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Violeta Popov, MD, PhD, FACG
February 3, 2022 at Noon Eastern

Disclosures:

Speaker:
Mihir Wagh, MD
Consultant: Boston Scientific, Olympus, Medtronic, Fujifilm, Incyte and Conmed; Grant/Research Support: Steris/US Endoscopy

Moderator:
Kelli DeLay, MD
Dr. DeLay, faculty for this educational event, has no relevant financial relationship(s) with ineligible companies to disclose.

*All of the relevant financial relationships listed for these individuals have been mitigated
Endoscopic myotomy: Update on POEM and GPOEM

Mihir S. Wagh, MD, FACG, FASGE

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Associate Professor of Medicine
Interventional Endoscopy
Division of Gastroenterology
University of Colorado

Agenda

Part 1: POEM
- Indications, techniques and outcomes
  - Long term outcomes
  - POEM vs Pneumatic Dilation (PD)
  - POEM vs Laparoscopic Heller Myotomy (LHM)

- Part 2: G-POEM
  - Indications and outcomes; is it real?
POEM: Technique

Mittal C and Wagh MS. Am J Gastro 2017

Posterior sub-mucosal injection
Indications

• Achalasia

• Other spastic esophageal motility disorders
  – DES
  – Jackhammer esophagus
POEM: Outcomes

Peroral endoscopic myotomy: A meta-analysis

• 36 studies (upto March 2016) involving 2373 patients

• Clinical success (Eckardt score ≤3) achieved in 98%

• After a mean follow-up of 8 months:
  - Symptomatic GER 8.5% (95%CI 4.9%-13%)
  - Esophagitis on EGD 13% (95%CI 5.0%-23%)
  - Abnormal acid exposure 47% (95%CI 21%-74%)

Conclusions:
POEM appears to be safe and effective based on the large body of current evidence, and warrants consideration as first-line therapy when an expert operator is available

Akintoye E et al. Endosc 2017

Long-term outcomes of per-oral endoscopic myotomy in achalasia patients with a minimum follow-up of 4 years: A multicenter study

• Retrospective multicenter study; 146 patients from 11 academic medical centers

• Median follow-up was 55 months (IQR 49.9-60.6)

• Clinical response in 139 (95.2 %) at follow-up of ≥ 48 months

• Adverse events (6 mucosotomies, 2 pneumothorax) in 8 patients (5.5 %)

• Symptomatic reflux in 45 (32.1 %), while 35.3 % of patients were using daily PPI at 48 months post POEM

Brewer Gutierrez OI et al. Endosc Int Open 2020
Conclusion

• POEM is a durable and safe procedure with an acceptably low adverse event rate and an excellent long-term clinical response

Brewer Gutierrez OI et al. Endosc Int Open 2020

POEM vs Pneumatic Dilation

• Multicenter study / 6 sites (5 countries)

• 133 patients randomized to POEM (n = 67) or pneumatic dilation 30-mm and 35-mm balloon (n = 66)

Ponds FA et al. JAMA 2019
POEM vs Pneumatic dilation

- Treatment success in 58/63 (92%) in POEM group vs 34/63 (54%) in pneumatic dilation group (p < 0.001)
- Reflux esophagitis occurred more often in the POEM group than in the pneumatic dilation group (41% vs 7%, p = 0.002)
- Two serious adverse events after PD
  - 1 perforation
  - 1 chest pain requiring 1 admission
- No serious adverse events after POEM

CONCLUSIONS:
- Compared to pneumatic dilation, POEM resulted in a significantly higher success rate at 2 years
- These findings support consideration of POEM as an initial treatment option for patients with achalasia

POEM vs Laparoscopic Heller Myotomy

Multicenter randomized trial comparing POEM with LHM plus Dor’s fundoplication in patients with symptomatic achalasia

Werner YB et al. N Engl J Med Dec 5, 2019
Endoscopic or Surgical Myotomy in Patients with Idiopathic Achalasia

RESULTS
• 221 patients randomly assigned to POEM (112 patients) or LHM plus Dor’s fundoplication (109 patients)
• Clinical success at 2-year follow-up was 83.0% in the POEM group and 81.7% of patients in the LHM group (P=0.007 for noninferiority)

CONCLUSIONS
• POEM was noninferior to LHM plus Dor’s fundoplication in controlling symptoms of achalasia at 2 years
• Gastroesophageal reflux was more common among patients who underwent POEM than among those who underwent LHM
Anterior vs Posterior Myotomy

Efficacy of anterior versus posterior per-oral endoscopic myotomy for treating achalasia: A randomized, prospective study

- 63 consecutive patients with achalasia without prior treatment randomized to anterior group (n=31) or posterior group (n=32)

