

# Achalasia and gastroparesis: Coexisting entities or consequence of therapy?



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No association has been reported between achalasia and gastroparesis despite similar pathophysiologic mechanisms and therapeutic options. A literature review shows only two reports of patients with both disorders for whom esophageal peroral endoscopic myotomy (POEM) and gastric (G-POEM) were performed. We have observed a number of patients with both conditions and question the possibility that their coexistence is not rare. We further propose a novel explanation for the increased incidence of gastroesophageal reflux disease (GERD) following treatment of achalasia.

Seven patients underwent POEM for achalasia with a resolution of dysphagia. A few months later, the patients developed symptoms of gastroparesis and new-onset GERD. G-POEM was performed successfully, and all patients had resolution or significant improvement in their GERD symptoms. Most patients were off proton pump inhibitors (PPIs) or using PPIs as needed only.

Concurrent or consecutive achalasia and gastroparesis raise the question of an alternative explanation for symptomatic GERD after POEM if the conditions either coexist or gastroparesis follow as a consequence of POEM by an unknown mechanism. In our patients, treatment of gastroparesis by G-POEM resolved reflux symptoms. Whether patients with achalasia have underlying, subclinical delayed gastric emptying is an impor-

tant topic that warrants study and raises the question of performing gastric emptying study on all patients with achalasia before or after POEM.

## Introduction

Achalasia is a neurodegenerative disorder of the esophagus that leads to significant morbidity and decreased quality of life. It affects individuals of both sexes and all ages, with a prevalence of 27.1 per 100,000 persons [1]. Symptom onset is typically insidious and usually includes several months to years of dysphagia and progressive weight loss before a diagnosis is made.

Gastroparesis is a syndrome of delayed gastric emptying in the absence of obstruction that is associated with substantial morbidity and frequent hospitalizations. It affects all ages, with female predominance increasing with age [2]. According to epidemiologic studies based on typical symptoms and imaging studies, the estimated prevalence is 24 per 100,000 individuals and 38 per 100,000 in women. However, it is widely perceived that gastroparesis prevalence is much higher, reaching 1.8% in pediatric patients and 4% in adults [3]. Gastroparesis manifests with the classical symptomology of nausea, vomiting, early satiety, bloating, and abdominal pain. We have ob-

served a number of patients with both conditions and question the possibility that their coexistence is not rare and may have a common etiology.

## Pathophysiology

The myenteric plexus is a part of the enteric nervous system (ENS) that consists of postganglionic neurons situated between the circular and longitudinal smooth muscle layers. These neurons differentiate into excitatory and inhibitory types; both produce neuromodulators in a coordinated fashion to create a contraction-relaxation balance essential for the motility function of the gastrointestinal tract [4]. The lower esophageal sphincter (LES), pyloric, and rectal plexuses are examples.

The hallmark of achalasia is a failure of the LES to relax adequately with swallowing, together with non-peristaltic or abnormal contractions of the esophagus's smooth muscle. The inhibitory ganglia in the myenteric plexus of the esophagus are impaired in achalasia, which was proven on histologic examination of esophagectomy specimens [5].

The pathophysiology of gastroparesis is complex. Depletion of the interstitial cells of Cajal (ICC) has been reported as the main finding in multiple studies. When assessed by gastric emptying scintigraphy (GES), abnormally prolonged gastric emptying correlated with depletion of ICC in the pylorus. These findings support pyloric dysfunction as a key component in the pathology of gastroparesis [6].

## Therapeutic options

In achalasia, current therapies with good outcomes focus on reducing the LES pressure to allow passage of food into the stomach, thereby improving symptoms. Esophageal peroral endoscopic myotomy (POEM) has shown excellent outcomes and provided an alternative to laparoscopic Heller myotomy (LHM) while avoiding surgery-related morbidity. A meta-analysis of 53 studies of LHM and 21 articles about POEM revealed POEM to be more effective in improving dysphagia than LHM. However, the incidence of GERD was higher following POEM [7].

Similarly, in gastroparesis, pylorus-focused therapies have gained interest lately, including pyloroplasty and G-POEM. Building on the experience obtained from esophageal POEM, the first successful G-POEM in a human was described by Khashab et al. in 2013 [8]. Since then, G-POEM has emerged as a promising treatment for gastroparesis resulting in significant improvement in GCSI (Gastric Cardinal Symptom Index) and quality of life.

