



Pacific Northwest **GI and Liver Update**

Powered by: Liver Institute Northwest

*A conference featuring cutting-edge clinical
updates on the latest advances in the field*

September 15 –16, 2023



Endoscopic Treatments for GERD: An Update on Transoral Incisionless Fundoplication

V. Raman Muthusamy, MD, MAS

Medical Director of Endoscopy, UCLA Health System

Professor of Clinical Medicine

David Geffen School of Medicine at UCLA

Disclosures

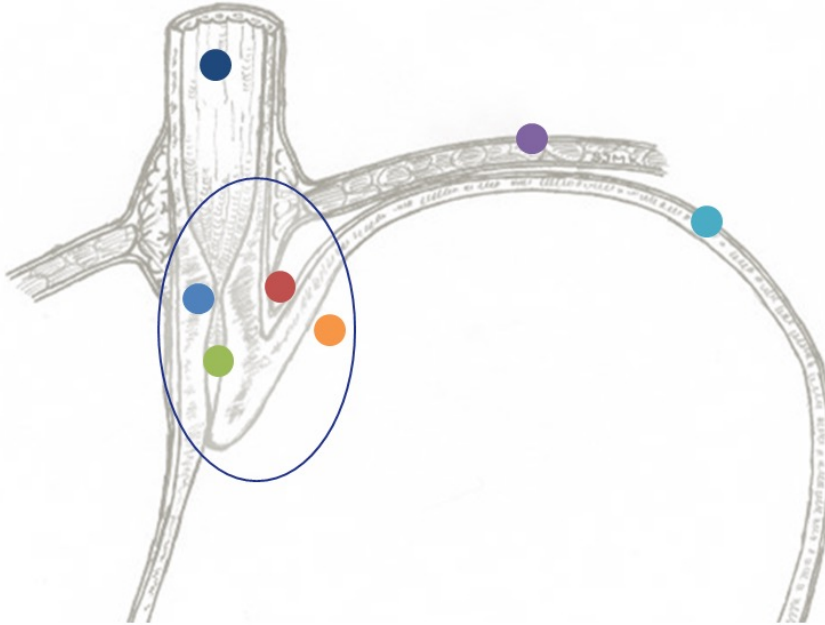
- Consultant, Research Support - Boston Scientific
- Consultant, Research Support - Medtronic
- Honoraria Recipient - Ethicon/Torax Medical
- Consultant – Interpace Diagnostics
- Consultant – Medivators
- Stockholder - Capsovision

Overview

- Why have prior endoscopic anti-reflux devices failed?
- The TIF procedure
- Indications, Patient work-up and Post-TIF care
- Evidence Summary
- Conclusions

Anatomy of the GEJ

Anatomy: Normal Valve Structures

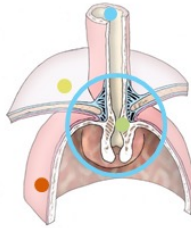


- **Esophagus**
- **Lower Esophageal Sphincter (LES)**
 - Relaxes to allow swallowing
- **Angle of HIS**
- **Z Line**
 - Marks where stomach and esophagus meet
- **Diaphragm**
- **Fundus**
- **Gastroesophageal Flap Valve (GEV)**
 - 180° flap valve, maintains closure against lesser curve of stomach
 - Is closed by pressure in the stomach to prevent reflux

Anatomical Causes for GERD

Normal

Normal, strongly established GEV



The antireflux barrier is an anatomically complex zone whose integrity has been attributed to:

● Esophagus

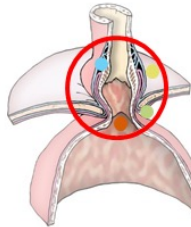
● Diaphragm

● Stomach

● Lower Esophageal Sphincter (LES)

GERD

Deficiencies



● Phreno-esophageal Membranes

- Deterioration results in loss of elasticity
- GEJ not returned to abdominal cavity following swallow

● Angle of His

- Loss of angle decreases barrier strength

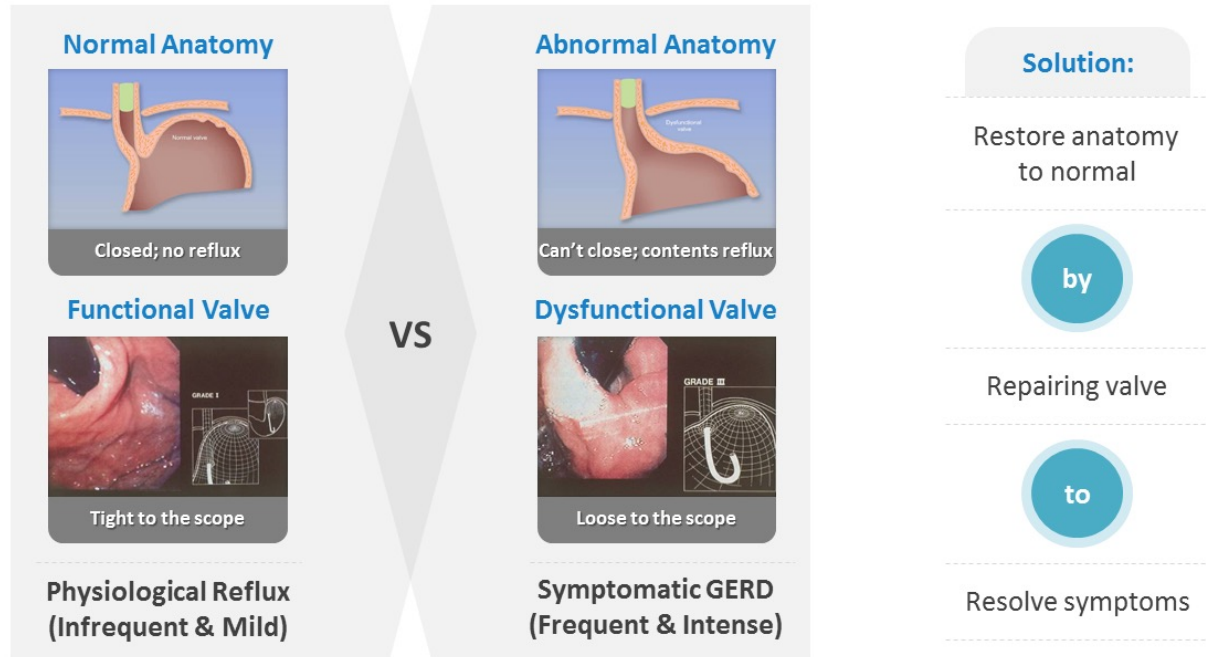
● Hiatal hernia

- Gastro-esophageal junction above diaphragm, reduces function of valve when in negative pressure thoracic cavity environment

