



Notable Grand Rounds
of the

**Michael & Marian Ilitch
Department of Surgery**

Wayne State University
School of Medicine

Detroit, Michigan, USA

Stephanie Joseph, MD

**A DIVE INTO THE THIRD SPACE:
THIRD SPACE ENDOSCOPY AND BEYOND**

May 13, 2026

About Notable Grand Rounds

These assembled papers are edited transcripts of didactic lectures given by mainly senior residents, but also some distinguished attending and guests, at the Grand Rounds of the Michael and Marian Ilitch Department of Surgery at the Wayne State University School of Medicine.

Every week, approximately 50 faculty attending surgeons and surgical residents meet to conduct postmortems on cases that did not go well. That "Mortality and Morbidity" conference is followed immediately by Grand Rounds.

This collection is not intended as a scholarly journal, but in a significant way it is a peer reviewed publication by virtue of the fact that every presentation is examined in great detail by those 50 or so surgeons.

It serves to honor the presenters for their effort, to potentially serve as first draft for an article for submission to a medical journal, to let residents and potential residents see the high standard achieved by their peers and expected of them, and by no means least, to contribute to better patient care.

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A Dive Into the Third Space: Third Space Endoscopy and Beyond

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Editor's Note: This is an edited summary of a Grand Rounds talk given by Dr. Joseph on May 13, 2026 at the Ilitch Department of Surgery, Wayne State University School of Medicine.

Introduction

The evolution of gastrointestinal endoscopy has progressed far beyond its original diagnostic role. Over the past several decades, endoscopy has advanced from a purely observational modality to a therapeutic platform capable of increasingly sophisticated interventions. Third space endoscopy (TSE) represents one of the most significant developments in this progression, creating the possibility of performing incisionless surgical procedures through the gastrointestinal lumen by exploiting the submucosal plane as an operative working space.

Third space endoscopy refers to a collection of advanced endoscopic techniques that access and operate within the submucosal layer of the gastrointestinal tract. Conceptually, the gastrointestinal tract may be divided into three spaces. The first space is the intraluminal space. The second space is the extraluminal or peritoneal cavity. The “third space” is the submucosal layer itself, which can be transformed into a working tunnel that allows intervention on deeper structures while preserving mucosal integrity.

This approach has dramatically expanded the capabilities of therapeutic endoscopy. Through submucosal tunneling techniques, endoscopists can now perform myotomies, tumor dissections, tissue harvesting, biopsies of muscular or neural tissue, placement of monitoring devices, and even anatomical reshaping procedures. The field therefore represents a transition from diagnostic endoscopy to therapeutic endoscopy and ultimately toward true endoscopic surgery.

The development of third space procedures has depended upon advances in instrumentation and visualization. Essential tools include high-definition gastroscopes with larger working channels, carbon dioxide insufflation systems, esophageal overtubes, electrosurgical knives, injection needles, clipping systems, and endoscopic suturing platforms. Carbon dioxide insufflation is preferred because of its rapid absorption and reduced risk of gas-related complications, similar to its use in laparoscopic surgery. Overtubes facilitate repeated atraumatic instrument exchange through the esophagus, functioning analogously to laparoscopic trocars.

A wide variety of third space procedures have now been described. These include peroral endoscopic myotomy (POEM), gastric POEM (G-POEM), Zenker's POEM (Z-POEM), diverticular POEM (D-POEM), submucosal tunneling endoscopic resection (STER), tunneled endoscopic full-thickness resection, and endoscopic sleeve gastropasty (ESG), among others. The present discussion focuses primarily on several of the most clinically relevant and widely adopted procedures: POEM, POEM with fundoplication (POEM+F), G-POEM, and ESG.

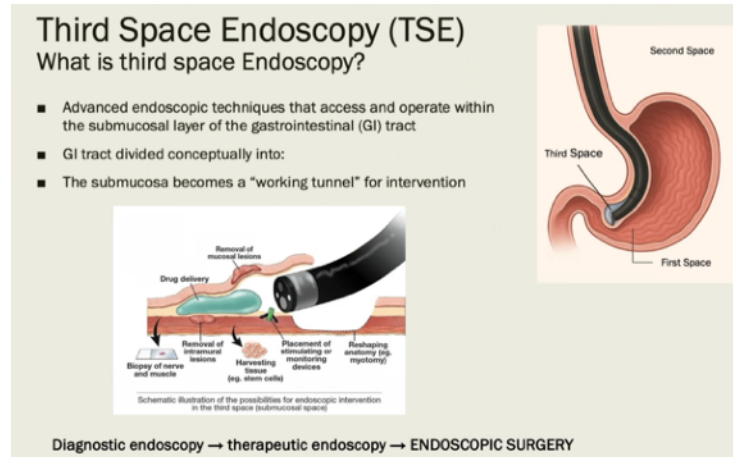


Fig. 1. Conceptual illustration of third space endoscopy and the submucosal working tunnel.

