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## EDITORIAL

- 3456 Effective roles of exercise and diet adherence in non-alcoholic fatty liver disease  
*Zhu W*
- 3461 Gastroesophageal reflux following peroral endoscopic myotomy for achalasia: Bumps in the road to success  
*Itskoviz D, Malnick SDH*

## ORIGINAL ARTICLE

## Observational Study

- 3465 Diagnostic delay in inflammatory bowel diseases in a German population  
*Blüthner E, Dehe A, Büning C, Siegmund B, Prager M, Maul J, Krannich A, Preiß J, Wiedenmann B, Rieder F, Khedraki R, Tacke F, Sturm A, Schirbel A*
- 3479 Prevalence of *Helicobacter pylori* infection among patients with esophageal carcinoma  
*López-Gómez M, Morales M, Fuerte R, Muñoz M, Delgado-López PD, Gómez-Cerezo JF, Casado E*

## Basic Study

- 3488 Leech *Poecilobdella manillensis* protein extract ameliorated hyperuricemia by restoring gut microbiota dysregulation and affecting serum metabolites  
*Liu X, Liang XQ, Lu TC, Feng Z, Zhang M, Liao NQ, Zhang FL, Wang B, Wang LS*
- 3511 *Calculus bovis* inhibits M2 tumor-associated macrophage polarization via Wnt/ $\beta$ -catenin pathway modulation to suppress liver cancer  
*Huang Z, Meng FY, Lu LZ, Guo QQ, Lv CJ, Tan NH, Deng Z, Chen JY, Zhang ZS, Zou B, Long HP, Zhou Q, Tian S, Mei S, Tian XF*

## LETTER TO THE EDITOR

- 3534 Defining failure of endoluminal biliary drainage in the era of endoscopic ultrasound and lumen apposing metal stents  
*Ali FS, Guha S*
- 3538 Evaluating the role of large language models in inflammatory bowel disease patient information  
*Gong EJ, Bang CS*

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## Gastroesophageal reflux following peroral endoscopic myotomy for achalasia: Bumps in the road to success

David Itskoviz, Stephen David Howard Malnick

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### Abstract

Achalasia can significantly impair the quality of life. The clinical presentation typically includes dysphagia to both solids and liquids, chest pain, and regurgitation. Diagnosis can be delayed in patients with atypical presentations, and they might receive a wrong diagnosis, such as gastroesophageal reflux disease (GERD), owing to overlapping symptoms of both disorders. Although the cause of achalasia is poorly understood, its impact on the motility of the esophagus and gastroesophageal junction is well established. Several treatment modalities have been utilized, with the most common being surgical Heller myotomy with concomitant fundoplication and pneumatic balloon dilatation. Recently, peroral endoscopic myotomy (POEM) has gained popularity as an effective treatment for achalasia, despite a relatively high incidence of GERD occurring after treatment compared to other modalities. The magnitude of post-POEM GERD depends on its definition and is influenced by patient and procedure-related factors. The long-term sequelae of post-POEM GERD are yet to be determined, but it appears to have a benign course and is usually manageable with clinically available modalities. Identifying risk factors for post-POEM GERD and modifying the POEM procedure in selected patients may improve the overall success of this technique.

**Key Words:** Achalasia; Per-oral endoscopic myotomy; Gastroesophageal reflux; Pneumatic dilatation; Heller myotomy; Proton pump inhibitor; Acidic fermentation

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**Core Tip:** Peroral endoscopic myotomy (POEM) is a valuable treatment for achalasia, although the occurrence of gastroesophageal reflux disease (GERD) following this procedure is a major concern among patients and caregivers. In this editorial, we will address the true meaning of acidic reflux after POEM, discuss the factors that need to be taken into account to prevent post-POEM GERD, and outline the treatment options available when it occurs.

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## INTRODUCTION

Achalasia is a rare esophageal motility disorder, with a reported incidence of approximately 1 per 100000 persons per year. The clinical presentation typically includes dysphagia to both solids and liquids, chest pain, and regurgitation. Diagnosis may also be delayed or mistaken as gastroesophageal reflux disease (GERD) owing to atypical presentations or overlapping symptoms.

## DIAGNOSIS AND TREATMENT

The etiology of achalasia is still unknown, but the pathophysiology is characterized by impaired lower esophageal sphincter relaxation with concomitant peristalsis dysfunction in the esophageal smooth muscles. The diagnosis involves careful consideration of the clinical scenario, together with the results of esophagogastroduodenoscopy, contrast esophagogram, and high-resolution manometry (HRM). The gold standard for diagnosing achalasia is HRM, as it allows an objective and reproducible measurement of dynamic esophageal pressure over time and space. This technique also enables the subcategorization of patients with achalasia into different subtypes according to the Chicago Classification 4.0.

