Endoscopic Treatment of GERD:
The Good, the Bad, and the Ugly

Jay Jacobs, MD
Assistant Professor of Medicine
Joy McCann Culverhouse Center for Swallowing Disorders
University of South Florida
Disclosures

- None
Three Main Objectives

- Summarize the “old reliable” = Nissen fundoplication
- Review new treatments of GERD
- Discuss six key subjective and objective outcome measurements
Outline

- “Burden of GERD”
- “Burden of PPI Use” and healthcare utilization
- Why do people get GERD?
- What is the “ideal treatment” for GERD?
- Gold standard: Nissen fundoplication
Outline

- Endoluminal Treatments
  - Stretta
  - Transoral incisionless fundoplication (TIF)
- LINX
- Evaluate six key elements
  - Symptom control
  - Decreased PPI use
  - Increased LES pressure
  - Normalization of pH
  - Safety profile
  - Durability
Burden of GERD

- A very common disease
- Up to 60% of adults will experience GERD within a 12 month period
  - 20-30% will have weekly symptoms
- 5-25% of adults worldwide have some symptoms within a 3 month period
- GERD diagnosis increased 216% from 1998 to 2005

Healthline.com
Walgreens – Downtown Tampa
Proton Pump Inhibitors

- In 2007, over 108 million prescriptions were written for PPIs
  - 6th ranked class of medication in terms of # of prescriptions
- In 2008, U.S. sales of PPIs reached $13.9 Billion,
  - 3rd highest grossing class of medication

Healthline.com
Why Do People Get GERD?

- Pathiophysiology of GERD is complex
  - Multiple functional and anatomical processes at the GEJ which promote reflux
  - Weak LES pressure
  - Disruption of the integrity of the anatomical barrier at the GEJ
  - Crural diaphragm separates from LES due to upward slippage of proximal stomach → hiatal hernia
  - TLESRs: brief episodes of LES relaxation unrelated to swallowing or peristalsis
The “Ideal GERD Treatment”

- Augment LES pressure
- Reduce the number of TLESRs
- Improve esophageal clearance of refluxed gastric contents
- Accelerate gastric emptying
- Augment mucosal resistance
- Neutralize gastric acidity

Unfortunately, this does not exist
Fears of Long-Term PPI Use

- Enteric infections
- Pneumonia
- Low B12, Mg
- Bone disease
- Renal disease
- Dementia
- CVAs
Our Patients’ Concerns

- Decreased quality of life, well-being
- Complications of uncontrolled GERD
  - Esophagitis, Strictures
  - Extraesophageal symptoms
  - Barrett’s esophagus, esophageal cancer
- Financial burden of chronic PPI use
- Potential SEs of chronic PPI use
- Do I really need “actual surgery” for this?
  - Can’t I have something “less invasive?”
Development of Endoscopic Antireflux Therapy

- Born to address these challenges/concerns
  - To treat refractory GERD
  - To eliminate long-term PPI use
  - To eliminate the need for antireflux surgery
Nissen Fundoplication

- First performed in 1955 by Dr. Rudolph Nissen
- Fundus wrapped around lower portion of the esophagus to create a physical barrier and reinforce the LES
- Over 20-30K performed each year
Nissen – LOTUS Study

- Open, parallel-group, multicenter, RCT conducted in 11 European countries
- 248 patients → Laparoscopic surgery
- 266 patients → Esomeprazole (allowed to dose escalate)
- In both groups:
  - Mean age 45
  - Majority male (~70%)
  - Mean BMI 27

Nissen – LOTUS Study – 5 year F/U

- Decreased heartburn in LARS group (QoL scale)

Nissen – LOTUS Study – 5 year F/U

- Decreased regurgitation in LARS group (QoL scale)

Nissen – LOTUS Study – pH F/U

- Repeat 24-hour pH testing off therapy
- At 5 years, total time pH < 4
  - Esomeprazole group: 8.8% → 1.9%
  - LARS group: 8.6% → 0.7%
- Normalization of esophageal acid exposure after 5 years:
  - 72% in the esomeprazole group
  - 90% in the LARS group

