

Third Space Endoscopy: To Infinity and Beyond

Mouen Khashab, MD, MASGE

Professor of Medicine

Director of Therapeutic Endoscopy

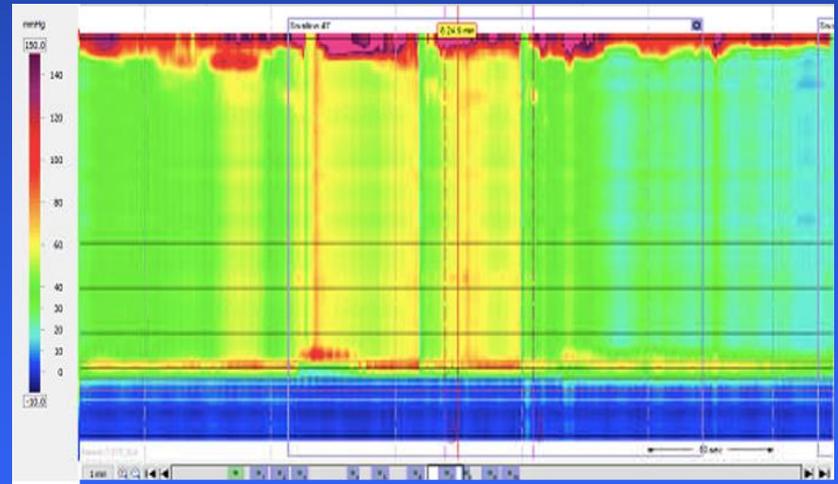
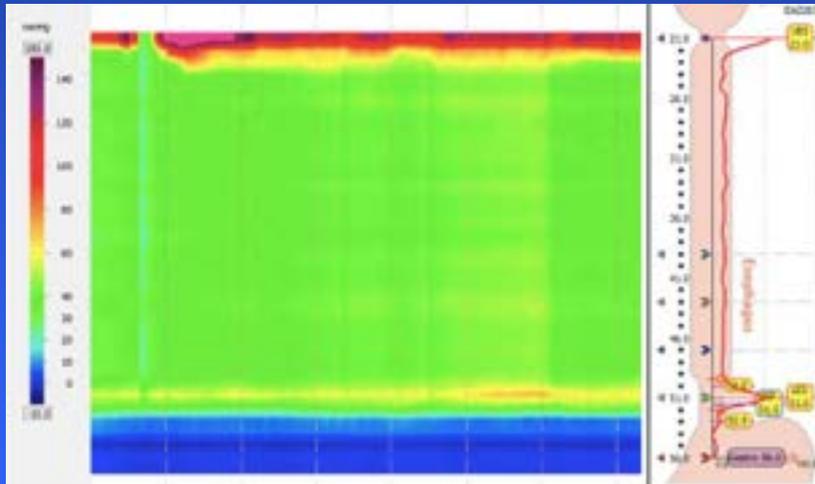
The Johns Hopkins Hospital

Baltimore, Maryland

HREM

Composite swallow

Swallow # 7



PD or POEM?

JAMA | Original Investigation

Effect of Peroral Endoscopic Myotomy vs Pneumatic Dilation
on Symptom Severity and Treatment Outcomes Among
Treatment-Naive Patients With Achalasia
A Randomized Clinical Trial

JAMA. 2019;322(2):134-144.

Comprehensive Analysis of Adverse Events Associated With Per Oral Endoscopic Myotomy in 1826 Patients: An International Multicenter Study

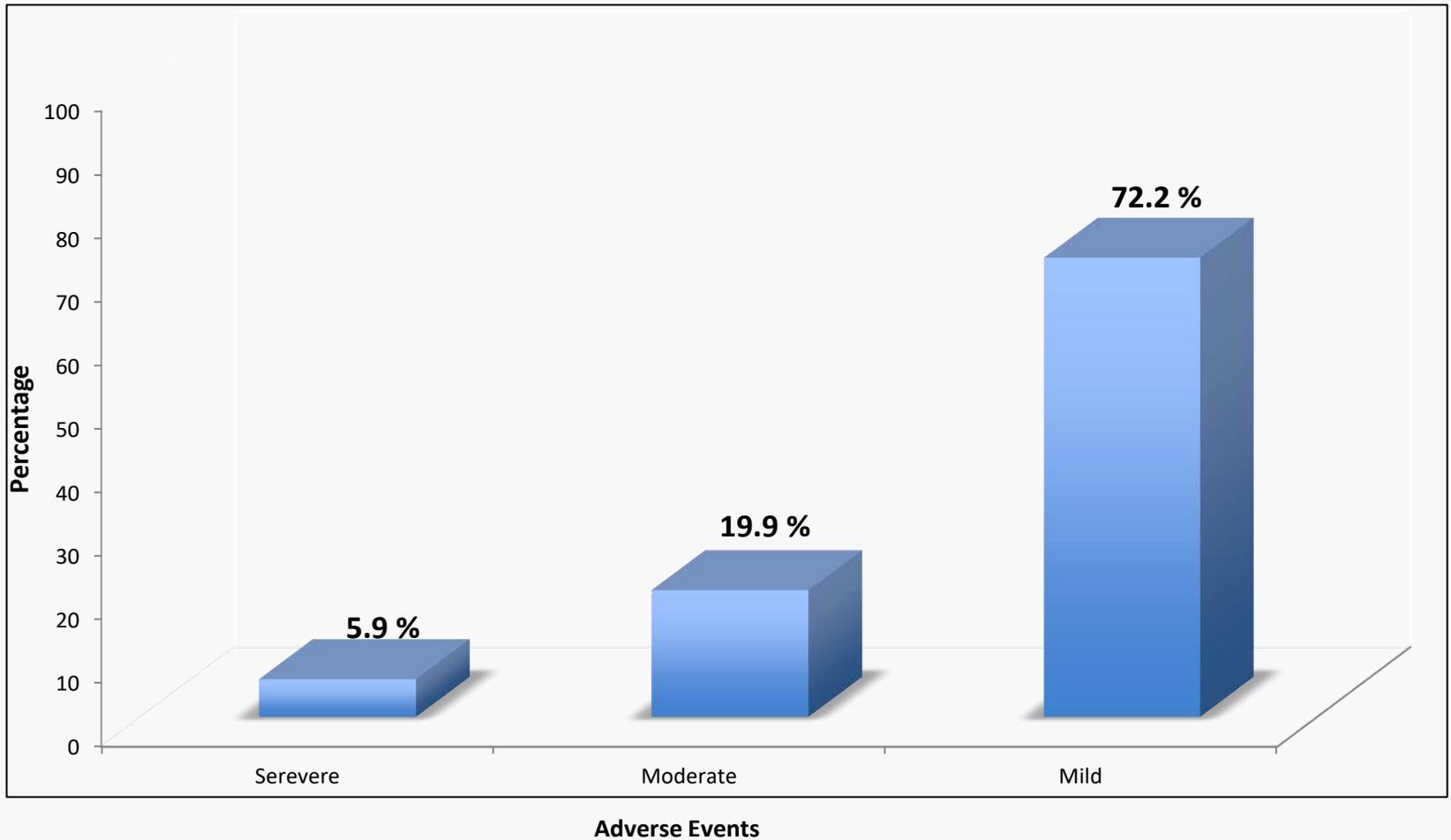
Yamile Haito-Chavez, MD¹, Haruhiro Inoue, MD, PhD², Kristin W. Beard, MD³, Peter V. Draganov, MD⁴, Michael Ujiki, MD⁵, Burkhard H.A. Rahden, MD⁶, Pankaj N. Desai, MD⁷, Mathieu Pioche, MD, PhD⁸, Bu Hayee, MBBS, PhD⁹, Aryn Haji, MD⁹, Payal Saxena, MD¹⁰, Kevin Reavis, MD³, Manabu Onimaru, MD, PhD², Valerio Balassone, MD², Jun Nakamura, MD, PhD², Yoshitaka Hata, MD², Dennis Yang, MD⁴, Davinderbir Pannu, MD⁴, Ali Abbas, MD⁴, Yaseen B. Perbtani, MD⁴, Lava Y. Patel, MD⁵, Jorg Filser, MD⁶, Sabine Roman, MD, PhD⁸, Jerome Rivory, MD⁸, Francois Mion, MD⁸, Thierry Ponchon, MD, PhD⁸, Silvana Perretta, MD¹¹, Vivien Wong, MD¹¹, Roberta Maselli, MD¹², Saowanee Ngamruengphong, MD¹, Yen-I Chen, MD¹, Majidah Bukhari, MD¹, Gulara Hajiyeva, MD¹, Amr Ismail, MD¹, Renata Pieratti, MD¹, Vivek Kumbhari, MD¹, Gerson Galdos-Cardenas, MD, PhD¹³, Alessandro Repici, MD¹² and Mouen A. Khashab, MD¹

Am J Gastroenterol 2017; 112:1267–1276

Results

- 1826 patients underwent POEM.
- 137 patients with AEs.
- Total of 156 AEs.
- Overall incidence of AEs: 7.5%.
- No mortality related to POEM.

