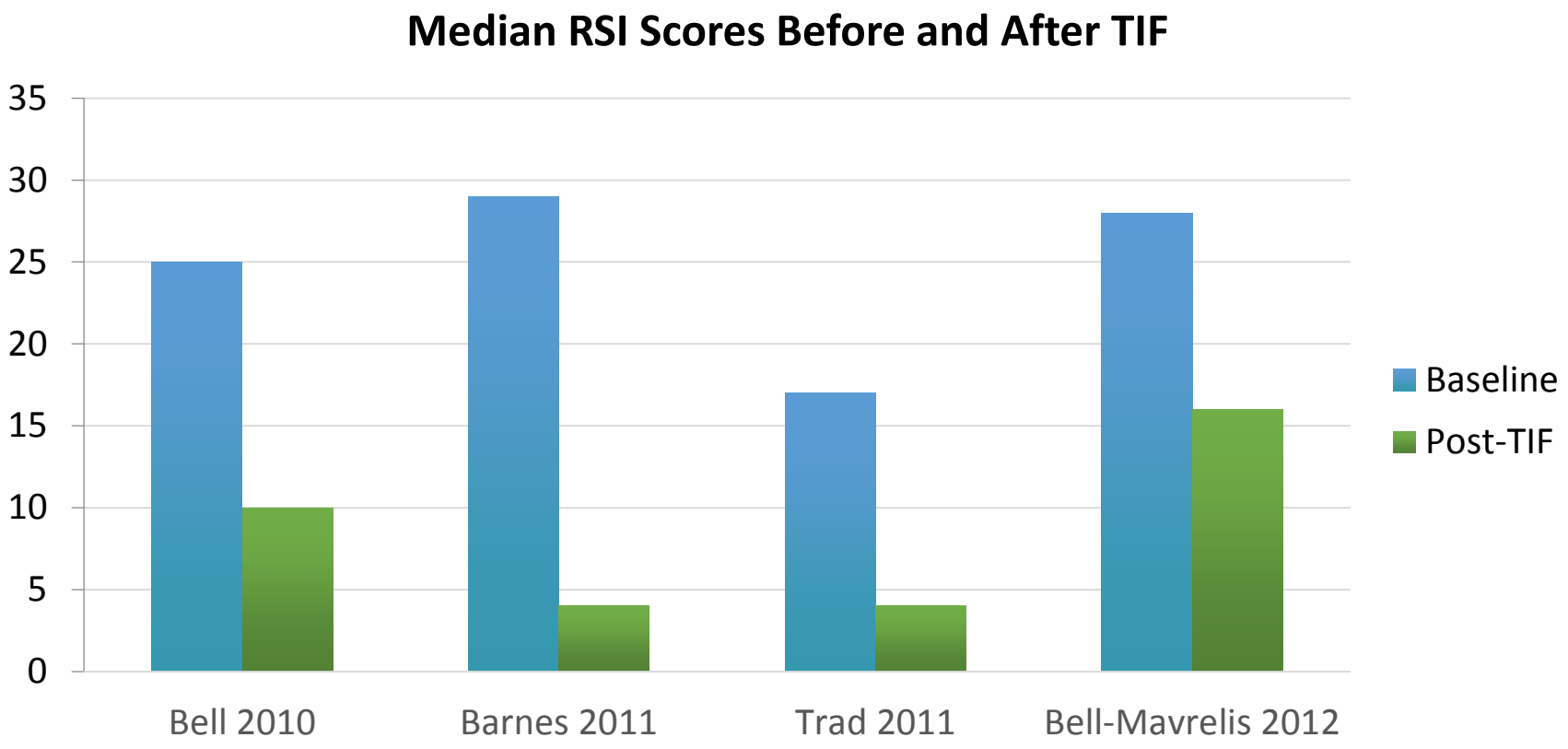
Effect on Atypical GERD symptoms

Table 1. *The Reflux Symptom Index (RSI)*

Within the last month, how did the following problems affect you? *Circle the appropriate response.*	0 = No Problem 5 = Severe Problem					
1. Hoarseness or a problem with your voice	0	1	2	3	4	5
2. Clearing your throat	0	1	2	3	4	5
3. Excess throat mucus or postnasal drip	0	1	2	3	4	5
4. Difficulty swallowing food, liquids, or pills	0	1	2	3	4	5
5. Coughing after you ate or after lying down	0	1	2	3	4	5
6. Breathing difficulties or choking episodes	0	1	2	3	4	5
7. Troublesome or annoying cough	0	1	2	3	4	5
8. Sensations of something sticking in your throat or a lump in your throat	0	1	2	3	4	5
9. Heartburn, chest pain, indigestion, or stomach acid coming up	0	1	2	3	4	5
	TOTAL					

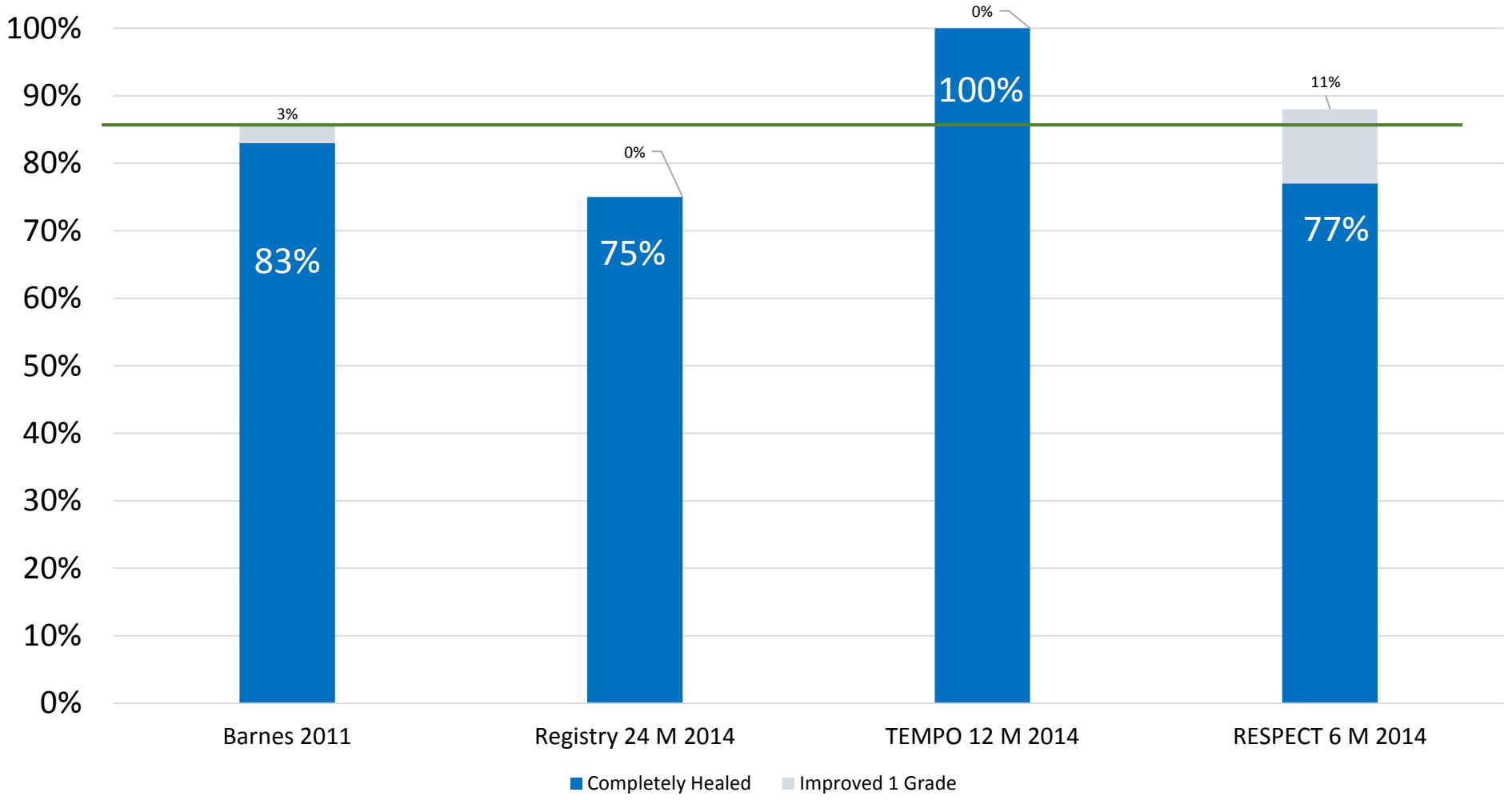
Journal of Voice, Vol. 16, No. 2, 2002

Effect on Atypical GERD symptoms



Healing of Esophagitis

*US Studies (TIF 2.0) – 4 studies; n= 79 patients (wt. avg. f/u at 9 mos.)