Nissen – 10 year Follow-Up of Symptoms

- 2007 Study
- 829 patients who underwent lap Nissen
  239 (44%) > 10 years prior
- Symptom scores for heartburn
  \[8.8 \pm 3.2 \rightarrow 2.3 \pm 2.8\] post surgery
- 80% of patients rate symptoms as almost completely resolved or greatly improved

PPI Use After Nissen

- Overall, decreased, but more than one would think
- Study of 102 patients S/P Nissen from 1997-2000
  - Median post-surgical f/u 3 years
  - 53 patients (52%) on the same dose or decreased dose of PPI as before surgery
- Nationwide Danish Registry of 3,465 pts
  - 5, 10, and 15 year risks of taking a PPI were 29.4%, 41.4%, and 56.6% respectively

Madan A. Aliment Pharmacol Ther 2006;23(5):601-5
Nissen – Safety

- Overall a safe operation
- Wrap too high or too tight
- Recurrent hernia
- GI symptoms
  - Dysphagia, inability to vomit, gas bloat
Nissen – Need for Re-Do

- Estimated risk is up to 10%
- 16-year follow-up
  – 47 / 595 (7.9%) required re-do
- 20-year f/u of 1209 patients who underwent Nissen

<table>
<thead>
<tr>
<th>Reason</th>
<th>Nissen (n = 1209)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent reflux</td>
<td>20 (1.7)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>76 (6.3)</td>
</tr>
<tr>
<td>Hiatus hernia</td>
<td>38 (3.1)</td>
</tr>
<tr>
<td>Other reason</td>
<td>9 (0.7)</td>
</tr>
<tr>
<td>Total (all reasons)</td>
<td>143 (11.8)</td>
</tr>
</tbody>
</table>

Vignal JC et al. J Visc Surg 2012;149(1)
# Nissen – Summary

<table>
<thead>
<tr>
<th></th>
<th>Nissen Fundoplication</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYMPTOM CONTROL</td>
<td></td>
</tr>
<tr>
<td>DECREASED PPI USE</td>
<td></td>
</tr>
<tr>
<td>INCREASED LES PRESSURE</td>
<td></td>
</tr>
<tr>
<td>NORMALIZATION OF pH</td>
<td></td>
</tr>
<tr>
<td>SAFETY</td>
<td></td>
</tr>
<tr>
<td>DURABILITY</td>
<td></td>
</tr>
</tbody>
</table>
Radiofrequency Therapy (Stretta)

- Mederi Therapeutics, Inc.
- Originally cleared by the FDA in 2000
- Transoral catheter delivers low power RF energy through electrodes
  - Generates tissue temperatures (65°C to 85°C) at the end of the catheter to the LES and gastric cardia
- Outpatient procedure, takes ~ 1 hour
Stretta System

Reflux - weak muscle allows stomach contents to reflux into esophagus
Stretta Therapy - treats muscle with radiofrequency energy
Post-Stretta - thicker muscle prevents reflux
Stretta

- Definitive mechanism of action vis-à-vis GERD is not entirely clear
- Local inflammation
  - Collagen deposition
  - Muscular thickening of the LES
  - Improved barrier function
  - Neurolysis
  - Reduction in tissue compliance
  - Reduction in TLESRs
Four RCTs

- RF versus sham (2003)
- RF versus PPI (2008)
- Single and double dose RF versus sham (2010)
- RF versus sham (2012)

------------------------------------------

- Large Meta-analysis of all four (USF-2015)

Corley DA et al. Gastroenterology 2003;125:668-676
RCT #1 – RF versus Sham (2003)

- 35 patients → RF
- 29 patients → sham procedure
- Included patients:
  - Partially response to PPIs, positive pH study
  - Normal peristalsis and sphincter relaxation
  - 2 cm or smaller HH, No Barrett’s
- Follow-up at 6 and 12 months
- Primary outcomes:
  - Reflux symptoms and QoL
- Secondary outcomes:
  - Medication use, LES pressure, and esophageal acid exposure

Corley DA et al. Gastroenterology 2003;125:668-676
RCT #1 – RF versus Sham (2003)

At 6 months, no significant difference in daily medication use, esophageal acid exposure time, or LES pressure.