## Case presentations

Case #1 was a 66-year-old woman with a long history of achalasia. She underwent LHM with partial fundoplication 17 years before, followed by posterior LHM 1 year later for persistent dysphagia. She continued to have dysphagia and subsequently underwent POEM. Her dysphagia resolved, and LES pressure normalized on post-POEM manometry. Eight weeks later, she developed heartburn, regurgitation, post-prandial bloating,

and early satiety. A pH study revealed a DeMeester score of 107.4 on day 1 and 43 on day 2 (normal <14.7). GES revealed 15% emptying at 4 hours. Notably, a GES done before POEM was normal. G-POEM was performed and the patient had an improvement in her symptoms and her GCSI improved from 2.5 to 0.22 after G-POEM. Six months later, the patient stopped using PPIs and was in good condition with no heartburn or post-prandial symptoms.

Case #2 was a 70-year-old woman with achalasia who had undergone pneumatic dilation 4 years before, but dysphagia recurred. POEM was performed with the resolution of dysphagia. One month later, she developed constant regurgitation, emesis, heartburn, and weight loss. GES revealed delayed gastric emptying. She underwent successful G-POEM and her symptoms improved. GCSI improved from 3.0 before G-POEM to 1.8 after G-POEM. Six months later, the patient continued to be asymptomatic.

Case #3 was a 28-year-old woman with Joubert syndrome and chronic kidney disease who underwent POEM for achalasia. Five months later, she began to complain of heartburn, severe nausea, and regurgitation. GES showed 44% gastric emptying at 4 hours. G-POEM was successfully performed 6 months later. Her symptoms improved significantly and GCSI improved from 2.8 before G-POEM to 0.22 after G-POEM. At 6-month follow-up, she continued to be doing well and was off-PPIs.

Case #4 was a 79-year-old woman with achalasia who underwent POEM with a resolution of dysphagia. However, 2 months later, she developed mild nausea, bloating, and regurgitation. GES showed 69% gastric emptying at 4 hours. G-POEM was performed 6 months later, resulting in significant improvement in nausea and bloating, but she continued to have intermittent regurgitation. GCSI improved from 2.5 before G-POEM to 0.2 after G-POEM. She continued PPIs as needed.

Case #5 was a 67-year-old man with achalasia. He underwent POEM with a significant improvement in dysphagia. Three months later, he developed new-onset GERD. A 48-hour pH study showed a total DeMeester score of 62. GES showed 60% gastric emptying at 4 hours. G-POEM was performed 9 months later, resulting in significant improvement in regurgitation and in GCSI (4.1 before G-POEM vs. 1.05 after G-POEM). She continued to use once-daily PPIs.

Case #6 was a 44-year-old man with achalasia who underwent POEM with a resolution of dysphagia. Four months later, he developed regurgitation. A 48-hour PH study showed a total DeMeester score of 22.4 and GES showed delayed gastric emptying. G-POEM was performed, resulting in a significant resolution of her symptoms and in GCSI (2.0 before G-POEM to 0.7 after G-POEM). She continued to use a PPI once daily.

Case #7 was a 69-year-old woman with achalasia. He underwent POEM with a resolution of dysphagia. Four months later, he developed regurgitation. A 48-hour pH study showed a total DeMeester score of 15.1. GES showed 44% gastric emptying at 4 hours. G-POEM was performed 1 month later, resulting in significant improvement in regurgitation. GCSI improved from 3.2 before G-POEM to 0.8 after G-POEM. The patient continued to use a PPI once daily.

► **Table 1** Baseline patient characteristics.

| Patient | Age (yr) | Sex    | Initial symptoms              | Comorbidity   | Prior therapy             |
|---------|----------|--------|-------------------------------|---|---------------------------|
| #1      | 66       | Female | Dysphagia, weight loss        | Gallstones, osteoporosis, depression  | LHM, repeat posterior LHM |
| #2      | 70       | Female | Dysphagia                     | Breast cancer treated with chemoradiation therapy, sarcoidosis                          | Pneumatic dilation        |
| #3      | 28       | Female | Dysphagia, weight loss >20 lb | Joubert syndrome, hypertension, chronic kidney disease, anemia, coronary artery disease | None                      |
| #4      | 79       | Female | Dysphagia                     | Hypertension  | None                      |
| #5      | 67       | Male   | Dysphagia                     | Hypertension  | None                      |
| #6      | 44       | Male   | Dysphagia                     | none  | None                      |
| #7      | 69       | Female | Dysphagia                     | Hypertension, atrial fibrillation   | None                      |

## Discussion


Gastroparesis and achalasia are two apparently distinct gastrointestinal disorders but with very much in common. Both disorders occur with about the same frequency and progress in similar insidious fashions until an end-stage of muscle “hypertrophy” is reached. Both diseases have uncertain etiology and pathophysiology, yet degenerative changes in anatomically respective parts of the ENS are thought to be the most direct cause. Very limited data exist on the occurrence of simultaneous achalasia and gastroparesis. However, anecdotal reports from experts suggest this concurrence is not rare.