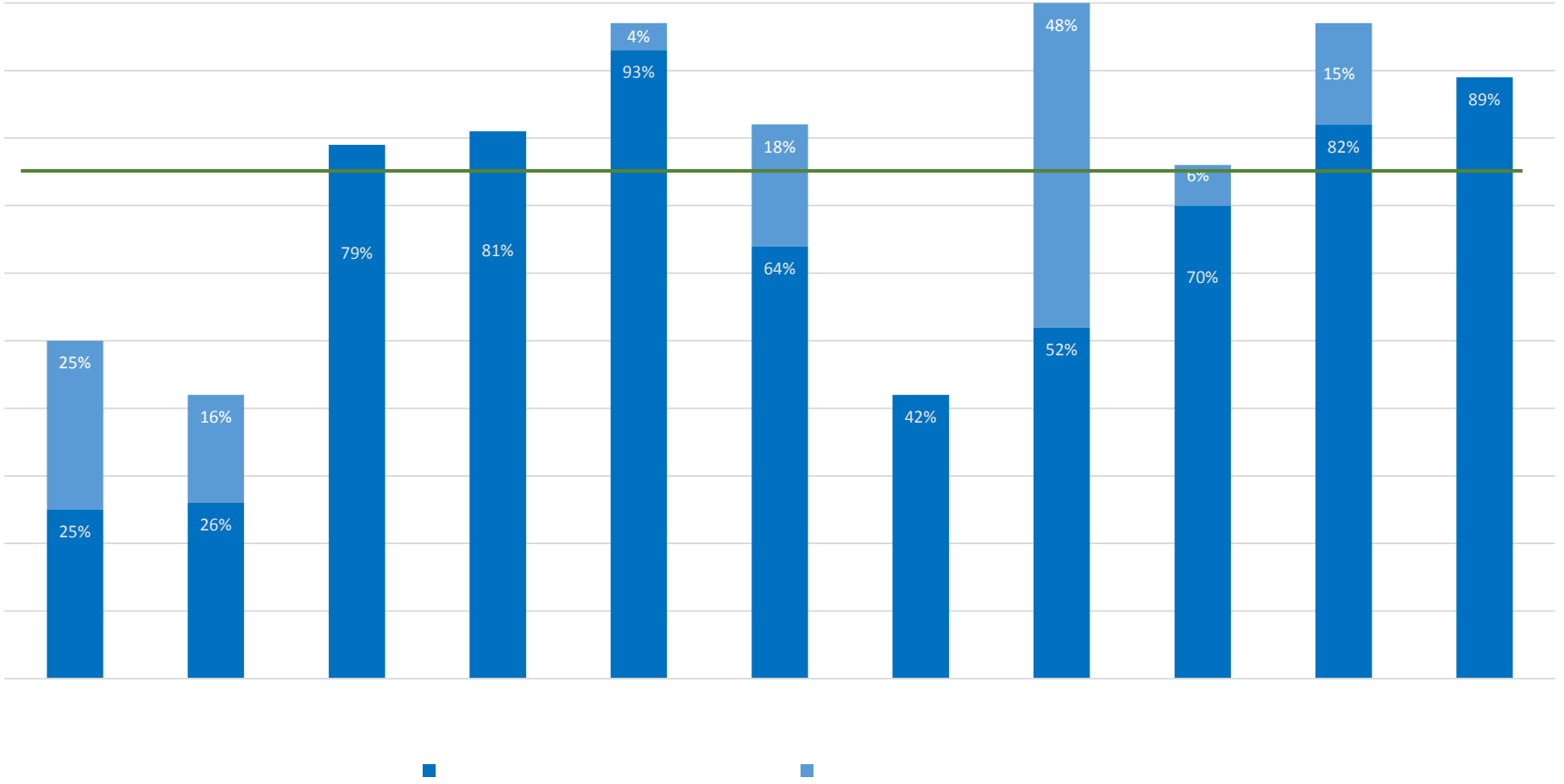


85% Completely Healed / 6% Improved*

Horizontal Orange Line — Wt. Avg. % of Patients Esophagitis Completely Healed

PPI Use

US Studies (TIF 2.0) – 11 studies; n=520 patients (wt. avg. f/u at 10 mos.)

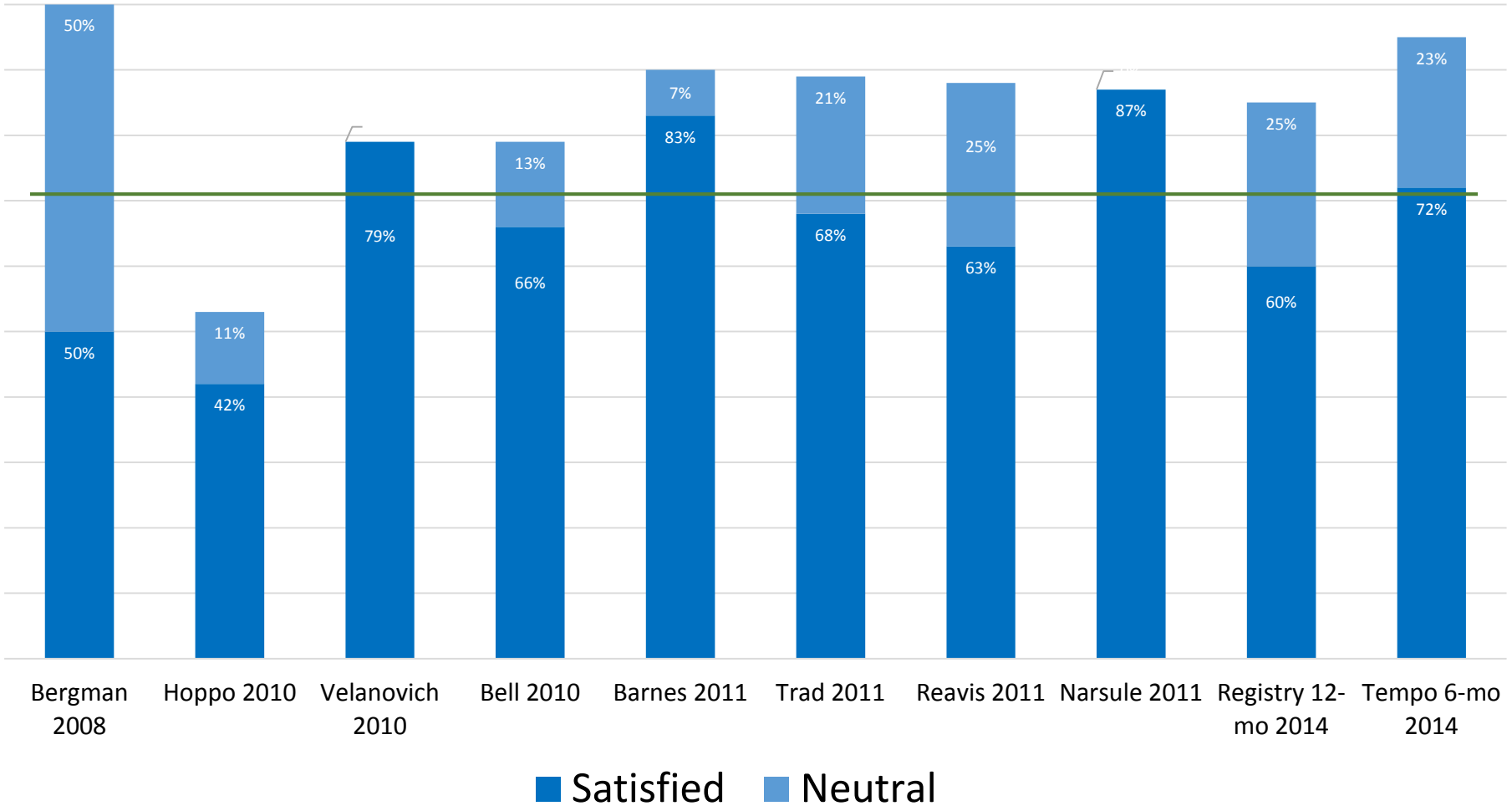


75% Completely Off / 10 % Occasional Use

Horizontal Orange Line — Wt. Avg. % of Patients Completely OFF PPI

Patient Satisfaction

US Studies (TIF 2.0) – 10 studies; n=410 patients (wt. avg. f/u at 8 mos.)