Peroral Endoscopic Myotomy (POEM)

Peroral endoscopic myotomy is the most extensively validated third space endoscopic procedure worldwide. Originally described by Dr. Haruhiro Inoue in animal models in 2008 and first performed in humans in 2010, POEM was developed as an incisionless treatment for achalasia and related esophageal motility disorders.

The goal of POEM is analogous to that of laparoscopic Heller myotomy: division of the lower esophageal sphincter musculature to relieve functional obstruction and improve esophageal emptying. The procedure begins with submucosal injection of saline mixed with methylene blue or indigo carmine to create a safe working plane between mucosa and muscularis propria. A mucosal incision is then created, allowing entry into the submucosal space. Using electrosurgical dissection and continued injection, a submucosal tunnel is extended distally across the gastroesophageal junction and proximally along the esophagus. Once the muscular layer is exposed, selective or full-thickness myotomy is performed.

In the original Inoue technique, only the circular muscle fibers were divided. More

extensive full-thickness myotomy is also possible, although this may increase the risk of perforation and postoperative gastroesophageal reflux disease (GERD). The completed myotomy generally extends approximately 6 cm proximally within the esophagus and 2–3 cm distally onto the gastric cardia, paralleling the extent of a conventional Heller myotomy.

Current Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and American Gastroenterological Association guidelines support POEM as an effective treatment for achalasia. For type I and type II achalasia, POEM and laparoscopic Heller myotomy are considered comparable treatment options. However, for type III achalasia, POEM is generally favored because of its ability to extend the myotomy proximally along the esophagus to address diffuse spastic contractions.

Type III achalasia is characterized by spastic contractions involving multiple esophageal segments. The endoscopic approach allows essentially unrestricted access to the full esophageal length, whereas laparoscopic Heller myotomy is generally confined to the distal esophagus and lower esophageal sphincter. This capacity to tailor myotomy length is one of POEM's principal advantages.

Patient selection remains important. Significant esophageal distortion, tortuosity, or large hiatal hernias may make endoscopic tunneling technically difficult. Likewise, patients with severe preexisting reflux disease may be less suitable candidates because POEM does not traditionally include an antireflux procedure.

POEM Versus Laparoscopic Heller Myotomy

The landmark randomized controlled trial comparing POEM with laparoscopic Heller

myotomy plus Dor fundoplication was published in 2019 in the *New England Journal of Medicine*. The study enrolled 221 patients with symptomatic achalasia and randomized them to either POEM or laparoscopic Heller myotomy with fundoplication.

Clinical success was defined using the Eckardt symptom score, a validated scoring system incorporating dysphagia, regurgitation, chest pain, and weight loss. Scores range from 0 to 12, with scores greater than 3 considered abnormal.

At two-year follow-up, POEM achieved clinical success rates of approximately 83%, compared with 81.7% for laparoscopic Heller myotomy, demonstrating noninferiority between the procedures. Additional meta-analyses with longer-term follow-up have confirmed broadly comparable treatment success, dysphagia improvement, complication rates, and hospital outcomes between POEM and laparoscopic myotomy.

POEM offers several attractive features. It is entirely incisionless, associated with shorter operative times and reduced hospital stays, and allows rapid return to normal activity. However, postoperative GERD remains its principal limitation. Multiple studies have demonstrated significantly higher rates of reflux esophagitis and proton pump inhibitor use after POEM compared with laparoscopic Heller myotomy with fundoplication.

This concern is particularly important because many achalasia patients exhibit diminished esophageal sensation and may therefore develop clinically silent reflux injury. As a result, long-term endoscopic surveillance and proton pump inhibitor therapy are frequently recommended after POEM.

POEM With Fundoplication (POEM+F)

To address the problem of postoperative reflux, Inoue later developed POEM with fundoplication, also termed POEM+F or endoscopic Heller-Dor myotomy. Introduced in 2019, this procedure combines standard POEM with an endoscopic fundoplication created entirely through the submucosal tunnel.

After completion of the myotomy, the endoscopist intentionally enters the peritoneal cavity and identifies the gastric fundus. Using grasping devices and endoscopic clips, the gastric fundus is retracted into the distal esophagus and secured in a configuration intended to mimic a Dor fundoplication. Simultaneous retroflexed intraluminal visualization allows assessment of the resulting antireflux valve. The mucosal entry site is then closed with clips.

Early United States experience with POEM+F, reported in 2023, demonstrated technical feasibility and promising symptom control. Six patients underwent the procedure with 100% technical success and no major adverse events. Mean Eckardt scores improved substantially, and postoperative reflux symptom scores were low.