● Increased TLESR

- Transient lower esophageal sphincter relaxations decrease valve competency

Anatomy: The Mechanics of Symptoms



Endoluminal (Endoscopic) Treatment of GERD

— Thermal methods

- Limit GER by collagen deposition around cardia

— Suturing / stapling methods

- Alter angle of His or elongate/augment LES

— Injection / bulking implant methods

- Augment LES tone with mass effect

Endoscopic Approaches

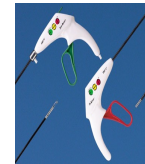
- Thermal Therapy

- Curon Stretta (Radiofrequency Energy)



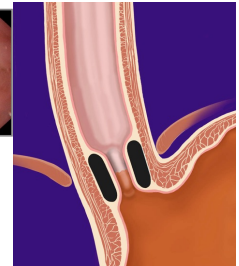
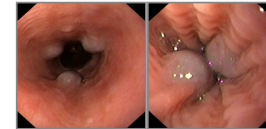
- Endoscopic Fundoplication

- Bard Endocinch
- Wilson Cook ESD
- NDO Plicator



- “Bulking Agents”

- Microvasive Enteryx
- Medtronic Gatekeeper



Endoluminal Treatment: Approved devices

- **FDA approval Dates**
 - EndoCinch – March 2000
 - Stretta system – April 2000
 - Enteryx – April 2003
 - NDO Plicator – April 2003

My View of Endoscopic Antireflux Technologies: 2005-2018



Overview

- Why have prior endoscopic anti-reflux devices failed?
- **The TIF procedure**
- Indications, Patient work-up and Post-TIF care
- Evidence Summary
- Conclusions

Terminology

- Transoral incisionless fundoplication (TIF) is the name of the procedure
- EsophyX is the name of the device used to perform the TIF procedure



The EsophyX Device: How it works....

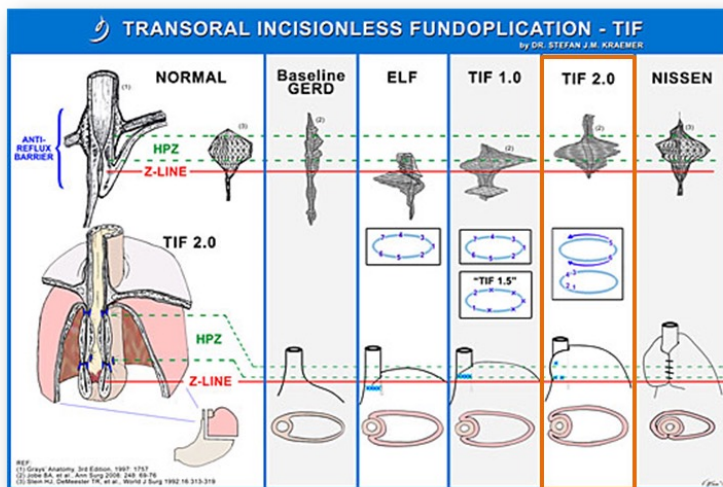


History of TIF

- 2005 - Endoluminal Fundoplication
 - Gastrogastric plication; 10 fasteners; below z-line
- 2007 – TIF 1.0 (also year of FDA approval)
 - Esophagogastric plication; 12 fasteners; 1 cm above z-line
- 2009 – TIF 2.0
 - Up to 23 fasteners placed
 - More proximal placement of fasteners (1-3 cm above z-line)
 - > 20,000 procedures performed
 - EsophyX Z+ device introduced in November 2017