72% Satisfied /14% Neutral Post-TIF procedure

Horizontal Orange Line — Wt. Avg. % of Patients Satisfied Post-TIF procedure

TEMPO

TIF **E**sophyX vs **M**edical **P**PI **O**pen Label Trial

Surgical Innovation
1–15

DOI: 10.1177/1553350614526788
sri.sagepub.com
SAGE

Transoral Incisionless Fundoplication Effective in Eliminating GERD Symptoms in Partial Responders to Proton Pump Inhibitor Therapy at 6 Months: The TEMPO Randomized Clinical Trial

Karim S. Trad, MD[1,2], William E. Barnes, MD[3], Gilbert Simoni, MD[4], Ahmad B. Shughoury, MD[5,6], Peter G. Mavrelis, MD[5,6], Mamoon Raza, MD[7,8], Jeffrey A. Heise, MD[9], Daniel G. Turgeon, MD[1,2], and Mark A. Fox, MD[10,11]

US-based, multicenter (N=7), prospective, open label, randomized comparative study

Table 1. Inclusion and Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
Age: 18-80 years	Body mass index (BMI) >35 kg/m^2
Gastroesophageal reflux disease duration: >1 year	Hiatal hernia >2 cm in axial length and/or >2 cm in greatest transverse dimensions
History of daily proton pump inhibitors (PPIs) use >6 months	Esophagitis grade C or D; Barrett's esophagus >2 cm; esophageal ulcer; fixed esophageal stricture or narrowing
Troublesome atypical symptoms and/or regurgitation (*with or without heartburn*) while on daily PPI therapy	Portal hypertension and/or varices
Abnormal 48-hour pH off PPIs (total % time pH < 4 > 5.3%)	Active gastroduodenal ulcer disease
Hill grade I or II	Gastroparesis, gastric outlet obstruction, or stenosis
Willingness to undergo pH testing	Coagulation disorder
Willingness to adhere to postoperative diet for 6 weeks	History of any of the following: resective gastric or esophageal surgery, antireflux surgery with anatomy unsuitable for transoral incisionless fundoplication (TIF) procedure per physician judgment, cervical spine fusion, Zenker's diverticulum, esophageal epiphrenic diverticulum, achalasia, scleroderma ordermatomyositis, eosinophilic esophagitis, or cirrhosis
Availability for follow-up visits	Pregnancy or plans of pregnancy in the 12 months following treatment
Willingly and cognitively signed informed consent	Enrollment in another device or drug study that may confound the results

Study Design

Treatment Group (n=39):

TIF -> Discontinue all PPIs at 14 days after procedure

Control Group (n=21):

Maximal dose PPI

Initial Evaluation:

EGD, 48 hour pH Monitoring,

Symptom Assessment using RSI, RDQ, GERD-HRQL

Follow up:

At 2 weeks, 3 months, 6 months

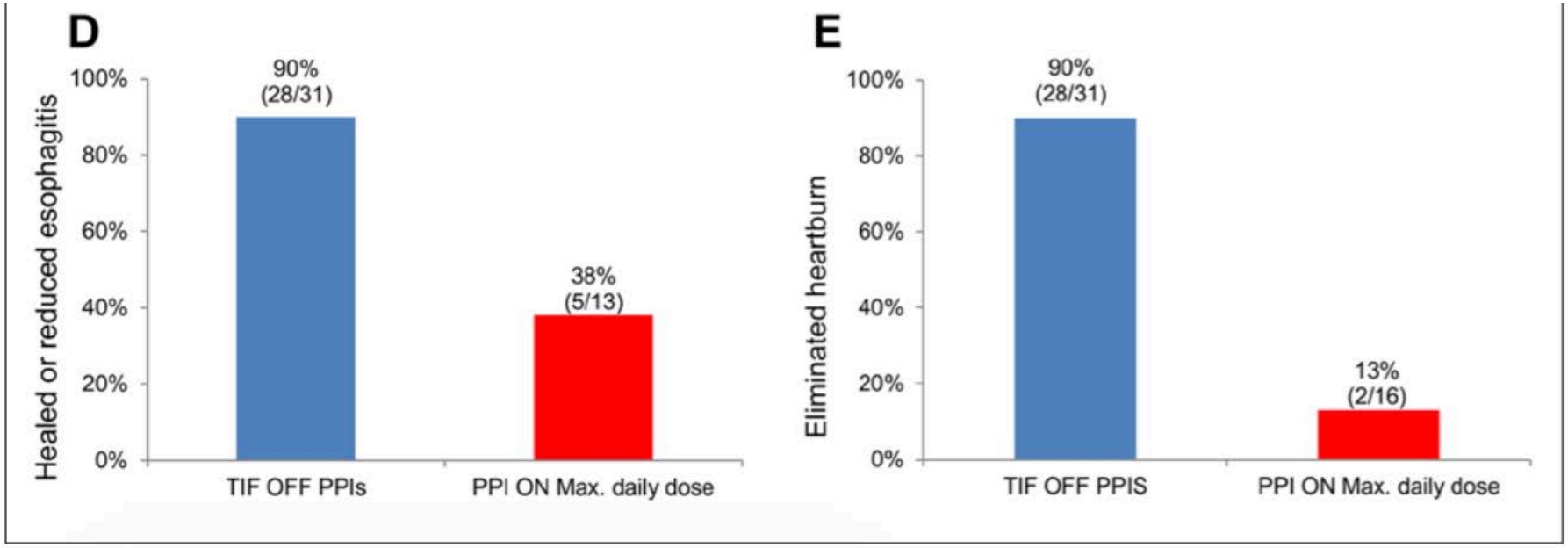
At 6 months, repeat EGD with 48 hour pH monitoring

(TIF – off PPIs, control – on PPIs)

