What's next in new technology Benign Esophagus

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Cleveland Clinic Foundation

GTSC 2022, Bonita Springs, FL



Disclosures

- No relevant commercial disclosures
- Unrelated disclosures
 - -Smiths Medical-Consultant
 - -Bristol Myers Squibb-Speaker
 - —Chromacode-Royalties



Learning Objectives

- Become familiar with emerging technologies for the detection of Barrett's esophagus
- Understand the mechanism of the new ant-reflux platforms
- Describe the role or third space endoscopy in the treatment of benign esophageal disorders.

Themes

- Barrett's Esophagus-Diagnosis and Eradication
- Anti-Reflux procedure
- Third space Endoscopy

Barrett's Esophagus Diagnostics and Prognostics



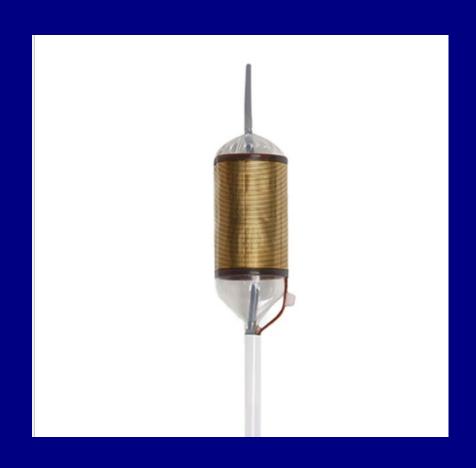
Treatment for Barrett's Esophagus



Treatment of BE in 2000



Treatment of BE in 2022





Barrx[™] 360 Barrx[™] 90 https://www.medtronic.com/covidien/en-us/products/gastrointestinal-rf-ablation.html

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

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VOL. 360 NO. 22

Radiofrequency Ablation in Barrett's Esophagus with Dysplasia

Nicholas J. Shaheen, M.D., M.P.H., Prateek Sharma, M.D., Bergein F. Overholt, M.D., Herbert C. Wolfsen, M.D., Richard E. Sampliner, M.D., Kenneth K. Wang, M.D., Joseph A. Galanko, Ph.D., Mary P. Bronner, M.D., John R. Goldblum, M.D., Ana E. Bennett, M.D., Blair A. Jobe, M.D., Glenn M. Eisen, M.D., M.P.H., M. Brian Fennerty, M.D., John G. Hunter, M.D., David E. Fleischer, M.D., Virender K. Sharma, M.D., Robert H. Hawes, M.D., Brenda J. Hoffman, M.D., Richard I. Rothstein, M.D., Stuart R. Gordon, M.D., Hiroshi Mashimo, M.D., Ph.D., Kenneth J. Chang, M.D., V. Raman Muthusamy, M.D., Steven A. Edmundowicz, M.D., Stuart J. Spechler, M.D., Ali A. Siddiqui, M.D., Rhonda F. Souza, M.D., Anthony Infantolino, M.D., Gary W. Falk, M.D., Michael B. Kimmey, M.D., Ryan D. Madanick, M.D., Amitabh Chak, M.D., and Charles J. Lightdale, M.D.

LGD: 90.5% eradication of dysplasia

HGD: 81.0 % eradication of dysplasia

New Technologies in Diagnostics and Prognostics

- Cytosponge
- Esocheck
- TissueCypher
- WATS 3D

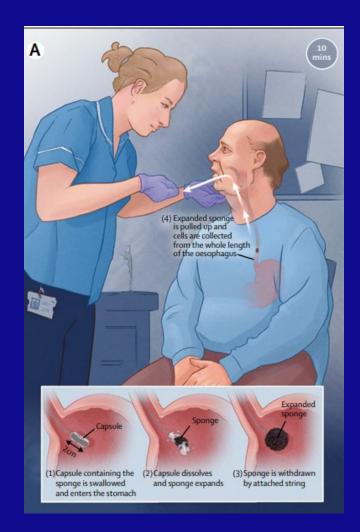
Cytosponge™

Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial

Rebecca C Fitzgerald, Massimiliano di Pietro, Maria O'Donovan, Roberta Maroni, Beth Muldrew, Irene Debiram-Beecham, Marcel Gehrung, Judith Offman, Monika Tripathi, Samuel G Smith, Benoit Aigret, Fiona M Walter, Greg Rubin, on behalf of the BEST3 Trial team*, Peter Sasieni



Cytosponge™





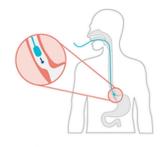
https://refluxuk.com/symptoms-and-diagnosis/diagnostic-tests/cytosponge/



Lancet 2020; 396: 333-44

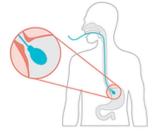
Esocheck™

The Esocheck cell collection device consists of a capsule containing a small balloon with a textured surface to enhance cell collection.





