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Reflux after peroral endoscopic myotomy: The dilemma and the options

Management of post POEM Reflux

priya hazrah

Abstract

Per oral endoscopic myotomy (POEM) is rapidly emerging as the treatment of choice for achalasia cardia, but its success is marred by problematic reflux. Although symptomatic reflux rates are low and often comparable to that after laparoscopic Hellers myotomy (LHM), a high incidence of pathologic reflux has been noted after POEM. This poses a dilemma as to what is true reflux, and in determining the indications and optimal endpoints for managing post-POEM reflux. The two pertinent reasons for the difference in reflux rates between LHM and POEM are the variation in length and location of myotomy and the absence of an anti-reflux procedure in POEM. Proton pump inhibitor (PPI) remains the most sought-after treatment of POEM derived reflux. Nevertheless, modifications in the procedural technique of POEM and the addition of endoscopic fundoplication can probably emerge as a game changer. This article briefly reviews the incidence, causes, controversies, predictive factors and management strategies related to post-POEM reflux.

Key Words: Achalasia, Per-oral endoscopic myotomy, Laparoscopic Heller myotomy, Transoral incisionless fundoplication, Gastroesophageal reflux disease, Pathologic reflux, Proton pump inhibitor, Endoscopic fundoplication, EndoFLIP tailored myotomy, Sling-fiber preserving myotomy .

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Core Tip: The incidence of symptomatic gastroesophageal reflux disease differs from that of pathologic reflux, as observed in endoscopy and pH studies after peroral endoscopic myotomy (POEM). Pathologic reflux is more common after POEM than laparoscopic Hellers Myotomy. It is attributed to difference in the technique used or because an anti-reflux procedure is not routinely added to POEM. Post-POEM reflux

can be managed with proton pump inhibitors or surgically with new emerging operative techniques.

INTRODUCTION

Peroral endoscopic myotomy (POEM), a scarless approach to the treatment of achalasia, is rapidly emerging as an effective alternative to laparoscopic Heller myotomy (LHM). Gastroesophageal reflux disease (GERD), an important concern after POEM[1] depends upon its definition as well as patient and procedure-related factors. Recent metanalyses have reported equivalent or better dysphagia relief with POEM when compared with LHM[2,3]. POEM achieves dysphagia relief to the tune of 90% at 2–3 years and > 80%–90% at 5 years[4,5]. However, a high incidence of pathologic reflux is noted after POEM than after LHM, the cause of which remains a dilemma[1,2,3]. The routine addition of anti-reflux procedures to LHM is one of the reasons for comparatively lower reflux rates. However, other factors may also be responsible, particularly the location and extent of myotomy in POEM. In this article we reflect upon the issue of reflux after POEM, its incidence, the discrepancy between symptomatic and pathologic reflux, the possible causes and highlight the novel techniques being investigated to tackle the issue.

MAIN TEXT

REFLUX AFTER POEM INCIDENCE AND CONCERNS.

Incidence:

Reflux after POEM can be erosive or non-erosive and is assessed subjectively based on symptom grading, quality of life (QOL) studies, proton pump inhibitor (PPI) requirement or more objectively with grades of esophagitis on endoscopy, pH measurement studies, high resolution manometry and impedance planimetry. Post-POEM reflux has been reported to be in the ranges of 9%–43%, 13–68%, and 38%–57% for symptomatic GERD, reflux esophagitis, and positive pH studies respectively[4]. Erosive esophagitis is more common after POEM than after LHM[2].

Symptomatic vs pathologic reflux, what is true reflux?

It is important to note that the incidence of symptomatic reflux after POEM is much lower than that of pathologic reflux as inferred from endoscopic evaluation and pH manometry in most studies. Hence subjective QOL survey metrics do not often corroborate with endoscopic findings of esophagitis[4, 6-10]. The reason for the above discrepancy remains elusive. However, denervation or compromise of mucosal vascularity during tunnel creation and other pathological changes like aganglionosis or squamous metaplasia merits investigation. In addition, mucosal entry point ulcer in POEM has a propensity to be confused with erosive ulcer in early follow up[4]. Reflux after POEM is not only attributable to a lax lower esophageal sphincter (LES) but also to ineffective clearance of refluxate from the distal esophagus. Furthermore, fermentation of undigested food in the distal esophagus can result in erroneous pH findings which can confound the incidence of true reflux[1, 11, 12].

Temporal progression of reflux:

Erosive esophagitis with progression to Barrett's though rare, has been reported after POEM, thereby emphasizing the need for long-term follow-up post-POEM[6,13]. Some studies have observed a delayed onset of reflux esophagitis after POEM[14]. In contrast, reflux has been reported to decrease with time in other studies[4]. This highlights the need for prolonged surveillance after POEM.

The lack of adequate long-term results after POEM, limits conclusions on the temporal outcome of POEM with respect to dysphagia relief and reflux. Moreover, the inconsistency between subjective GERD symptomatology and objective GERD metrics raises concerns regarding the ideal methodology to investigate and treat POEM-derived reflux.