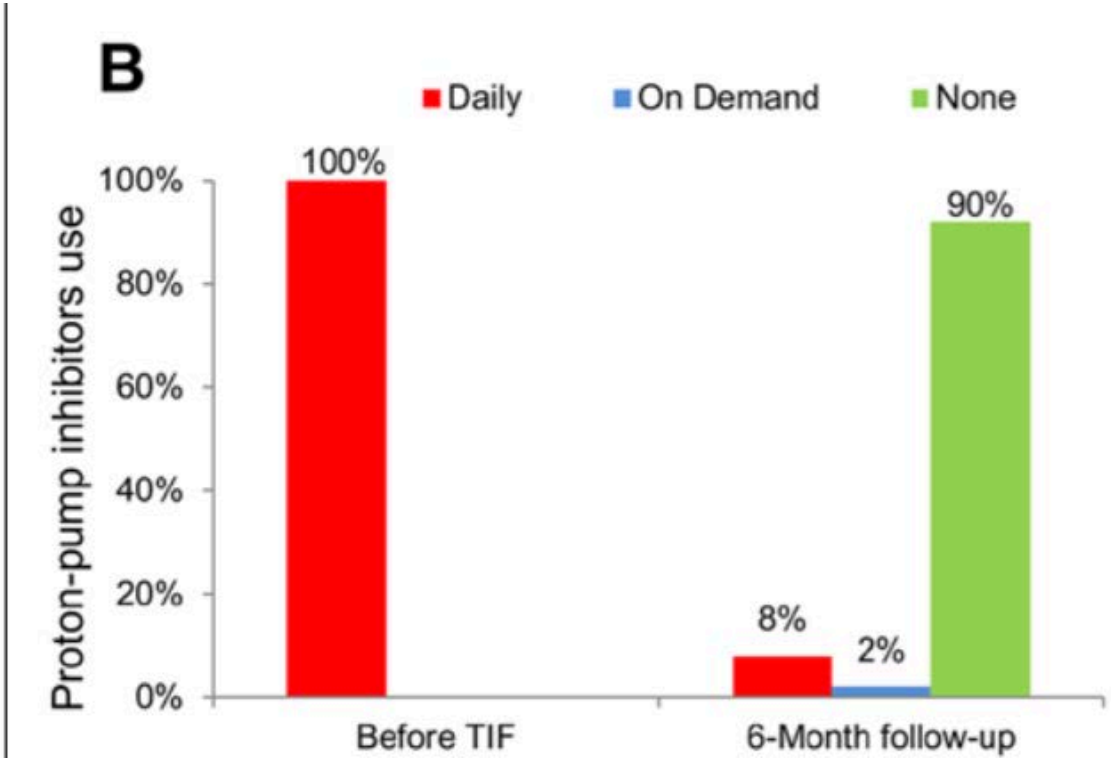
TEMPO Results

Esophagitis Healing

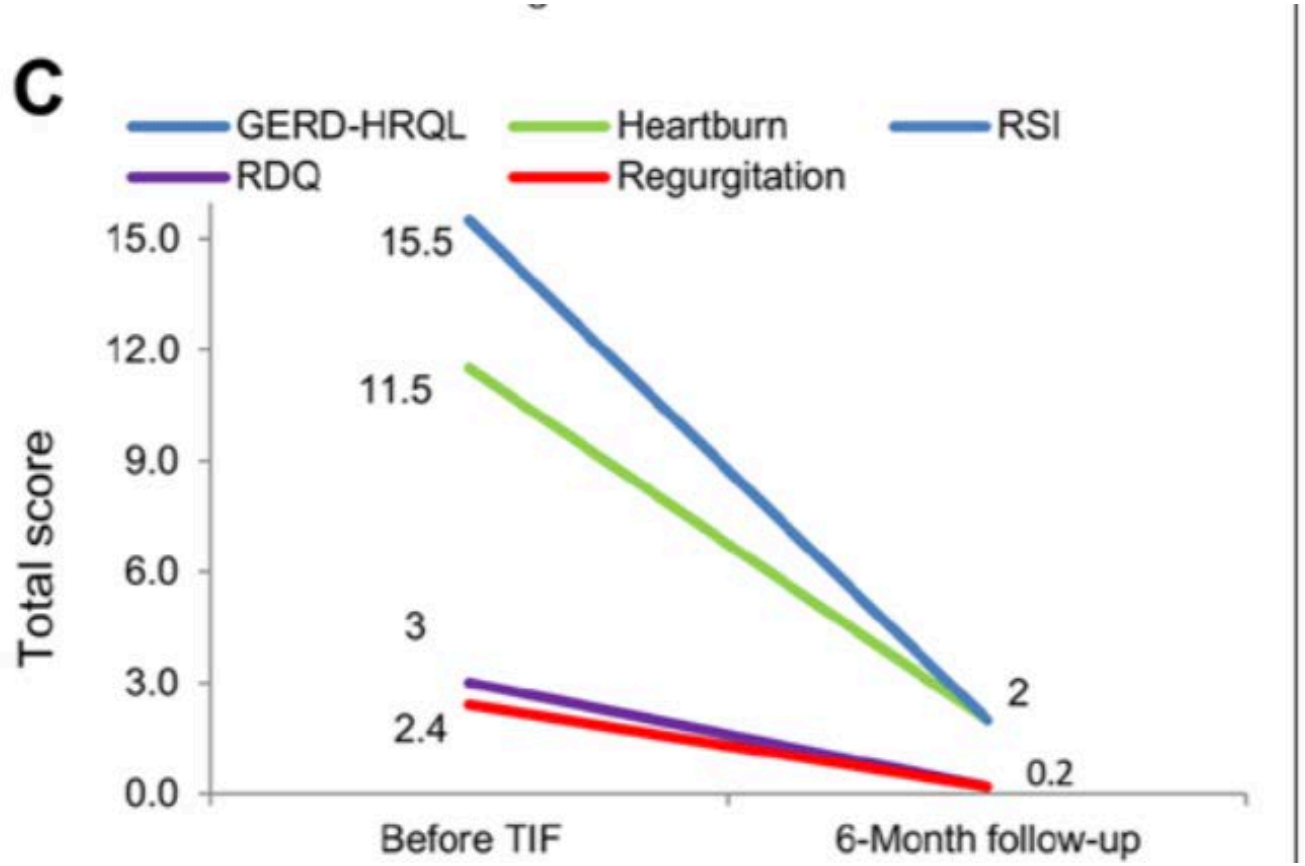
Heartburn Elimination



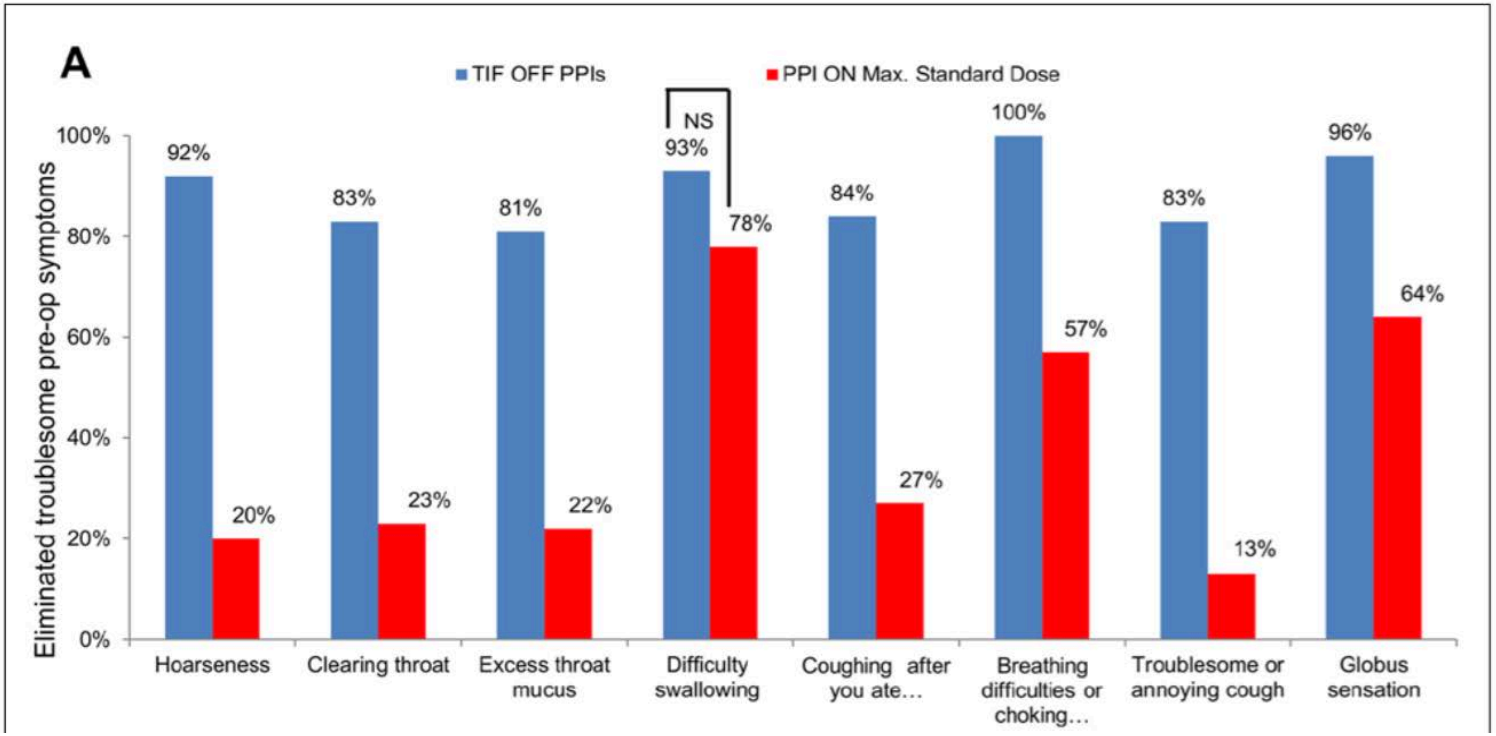
Results – PPI Use



Results – Symptom Scores



Results – Atypical Symptoms

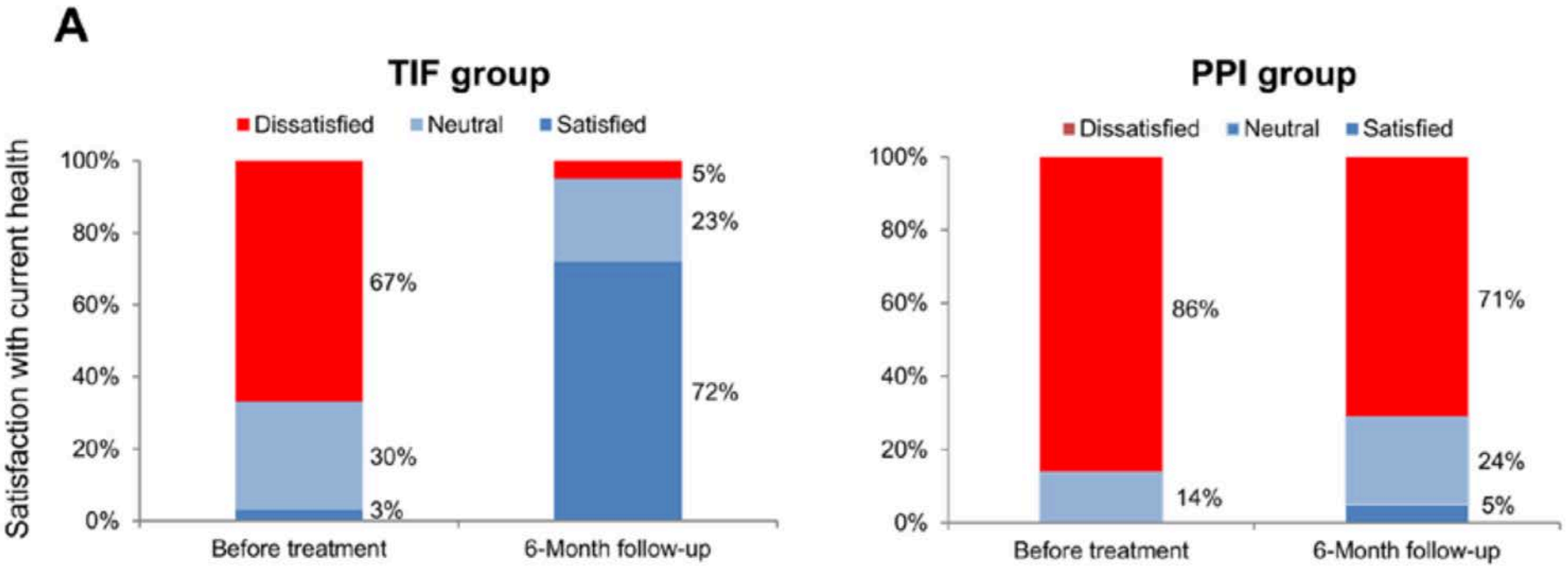


- TIF produced better better symptom improvement for atypical symptoms high dose PPI, and provided a durable response at 6 months

Results – Objective

- TIF improved ambulatory pH metrics, but was not better than maximal dose PPI
- Normalization of esophageal acid exposure was not achieved following TIF in all patients

Results – Satisfaction



Patients who undergo TIF reported a higher satisfaction with their current health than those who remain on standard medical therapy

TEMPO 5 Yr Follow up

Trad et al. Surgical Innovation 2018, Vol. 25(2) 149–157

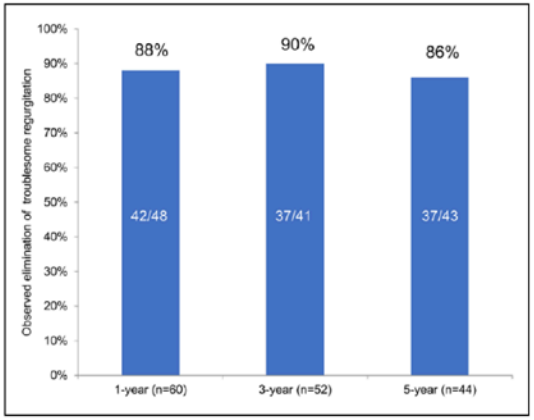


Figure 2. Elimination of troublesome regurgitation, as assessed by the Reflux Disease Questionnaire at the 1-, 3-, and 5-year follow-ups.

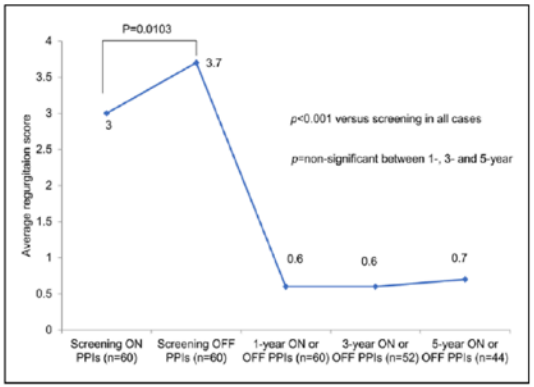


Figure 3. Regurgitation score, as assessed by the Reflux Disease Questionnaire, at screening and the 1-, 3-, and 5-year follow-ups.

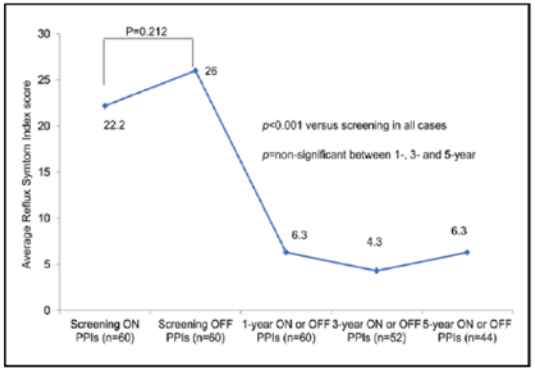


Figure 4. Reflux Index Score at screening and 1-, 3-, and 5-year follow-up assessments.