Nevertheless, important limitations remain. The fundoplication component carries a technical failure rate of approximately 5–8%, adds roughly 45 minutes to operative time, and appears susceptible to wrap degradation over time. Approximately one-quarter of patients demonstrate degradation of the wrap by three years, and long-term durability beyond five years remains uncertain. Consequently, although POEM+F is conceptually appealing, its ultimate role relative to conventional laparoscopic Heller-Dor procedures remains to be determined.

Gastric Peroral Endoscopic Myotomy (G-POEM)

Gastric POEM extends third space principles to treatment of medically refractory gastroparesis. First described in humans in 2013, G-POEM targets the pyloric sphincter as a contributor to impaired gastric emptying.

The procedural steps closely mirror those used in esophageal POEM. A submucosal bleb is created within the gastric antrum, followed by mucosal incision and submucosal tunneling toward the pylorus. Once the pyloric musculature is exposed, pyloromyotomy is performed, generally including full-thickness division of the pyloric sphincter. The mucosal entry site is then closed with clips.

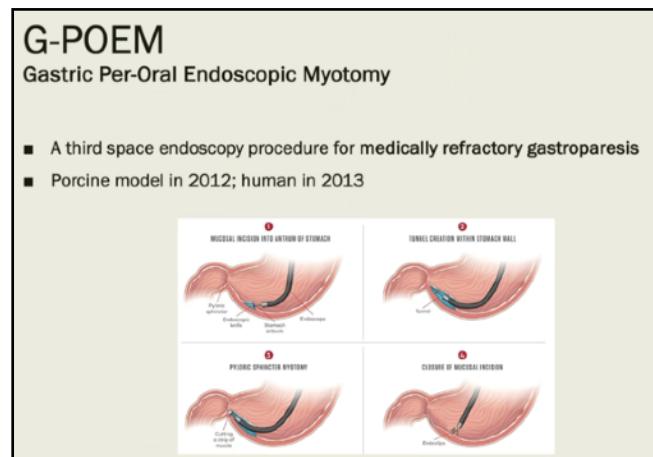


Fig. 2. Sequential steps of G-POEM including mucosal incision, tunnel creation, pyloromyotomy, and closure.

According to current guidelines, ideal candidates for G-POEM are patients with medically refractory gastroparesis who demonstrate delayed gastric emptying with greater than 20% retention at four hours on gastric emptying studies and who exhibit moderate-to-severe symptoms, particularly nausea and vomiting. Symptom severity is commonly assessed using the Gastrointestinal Cardinal Symptom Index (GCSI).

Although randomized trials remain limited, retrospective comparative studies have suggested that G-POEM achieves outcomes comparable or potentially superior to laparoscopic pyloromyotomy. Reported advantages include reduced invasiveness, shorter operative time, and preservation of future surgical options.

Not all patients respond equally well. Certain symptom profiles, particularly predominant abdominal pain, appear less responsive to pyloric interventions. Additionally, dumping syndrome remains a recognized potential complication. As with other advanced endoscopic procedures, the technical learning curve is substantial.

Endoscopic Sleeve Gastroplasty (ESG)

Endoscopic sleeve gastroplasty differs somewhat from pure third space procedures and more closely resembles natural orifice transluminal endoscopic surgery (NOTES). ESG is an incisionless restrictive bariatric procedure intended to replicate some of the physiological effects of laparoscopic sleeve gastrectomy without gastric resection.

First reported in 2013 by Dr. Barham Abu Dayyeh at the Mayo Clinic, ESG reduces gastric volume through full-thickness endoscopic suturing and plication of the greater curvature. Patients with class I and II obesity, typically with body mass index values between 30 and 40 kg/m², are considered the best candidates.

The procedure is performed under general anesthesia using

a specialized endoscopic suturing platform. A tissue helix device engages the gastric wall and pulls tissue into the suturing system, allowing full-thickness bites to be placed in a U- or O-shaped pattern along the greater curvature. Sequential cinching of these sutures tubularizes the stomach lumen, creating a sleeve-like anatomy.

