Endoscopic Treatments of GERD
Introduction

- Standard care for GERD
  - Lifestyle modification
  - Acid suppression
  - Surgical fundoplication
    - Incomplete response to medical management

⇒ 30~40% : poorly controlled reflux despite PPI therapy
Introduction

- Concerns about treatment
  - Long-term PPI therapy
    - Osteopenia, dementia, CKD, coronary artery disease
  - Surgical fundoplication
    - Invasive procedure
    - Dysphagia, diarrhea, gas bloat syndrome

→ Need for a minimally invasive procedure
Introduction

- Endoscopic therapies for GERD
  - Reinforcement of LES by injection
  - Endoscopic fundoplication
    - Transoral incisionless fundoplication (TIF) using EsophyX, MUSE
  - Radiofrequency energy delivery to LES
    - Using Stretta device
Transoral incisionless fundoplication
TIF using EsophyX device

- FDA approved in 2007
- Creation of a gastric fundal wrap with plication
TIF using Esophyx device

- **Technique**
  - General anesthesia
  - **Endoscopy**
    - Evaluate for a hiatal hernia
    - Assess Hill grade of valve
    - Rule out mucosal abnormality
TIF using EsophyX device

- Technique
  - Attach Esophyx device
  - Non-absorbable polypropylene fastners
  - Create a 200°~300° partial fundoplication with a valve of 3~5cm
  - Multiple iterations
Efficacy of TIF

- Improvement in GERD symptoms
- Cessation or reduction of PPI use
- Reduction in esophageal acid exposure (EAE) time
- Clinical improvement
# Efficacy of TIF

- **RESPECT trial**
  - TIF + placebo medication vs sham procedure + PPI

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<tbody>
<tr>
<td>Transoral incisionless fundoplication (TIF)</td>
<td>Hunter et al. [13] RESPECT Trial (2015)</td>
<td>6 months</td>
<td>67% of TIF patients no longer had regurgitation vs. 45% in sham group ($p = 0.023$)</td>
<td>Not available</td>
<td>- TIF patients had decrease in esophageal acid exposure time from 9.3 before TIF to 6.4 after ($p &lt; 0.001$) - Mean</td>
<td></td>
<td>Temporary abdominal pain, Chest pain, Dysphagia, Nausea</td>
</tr>
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DeMeester score improved in TIF ($p < 0.001$)
Efficacy of TIF

- TEMPO trial
  - TIF vs high-dose PPI
  - Similar results

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<tr>
<td>Trad et al. [14] TEMPO Trial (2017)</td>
<td>Randomized controlled trial Crossover study</td>
<td>3 years</td>
<td>Average Reflux Symptom Index score improved from 22.2 to 4 at 3-year post-TIF ($p &lt; 0.0001$)</td>
<td>At 3 years, 71% of TIF patients stopped PPI therapy</td>
<td>- Esophageal acid exposure time improved from 10.5 to 7.8 at 3 years ($p = 0.03$)</td>
<td>Subjective Objective</td>
<td>Not available at 3 years</td>
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### Efficacy of TIF

- **Systematic review**

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<tr>
<td>Wendling et al. [15] (2013)</td>
<td>Systematic review</td>
<td>8.5 months</td>
<td>GERD-HRQL score was improved (21.9 vs. 5.8, p &lt; 0.0001)</td>
<td>The PPI discontinuation rate was 67% across studies</td>
<td>Inconsistent results in esophageal acid exposure times</td>
<td>Subjective</td>
<td>Hemorrhage (1.2%), esophageal perforation (0.7%), pneumothorax (0.4%), TIF failure (7.2%)</td>
</tr>
<tr>
<td>Huang et al. [18] (2016)</td>
<td>Systematic review</td>
<td>Variable</td>
<td>Improved total number of refluxes following TIF vs. PPI/sham (24.5 vs. 5.4, p ≤ 0.0001)</td>
<td>No significant improvement/-reduction in PPI use</td>
<td>No significant improvement in esophageal acid exposure times</td>
<td>Subjective</td>
<td>Perforation (7/781), Bleeding (5/781), Pneumothorax (4/781), Death (1/781)</td>
</tr>
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Most of the patients resumed PPI at reduced dosage during long-term f/u.
### Efficacy of TIF

- **TIF vs laparoscopic fundoplication**
  - No RCT

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<tr>
<td>Toomey et al. [17] (2014)</td>
<td>Case-control (TIF vs. laparoscopic Nissen vs. Toupet fundoplication)</td>
<td>Not available</td>
<td>Similar symptom reduction rates between all 3 groups</td>
<td>Not available</td>
<td>Not available</td>
<td>Subjective</td>
<td>None with TIF</td>
</tr>
<tr>
<td>Frazzoni et al. [11] (2011)</td>
<td>Open-label trial (TIF vs. laparoscopic fundoplication)</td>
<td>3 months</td>
<td>Continued reflux symptoms on follow up in TIF group compared to surgical group ($p = 0.003$)</td>
<td>Not available</td>
<td>- EAE time normal in 50% of patients post TIF vs. 100% post-surgery ($p = 0.033$)</td>
<td>Laparoscopic fundoplication more effective objectively and subjectively</td>
<td>Not available</td>
</tr>
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TIF: shorter operative time, length of stay
Efficacy of TIF