Abbreviation: PPI, proton pump inhibitor.

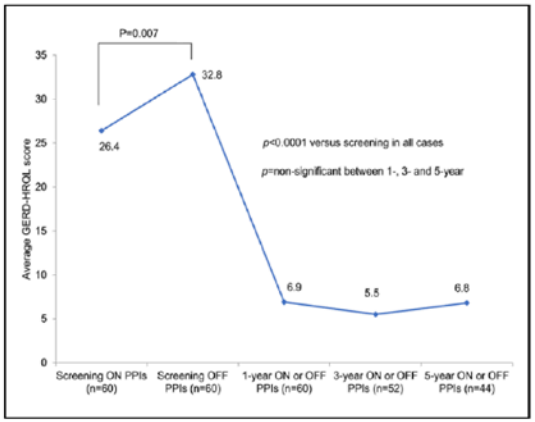


Figure 5. Gastroesophageal Reflux Disease Health-Related Quality of Life (GERD-HRQL) questionnaire, at screening and 1-, 3-, and 5-year follow-up assessments.

RESPECT

Randomized **E**sophyX vs **S**ham, **P**lac**e**bo-**C**ontrolled **T**ransoral Fundoplication Trial

[redacted]

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

John G. Hunter, Peter J. Kahrilas, Reginald C.W. Bell, Erik B. Wilson, Karim S. Trad, James P. Dolan, Kyle A. Perry, Brant K. Oelschlager, Nathaniel J. Soper, Brad E. Snyder, Miguel A. Burch, William Scott Melvin, Kevin Reavis, Daniel G. Turgeon, Eric S. Hungness, Brian S. Diggs

US-based, Multicenter (N=8), prospective sham-controlled randomized trial

Inclusion criteria:

Age 18-80

>6 months symptoms despite at least 40mg daily PPI

Abnormal ambulatory pH monitoring

Exclusion criteria:

Hiatal hernia >2 cm

BMI >35

LA Class C and D esophagitis

Study Design

Treatment group (2:1 Randomization):

- EGD with TIF
- 2 weeks 40mg omeprazole
- Then placebo for remainder of study

Control group:

- EGD with passage of 50 French Dilator for 15 minutes (sham procedure)
- 2 weeks 40mg omeprazole
- Then 40mg omeprazole for remainder of study