The clinical presentation of concurrent achalasia and gastroparesis varies. In our experience, most patients present with symptoms of achalasia first. The patients in this report presented with dysphagia, which resolved in all patients after successful POEM (► **Table 1**). Symptoms of gastroparesis did not clearly manifest until after adequate treatment of achalasia was achieved. All patients had developed heartburn and regurgitation. Three patients also complained of nausea and bloating with vomiting or abdominal pain. The average time between esophageal POEM and gastroparesis symptoms presentation was 3 months. GES showed evidence of delayed emptying at 4 hours. G-POEM was technically successful in all patients (► **Video 1**). After 1 month, patients reported the ability to tolerate oral intake of all kinds of food and their nausea, bloating, and reflux symptoms improved (► **Table 2**). At 6-month follow-up visits, four patients were off PPIs and three patients continued as-needed PPIs.

Patients with achalasia or gastroparesis respond poorly to medical therapy. There are two main factors responsible for this inadequate response: (1) the available pharmacologic therapy is limited in efficacy and is non-specific; and (2) both diseases manifest in advanced stages where hypertrophy reaches an irreversible point. Endoscopic myotomy has been particularly successful in treating achalasia. Symptom resolution and improvement in objective measures are seen in >90% of patients. There is currently no reliable way to predict which patients are likely to respond to G-POEM.

Although POEM is very effective in improving dysphagia, the incidence of GERD following POEM may be problematic. The in-

► **VIDEO**



► **Video 1** Video of outcome of G-POEM

cidence varies based on the measurements used to establish the diagnosis. Meta-analyses reported erosive esophagitis in 13% to 29.4% of patients, but abnormal pH studies have been found in 39% to 47.5% of patients. Surprisingly, the rates of symptomatic GERD after POEM are lower than those for erosive esophagitis and abnormal pH studies [9]. The etiological mechanism of GERD following myotomy is unclear. Different hypotheses have been suggested, but studies are conflicting [10]. This brief report of concurrent or consecutive achalasia and gastroparesis suggests an alternative etiology for symptomatic GERD after POEM. Future study is needed to elucidate if the conditions either coexist before treatment or gastroparesis follows as a consequence of POEM by an unknown mechanism. In our patients, treatment of gastroparesis by G-POEM almost completely resolved symptoms of GERD.

Our study has a few limitations. It was small study, despite being conducted at two large academic medical centers. The pH testing after G-POEM was not done for patients who had significant improvement in their GERD symptoms; therefore, the potential role of G-POEM in improving post-esophageal myotomy GERD symptoms requires further evaluation, preferably in a study with a prospective, controlled, design.

▶ **Table 2** Patient outcomes at 1-month follow-up.

| Pa-tient | POEM           |                           |                          | New-onset GERD     |                    |   |                | G-POEM                               |                    |               |                    | GERD post G-POEM  |                    |                     |           |         |
|----------|----------------|---------------------------|--------------------------|--------------------|--------------------|---|----------------|--------------------------------------|--------------------|---------------|--------------------|-------------------|--------------------|---------------------|-----------|---------|
|          | POEM ap-proach | Eckardt score before POEM | Eckardt score after POEM | Dysphagia symptoms | Early and late AEs | GERD symptoms                           | Symp-tom onset | pH Study                             | G-POEM approach    | GES post-POEM | GCSI before G-POEM | GCSI after G-POEM | Early and late AEs | pH study            | Symp-toms | PPI use |
| #1       | Anterior       | 4                         | 0                        | Resolved           | none               | Heartburn, regurgitation                | 8 weeks        | DM score 107.4 on Day 1, 43 on Day 2 | Lesser curve       | 15%           | 2.5                | 0.22              | none               | N/A                 | Resolved  | Off     |
|          | Posterior      | 5                         | 0                        | Resolved           | none               | Heartburn, regurgitation, emesis        | 4 weeks        | N/A                                  | Lesser curva-ture  | <85%          | 3.0                | 1.8               | none               | N/A                 | Resolved  | Off     |
| #3       | Posterior      | 5                         | 1                        | Resolved           | none               | Heartburn, severe nausea, regurgitation | 20 weeks       | N/A                                  | Lesser curva-ture  | 44%           | 2.8                | 0.22              | none               | N/A                 | Resolved  | 40 mg   |
|          | Posterior      | 6                         | 1                        | Resolved           | none               | Nausea, bloating, regurgitation         | 8 weeks        | N/A                                  | Lesser curva-ture  | 69%           | 2.5                | 0.2               | none               | N/A                 | Im-proved | prn     |
| #5       | Posterior      | 8                         | 4                        | Improved           | none               | Heartburn, regurgitation                | 12 weeks       | Total DM score 62                    | Greater curva-ture | 60%           | 4.1                | 1.05              | none               | N/A                 | Resolved  | 40 mg   |
|          | Posterior      | 6                         | 1                        | Resolved           | none               | Regurgitation                           | 20 weeks       | N/A                                  | Greater curva-ture | 88%           | 2                  | 0.7               | none               | Total DM score 22.4 | Im-proved | 40 mg   |
| #7       | Posterior      | 6                         | 1                        | Resolved           | none               | Nausea, regurgi-tation                  | 16 weeks       | Total DM score 15.1                  | Greater curva-ture | 44%           | 3.2                | 0.8               | none               | N/A                 | Resolved  | 40 mg   |

