World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2025 December 16; 17(12): 111206

DOI: 10.4253/wjge.v17.i12.111206

ISSN 1948-5190 (online)

MINIREVIEWS

Mastering the third space: Innovations in intramural endoscopic surgery for gastrointestinal disorders

Gabriela Restrepo-Rodas, John Rodriguez

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade B

Novelty: Grade B, Grade B

Creativity or Innovation: Grade B, Grade B

Scientific Significance: Grade B, Grade B

P-Reviewer: Tahseen MU, MD, MRCP, Research Fellow, Researcher, Pakistan; Tiwari A, MD, Consultant, DM, India

Received: June 25, 2025

Revised: August 17, 2025

Accepted: November 11, 2025

Published online: December 16, 2025

Processing time: 174 Days and 3.8 Hours

Gabriela Restrepo-Rodas, John Rodriguez, General Surgery, Cleveland Clinic Abu Dhabi, Abu Dhabi 00000, United Arab Emirates

Gabriela Restrepo-Rodas, College of Medicine and Health Sciences, Khalifa University, Abu Dhabi 00000, United Arab Emirates

John Rodriguez, College of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH 44195, United States

Corresponding author: John Rodriguez, MD, FACS, General Surgery, Cleveland Clinic Abu Dhabi, 59 Hamouda Bin Ali Al Dhaheri St, Abu Dhabi 00000, United Arab Emirates.
rodrigj2@ccad.ae

Abstract

Third-space endoscopy, also known as intramural surgery, represents a major evolution in minimally invasive gastrointestinal interventions. While natural orifice transluminal endoscopic surgery provided early conceptual groundwork, third-space endoscopy builds upon it by maintaining interventions within the submucosal layer, offering improved precision and reduced risk. The creation of a controlled submucosal working space enables precise therapeutic interventions while potentially reducing the morbidity associated with traditional surgical approaches. Among its most impactful applications are the peroral endoscopic myotomy techniques, including cricopharyngeal, esophageal, gastric, and Zenker's myotomies. These procedures have redefined the management of cricopharyngeal bar, achalasia, gastroparesis, and Zenker's diverticulum, respectively. These techniques offer durable symptom relief with reduced recovery times. Over the past five years, refinements in technique, advancements in instrumentation, technology, and improved patient selection have expanded indications and enhanced safety. However, challenges remain, including the limited standardization and accessibility to specialized training. This review provides a comprehensive analysis of the evolution, technical refinements, and clinical outcomes of third-space endoscopy, with a focus on its expanding role in foregut surgery. By consolidating current evidence and highlighting future directions, we aim to provide a critical perspective on the impact of intramural surgery and its potential to further transform the management of complex gastrointestinal disorders.

Key Words: Third-space endoscopy; Cricopharyngeal; Esophageal; Gastric; Zenker

©The Author(s) 2025. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Third-space endoscopy has redefined the management of complex foregut disorders through techniques such as cricopharyngeal, esophageal, gastric, and Zenker's myotomies. These procedures offer effective, less invasive alternatives to traditional surgery, with growing evidence of durable outcomes. This review outlines key technical refinements and clinical milestones that have expanded their indications and safety. Emerging innovations such as artificial intelligence models and precision-based techniques signal the next frontier. These advancements are expanding the scope and safety of third-space endoscopy, moving it closer to broader clinical adoption and personalized surgical care.

Citation: Restrepo-Rodas G, Rodriguez J. Mastering the third space: Innovations in intramural endoscopic surgery for gastrointestinal disorders. *World J Gastrointest Endosc* 2025; 17(12): 111206
URL: https://www.wjgnet.com/1948-5190/full/v17/i12/111206.htm
DOI: https://dx.doi.org/10.4253/wjge.v17.i12.111206

INTRODUCTION

The evolution of endoscopic minimally invasive gastrointestinal (GI) interventions has been marked by the delineation of three anatomical "spaces" for endoscopic procedures. The first space refers to the luminal cavity of the GI tract, while the second encompasses access to the peritoneal cavity through natural orifices[1]. The establishment of third-space endoscopy (TSE), or intramural surgery, introduced a novel domain within the submucosal layer of the GI wall, enabling therapeutic interventions without breaching the serosal surface[1,2]. Similar to natural orifice transluminal endoscopic surgery, TSE leverages a natural orifice for access, but remains within the GI wall[1]. The conceptual foundation of TSE was laid by Sumiyama *et al*[2] in 2007 through the development of the submucosal endoscopy with mucosal flap safety valve technique. This approach involved creating a submucosal tunnel, allowing access to deeper layers of the GI tract while maintaining mucosal integrity to prevent contamination. Initial feasibility was confirmed in *ex vivo* models, subsequently transitioning to *in vivo* applications[2,3].

Despite being a relatively novel concept, the therapeutic landscape of TSE has expanded rapidly. Clinical applications of TSE have increased significantly since its inception with the development of peroral endoscopic myotomy (POEM)[1,4]. POEM involves several steps, which begin with the creation of a mucosal incision and submucosal tunneling, followed by a myotomy of the circular muscle fibers and closure of the entry site[4,5]. Similar principles were first applied to the endoscopic management of Zenker's diverticulum (ZD) in 1995, though the creation of the submucosal tunnel that characterizes Zenker's POEM (Z-POEM) technique did not arrive until 2016[6,7]. Similarly, the esophageal POEM (E-POEM) was introduced by Inoue *et al*[8] in 2008 for achalasia. A parallel technique was later adapted by Khashab *et al*[9] in 2013 to create the gastric POEM (G-POEM) for gastroparesis (GP). Then, in 2020, Al Ghamdi *et al*[10] described its use for cricopharyngeal (C-POEM) bars. While previous reviews have provided thorough foundational knowledge, emerging technologies, such as artificial intelligence (AI), as well as new studies, are poised to further refine TSE by enhancing procedural planning and real-time decision-making. This review aims to provide a comprehensive analysis of the evolution, technical refinements, and recent clinical outcomes of TSE, with a focus on its expanding role in foregut surgery. By integrating recent advancements and exploring future directions, we seek to contribute to the ongoing evolution of minimally invasive GI interventions.

METHODOLOGY

This narrative review aimed at providing a critical and clinically relevant overview of TSE with a focus on POEM techniques. A comprehensive literature search was conducted in PubMed Central to identify relevant studies on TSE, focusing on POEM techniques. The search strategy utilized a combination of keywords, including "Cricopharyngeal bar POEM", "C-POEM", "Esophageal POEM", "E-POEM", "Gastric POEM", "G-POEM", "Zenker's POEM", "Z-POEM", "third-space endoscopy", "submucosal endoscopy", "endoscopic myotomy", "intramural surgery", and "artificial intelligence". Boolean operators were applied to refine the search, and filters were set to exclude studies related to laparoscopic, open, and robotic approaches. The search encompassed articles published between January 1, 2020, and August 04, 2025, to ensure the inclusion of the most recent and relevant data. Only articles published in English and Spanish were considered. Initial screening was performed individually by both authors. Studies were categorized based on the specific POEM technique evaluated: C-POEM, E-POEM, G-POEM, or Z-POEM.

TECHNICAL ASPECTS OF POEM PROCEDURES

POEM procedures share a foundational approach, beginning with a comprehensive preoperative assessment to confirm

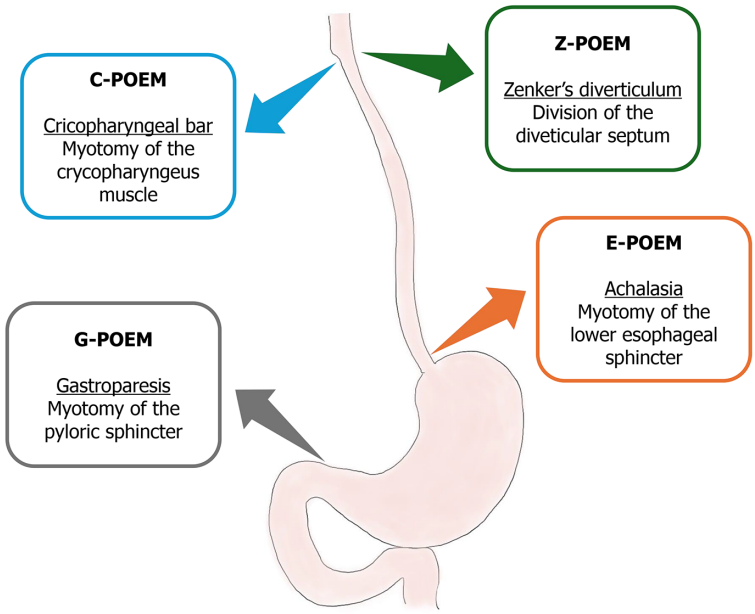


Figure 1 Peroral endoscopic myotomy techniques. Original schematic diagram of muscles targeted during each procedure. C-POEM: Cricopharyngeal peroral endoscopic myotomy; Z-POEM: Zenker's peroral endoscopic myotomy; G-POEM: Gastric peroral endoscopic myotomy; E-POEM: Esophageal peroral endoscopic myotomy.