Study Design

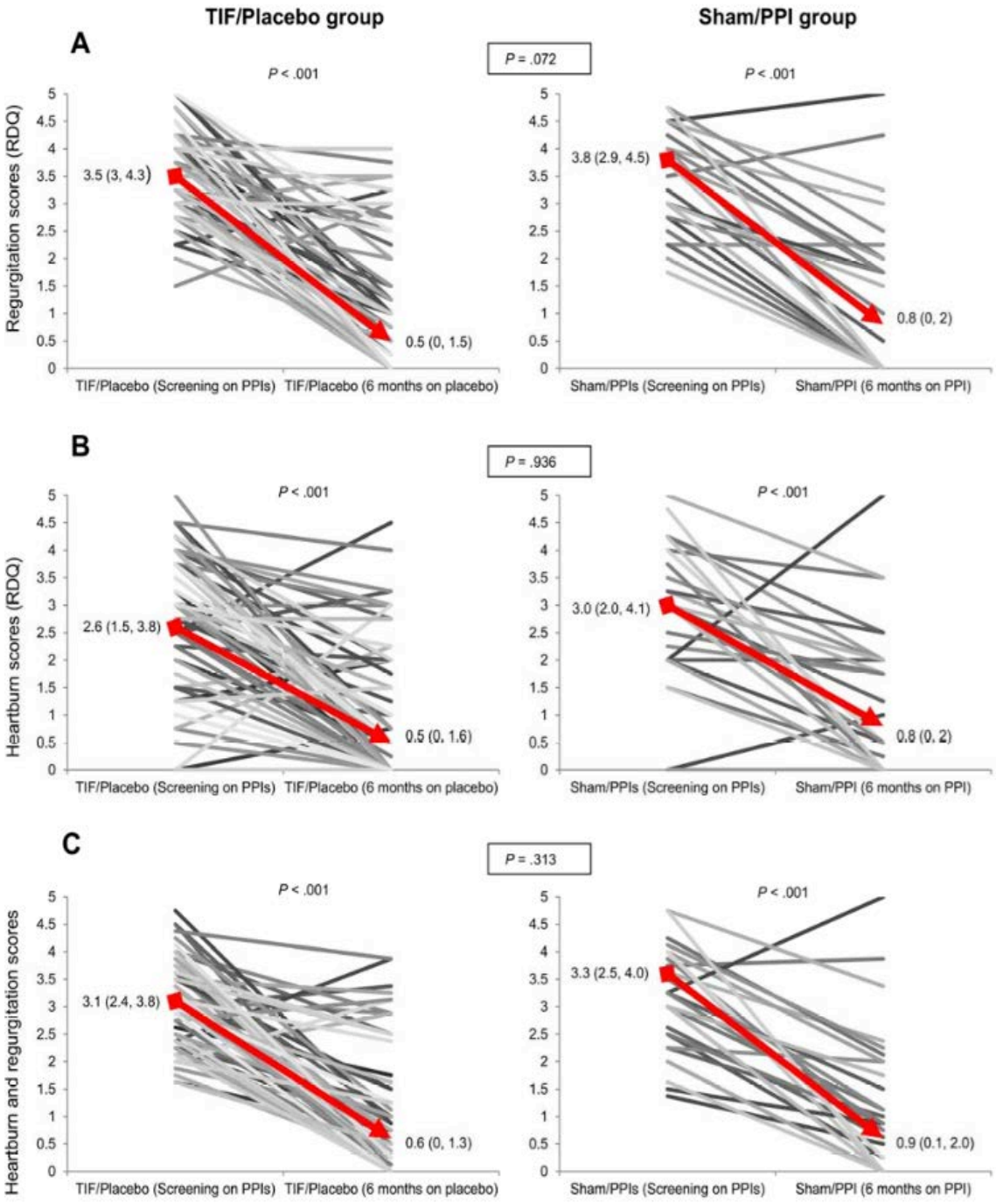
Follow up:

- At weeks 2, 12, and 26 weeks evaluated using Questionnaires
- If troublesome symptoms at week 2, medical therapy was increased to twice daily (placebo BID or omeprazole BID)
- If symptoms persisted at week 12, patients were allowed to crossover to other treatment arm (“early failures”)
- At 26 weeks completed questionnaires on and off therapy, had EGD with 48-hour ambulatory pH monitoring off therapy

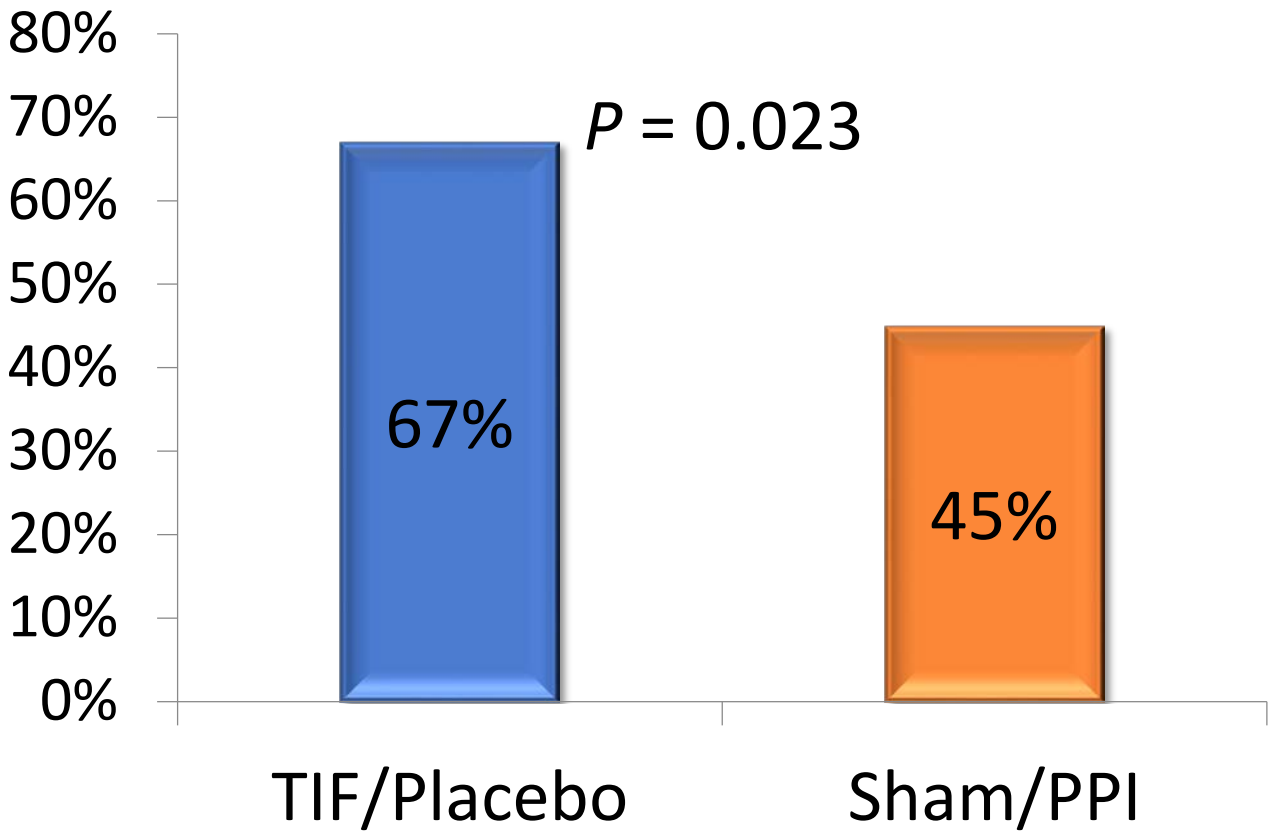
Results

- TF/Placebo Group n= 87
- Sham/PPI Group n=42

- TIF with placebo resulted in symptom improvement across a number of validated symptom scoring systems
- The degree however was roughly equivalent to standard medical therapy and a sham procedure



Resolution of troublesome regurgitation as evaluated by RDQ per Montreal Consensus definition at 6-M follow-up