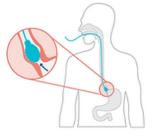
The patient swallows a capsule, which is attached to a thin catheter, until the capsule reaches the stomach.



Contract of the second

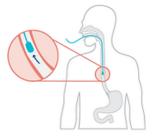
2 Inflate

The balloon is inflated to expose the ridges and then withdrawn allowing them swab the targeted area of the esophagus, collecting cells on the balloon's surface.











The balloon covered with sampled cells is placed in a preservation solution for transport to a diagnostic testing facility.

EsoGuard™ is a laboratory developed test which analyzes 31 methylated biomarkers

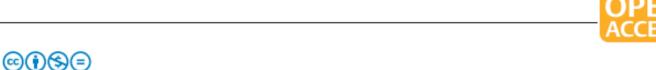
https://www.luciddx.com/esocheck
The FDA has given 510(k) clearance to the EsoCheck Cell Collection Device



TissueCypher™

Original article # Thieme

TissueCypher Barrett's esophagus assay impacts clinical decisions in the management of patients with Barrett's esophagus



Authors

David L. Diehl¹, Harshit S. Khara¹, Nasir Akhtar¹, Rebecca J. Critchley-Thorne²

- Tissue needed (biopsy)
- Whole slide quantitative image analysis after multiplex immunofluorescent labelling of 15 quantitative measures of biomarkers and generation of risk scores.
- Locked prediction algorithm
- Commercially available.

Endoscopy International Open 2021; 09: E348–E355 | © 2021.

https://tissuecypher.com/tissuecypher-technology/



TissueCypher™

Independent Blinded Validation of a Tissue Systems Pathology Test to Predict Progression in Patients With Barrett's Esophagus

Jon M. Davison, MD¹, John Goldblum, MD², Udhayvir Singh Grewal, MBBS², Kevin McGrath, MD¹, Kenneth Fasanella, MD¹, Christopher Deitrick, BS¹, Aaron D. DeWard, PhD³, Emily A. Bossart, PhD³, Stephen L. Hayward, PhD³, Yi Zhang, PhD³, Rebecca J. Critchley-Thorne, PhD³ and Prashanthi N. Thota, MD²

Findings: ND BE patients who scored high-risk progressed at a higher rate (26%) than patients with subspecialist-confirmed LGD (21.8%) at 5 years



Wide-area trans-epithelial sampling with three-dimensional computer-assisted analysis



Clinical utility of wide-area transepithelial sampling with three-dimensional computer-assisted analysis (WATS^{3D}) in identifying Barrett's esophagus and associated neoplasia

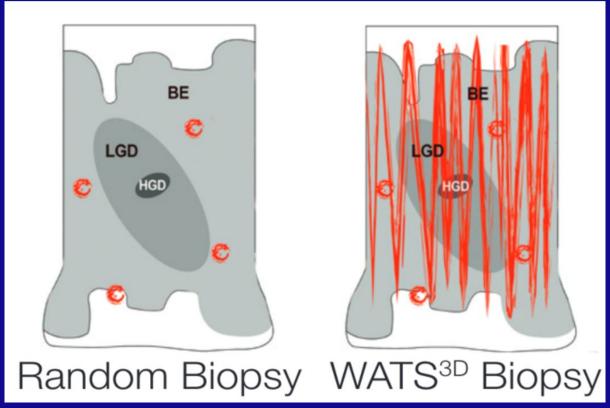
Vivek Kaul, ¹⁰¹ Seth Gross, ² F. Scott Corbett, ³ Zubair Malik, ¹⁰⁴ Michael S. Smith, ¹⁰⁴ Christina Tofani, ⁶ Anthony Infantolino ⁶

432 consecutive patients (2013-2018) with WATS-3D positive for BE and negative biopsy.