Symptom improvement persisted at 12 months.
RCT #2 – RF versus PPI (2008)

- 20 patients → RF
- 16 patients → PPI
- Included patients:
  - Positive pH study and/or esophagitis
  - Required maintenance PPI therapy
- Endpoints:
  - Primary - Stop or decrease PPI dose to < 50% of current dose
  - Secondary - 24-hour distal acid exposure and GERD-HRQOL scores

RCT #2 – RF versus PPI (2008)

- **At 6 months:**
  - 78% of RF patients reduced or stopped PPIs
- **At 12 months:**
  - This decreased to 56%
- **Most patients remained on a PPI**
- **At 12 months, no difference in:**
  - Heartburn scores
  - QoL surveys
  - Mean daily dose of PPI

RCT #2 – RF versus PPI (2008)

- No change in distal acid exposure
Large Meta-analysis of 4 RCTs (USF)

- % Time pH < 4 over 24 hours
  - 81 Stretta patients and 72 sham patients

- No significant benefit of Stretta over sham

Large Meta-analysis of 4 RCTs (USF)

- **Mean LES pressure**
  - 58 Stretta patients and 52 sham patients

- No statistically significant benefit of Stretta over sham

Large Meta-analysis of 4 RCTs (USF)

- Ability to stop PPI
  - 65 Stretta patients and 53 sham patients

- No statistical advantage of Stretta over sham

Large Meta-analysis of 4 RCTs (USF)

- **HRQoL**
  - 47 Stretta patients and 41 sham patients

- No statistically significant benefit of Stretta over sham

Stretta – Large Meta-analysis 2012

- 18 Studies composed of 1441 patients
  - 2 RCT and 18 case series
- Mean age 47.5 ± 7.2 years
- Men 52.9%
- Mean follow-up interval = 17.1 ± 15.5 mo.
- Evaluated (pre and post)
  - QoL, symptoms scores
  - Esophageal acid exposure
  - DeMeester Score
  - LES pressure
Pre and Post Stretta QoL Measures

Subjective Outcome Measurements

<table>
<thead>
<tr>
<th>Outcome Variables</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</th>
</tr>
</thead>
<tbody>
<tr>
<td>GERD-HRQL score</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 score</td>
<td>4</td>
<td>250</td>
<td>25.2</td>
<td>3.30</td>
<td>4.97</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>
</tr>
<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>
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<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>
</tbody>
</table>

Objective Outcome Measurements

<table>
<thead>
<tr>
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<th>Pre-Stretta</th>
<th>Post-Stretta</th>
<th>P</th>
</tr>
</thead>
<tbody>
<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>
</tr>
<tr>
<td>Johnson-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 (mm Hg)</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>

Stretta – Meta-analysis Conclusions

- Significant improvement in heartburn and QoL scores
- Objective measurements (acid exposure and DeMeester score) did not normalize
- No significant increase in LES pressure
## Safety