Results

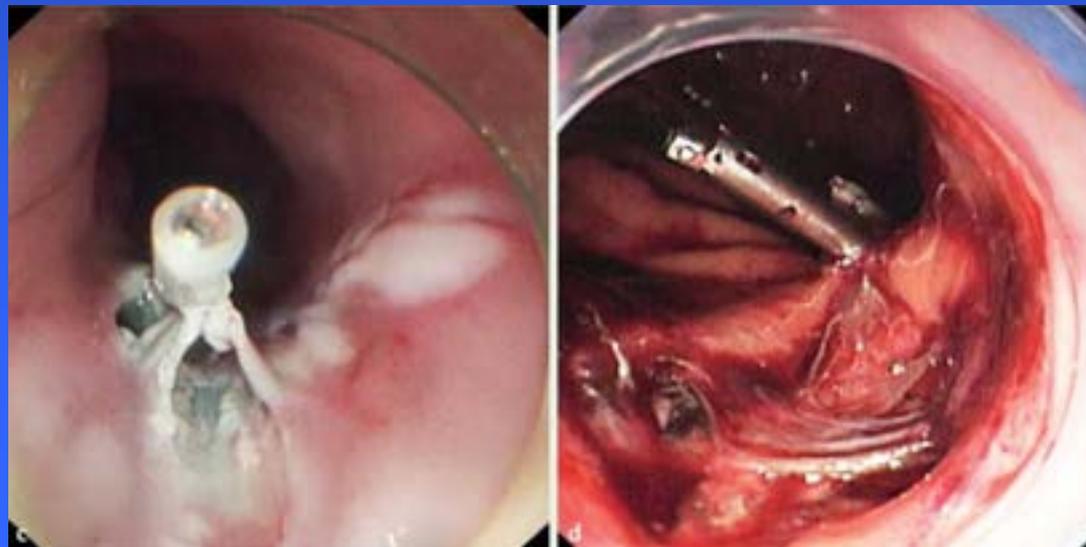


Results

| Severe AEs 9 (5.9%) | n | % | Treatment |
|------------------------|---|------|---|
| • Intraprocedure | 4 | 2.6 | |
| Bleeding | 2 | 1.3 | Taponade with a Segstaken-Blakemore tube (1/2) Surgery (1/2) |
| Cardiac Arrhythmia | 1 | 0.65 | |
| Esophageal perforation | 1 | 0.65 | Surgery |
| • First 48 hours | 4 | 2.6 | |
| Esophageal leak | 2 | 1.3 | Endoscopic therapy : clipping (1/2) Surgery (1/2) |
| Pneumomediastinum | 1 | 0.65 | Conservative treatment |
| Pneumonia | 1 | 0.65 | Conservative treatment |
| • After 48 hours | 1 | 0.65 | |
| Empyema | 1 | 0.65 | Surgery |

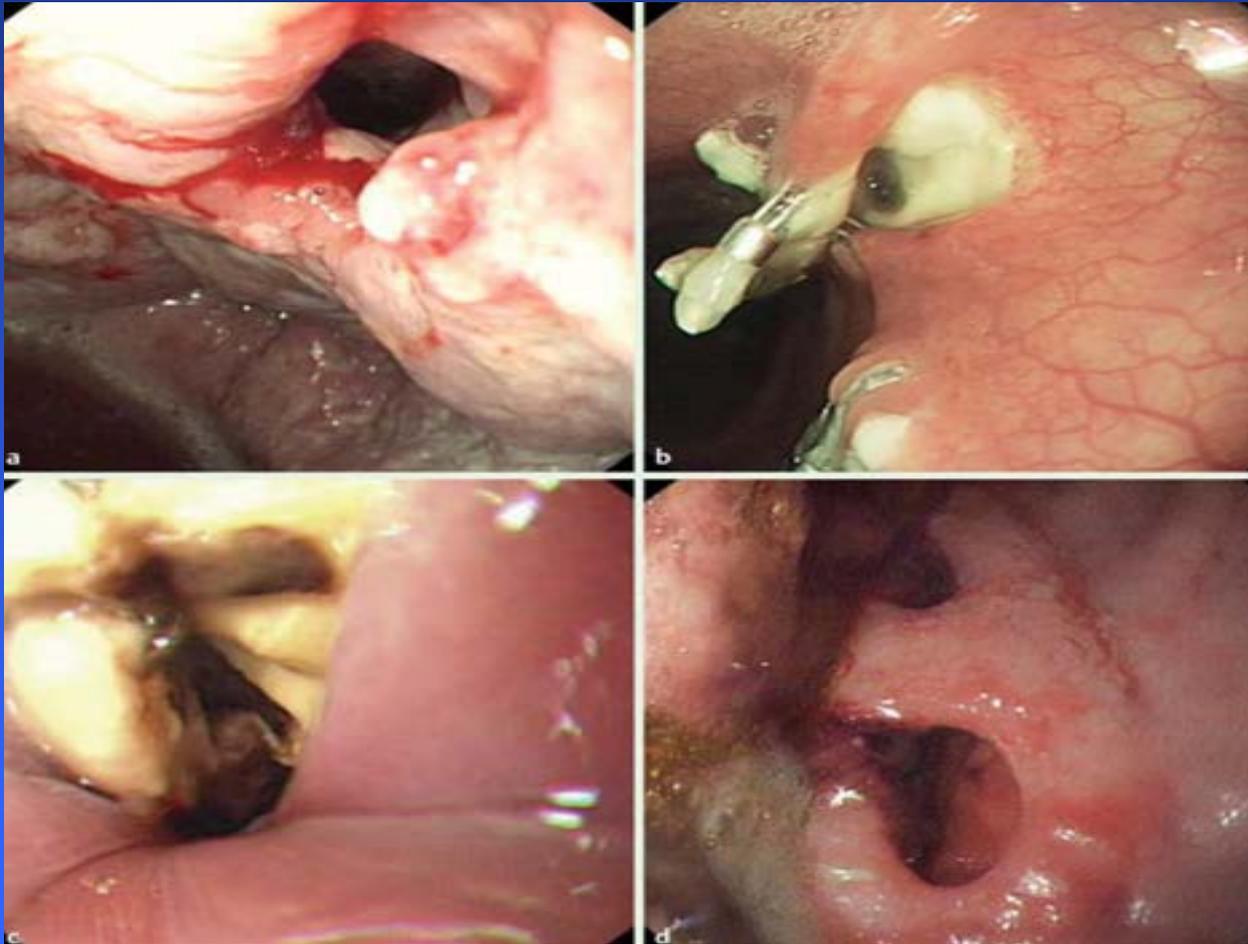


**Type I
mucosal
injury**



**Type II
mucosal
injury**

Delayed mucosal barrier failure



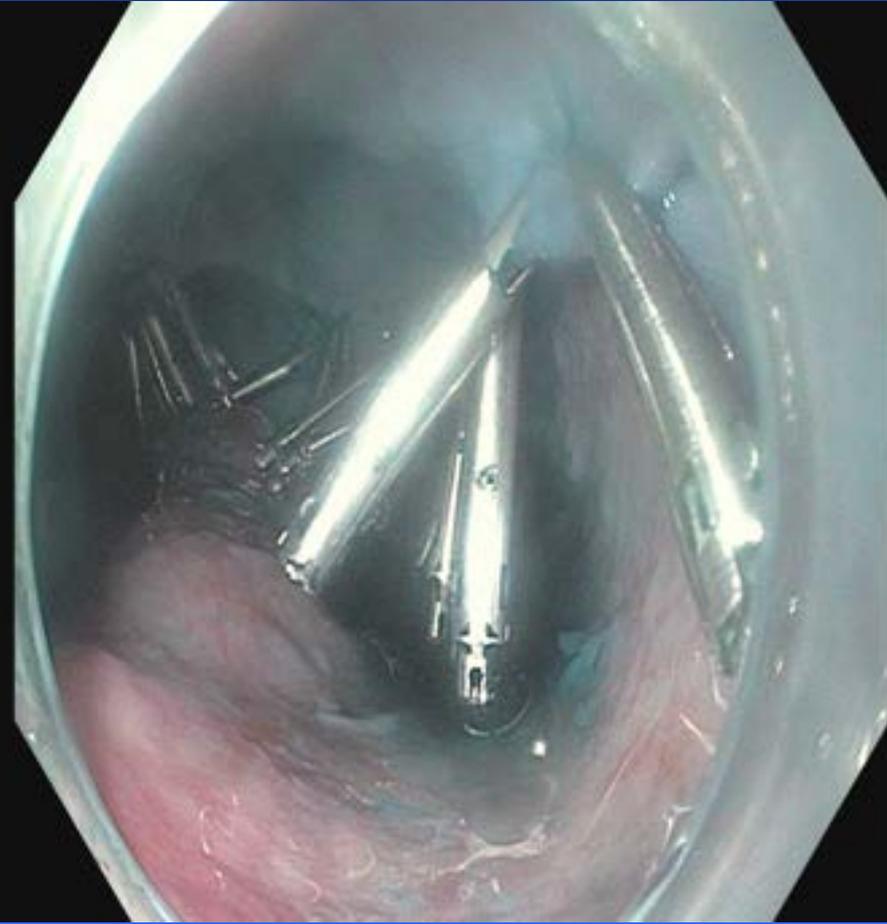
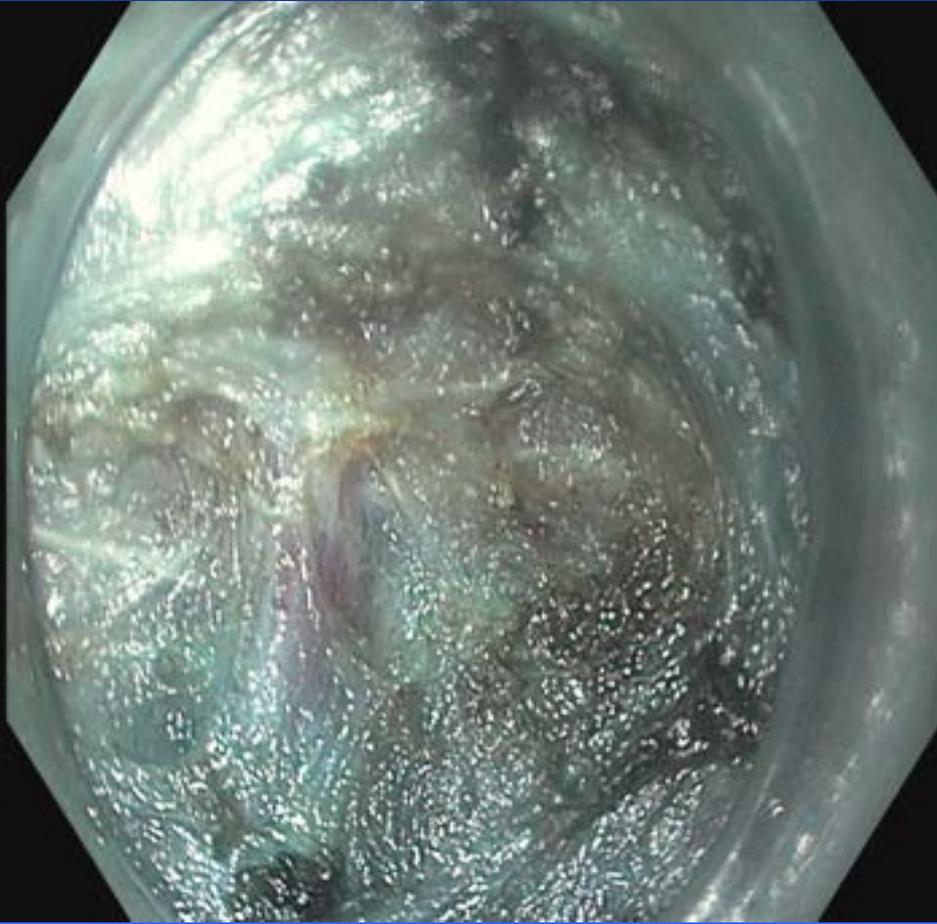
Mucosal injury at the cardia may occur and can be treated with clips (mucosotomy)