The MERIT trial, a multicenter randomized study published in 2022, demonstrated significantly greater excess weight loss with ESG compared with lifestyle modification alone. Patients undergoing ESG achieved approximately 49.2% excess weight loss at

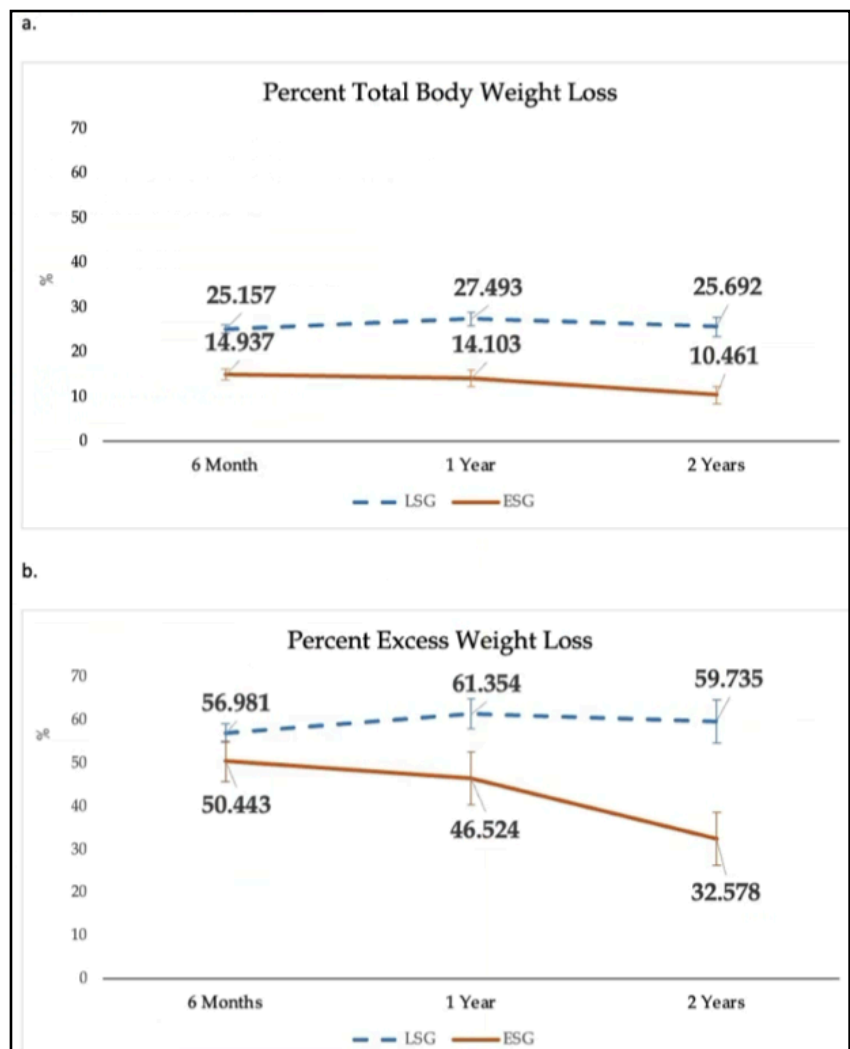


Fig. 3. Comparative weight loss outcomes after ESG versus laparoscopic sleeve gastrectomy

52 weeks, compared with only 3.2% in controls. Additionally, 80% of ESG patients demonstrated improvement in obesity-related comorbidities.

Comparisons between ESG and laparoscopic sleeve gastrectomy have shown that although laparoscopic sleeve gastrectomy produces substantially greater weight loss, ESG provides meaningful improvement in obesity-related comorbidities with shorter hospital stays and fewer complications.

One unresolved question is why ESG does not achieve the same degree of weight loss as laparoscopic sleeve gastrectomy. Several factors likely contribute. Unlike surgical sleeve gastrectomy, ESG does not remove gastric tissue, leaving residual absorptive surface and hormonal activity intact. Additionally, the degree of gastric tubularization is more difficult to standardize endoscopically than surgically using a bougie.

Future directions may include combining ESG with pharmacologic therapies such as glucagon-like peptide-1 receptor agonists, although this approach has not yet been fully studied.

Future Directions and Conclusion

Third space endoscopy represents the next major step in the continuing evolution of minimally invasive gastrointestinal surgery. The progression from open surgery to laparoscopy, robotic surgery, and now incisionless endoluminal interventions reflects a broader movement toward reduced physiologic disruption and faster recovery while preserving therapeutic efficacy.

POEM has already established itself as a durable and highly effective therapy for achalasia, particularly type III disease. G-POEM is emerging as a promising intervention for refractory gastroparesis. ESG offers a minimally invasive option for carefully selected bariatric patients. Meanwhile, newer procedures such as POEM+F and Z-POEM continue to expand the therapeutic reach of third space techniques.

Despite these advances, important challenges remain. Long-term durability data are still evolving. GERD after POEM continues to be a significant concern. Technical learning curves are steep, requiring substantial procedural volume and specialized expertise. Standardization of techniques and long-term comparative outcomes will be essential as these procedures become more widely adopted.

Nevertheless, third space endoscopy has fundamentally altered the boundaries between surgery and endoscopy. The submucosal tunnel has become not merely an anatomical plane, but a new operative frontier.

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