### MAUDE Database

- **4 Deaths**
- **6 Perforations**

### Table of Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Hospitalization</th>
<th>Reason</th>
<th>Permanent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>Esophageal perforation</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>N/A</td>
<td>Gastroparesis</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>Severe gastrointestinal bleed (requiring transfusion)</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>Esophageal perforation/ aspiration</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Yes</td>
<td>Esophageal perforation</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>Aspiration pneumonia/ esophageal perforation</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>N/A</td>
<td>Pleural effusion requiring thoracentesis</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>Yes</td>
<td>Aspiration pneumonia/ respiratory failure</td>
<td>Yes, death</td>
</tr>
<tr>
<td>9</td>
<td>N/A</td>
<td>Systemic inflammatory response syndrome</td>
<td>N/A</td>
</tr>
<tr>
<td>10</td>
<td>Yes</td>
<td>Mucosal tear</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>Yes</td>
<td>Atrial fibrillation</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>Yes</td>
<td>Esophageal perforation/ aspiration pneumonia/ respiratory failure</td>
<td>Yes, death</td>
</tr>
<tr>
<td>13</td>
<td>Yes</td>
<td>Esophageal perforation</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>Yes</td>
<td>Systemic inflammatory response syndrome</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>Yes</td>
<td>Esophageal perforation</td>
<td>No</td>
</tr>
<tr>
<td>16</td>
<td>No</td>
<td>Scarring from electrode on back</td>
<td>Yes</td>
</tr>
<tr>
<td>17</td>
<td>Yes</td>
<td>Bradycardia</td>
<td>Yes, death</td>
</tr>
<tr>
<td>18</td>
<td>No</td>
<td>Device malfunction</td>
<td>No</td>
</tr>
<tr>
<td>19</td>
<td>N/A</td>
<td>Device malfunction</td>
<td>No</td>
</tr>
<tr>
<td>20</td>
<td>N/A</td>
<td>Device malfunction</td>
<td>No</td>
</tr>
<tr>
<td>21</td>
<td>No</td>
<td>Hospitalization for unknown reason</td>
<td>Unknown</td>
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<tr>
<td>22</td>
<td>No</td>
<td>Device malfunction</td>
<td>No</td>
</tr>
<tr>
<td>23</td>
<td>No</td>
<td>Gastroparesis</td>
<td>Yes</td>
</tr>
<tr>
<td>24</td>
<td>Yes</td>
<td>Boorehaves/chest tube</td>
<td>No</td>
</tr>
<tr>
<td>25</td>
<td>Yes</td>
<td>Bradycardia/death</td>
<td>Yes, death</td>
</tr>
<tr>
<td>26</td>
<td>No</td>
<td>Device malfunction</td>
<td>No</td>
</tr>
</tbody>
</table>

Manufacturer and User Facility Device Experience Database


UNIVERSITY OF SOUTH FLORIDA
### Stretta – Summary

<table>
<thead>
<tr>
<th></th>
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<tr>
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<tr>
<td>SAFETY</td>
<td></td>
</tr>
<tr>
<td>DURABILITY</td>
<td></td>
</tr>
</tbody>
</table>
Transoral Incisionless Fundoplication
- EsophyX device inserted transorally
- Deploys ~ 20 full thickness fasteners circumferentially → wraps fundus around the distal esophagus to re-establish the anti-reflux barrier
- Takes approximately 1 hour

Source: Medgadget.com
## Multiple Iterations

<table>
<thead>
<tr>
<th>Name</th>
<th>Acronym</th>
<th>Fastener Placement</th>
<th>Plication Type</th>
<th>Wrap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoluminal Fundoplication</td>
<td>ELF</td>
<td>Below Z line</td>
<td>Gastrogastric</td>
<td>No</td>
</tr>
<tr>
<td>Transoral Incisionless Fundoplication 1.0</td>
<td>TIF 1.0</td>
<td>Above Z line 1 cm</td>
<td>Esophagogastric</td>
<td>No</td>
</tr>
<tr>
<td>Transoral Incisionless Fundoplication 2.0</td>
<td>TIF 2.0</td>
<td>1-3 cm above Z line; more length along greater curve of the stomach</td>
<td>Esophagogastric</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Source: Endogastricsolutions
<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>N</th>
<th>Intervention</th>
<th>Reduction in reflux symptoms</th>
<th>HRQL</th>
<th>Stopped or decreased PPI use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunter et al. [44]</td>
<td>RCT</td>
<td>129</td>
<td>Sham versus TIF</td>
<td>22% improvement with TIF, $P = 0.023$</td>
<td>8% improvement with TIF, $P = 0.108$</td>
<td>12% improvement with TIF, $P = 0.541$</td>
</tr>
<tr>
<td>Trad et al. [45]</td>
<td>RCT</td>
<td>63</td>
<td>PPI versus TIF</td>
<td>47% improvement with TIF, $P &lt; 0.001$</td>
<td>80% improvement with TIF, $P &lt; 0.001$</td>
<td>58% improvement with TIF, $P &lt; 0.001$</td>
</tr>
<tr>
<td>Witteeman et al. [46]</td>
<td>RCT</td>
<td>60</td>
<td>PPI versus TIF</td>
<td>55% improvement with TIF, $P &lt; 0.001$</td>
<td>51% improvement with TIF, $P &lt; 0.001$</td>
<td>10% improvement with TIF, $P &gt; 0.05$</td>
</tr>
<tr>
<td>Hakansson et al. [47]</td>
<td>RCT</td>
<td>44</td>
<td>Sham versus TIF</td>
<td>66% improvement with TIF, $P &lt; 0.0001$</td>
<td>29% improvement with TIF, $P = 0.0005$</td>
<td>41% improvement with TIF, $P = 0.01$</td>
</tr>
</tbody>
</table>
**A)** Only total number of reflux episodes normalized (NOT DeMeester or total time pH < 4) among TIF patients