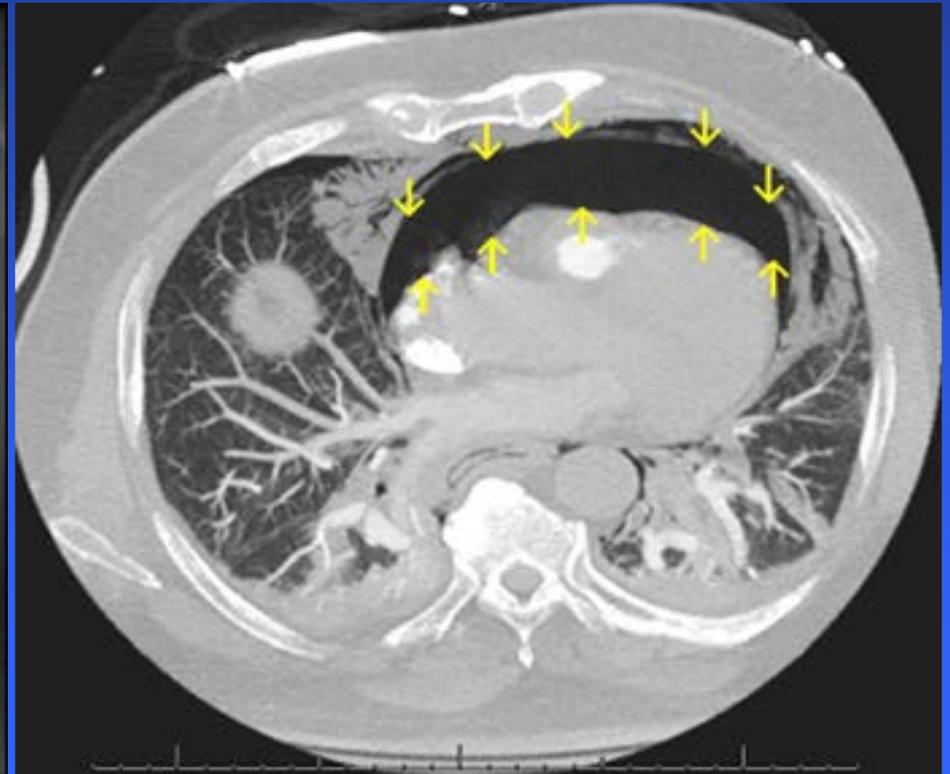
POEM - Bleeding

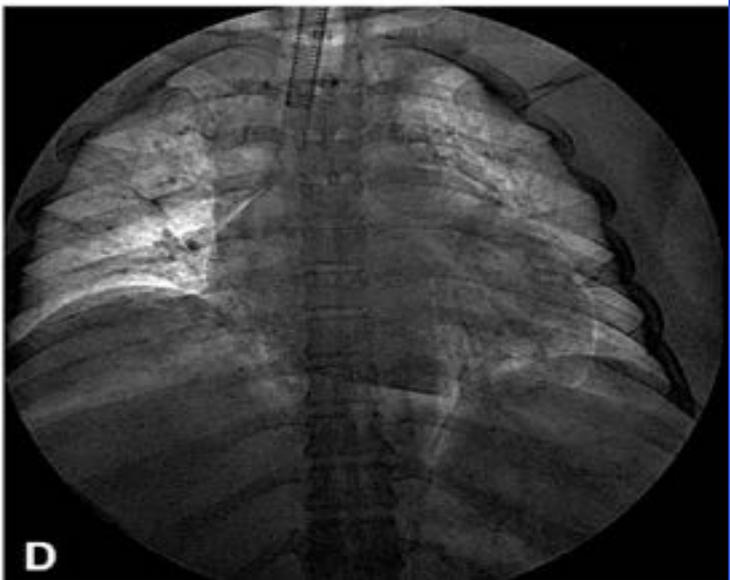
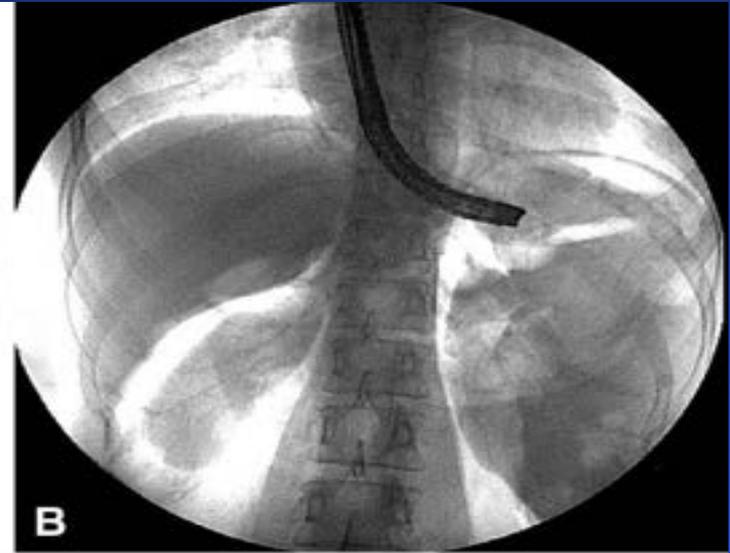
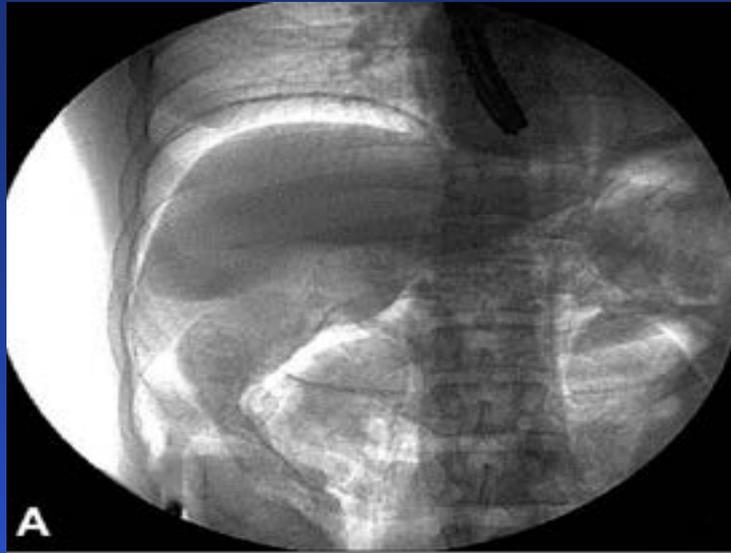


Extensive Submucosal Fibrosis



Cardiac arrest during POEM !!





Tension Pneumoperitoneum



PD or POEM?