diagnosis and plan the intervention[11,12]. An initial esophagogastroduodenoscopy (EGD) is performed to evaluate the esophageal or gastric anatomy and to strategize the procedure. POEM procedures share a unifying framework involving submucosal tunneling and selective myotomy, but differ based on anatomical target, technical nuance, and disease indication (Table 1). They commence with the selection of the submucosal entry point, which varies based on the specific POEM technique (Figure 1)[13]. Then, a submucosal bleb is created at the chosen entry point by injecting a solution, facilitating the formation of a submucosal tunnel through careful dissection. Subsequently, the myotomy is performed, with the site and length tailored to the specific procedure[14]. The procedure concludes with the closure of the mucosal entry using hemostatic clips, such as through-the-scope or over-the-scope clips, ensuring proper alignment of the mucosal edges[15]. Special considerations depending on the specific procedure are delineated below. While procedural steps and instrumentation have become more refined, the lack of standardized definitions for clinical success and adverse events remains a major limitation across the literature. These discrepancies hinder direct comparisons and introduce heterogeneity into outcome analyses. In Table 2, we have synthesized the best available evidence to provide a comparative framework across POEM variants.

C-POEM surgical technique

The procedure begins with endoscopic identification of the cricopharyngeus muscle (CPM), followed by a submucosal entry approximately 1.5 cm to 2 cm proximal to its location[16]. A Triangle Tip Knife in probe mode can be used to create a 4-5 cm submucosal tunnel within the hypopharynx, offering controlled dissection despite the narrow workspace[17]. Once the tunnel is extended to expose the CPM, complete myotomy is performed using the electrocautery knife of choice [4,18]. The mucosal entry is then closed with hemostatic clips[16,19].

E-POEM surgical technique

A submucosal bleb is raised 10-15 cm proximal to the esophagogastric junction, where the mucosal incision is then made [8]. A 2-3 cm submucosal tunnel is carefully dissected in the direction of the stomach[14]. The myotomy is then performed, typically 7-10 cm in length, extending through the lower esophageal sphincter (LES) and into the gastric cardia, either in an antegrade or retrograde fashion[11]. Depending on operator preference, the myotomy may be limited to the inner circular muscle or be performed as a full-thickness dissection involving both circular and longitudinal layers [20]. The mucosal incision is closed with hemostatic clips to ensure a secure seal.

G-POEM surgical technique

The G-POEM procedure begins with a mucosal entry point approximately 3-5 cm proximal to the pylorus along the lesser curvature[12]. A submucosal tunnel is then dissected until the pyloric ring is visualized. Complete myotomy of the pyloric sphincter is performed, in some instances extending 1-3 cm into the antrum[21]. The mucosal flap is subsequently closed using endoscopic clips or endoscopic suturing devices such as the OverStitch system, both of which have exhibited reliable outcomes[15].

Z-POEM surgical technique

Z-POEM involves exposing the septum under direct endoscopic vision, with the mucosal entry point typically 3 cm

Table 1 Key differences of peroral endoscopic myotomy procedures

POEM type	Primary Indication	Target anatomy	Submucosal entry point	Myotomy site	Myotomy length
C-POEM	Cricopharyngeal bar/UES dysfunction	Upper esophageal sphincter (cricopharyngeal muscle)	2-3 cm proximal to the cricopharyngeal bar	Cricopharyngeal muscle	Approximately 2 cm
E-POEM	Esophageal achalasia	Esophageal body and LES	10-14 cm proximal to EGJ	Circular ± longitudinal layers of esophagus and LES	7-10 cm
G-POEM	Refractory gastroparesis	Pyloric sphincter	3-5 cm proximal to pylorus	Pyloric muscle ± distal antrum	2-3 cm
Z-POEM	Zenker's diverticulum	Cricopharyngeal muscle and diverticular septum	3 cm proximal to septum or directly over it	Cricopharyngeal muscle and septum	Approximately 2 cm

All terms have been standardized; and time and distance units have been harmonized for consistency. POEM: Peroral endoscopic myotomy; C: Cricopharyngeal; E: Esophageal; G: Gastric; Z: Zenker.

Table 2 Comparative outcomes of peroral endoscopic myotomy procedures

Poem type	Sample size (range)	Technical success	Clinical success	Adverse events	Follow-up duration
C-POEM	1-27 (mostly case series)	100% (limited data)	100% (largest series)	Approximately 4%-6% (leaks, edema)	Short to mid-term (≤ 12 months)
E-POEM	Dozens to hundreds (multiple studies)	> 95% across studies	Approximately 90%-95%	9%-43% GERD (variable by myotomy length/type)	Up to 5 years in RCTs
G-POEM	30-150 per study (systematic reviews included)	Approximately 95%-100%	Approximately 70%-85% (long-term 76.6%)	5%-10% (bleeding, leak, BAG, dumping)	1-5 years
Z-POEM	30-100+ in comparative studies	Approximately 95%	90%-95%	Approximately 5%-6% (perforation, bleeding)	1-2 years

POEM: Peroral endoscopic myotomy; C: Cricopharyngeal; E: Esophageal; G: Gastric; Z: Zenker; BAG: Bile acid reflux; RCT: Randomized control trial.

proximal to or directly over the septum[12]. A deep submucosal tunnel of approximately 3 cm is dissected, allowing division of the cricopharyngeal muscle using a surgical knife[14]. The procedure concludes with flap closure using endoscopic clips.

CRICOPHARYNGEAL POEM

Cricopharyngeal bar (CPB), also known as cricopharyngeal achalasia, is a rare motility disorder primarily affecting the CPM of the upper esophageal sphincter[22,23]. While many patients remain asymptomatic, others may experience significant dysphagia[18]. Diagnosis involves a combination of radiologic imaging, endoscopic assessment, and high-resolution manometry[22]. Traditional management strategies include botulinum toxin injections and endoscopic balloon dilation, but recent years have seen the emergence of C-POEM as a minimally invasive and targeted approach[10,16].

Earlier work by Kocdor *et al*[24] synthesized outcomes of various interventions for CPB, reporting higher success rates for endoscopic approaches over botulinum toxin and open surgery, yet those techniques used CO_2 laser rather than third-space surgery. Their analysis revealed complication rates up to 6%, including perforation, edema, and mediastinitis[24]. Therefore, further techniques were explored. In 2020, Al Ghamdi *et al*[10] adapted the POEM technique, originally used for ZD, to CPB. Subsequently, a series of successful case reports by Al Ghamdi[25] reinforced the safety and efficacy of this emerging technique. The largest series to date, involving 27 patients, displayed 100% technical and clinical success, with only one complication of post-procedure leakage. For such cases, Navarro *et al*[26] recommend the use of a novel through-the-scope suturing system for closure of leaks in narrow anatomical spaces such as the GI tract, where working space is limited. Despite promising results, C-POEM remains technically demanding due to limited maneuverability in the hypopharynx and the natural convexity of the CPM, which often necessitates a longer mucosotomy[18]. These factors can be associated with an increased risk of mucosal leaks[16,18,25]. While early evidence supports the feasibility and safety of C-POEM, current data are limited to small case series[16,18,19,23,25]. Future studies should explore comparative efficacy between C-POEM, CO_2 laser myotomy, and botulinum toxin injections, and assess long-term outcomes in larger patient cohorts. For now, C-POEM is best suited to centers with established expertise in TSE.