- Predictors of a positive outcome with EsophyX
  - Hill grade 1 or 2
  - No hiatal hernia or Deformity < 2cm
  - Normal motility
  - Use of 20 or more fasteners
Complications of TIF

- Severe complications: rare
  - Esophageal perforation: 7 patients
  - Bleeding: 5 patients
  - Pneumothorax: 4 patients
Complications of TIF

- Common adverse events
  - Dysphagia
  - Chest pain
  - Bloating
  - Pharyngeal irritation
Stretta

- FDA approved in 2000
- Delivery of radiofrequency energy to muscle layer of LES
Technique

- Upper endoscopy
  - Visualize squamocolumnar junction (SCJ)
  - Measure SCJ distance from the incisors

- Stretta catheter
  - Advance over a guidewire
  - Deliver thermal energy to the muscularis propria
  - 1cm proximal to SCJ ~ LES ~ gastric cardia
Stretta

- Mechanism: not entirely understood
  - Thermal injury: scar tissue formation, neurolysis, ↑collagen deposition
  
  ↓LES thickness
  - Variable correction of LES incompetence
  - ↓Frequency, intensity of TLESR
### Efficacy of Stretta

- **Randomized sham-controlled trial**

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<td>Stretta</td>
<td>Randomized controlled trial (Stretta vs. sham crossover study)</td>
<td>6–12 months</td>
<td>-Improved mean heartburn score by 61 vs. 33% in sham ($p = 0.05$)</td>
<td>No difference between both groups ($n = 17$ (55%) in Stretta vs. $n = 14$ (61%) in sham $p = 0.67$)</td>
<td>-Median 24 h pH $&lt; 4$: 10.7 in Stretta vs. 9.9 in sham ($p = 0.79$)</td>
<td>Subjective: Chest pain (11%) Nausea/vomiting (9%) Abdominal Pain (3%) Bleeding esophageal ulcer (3%)</td>
<td></td>
</tr>
<tr>
<td>Corley et al. [29] (2002)</td>
<td>Randomized controlled trial (Stretta vs. sham crossover study)</td>
<td>6–12 months</td>
<td>-Improved mean HRQL score by 61 vs. 30% in sham ($p = 0.03$)</td>
<td>Subjective:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coron et al. [30] (2008)</td>
<td>Randomized controlled trial (Stretta vs. PPI)</td>
<td>12 months</td>
<td>No difference between groups in HR-QOL scores ($p = 0.5$) - No significant difference between groups in 18/20 patients stopped/decreased PPI use in Stretta vs. 8/16 in the PPI group ($p = 0.01$)</td>
<td>No difference in esophageal acid exposure between both groups ($p = 0.27$) - No difference in esophagitis ($p = 0.97$)</td>
<td>Subjective:</td>
<td></td>
<td></td>
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64 patients

43 patients
### Efficacy of Stretta

- **Randomized sham-controlled trial**

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<td>Aziz et al. [31] (2010)</td>
<td>Randomized controlled trial (single dose vs. double dose Stretta vs. sham)</td>
<td>12 months</td>
<td>- HRQOL score improved in double Stretta vs. single Stretta ($p &lt; 0.05$), in double Stretta vs. sham ($p &lt; 0.05$). No improvement in single Stretta compared to sham ($p &gt; 0.05$)</td>
<td>Significant reduction or going off PPI in Stretta groups compared to sham ($p &lt; 0.001$)</td>
<td>Esophageal acid exposure time in - Sham</td>
<td>Group 9 ± 1.2 6.2 to 8.2 ± 3.1 min ($p &gt; 0.05$)</td>
<td>Prolonged gastroparesis (16.6% in double Stretta), Mucosal laceration (8.3% in Stretta groups), Pleural effusion (8.3% in single Stretta group), Abdominal pain (8.3% in all groups)</td>
</tr>
<tr>
<td>Arts et al. [27] (2012)</td>
<td>Randomized controlled trial (Stretta vs. sham crossover study)</td>
<td>3–6 months</td>
<td>Stretta/sham: Symptom score improved ($p &lt; 0.005$) after Stretta but not after sham Sham/Stretta: No initial improvement in score ($p = $ NS) but improved after Stretta ($p &lt; 0.05$)</td>
<td>- No improvement in EAE or LES pressure.</td>
<td>Subjective</td>
<td>Not available</td>
<td></td>
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</table>

- Higher dose Stretta 36 patients
- Double dose 3 arms

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**Note:** Stretta is a procedure used to treat GERD by creating a barrier at the GEJ. The table summarizes the efficacy of different dosing regimens in randomized sham-controlled trials.
### Meta-analysis