JAMA | Original Investigation

Effect of Peroral Endoscopic Myotomy vs Pneumatic Dilation
on Symptom Severity and Treatment Outcomes Among
Treatment-Naive Patients With Achalasia
A Randomized Clinical Trial

JAMA. 2019;322(2):134-144.

| | POEM | | Pneumatic Dilatation | | Unadjusted Absolute Difference, % (95% CI) ^a | Unadjusted Risk Ratio (95% CI) | P Value ^b |
|--------------------------------------|----------|-----|----------------------|------|---|--------------------------------|----------------------|
| | No. (%) | SD | No. (%) | SD | | | |
| 2-y Follow-up (primary end point) | (n = 63) | | (n = 63) | | | | |
| Overall treatment success | 58 (92) | 3.4 | 34 (54) | 6.3 | 38 (22 to 52) | 1.71 (1.34 to 2.17) | <.001 |
| Reasons for failure ^c | | | | | | | |
| Eckardt score >3 | 5 (8) | 3.4 | 28 (44) | 6.2 | 36 (20 to 50) | | <.001 |
| Re-treatment | 5 (8) | 3.4 | 26 (41) | 10.5 | 33 (17 to 47) | | <.001 |
| Treatment-related SAEs | 0 | 0 | 1 (1.6) | 1.6 | 1.6 (-5 to 10) | | >.99 |
| 3-mo Follow-up (secondary end point) | (n = 64) | | (n = 65) | | | | |
| Overall treatment success | 63 (98) | 1.8 | 52 (80) | 5 | 18 (7 to 30) | 1.23 (1.09 to 1.40) | .001 |
| Reasons for failure ^c | | | | | | | |
| Eckardt score >3 | 1 (2) | 1.8 | 12 (18) | 4.8 | 16 (5 to 29) | | .002 |
| Re-treatment | 1 (2) | 1.8 | 11 (17) | 4.7 | 15 (4 to 27) | | .004 |
| Treatment-related SAEs | 0 | 0 | 1 (2) | 1.7 | 2 (-5 to 9) | | >.99 |
| 1-y Follow-up (secondary end point) | (n = 64) | | (n = 64) | | | | |
| Overall treatment success | 61 (95) | 2.7 | 42 (66) | 5.9 | 31 (17 to 45) | 1.45 (1.21 to 1.75) | <.001 |
| Reasons for failure ^c | | | | | | | |
| Eckardt score >3 | 3 (5) | 2.7 | 21 (33) | 5.9 | 28 (14 to 42) | | <.001 |
| Re-treatment | 3 (5) | 2.7 | 19 (30) | 5.7 | 25 (11 to 38) | | <.001 |
| Treatment-related SAEs | 0 | 0 | 1 (1.6) | 1.6 | 2 (-5 to 9) | | >.99 |

| Endoscopic reflux esophagitis ^e | (n = 54) | (n = 29) | | |
|--|----------|----------|---------------|------------|
| No. (%) | 22 (41) | 2 (7) | 34 (12 to 49) | .002 (.03) |
| SD | 6.5 | 4.7 | | |
| Grade, No. (%) | | | | |
| A | 17 (31) | 2 (7) | | |
| B | 2 (4) | 0 | | |
| C | 3 (6) | 0 | | |
| D | 0 | 0 | | |
| PPI use, No (%) | 24 (41) | 7 (21) | 20 (1 to 38) | .004 (.04) |
| SD | 6.5 | 7 | | |
| Reflux esophagitis, No. (%) | 10 (42) | 0 | | |
| No reflux esophagitis, No. (%) | 14 (58) | 7 (100) | | |

LHM or POEM

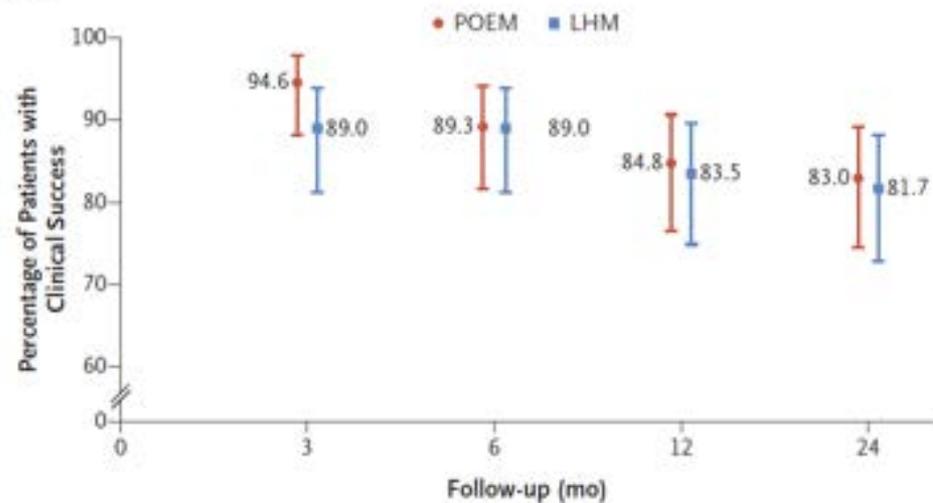
ORIGINAL ARTICLE

Endoscopic or Surgical Myotomy in Patients with Idiopathic Achalasia

Yuki B. Werner, M.D., Bengt Hakanson, M.D., Jan Martinek, M.D.,
Alessandro Repici, M.D., Burkhard H.A. von Rahden, M.D.,
Albert J. Bredenoord, M.D., Raf Bisschops, M.D., Helmut Messmann, M.D.,
Marius C. Vollberg, M.Sc., Tania Noder, R.N., Jan F. Kersten, M.Sc.,
Oliver Mann, M.D., Jakob Izbiccki, M.D., Alexander Pazdro, M.D.,
Uberto Fumagalli, M.D., Riccardo Rosati, M.D., Christoph-Thomas Germer, M.D.,
Marlies P. Schijven, M.D., Alice Emmermann, M.D., Daniel von Renteln, M.D.,
Paul Fockens, M.D., Guy Boeckxstaens, M.D., and Thomas Rösch, M.D.

N Engl J Med 2019;381:2219-29

A Clinical Success



No. at Risk

| | | | | |
|------------------------------------|---------|---------|---------|---------|
| POEM (no. of imputed observations) | 112 (4) | 112 (6) | 112 (5) | 112 (4) |
| LHM (no. of imputed observations) | 109 (3) | 109 (7) | 109 (7) | 109 (5) |

Table 2. Clinical and Objective Evaluation of Gastroesophageal Reflux Disease (a Secondary End Point) over Time.*

| Measure | 3 Months | | 2 Years | |
|---|-----------------------|----------------------|-----------------------|----------------------|
| | POEM Group (N=112) | LHM Group (N=109) | POEM Group (N=112) | LHM Group (N=109) |
| Clinical scores | | | | |
| Mean DeMeester clinical score (95% CI) | 0.9 (0.6–1.1) | 0.5 (0.3–0.7) | 1.2 (0.9–1.5) | 1.0 (0.6–1.0) |
| Daily reflux symptoms — no./total no. (%) | 5/108 (4.6) | 2/105 (1.9) | 7/107 (6.5) | 2/103 (1.9) |
| Occasional reflux symptoms — no./total no. (%) | 42/108 (38.9) | 29/105 (27.6) | 49/107 (45.8) | 45/103 (43.7) |
| Daily proton-pump inhibitor use — no./total no. (%) | 25/108 (23.1) | 16/105 (15.2) | 41/106 (38.7) | 20/103 (19.4) |
| Occasional proton-pump inhibitor use — no./total no. (%) | 8/108 (7.4) | 13/105 (12.4) | 15/106 (14.2) | 8/103 (7.8) |
| LA Classification grade of reflux esophagitis — no./total no. (%)† | | | | |
| Overall, grades A to D | 57/100 (57) | 19/96 (20) | 38/87 (44) | 23/78 (29) |
| Grade A | 32/100 (32) | 13/96 (14) | 18/87 (21) | 13/78 (17) |
| Grade B | 19/100 (19) | 3/96 (3) | 16/87 (18) | 5/78 (6) |
| Grade C | 5/100 (5) | 2/96 (2) | 4/87 (5) | 2/78 (3) |
| Grade D | 1/100 (1) | 1/96 (1) | 0/87 | 3/78 (4) |
| Esophageal acid exposure‡ | | | | |
| Mean acid exposure time (95% CI) — % | 7.1 (5.4–8.9) | 6.7 (4.1–9.3) | 5.7 (2.8–8.5) | 5.4 (2.2–8.5) |
| Acid exposure time >4.5% — no./total no. (%) | 41/93 (44) | 27/82 (33) | 21/70 (30) | 17/56 (30) |

ASGE guideline on the management of achalasia



Mouen A. Khashab, MD,^{1,*} Marcelo F. Vela, MD,^{2,*} Nirav Thosani, MD,^{3,*} Deepak Agrawal, MD, MPH, MBA,⁴ James L. Buxbaum, MS, FASGE,⁵ Syed M. Abbas Fehmi, MD, MSc, FASGE,⁶ Douglas S. Fishman, MD, FAAP, FASGE,⁷ Suryakanth R. Gurudu, MD, FASGE,² Laith H. Jamil, MD, FASGE,⁸ Terry L. Jue, MD, FASGE,⁹ Bijun Sai Kannadath, MBBS, MS,⁵ Joanna K. Law, MD,¹⁰ Jeffrey K. Lee, MD, MAS,¹¹ Mariam Naveed, MD,¹² Bashar J. Qumseya, MD, MPH,¹³ Mandeep S. Sawhney, MD, MS, FASGE,¹⁴ Julie Yang, MD, FASGE,¹⁵ Sachin Wani, MD, ASGE Standards of Practice Committee Chair¹⁶