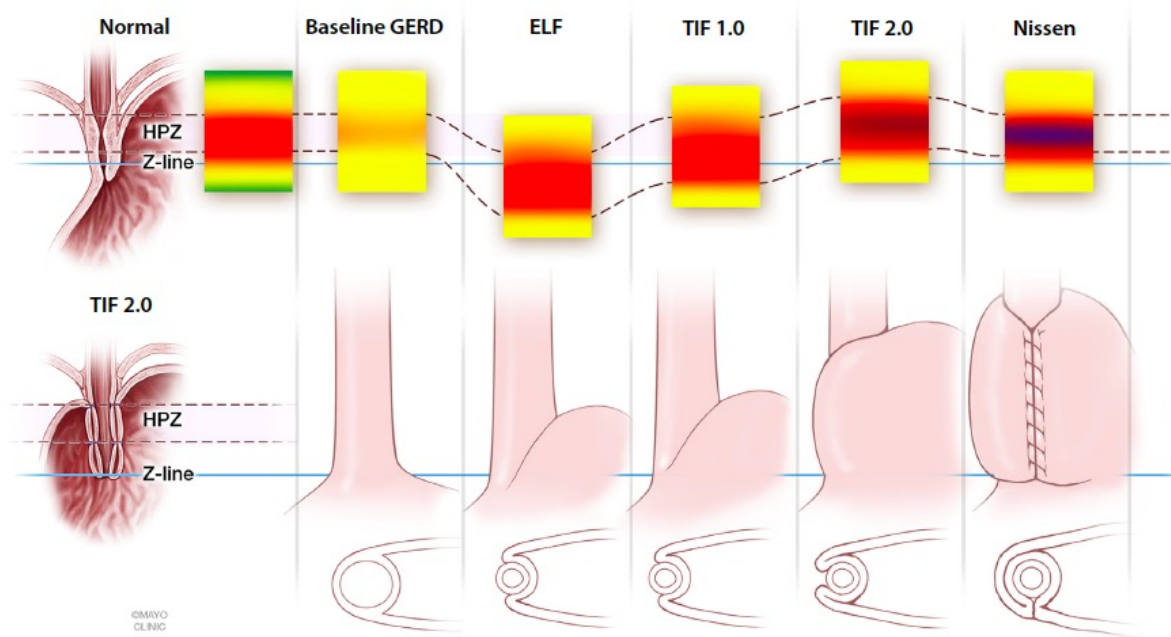
Evolution of TIF

TIF Procedure Evolution



	Transoral Incisionless Fundoplication 2.0	Transoral Incisionless Fundoplication 1.0	Endoluminal Fundoplication (ELF)
Commercial Introduction	2009	2007	2005
Commercial Cases to Date	22,051	673	186
% of Total Commercial Cases	96%	3%	1%
Plication Type	Esophago-gastric	Esophago-gastric	Gastro-gastric
Fastener Placement	1-3cm Above Z-line; more length along greater curve of stomach	Above Z-line, 1cm	Below Z-line
Average # of Fasteners	12 – 23	12	10
Wrap	Yes	No	No

Impact of Device Modifications



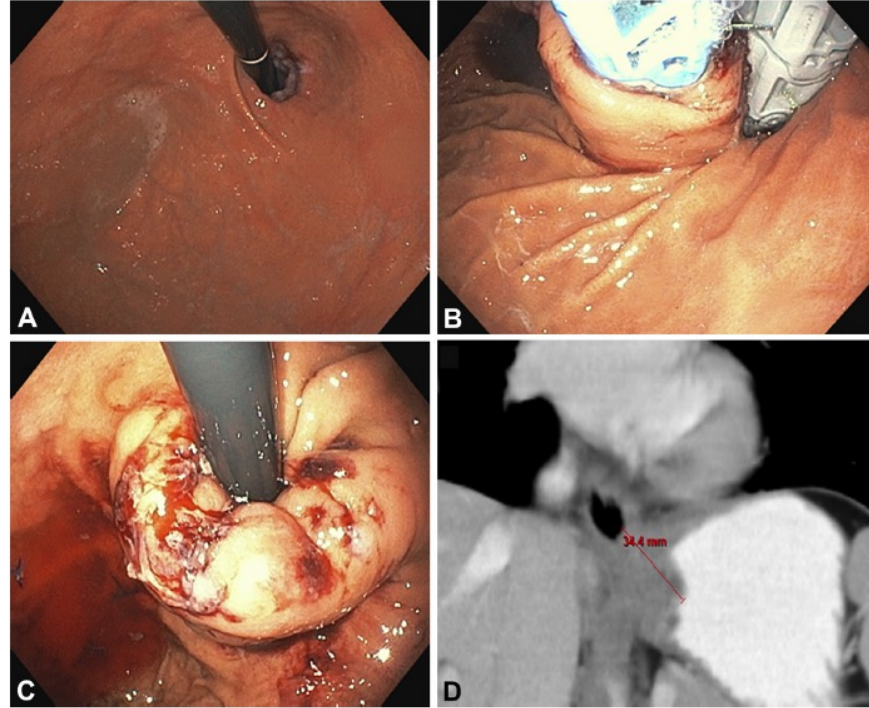
TIF vs. Lap Fundoplication



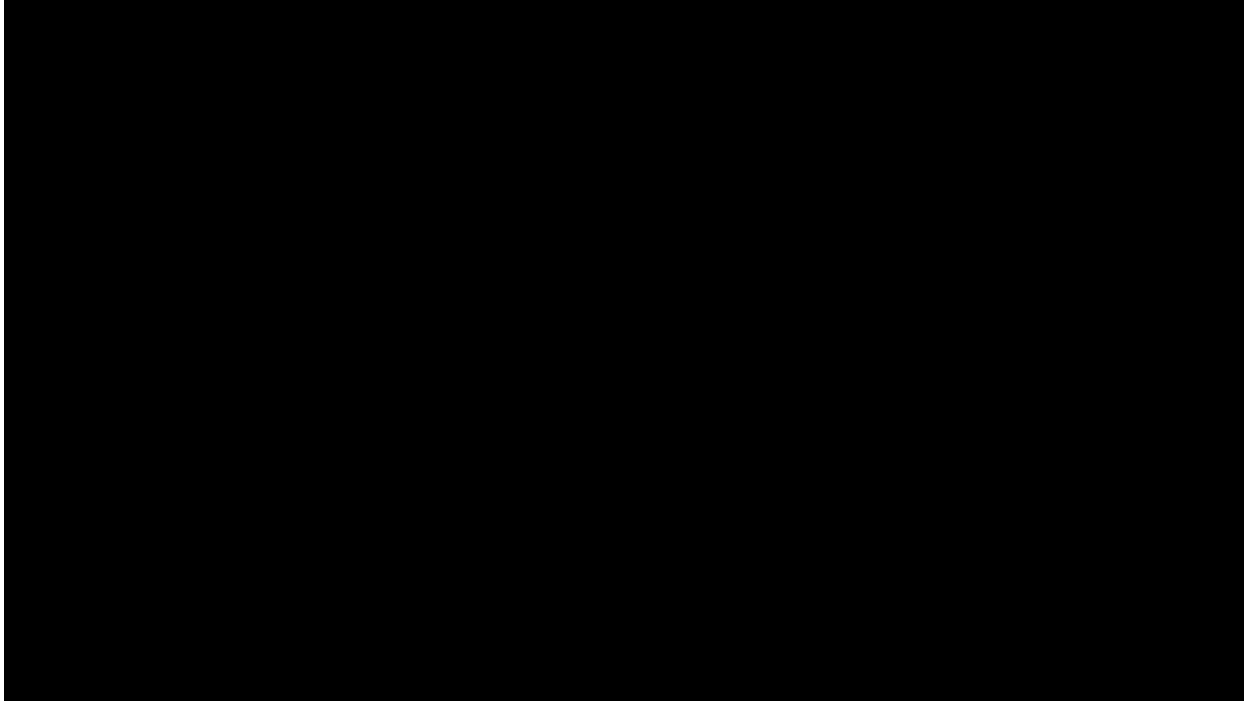
Principles Of Antireflux Surgery	TIF® Procedure	Laparoscopic Fundoplication
Reduce hiatal hernia ≤ 2 cm	✓	✓
Repair hiatal hernia > 2 cm and close crura*	✓*	✓
Elongate the intra-abdominal esophagus	✓	✓
Fundoplication	✓	✓
• Approximate and tighten the fundus around the distal esophagus	✓	✓
• Recreate the dynamics of the angle of His	✓	✓
• Restore the distal high pressure zone	✓	✓

*As of June 22, 2017, EsophyX® device indication was expanded to include patients with hiatal hernias larger than 2cm when a laparoscopic hiatal hernia repair (HHR) reduces the hernia to 2 cm or less.

