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EDITORIAL

Gastroesophageal reflux after per-oral endoscopic myotomy: Management literature

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Abstract

In this editorial, we respond to a review article by Nabi *et al*, in which the authors discussed gastroesophageal reflux (GER) following peroral endoscopic myotomy (POEM). POEM is presently the primary therapeutic option for achalasia, which is both safe and effective. A few adverse effects were documented after POEM, including GER. The diagnostic criteria were not clear enough because approximately 60% of patients have a long acid exposure time, while only 10% experience reflux symptoms. Multiple predictors of high disease incidence have been identified, including old age, female sex, obesity, and a baseline lower esophageal sphincter pressure of less than 45 mmHg. Some technical steps during the procedure, such as a lengthy or full-thickness myotomy, may further enhance the risk. Proton pump inhibitors are currently the first line of treatment. Emerging voices are increasingly advocating for the routine combining of POEM with an endoscopic fundoplication method, such as peroral endoscopic fundoplication or transoral incisionless fundoplication. However, more research is necessary to determine the safety and effectiveness of these procedures in the long term for patients who have undergone them.

Key Words: Achalasia; Per-oral endoscopic myotomy; Gastroesophageal reflux disease; Transoral incisionless fundoplication; Peroral endoscopic fundoplication

Core Tip: In this editorial, we discuss the current objective measures for diagnosing gastroesophageal reflux (GER) after peroral endoscopic myotomy (POEM). We also review the factors that contribute to this adverse event, including patient and technique-related characteristics. Furthermore, we provide a list of all published studies on the various treatment options available for post-POEM GER, such as proton pump inhibitors, peroral endoscopic fundoplication, and transoral incisionless fundoplication.

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INTRODUCTION

Achalasia is a disorder of esophageal motility. Its defining characteristics are the lower esophageal sphincter's (LES) ineffective relaxation and the absence of esophageal peristalsis[1]. Peroral endoscopic myotomy (POEM) is considered the gold standard for managing achalasia[2]. After being introduced 16 years ago, we gained a better understanding of the procedure, its long-term sequence, and its outcomes[3]. Despite the high safety profile of POEM procedures done by third-space endoscopy experts, adverse events (AEs) are still reported. One of the notable AEs after POEM is gastroesophageal reflux (GER)[4]. In a meta-analysis, Repici *et al*[5] found that the incidence of GER was significantly higher following POEM than laparoscopic Heller myotomy. In this editorial, we briefly discuss the predictors of post-POEM GER and the different diagnostic and therapeutic strategies.

THE TRUTH ABOUT GERD

The Lyon consensus in 2018 determined that clinical history, questionnaire data, and response to antisecretory medication are inadequate on their own to definitively diagnose GER disease (GERD)[6]. A definitive diagnosis could be made based on the findings of objective tests. Endoscopic findings include grade C and D erosive esophagitis according to Los Angeles classification (LA), a long segment of Barret's esophagus, or strictures. At the same time, an acid exposure time (AET) of > 6% is considered diagnostic along with the subjective methods. The consensus did not include recommendations for diagnosing post-POEM GER, despite multiple studies indicating a high prevalence of GER after POEM, with rates as high as 60% in some instances[1,7,8]. Further clarification is needed regarding the term GER when describing the sequelae in patients who have undergone POEM. Several post-POEM investigations characterize GER as having a DeMeester score over 14.7 or an esophageal pH below 4 for over 5% of the observation period, similar to diagnosing GER unrelated to POEM[1,9]. According to objective testing using 24-h pH monitoring, almost 50% of those individuals have a high AET[10]. Despite the high incidence rate, only 10% of patients are symptomatic[9]. In those patients, a high AET can be attributed to either real GER, characterized by an acute decrease in pH below 3 with sluggish clearance during pH monitoring, or to fermentation of residual food due to long-standing achalasia, resulting in a gradual reduction in pH usually above 3.7[11]. Diagnosis of GER using pH monitoring should be postponed for more than 1 mo following POEM to prevent inaccurate results due to mucosal edema and damage[10].

PRECARIOUS PREDICTORS

Predicting GER after POEM has been challenging due to the lack of a standardized diagnostic approach, making it difficult to rely on previous data. In 2021, a meta-analysis was conducted by Mota *et al*[12] on the published studies in the literature discussing the risk factors for predicting the occurrence of GER after POEM. The study found that full-thickness myotomy, using a posterior myotomy approach, endoscopic findings, pH monitoring, and symptoms were more commonly associated with GER. The authors recommended using circular and anterior myotomy to minimize the risk of post-POEM GER. A study conducted by Wang *et al*[13] investigated the incidence of GERD in individuals who had undergone POEM. The diagnosis of GERD was made based on abnormal acid exposure along with symptoms and/or esophagitis. The study reported that patients who received a full-thickness myotomy had a higher likelihood of developing GERD after POEM (37.5%) in comparison to those who underwent a selective myotomy (12.5%). However, in another retrospective comparison study of 234 patients who underwent POEM, there was no significant difference in the incidence of GER between the full-thickness and circular myotomy groups[14]. Other reported risk factors for post-POEM GER include baseline LES pressure below 45 mmHg, obesity, female sex, and age over 65 years[1,7,15].

