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 at least 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
HOW STRETTA WORKS

• Concentrated RF energy delivered to tissue

• Multi-level thermal treatment remolds 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


- 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
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
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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.

Gastroesophageal reflux disease (GERD) is the most common principal gastrointestinal 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

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Studies (n)</th>
<th>Patients (n)</th>
<th>Mean Follow-up (mo)</th>
<th>Pre-Stretta</th>
<th>Post-Stretta</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUBJECTIVE MEASUREMENTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>GERD-HRQL</td>
<td>9</td>
<td>433</td>
<td>19.8</td>
<td>26.11</td>
<td>9.25</td>
<td>0.0001</td>
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<tr>
<td>QOLRAD</td>
<td>4</td>
<td>250</td>
<td>25.2</td>
<td>3.30</td>
<td>9.25</td>
<td>0.0010</td>
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<tr>
<td>SF-36 Physical</td>
<td>6</td>
<td>299</td>
<td>9.5</td>
<td>36.45</td>
<td>46.12</td>
<td>0.0001</td>
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<tr>
<td>SF-36 Mental</td>
<td>5</td>
<td>264</td>
<td>10.0</td>
<td>46.79</td>
<td>55.16</td>
<td>0.0015</td>
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<tr>
<td>Heartburn Score</td>
<td>9</td>
<td>525</td>
<td>24.1</td>
<td>3.55</td>
<td>1.19</td>
<td>0.0001</td>
</tr>
<tr>
<td>Satisfaction Score</td>
<td>5</td>
<td>366</td>
<td>21.9</td>
<td>1.43</td>
<td>4.07</td>
<td>0.0006</td>
</tr>
<tr>
<td><strong>OBJECTIVE MEASUREMENTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Esophageal Acid Exposure (%Ph&lt;4)</td>
<td>11</td>
<td>364</td>
<td>11.9</td>
<td>10.29</td>
<td>6.51</td>
<td>0.0003</td>
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<tr>
<td>DeMeester score</td>
<td>7</td>
<td>267</td>
<td>13.1</td>
<td>44.37</td>
<td>28.53</td>
<td>0.0074</td>
</tr>
<tr>
<td>LES pressure</td>
<td>7</td>
<td>263</td>
<td>8.7</td>
<td>16.54</td>
<td>20.24</td>
<td>0.0302</td>
</tr>
</tbody>
</table>

Radiofrequency Energy Delivery to the Lower Esophageal Sphincter Reduces Esophageal Acid Exposure and Improves GERD Symptoms: A Systematic Review and Meta-analysis.
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

• 28 Studies, 2468 Patients, up to 10-yrs follow-up (avg 25 months)
New Stretta Meta-Analysis 2017

<table>
<thead>
<tr>
<th>STATISTICALLY SIGNIFICANT IMPROVEMENTS/REDUCTIONS POST STRETTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid Exposure Time</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>0%</td>
</tr>
<tr>
<td>10%</td>
</tr>
<tr>
<td>20%</td>
</tr>
<tr>
<td>30%</td>
</tr>
<tr>
<td>40%</td>
</tr>
<tr>
<td>50%</td>
</tr>
<tr>
<td>60%</td>
</tr>
<tr>
<td>70%</td>
</tr>
</tbody>
</table>

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)

- 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)
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)

Preamble

The following clinical spotlight review provides information for physicians who manage and treat esophagopharyngeal reflux disease (GERD) supporting their safety and efficacy in clinical practice.

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 48 months 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

- **Normal Anatomy**
  - Fully Functional Valve Prevents Reflux
  - Dysfunctional Valve
  - Reconstruct natural physical barrier to reflux

- **Lower Esophageal Sphincter (LES)**
- **Angle of HIS**
- **Gastroesophageal Flap Valve (GEV)**
- **Fundus**
- **Diaphragm**

*Gray's Anatomy, 1997*
## Surgical Treatment

### Surgical Objectives of Treatment

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Nissen</th>
<th>TIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recreates Angle of HIS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tightens greater curve side of cardia to lesser curve</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Submerges distal esophagus into proximal stomach</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Restores intraabdominal esophageal length</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Reduces hiatal hernia</td>
<td>Yes</td>
<td>&lt;2cm</td>
</tr>
<tr>
<td>Creates a valve the length of the fundoplication</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tightens phrenoesophageal membrane</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
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

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

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

**TOTAL**

*Journal of Voice, Vol. 16, No. 2, 2002*
Effect on Atypical GERD symptoms

Median RSI Scores Before and After TIF

Combined 270 patients with average Follow up 7 months

All p < 0.01

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

83%  75%  100%  77%  11%


Completely Healed  Improved 1 Grade

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.)