PREDICTIVE FACTORS OF REFLUX AFTER POEM:

It remains unclear as to what causes higher reflux after POEM. The proposed risk factors can be patient-centric variables or operation related factors.

Patient-centric variables for post-POEM GERD:

Several patient centric variables like advancing age, sex, high BMI (body mass index), alcohol use, low preoperative LES pressure (< 45mm) , high preoperative Eckardt score, long duration of symptoms, type of achalasia, sigmoid esophagus, prior therapy for achalasia (LHM/dilatation), high integrated relaxation pressure (IRP) have been suggested to variably correlate with post POEM reflux in individual studies[11,15-19]. On the contrary, parameters such as sex, age, BMI, type of achalasia, lower esophageal sphincter pressure and previous therapies have not been shown to be predictive of post-POEM GERD in other studies and metanalyses[20,21].

Operation-related predictive factors for post POEM reflux:

Full-thickness myotomy, length of gastric myotomy, length of esophageal myotomy, anterior location of myotomy, non-preservation of gastric sling fibers and blown-out myotomy have been proposed to predispose to reflux.

MYOTOMY AND REFLUX AFTER POEM, CAN MODIFICATION OF OPERATIVE TECHNIQUE REDUCE REFLUX?

The crux of achalasia treatment is a delicate balance between achieving a good dysphagia relief without causing significant reflux. One of the reasons for better dysphagia relief but increased reflux rates after POEM compared to LHM could be attributed to the longer length of myotomy practiced in POEM[2]. A longer myotomy may provide better relief of dysphagia but predispose to reflux. In contrast, a short myotomy can result in inadequate dysphagia relief. Furthermore, the location of myotomy is variable in POEM and is more constant in LHM. In a large-scale multicenter cohort from Japan, posterior myotomy, esophageal myotomy > 10 cm, and gastric myotomy > 2 cm were found to be independently associated with reflux

esophagitis[19]. However, in an earlier small-volume study, the same authors noted no POEM-related factors to be predictive of GERD and advocated extended gastric myotomy[22].

The following modifications during POEM procedure have been suggested to circumvent the problem of reflux.

Short gastric myotomy: The length of gastric myotomy has been proposed to influence reflux, with longer myotomy resulting in greater reflux. A < 2 cm gastric myotomy has been observed to significantly reduce reflux[4]. A study comparing short *vs* long gastric myotomies (> 2.5 cm) concluded that there were no differences in post-POEM reflux rates, but severe esophagitis was significantly lower in the short myotomy group[14]. A total myotomy length > 7 cm has also been shown to increase PPI requirement after POEM[23]. However, a retrospective trial found no difference in GERD using a 7 cm cut-off for total length of myotomy[24]. Another study evaluating short and long myotomy found no difference in dysphagia relief or GERD[25]. However, the authors classified a short myotomy as one with 8 cm length, which would qualify as a long myotomy in other studies. Moreover, the extent of gastric myotomy was not considered a criterion[25]. Another randomized study comparing short and long esophageal myotomies (≤ 3 cm *vs* ≥ 6 cm) found similar rates of dysphagia relief and GERD[26]. However, it is pertinent to note that the length of gastric myotomy was the same in both groups in the study[26]. A recent randomized trial evaluating short *vs* long myotomy based upon length of esophageal myotomy concluded that both procedures exhibited similar dysphagia relief and GERD rates[27]. Contrarily significant lower rates of GERD were noted in short esophageal myotomy (3-4 cm) group with constant gastric myotomy length[28]. Two systematic reviews and metaanalyses have documented equivalent dysphagia relief but lower pathologic reflux with shorter myotomies[29,30]. These conflicting results could be attributed to the variable extents of esophageal and gastric myotomies in most studies which confound comparisons.

Only circular muscle myotomy: Only circular muscle myotomy as opposed to a full thickness myotomy has been noted to decrease reflux[4,21,31].

Anterior or posterior myotomy? It needs to be emphasized that myotomy is always anterior in LHM but can be either anterior or posterior in POEM. Anterior myotomy has been proposed to reduce reflux in a metaanalysis which also corroborates with findings of a large multi-center trial suggesting posterior myotomy to be a factor linked to reflux[19,21]. The location of the angle of His at 8 '0' clock position may explain the higher GERD rates with posterior myotomy[21]. Conversely, according to the observations of two other systematic reviews and metaanalyses, the location of myotomy in POEM (anterior *vs* posterior) has not been shown to have any compelling effect on reflux rates[32,33].

Sling fiber preserving myotomy: Preservation of gastric sling fibers (sling fiber preserving POEM) appears to be promising in nascent studies[14,34]. Grade C esophagitis was observed in 44.1% of conventional POEM *vs* 18.5% of patients undergoing sling fiber preservation myotomy[34]. However, a recent randomized trial did not observe any benefit of sling fiber preservation in POEM with regard to esophagitis, acid exposure time, De Meester score, reflux symptoms and PPI use[35].