Endoscopic Imaging Pre- and Post-TIF



Schematic Video of TIF Procedure



Overview

- Why have prior endoscopic anti-reflux devices failed?
- The TIF procedure
- **Indications, Patient work-up and Post-TIF care**
- Evidence Summary
- Conclusions

Indications

- Age 18+
- Partial to incomplete response of daily GERD(> 1 yr) symptoms to PPI (> 6 mos)
- Hill Grade 1-2 flap valve
- Proven GERD by endoscopy, pH study or barium imaging
- Hiatal hernia ≤ 2 cm
- Abnormal pH or endoscopy while on PPI

Contraindications

Patients with:



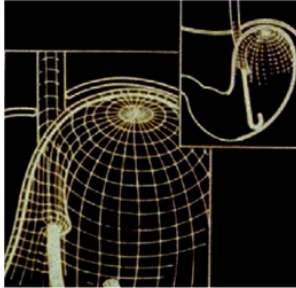
- BMI ≥ 35
- Hiatal hernia > 2cm
- Paraesophageal hernia
- Bleeding disorders
- Severe esophagitis
- Esophageal diverticulae
- Esophageal varices
- Esophageal infections or fungal disease
- Esophageal stenosis
- Strictures
- Obstructions
- Limited neck mobility
- Osteophytes of the spine
- Chronic cough
- Any kind of normal or abnormal esophageal anatomy which would not permit insertion of a device



Assessing the GEJ: Hill Grade

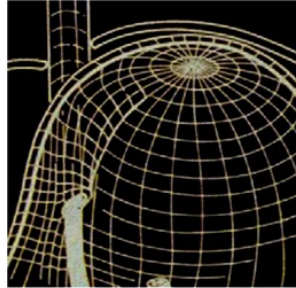
Hill Grade

Grade I



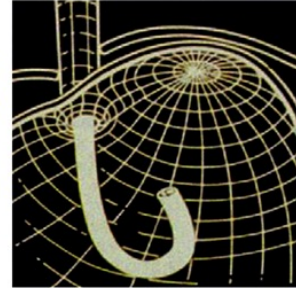
Normal ridge of tissue approximates closely to the scope

Grade II



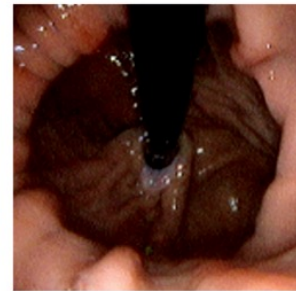
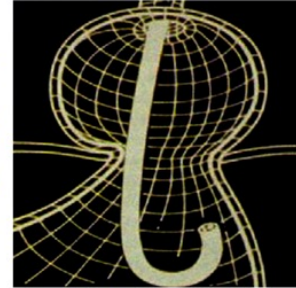
Ridge is slightly less well defined and opens with respiration

Grade III



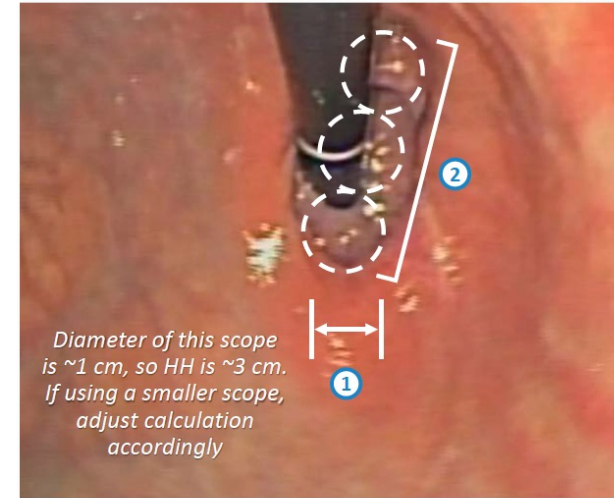
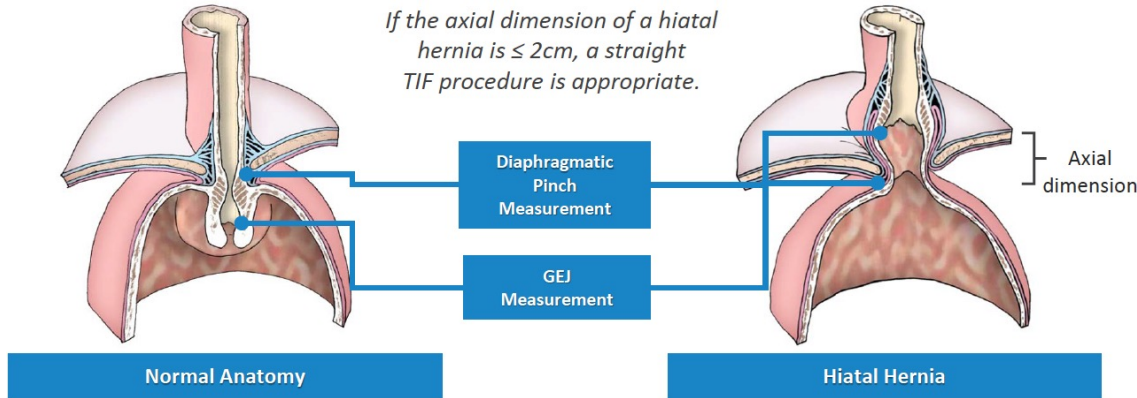
Ridge is effaced and the hiatus is patulous