ESOPHAGEAL POEM

Achalasia is a neurodegenerative esophageal motility disorder characterized by the progressive degeneration of inhibitory neurons in the myenteric plexus, resulting in impaired relaxation of the LES and loss of peristalsis[27]. Clinically, it manifests as dysphagia, chest pain, regurgitation, and weight loss[28]. Since its introduction by Calabrese *et al*[29] in 2007, the E-POEM has become a mainstay alternative to laparoscopic Heller myotomy (LHM) and pneumatic dilation in treating achalasia. Current guidelines by the American Gastroenterological Association (AGA) and the Society of American Gastrointestinal and Endoscopic Surgeons recommend that patients being considered for E-POEM undergo a comprehensive diagnostic evaluation, including an EGD, high-resolution manometry, and a timed barium esophagogram, along with a careful review of medications[29,30]. E-POEM is particularly indicated for type III achalasia, although it is also an effective treatment option for types I and II[29,30].

As the procedure has gained widespread adoption, attention has turned to optimizing technique and minimizing postoperative complications, particularly gastroesophageal reflux disease (GERD). Several studies have investigated the effect of myotomy length on clinical outcomes. Ghazaleh *et al*[31] conducted a meta-analysis and found that although short (3-7 cm) and long myotomies (> 7 cm) achieved comparable clinical success, the shorter approach was associated with a reduced operative time and significantly lower rates of postoperative GERD. Similarly, a larger meta-analysis by Diab *et al*[32] supported these findings and advocated for short myotomies to minimize reflux without compromising efficacy. Another technical consideration is whether the myotomy should be full-thickness. A systematic review by Dhoop *et al*[20] found that both full-thickness and circular-only myotomies had similar short- and long-term success rates. However, full-thickness myotomies were associated with greater postoperative pain and longer hospital stays. While there was an initial association between full-thickness myotomy and increased GERD and esophagitis, these outcomes may have been confounded by previous interventions or differences in postoperative proton pump inhibitor use.

Reported complication rates vary across studies. E-POEM carries a perforation risk of < 1%, delayed bleeding in 0.2%-0.4%, and post-POEM reflux in up to 40%, though rates vary by study design and follow-up period[28,33]. The reported incidence of GERD following E-POEM ranges widely from 9% to 43%, particularly when assessed with objective measures such as pH monitoring or endoscopic evaluation[34]. In a long-term randomized controlled trial comparing E-POEM with LHM plus Dor fundoplication, Hugova *et al*[33] reported that patients in the E-POEM group had significantly higher acid exposure times both during the first follow-up and at five years post-procedure. To address these concerns, emerging strategies aim to mitigate GERD risk following E-POEM. One such approach is the combination of E-POEM with endoscopic fundoplication (E-POEM + F). Kamal *et al*[28] conducted a systematic review assessing the safety and feasibility of this combined approach, reporting a post-procedure esophagitis rate of 18%. A study by Bapaye *et al*[35] comparing E-POEM + F to standard E-POEM found significantly lower rates of GERD in the E-POEM + F group, with over 75% of patients maintaining wrap integrity at a 3-year follow-up. These promising findings suggest that E-POEM + F may offer a valuable compromise between therapeutic efficacy and long-term reflux control. However, future trials are needed to compare E-POEM + F with LHM plus fundoplication under similar clinical conditions to accurately determine the superiority of one approach over the other. Transoral Incisionless Fundoplication is also emerging as an effective alternative to long-term proton pump inhibitor use for post-POEM GERD, as it helps restore the GE valve function[36]. Long-term efficacy of E-POEM has been evaluated both in systematic reviews and retrospective studies[37,38]. Despite showing comparable complications to LHM, E-POEM did not prove superior beyond two years[38]. Further high-quality, randomized studies are needed to examine long-term outcomes and establish superiority.

GASTRIC POEM

GP is a chronic gastric motility disorder characterized by delayed gastric emptying in the absence of mechanical obstruction. It can manifest with symptoms such as nausea, vomiting, early satiety, bloating, and abdominal pain[39]. Its pathophysiology remains incompletely understood, though dysfunction in antral contractions and pyloric relaxation is believed to play central roles in impaired gastric emptying[21]. Interstitial cells of Cajal have been proposed as key contributors to this dysfunction. Yang *et al*[40] demonstrated the feasibility of obtaining pyloric muscle biopsies during G-POEM, noting a higher degree of fibrosis in patients with poor response to the procedure. However, a subsequent study by Mubashir *et al*[41] found no correlation between Cajal cell counts in G-POEM biopsies and clinical outcomes, highlighting the need for further research to clarify the roles of fibrosis and Cajal cell pathology in GP pathogenesis. The treatment of GP typically follows a stepwise approach, starting with dietary modifications and pharmacological therapy, progressing to endoscopic interventions, and ultimately considering surgical options such as partial gastrectomy for refractory cases[42]. Among the available endoscopic options are pyloric balloon dilation, intrapyloric botulinum toxin injection, and G-POEM, with the latter emerging as a particularly promising therapy since its introduction[9,21]. G-POEM has showcased excellent efficacy in decreasing symptom burden regardless of the GP etiology[43,44]. In 2023, the AGA endorsed G-POEM as a treatment for refractory GP in patients who meet specific criteria: The absence of mechanical obstruction on EGD, > 20% gastric retention at 4 hours on a solid-phase gastric emptying scan, and moderate-to-severe symptom burden[21,42].

Comparative studies suggest favorable outcomes with G-POEM. A randomized control trial by Gonzalez *et al*[45] reported superior, though not statistically significant, clinical efficacy of G-POEM compared to botulinum toxin injection; a result likely limited by a small sample size. In a retrospective review, Eriksson *et al*[46] found that laparoscopic pyloroplasty resulted in greater improvement in gastric emptying than G-POEM, though both procedures led to significant symptom improvement. Therefore, the clinical significance of the difference remains uncertain. The minimally invasive

nature of G-POEM facilitates same-day discharge, as stated by Salame *et al*[47] and Landreneau *et al*[48], who reported low readmission rates within 15 postoperative days. Long-term outcomes of G-POEM are encouraging. A systematic review by Mandarino *et al*[49] showed a 70% success rate at one year, while Wills *et al*[50] reported a 76.6% patient satisfaction rate at five years using the Gastroparesis Cardinal Symptom Index. Nonetheless, the field would benefit from larger prospective studies with objective assessment tools and long-term follow-up. Complications, although relatively infrequent, must be acknowledged. These include pain, bleeding, perforation, rapid gastric emptying, and bile acid reflux [42]. A systematic review by Shargo *et al*[51] reported dumping syndrome and bile acid gastritis incidences of 3.2% and 0%-15.4%, respectively, across G-POEM and pyloroplasty, suggesting underreporting and highlighting the need for future studies to determine the true incidence and risk factors.

ZENKER'S POEM

ZD, the most common esophageal diverticulum, forms in the hypopharynx between the thyropharyngeal and cricopharyngeal muscles[52,53]. It typically presents with dysphagia in 80%-90% of cases, along with regurgitation of undigested food, halitosis, and chest discomfort[53]. Surgical repair is indicated in symptomatic patients, with endoscopic approaches gaining popularity over traditional open surgery[54]. Endoscopic treatment has shown high efficacy, with Spadaccini *et al*[55] reporting a pooled clinical success rate of 93.4% and an overall adverse event rate of 4.9%. Available endoscopic techniques include Z-POEM, Flexible Endoscopic Septum Division (FESD), a technique involving direct incision of the septum using a flexible endoscope, and Peroral Endoscopic Septotomy[53].

Recent technical modifications aim to streamline the procedure and improve outcomes, with some of these new techniques renamed as "hybrid" procedures[53]. Mavrogenis *et al*[56] evaluated standard Z-POEM against single-tunnel and tunnel-free variations. The tunnel-free approach, involving mucosotomy directly over the septum followed by direct myotomy, reduced operative time without compromising efficacy. Almario *et al*[57] proposed an additional mucosal incision post-myotomy to prevent the formation of large mucosal flaps, which may exacerbate symptoms in the future. Zhang *et al*[54] recommend tailoring the technique to each patient's characteristics, such as adding mucosotomy for larger diverticula, to maximize effectiveness and minimize operative time. While these innovations show promise, their long-term utility requires further validation.

