Trans-oral Incisionless Fundoplication (TIF) for GERD: When, Why & How

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Guiding Principles

- GERD IS A SPECTRUM DISEASE
- TREATMENT SHOULD BE INDIVIDUALIZED
- ENDOSCOPY & AMBULATORY PH IS KEY IN DETERMINING MECHANISM FOR GERD
- ENDOSCOPIC TREATMENT OPTIONS APPROPRIATE IN EARLY PHASE
All these patients have GERD, but in different parts of the spectrum

Status of the LES and Esophageal Acid Exposure

918 GERD patients with abnormal 24 hr pH score

Shahin & DeMeester DDW 2013

Mechanism of Action – Dynamic failure

Concept: Effacement Cause Dynamic Failure of the LES & its Exposure to the acid pocket
Anti-GERD Procedural Options

- Nissen Fundoplication
- Linx
- Stretta RF procedure
- TIF procedure with Esophyx device
- Muse procedure
- Apollo Overstitch

How to choose appropriate procedure/surgery?

- EGD
  - Hiatal hernia – length
  - Hill Grade – diaphragmatic hiatus – width
  - Presence of esophagitis – LA class
- pH study – upright vs supine reflux
- Esophageal manometry – on selected patients

Hiatal Hernia
Hill Grade

Esophagitis

Bravo pH
Esophageal manometry – Careful with the mimickers

Normal

Achalasia

Scleroderma

Where is my patient on the GERD Spectrum

Normal

Staining

Staining

Pancreas/duodenal
TIF procedure with EsophyX Device

Plication, Fastener Placement, Finished Valve

TIF Procedure Overview

270 degrees, 3 cm
Tissue Mold
Rotates stomach tissue around the distal esophagus superior to the z-line and compresses tissue prior to plication

Helical Retractor
Retracts stomach toward the esophagus and retracts gastroesophageal junction in the abdomen

Stylets & Fasteners
Transect apposed esophago-gastric tissues and provide tissue compression throughout the healing process

Invaginator
Reduces a hiatal hernia and positions fundoplication caudal to the diaphragm

EsophyX Z device
Used in concert, the elements of EsophyX device enable a true transoral fundoplication.
EsophyX TIF Procedure Evolution

<table>
<thead>
<tr>
<th>Name</th>
<th>Commercial Introduction</th>
<th>Commercial Cases (of 18,000)</th>
<th>% of Total Commercial Cases (of 18,000)</th>
<th>Plication Type</th>
<th>Fastener Placement</th>
<th>Avg. # of Fasteners</th>
<th>Wrap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transoral Incisionless Plication 2.0 (TIF 2.0)</td>
<td>2009</td>
<td>2068</td>
<td>95%</td>
<td>Esophagogastric</td>
<td>1 incision above Z-line, more length along the greater curvature of the stomach</td>
<td>12 to 22</td>
<td>Yes</td>
</tr>
<tr>
<td>Transoral Incisionless Plication 1.0 (TIF 1.0)</td>
<td>2007</td>
<td>472</td>
<td>3.2%</td>
<td>Esophagogastric</td>
<td>Above Z-line, 2cm</td>
<td>12</td>
<td>No</td>
</tr>
<tr>
<td>Endoluminal Plication (ELP)</td>
<td>2005</td>
<td>186</td>
<td>1.0%</td>
<td>Gastrogastric</td>
<td>Below Z-line</td>
<td>18</td>
<td>No</td>
</tr>
</tbody>
</table>

TIF procedure evolution

Mechanism of Action – similar to Lap Nissen

<table>
<thead>
<tr>
<th>Principles of Laparoscopic Nissen Fundoplication</th>
<th>TIF</th>
<th>Endoluminal Fundoplication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce Relativities 2 cm above Z-line</td>
<td>D2</td>
<td>D2</td>
</tr>
<tr>
<td>Repair Relativities in Z-line and other areas</td>
<td>D2</td>
<td>D2</td>
</tr>
<tr>
<td>Untangle the intrathoracic esophagus</td>
<td>D3</td>
<td>D3</td>
</tr>
<tr>
<td>Fundoplication</td>
<td>D3</td>
<td>D3</td>
</tr>
<tr>
<td>Approximate and tighten the fundus around the initial esophagus</td>
<td>D3</td>
<td>D3</td>
</tr>
<tr>
<td>Secure the esophagus at the angle of His</td>
<td>D3</td>
<td>D3</td>
</tr>
<tr>
<td>Restore the distal high pressure zone</td>
<td>D2</td>
<td>D2</td>
</tr>
</tbody>
</table>
**pH Changes Post TIF**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Pre</th>
<th>Post</th>
<th>p</th>
<th>Normalized pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bell and Freeman</td>
<td>18</td>
<td>37.1</td>
<td>16.9</td>
<td>&lt;0.001</td>
<td>54%</td>
</tr>
<tr>
<td>Cadoret al</td>
<td>71</td>
<td>34</td>
<td>28</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Petersen et al</td>
<td>14</td>
<td>32.5</td>
<td>19.3</td>
<td>&lt;0.01</td>
<td>43%</td>
</tr>
<tr>
<td>TIF registry</td>
<td>20</td>
<td>34.4</td>
<td>17.2</td>
<td>&lt;0.001</td>
<td>55%</td>
</tr>
<tr>
<td>Tempo</td>
<td>39</td>
<td>35.3</td>
<td>25.3</td>
<td>0.016</td>
<td>45%</td>
</tr>
<tr>
<td>Respect</td>
<td>76</td>
<td>33.6</td>
<td>23.9</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Commercial Experience Overview**