Results:
- Mean follow-up of 15.5 months
- No significant difference in general characteristics, treatment success, pre- and postoperative esophageal manometry, Eckardt score, and adverse events (P > 0.05)

Tan Y et al. GIE 2018
Efficacy of anterior versus posterior per-oral endoscopic myotomy for treating achalasia: A randomized, prospective study

Conclusions:
The short-term treatment efficacy, manometry outcomes, and adverse events were comparable between the anterior and posterior myotomy groups

Tan Y et al. GIE 2018

Outcomes of anterior versus posterior peroral endoscopic myotomy 2 years post-procedure: Prospective follow-up results from a randomized clinical trial

• 150 patients were initially randomized and 138 completed the 1-year follow-up
• Of the 138, 111 (anterior group 54, posterior group 57) also completed ≥2 years of follow-up
• Overall clinical success decreased from 89% to 82%
• At ≥2 years post-POEM, clinical success was achieved in 46/54 (85%) and 45/57 (79%) in the anterior and posterior groups, respectively (P = 0.43)
• GERDQ score was 6 (interquartile range 6–8; P= 0.08) in both treatment groups

Conclusions
• The anterior and posterior POEM techniques remained equally effective at 2 years
• GERD outcomes were also similar in both groups during medium-term follow-up

Ichkhanian Y et al. Endosc 2020
POEM and Acid Reflux

Gastroesophageal reflux disease after peroral endoscopic myotomy is unpredictable, but responsive to proton pump inhibitor therapy: A large, single-center study

- 209 patients (194 patients with non-sigmoid achalasia); comprehensive evaluation of GERD completed in 167 patients (86.1%)
- A high DeMeester score (> 14.72), reflux esophagitis, and symptomatic GERD were identified in 47.9%, 41.9%, and 29.3% of patients, respectively
- On logistic regression analysis, type of achalasia, technique of POEM (anterior vs. posterior), pre- or post-POEM esophageal manometry variables, and patient characteristics were not associated with post-POEM GERD
- Erosive esophagitis responded to PPI therapy in majority of patients (81.4%)

Conclusion
- Incidence of GERD is high after POEM
- Most of the reflux esophagitis is mild and responsive to PPI therapy
- There are no procedural or patient-related variables that appear to affect the incidence of post-POEM GERD

Nabi Z et al. Endosc 2020
**POEM in Special Situations**

- Can be effectively performed even after prior therapies
  - Post Heller myotomy (POEM easier than re-do Heller)
  - After pneumatic dilation and botulinum toxin (Botox)
  - After failed POEM

- Has been safely performed in pediatric patients as well

- Long proximal myotomy (tailored to spastic esophageal segment on esophageal manometry) can be performed in
  - Type 3 (spastic) achalasia
  - Other spastic motility disorders (DES and Jackhammer esophagus)

**Long-term Outcomes of Per-oral Endoscopic Myotomy in Spastic Esophageal Motility Disorders: A Large, Single-Center Study**

- Retrospective analysis of 74 patients with spastic esophageal motility disorders including type III in 53, DES in 11, and JHE in 10 patients

- Median follow-up was 47.5 months (range: 2 to 77 mo)

- Short-term (1 to 3 y) clinical success in 85.2%
- Long-term (>5 y) clinical success in 82.6%

- No significant difference in the clinical success between type III achalasia and JHE/DES

Nabi Z et al. J Clin Gastroenterol 2020
So, what have we learned in the last decade?

- POEM is a safe, effective and durable treatment option for achalasia and spastic esophageal motility disorders
- POEM has a higher success rate than pneumatic dilation
- POEM is non-inferior to laparoscopic Heller myotomy with Dor fundoplication but has higher rate of acid reflux
- No difference in outcomes between anterior and posterior myotomy
- Similar outcomes between (traditional) long myotomy and short myotomy (but short myotomy is faster)

Summary

POEM
- Is a safe and effective option for treatment of achalasia and spastic esophageal motility disorders
- Less invasive and as effective as Heller myotomy
- More effective than botulinum toxin (Botox) injections and pneumatic dilation
- GERD after POEM remains a concern
- Should be considered for treatment of achalasia in specialized centers based on available expertise
Part 2

Agenda

• Is GPOEM effective (does it work)?
  – Symptom improvement and mid / long-term outcomes

• How does GPOEM work?
  – Objective evidence for improved gastric emptying

• Which patients/symptoms are more likely to respond to GPOEM?