**B)** Only 54% of TIF patients had pH normalization

**C)** No improvement in esoph acid exposure. Only 29% had pH normalization

---

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Patients</th>
<th>Intervention</th>
<th>Post-intervention esophageal acid exposure (% time pH &lt; 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunter et al. [44]</td>
<td>RCT</td>
<td>129</td>
<td>Sham vs TIF</td>
<td>3 % more time with TIF, $P = 0.003$</td>
</tr>
<tr>
<td>Trad et al. [45]</td>
<td>RCT</td>
<td>63</td>
<td>PPI vs TIF</td>
<td>2 % more time with TIF, $P &lt; 0.001$</td>
</tr>
<tr>
<td>Witteman et al. [46]</td>
<td>RCT</td>
<td>60</td>
<td>PPI vs TIF</td>
<td>13 % less time with TIF, $P = 0.228$</td>
</tr>
<tr>
<td>Hakansson et al. [47]</td>
<td>RCT</td>
<td>44</td>
<td>Sham vs TIF</td>
<td>49 % more time with TIF, $P = 0.003$</td>
</tr>
</tbody>
</table>

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Trad KS et al. Surg Innov 2015;22.
TIF – 12 Month Follow-Up Data

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>No.</th>
<th>Comparator</th>
<th>Reduction in reflux symptoms</th>
<th>HRQL</th>
<th>Stopped or decreased PPI use</th>
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<tr>
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<td>129</td>
<td>Sham versus TIF</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
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<td>63</td>
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<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Witteman et al. [46]</td>
<td>RCT</td>
<td>60</td>
<td>PPI versus TIF</td>
<td>27% improvement with TIF, $P &lt; 0.05$</td>
<td>10% improvement with TIF, $P &lt; 0.05$</td>
<td>8% improvement with TIF, $P &gt; 0.05$</td>
</tr>
<tr>
<td>Hakansson et al. [47]</td>
<td>RCT</td>
<td>44</td>
<td>Sham versus TIF</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

At 1 year →
60% on PPIs
< 30% with normal pH
**Not much long-term follow-up on these patients
TIF – Durability

- Few studies follow patients past 6-12 months
- One European study (2013):
  - 12/66 (18%) underwent revision ~ 2 years
  - 2 Nissens and 10 TIF
  - Highly insufficient gastroesophageal valve (Hill Grade 3 or 4)

### TIF – Safety

- **MAUDE Database – 5 years (2011-2016)**
  - 59 reports

<table>
<thead>
<tr>
<th>Incident / Complication</th>
<th>Number of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equipment Malfunction</td>
<td>24</td>
</tr>
<tr>
<td><strong>Perforation</strong></td>
<td><strong>22</strong></td>
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<tr>
<td>GI Bleeding</td>
<td>7</td>
</tr>
<tr>
<td>Likely Perforation / Abscess</td>
<td>3</td>
</tr>
<tr>
<td>Laceration / Tear</td>
<td>2</td>
</tr>
<tr>
<td>Mouth / Tongue Bleeding</td>
<td>2</td>
</tr>
<tr>
<td>Pleural Effusion</td>
<td>1</td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>1</td>
</tr>
</tbody>
</table>
# TIF – Summary

<table>
<thead>
<tr>
<th></th>
<th>TIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYMPTOM CONTROL</td>
<td></td>
</tr>
<tr>
<td>DECREASED PPI USE</td>
<td></td>
</tr>
<tr>
<td>INCREASED LES PRESSURE</td>
<td></td>
</tr>
<tr>
<td>NORMALIZATION OF pH</td>
<td></td>
</tr>
<tr>
<td>SAFETY</td>
<td></td>
</tr>
<tr>
<td>DURABILITY</td>
<td></td>
</tr>
</tbody>
</table>
LINX