Grade IV

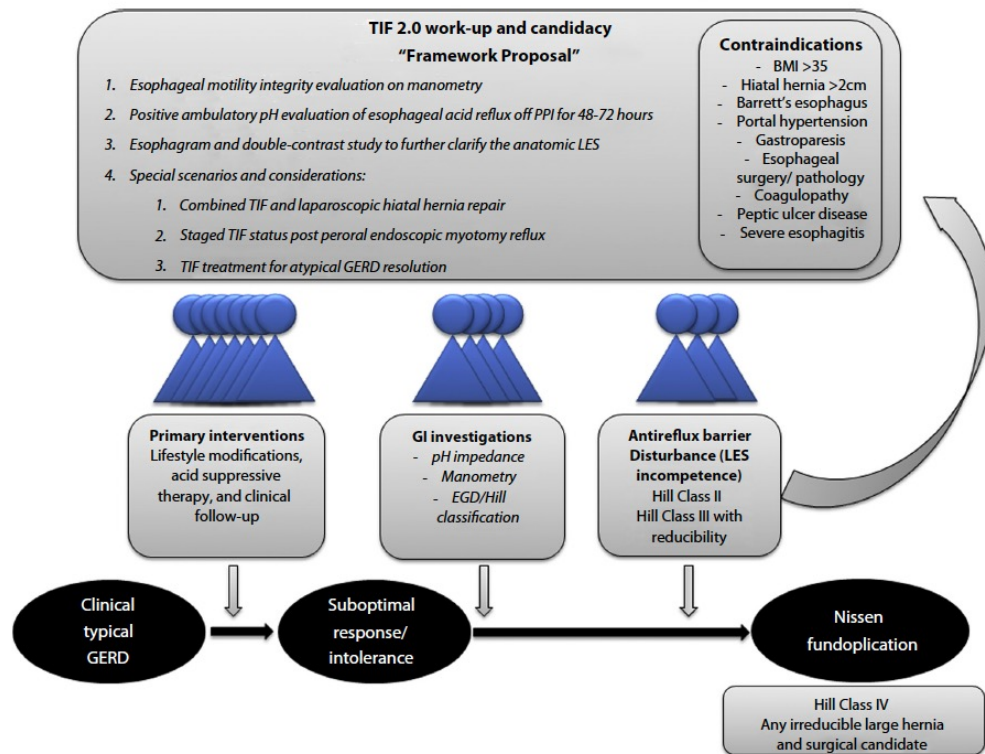


Hiatus is wide open at all times and the sphincter is displaced axially

Axial and Transverse Hiatal Hernia Measurements



Patient Selection



Procedure and Post-procedure management

- General anesthesia
- 45 min procedure time (range 30-60 min)
- 2 operators (one for scope; one for EsophyX device)
- Intraop paralysis/PEEP 5-10 cm H₂O may aid in avoiding diaphragm during plication
- Prophylactic antibiotics as well as IVF and antiemetics typically given intra-procedurally
- Typically observed overnight

Upon Discharge....



Medications post-op prescriptions including:

- ▶ Analgesic for moderate to severe pain
- ▶ Antiemetic to control nausea and vomiting
- ▶ Anti-gas agent to relieve bloating and discomfort
- ▶ Laxative to control constipation and straining
- ▶ PPIs – short term, reduce risk of rebound



Post-procedure: Diet

- Day 0-3
 - Clear liquid diet
- Day 4-14
 - Blenderized/full liquid diet
- Week 3-4
 - Pureed foods
- Week 5-6
 - Medium soft foods

Food Guide						
Yes ☒ No ☐		Post Procedure	Day 0-3	Day 4-14	Weeks 3-4	Weeks 5-6
Clear liquids, low in sugar		Water (non-carbonated)	☒	☒	☒	☒
		Milk, decaffeinated tea, caffeine free drinks	☒	☒	☒	☒
		Diet and decaffeinated drinks, diluted electrolyte drinks	☒	☒	☒	☒
		Broth of any kind, strained soups (not tomato based)	☒	☒	☒	☒
		Diluted, light or diet apple or white grape juice	☒	☒	☒	☒
		Non-acidic fruit or vegetable juice (without chunks)	☒	☒	☒	☒
		Liquid puddings and creams	☒	☒	☒	☒
		Sherbets, ice-creams, milk shakes (without chunks)	☒	☒	☒	☒
Full liquids		Drinkable yogurt (no chunks)	☐	☒	☒	☒
		Protein-enriched commercially available shakes	☐	☒	☒	☒
		Very liquid, potato-based mash	☐	☒	☒	☒
		Non-stringy vegetable mash	☐	☒	☒	☒
		Baby food	☐	☒	☒	☒
Soft texture, low fat food		Cottage cheese	☐	☐	☒	☒
		Oatmeal	☐	☐	☒	☒
		Well-cooked & pureed vegetables (mashed potatoes)	☐	☐	☒	☒
		Canned fruit (without skins)	☐	☐	☒	☒
		Bananas, melons, berries	☐	☐	☒	☒
		Soft eggs, tofu	☐	☐	☒	☒
		Moist, mashed boneless fish	☐	☐	☒	☒
		Well-cooked lean ground food (e.g. turkey)	☐	☐	☒	☒
Medium texture food		Small soft noodles	☐	☐	☐	☒
		Non-sticky rice	☐	☐	☐	☒
		Cereals (softened in milk)	☐	☐	☐	☒
		Soft cheeses	☐	☐	☐	☒

Post-procedure: Activity and F/u

❖ Activity

- Week 1: Short distance walking encouraged, minimal physical activity, no lifting > 5lbs
- Week 2: Slow climbing stairs allowed, no intense exercise, no lifting > 5 lbs., sex allowed
- Week 3-6: No intense exercise, may lift up to 25lbs.
- Week 7: Resume normal activity

❖ Follow-up

- 1-2 weeks post op
- 3 months
- If study, 6-9 months



Insurance Coverage

- Category 1 CPT code for TIF exists
 - 43210: TIF alone
 - 43281: TIF & Hernia repair
- Hybrid TIF (laparoscopic hernia reduction and endoscopic TIF) covered by all parties (Medicare and private insurance)
- Straight TIF (all endoscopic) covered by Medicare
- Authorization for straight TIF needed are with some private payors

