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Endoscopic Treatments of GERD

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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

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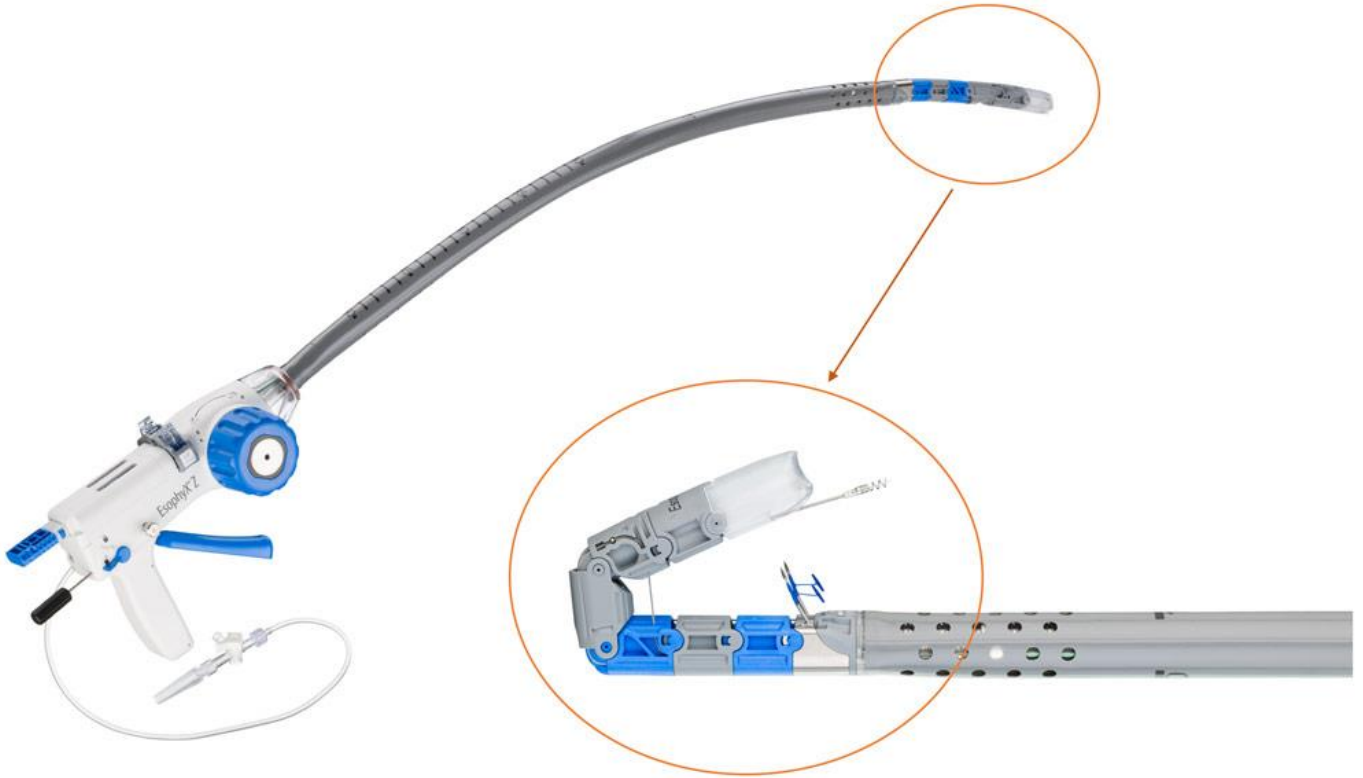
Transoral incisionless fundoplication

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

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Transoral incisionless fundoplication (TIF)							
Hunter et al. [13] RESPECT Trial (2015)	Randomized controlled trial (TIF vs. sham)	6 months	67% of TIF patients no longer had regurgitation vs. 45% in sham group ($p = 0.023$)	Not available	-TIF patients had decrease in esophageal acid exposure time from 9.3 before TIF to 6.4 after ($p < 0.001$) -Mean DeMeester score improved in TIF ($p < 0.001$)	Subjective Objective	Temporary abdominal pain Chest pain Dysphagia Nausea

Efficacy of TIF

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

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Trad et al. [14] TEMPO Trial (2017)	Randomized controlled trial Crossover study	3 years	Average Reflux Symptom Index score improved from 22.2 to 4 at 3-year post-TF ($p < 0.0001$)	At 3 years, 71% of TIF patients stopped PPI therapy	-Esophageal acid exposure time improved from 10.5 to 7.8 at 3 years ($p = 0.03$)	Subjective Objective	Not available at 3 years

Efficacy of TIF

- Systematic review

550 procedures

963 patients

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Wendling et al. [15] (2013)	Systematic review	8.5 months	-GERD-HRQL score was improved (21.9 vs. 5.9, $p < 0.0001$) -RSI score was improved (24.5 vs. 5.4, $p \leq 0.0001$)	The PPI discontinuation rate was 67% across studies	Inconsistent results in esophageal acid exposure times	Subjective	Hemorrhage (1.2%), esophageal perforation (0.7%), pneumothorax (0.4%), TIF failure (7.2%)
Huang et al. [16] (2016)	Systematic review	Variable	Improved total number of refluxes following TIF vs. PPI/sham	No significant improvement/-reduction in PPI use	No significant improvement in esophageal acid exposure times	Subjective	Perforation (7/781) Bleeding (5/781) Pneumothorax (4/781) Death (1/781)