POEM, peroral esophageal peroral endoscopic myotomy; AE, adverse event; GERD, gastroesophageal reflux disease; G-POEM, gastric peroral esophageal endoscopic myotomy; GES, gastric emptying scintigraphy; GCSI, Gastric Cardinal Symptom Index; PPI, proton pump inhibitor; DM, DeMeester.

## Conclusions

No association has hitherto been reported between achalasia and gastroparesis, and the studies on concurrent or consecutive presentations are scarce. The possibility of unmasking gastroparesis symptoms following adequate treatment of achalasia warrants evaluation. This report, although limited by small sample size, proposes an alternative explanation for new-onset GERD after POEM and raises important questions for further discussion: Do patients with achalasia have underlying, subclinical delayed gastric emptying? Should every patient undergoing POEM for achalasia be evaluated for delayed gastric emptying? Should planimetry of the LES and pylorus be performed in patients undergoing POEM for achalasia? Should we biopsy the antrum for ICC evaluation of all patients undergoing POEM for achalasia?

## Competing interests

Dr. Benias is a consultant for Boston Scientific, Medtronic, Fujifilm and Apollo endosurgery. Dr. Carr-Lock receives royalties from Steris and is a consultant for Boston Scientific.

## References

- [1] Sadowski DC, Ackah F, Jiang B et al. Achalasia: incidence, prevalence and survival. A population-based study. *Neurogastroenterol Motil* 2010; 22: e256–261
- [2] Rodriguez L, Irani K, Jiang H et al. Clinical presentation, response to therapy, and outcome of gastroparesis in children. *J Pediatr Gastroenterol Nutr* 2012; 55: 185–190
- [3] Rey E, Choung RS, Schleck CD et al. Prevalence of hidden gastroparesis in the community: the gastroparesis "iceberg". *J Neurogastroenterol Motil* 2012; 18: 34–42
- [4] Furness JB. The enteric nervous system and neurogastroenterology. *Nature Rev Gastroenterol Hepatol* 2012; 9: 286–294
- [5] Furuzawa-Carballeda J, Torres-Landa S, Valdovinos MA et al. New insights into the pathophysiology of achalasia and implications for future treatment. *World J Gastroenterol* 2016; 22: 7892–7907
- [6] Moraveji S, Bashashati M, Elhanafi S et al. Depleted interstitial cells of Cajal and fibrosis in the pylorus: Novel features of gastroparesis. *Neurogastroenterol Motil* 2016; 28: 1048–1054
- [7] Schlottmann F, Luckett DJ, Fine J et al. Laparoscopic Heller Myotomy versus peroral endoscopic myotomy (POEM) for achalasia: a systematic review and meta-analysis. *Ann Surgery* 2018; 267: 451–460
- [8] Khashab MA, Sharaiha RZ, Saxena P et al. Novel technique of auto-tunneling during peroral endoscopic myotomy (with video). *Gastrointest Endosc* 2013; 77: 119–122
- [9] Repici A, Fuccio L, Maselli R et al. GERD after per-oral endoscopic myotomy as compared with Heller's myotomy with fundoplication: a systematic review with meta-analysis. *Gastrointest Endosc* 2018; 87: 934–943 e18
- [10] Nabi Z, Ramchandani M, Kotla R et al. Gastroesophageal reflux disease after peroral endoscopic myotomy is unpredictable, but responsive to proton pump inhibitor therapy: a large, single-center study. *Endoscopy* 2020; 52: 643–651