IS PREVENTION BETTER THAN CURE?

The risk of post-POEM GER could be minimized during the procedure by some measures, including performing a short esophageal myotomy[10]. In surgical myotomy procedures, myotomies shorter than 1 cm can reduce the occurrence of GER, while myotomies longer than 2 cm have been shown to be more effective in relieving the symptoms of achalasia [16]. A recent meta-analysis found that for patients who underwent POEM, the safety and effectiveness of short esophageal myotomy (ranging from 2.76 cm to 5 cm) was comparable to that of standard esophageal myotomy. Additionally, the incidence rates of GER were similar in both groups; however, patients who received short myotomy treatment had a lower risk of developing erosive esophagitis[17]. One method to determine the least effective length for endoscopic myotomy is the double-scope technique, first introduced for POEM in 2016[18]. However, Grimes *et al*[19] conducted a randomized controlled trial involving 100 patients, divided into two groups: Those who underwent a (2.6 cm) myotomy with a single scope and those who underwent a longer myotomy (3.2 cm) with double scopes. The double-scope group exhibited a greater incidence of moderate esophagitis LA grade B. Another reported measure was preserving gastric sling muscle fibers during the procedure, as Shiwaku *et al*[20] demonstrated that it could be a safe way to reduce the incidence of post-POEM GER with a 90% success rate. The two-vessel penetrating sign was initially proposed in 2018 by Tanaka *et al*[21], it could serve as a useful indicator for identifying the myotomy's endpoint.

Multiple studies have discussed the treatment strategies for post-POEM GER (Table 1). In a consensus, Inoue *et al*[22] reported that proton pump inhibitors (PPIs) are the first line for treating post-POEM GER. The role of PPIs in patients who underwent POEM is a bit controversial since most cases with high AET are asymptomatic[22]. According to studies, the majority of patients who experienced symptoms of GER after POEM were effectively treated with PPIs, and the response was confirmed using objective tests[23,24]. Although numerous algorithms have been suggested for treating post-POEM GERD, Maydeo and Patil[10] presented the most comprehensive algorithm (Figure 1).