Overview

- Why have prior endoscopic anti-reflux devices failed?
- The TIF procedure
- Indications, Patient work-up and Post-TIF care
- **Evidence Summary**
- Conclusions

TIF: Primary References Used

REVIEW ARTICLE

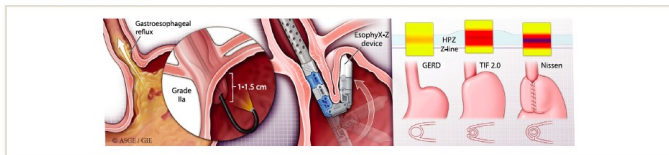
Endoscopic GERD therapy: a primer for the transoral incisionless fundoplication procedure

Fateh Bazerbachi, MD,¹ Kumar Krishnan, MD,² Barham K. Abu Dayyeh, MD, MPH¹

Rochester, Minnesota; Boston, Massachusetts, USA



GRAPHICAL ABSTRACT



Gastroenterology 2020;159:1504–1525

SPECIAL ARTICLE

State of Evidence in Minimally Invasive Management of Gastroesophageal Reflux: Findings of a Scoping Review



Michael F. Vaezi,¹ Nicholas J. Shaheen,² and V. Raman Muthusamy³

¹Division of Gastroenterology, Hepatology, and Nutrition, Vanderbilt University Medical Center, Nashville, Tennessee, ²Division of Gastroenterology, Hepatology, and Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, and ³Vatche and Tamar Manoukian Division of Digestive Diseases, David Geffen School of Medicine, University of California-Los Angeles, Los Angeles, California

Bazerbachi, Krishnan, Abu Dayyeh, Gastrointest Endosc 2019;90:370-83.
Vaezi MF, Shaheen NJ, Muthusamy VR. Gastroenterology. 2020 Oct;159(4):1504-1525.

TIF: The Evidence Base

- 5 systematic reviews
- 5 Randomized trials
 - 2 c/t sham, 2 c/t PPI, 1 c/t lap Nissen fundoplication
- Multiple cohort studies
- >140 publications with at least 1600 unique patients
- Longest available f/u are 8 and 10 yrs

Effectiveness: Summary

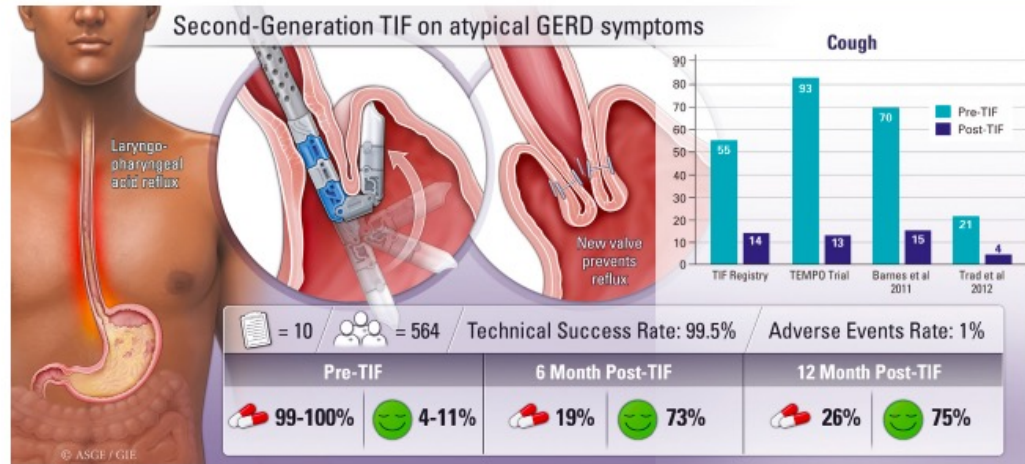
- Improved heartburn, regurgitation and GERD-related QOL scores c/t sham procedures
- Acid reflux is reduced and even normalized in 40-80% of patients.
- Impact on LES pressures not as well studied
- Reduced need for PPI therapy at 5 yrs
 - 40-90% able to stop PPI use at various stages of f/u
- **TIF appears to be superior to PPI in eliminating or reducing regurgitation or extra-esophageal symptoms**

Systematic Reviews of TIF

- Meta-analysis of 32 TIF studies
 - 1232 patients in 26 studies with TIF 2.0 protocol
 - Procedural success rate (immediate) = 99%; AE = 2.0%
 - Significant improvement in GERD-HRQOL and pH scores
 - Hernia reduction achieved in 91%
 - PPI elimination in 88%
- SR and Network Meta-analysis of only RCTs of Lap Nissen or TIF w/ sham or PPI
 - 7 studies, 1128 patients
 - TIF with best improvement in HRQOL
 - Nissen better with objective parameters (LES pressure and acid exposure)

TIF 2.0 for Atypical GERD Symptoms

- 10 studies; 564 pts
- RSI 6 & 12 mo data
- Tech success, Adv. Events, satisfaction, PPI use collected
- RSI
 - 6 mo – reduced by 15.72
 - 12 mo – reduced by 14.73



TIF 2.0 Data Summary

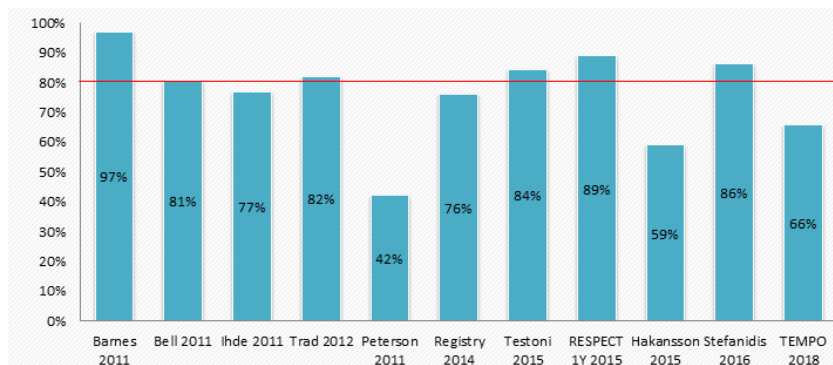
TIF 2.0 Procedure Delivers Consistent Results on Objective Outcome Measures