• Unanswered questions
Endoscopic therapy for gastroparesis

Gastric Per-Oral Endoscopic Myotomy (G-POEM)

or

Per-Oral Pyloromyotomy (POP)

Pyloric ring

Pyloromyotomy
G-POEM

• For gastroparesis refractory to medical therapy

• Gastroparesis Cardinal Symptoms Index (GCSI) score improved

• Gastric emptying study normalization or improvement in a significant proportion

• No major adverse events

Khashab MA et al. GIE 2017
Gonzalez JM et al. GIE 2017

Gastroparesis: Choosing the right patient for G-POEM

• Gastroparesis is associated with a wide spectrum of symptoms with varying presentations

• Poor prognostic factors in gastroparesis
  ➢ Obesity
  ➢ Female gender
  ➢ Smoking
  ➢ Abdominal pain as the dominant symptom
  ➢ Narcotic use
  ➢ Gastroesophageal reflux
  ➢ Depression / psychiatric illness
Gastroparesis Cardinal Symptom Index (GCSI)

Definitions

• Radiologic diagnosis of gastroparesis: > 10% gastric retention at 4 hours

• Clinical response:
  (1) Decrease of at least 1 point in the average total GCSI score with more than a 25% decrease in at least 2 subscales of cardinal symptoms
  (2) “Improvement” in Mean GCSI score

• Objective improvement:
  (1) “Improvement” in gastric emptying study or “reduction” in % gastric retention
  (2) Normalization of gastric emptying study

Definitions have been vague and often unvalidated
"Outcomes and quality-of-life assessment after gastric per-oral endoscopic pyloromyotomy"

- Retrospective study: 16 patients
- Improvement in GCSI scores (improved nausea/vomiting and early satiety subscales)
- No adverse events

Dacha S et al. GIE 2017

Improvement in gastric retention percentage on GES and QOL

Dacha S et al. GIE 2017
Association between duration or etiology of gastroparesis and clinical response after gastric per-oral endoscopic pyloromyotomy

- Single-center retrospective study over an 18-month period
- 40 patients with refractory gastroparesis (25 nondiabetic and 15 diabetic patients)

Results:
- Multivariate linear regression modeling showed longer duration of disease associated with a poorer long-term response

Mekaroonkamol P et al. GIE 2019

GCSI improvement after GPOEM

- GCSI significantly improved throughout the study period
  - Nausea/vomiting subscale showed sustained improvement through 18 months
  - No significant improvement in bloating

Etiology of gastroparesis was not associated with clinical improvement

Mekaroonkamol P et al. GIE 2019
GPOEM Improves Quality of Life and Reduces Health Care Use for Patients with Gastroparesis

- Retrospective study on 30 patients
- Outcomes compared with 7 patients with refractory gastroparesis who did not undergo the procedure (controls)

RESULTS:
- GPOEM significantly reduced GCSI scores
- Patients who had GPOEM had significant reductions in number of emergency department visits and hospitalizations

Long-term Outcome of Gastric Per-Oral Endoscopic Pyloromyotomy in Treatment of Gastroparesis

- Retrospective single center study; 90 patients
- 73 patients (81.1%) had a clinical response at initial follow-up (3 to 6 months)
- Follow-up at 36-months in only 7/90 patients

<table>
<thead>
<tr>
<th>Table 2: Long-Term Outcome of GPOEM</th>
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<tbody>
<tr>
<td>Patients eligible for survey</td>
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<td>Patients who achieved initial clinical response</td>
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<tr>
<td>Patients who failed to achieve initial clinical response</td>
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<tr>
<td>Lost to follow-up</td>
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<td>Surveyed patients who lost initial clinical response</td>
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<td>73 (91.1)</td>
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American College of Gastroenterology
Gastric peroral endoscopic myotomy for the treatment of refractory gastroparesis: a prospective single-center experience with mid-term follow-up

- 52 patients (median age 48 years, 88% female)
- Clinical response in 68%, 58%, and 48% at 1, 6, and 12-month follow-up

Prior pyloric botulinum toxin (Botox) injection and GPOEM
- 25 patients had prior botulinum toxin
- Significant response to G-POEM up to 12 months in 19 botulinum toxin responders
- GCSI scores decreased but did not achieve significance for clinical success in 6 botulinum toxin non-responders

Gregor L et al GIE 2021

Mid-term f/u at 24 months in only 11/52 patients

Mean 4-hour gastric retention was reduced 6 months after G-POEM (10.2%) compared with baseline (36.5%, P < .001) but no correlation between responders and non-responders

Gregor L et al GIE 2021

American College of Gastroenterology
SYMPTOM IMPROVEMENT AFTER GASTRIC PER-ORAL ENDOSCOPIC MYOTOMY DOES NOT MATCH GASTRIC EMPTYING TIMES: RESULTS OF A PROSPECTIVE STUDY

• 23 patients (mean age 48.1 years, 82.6% female); mean follow-up 12.9 months
  – idiopathic (60.9%),
  – diabetic (30.4%),
  – post-surgical (4.4%) and post-infectious (4.4%)