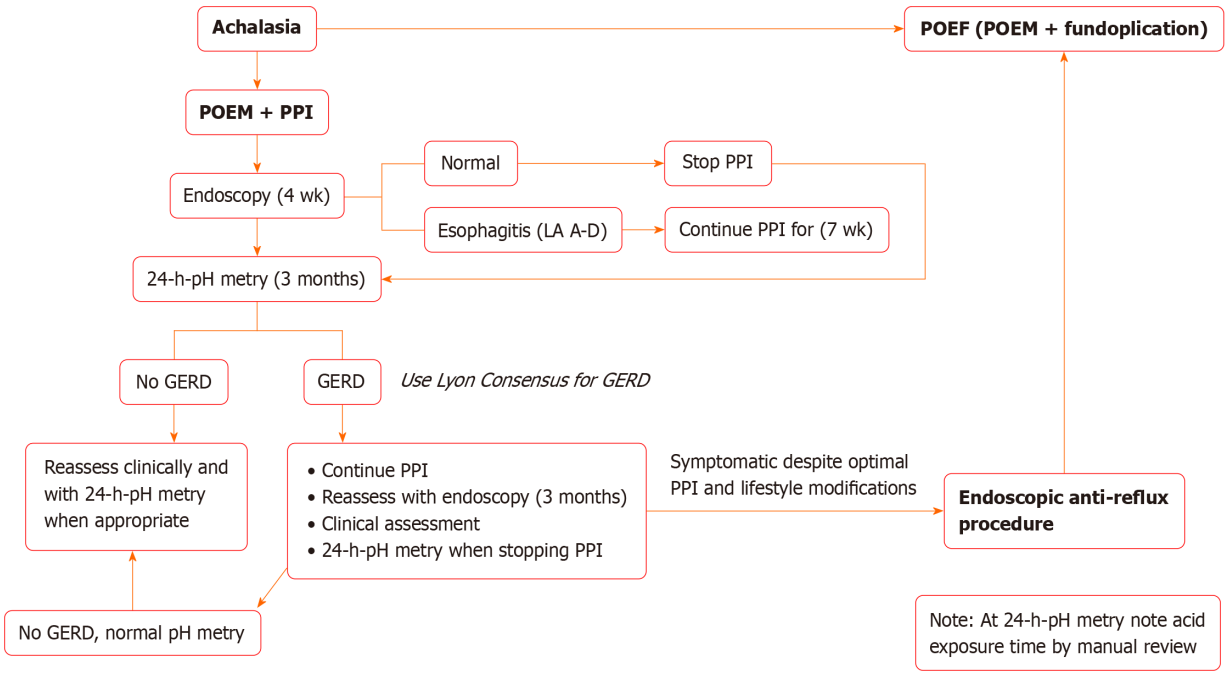

Figure 1 Algorithm of management of post-peroral endoscopic myotomy gastroesophageal reflux. The algorithm originally presented by Maydeo and Patil[10] to manage post-peroral endoscopic myotomy (POEM) gastroesophageal reflux. However, we added the option of initial fundoplication with POEM to the algorithm. EGD: Esophagogastroduodenoscopy; GERD: Gastroesophageal reflux disease; LA: Los Angeles; POEF: Peroral endoscopic fundoplication; PPI: Proton pump inhibitor.

There is a debate surrounding the incorporation of endoscopic fundoplication as a standard procedure alongside POEM. Multiple fundoplication approaches are being examined, either separate from POEM, such as transoral incisionless fundoplication (TIF)[25], or in combination with POEM, such as POEM with fundoplication (POEM + F)[26]. TIF is a therapeutic endoscopic approach used to treat chronic GERD patients[27]. Since its introduction in 2006[28], several studies have confirmed the viability of performing TIF following POEM[25,29-31]. Although most of these studies involved small groups, they demonstrated a safe and effective procedure that led to patients discontinuing the use of PPIs and resolving esophagitis.

The alternative fundoplication option is POEM + F. Inoue *et al*[26] introduced a novel endoscopic fundoplication to reduce post-POEM GER. The authors documented a reduction in the incidence of reflux symptoms with an intact wrap at 1-mofollow-up after the procedure. In a single-center study, 25 patients underwent POEM + F, in which 23 patients (92%) had a technically successful procedure. Follow-up endoscopy showed that 19 patients (82.6%) had an intact wrap, whereas only 3 patients (12%) experienced delayed complications due to endoloop or endoclip erosion of the mucosa,

Table 1 Studies reporting different treatment modalities for post-peroral endoscopic myotomy gastroesophageal reflux

Ref.	*n*	Treatment	Follow-up GER assessment method	Results and conclusion
Inoue *et al*[26], 2019	21	POEM + F	Not assessed	Technical success: 100%. Maintaining wrap at 2 mo: 95%. AE: 0%
Shrigiriwar *et al* [33], 2023	6	POEM + F + PPI	GERD-HRQL; RSI	Technical success: 100%. AE: 0%. GERD-HRQL score: 2.3 ± 3.7. RSI Score: 2.2 ± 2.5
Patil *et al*[35], 2021	20	POEM + F + PPI	24 h pHmetry; endoscopy	Technical success: 85%. Subcutaneous emphysema: 47%. Capnothorax: 17%. At 1 mo follow-up grade B esophagitis: 23.5%. At 3 mo pHmetry: High AET in those with loosening of wrap 100%. At 3 mo pHmetry: Normal AET in those who maintained wrap 100%. Maintaining wrap at 3 mo: 58.8%. Patient off PPI after 3 mo: 58.8%
Toshimori *et al* [36], 2020	1	POEF for refractory GERD with erosive esophagitis after POEM	Endoscopy	Technical success without notable AE with maintaining the wrap at a 10-mo follow-up endoscopy. Improved symptoms. No erosive esophagitis
Maydeo *et al*[37], 2023	30	EFTP	GERDQ; endoscopy. 24 pHmetry	Maintaining flap at 3 mo: 89.6%. AE: 13.8% "mild symptoms". Symptoms resolution and PPI stoppage after 6 mo: 72.4%. Improvement (> 50% from baseline) in AET: 96.6%. GERDQ improvement by > 50% at 6 mo: 55.2%
Bapaye *et al*[32], 2021	25	POEM + F	GERDQ; endoscopy; 24 pHmetry	Technical success: 92%. Maintaining wrap at 12 mo: 82.6%. AE: 12%. Abnormal AET at 2 mo: 11.1%. Erosive esophagitis at 2 mo: 18.2%
Ayoub *et al*[38], 2024	4	TIF + PPI	GERD-HRQL	75% of patients achieved either dose reduction or discontinuation of PPI. Pre-TIF GERD-HRQL: 20 ± 18.5. Post-TIF GERD-HRQL: 3.75 ± 6.2
Hoerter *et al*[39], 2022	1	TIF	Endoscopy	Technical success without notable AE. Absence of esophagitis at a 9-mo follow-up endoscopy
Kumta *et al*[40], 2015	1	TIF	Not assessed	Technical success without notable AE
DeWitt *et al*[41], 2024	17	TIF, cTIF	GERD-HRQL; endoscopy; 24 pHmetry	At 9 mo follow-up: Stopped PPI: 80%. Pre-TIF esophagitis: 88%. Post-TIF esophagitis: 50%. Pre-TIF total time reflux episode: 90.5 ± 46.9. Post-TIF total time reflux episode: 49.3 ± 32.3
Tyberg *et al*[25], 2018	5	PPI + TIF	Endoscopy	Technical success: 100%. Complete resolution of symptoms: 100%
Shiwaku *et al*[15], 2022	1886	PPI	Endoscopy	Complete resolution of symptoms: 100% at 5-yr follow up
Nabi *et al*[42], 2020	167	PPI	Endoscopy	Complete resolution of esophagitis: 81.4%
Brewer Gutierrez *et al*[43], 2020	67	PPI	Endoscopy; pHmetry	At 48 mo follow-up erosive esophagitis: 16%. 47.5 % had AET despite being on PPI