¹Division of Gastroenterology and Hepatology, University of Rochester Medical Center, Rochester, New York, ²Division of Gastroenterology, NYU Langone Medical Center, New York, New York, ³Suncoast Endoscopy of Sarasota, Gastroenterology Associates of Sarasota, Sarasota, Florida, ⁴Division of Gastroenterology, Temple University, Philadelphia, Pennsylvania, ⁵Department of Gastroenterology, Mount Sinai West Medical Center, New York, New York, ⁶Department of Gastroenterology, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, USA







	BE	LGD	HGD	Total
Total number of patients	317	98	17	432
Mean age (range)	60.5 (18-91)	69.1 (38-90)	66.9 (48-86)	62.7 (18-91)
Mean length of suspected Barrett's	1.5	4.1	4.5	2.3
segment (cm)				
Gender				
Male (%)	42	67	82	49
Female (%)	58	33	18	51
Ethnicity				
White (%)	79	97	82	83
Black/African American (%)	2	0	6	2
Hispanic/Latino (%)	7	1	6	6
Asian (%)	7	1	6	6
Other (%)	5	1	0	4

Table 2 Direct impact of WATS3D on the management of patients with be, LGD, and HGD

Action	BE (n = 317) n (%)	LGD (n = 98) n (%)	HGD (n = 17) n (%)	Total all BE and Dysplasia (n = 432) n (%)
Increased surveillance frequency of	_	29 (29.6)	5 (29.4)	34 (29.6)
dysplasia patients				
Ablation/Antireflux surgery	12 (3.7)	33 (33.7)	12 (70.6)	57 (13.2)
Ablation/EMR				
PPIs initiated	170 (53.6)	43 (43.9)	7 (41.2)	220 (50.9)
PPI dose increased	21 (6.65)	10 (10.2)	3 (17.6)	34 (7.9)
No change in patient management	7 (2.2)	5 (5.1)	1 (5.9)	13 (3.0)
Direct impact on patient	310 (97.8)	93 (94.9)	16 (94.1)	419 (97.0)
management				

BE, Barrett's esophagus; EMR, endoscopic mucosal resection; HGD, high-grade dysplasia; LGD, low-grade dysplasia; PPI, proton pump inhibitor; WATS^{3D}, wide-area transepithelial sampling with three-dimensional computer-assisted analysis.

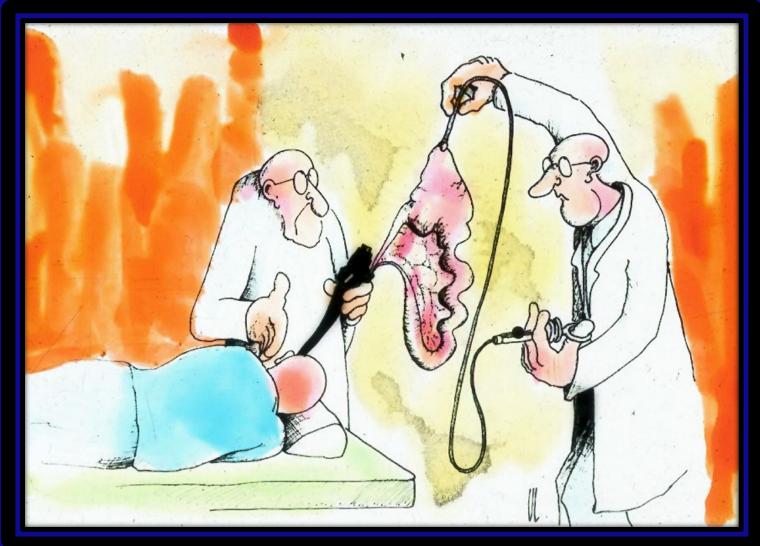
97% of patinets in this study had their management impacted



Anti-Reflux Procedures



Paradigm Shifts in GI Diseases



Laparoscopic Nissen Fundoplication: Preliminary Report

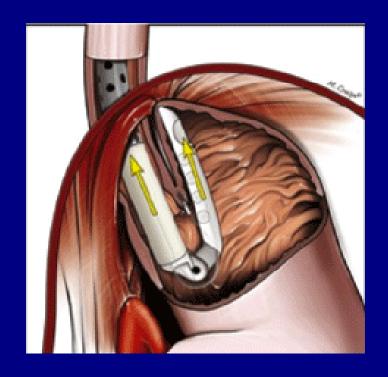
B. Dallemagne, M.D., J. M. Weerts, M.D., C. Jehaes, M.D., S. Markiewicz, M.D., and R. Lombard, M.D.