- 20,000+ procedures performed
- Severe adverse events (SAE): 0.38% (compared to colonoscopies: 1.6%)

- Perforation, laceration, or tear of the esophagus
- Pleural effusion
- GEJ leak
- GI bleeding
- Mediastinitis/mediastinal abscess
- Gastric perforation

**Summary: Recent Key Studies**
US studies (TIF 2.0) 10 studies; n= 527 patients
- PPI use
  75% completely off / 8% occasional use

US studies (TIF 2.0) 4 studies; n= 82 patients
- Healing of esophagitis
  82% completely healed / 4% improved

Level I: RESPECT

- A multi-center, randomized, single-blind, controlled TIF/Placebo vs. Sham/PPI trial
- To compare safety and effectiveness of TIF vs. PPIs in patients with “troublesome symptoms”, specifically regurgitation.
- 2:1 ratio TIF group (n=57) vs Sham/PPI group (n=45)

<table>
<thead>
<tr>
<th>Duration</th>
<th>6 months, 1 year w/ crossover</th>
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</thead>
<tbody>
<tr>
<td>Key Outcomes</td>
<td></td>
</tr>
<tr>
<td>Troublesome regurgitation was eliminated in 72%</td>
<td></td>
</tr>
<tr>
<td>Median heartburn score decreased from 17 to 5 at 6 months</td>
<td></td>
</tr>
<tr>
<td>Median heartburn score further decreased to 3, at &gt;1 year</td>
<td></td>
</tr>
<tr>
<td>72% of TIF pts off PPIs &gt;1 year</td>
<td></td>
</tr>
</tbody>
</table>

Level I: Tempo

- A multi-center, randomized, open-label, controlled TIF vs PPI trial
- To compare safety and efficacy of TIF vs. PPIs for the treatment of chronic medically refractory GERD.
- 2:1 ratio TIF Group (n=40) vs PPI group (n=23)

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<th>Duration</th>
<th>6 months, 1 year w/ crossover, 3 years</th>
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<tr>
<td>Key Outcomes</td>
<td></td>
</tr>
<tr>
<td>All outcome measures were stable at 1Y, 2Y &amp; 3Y follow up (seeing similar outcomes with 4 year data collection)</td>
<td></td>
</tr>
<tr>
<td>Esophagitis healed in 86% or patients at 3Y follow up</td>
<td></td>
</tr>
<tr>
<td>71% of pts. Off PPI at 3Y follow up</td>
<td></td>
</tr>
<tr>
<td>pH improvement remained stable at 3Y</td>
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</tbody>
</table>
Sustained elimination of regurgitation up to 4 years

Regurgitation scores
Improvement achieved at 1 year follow up remained stable up to 4 years
Sustained elimination of atypical symptoms up to 4 years

R1 scores
Sustained improvement in R1 scores up to 4 years

Global Sustained elimination of regurgitation atypical symptoms up to 4 years
Conclusions

- TIF provides durable long term control of regurgitation, heartburn, and atypical symptoms post procedure in a subset of chronic GERD patients with small (<2 cm) hiatal hernia
- TIF is a proven endoscopic alternative to control troublesome GERD symptoms in well selected patients with trouble some symptoms on maximum dose PPI before procedure
- TIF is now considered as an alternative treatment modality for a subset of GERD patients
- FDA expanded label, June 2017: patients with hiatal hernias larger than 2 cm may be included, when a laparoscopic hiatal hernia repair reduces the hernia to 2 cm or less

HRQL scores

Improvement achieved at 1 year follow up remained stable up to 4 years

Satisfaction of Current Health Condition Sustained up to 4 years
Medical Society Support

American Gastroenterological Association (AGA)

Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)

American College of Gastroenterology (ACG)

American Society of General Surgeons (ASGS)

AGA Technology Coverage Statement (April 2016)

“Recognizing that the AGA medical position statement on the management of GERD has not been updated since 2008, AGA convened a multi-disciplinary workgroup to develop a framework for selected services and procedures related to the diagnosis and treatment of GERD.”

“The goal of therapy is to control both the symptoms and mucosal damage.”

“This procedure delivers patient outcomes similar to those provided by conventional anti-reflux surgery (ARS) procedures and does not limit future treatment options.”

“In conclusion, the three-year plus evidence is sufficient to demonstrate sustainable improvement in health outcomes, symptom relief, decrease in PPI utilization and improvement in esophageal pH with transoral fundoplication.”

SAGES Spotlight Guideline Review (March 2017)

Recommendation: “++++/Strong Recommendation”

Symptom Control: “Compared with PPI treatment, TIF has clearly demonstrated to be more effective in controlling patient GERD symptoms six months post-procedure.”

Objective Outcomes: “Compared with sham controls, esophageal acid exposure time has been shown to improve significantly after TIF and be similar to that of patients on PPIs. Total number of reflux episodes were fewer compared with those on PPIs.”
Case scenario

Normal 48h pH study

Mr. Burn’s pH study note multiple episodes of pH<4 (arrows)