TIF 2.0 Studies

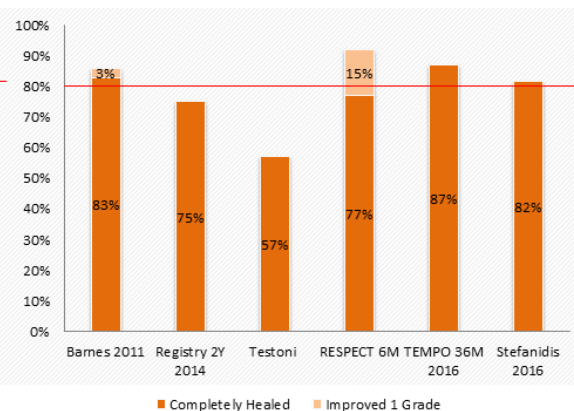
Percent of Patients
Off Daily PPI



Percent of Patients Esophagitis
Healed or Improved One Grade



Weighted incidence is 81% across 11 studies
with follow-up > 6 mo in 568 patients



Weighted incidence is 80% across 6 studies with
follow-up > 6 mo in 122 patients; 84% across
2 studies follow-up > 36mo in 56 patients

pH Parameters Following TIF Procedure

Adverse Events

- Serious adverse event (SAE) rate of 2.0-2.4% in the 2 largest meta-analyses
 - Nearly half (9/19) occurred with TIF 1.0 procedure
- This appears to be decreasing with time – likely due to operator experience and device refinements
- Most commonly reported SAEs:
 - Perforation – 0.9% (none in 5 RCT of TIF 2.0 technique)
 - Post-TIF bleeding – 0.6%
 - Pneumothorax – 0.5%

Systematic Reviews of TIF

- Long term (≥ 3 yrs) TIF F/u
- 8 studies; 418 pts
- Mean f/u 5.3 yrs (3-10 yrs)
- The pooled proportion of **patient-reported satisfaction** before and after TIF was 12.3% [12.3–35.1] and 70.6% [51.2–84.6] respectively, corresponding to an odds ratio of 21.4 [3.27–140.5].
- Pooled rates of patients **completely off PPIs and on occasional PPIs** were 53.8% [42.0%-65.1%] and 75.8% [67.6–82.6]
- Pooled mean **GERD-HRQL** scores off PPI were 26.1 [21.5–30.7] and 5.9 [0.35.1–11.4]
- Pooled rates of **heartburn and regurgitation** scores normalization were 73.0% [0.62–0.82] and 86% [75.0–91.0].

Review

Thieme

Long-term outcomes of transoral incisionless fundoplication for gastro-esophageal reflux disease: systematic-review and meta-analysis



Authors

Sabrina Testoni^{1,2}, Cesare Hassan^{1,2}, Giorgia Mazzoleni³, Giulio Antonelli², Lorella Fantì⁴, Sandro Passaretti⁴, Loredana Correale⁵, Giulia Martina Cavestro⁴, Pier Alberto Testoni⁴

Very Long Term Durability

- 10 yr data: Testoni et al, Endoscopy International Open 2019; 07: E647–E654
 - 50 pts, 14 with 10 yr f/u
 - 91.7% w/ 10 yr f/u had stopped or halved anti-secretory use
- 8 yr data: Chimukangara et al, Surg Endosc. 2019 April ; 33(4): 1304–1309.
 - 2007-2014; N=57
 - Median f/u 97 months; 23 w/ long term f/u
 - 73% on daily anti-secretory use; 78% satisfied/neutral w/ GERD management
- 9 year data: Bell RCW et al, Ther Adv Gastroenterol 2021 1-11.
 - Single Center Prospective Registry 11/08-7/15; N =151; no hernia repair; f/u in 131
 - 64% with >50% reduction in GERD-HRQL at 4.92 median yr f/u
 - 22% on daily PPI among those w/ > 5 yr f/u; 22% revised to LNF

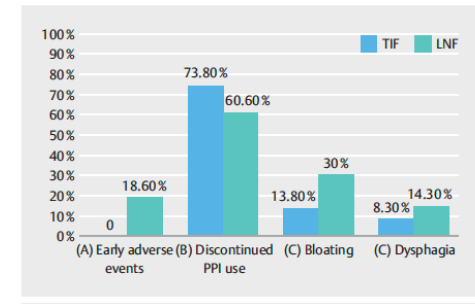
Concept of “C-TIF”

- Concomitant Surgical Hiatal Hernia Repair and TIF procedure
- For > 2 cm hiatal hernias
- Done in Operating Room
- 60 pts with > 2 cm hiatal hernia; 2018-2020
- 100% technical success
- Reflux Disease Questionnaire for frequency and severity improved significantly from (17.4 to 4.72; $p < 0.01$ and 16.7 to 4.56; $p < 0.05$, respectively) at 6 mos.
- GERD HRQL scores decreased in heartburn (23.26 to 7.37; $p < 0.01$) and regurgitation (14.26 to 0; $p = 0.05$).
- Reflux Symptom Index decreased after cTIF (17.7 to 8.1 post cTIF; $p < 0.01$).
- Mean DeMeester score decreased from 43.7 to 4.9 and acid exposure time decreased from 12.7% to 1.28% post cTIF ($p = 0.06$).