Summary: Twelve patients presenting with symptomatic esophagitis associated with hiatal hernia and gastroesophageal reflux underwent operative management under laparoscopic guidance. The antireflux procedure employed was the Nissen fundoplication. The authors completed the operation laparoscopically in nine patients. Postoperatively, patients were evaluated with repeat fiberoptic endoscopy, esophageal manometry, and barium contrast studies. Postoperative results were considered excellent on the basis of these studies and complete control of symptoms. The mortality rate was 0%. The only major operative complication was a pneumonia that occurred in one patient. At 1 month follow-up, six patients were totally asymptomatic. The authors conclude that laparoscopic treatment of gastroesophageal reflux associated with a train is feasible by a procedure that has already proven its value during the words: Hiatal hernia—Gastroesophageal reflux—Esophagearoscopy.

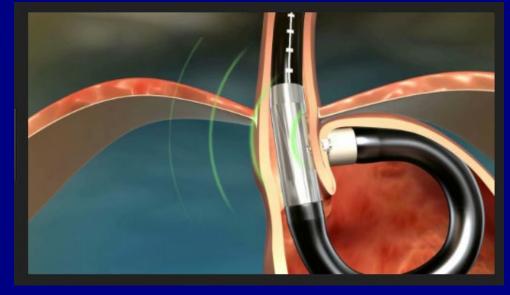
Paradigm Shifts in GI Diseases



Trans-Oral Incisional Fundoplication



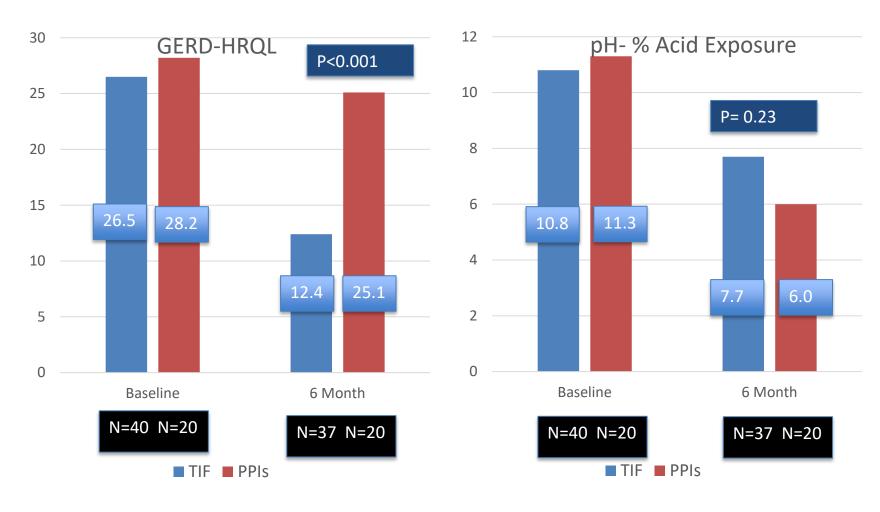
EsophyX



Medigus

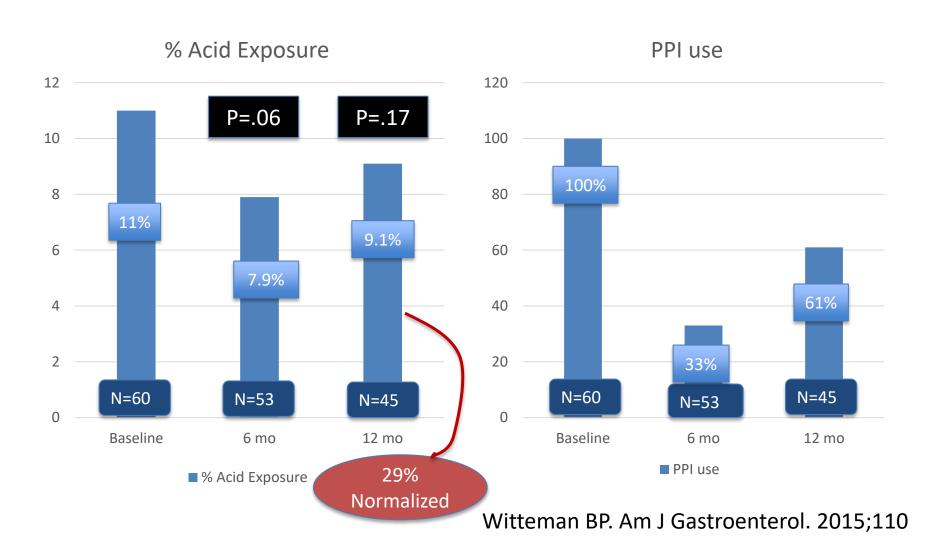