- Small flexible band of interlinked titanium beads with magnetic cores
- Helps LES resist opening to increased gastric pressure → prevents reflux
- Force of swallowing, esophageal peristalsis break the bond → allows food/liquid to pass
- Closes LES after swallowing to restore reflux barrier
  - Designed to augment the LES
LINX – Placed Laparoscopically

Sizing tool determines the appropriate size LINX system

LINX positioned around the LES using suture tails

Ends of the LINX system are aligned

Source: toraxmedical.com
### Single-Arm Prospective Studies

<table>
<thead>
<tr>
<th>Type</th>
<th>N</th>
<th>Follow-up duration</th>
<th>GERD-HRQL score</th>
<th>Patients satisfied with GERD outcome</th>
<th>Patients off PPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single center</td>
<td>100</td>
<td>3 years (95% f/u)</td>
<td>Baseline: 24</td>
<td>87%</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 year: 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multicenter</td>
<td>44</td>
<td>3.7 years (&lt; 50% f/u)</td>
<td>Baseline: 25.7</td>
<td>86% (2 years)</td>
<td>90% (1 year)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 year: 3.8</td>
<td></td>
<td>86% (2 years)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>80% (4 years)</td>
</tr>
<tr>
<td>Multicenter</td>
<td>100</td>
<td>3 years (85% f/u)</td>
<td>Baseline: 27</td>
<td>94% (3 years)</td>
<td>87% (3 years)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 year: 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single center</td>
<td>66</td>
<td>5.8 months</td>
<td>Baseline: 26</td>
<td>92%</td>
<td>83%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 6 months: 6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sheu EG. Curr Opin Gastroenterol 2015;31(4):334-8
## Single-Arm Prospective Studies

<table>
<thead>
<tr>
<th>Type</th>
<th>N</th>
<th>Follow-up duration</th>
<th>Patients with normalized pH study</th>
<th>Patients having device removed</th>
<th>Patients with dysphagia</th>
<th>Patients able to belch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single center</td>
<td>100</td>
<td>3 years (95% f/u)</td>
<td>67%</td>
<td>3%</td>
<td>2% dilation</td>
<td>99%</td>
</tr>
<tr>
<td>Multicenter</td>
<td>44</td>
<td>3.7 years (&lt; 50% f/u)</td>
<td>77% (1 year)</td>
<td>6.8%</td>
<td>43%</td>
<td>100% (3 months)</td>
</tr>
<tr>
<td>Multicenter</td>
<td>100</td>
<td>3 years (85% f/u)</td>
<td>58% (1 year)</td>
<td>4%</td>
<td>68% (19% dilation)</td>
<td>97%</td>
</tr>
<tr>
<td>Single center</td>
<td>66</td>
<td>5.8 months</td>
<td></td>
<td>0%</td>
<td>6% dilation</td>
<td></td>
</tr>
</tbody>
</table>
Prospective Multicenter European Registry (2014)

- 202 LINX patients
- 47 Nissen fundoplication patients
- One year follow-up
- GERD-HRQOL
  - LINX: 20 → 3
  - Nissen: 23 → 3.5
- Regurgitation symptoms
  - LINX: 58.2% → 3.1%
  - Nissen: 60% → 13%

Prospective Multicenter European Registry (2014)

- Discontinuation of PPIs:
  - 81.8% LINX vs. 63% Nissen (p = 0.009)

- Re-operation
  - 4% LINX vs. 6.4% Nissen

<table>
<thead>
<tr>
<th>Measure</th>
<th>% of patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MSAD</td>
<td>LF</td>
</tr>
<tr>
<td>Bloating and gassy feeling(^a)</td>
<td>10.0</td>
<td>31.9</td>
</tr>
<tr>
<td>Difficulty swallowing(^a)</td>
<td>7.0</td>
<td>10.6</td>
</tr>
<tr>
<td>Ability to belch</td>
<td>98.4</td>
<td>88.9</td>
</tr>
<tr>
<td>Ability to vomit(^b)</td>
<td>91.3</td>
<td>44.4</td>
</tr>
</tbody>
</table>
Safety

- Four year follow-up of 44 patients
- 42/44 (95.5%) free from a serious event
- 1 patient → dysphagia → removal
- 20/44 (43%) mild dysphagia, resolved by 3 months
- No erosions
- 1 patient → removal for MRI
Safety – Device Erosion

- Review of MAUDE database and literature
  - Approximately 10-15 reports of device erosion

MRI with LINX?