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

- Bergman 2008
- Hoppo 2010
- Velanovich 2010
- Bell 2010
- Barnes 2011
- Trad 2011
- Oeslhlager 2011
- Narsule 2011
- Registry 24-mo

- TEMPO 12-mo 2014
- RESPECT 6-mo 2014

75% Completely Off / 10 % Occasional Use
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 EsophyX vs Medical PPI Open Label Trial

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>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 18-80 years</td>
<td>Body mass index (BMI) &gt;35 kg/m²</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease duration: &gt;1 year</td>
<td>Hiatal hernia &gt;2 cm in axial length and/or &gt;2 cm in greatest transverse dimensions</td>
</tr>
<tr>
<td>History of daily proton pump inhibitors (PPIs) use &gt;6 months</td>
<td>Esophagitis grade C or D; Barrett’s esophagus &gt;2 cm; esophageal ulcer; fixed esophageal stricture or narrowing</td>
</tr>
<tr>
<td>Troublesome atypical symptoms and/or regurgitation (with or without heartburn) while on daily PPI therapy</td>
<td>Portal hypertension and/or varices</td>
</tr>
<tr>
<td>Abnormal 48-hour pH off PPIs (total % time pH &lt; 4 &gt; 5.3%)</td>
<td>Active gastroduodenal ulcer disease</td>
</tr>
<tr>
<td>Hill grade I or II</td>
<td>Gastroparesis, gastric outlet obstruction, or stenosis</td>
</tr>
<tr>
<td>Willingness to undergo pH testing</td>
<td>Coagulation disorder</td>
</tr>
<tr>
<td>Willingness to adhere to postoperative diet for 6 weeks</td>
<td>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, dermatomyositis, eosinophilic esophagitis, or cirrhosis</td>
</tr>
<tr>
<td>Availability for follow-up visits</td>
<td>Pregnancy or plans of pregnancy in the 12 months following treatment</td>
</tr>
<tr>
<td>Willingly and cognitively signed informed consent</td>
<td>Enrollment in another device or drug study that may confound the results</td>
</tr>
</tbody>
</table>
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

[Bar charts showing percentages of healed or reduced esophagitis and eliminated heartburn for TIF OFF PPIs and PPI ON Max. daily dose.]
Results – PPI Use

The bar chart illustrates the percentage of patients using proton-pump inhibitors (PPIs) before and after TIF therapy. Before TIF, 100% of patients were using PPIs daily. After the 6-month follow-up, the percentage of daily users decreased to 8%, and the percentage of patients who did not use PPIs increased to 90%.
Results – Symptom Scores
Results – Atypical Symptoms

- TIF produced 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.
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 EsophyX vs Sham, Placebo-Controlled Transoral Fundoplication Trial

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

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

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
### Table 2. Significant Adverse Events

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

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
“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 Endosc, online May 2013
Effect of transoral incisionless fundoplication on reflux mechanisms

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Abstract

Objectives Transoral incisionless fundoplication (TIF) is a new endoscopic treatment option for gastroesophageal reflux disease (GERD). The mechanisms of the anti-reflux effect of this new procedure have not been fully understood. We therefore conducted this exploratory study to evaluate the effect of TIF on reflux mechanisms using high-resolution impedance-pH monitoring, high-resolution impedance monitoring and an ambulatory manometry study before and after TIF.

Methods GERD patients (N = 15; 11 males, mean age 41 years, range 23–66), dissatisfied with medical therapy, were studied before and 6 months after TIF. HRM was performed 90 min after a prandial meal and impedance-pH monitoring was performed before and after TIF.

Results TIF reduced the number of postprandial TLESRs (16.8 ± 1.5 vs. 9.2 ± 1.3, p < 0.01) and the number of reflux episodes (90 min postprandial combined high-resolution impedance-pH monitoring) after TIF (5.6 ± 0.6, p < 0.01), but the proportion of episodes associated with reflux was unaltered (56 ± 24 vs. 54 ± 30%). TIF also led to a decrease in EGJ distensibility (EndoFlap).

Conclusion Decreased TLESRs likely important mechanism for TIF. TIF permits belching.

TIF Effects on Reflux Mechanisms

- 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

Endoscopic

RF  TIF

Mild GERD

Early disease, no anatomic correction required

Severe GERD

Anatomic correction warranted
Thank you for your attention

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