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<tr>
<td>Perry et al. [32] (2012)</td>
<td>Meta-analysis</td>
<td>Variable</td>
<td>Stretta improves heartburn scores ( p = 0.001 ) and GERD-HRQL score ( p = 0.001 )</td>
<td>No improvement in esophageal acid exposure times and LES pressure</td>
<td>Very low evidence</td>
<td>Esophageal perforation, pleural effusion, aspiration pneumonia, bradycardia, death</td>
<td></td>
</tr>
<tr>
<td>Lipka et al. [33] (2015)</td>
<td>Meta-analysis</td>
<td>Variable</td>
<td>No difference in HRQL scores compared to control group (sham or PPI)</td>
<td>No difference in ability to stop PPI between Stretta and control group</td>
<td>No difference in esophageal acid exposure time</td>
<td>No difference in LES pressure</td>
<td></td>
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- **Total studies:** 18
- **Total patients:** 1,441
- **RCTs:** 4
- **Patients per RCT:** 165
### Long-term efficacy

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<tr>
<td>Dughera et al. [34] (2014)</td>
<td>Randomized Controlled Trial</td>
<td>8 years</td>
<td>Decrease in heartburn score and GERD-HRQL scores at 4 years ($p = 0.001$) and at 8 years ($p = 0.003$)</td>
<td>At 4 years: 21/26 were off PPI - After 8 years: 21/26 were off PPIs.</td>
<td>Median LES pressure: no significant amelioration at 4 and 8 years ($p = 0.001$) but back to baseline at 8 years</td>
<td>Subjective</td>
<td>Transient severe gastroparesis in one patient</td>
</tr>
</tbody>
</table>
Complications of Stretta

- Serious adverse events
  - Esophageal perforation
  - Permanent gastroparesis
  - Aspiration pneumonia
  - Cardiac arrest
Complications of Stretta

- Minor adverse events
  - Dysphagia
  - Odynophagia
  - Hoarseness
  - Epigastric, retrosternal discomfort
Endoscopic fundoplication using MUSE™
MUSE™

- FDA approved in 2014
- An ultrasound and video-guided endoscopic stapler
- Creation of partial anterior fundoplication
Technique

- General anesthesia
- Staple cartridge
  - 3cm proximal to GE junction
- Two screws
  - Compress fundus against esophagus
- Tissue thickness
  - Monitoring using US
  - 1.4 ~ 1.6 cm: stapler fire
### Efficacy of MUSE™

- **Multicenter prospective trial**

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<tr>
<td>Medigus Ultrasonic Surgical Endostapler (MUSE)</td>
<td>Open-label trial</td>
<td>6 months</td>
<td>- GERD-HRQL score dropped to 6 when tested off PPI at 6 months compared to 15 at baseline on PPI ($p &lt; 0.001$) and a 29 off PPI ($p &gt; 0.001$)</td>
<td>64% of patients stopped using PPI</td>
<td>- EAE time: 10.9% at baseline off PPI vs. 7.3% at 6 months off PPI ($p &lt; 0.001$)</td>
<td>- No difference in manometric findings at 6 months compared to baseline</td>
<td>Pain + fever: Pneumothorax GI bleed, Pleural effusion, Esophageal leak</td>
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66 patients
### Multicenter prospective trial - follow up data

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<tr>
<td>Kim et al. [36] (2016)</td>
<td>Open-label trial</td>
<td>4 years</td>
<td>Decrease in the GERD-HRQL score to 5.3 ± 5.8 at 4 years vs. 29.1 ± 5.6 at baseline and 8.9 ± 8.3 at 6 months (p &lt; 0.01)</td>
<td>Less patients off PPI compared to baseline.</td>
<td>No significant difference in EAE times</td>
<td>Subjective</td>
<td>None</td>
</tr>
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</table>
Complications of MUSE™

- Serious adverse events
  - Pneumothorax
  - Bleeding
  - Esophageal perforation

- Common side effects
  - Chest pain (22%)
  - Sore throat (15%)
Summary

- **TIF with EsophyX**
  - Symptom control, PPI reduction/cessation up to 6 years
  - Improvement in objective parameters

- **Stretta**
  - ↓GERD symptoms, ↑QoL scores up to 8 year post-intervention
  - No consistent improvement in objective parameters

- **MUSE™**
  - Advantages over Esophyx: having US guidance, single operator
  - Not enough evidence
Final considerations

- Careful patient selection
  - Non-erosive reflux disease or Los Angeles grade A/B
  - Without severe anatomic distortion
    - Large hiatal hernia, severe esophageal dysmotility
  - Unwilling to take long-term PPI
  - Averse to fundoplication
  - Symptoms in spite of PPI use
Final considerations

- Patient education
  - Not an alternative to medical therapy or surgical fundoplication
  - Side effects can be serious

- Adequate endoscopist training
Conclusion

- Endoscopic therapies
  - Offer an treatment option
  - Bridge the gap between medical therapy and surgical fundoplication
Thank you for your attention