Pictures sourced from device websites

Dutch Trial – 6 month Data



Witteman BP. Am J Gastroenterol. 2015;110

Dutch Trial – 12mo after TIF



Meta-Analysis

Efficacy of transoral incisionless fundoplication (TIF) for the treatment of GERD: a systematic review with meta-analysis

Xiaoquan Huang^{1,2} · Shiyao Chen^{1,2,3} · Hetong Zhao⁴ · Xiaoqing Zeng³ · Jingjing Lian^{1,2} · Yujen Tseng³ · Jie Chen³

Meta-Analysis

- 18 studies
- 963 patients
- 5 RCT
- 13 observational studies
- 2007-2015

Meta-Analysis

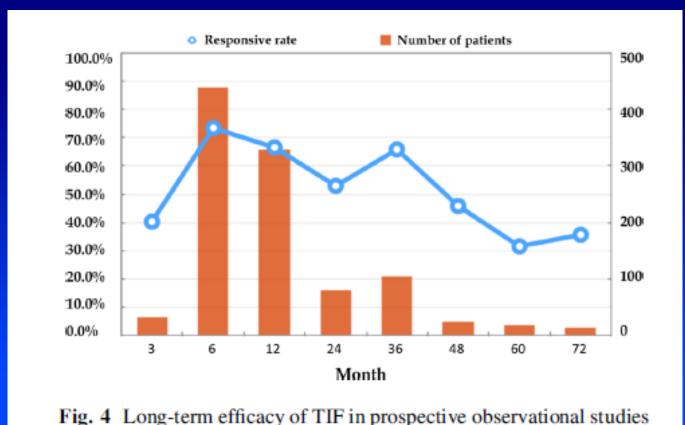


Fig. 4 Long-term efficacy of TIF in prospective observational studies

Meta-Analysis Conclusions

 TIF is an alternative intervention in controlling GERD-related symptoms with comparable short-term patient satisfaction.
 Long-term results showed decreased efficacy with time.
 Patients often resume PPIs at reduced doses in the near future.

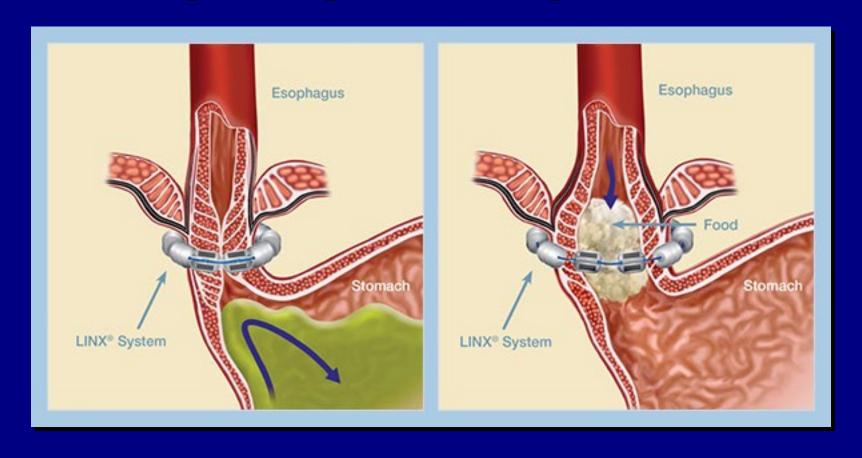
TIF Pros

- Trans oral fundoplication is an alternative to PPIs
- Low side effect rate
- No Incisions
- ? Low complication rate (0.41% of 17000 patients)*
- Low rate of Dysphagia, bloating, and other post-fundoplication symptoms (but do exist)