Intra-operative impedance planimetry (endoluminal functional luminal imaging probe -EndoFLIP) assisted myotomy: Intraoperative EndoFLIP can be used to tailor the length of the myotomy to a shorter extent and help predict reflux[10,23,36]. Distensibility index and a final cross-sectional area in intra-operative endoFLIP can predict the likelihood of esophagitis in postoperative esophagogastroduodenoscopy[10]. Due to variability of impedance finding amongst patients with achalasia a pre-post change in impedance planimetry rather than a single point intra-operative measurement is likely to be more useful[10].

MANAGEMENT OF POEM ASSOCIATED REFLUX.

The options for managing post POEM reflux include:

PPIs

Endoscopic fundoplication: Transoral incisionless fundoplication / peroral fundoplication

Laparoscopic fundoplication

Stretta, magnetic rings, electric stimulation.

PPIs:

PPIs have been the mainstay of management of pathologic reflux after POEM. Most cases of post-POEM GERD partially resolve with PPIs. Symptom resolution has been reported to occur in 66%-100% patients[6]. PPI therapy can also lead to the resolution of erosive GERD[37]. However, interventions may be needed in the event of escalation of GERD symptoms or complications and to mitigate long-term PPI use. Given the incongruence in rates of symptomatic and objective reflux, it remains to be determined whether PPI should be used for achieving only symptomatic relief or also for objective endpoints such as resolution of esophagitis and normalization of pH abnormalities. There is lack of clarity on the duration of PPI therapy and the incidence of recurrent symptoms after discontinuing medical therapy. PPI-refractory GERD is another issue that needs to be addressed. PPI-refractory post-POEM GERD was noted in 6.8% of patients in a study and was proposed to be related to CYP2C19 variability. Exploration of the use of PPIs less affected by CYP2C19 pharmacogenetics such as rabeprazole in the scenario, or opting for fundoplication was suggested[6,38].

Endoscopic fundoplication:

Currently the lower incidence of reflux after LHM as opposed to that after POEM is mostly attributed to the routine addition of an anti-reflux procedure to LHM. Therefore, addition of anti-reflux procedures such as endoscopic or laparoscopic fundoplication to POEM can emerge as a game changing strategy.

Transoral incisionless fundoplication (TIF): TIF was initially described as a procedure to treat GERD. This technique reconfigures tissue from inside the stomach to create a gastroesophageal valve and wrapping of fundus around the esophagus using

endo stapling techniques such as the EsophyX(®) device and the MUSE(TM) system[39]. Being performed entirely using the endoscopic approach, TIF has the propensity to emerge as an attractive adjunct to POEM for reducing reflux[39,40]. It may fare better when done in conjunction with intraoperative impedance planimetry[41]. TIF may also be combined with laparoscopic hiatal hernia repair[42]. In a pilot study PPI was discontinued in 75% patients post TIF at 3 months[43]. In a multicenter study of 12 patients who underwent post POEM TIF, technical success was noted in all patients as regards the reduction in frequency of daily GERD symptoms in subjective assessments as well as in pH studies[44]. TIF can be added to POEM intraoperatively in the same sitting or subsequently in follow up.

Per oral endoscopic fundoplication (POEM fundoplication, POEM F): POEM F is being investigated as an option for adding fundoplication during POEM[45-48]. After completing POEM the endoscope is advanced through the submucosal tunnel into the peritoneal cavity and a mechanical barrier zone/wrap is created at the gastroesophageal junction using endoclips and an endoloop[45,46]. In a study with POEM F involving 25 patients, abnormal esophageal acid exposure time was seen in 11% and borderline GERD in 18.2% at 12 months follow-up[47].

Laparoscopic fundoplication:

Laparoscopic fundoplication remains a viable option for treatment of POEM related reflux, particularly that refractory to medical therapy, although increased mediastinal adhesion may be noted[6,49].

Other techniques:

Other minimally invasive techniques used for treatment of GERD, such as Stretta, electric stimulation, magnetic sphincter augmentation and anti-reflux mucosectomy merits investigation in post-POEM reflux[50].

FUTURE RESEARCH

Post POEM reflux can have health-related and economic implications in the long term. Therefore, long-term outcomes of post-POEM reflux, its causes, prevention, and management options can emerge as arenas for potential future research.

CONCLUSION

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There is a higher incidence of pathologic reflux after POEM than after LHM. The routine addition of an antireflux procedure to LHM is proposed to cause the discrepancy. However, various other modifiable POEM-related factors may be contributory. PPI remains the mainstay of treatment for post-POEM reflux, but novel minimally invasive techniques such as endoscopic fundoplication appears promising.

ORIGINALITY REPORT

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SIMILARITY INDEX

PRIMARY SOURCES

1

Hironari Shiwaku, Hiroki Sato, Yuto Shimamura, Hirofumi Abe et al. "Risk factors and long-term course of gastroesophageal reflux disease after peroral endoscopic myotomy: A large-scale multicenter cohort study in Japan", Endoscopy, 2022

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