• Technical success was 100%

• Clinical success in 18/23 (78.3%) patients; mean GCSI scores pre and post GPOEM (3.4 ± 0.9 pre vs 2.0 ± 1.7 post, p<0.01)

• No correlation between improvement in symptoms and gastric emptying time

Han S et al. DDW 2021

G-POEM: Systematic review and meta-analysis using surgical pyloroplasty as a comparator group

• 332 and 375 patients underwent G-POEM (11 studies) and surgical pyloroplasty (7 studies), respectively

• Pooled rate of clinical success, based on the GCSI score, with G-POEM was 75.8% (95% CI 68.1 - 82.1, I² = 50) and with surgical pyloroplasty was 77.3% (95% CI 66.4 - 85.4, I² = 0), p = 0.81

• Pooled rate of clinical success, based on the 4-hour GES results, with G-POEM was 85.1% (95% CI 68.9 - 93.7, I² = 74) and with surgical pyloroplasty was 84% (95% CI 64.4 - 93.8, I² = 81), p = 0.91

• Overall adverse events were comparable

• Based on meta-regression analysis, idiopathic gastroparesis, prior treatment with botulinum toxin and gastric stimulator seemed to predict clinical success with G-POEM

Mohan BP et al. Surg Endosc 2020
Pyloric planimetry (functional lumen imaging probe) and GPOEM

- Retrospective analysis\(^1\) of 37 patients from 5 centers
  - Clinical success was achieved in 26 (70\%) patients
  - Post G-POEM pyloric cross-sectional area (CSA) and distensibility index (DI) were significantly higher in the clinical success group

- Prospective single center study\(^2\), 52 patients
  - Functional lumen imaging probe: significant improvement in both pyloric cross-sectional area and pyloric distensibility index (PDI) at 6 and 12 months
  - No statistical difference in PDI between clinical responders and non-responders (as defined by >1 point improvement in GCSI) at baseline or at 6 months

\(^1\) Vosoughi K et al. GIE 2020
\(^2\) Gregor L et al GIE 2021
GPOEM vs sham

- Prospective, randomized, single-blind trial
- 41 patients (46% men; median age, 46 years)
- GPOEM (n = 21) or sham procedure (n = 20)
- Sham procedure patients offered crossover G-POEM at 6 months if symptoms persisted

Hustak R et al. Abstr OP005. UEGW; Oct 3-5, 2021 (virtual meeting)

Treatment success (>50% reduction in GCSI)
- 74% (95% CI, 51-89) in the G-POEM group
- 18% (95% CI, 5-42) in the sham group

Mean GCSI score improved significantly after GPOEM from 3.48 ± 0.58 → 1.18 ± 0.87 compared to 3.23 ± 0.65 → 2.59 ± 1.05 after sham

Decreased median gastric retention at 4 hours (22% → 7% with GPOEM vs 26% → 21% sham)

Hustak R et al. Abstr OP005. UEGW; Oct 3-5, 2021 (virtual meeting)
GPOEM vs sham

• Crossover arm 6-month follow-up (n = 11)
  – Treatment success in 9 (82%; 95% CI: 52–95)
  – GCSI decreased from 3.2 following sham to 1.1 (P = 0.005) after G-POEM
  – Decrease in median gastric retention (20% → 4%)

• Adverse events
  – No severe adverse events
  – One patient in the G-POEM group developed severe dumping syndrome that required drug treatment

Hustak R et al. Abstr OP005. UEGW; Oct 3-5, 2021 (virtual meeting)

Questions and concerns

• Majority of data for GPOEM is retrospective and with small numbers of patients

• Definitions for outcomes are not validated

• Gastric emptying study may not correlate with symptoms (improvement) and may not be the best assessment for effects of pyloromyotomy

• No clear predictors for success

• Unanswered questions
  - Which etiology of gastroparesis is best suited for GPOEM?
  - Which symptoms are most responsive to GPOEM?
  - Is gastric emptying test and/or functional lumen imaging probe helpful before or after GPOEM?
  - Does pyloric botulinum toxin injection predict response to GPOEM?
Summary

• GPOEM is a safe and effective endoscopic option for select patients with refractory gastroparesis
  ➢ Improvement in symptoms and QOL

• Careful patient selection is essential for ensuring clinical success and reducing risk of adverse events after GPOEM

• Set realistic expectations for outcomes (disease will not be cured with GPOEM)

• Use caution in
  – Patients on narcotics
  – Marijuana and other illicit drug use
  – Psychiatric illnesses, eating disorders
  – Chronic abdominal pain as main symptom

Thank You
Questions?

Speaker:
Mihir Wagh, MD

Moderator:
Kelli DeLay, MD

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