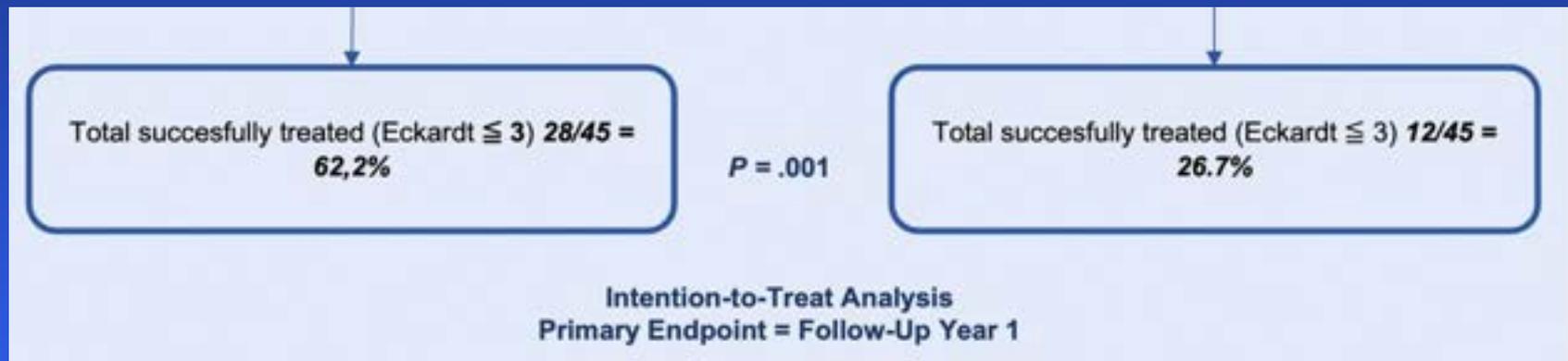
1. Laparoscopic Heller myotomy, pneumatic dilation, and POEM are effective therapeutic modalities for patients with achalasia. Decision between these treatment options should depend on achalasia type, local expertise, and patient preference. ⊕ ⊕ ⊕ ⊕

2. We recommend against the use of botulinum toxin injection as definitive therapy for achalasia patients. Botulinum toxin injection may be reserved for patients who are not candidates for other definitive therapies. ⊕ ⊕ ⊕ ○

The Efficacy of Peroral Endoscopic Myotomy vs Pneumatic Dilatation as Treatment for Patients With Achalasia Suffering From Persistent or Recurrent Symptoms After Laparoscopic Heller Myotomy: A Randomized Clinical Trial

Caroline M. G. Saleh, Pietro Familiari, Barbara A. J. Bastiaansen, Paul Fockens, Jan Tack, Guy Boeckxstaens, Raf Bisschops, Aaltje Lei, Marlies P. Schijven, Jan Guido Costamagna, and Albert J. Bredenoord

Gastroenterology 2023



| Variable | POEM, n (%) | PD, n (%) | P Value ^a |
|-----------------------------|--------------|------------|----------------------|
| Reflux esophagitis (n = 75) | 12/35 (34.3) | 6/40 (15) | .062 |
| Grade A | 7/35 (20) | 4/40 (10) | NA |
| Grade B | 4/35 (11.4) | 1/40 (2.5) | NA |
| Grade C | 1/35 (2.9) | 1/40 (2.5) | NA |
| Grade D | 0 (0) | 0 (0) | NA |
| PPI use (n = 87) | 29 (69) | 26 (57.8) | 0.374 |

ASGE guideline on the management of achalasia



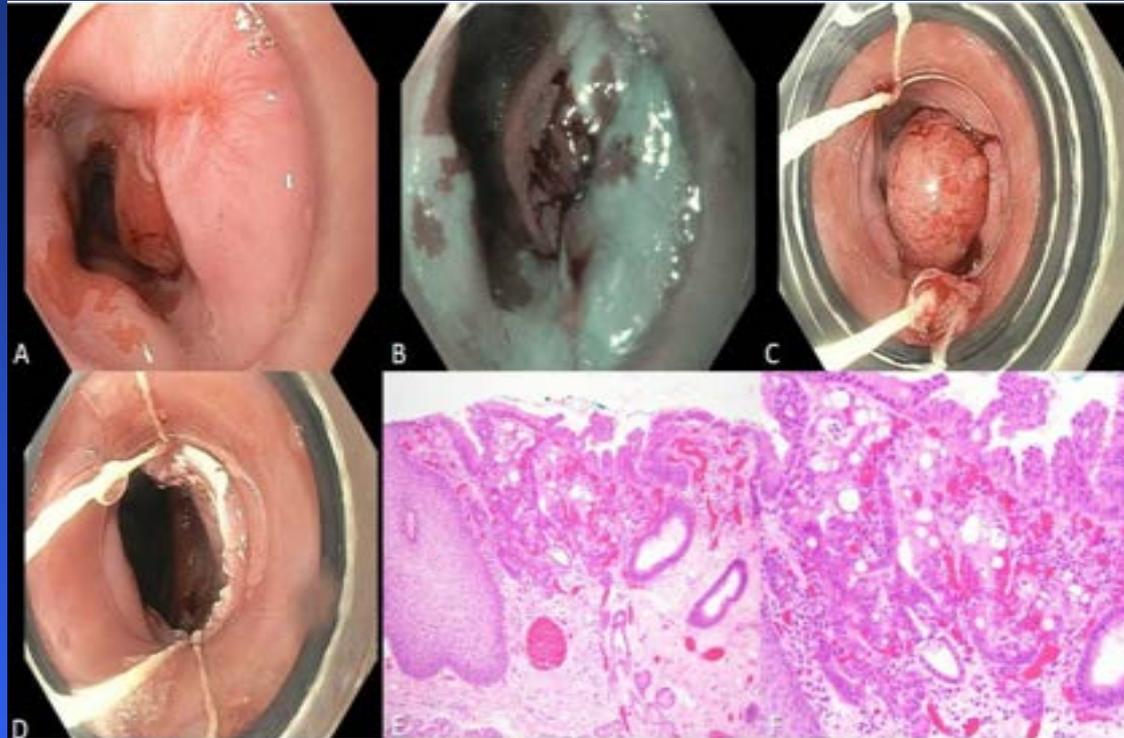
Mouen A. Khashab, MD,^{1,*} Marcelo F. Vela, MD,^{2,*} Nirav Thosani, MD,^{3,*} Deepak Agrawal, MD, MPH, MBA,⁴ James L. Buxbaum, MS, FASGE,⁵ Syed M. Abbas Fehmi, MD, MSc, FASGE,⁶ Douglas S. Fishman, MD, FAAP, FASGE,⁷ Suryakanth R. Gurudu, MD, FASGE,² Laith H. Jamil, MD, FASGE,⁸ Terry L. Jue, MD, FASGE,⁹ Bijun Sai Kannadath, MBBS, MS,⁵ Joanna K. Law, MD,¹⁰ Jeffrey K. Lee, MD, MAS,¹¹ Mariam Naveed, MD,¹² Bashar J. Qumseya, MD, MPH,¹³ Mandeep S. Sawhney, MD, MS, FASGE,¹⁴ Julie Yang, MD, FASGE,¹⁵ Sachin Wani, MD, ASGE Standards of Practice Committee Chair¹⁶

1. Laparoscopic Heller myotomy, pneumatic dilation, and POEM are effective therapeutic modalities for patients with achalasia. Decision between these treatment options should depend on achalasia type, local expertise, and patient preference. ⊕ ⊕ ⊕ ⊕

2. We recommend against the use of botulinum toxin injection as definitive therapy for achalasia patients. Botulinum toxin injection may be reserved for patients who are not candidates for other definitive therapies. ⊕ ⊕ ⊕ ○