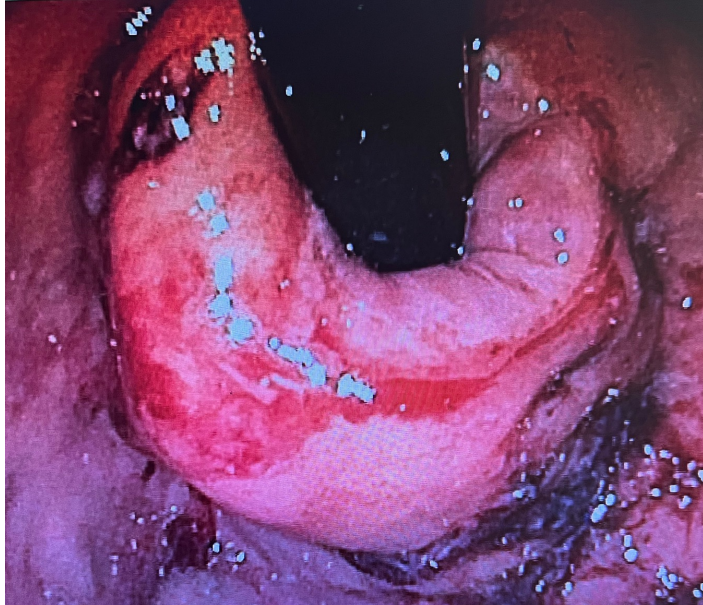
C-TIF vs. Laparoscopic Nissen Fundoplication

- Multicenter, retrospective; N=125 TIF and 70 LNF
- HH 2-5 cm in size; both groups got HH repair and fundoplication
- No difference in: stop/reduction in PPI use, dysphagia, esophagitis, disruption of wrap or HH recurrence
- TIF had shorter hospital stay, lower 30 d readmission, less bloating and lower early and serious AE

Length of hospital stay (days, median [IQR])	1 (1-1)	2 (1-2)	<0.001
Readmission in 30 days [n (%)]	0	3 (4.3)	0.013
Adverse event [n (%)]			
• Early (<30 days)	0	13 (18.6)	<0.001
• Early serious	0	3 (4.3)	<0.001
• Late (30 days to 1 year)	0	0	-
• Late serious	0	0	-
• 1-year mortality [n (%)]	0	0	-
At 6 months [n (%)]			
• Discontinued PPI use	76 (73.8)	40 (60.6)	0.07
• Decreased PPI use	88 (85.4)	55 (83.3)	0.71
• Start PPI use	0	0	-
• Bloating (new or worse than baseline)	15 (13.8)	21 (30.0)	0.009



TIF vs. LNF



TIF



Endoscopic view of LNF

Additional Recent Data

- **Cost Effectiveness**

- TIF cost effective compared to surgery or medical therapy (BID PPI) over 10 yrs & lifetime
- Costs: TIF 2.0 (\$ 13,978.63) vs. \$ 17,658.47 for LNF and \$10,931.49 for PPI.
- Compared to the PPI strategy, TIF 2.0 was cost-effective with an incremental cost of \$ 3,047 and incremental effectiveness of 0.29 QALYs, resulting in an ICER of \$ 10,423.17 /QALY gained.
- TIF 2.0 dominated LNF

- **Learning Curve**

- Proficiency achieved at 18-20 procedures; Maximum plication efficiency after 26 procedures
- Overall procedure time about 39 min after 44 procedures

- **TIF to Revise Prior LNF (N=20)**

- Esophagitis healed in 78% of patients & significantly improved GERD-HRQL and RSI scores.
- Mean acid exposure time decreased from $12\% \pm 17.8$ to $0.8\% \pm 1.1$ ($p = 0.028$) with 9 patients with normalized pH post-TIF.

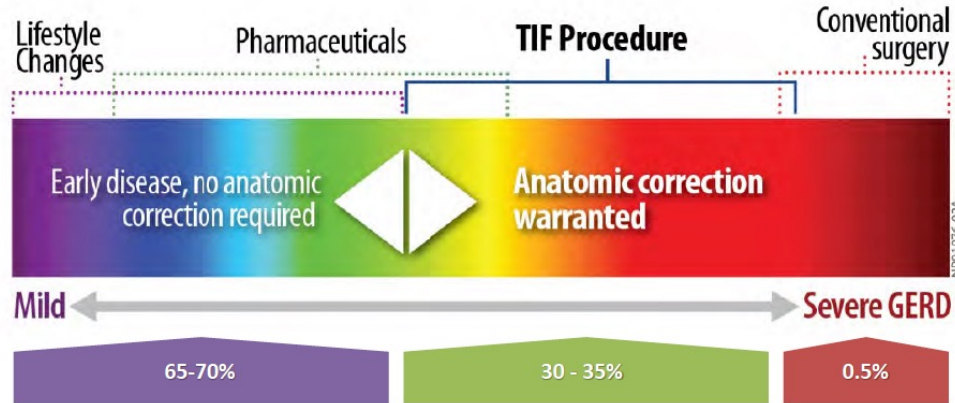
McCarty TR et al, Endosc Int Open 2022; 10:E923-E932.

Dbouk M et al, Endosc Int Open 2021; 9:E1785-E1791.

Ghosh G. et al, Surgical Endoscopy, 2023, Vol. 37, p. 3701–3709.

When to Use TIF?

Of the ~6.7M uncontrolled GERD sufferers, <30K elect surgery
(due to invasiveness, high complication rates and side-effect profile)



Reference: Reavis KM, Perry KA. Expert Rev Med Devices. 2014 Jul;11(4): 341-50.
Subramanian, CR and Triadafilopoulos G. Refractory gastroesophageal reflux disease. Gastroenterol. Rep. (2015) 3 (1): 4153.

My Thoughts on Why to Use TIF

- For patients who don't desire long-term medications (concerns about long-term side effects, drug interactions, compliance issues)
- GERD symptoms controlled by PPI but with persistent regurgitation or supra-esophageal symptoms
- Adequate fundoplication but not so tight as to lead to dysphagia/gas bloat (about 80% reduction in these symptoms c/w Nissen)
- Easy to revise
- Doesn't eliminate future surgical fundoplication as an option if needed or desired

Summary/Conclusions

- TIF appears to be a safe, effective and relatively durable technique anti-reflux procedure that improves symptoms, reduces PPI use and improves and often normalizes objective parameters of reflux (pH study)
- Careful patient selection and pre-procedure workup (hernia assessment) is essential to achieving clinical success
- The technique does not preclude subsequent fundoplication and may also be used after failed prior fundoplication

Robert G. Kardashian Center for Esophageal Health