Z-POEM, first described in 2016, has proven to be a safe and effective option, achieving a pooled technical success of 95% and an adverse event rate of 6% in a systematic review by Kamal *et al*[58]. Comparative studies further support its utility. Singh *et al*[59] found that while both Z-POEM and FESD showcased high technical success and similar safety profiles, Z-POEM offered significantly superior clinical success ($P = 0.001$). In contrast, Sarkis *et al*[60] reported fewer and less severe adverse events with Z-POEM than with FENKS (a modification of FESD that employs a needle-type knife for direct septal division). Furthermore, Spadaccini *et al*[55] showed equivalent safety and efficacy between Z-POEM and Peroral Endoscopic Septotomy. In 2023, the AGA endorsed the use of Z-POEM for diverticula of all sizes, including those under 3 cm, citing its capacity for deep and complete septotomy (a limitation of traditional techniques that may lead to recurrence)[61,62]. Z-POEM offers an additional technical advantage by allowing controlled myotomy while reducing the risk of perforation[1]. In contrast to open surgery, Sarkis *et al*[60] declared that, in high-volume centers with standardized protocols, same-day discharge is feasible and safe. Steinway *et al*[63] assessed the durability of Z-POEM, reporting a 94% initial clinical success rate with only 6.7% recurrence at two years, affirming its long-term efficacy. Nevertheless, potential complications, including perforation, pneumoperitoneum, bleeding, and pneumothorax, must be considered.[58] Future research should focus on standardized comparisons of existing techniques and hybrid approaches that combine elements of FESD and Z-POEM. Such strategies may offer optimized outcomes while minimizing complexity[53].

INNOVATIONS IN TSE

AI integration

As TSE continues to evolve, innovations aimed at enhancing safety, efficacy, and personalization are emerging across various fronts. One promising area involves the integration of AI, particularly with computer vision and machine learning. Intraoperative vessel detection is emerging as an interesting tool to help prevent bleeding, a major adverse event that can obscure the operative field and hamper corrective actions[64]. Scheppach *et al*[65] developed a real-time vessel detection algorithm that improved both the accuracy and speed of vessel recognition for endoscopists, regardless of experience level, achieving a 10% increase in detection compared to standard visualization. Similarly, Egibgo *et al*[66] introduced a machine learning model capable of detecting vessels with 85% sensitivity and a false-positive rate of 0.75 per minute. However, challenges remain. As Schoon[67] noted, most bleedings occur during circumferential myotomies, an area not yet covered by existing AI models. Consequently, future research must validate these algorithms in live clinical settings and extend their scope to critical procedural steps. AI's utility extends beyond procedural guidance to preoperative risk stratification. Takahashi *et al*[68] employed machine learning to stratify patients with achalasia by phenotype and risk of symptom persistence following E-POEM, using preoperative demographic data and high-resolution manometry results. Such models could play a pivotal role in customizing therapeutic strategies and improving long-term outcomes.

Robotics assistance in TSE

Another promising frontier is robotics. Current TSE challenges, such as restricted working space, need for traction, and a steep learning curve, could potentially be mitigated by robotic assistance[69]. Flexible robotic platforms like the Flex Robotic System (Medrobotics) and the Endoluminal Surgical System (CloubrisMX) are being adapted for colorectal interventions and may soon enter the third space[70-72]. In a proof-of-concept, Moura *et al*[73] used the Flex Robotic System to successfully treat Zenker's diverticulum endoscopically in an *ex vivo* animal model, suggesting a possible future extension of robotic applications into the submucosal space. The feasibility and safety of robotic-assisted techniques in TSE are currently being explored in ongoing clinical trials. No. NCT01394861 is evaluating a masterslave robotic platform for endoscopic submucosal dissection, while No. NCT06581718 is assessing a novel robotic system for flexible endoscopy procedures[74,75].

Equally transformative is the shift toward precision endoscopy. Tailoring the length and location of the myotomy according to patient anatomy and disease phenotype is gaining momentum[36]. In E-POEM, Mandarino[13] advocated for shorter, personalized myotomies, supported by intraoperative tools such as the Functional Luminal Imaging Probe (FLIP), a device that measures esophageal distensibility and helps dynamically identify the LES to guide the extent of the myotomy. Holmstrom *et al*[76] used FLIP in achalasia patients to identify who needed an extended myotomy, achieving improved outcomes in nearly half of the cases. Farooq *et al*[77] applied FLIP to G-POEM and determined that a sustained clinical response correlated with durable pyloric distensibility improvements measured at 6 months. Recent technical developments in TSE, including the Speedboat-RS2 and HybridKnife® flex, have been developed to improve procedural precision, hemostasis, and efficiency while minimizing thermal injury[78]. These innovations, from AI to robotics and FLIP-guided customization, are propelling TSE into a new era of safety, efficiency, and individualized care. Actionable steps for integration include simulation-based curricula with FLIP and robotic models, incorporation of AI-based feedback in skill assessment, and use of video annotation platforms for endoscopic coaching[78].

CHALLENGES

Despite the promising trajectory of TSE, some challenges persist. A main challenge is the steep learning curve and the high level of technical expertise required to safely perform these procedures. TSE demands a nuanced understanding of tissue dynamics and anatomical navigation. According to Roser *et al*[79], successful TSE necessitates a stepwise training model that integrates both theoretical knowledge and hands-on skill acquisition to reduce complications and optimize outcomes. Wei *et al*[80] described three primary training pathways currently available in the United States: Formal fellowships in TSE, traditional master-apprentice mentorships, and participation in live instructional courses with proctored procedures. Nonetheless, these methods remain inconsistently adopted, and limited standardized curricula currently exist, limiting the widespread dissemination of TSE. Similarly, patient selection remains critical for optimal outcomes. Patients with severe fibrosis, distorted anatomy from prior interventions, or limited submucosal space may be suboptimal candidates. Moreover, high procedural costs, and limited availability of advanced endoscopy units present additional barriers to wider adoption[28,48].

LIMITATIONS

This review sought to consolidate and synthesize recent developments in TSE across its primary procedural variants - C-POEM, E-POEM, G-POEM, and Z-POEM. However, several limitations must be acknowledged. First, the review was not based on a systematic evaluation of study quality, and much of the data are derived from heterogeneous studies with variable designs, sample sizes, outcome measures, and follow-up periods, introducing the risk of publication bias. Second, many of the innovations discussed - particularly in C-POEM, robotic assistance, and AI-guided enhancements - are supported by early-phase studies or single-center reports, limiting the generalizability of conclusions. Furthermore, a lack of long-term randomized comparative trials against surgical alternatives continues to hinder definitive outcome comparisons. Questions regarding cost-effectiveness and the scalability of advanced tools like robotics and AI also remain largely unanswered, especially in low-resource settings. Nevertheless, this review aimed to provide a broad, balanced, and transparent overview of current trends and innovations while highlighting areas in need of further research.

CONCLUSION

TSE represents a paradigm shift in minimally invasive surgery, offering targeted solutions for a range of GI motility disorders. C-POEM, E-POEM, G-POEM, and Z-POEM each hold distinct clinical indications and technical adaptations, with mounting evidence supporting their safety and efficacy. Recent innovations, including AI-driven vessel detection, robotic assistance, and personalized procedural tailoring using tools like FLIP, are expanding the potential of these techniques. Future priorities include comparative trials against surgical standards, development of standardized training pathways, and health economics analyses to assess cost-effectiveness across healthcare settings. These efforts will be critical to the responsible integration of third-space techniques into routine care.

FOOTNOTES

Author contributions: All authors wrote the original draft, investigation, review-editing, and final approval.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Open Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

Country of origin: United Arab Emirates

ORCID number: Gabriela Restrepo-Rodas 0000-0002-8324-3969; John Rodriguez 0009-0004-3082-047X.