Post POEM GERD



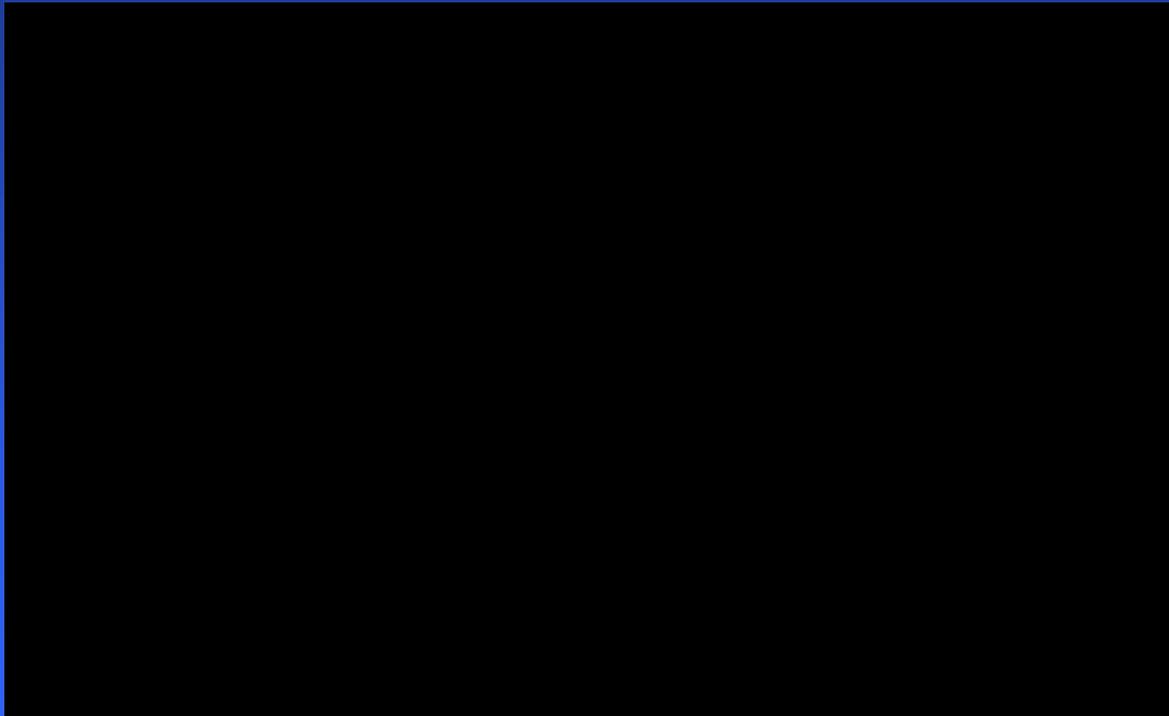


Ichkhanian, Benias, Khashab. Gut 2019;68:2107–2110

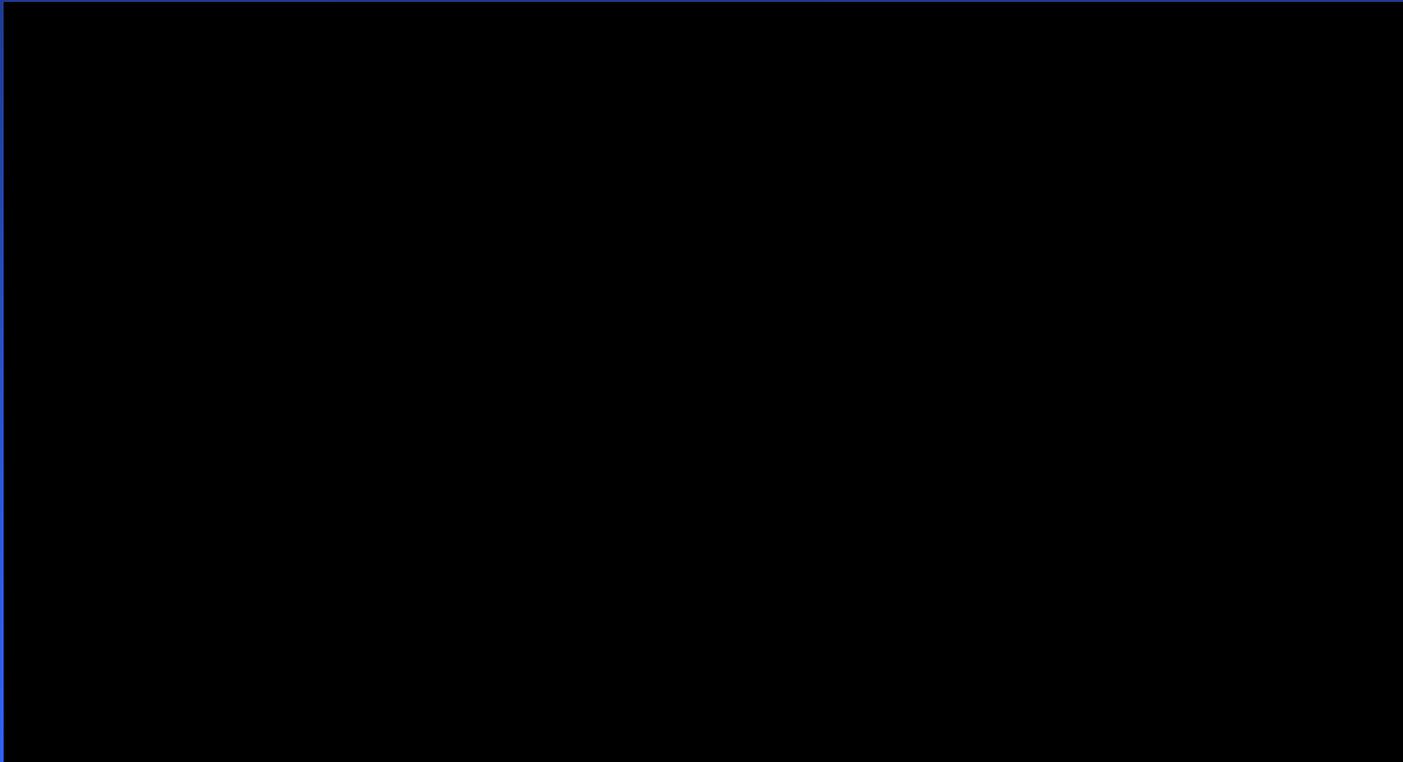
What is your recommended treatment?

- a. Dietary modification alone
- b. Calcium channel blocker alone
- c. Botulinum toxin injection
- d. Pneumatic dilation to 30-35mm
- e. Heller Myotomy with partial fundoplication
- f. POEM
- g. POEM-F

POEM-F (part 1)



POEM-F

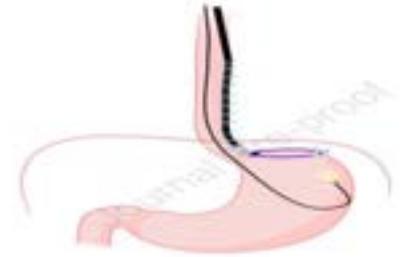


EndoFlip

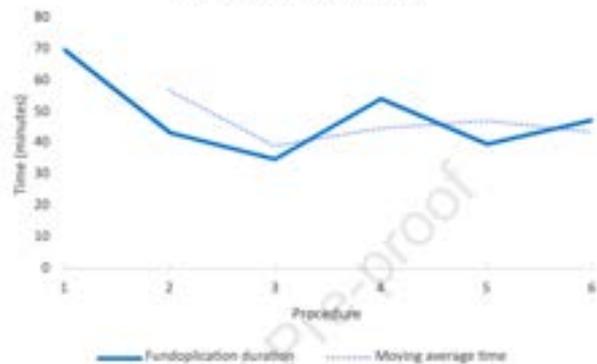
| | Diameter | CSA | Pressure | DI | Compliance |
|----------------------|----------|-----|----------|-----|------------|
| Baseline | 5 | 20 | 26.4 | 0.8 | 59.7 |
| After myotomy | 14.4 | 162 | 17.7 | 9.4 | 222.6 |
| After fundoplication | 11.1 | 97 | 29.9 | 3.2 | 89.1 |

Technical Details and Outcomes of Peroral Endoscopic Myotomy with Fundoplication: The First U.S. Experience.

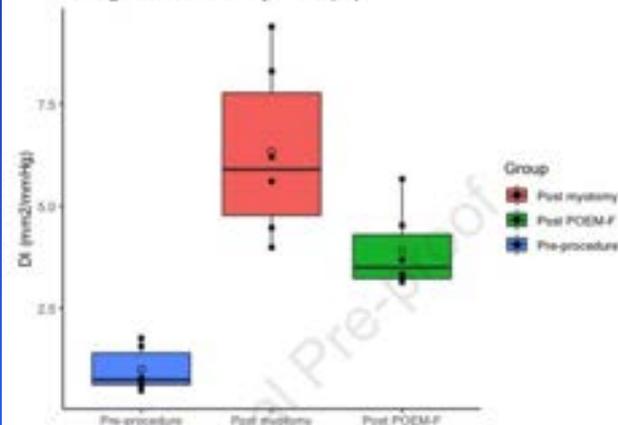
Apurva Shrigiriwar, MD, Linda Y. Zhang, MD, Bachir Ghandour, MD, Michael Bejjani, MD, Shruti Mony, MD, Amol Bapaye, MD (MS), FASGE, FSGEI, FISG, FJGES, Mouen A. Khashab, MD, MASGE



Fundoplication duration



Changes in Distensibility Index (DI)



GIE
2023

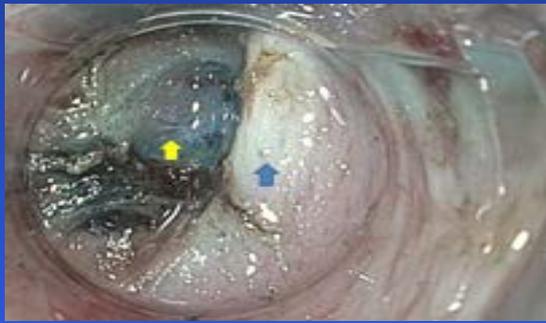


G-POEM

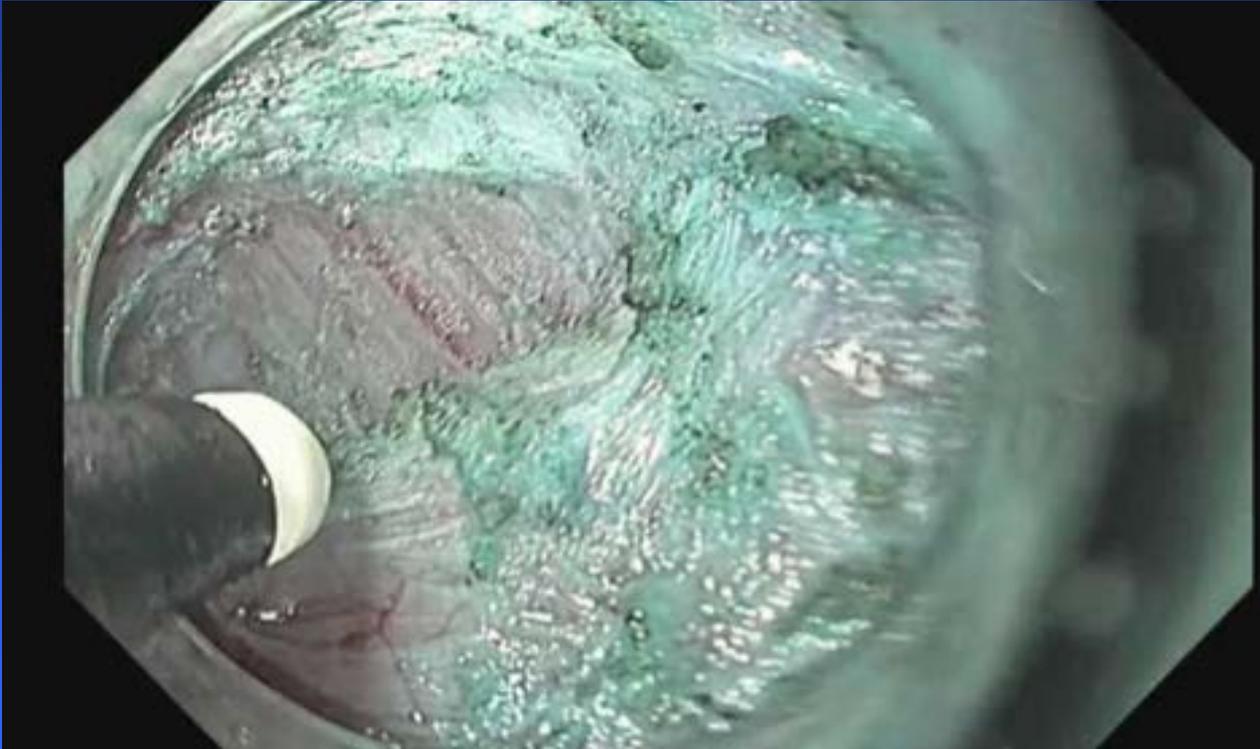
THINKING OUTSIDE THE BOX

Gastric peroral endoscopic myotomy for refractory gastroparesis:
first human endoscopic pyloromyotomy (with video) 