TIF Cons

- Inferior control to fundoplication
- Conversion to conventional anti-reflux surgery can be challenging
- Leaves its role unclear in the spectrum of GERD therapy
- Given the continued abnormal acid exposure, its role in cancer risk reduction is at best uncertain

LINX® Magnetic Sphincter Augmentation





SYSTEMATIC REVIEW

LINX® reflux management system to bridge the "treatment gap" in gastroesophageal reflux disease: A systematic review of 35 studies

Dimitrios Schizas, Aikaterini Mastoraki, Eleni Papoutsi, Vassilis G Giannakoulis, Prodromos Kanavidis, Diamantis Tsilimigras, Dimitrios Ntourakis, Orestis Lyros, Theodore Liakakos, Dimitrios Moris

LINX®

- OR time 27-73 min
- 75-100% cessation of PPI post-op (2511 pts in 35 studies)
- Dysphagia 6-83%
 - 2% device removal
- Post-op Dilation 8%
- Device Erosion 0.3% at 4 years
 - From registry of 9453 patients

Anti-Reflux Mucosotomy (ARM)

ORIGINAL ARTICLE

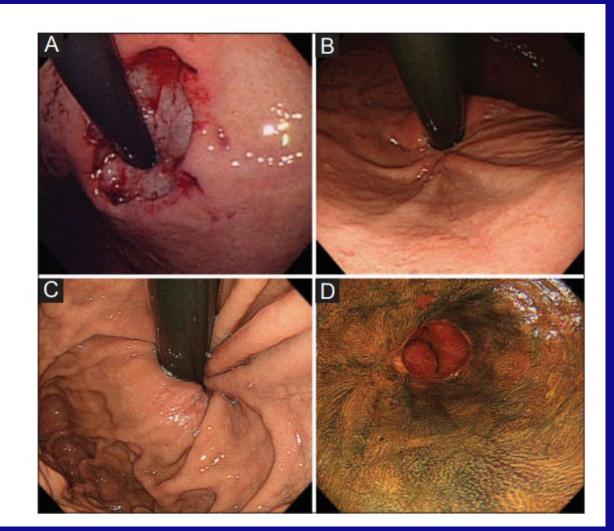
Annals of Gastroenterology (2014) 27, 346-351

Anti-reflux mucosectomy for gastroesophageal reflux disease in the absence of hiatus hernia: a pilot study

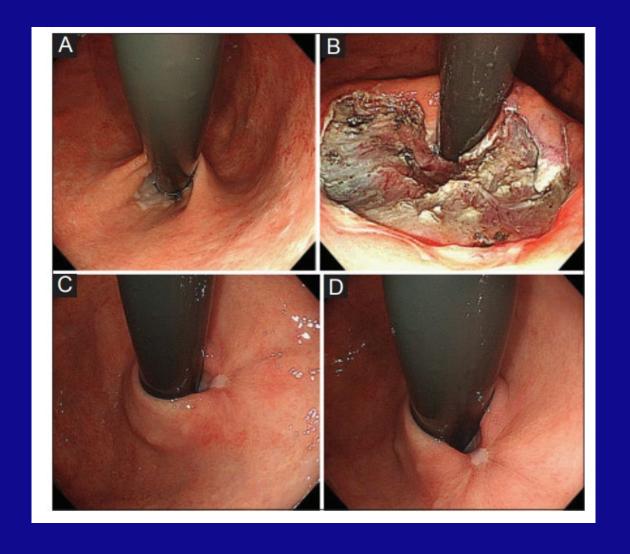
Haruhiro Inoue^a, Hiroaki Ito^a, Haruo Ikeda^a, Chiaki Sato^a, Hiroki Sato^a, Chainarong Phalanusitthepha^a, Bu'Hussain Hayee^b, Nikolas Eleftheriadis^a, Shin-ei Kudo^c