S-Editor: Bai SR
L-Editor: A
P-Editor: Zhao YQ

REFERENCES

1 **Shanbhag AB**, Thota PN, Sanaka MR. Recent advances in third space or intramural endoscopy. *World J Gastrointest Endosc* 2020; **12**: 521-531 [*RCA*] [PMID: 33362905 DOI: 10.4253/wjge.v12.i12.521] [FullText] [Full Text(PDF)]
2 **Sumiyama K**, Gostout CJ, Rajan E, Bakken TA, Knipschield MA, Marler RJ. Submucosal endoscopy with mucosal flap safety valve. *Gastrointest Endosc* 2007; **65**: 688-694 [*RCA*] [PMID: 17324411 DOI: 10.1016/j.gie.2006.07.030] [FullText]
3 **Pasricha PJ**, Hawari R, Ahmed I, Chen J, Cotton PB, Hawes RH, Kalloo AN, Kantsevoy SV, Gostout CJ. Submucosal endoscopic esophageal myotomy: a novel experimental approach for the treatment of achalasia. *Endoscopy* 2007; **39**: 761-764 [*RCA*] [PMID: 17703382 DOI: 10.1055/s-2007-966764] [FullText]
4 **Norton BC**, Papaefthymiou A, Telese A, Murray C, Murino A, Johnson G, Bisschops R, Haidry R. The A to Z of Peroral Endoscopic Myotomy. *J Clin Gastroenterol* 2025; **59**: 110-120 [*RCA*] [PMID: 39774595 DOI: 10.1097/MCG.0000000000002082] [FullText]
5 **Mohapatra S**, Esaki M, Fukami N. Advances in Third Space Endoscopy. *Gastroenterol Clin North Am* 2024; **53**: 747-771 [*RCA*] [PMID: 39489585 DOI: 10.1016/j.gtc.2024.08.020] [FullText]
6 **Ishioka S**, Sakai P, Maluf Filho F, Melo JM. Endoscopic incision of Zenker's diverticula. *Endoscopy* 1995; **27**: 433-437 [*RCA*] [PMID: 8549440 DOI: 10.1055/s-2007-1005736] [FullText]
7 **Li QL**, Chen WF, Zhang XC, Cai MY, Zhang YQ, Hu JW, He MJ, Yao LQ, Zhou PH, Xu MD. Submucosal Tunneling Endoscopic Septum Division: A Novel Technique for Treating Zenker's Diverticulum. *Gastroenterology* 2016; **151**: 1071-1074 [*RCA*] [PMID: 27664512 DOI: 10.1053/j.gastro.2016.08.064] [FullText]
8 **Inoue H**, Minami H, Satodate H, Kudo S. First Clinical Experience of Submucosal Endoscopic Esophageal Myotomy for Esophageal Achalasia with No Skin Incision. *Gastrointest Endosc* 2009; **69**: AB122 [DOI: 10.1016/j.gie.2009.03.133] [FullText]
9 **Khashab MA**, Stein E, Clarke JO, Saxena P, Kumbhari V, Chander Roland B, Kalloo AN, Stavropoulos S, Pasricha P, Inoue H. Gastric peroral endoscopic myotomy for refractory gastroparesis: first human endoscopic pyloromyotomy (with video). *Gastrointest Endosc* 2013; **78**: 764-768 [*RCA*] [PMID: 24120337 DOI: 10.1016/j.gie.2013.07.019] [FullText]
10 **Al Ghamdi SS**, Farha J, Runge TM, Ichkhanian Y, Khashab MA. No pouch, no problem: successful endoscopic division of a symptomatic cricopharyngeal bar using a modified peroral endoscopic myotomy technique for Zenker's diverticulum. *VideoGIE* 2020; **5**: 281-282 [*RCA*] [PMID: 32642611 DOI: 10.1016/j.vgie.2020.03.006] [FullText] [Full Text(PDF)]
11 **Tat C**, Barajas-Gamboa JS, Kroh M. Principles of Intramural Surgery. *Surg Clin North Am* 2020; **100**: 1169-1182 [*RCA*] [PMID: 33128886 DOI: 10.1016/j.suc.2020.08.003] [FullText]
12 **Restrepo-Rodas G**, Barajas-Gamboa JS, Dang JT, Piechowska-Jóźwiak MI, Khan M, Diaz Del Gobbo G, Abdallah M, Moreno C, Abril C, Pantoja JP, Guerron AD, Corcelles R, Kroh M, Rodriguez J. Seven-Year Experience of Intramural Surgery in the Middle East: A Safety and Feasibility Analysis. *J Clin Med* 2024; **13**: 3989 [*RCA*] [PMID: 38999553 DOI: 10.3390/jcm13133989] [FullText]
13 **Mandarino FV**, Vespa E, Barchi A, Fasulo E, Sinagra E, Azzolini F, Danese S. Precision Endoscopy in Peroral Myotomies for Motility Disorders of the Upper Gastrointestinal Tract: Current Insights and Prospective Avenues-A Comprehensive Review. *Life (Basel)* 2023; **13**: 2143 [*RCA*] [PMID: 38004283 DOI: 10.3390/life13112143] [FullText] [Full Text(PDF)]
14 **Barajas-Gamboa J**, Corcelles R, Kroh M. Endoscopic Intramural Surgery Part II: Muscular Division. *Dig Dis Interv* 2018; **02**: 368-374 [DOI: 10.1055/s-0038-1676504] [FullText]
15 **Hustak R**. How to close mucosal incisions? *Best Pract Res Clin Gastroenterol* 2024; **71**: 101938 [*RCA*] [PMID: 39209420 DOI: 10.1016/j.bpg.2024.101938] [FullText]
16 **Elmunzer BJ**, Moran RA. Peroral endoscopic myotomy for cricopharyngeal bar. *VideoGIE* 2020; **5**: 378-379 [*RCA*] [PMID: 32821871 DOI: 10.1016/j.vgie.2020.04.020] [FullText] [Full Text(PDF)]
17 **Fraile López M**, Cobas Bravo Á, Fernández Gil PL, Moris Felgueroso M, Rodríguez Duque JC, López Arias MJ, Cuadrado Lavín A, Terán Lantarón Á. Triangle-Tip Jet Knife used as "probe mode" during C-POEM for the treatment of cricopharyngeal achalasia. *Rev Esp Enferm Dig* 2025 [*RCA*] [PMID: 39898723 DOI: 10.17235/reed.2025.11073/2025] [FullText]
18 **Pittala K**, Reinhart N, Sujka JA, Velanovich V, DuCoin CG. Novel Per-Oral Cricopharyngotomy for Cricopharyngeal Bar: Feasibility Study With Emphasis on Technical Limitations. *Cureus* 2023; **15**: e36663 [*RCA*] [PMID: 37102013 DOI: 10.7759/cureus.36663] [FullText]
19 **Norton B**, Papaefthymiou A, Telese A, Aslam N, Murray C, Haidry R. Peroral endoscopic myotomy for the management of symptomatic cricopharyngeal bar (C-POEM): a case series and video demonstration. *Ann Gastroenterol* 2024; **37**: 251-254 [*RCA*] [PMID: 38481774 DOI:

10.20524/aog.2024.0856] [FullText] [Full Text(PDF)]

20 **Dhoop S**, Abu-Rumaileh M, Sayeh W, Ghazaleh S, Lombardi C, Patel M, Sawaf B, Lee-Smith W, Zhou A, Nawras A, Alastal Y. Efficacy and safety of full-thickness versus circular peroral endoscopic myotomy for treatment of achalasia: a systematic review and meta-analysis. *Ann Gastroenterol* 2025; **38**: 143-155 [*RCA*] [PMID: 40124428 DOI: 10.20524/aog.2025.0946] [FullText] [Full Text(PDF)]

21 **Khashab MA**, Wang AY, Cai Q. AGA Clinical Practice Update on Gastric Peroral Endoscopic Myotomy for Gastroparesis: Commentary. *Gastroenterology* 2023; **164**: 1329-1335.e1 [*RCA*] [PMID: 37086247 DOI: 10.1053/j.gastro.2023.02.027] [FullText]

22 **Albeniz E**, Estremera-Arevalo F. Cricopharyngeal achalasia and upper oesophageal endoscopic myotomy (CP-POEM). *Best Pract Res Clin Gastroenterol* 2024; **71**: 101937 [*RCA*] [PMID: 39209419 DOI: 10.1016/j.bpg.2024.101937] [FullText]

23 **Duarte-Chavez R**, Wey B, Kahaleh M. Adaptation of peroral endoscopic myotomy for cricopharyngeal bar. *VideoGIE* 2023; **8**: 148-150 [*RCA*] [PMID: 37095833 DOI: 10.1016/j.vgie.2022.12.003] [FullText]

24 **Kocdor P**, Siegel ER, Tulunay-Ugur OE. Cricopharyngeal dysfunction: A systematic review comparing outcomes of dilatation, botulinum toxin injection, and myotomy. *Laryngoscope* 2016; **126**: 135-141 [*RCA*] [PMID: 26360122 DOI: 10.1002/lary.25447] [FullText]

25 **Al Ghamdi SS**, Bejjani M, Hernández Mondragón OV, Parsa N, Yousaf MN, Aghaie Meybodi M, Ghandour B, Krustri C, Phalanusitthepha C, Ngamruengphong S, Nieto JM, Khashab MA. Peroral endoscopic myotomy for management of cricopharyngeal bars (CP-POEM): a retrospective evaluation. *Endoscopy* 2022; **54**: 498-502 [*RCA*] [PMID: 34710910 DOI: 10.1055/a-1646-1151] [FullText]

