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Gastro esophageal reflux following peroral endoscopic myotomy for Achalasia:
Bumps in the road to success

Post POEM GERD

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Abstract
Achalasia can significantly impair quality of life. The clinical presentation is usually with dysphagia to both solids and liquids, chest pain and regurgitation. Diagnosis can be delayed in patients with atypical presentations and patients might receive a wrong diagnosis such as gastro-esophageal reflux disease (GERD) since symptoms of both disorders might overlap. Although the cause of achalasia is poorly understood, the motility effect on the esophagus and gastro-esophageal junction is well defined. Several treatment modalities have been utilized but the most common are the surgical Heller myotomy with concomitant fundoplication and the pneumatic balloon dilatation. Recently, peroral endoscopic myotomy (POEM) has gained popularity as an effective treatment for achalasia, although the rate of GERD occurring post treatment is high relatively to the former treatment modalities. The magnitude of post POEM GERD depends on the very definition of GERD and is related to several patient and procedure factors. The long term sequelae of post POEM GERD is yet to be determined but it appears to have a benign course and is usually manageable by clinically available modalities. Identification of risk factors for post-POEM GERD and modifying the POEM procedure in 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

Core Tip: Peroral endoscopic myotomy (POEM) is a valuable tool in treatment of achalasia, although the occurrence of gastroesophageal reflux disease (GERD) following this procedure is a major concern among patients and care-givers. In this editorial we will address the true meaning of acidic reflux post POEM and will point the factors to be taken into account in order to prevent post POEM GERD occurrence and how to treat it when it occurs.
INTRODUCTION

Achalasia is a rare esophageal motility disorder with a reported incidence of ~1 per 100,000 persons per year. The clinical presentation is usually with dysphagia to both solids and liquids, chest pain and regurgitation. Diagnosis can also be delayed or GERD diagnosed in error due to atypical presentations or overlap of symptoms.

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.

Diagnosis of achalasia results form a careful consideration of the clinical scenario, together with the results of esophago-gastro-duodenoscopy (EGD), contrast esophagogram and high-resolution manometry (HRM). The gold standard for diagnosing achalasia is HRM which allows an objective and reproducible measurement of dynamic esophageal pressure over time and space which also enables the subcategorization of patients with achalasia to 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 EGD. 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 disturbance - impaired relaxation of the lower esophageal sphincter. Pharmacological treatment options ineffective except for endoscopic guided botulinum toxin injection at the lower esophageal sphincter which has short-lived effectiveness. The classic treatment has been either pneumatic dilatation of the esophagus or Heller myotomy performed surgically, usually with concomitant creation of a gastric fundoplication. [4-1]

In 2010, Professor Haruhiro Inoue[5] published his experience with 43 achalasia patients treated with peroral endoscopic myotomy (POEM). Since then, this treatment
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 by selectively dissecting the muscle fibers in that tunnel. While POEM is considered an effective and safe procedure, the development of post POEM gastro esophageal reflux disease remains a challenge. In the surgically based myotomy, the anti-reflux mechanism is partially restored by creating a fundoplication, but this is not the case in the classical POEM procedure.

In this issue of World Journal of Gastroenterology, Nabi Z et al[1] comprehensively review the clinical significance and approach to post POEM GERD. The first issue is how do we 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?

Apparently, a significant number of post-POEM patients will have evidence of esophageal acid exposure, but most will be asymptomatic. More so, even in patients with esophageal acid exposure, the incidence of severe esophagitis is relatively low[6,7]. Dewitt et al[8] described recently 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 (RSA) was as low as 17.1-20.9% in symptomatic patients. Karyampudi et al[9] compared 50 patients with post-POEM GERD with non-achalasia related GERD. They found a positive RSA in only 6% of post-POEM GERD patients compared with 56% in the control group. It is also important to note that documentation of acidic environment in post-POEM esophagus can be related to acidic fermentation of the esophagus secondary to motility disturbances and food stasis and not to real acid reflux from the stomach. The incidence of true acid reflux is significantly less evident when we drill down and look for the acid exposure pattern in these patients.[10,11]

The second question that comes to mind is what is the clinical significance of post POEM GERD besides the patients’ symptoms? Since we are dealing with a relatively new procedure, the available data is limited, and yet, it appears that development of GERD related complications, such as Barrett’s esophagus and peptic strictures, is
infrequent and it is estimated that we can avoid even these uncommon complications with a relatively available drugs such as proton pump inhibitors and possibly potassium-competitive acid blockers (P-CABs).[6,12]

Shiwaku et al.[13] found an incidence of 7.5% of severe reflux esophagitis among a cohort of 2905 patients who underwent POEM. They found an association between older age ( > 65 years), previous achalasia treatments, Eckardt score ≥ 7, sigmoid- type achalasia and long ( > 10cm) myotomy and the development of severe reflux esophagitis. Another retrospective study of 183 post POEM patients reported an incidence of severe GERD in 19.5% of patients[14]. 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, i.e Barrett’s esophagus and peptic stricture[15].

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

The fourth and last question is how easily can we treat patients with post POEM GERD? It appears that the primary treatment regimen is similar to any other GERD patients with proton pump inhibitors (PPI). This well-known class of drugs seem to work well in post POEM GERD patients. Other more instrumental methods to treat GERD are also effective and available. A recent review of 8 studies including 3568 patients found that PPI treatment is effective and leads to complete resolution of symptoms in most of 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 might be complicated in post POEM patients, and yet, by taking specific actions such as looking for the risk factors in our patients and by refining the POEM procedure in these patients, we might make the road to success in treating achalasia a little smoother.