Functional lumen imaging probe (FLIP or endoFLIP) is a high-resolution impedance system that measures esophageal distensibility and has a good correlation with HRM. FLIP is performed during sedated esophagogastroduodenoscopy. It has the advantage of aiding diagnosis in patients intolerant of HRM and providing immediate feedback on the effectiveness of treatment.

Treatment goals for achalasia center on the main pathophysiological issue: impaired relaxation of the lower esophageal sphincter. Pharmacological treatment options have proven to be ineffective, except for endoscopic botulinum toxin injections at the lower esophageal sphincter, which have only short-lived effectiveness. The classic treatment for achalasia has been either pneumatic dilatation of the esophagus or Heller myotomy performed surgically, usually with concomitant creation of a gastric fundoplication[1-4].

In 2010, Inoue and Kudo[5] published their experience with 43 achalasia patients treated with peroral endoscopic myotomy (POEM). Since then, this approach has gained popularity as a treatment modality for achalasia patients. POEM is performed under endoscopic guidance by creating a submucosal tunnel in the esophagus and stomach cardia and selectively dissecting the muscle fibers in that tunnel. While POEM is considered an effective and safe procedure, the development of post-POEM GERD remains a challenge. In surgical myotomy, the anti-reflux mechanism is partially restored by creating a fundoplication, but this is not the case in the classical POEM procedure.

## POST-POEM GERD

Nabi *et al*[1] have comprehensively reviewed the clinical significance and approach to post-POEM GERD. The first question addressed is how to define post-POEM GERD. Should we rely on patient-reported symptoms, objectively look for esophagitis and measure esophageal exposure to acid, or perhaps combine all of the above outcomes?

A significant number of post-POEM patients show evidence of esophageal acid exposure, but most remain asymptomatic. Moreover, even in patients with proven esophageal acid exposure, the incidence of severe esophagitis is relatively low[6,7]. Dewitt *et al*[8] recently described a cohort of 149 patients who underwent POEM and were followed up after at least 6 months with pH-metry. They found that a positive reflux symptom association was as low as 17.1%-20.9% in symptomatic patients. Karyampudi *et al*[9] compared 50 patients with post-POEM GERD to those with non-achalasia-related GERD and found a positive reflux symptom association in only 6% of post-POEM GERD patients compared to 56% in the control group. It is also important to note that the documentation of an acidic environment in the post-POEM esophagus can be related to acidic fermentation secondary to motility disturbances and food stasis and not to actual acid reflux from the stomach. The incidence of actual acid reflux is significantly less evident when we examine the acid exposure pattern in these patients[10,11].

The second question that arises is regarding the clinical significance of post-POEM GERD besides the patients' symptoms. Given that POEM is a relatively new procedure, the available data are limited, and yet, it appears that the development of GERD-related complications, such as Barrett's esophagus and peptic strictures, is infrequent. It is estimated that even these uncommon complications can be avoided with readily available drugs such as proton pump inhibitors and, possibly, potassium-competitive acid blockers[6,12].

Shiwaku *et al*[13] found a 7.5% incidence of severe reflux esophagitis in a cohort of 2905 patients who underwent POEM. They found an association between the development of severe reflux esophagitis and older age (> 65 years), previous achalasia treatments, an Eckardt score  $\geq 7$ , sigmoid-type achalasia, and long (> 10 cm) myotomy. Another retrospective study involving 183 post-POEM patients reported an incidence of severe GERD in 19.5% of patients[14]. A recent systematic review and meta-analysis of 11 studies, including 2342 post-POEM patients with a median follow-up of 48 months, reported only 3 cases of significant reflux-related consequences, such as Barrett's esophagus and peptic stricture[15].

The third question is whether we can predict which patients are prone to develop post-POEM GERD, and, if so, whether we can offer them any preventive measures. Nabi *et al*[1] address several risk factors in their review, such as obesity, female sex, and the presence of a hiatal hernia. In addition, they discuss several technical aspects of the procedure that might mitigate the risk of post-POEM GERD, such as limiting the length of the gastric myotomy, preserving the sling fibers during myotomy, and even combining the creation of a gastric fundoplication during the POEM procedure *via* the natural orifice transluminal endoscopic surgery approach, which appears to be safe and effective in experienced hands, although its generalizability is yet to be determined[16-18].

The fourth and last question is how easily we can treat patients with post-POEM GERD. It appears that the primary treatment regimen is similar to that for any other GERD patients, involving proton pump inhibitors. This well-known class of drugs seems to work well in post-POEM GERD patients. Other more instrumental methods to treat GERD are also effective and available. A recent review of eight studies including 3568 patients found that treatment using proton pump inhibitors is effective and leads to complete resolution of symptoms in most post-POEM patients dealing with GERD[19].

## CONCLUSION

POEM is an effective treatment for achalasia patients, but GERD remains an important side effect of this procedure. Defining the true incidence and impact of GERD in post-POEM patients can be challenging. However, by identifying specific risk factors in our patients and refining the POEM procedure accordingly, we can make the road to success in treating achalasia a little smoother.

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