26 **Navarro Almario JA**, Mehta A, Khashab M. Through-the-scope suturing for closure of contained leak after cricopharyngeal peroral endoscopic myotomy. *VideoGIE* 2024; **9**: 57-60 [*RCA*] [PMID: 38357016 DOI: 10.1016/j.vgie.2023.10.003] [FullText] [Full Text(PDF)]

27 **Kim GH**, Park H, Jung KW, Kim MJ, Kim YJ, Lee JM, Lee BE, Min YW, Kim JH, Na HK, Ahn JY, Lee JH, Kim DH, Choi KD, Song HJ, Lee GH, Jung HY, Kim HJ; Big Data Study Group Under the Korean Society of Neurogastroenterology and Motility. Incidence, Morbidity, and Mortality of Achalasia: A Nationwide, Population-Based Cohort Study in South Korea. *Gut Liver* 2023; **17**: 894-904 [*RCA*] [PMID: 36987382 DOI: 10.5009/gnl220334] [FullText]

28 **Kamal F**, Khan MA, Lee-Smith W, Sharma S, Acharya A, Farooq U, Ejaz Z, Aziz M, Gangwani MK, Hayat U, Kumar A, Schlachterman A, Loren D, Kowalski T. Feasibility and safety of peroral endoscopic myotomy with fundoplication in patients with achalasia: a systematic review and meta-analysis. *Ann Gastroenterol* 2024; **37**: 403-409 [*RCA*] [PMID: 38974079 DOI: 10.20524/aog.2024.0890] [FullText] [Full Text(PDF)]

29 **Calabrese EC**, Kindel T, Slater BJ, Marks J, Swanstrom L, Saxena P, Docimo S, Athanasiadis DI, Hanna NM, Stefanidis D, Rooker C, Maddern G, Kohn GP. 2024 Update to SAGES guidelines for the use of peroral endoscopic myotomy (POEM) in the treatment of achalasia. *Surg Endosc* 2025; **39**: 4027-4037 [*RCA*] [PMID: 40399617 DOI: 10.1007/s00464-025-11789-z] [FullText]

30 **Yang D**, Bechara R, Dunst CM, Konda VJA. AGA Clinical Practice Update on Advances in Per-Oral Endoscopic Myotomy (POEM) and Remaining Questions-What We Have Learned in the Past Decade: Expert Review. *Gastroenterology* 2024; **167**: 1483-1490 [*RCA*] [PMID: 39425737 DOI: 10.1053/j.gastro.2024.08.038] [FullText]

31 **Ghazaleh S**, Beran A, Khader Y, Nehme C, Chuang J, Sharma S, Aziz M, Khan Z, Elzanaty AM, Burlen J, Nawras A. Short versus standard peroral endoscopic myotomy for esophageal achalasia: a systematic review and meta-analysis. *Ann Gastroenterol* 2021; **34**: 634-642 [*RCA*] [PMID: 34475733 DOI: 10.20524/aog.2021.0644] [FullText] [Full Text(PDF)]

32 **Diab AF**, Sujka JA, Mitra C, Hamza A, Ananthan YD, Docimo S, DuCoin CG. Short Versus Long Myotomy Length in Peroral Endoscopic Myotomy for Achalasia: Comparable Efficacy with Potential Reduction in Incidence of Reflux-A Meta-Analysis of 10 Comparative Studies. *J Laparoendosc Adv Surg Tech A* 2025; **35**: 300-312 [*RCA*] [PMID: 40173097 DOI: 10.1089/lap.2024.0397] [FullText]

33 **Hugova K**, Mares J, Hakanson B, Repici A, von Rahden BHA, Bredenoord AJ, Bisschops R, Messmann H, Ruppenthal T, Mann O, Izbicki J, Harustiak T, Fumagalli Romario U, Rosati R, Germer CT, Schijven M, Emmermann A, von Renteln D, Dautel S, Fockens P, Boeckxstaens G, Rösch T, Martinek J, Werner YB. Per-oral endoscopic myotomy versus laparoscopic Heller's myotomy plus Dor fundoplication in patients with idiopathic achalasia: 5-year follow-up of a multicentre, randomised, open-label, non-inferiority trial. *Lancet Gastroenterol Hepatol* 2025; **10**: 431-441 [*RCA*] [PMID: 40112837 DOI: 10.1016/S2468-1253(25)00012-3] [FullText]

34 **Hazrah P**. Reflux after peroral endoscopic myotomy: The dilemma and the options. *World J Gastroenterol* 2025; **31**: 100510 [*RCA*] [PMID: 39958445 DOI: 10.3748/wjg.v31.i6.100510] [FullText] [Full Text(PDF)]

35 **Bapaye A**, Yewale R, Shah J, Bale R A, Ansari J, Borkar M, Bapaye H, Pujari R, Gadhikar H. Long-term (3-year) composite gastroesophageal reflux outcomes of peroral endoscopic myotomy with or without concomitant endoscopic fundoplication in matched cohorts of achalasia. *Gastrointest Endosc* 2025; S0016-5107(25)01622 [*RCA*] [PMID: 40288696 DOI: 10.1016/j.gie.2025.04.029] [FullText]

36 **Christodoulidis G**, Tsagkidou K, Koumarelas KE, Kouliou MN. Advances and challenges in peroral endoscopic myotomy: Safety, precision, and post-procedure management. *World J Gastroenterol* 2025; **31**: 97574 [*RCA*] [PMID: 39926218 DOI: 10.3748/wjg.v31.i5.97574] [Full Text] [Full Text(PDF)]

37 **Onimaru M**, Inoue H, Fujiyoshi Y, Abad MRA, Nishikawa Y, Toshimori A, Shimamura Y, Tanabe M, Sumi K, Ikeda H. Long-term clinical results of per-oral endoscopic myotomy (POEM) for achalasia: First report of more than 10-year patient experience as assessed with a questionnaire-based survey. *Endosc Int Open* 2021; **9**: E409-E416 [*RCA*] [PMID: 33655041 DOI: 10.1055/a-1333-1883] [FullText] [Full Text (PDF)]

38 **Ma O**, Brar K, McCluskey S, Morris-Janzen D, Peabody J, Turner S. Long-term outcomes after per-oral endoscopic myotomy versus laparoscopic Heller myotomy in the treatment of achalasia: a systematic review and meta-analysis. *Surg Endosc* 2025; **39**: 5985-5994 [*RCA*] [PMID: 40624423 DOI: 10.1007/s00464-025-11895-y] [FullText]

39 **Vasatko M**, Evinova E, Hugova K, Simkova D, Yepishkina K, Amin S, Martinek J. Endoscopic pyloromyotomy for treatment of gastroparesis: A new standard or still an experimental approach? *Best Pract Res Clin Gastroenterol* 2024; **71**: 101910 [*RCA*] [PMID: 39209413 DOI: 10.1016/j.bpg.2024.101910] [FullText]

40 **Yang D**, Hasan MK, Bani Fawwaz B, Farooq A, Zhang Y, Khan HM, Brar TS, Singh S, Viana A, Singh G, Kadkhodayan K, Arain MA, Cosgrove N, Jain D, Inayat I, Singh C. Quantification of interstitial cells of Cajal and fibrosis during gastric per-oral endoscopic myotomy and its association with clinical outcomes. *Endosc Int Open* 2024; **12**: E585-E592 [*RCA*] [PMID: 38654965 DOI: 10.1055/a-2290-0502] [FullText] [Full Text(PDF)]

41 **Mubashir M**, Raza D, Neice M, Novacic S, Maloz M, Aburumman R, Pass B, Roppolo N, Dies R, Arora K, Traylor J, Takei H, Hossain MI, Bhuiyan MAN, Cai Q. Impact of Interstitial Cells of Cajal Density and Other Factors on Clinical Outcomes Following G-POEM in Gastroparesis Patients. *Dig Dis Sci* 2025; **70**: 2621-2627 [*RCA*] [PMID: 40323492 DOI: 10.1007/s10620-025-09020-z] [FullText]

42 **Camilleri M**, Kuo B, Nguyen L, Vaughn VM, Petrey J, Greer K, Yadlapati R, Abell TL. ACG Clinical Guideline: Gastroparesis. *Am J Gastroenterol* 2022; **117**: 1197-1220 [*RCA*] [PMID: 35926490 DOI: 10.14309/ajg.0000000000001874] [FullText]