Digestive Diseases Center, Showa University Koto-Toyosu Hospital, Tokyo, Japan; King's College Hospital NHS Foundation Trust, London, UK; Digestive Disease Center, Showa University Northern Yokohama Hospital, Yokohama, Japan

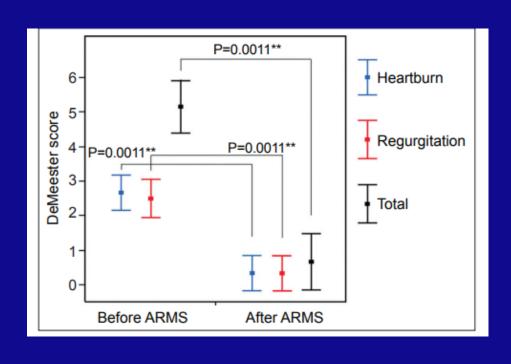
Circumferential ARM



Cresentic ARM



Anti-Reflux Mucosotomy (ARM)



- 10 patients
- Stricture with circumferential ARM
- PPI cessation after 40 days in all 10 patients

Third Space Endoscopy

Per Oral Pyloromyotomy

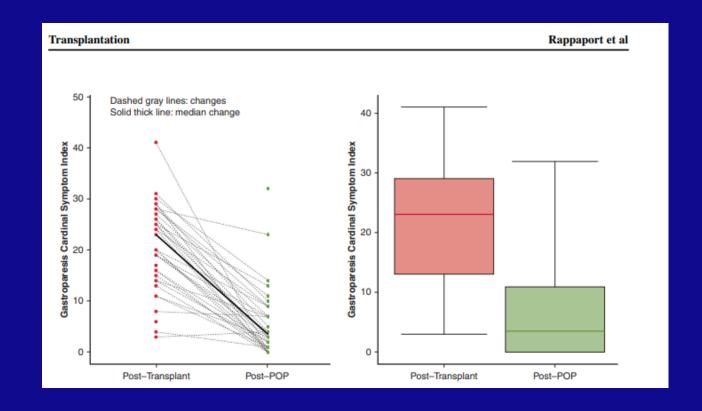
Rappaport et al Transplantation

Endoscopic pyloromyotomy is feasible and effective in improving post-lung transplant gastroparesis

Jesse M. P. Rappaport, MD, Siva Raja, MD, PhD, Scott Gabbard, MD, Lucy Thuita, MS, Madhusudhan R. Sanaka, MD, Eugene H. Blackstone, MD, and Usman Ahmad, MD, for the Cleveland Clinic Lung Transplantation Center