Khashab et al. 2013 Nov;78(5):764-8



G- POEM



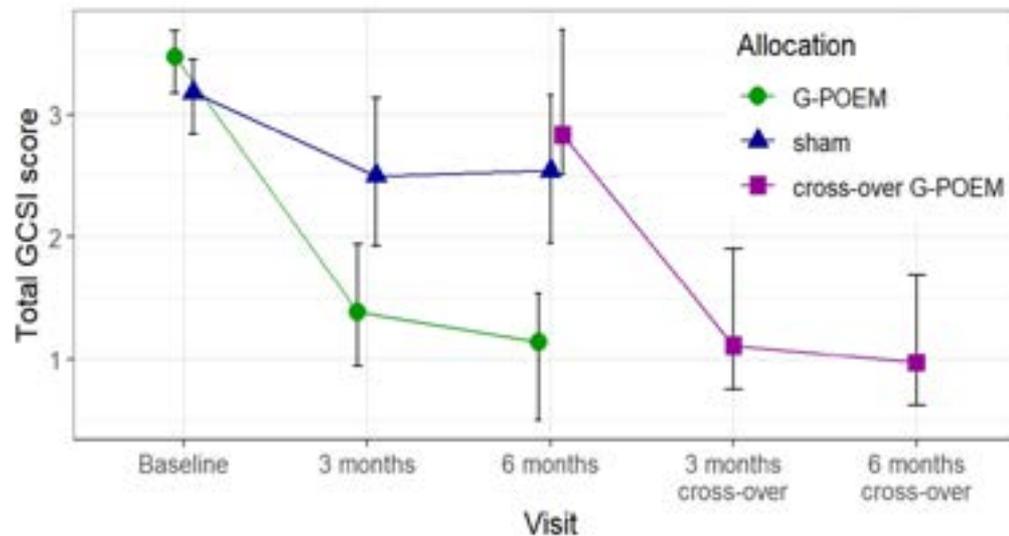
Double G-POEM



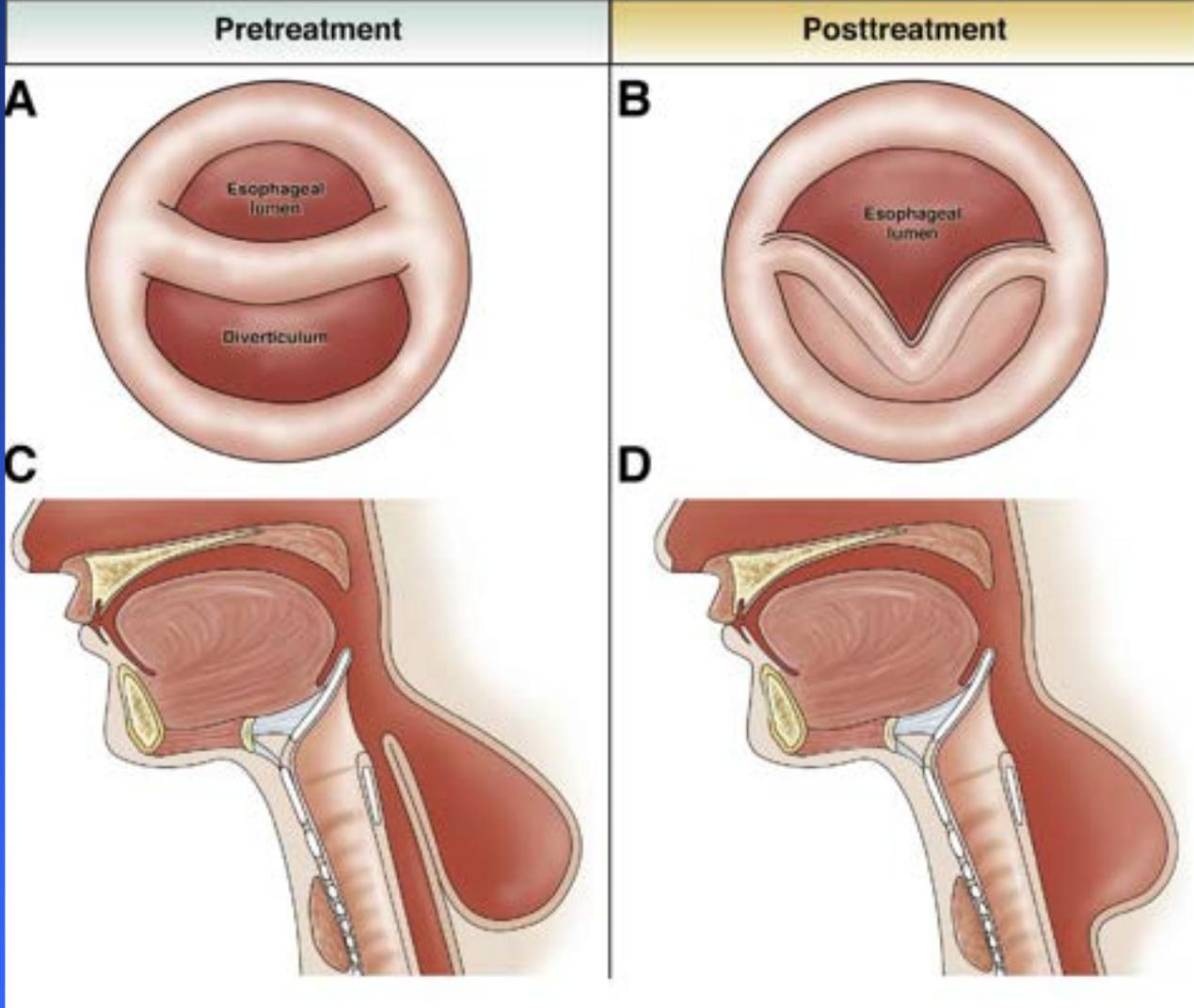
G-POEM

Endoscopic pyloromyotomy for the treatment of severe and refractory gastroparesis: a pilot, randomised, sham-controlled trial

Jan Martinek¹, Rastislav Hustak^{2,3}, Jan Mares⁴, Zuzana Vackova¹, Julius Spicak¹, Eva Kieslichova⁵, Marie Buncova⁶, Daniel Pohl⁷, Sunil Amin⁸, Jan Tack⁹



Z POEM

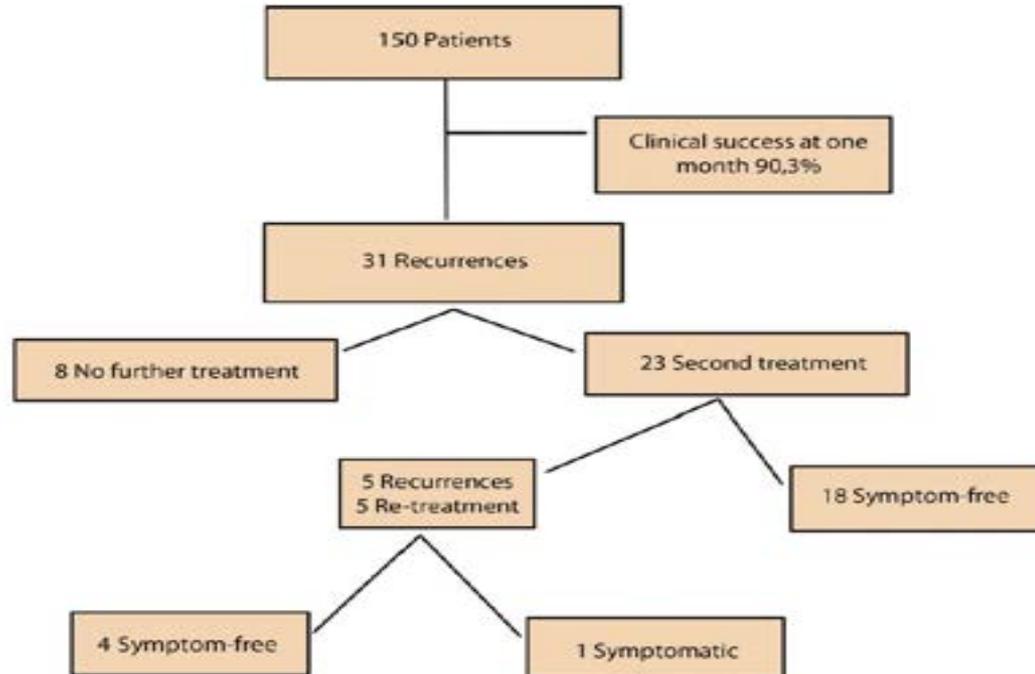


Endoscopic treatment for Zenker's diverticulum: long-term results (with video)