43 **Malik S**, Loganathan P, Khan K, Mohan BP, Adler DG. Efficacy and safety of gastric peroral endoscopic myotomy across different etiologies of gastroparesis: systematic review and meta-analysis. *Gastrointest Endosc* 2025; **101**: 54-67.e6 [*RCA*] [PMID: 39181473 DOI: 10.1016/j.gie.2024.08.024] [FullText]

44 **Dolan RD**, McCarty TR, Bazarbashi AN, Thompson CC. Efficacy and Safety of Gastric Per-Oral Endoscopic Myotomy (G-POEM): A Systematic Review and Meta-Analysis. *J Clin Gastroenterol* 2025; **59**: 325-334 [*RCA*] [PMID: 38683239 DOI: 10.1097/MCG.0000000000002010] [FullText]

45 **Gonzalez JM**, Mion F, Pioche M, Garbay V, Baumstarck K, Boucekine M, Debourdeau A, Rivory J, Barthet M, Vitton V. Gastric peroral endoscopic myotomy versus botulinum toxin injection for the treatment of refractory gastroparesis: results of a double-blind randomized controlled study. *Endoscopy* 2024; **56**: 345-352 [*RCA*] [PMID: 38141620 DOI: 10.1055/a-2235-3286] [FullText]

46 **Eriksson SE**, Chrysostome ML, Sarici IS, Nguyen J, Zheng P, Ayazi S. Pyloric drainage interventions for gastroparesis: a comparison of laparoscopic pyloroplasty and gastric peroral endoscopic myotomy (G-POEM) outcomes. *Surg Endosc* 2025; **39**: 3514-3524 [*RCA*] [PMID: 40251315 DOI: 10.1007/s00464-025-11731-3] [FullText] [Full Text(PDF)]

47 **Salame M**, Ichkhanian Y, Hadaki N, Wo JM, Stainko SA, Saito A, Siwiec RM, Nowak TV, Li A, Hwang JH, Yang J, Broucek J, Esfandyari T, Joseph S, Ujiki M, Williams AE, Moremen JR, Gouda Z, Schlachterman A, Hugova K, Martinek J, Geng CX, Podboy A, Wang AY, Lajin M, Miller P, Gregor L, Albunni H, Dewitt JM, Al-Haddad MA. Safety of same-day discharge after gastric peroral endoscopic myotomy in patients with refractory gastroparesis: an international multicenter study. *Gastrointest Endosc* 2025; **102**: 595-599.e1 [*RCA*] [PMID: 39983999 DOI: 10.1016/j.gie.2025.02.020] [FullText]

48 **Landreneau JP**, Strong AT, Ponsky JL, Tu C, Kroh MD, Rodriguez JH, El-Hayek K. Enhanced recovery outcomes following per-oral pyloromyotomy (POP): a comparison of safety and cost with same-day discharge versus inpatient recovery. *Surg Endosc* 2020; **34**: 3153-3162 [*RCA*] [PMID: 31482346 DOI: 10.1007/s00464-019-07085-2] [FullText]

49 **Mandarino FV**, Barchi A, Salmeri N, Azzolini F, Fasulo E, Dell'Anna G, Vespa E, Sinagra E, Jacques J, Danese S. Long-term efficacy (at and beyond 1 year) of gastric peroral endoscopic myotomy for refractory gastroparesis: A systematic review and meta-analysis. *DEN Open* 2025; **5**: e70021 [*RCA*] [PMID: 39372285 DOI: 10.1002/deo2.70021] [FullText] [Full Text(PDF)]

50 **Wills MV**, Farah A, Moussally M, Chaivanijchaya K, Lee S, Barajas-Gamboa JS, Dang J, Strong A, Navarrete S, Kroh M, Allemang M. Long term outcomes of gastric per oral endoscopic myotomy (GPOEM) in patients with gastroparesis. *Am J Surg* 2025; **243**: 116203 [*RCA*] [PMID: 39900511 DOI: 10.1016/j.amjsurg.2025.116203] [FullText]

51 **Shargo R**, Poonen-Honig I, Thélin C, DuCoin CG, Mhaskar R, Docimo S, Sujka JA. Dumping Syndrome and Bile Acid Reflux Following Pyloroplasty and Gastric Peroral Endoscopic Myotomy (G-POEM) for Refractory Gastroparesis: A Systematic Review. *Cureus* 2025; **17**: e79056 [*RCA*] [PMID: 40104464 DOI: 10.7759/cureus.79056] [FullText] [Full Text(PDF)]

52 **Maehata T**, Sato Y, Nakamoto Y, Kato M, Kawashima A, Kiyokawa H, Yasuda H, Yamamoto H, Tateishi K. Updates in the Field of Submucosal Endoscopy. *Life (Basel)* 2022; **13**: 104 [*RCA*] [PMID: 36676053 DOI: 10.3390/life13010104] [FullText]

53 **Dell'Anna G**, Fasulo E, Fanizza J, Barà R, Vespa E, Barchi A, Cecinato P, Fuccio L, Annese V, Malesci A, Azzolini F, Danese S, Mandarino FV. The Endoscopic Management of Zenker's Diverticulum: A Comprehensive Review. *Diagnostics (Basel)* 2024; **14**: 2155 [*RCA*] [PMID: 39410559 DOI: 10.3390/diagnostics14192155] [FullText] [Full Text(PDF)]

54 **Zhang LY**, Nieto J, Ngamruengphong S, Repici A, Khashab MA. Zenker's diverticulum: advancing beyond the tunnel. *VideoGIE* 2021; **6**: 562-567 [*RCA*] [PMID: 34917870 DOI: 10.1016/j.vgie.2021.08.003] [FullText] [Full Text(PDF)]

55 **Spadaccini M**, Maselli R, Chandrasekar VT, Patel HK, Fugazza A, Galtieri PA, Pellegatta G, Attardo S, Carrara S, Anderloni A, Desai P, Alkandari A, Sharma P, Khashab MA, Repici A. Submucosal tunnelling techniques for Zenker's diverticulum: a systematic review of early outcomes with pooled analysis. *Eur J Gastroenterol Hepatol* 2021; **33**: e78-e83. [*RCA*] [PMID: 34907984 DOI: 10.1097/MEG.0000000000002318] [FullText]

56 **Mavrogenis G**, Zachou M, Tsevgas I, Markoglou K, Zachariadis D, Spanomanoli A, Chatzis M, Bazerbachi F. Tunnel-free peroral endoscopic myotomy reduces procedural time and maintains efficacy in Zenker's diverticulum. *Ann Gastroenterol* 2024; **37**: 509-513 [*RCA*] [PMID: 39238796 DOI: 10.20524/aog.2024.0902] [FullText] [Full Text(PDF)]

57 **Almario JA**, Mehta A, Shrigiriwar A, Fayyaz F, El-Sherbiny M, Essam K, Haggag H, Yousef K, Abdallatef AA, Elkholy S, Canakis A, Kim RE, Yang D, Puga-Tejada M, Alcívar-Vásquez J, Egas-Izquierdo M, Del Valle RS, Cunto D, Baquerizo-Burgos J, Arevalo-Mora M, Robles-Medranda C, Borkowicz A, Kamiński MF, Lajin M, Kedia P, Khashab MA. Short-term clinical and technical outcomes of a modified Zenker's peroral endoscopic myotomy with mucosal flap incision. *Endoscopy* 2025; **57**: 348-353 [*RCA*] [PMID: 39447609 DOI: 10.1055/a-2451-2869] [FullText]

58 **Kamal F**, Khan MA, Lee-Smith W, Sharma S, Marella HK, Iqbal U, Mcdonough S, Aslam A, Ismail MK, Tombazzi C, Adler DG. Peroral Endoscopic Myotomy Is a Safe and Feasible Option in Management of Esophageal Diverticula: Systematic Review and Meta-Analysis. *Dig Dis Sci* 2021; **66**: 3242-3249 [*RCA*] [PMID: 33123940 DOI: 10.1007/s10620-020-06678-5] [FullText]

59 **Singh S**, Chandan S, Bapaye J, Brar HS, Mohammed A, Kassab LL, Bhat I, Singh S, Bapaye A, Yang D. Peroral endoscopic myotomy (Z-POEM) versus flexible endoscopic septotomy (FES) for treatment of Zenker's diverticulum: does either make the cut? A systematic review and meta-analysis of outcomes. *Ann Gastroenterol* 2025; **38**: 20-27 [*RCA*] [PMID: 39802284 DOI: 10.20524/aog.2024.0934] [FullText] [Full Text (PDF)]