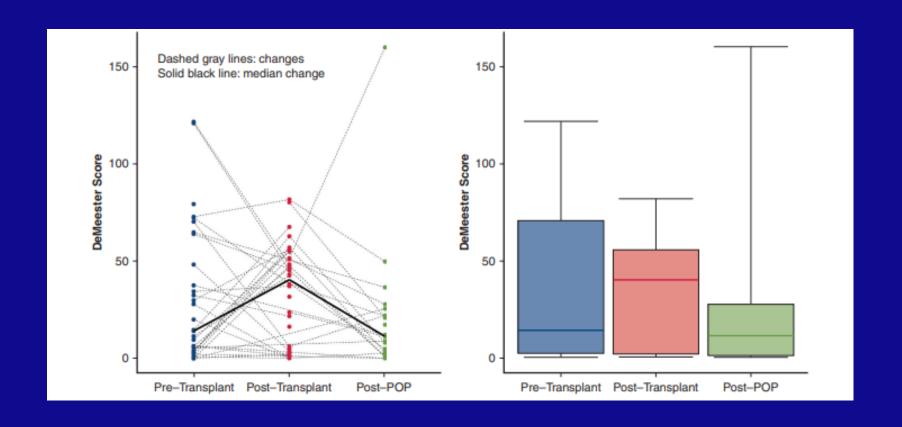


Per Oral Pyloromyotomy



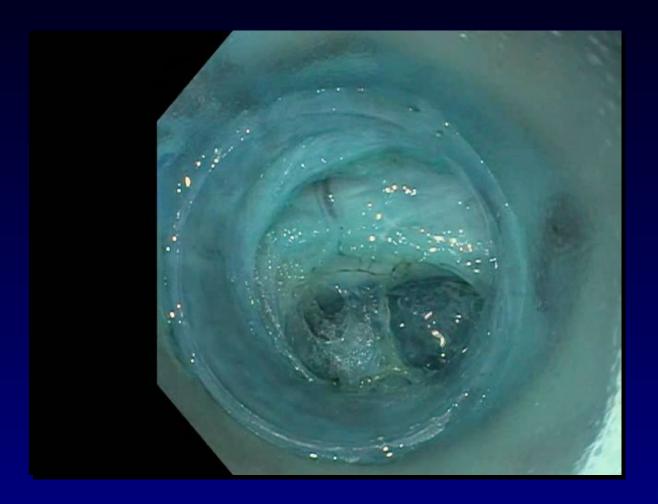


Per Oral Pyloromyotomy





Third Space Endoscopy G-POEM/POP





STER

REVIEW ARTICLE

Annals of Gastroenterology (2017) 30, 262-272

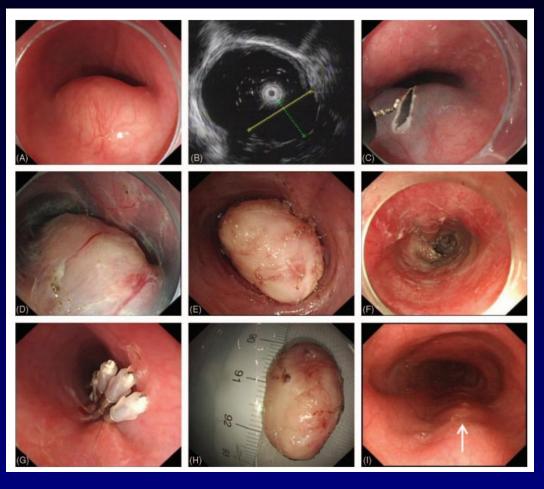
Submucosal tunneling endoscopic resection of upper gastrointestinal tract tumors arising from muscularis propria

Deepanshu Jain^a, Aakash Desai^b, Ejaz Mahmood^a, Shashideep Singhal^b

Albert Einstein Medical Center, Philadelphia; University of Texas Health Science Center at Houston, USA



STER





STER

TABLE 1.	Clinicopathological	Characteristics	of	180	Upper	
Gastrointestinal SMTs Treated by STER						

Patients			
Age, median (range), yr	49 (18-77)		
Sex, male/female	120/60		
Lesions			
Size, median (range), cm	2.6 (2.0-5.0)		
Shape, n (%)			
Regular	131(72.8%)		
Irregular	49 (27.2%)		
Location, n (%)			
Upper Esophagus	7 (3.9%)		
Middle Esophagus	66 (36.7%)		
Lower Esophagus	51 (28.3%)		
Esophagogastric junction	43 (23.9%)		
Stomach	13 (7.2%)		
Layer			
Superficial MP	58 (32.2%)		
Deep MP	122 (67.8%)		
Histopathology, n (%)			
Leimyoma	146 (81.1%)		
GIST	28 (15.6%)		
Schwannoma	4 (2.2%)		
Clarifying fibrous tumors	2 (1.1%)		
Technique, n (%)			
En bloc	163 (90.6%)		
Procedure time, median (range), min	45 (15-200)		
Complications, n (%)	15 (8.3%)		
Pneumothorax/hydrothorax	10 (5.5%)		
Major bleeding	2 (1.1%)		
Mucosal injury	2 (1.1%)		
Esophageal-pleural fistula	1 (0.6%)		
Follow-up, median (rang, mo)	36 (28-51)		
Recurrence	0 (0%)		
Metastasis	0 (0%)		

- Median Size 2.6 cm
- Most commonly in the mid to distal esophagus
- Leiomyoma 81%
- Median Procedure time 45 min
- Follow up 36 months



Final Thoughts

- Molecular detection of high risk Barrett's esophagus very promising but not mainstream yet
- Endoscopic therapies have yet to demonstrate durability but have uses in specific clinical arenas
- Third space endoscopy is here to stay but require an additional skill set

The battlefields of surgery are littered with the remains of new operations, which foundered and perished in the follow up clinic.

Mr. Ronald Belsey MD