Vincent Huberty, MD,¹ Souraya El Bacha, MD,¹ Daniel Blero, MD, PhD,¹ Olivier Le Moine, MD, PhD,¹ Sergio Hassid, MD, PhD,² Jacques Devière, MD, PhD¹

Brussels, Belgium

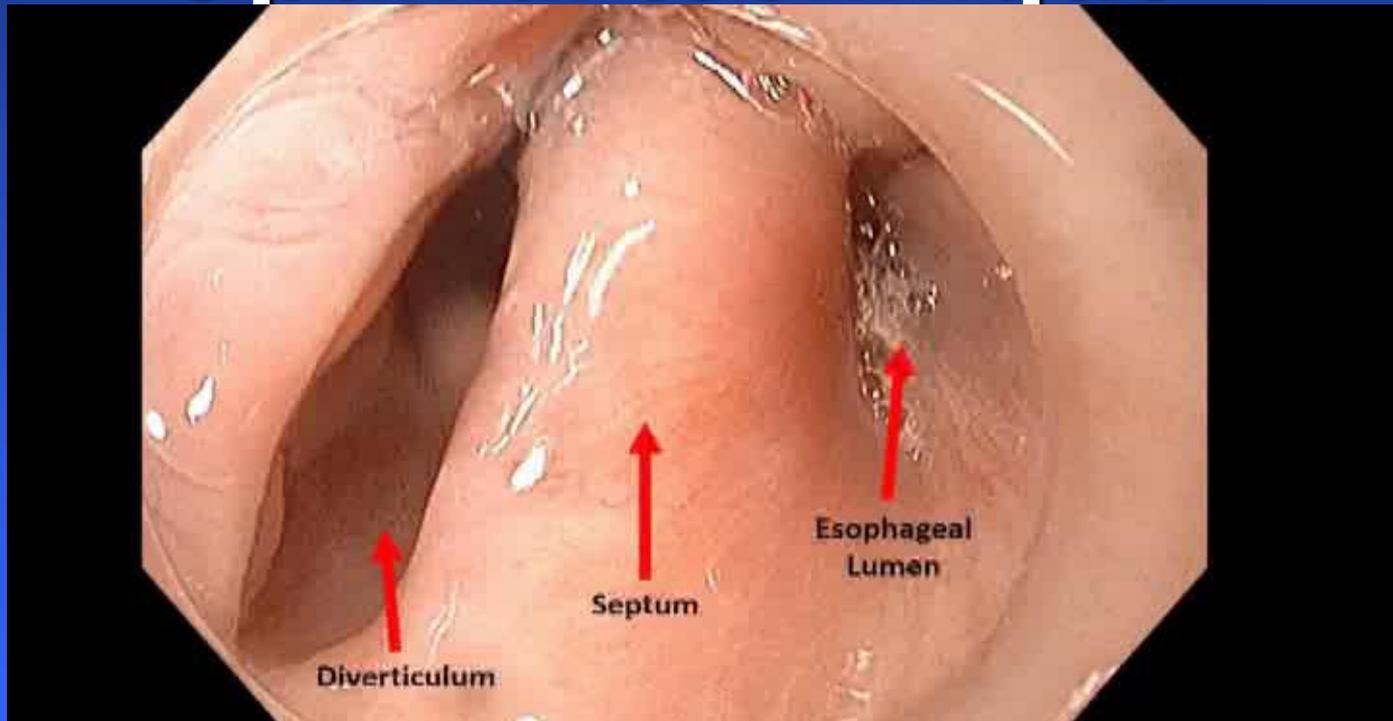
Gastrointest Endosc 2013;77:701-7.



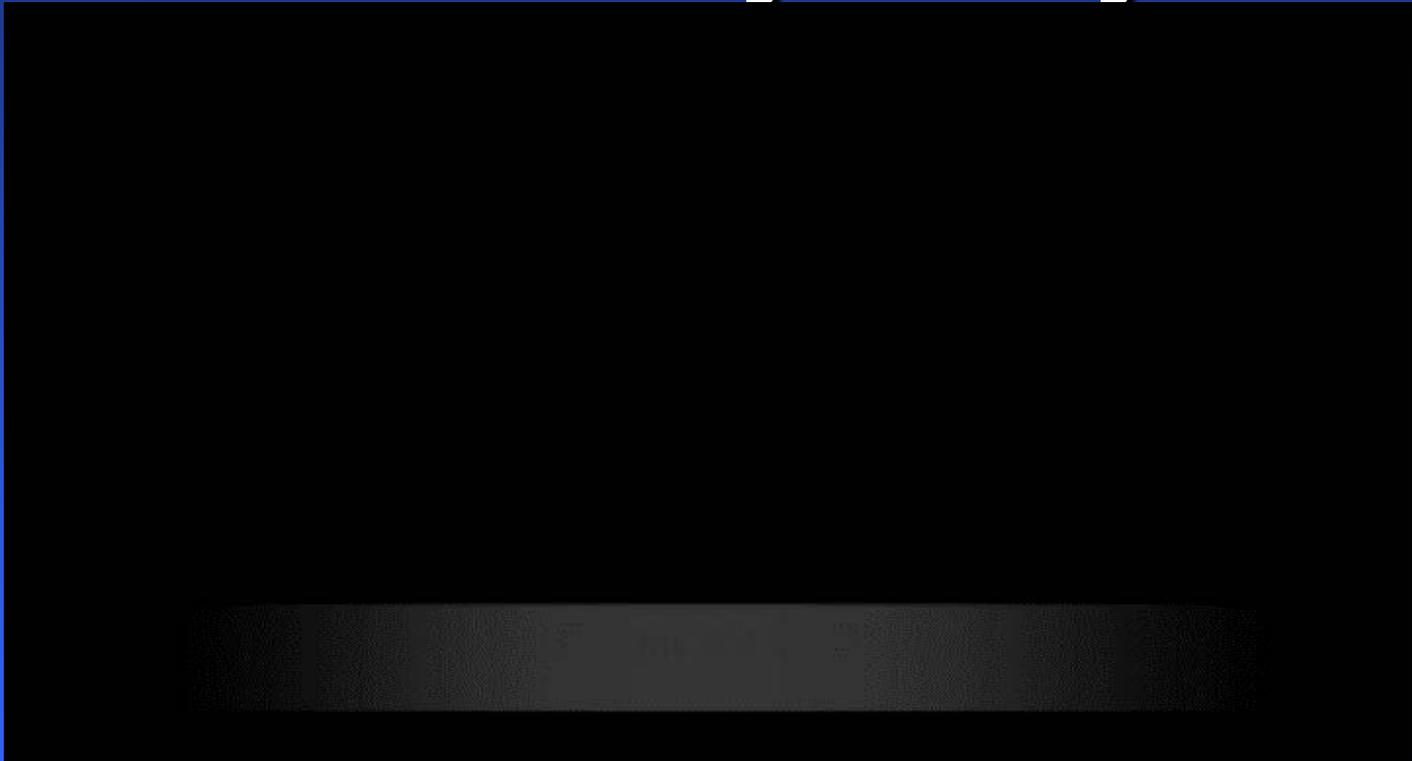
**Recurrence
rate: 23%**

Z-POEM

Optimal technique



CP Bar Myotomy



Z-POEM + MFI

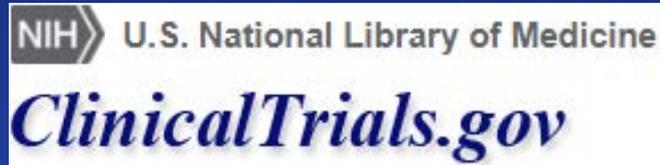


An international study on the use of peroral endoscopic myotomy in the management of Zenker's diverticulum

Juliana Yang, MD,¹ Stephanie Novak, MD,² Michael Ujiki, MD,² Óscar Hernández, MD,³ Pankaj Desai, MD,⁴ Petros Benias, MD,⁵ David Lee, MD,⁶ Kenneth Chang, MD,⁶ Bricau Bertrand, MD,⁷ Maximilien Barret, MD,⁷ Nikhil Kumta, MD,⁸ Xianhui Zeng, MD,⁹ Bing Hu, MD,⁹ Konstantinos Delis, MD,¹⁰ Mouen A. Khashab, MD¹

| | |
|---|-----------------------|
| | N=75 |
| Clinical success %(n) | 92% (69) |
| Technical success %(n) | 97.3% (73) |
| Mean POEM procedure time (min) (mean±std) | 52.4±2.9 |
| Repeat interventions | |
| Surgical interventions (n) | 0 |
| Endoscopic interventions (n) | 1 |
| Post-procedure follow-up days (median, IQR) | 291.5 (IQR 103.5-436) |
| Days of hospitalization (mean±std) | 1.8±0.2 |
| Preprocedure dysphagia score (mean±std) | 1.96±0.68 |
| Postprocedure dysphagia score (mean±std) | 0.25±0.52 |

GIE 2019



Comparison of Zenker's Diverticulum Treatment Using Peroral Endoscopic Myotomy and Flexible Endoscopy Septotomy. (ZIPPY)

Conclusions

- Third Space Endoscopy → Exciting results
- POEM is safe and effective in the management of achalasia/GP
- Severe adverse events are uncommon but may occur
- Z POEM is a promising technique for the management of symptomatic Zenker's Diverticula.

Thank you