Most of the patients resumed PPI at reduced dosage during long-term f/u

Efficacy of TIF

- TIF vs laparoscopic fundoplication
  - No RCT

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Toomey et al. [17] (2014)	Case-control (TIF vs. laparoscopic Nissen vs. Toupet fundoplica-tion)	Not available	Similar symptom reduction rates between all 3 groups	Not available	Not available	Subjective	None with TIF
Frazzoni et al. [11] (2011)	Open-label trial (TIF vs. laparoscopic fundoplica-tion)	3 months	Continued reflux symptoms on follow up in TIF group compared to surgical group ($p = 0.003$)	Not available	-EAE time normal in 50% of patients post TIF vs. 100% post-surgery ($p = 0.033$)	Laparoscopic fundoplica-tion more effective objectively and subjectively	Not available

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

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Stretta

Stretta

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

Stretta

- 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

64 patients

43 patients

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Stretta							
Corley et al. [29] (2002)	Randomized controlled trial (Stretta vs. sham crossover study)	6–12 months	-Improved mean heartburn score by 61 vs. 33% in sham ($p = 0.05$) -Improved mean HRQL score by 61 vs. 30% in sham ($p = 0.03$)	No difference between both groups ($n = 17$ (55%) in Stretta vs. $n = 14$ (61%) in sham $p = 0.67$)	-Median 24 h pH < 4: 10.7 in Stretta vs. 9.9 in sham ($p = 0.79$)	Subjective	Chest pain (11%) Nausea/vomiting (9%) Abdominal Pain (3%) Bleeding esophageal ulcer (3%)
Coron et al. [30] (2008)	Randomized controlled trial (Stretta vs. PPI)	12 months	-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 ($p = 0.01$)	-No difference in esophageal acid exposure between both groups ($p = 0.27$) -No difference in esophagitis ($p = 0.97$)	Subjective	4 patients with transient epigastric discomfort, transient odynophagia, 2 fever episodes

Efficacy of Stretta

- Randomized sham-controlled trial

Higher dose Stretta
36 patients

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Aziz et al. [31] (2010)	Randomized controlled trial (single dose vs. double dose Stretta vs. sham)	12 months	-HRQL score improved in double Stretta vs. single Stretta ($p < 0.05$), in double Stretta vs. sham ($p < 0.05$). -No improvement in single Stretta compared to sham ($p > 0.05$)	Significant reduction or going off PPI in Stretta groups compared to sham ($p < 0.001$)	Esophageal acid exposure times in: -Sham group: 9.9 ± 2.6 to 8.2 ± 3.1 min ($p > 0.05$) -Single Stretta group: 9.4 ± 3.4 to 6.7 ± 2.8 min($p < 0.01$) -Double Stretta: 8.8 ± 2.8 to5.2 ± 2.4 min ($p < 0.01$)	Subjective Objective	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)
Arts et al. [27] (2012)	Randomized controlled trial (Stretta vs. sham crossover study)	3–6 months	Stretta/sham: Symptom score improved ($p < 0.005$) after Stretta but not after sham Sham/Stretta: No initial improvement in score (p = NS) but improved after Stretta ($p < 0.05$)	Stretta/sham: no improvement Sham/Stretta: no improvement	-No improvement in EAE or LES pressure.	Subjective	Not available

3 arms

Double dose

Efficacy of Stretta

- Meta-analysis

18 studies
1441 patients

4 RCTs
165 patients

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Perry et al. [32] (2012)			Stretta improves heartburn scores (p = 0.001) and GERD-HRQL score (p = 0.001)		No improvement in esophageal acid exposure times and LES pressure		
Lipka et al. [33] (2015)	Meta-analysis	Variable	-No difference in HRQL scores compared to control group (sham or PPI)	-No difference in ability to stop PPI between Stretta and control group	-No difference in esophageal acid exposure time -No difference in LES pressure	Very low evidence	Esophageal perforation, pleural effusion, aspiration pneumonia, bradycardia, death

Efficacy of Stretta

- Long-term efficacy

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Dughera et al. [34] (2014)	Randomized Controlled Trial	8 years	Decrease in heartburn score and GERD-HRQL scores at 4 years (p = 0.001) and at 8 years (p = 0.003)	-At 4 years: 21/26 were off PPI -After 8 years: 21/26 were off PPIs.	-Median LES pressure: no significant amelioration at 4 and 8 years -Mean esophageal acid exposure: significant improved at 4 years (p = 0.001) but back to baseline at 8 years	Subjective	Transient severe gastroparesis in one patient

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

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Endoscopic fundoplication using MUSE™

MUSE™

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

MUSE™

- Technique
  - General anesthesia
  - Staple catridge
    - 3cm proximal to GE junction
  - Two screws
    - Compress fundus against esophagus
  - Tissue thickness
    - Monitoring using US
    - 1.4 ~ 1.6cm : stapler fire

Efficacy of MUSE™

- Multicenter prospective trial

66 patients

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Medigus Ultrasonic Surgical Endostapler (MUSE)							
Zacherl et al. [35] (2015)	Open-label trial	6 months	-GERD-HRQL score dropped to 6 when tested off PPI at 6 months compared to 15 at baseline on PPI ($p <$ 0.001) and a 29 off PPI ($p >$ 0.001)	64% of patients stopped using PPI	-EAE time: 10.9% at baseline off PPI vs. 7.3% at 6 months off PPI ($p <$ 0.001) -No difference in manometric findings at 6 m months compared to baseline	Subjective Objective	Pain + fever Pneumothorax GI bleed Pleural effusion Esophageal leak

Efficacy of MUSE™

- Multicenter prospective trial - follow up data

Study (year)	Study design	Total follow-up time	Subjective improvement with endoscopic procedure	Off PPI therapy after endoscopic procedure	Objective improvement after endoscopic procedure	Efficacy of endoscopic procedure	Complications after endoscopic procedure
Kim et al. [36] (2016)	Open-label trial	4 years	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 ($p < 0.01$)	Less patients off PPI compared to baseline.	No significant difference in EAE times	Subjective	None

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

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Thank you for your attention