- New version of LINX is MR conditional up to 1.5 Tesla
- LINX before 5/22/15 = 0.7 Tesla
- LINX may need to be removed

Source: toraxmedical.com
Contraindications

- Allergies to titanium, steel, nickel, iron
- Hernia $\geq$ 3 cm
- Not studied in Barrett’s, LA Grades C/D esophagitis, BMI $> 35$
- Be careful with pre-op dysphagia, esophageal motility disorders
  - LINX is a circumferential intervention
### LINX – Summary

<table>
<thead>
<tr>
<th>Feature</th>
<th>LINX</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYMPTOM CONTROL</td>
<td>Yes</td>
</tr>
<tr>
<td>DECREASED PPI USE</td>
<td>Yes</td>
</tr>
<tr>
<td>INCREASED LES PRESSURE</td>
<td>? (Probably)</td>
</tr>
<tr>
<td>NORMALIZATION OF pH</td>
<td>~ 60-70%</td>
</tr>
<tr>
<td>SAFETY</td>
<td></td>
</tr>
<tr>
<td>DURABILITY</td>
<td></td>
</tr>
</tbody>
</table>
Patient Selection Considerations and Recommendations

- Esophageal manometry in all patients!
- pH testing in almost all patients
  - Abnormal study should NOT be the sole criteria for intervention
- Be careful with the anxious / depressed patient!
  - Is IBS driving their symptoms?
Predicting Response to Nissen

- Hiatal hernia $>$ 4 cm, baseline HB/regurgitation, % time pH $<$ 4 is greater than 10%

Approximate Cost

<table>
<thead>
<tr>
<th></th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nissen</td>
<td>$12,000 - $20,000</td>
</tr>
<tr>
<td>Stretta</td>
<td>~ $3,000</td>
</tr>
<tr>
<td>TIF</td>
<td>Cost to hospital ~ $6,500</td>
</tr>
<tr>
<td>LINX</td>
<td>Device costs ~ $5,000 + Surgical Cost</td>
</tr>
</tbody>
</table>

Sources: newsmax.com, beckersasc.com, massdevice.com
# Does Insurance Cover All This?

<table>
<thead>
<tr>
<th></th>
<th>Nissen</th>
<th>Stretta</th>
<th>TIF</th>
<th>LINX</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCBS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aetna</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humana</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Medicare</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Considered investigational / experimental

* Evaluation on a case by case basis
  Is it medically necessary?
  Supportive documentation required

Companies provide assistance with obtaining reimbursement
<table>
<thead>
<tr>
<th></th>
<th>Nissen</th>
<th>Stretta</th>
<th>TIF</th>
<th>LINFX</th>
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<tbody>
<tr>
<td><strong>SYMPTOM CONTROL</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PPI USE</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>LESP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NORMALIZATION of pH</strong></td>
<td></td>
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<td><strong>SAFETY</strong></td>
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<td><strong>DURABILITY</strong></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Summary

- GERD is a common disease
- Newer treatments must be measured against the "gold standard"
  - Symptoms, pH control, safety, durability
- Stretta improves symptoms, but does not improve objective measurements
  - A very expensive antacid
- Durability of TIF is unclear; perforation risk
- LINX appears to be very promising
Summary

- Objective outcome measurements do not always parallel subjective outcome measurements
- Sometimes, newer is not always better
- ***Proper patient selection is critical***
To This Point…

- The Good
  - Nissen fundoplication
- The “Promising”
  - LINX
- The Bad / Ugly
  - TIF
  - Stretta