60 **Sarkis Y**, Al-Haddad M, Stainko S, Wreglesworth L, Ashcraft K, DeWitt J. Safety of same day discharge after Zenker's diverticulum peroral endoscopic myotomy. *Dig Liver Dis* 2025; **57**: 902-905 [*RCA*] [PMID: 39919979 DOI: 10.1016/j.dld.2025.01.188] [FullText]

61 **Wagh MS**, Draganov PV. How to Approach a Patient with a Zenker's Diverticulum. *Gastroenterology* 2021; **160**: 10-14 [*RCA*] [PMID: 33220254 DOI: 10.1053/j.gastro.2020.11.018] [FullText]

62 **Mandavdhare HS**, Samanta J, Jafra A, Singh H, Gupta P. Recurrence after Zenker's peroral endoscopic myotomy despite complete septotomy: how far to go with myotomy on the esophageal side. *VideoGIE* 2022; **7**: 350-352 [*RCA*] [PMID: 36238802 DOI: 10.1016/j.vgie.2022.07.006] [FullText] [Full Text(PDF)]

63 **Steinway S**, Zhang L, Amundson J, Nieto J, Desai P, Jacques J, Bejjani M, Pioche M, Kumta N, Hernandez-Mondragon O, Ujiki M, Khashab M. Long-term outcomes of Zenker's peroral endoscopic myotomy (Z-POEM) for treatment of Zenker's diverticulum. *Endosc Int Open* 2023; **11**: E607-E612 [*RCA*] [PMID: 37397859 DOI: 10.1055/a-2067-9105] [FullText] [Full Text(PDF)]

64 **Yewale R**, Daphale A, Gandhi A, Bapaye A. Prevention, detection and management of adverse events of third-space endoscopy. *Indian J Gastroenterol* 2024; **43**: 872-885 [*RCA*] [PMID: 39259447 DOI: 10.1007/s12664-024-01665-4] [FullText]

65 **Scheppach MW**, Mendel R, Muzalyova A, Rauber D, Probst A, Nagl S, Römmele C, Yip HC, Lau LHS, Gölder SK, Schmidt A, Kouladouros K, Abdelhafez M, Walter BM, Meinikheim M, Chiu PWY, Palm C, Messmann H, Ebigbo A. Use of artificial intelligence in submucosal vessel

detection during third-space endoscopy. *Endoscopy* 2025; **57**: 760-766 [*RCA*] [PMID: 39909396 DOI: 10.1055/a-2534-1164] [FullText]

66 **Ebigbo A**, Mendel R, Scheppach MW, Probst A, Shahidi N, Prinz F, Fleischmann C, Römmele C, Goelder SK, Braun G, Rauber D, Rueckert T, de Souza LA Jr, Papa J, Byrne M, Palm C, Messmann H. Vessel and tissue recognition during third-space endoscopy using a deep learning algorithm. *Gut* 2022; **71**: 2388-2390 [*RCA*] [PMID: 36109151 DOI: 10.1136/gutjnl-2021-326470] [FullText] [Full Text(PDF)]

67 **Schoon EJ**. Can artificial intelligence help to reduce intraprocedural bleedings during third-space endoscopy? *Endoscopy* 2025; **57**: 767-768 [*RCA*] [PMID: 40228536 DOI: 10.1055/a-2570-6331] [FullText]

68 **Takahashi K**, Sato H, Shimamura Y, Abe H, Shiwaku H, Shiota J, Sato C, Hamada K, Ominami M, Hata Y, Fukuda H, Ogawa R, Nakamura J, Tatsuta T, Ikebuchi Y, Yokomichi H, Terai S, Inoue H. Achalasia phenotypes and prediction of peroral endoscopic myotomy outcomes using machine learning. *Dig Endosc* 2024; **36**: 789-800 [*RCA*] [PMID: 37886891 DOI: 10.1111/den.14714] [FullText]

69 **Chiu PW**, Zhou S, Dong Z. A Look into the Future of Endoscopic Submucosal Dissection and Third Space Endoscopy: The Role for Robotics and Other Innovation. *Gastrointest Endosc Clin N Am* 2023; **33**: 197-212 [*RCA*] [PMID: 36375883 DOI: 10.1016/j.giec.2022.09.006] [Full Text]

70 **Atallah S**, Sanchez A, Bianchi E, Larach SW. Envisioning the future of colorectal surgery: preclinical assessment and detailed description of an endoluminal robotic system (ColubrisMX ELS). *Tech Coloproctol* 2021; **25**: 1199-1207 [*RCA*] [PMID: 34224035 DOI: 10.1007/s10151-021-02481-0] [FullText]

71 **Arezzo A**. Endoluminal robotics. *Surgery* 2024; **176**: 1542-1546 [*RCA*] [PMID: 39217055 DOI: 10.1016/j.surg.2024.07.050] [FullText]

72 **Lam TLN**, Chiu PWY. Current Applications of Flexible Endoluminal Robotics for Colorectal Endoscopic Submucosal Dissection. *Tech Innov Gastrointest Endosc* 2023; **25**: 88-94 [DOI: 10.1016/j.tige.2022.10.005] [FullText]

73 **Moura DTH**, Aihara H, Thompson CC. Robotic-assisted surgical endoscopy: a new era for endoluminal therapies. *VideoGIE* 2019; **4**: 399-402 [*RCA*] [PMID: 31517160 DOI: 10.1016/j.vgie.2019.04.014] [FullText] [Full Text(PDF)]

74 **Asian Institute of Gastroenterology**, India. Endoscopic Submucosal Dissection (ESD)- Master Slave Robotic System - Human Study (ESD). [accessed 2025 Aug 8]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine. Available from: https://clinicaltrials.gov/study/NCT01394861 ClinicalTrials.gov Identifier: NCT01394861

75 **King's College Hospital NHS Trust**. Image-Enhanced Endoscopy in the Gastrointestinal TractImperial College London (2024) Eye Gaze Technology for Endoscopic Inspection of the Gastrointestinal Tract. [accessed 2025 Aug 8]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine. Available from: https://www.clinicaltrials.gov/study/NCT04085211 ClinicalTrials.gov Identifier: NCT04085211

76 **Holmstrom AL**, Campagna RAJ, Cirera A, Carlson DA, Pandolfino JE, Teitelbaum EN, Hungness ES. Intraoperative use of FLIP is associated with clinical success following POEM for achalasia. *Surg Endosc* 2021; **35**: 3090-3096 [*RCA*] [PMID: 32632483 DOI: 10.1007/s00464-020-07739-6] [FullText]

77 **Farooq A**, Bani Fawwaz B, Zhang Y, Hasan MK, Mian A, Khan H, Brar TS, Singh S, Viana A, Hayat M, Xiao Y, Aljohani W, Abbasi A, Chandan S, Pathak S, Kadkhodayan K, Arain MA, Cosgrove N, Jain D, Inayat I, Yang D. Prospective analysis of endoscopic measurement of pyloric impedance planimetry and its association with clinical outcomes of gastric peroral endoscopic myotomy. *Endoscopy* 2025; **57**: 1197-1205 [*RCA*] [PMID: 40404137 DOI: 10.1055/a-2619-4638] [FullText]

78 **Patil G**, Dalal A, Maydeo AP. Feasibility of Speedboat RS2 with bipolar radiofrequency energy for peroral endoscopic myotomy in patients with achalasia (with video). *Endosc Int Open* 2020; **8**: E998-E1001 [*RCA*] [PMID: 32743048 DOI: 10.1055/a-1165-0087] [FullText] [Full Text (PDF)]

79 **Roser D**, Nagl S, Ebigbo A. Navigating the learning landscape: Comprehensive training in third space endoscopy - training, techniques, and practical recommendations. *Best Pract Res Clin Gastroenterol* 2024; **71**: 101918 [*RCA*] [PMID: 39209422 DOI: 10.1016/j.bpg.2024.101918] [FullText]

80 **Wei MT**, Friedland S, Hwang JH. The Current Landscape of Endoscopic Submucosal Training in the United States. *Curr Gastroenterol Rep* 2025; **27**: 4 [*RCA*] [PMID: 39509015 DOI: 10.1007/s11894-024-00950-8] [FullText]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com

© 2025 Baishideng Publishing Group Inc. All rights reserved.