AE: Adverse event; AET: Acid exposure time; cTIF: Combined laparoscopic hernia repair and transoral incisionless fundoplication; EFTP: Endoscopic full-thickness plication GER: Gastroesophageal reflux; GERD: Gastroesophageal reflux disease; GERD-HRQL: Gastroesophageal reflux disease Health-Related Quality of Life; GERDQ: Gastroesophageal reflux disease questionnaire; POEF: Peroral endoscopic fundoplication; POEM: Peroral endoscopic myotomy; PPI: Proton pump inhibitor; RSI: Reflux symptom index; TIF: Transoral incisionless fundoplication.

which resolved spontaneously. Only 2 patients (11%) in this group developed GER after POEM[32]. In the United States, Shrigiriwar *et al*[33] conducted the first United States study with 6 patients and achieved a technical success rate of 100%. However, they did encounter some technical difficulties that need to be addressed in future research. These included the off-label use of endoscopic accessories in POEM + F and the need for surgical anatomy awareness before performing such a procedure.

In the Nabi *et al*[34] review article titled "Prediction, prevention, and management of gastroesophageal reflux after per-oral endoscopic myotomy: An update" and published in the *World Journal of Gastroenterology*, the authors provided a well-organized, comprehensive review of post-POEM GER in terms of risk factors, diagnosis, prevention, and management. They provided an algorithm for the evaluation and management of post-POEM GER. Also, they summarized the conclusions of the published papers with a simple and clear figure of the current understanding of post-POEM GER.

CONCLUSION

In our opinion, the diagnosis of GER after POEM should be determined using both objective and subjective approaches. Questionnaires and other subjective approaches for diagnosing GER can be used in conjunction with objective procedures

or to evaluate the quality of life of individuals suspected of having post-POEM GER. It has been reported that nearly 60% of patients undergoing POEM may experience AET. Therefore, performing pHmetry, especially in symptomatic patients, can prove to be helpful in assessing the need for an endoscopic anti-reflux procedure. However, delaying this testing for at least 1 mo after the POEM procedure is important to avoid inaccurate results due to mucosal edema and damage. Existing data on myotomy techniques indicate certain techniques that decrease the risk of developing GER. However, these data were inconclusive. Therefore, when performing the POEM procedure, the choice of myotomy technique should not be influenced by concerns about the development of post-POEM GER. Instead, the decision should be based on the specific circumstances of the procedure, such as the difficulty level, the complexity of using the double-scope technique, and the experience and preference of the endoscopist. However, a trial should be conducted to minimize the length of the myotomy and lower the risk of prolonged post-POEM erosive esophagitis. The first line of management for patients at risk of developing GER should always be PPIs, which are effective in treating esophagitis in most patients. POEM + F is promising yet in the early stages of development. However, this procedure needs the endoscopist to have a surgical background or be an expert in POEM and third-space endoscopic procedures, with a proficient surgical team available as a backup. Long-term studies are necessary to validate the substantial risk associated with the procedure and the long-term efficacy. In addition, accessories manufacturing companies should collaborate with endoscopists to design necessary accessories to prevent off-label use of items such as endoloop, which may lead to various risks such as tool change delays and losing position during the procedure.

FOOTNOTES

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