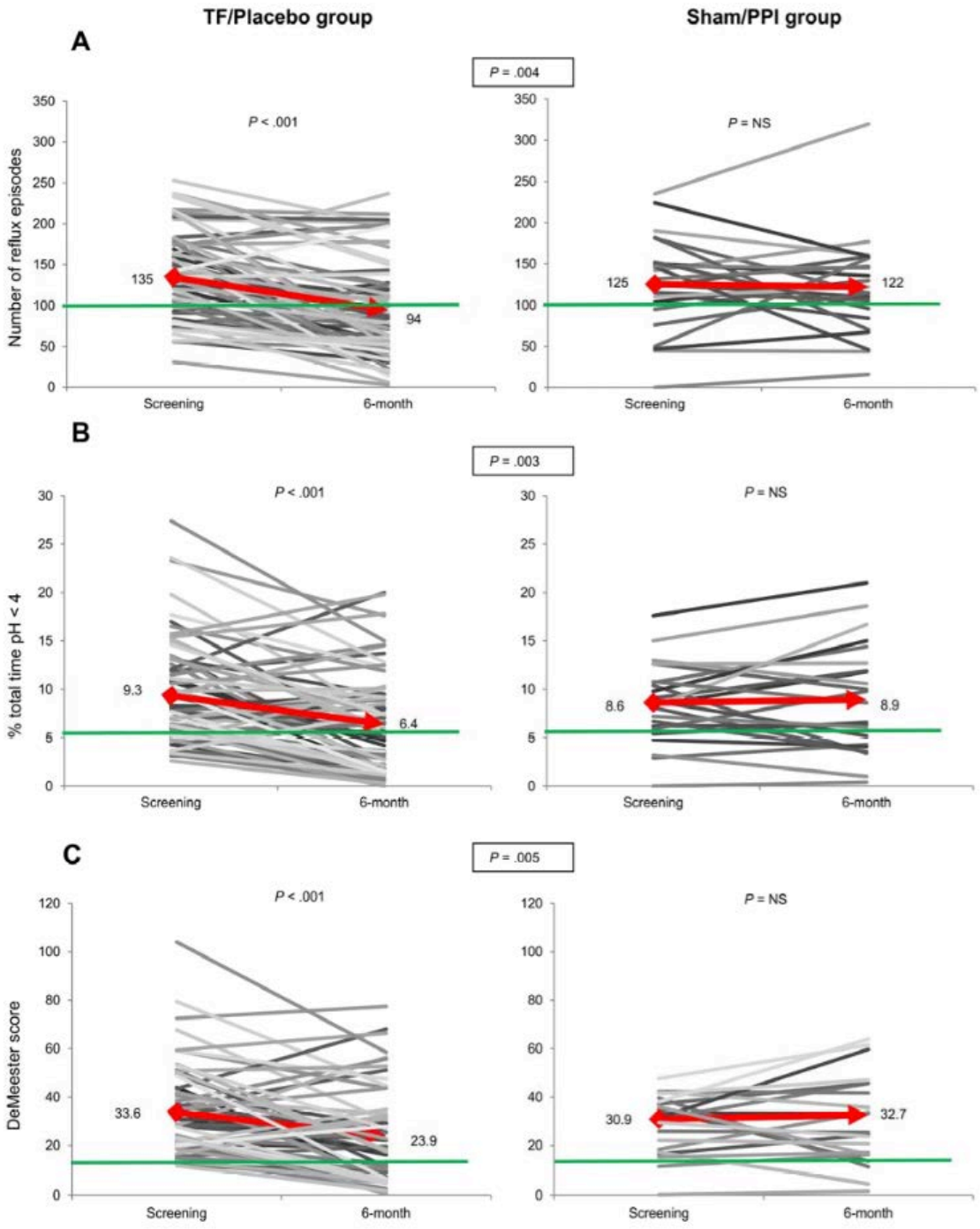


Hunter et al (2015)

Results – pH Testing

- TIF demonstrated a greater improvement in ambulatory pH metrics
- Normalization of esophageal acid exposure was not achieved following TIF

- Neither TIF nor the sham procedure resulted in significant worsening of dysphagia or bloating at the end of the study period



Significant Adverse Events

Table 2. Significant Adverse Events

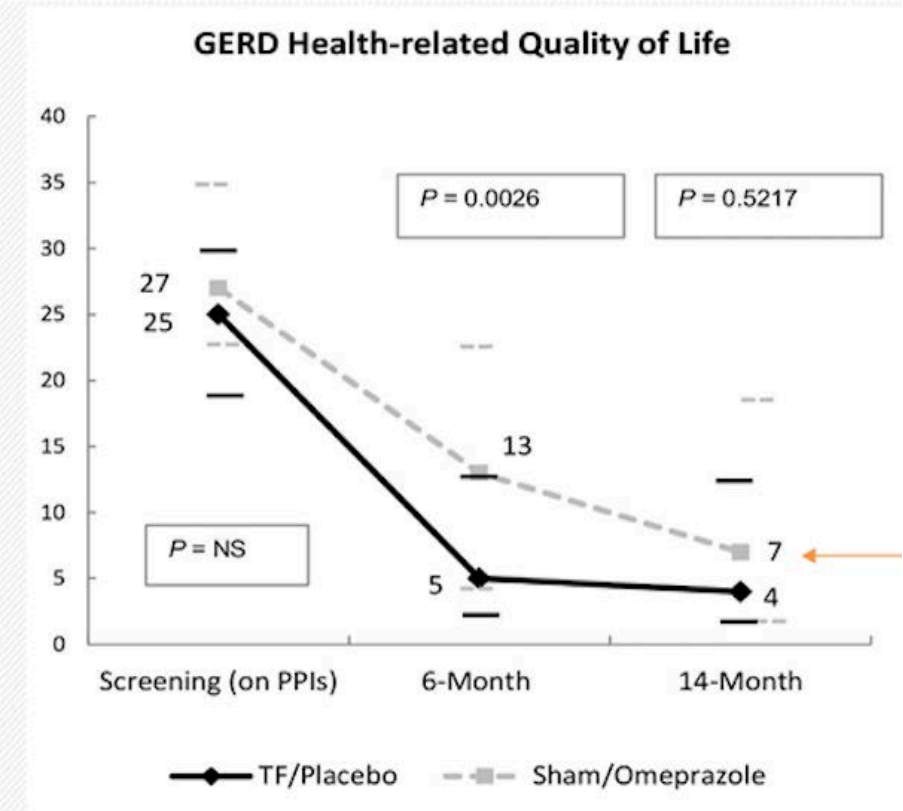
Randomization Group	Significant Adverse Event	Maximum Severity	Onset After Procedure	Duration
Sham	Nausea	Severe	PPD 1	2 Days
TF	Temporary epigastric /abdominal pain	Severe	PPD 5	2 Weeks
	Chest Pain	Severe	PPD 5	3 Days
	Musculoskeletal pain	Severe	PPD 1	1 Day
	Temporary epigastric /abdominal pain	Moderate	PPD 1	4 Weeks
	Dysphagia	Moderate	PPD 1	8 Days
	Dysphagia	Mild	PPD 1	1 Day
	Nausea	Mild	PPD 1	1 Day

Per protocol definition, the events reported above were classified as Serious Adverse Events as they required in-patient hospitalization or prolonged hospitalization.

RESPECT Trial Conclusion

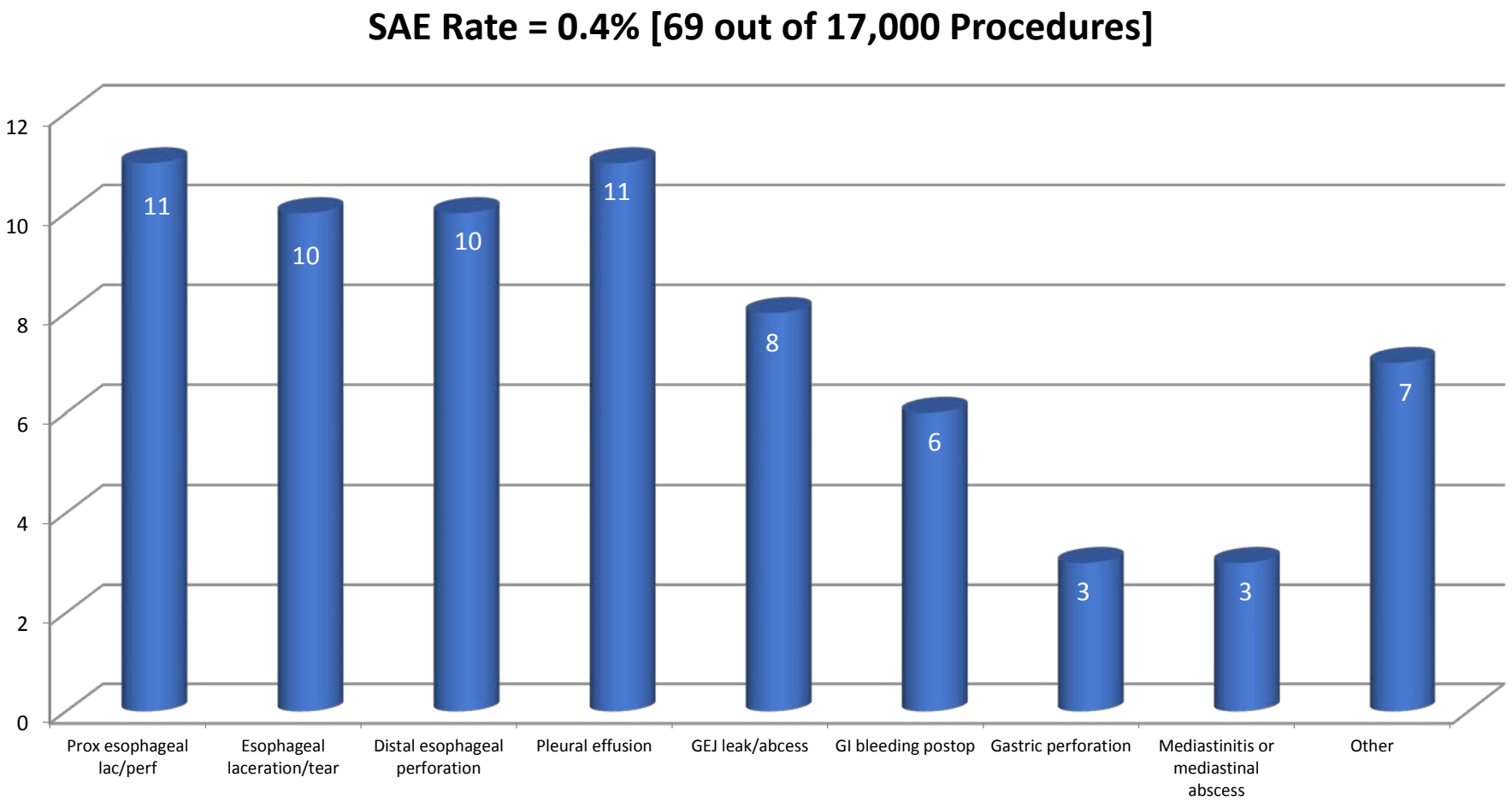
- In this sham-controlled randomized controlled trial, TIF was effective in eliminating troublesome GERD symptoms, especially regurgitation, with a low failure rate and good safety profile for 6 months.

Respect 14M Quality of Life



- After 6M evaluation and unblinding, sham patients were offered crossover to TIF procedure
- 76% crossed over to TIF Procedure
- Quality of Life improved to close to the TIF group

TIF SAE and Side Effects



"Overall, TIF appears to be safe with a relatively low rate of complications. The major complication rate across all studies was found to be 3.2 %. This is comparable to that of laparoscopic Nissen fundoplication." Wendling, Melvin, Surg Endoscp, online May 2013

Surg Endosc (2014) 28:941–949
DOI 10.1007/s00464-013-3250-7

Effect of transoral incisionless fundoplication on reflux mechanisms

Nicolaas F. Rinsma · Fabiënne G. Smeets · Daisy W. Bruls · Boudewijn F. Kessing · Nicole D. Bouvy · Ad A. M. Masclee · José M. Conchillo

Received: 8 April 2013 / Accepted: 30 September 2013 / Published online: 23 October 2013

Abstract
Objectives Transoral incisionless fundoplica… new endoscopic treatment option for gas… reflux disease (GERD). The mechanisms u… anti-reflux effect of this new procedure have … ied. We therefore conducted this explorative … uate the effect of TIF on reflux mechanisms … transient lower esophageal sphincter relaxati… and esophagogastric junction (EGJ) distensib…
Methods GERD patients ($N = 15$; 11 mal… 41 years, range 23–66), dissatisfied with med… were studied before and 6 months after TIF. … 90-min postprandial combined high-resolutio… and impedance-pH monitoring and an ambula… impedance monitoring. EGJ distensibility … using an endoscopic functional luminal i… before and directly after the procedure.
Results TIF reduced the number of postpra… (16.8 ± 1.5 vs. 9.2 ± 1.3; $p < 0.01$) and t… postprandial TLESRs associated with reflu… vs. 5.6 ± 0.6; $p < 0.01$), but the proportio… associated with reflux was unaltered (6… 69.9 ± 6.3 %). TIF also led to a decrease i… and proximal extent of reflux episodes and an improvement …

been introduced to fill the therapeutic gap between treatment with proton pump inhibitors (PPIs) and laparoscopic anti-reflux surgery (LARS). To date, most of these endoscopic techniques have failed, either because of a lack of long-term efficacy or due to complications of the procedure [1–4]. Transoral incisionless fundoplication (TIF) using the EsophyX device is a recently developed endoscopic treatment option for GERD. In this procedure, a partial fundoplication is created under general anesthesia by sequential retractions of tissue, fixed by multiple transmurally placed polypropylene fasteners [5]. Since its first introduction, several modifications have been made to the EsophyX device and to

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TIF Effects on Reflux Mechanisms

Surg Endosc 2014: 28: 941-949

- Netherlands
- 15 patients

- Studied pre-TIF vs 6 mos post-TIF
  - 90 min post prandial HRM
  - Impedence pH-monitoring
  - EGJ distensbility (Endoflip)

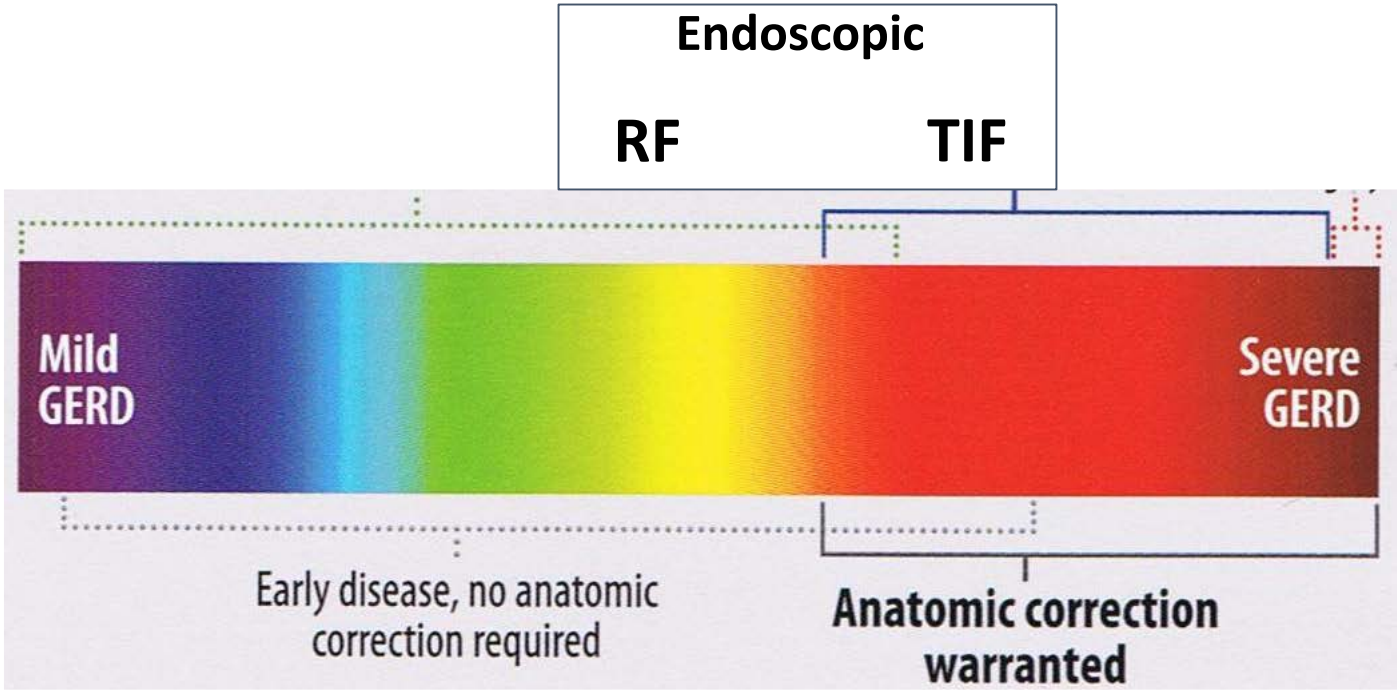
- Results:
  - TIF reduced TLESRs (16.8 vs 9.2 p<0.01)
  - Reduced # of liquid reflux episodes
  - Reduced the proximal extent of reflux episodes
  - No effect on # of gas reflux episodes
  - Less distensibility after TIF

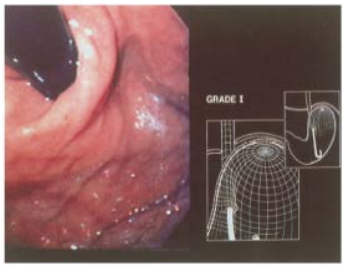
- Conclusion:
  - Decreased TLESR likely important mechanism
  - TIF permits belching

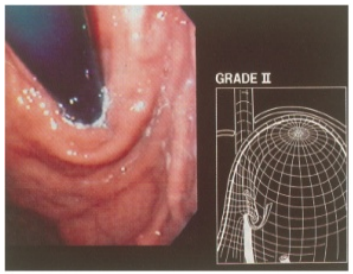
TIF Summary

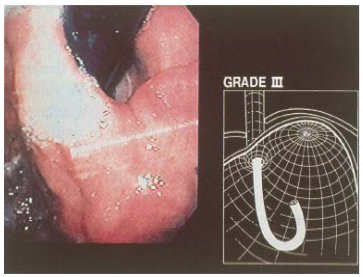
- Similar anti-reflux mechanism to Nissen fundoplication
- Generally tolerated well by patients
- Appears to have less short and long term side effects than Nissen (less gas / bloating)
- Long term durability studies have emerged

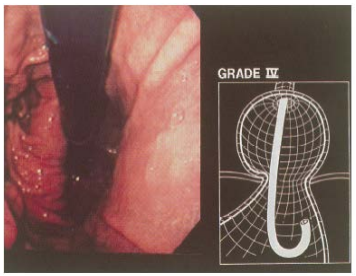
GERD Continuum











Thank you for your attention

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