# Gastroesophageal reflux disease after peroral endoscopic myotomy is unpredictable, but responsive to proton pump inhibitor therapy: a large, single-center study

## Authors

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## **ABSTRACT**

**Background** Gastroesophageal reflux disease (GERD) is an important concern after peroral endoscopic myotomy (POEM). However, there are limited data on the risk factors for post-POEM GERD and its responsiveness to proton pump inhibitors (PPIs). In this study, we aimed to analyze the variables affecting the occurrence of GERD and its response to PPI therapy.

Methods Consecutive patients with idiopathic achalasia who underwent POEM (December 2016 to January 2018) were evaluated for GERD using 24-hour pH impedance, esophagogastroduodenoscopy (EGD), and symptoms. Multivariate analysis was performed to identify the variables affecting the incidence of post-POEM GERD.

Results A total of 209 patients with esophageal motility disorders, including 194 patients with non-sigmoid achalasia, underwent POEM during the study period. Comprehensive evaluation of GERD was completed on 167 patients (86.1%): 47.3% women with a mean (standard deviation) age of 41 (14.42) years and body mass index of 22.2 (3.89) kg/m<sup>2</sup>; the majority (70.7%) were treatment naïve. A high DeMeester score (>14.72), reflux esophagitis, and symptomatic GERD were identified in 47.9%, 41.9%, and 29.3% of patients, respectively. On logistic regression analysis, type of achalasia, technique of POEM (anterior vs. posterior), pre- or post-POEM esophageal manometry variables, and patient characteristics were not associated with post-POEM GERD. Erosive esophagitis responded to PPI therapy in the majority of patients (81.4%).

Conclusion The incidence of GERD is high after POEM. Most of the reflux esophagitis is mild and responsive to PPI therapy. There are no procedural or patient-related variables that appear to affect the incidence of post-POEM GERD.

## Introduction

Peroral endoscopic myotomy (POEM) was introduced by Inoue and colleagues nearly a decade ago [1]. Since then, multiple studies have confirmed the safety and efficacy of POEM for the management of achalasia [2,3]; however, initial studies concentrated mainly on the feasibility and efficacy of POEM, and lacked a comprehensive evaluation of gastroesophageal reflux disease (GERD) [1, 4, 5]. Recent studies incorporating an objective evaluation of GERD have indicated that the incidence of GERD is high after POEM [6]. However, the existing literature is limited and divergent with regards to the incidence and risk factors for GERD after POEM [6-12]. The observed heterogeneity in the published studies may be due to the selection bias generated by the evaluation of selected patients. In addition, the response to proton pump inhibitor (PPI) therapy has not been objectively evaluated in previous studies.

In this study, we aimed to analyze the incidence and risk factors of post-POEM GERD and its response to PPI therapy in consecutive patients with idiopathic achalasia.

## Methods

The data on consecutive patients who underwent POEM (from December 2016 to January 2018) for idiopathic achalasia at a single tertiary center were analyzed from a prospectively maintained database. Patients who underwent comprehensive evaluation of GERD with data on all three parameters (symptoms, esophagogastroduodenoscopy [EGD] findings, and 24-hour pH analysis) were included in the study. Children < 18 years of age, patients with sigmoid achalasia or non-achalasia spastic esophageal motility disorders, and those who did not agree to the evaluation of GERD were excluded from the study.

Multiple factors were analyzed to identify the variables that affect the incidence of GERD after POEM (> Fig. 1). The study was approved by the institutional review board committee.

## **Pre-POEM** evaluation

The pre-POEM evaluation included symptom analysis using the Eckardt score, timed barium esophagogram, EGD, and high resolution esophageal manometry. The type of achalasia, integrated relaxation pressure (IRP), and lower esophageal sphincter (LES) pressure were recorded on esophageal manometry.

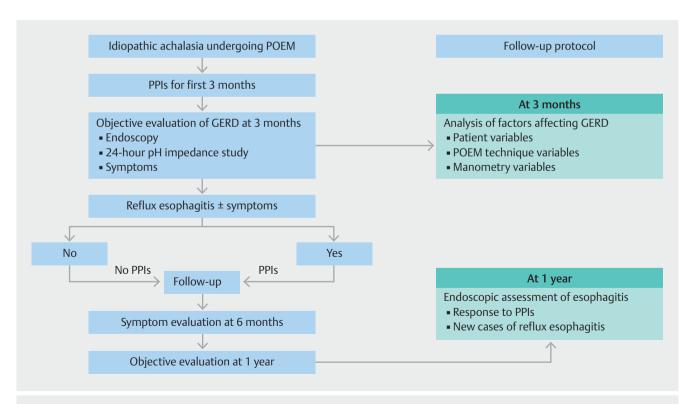
# POEM technique

The standard technique of POEM has been described previously [3,13]. In brief, POEM was performed via an anterior (1–2 o'clock) or posterior (5 o'clock) route by three experienced operators (Z.N., D.N.R., M.R.). Selective circular myotomy was done in the upper part of the tunnel and full-thickness myotomy towards the lower part of the tunnel. Myotomy was performed for a length of 2–3 cm beyond the gastroesophageal junction (GEJ). The length of esophageal myotomy was left to the discretion of the operating endoscopist.

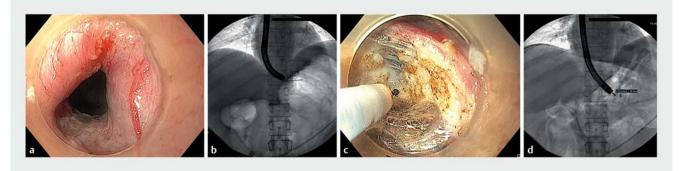
Extension of the submucosal tunnel into the stomach was identified using a change in vascular pattern; narrowing, followed by widening of submucosal space; and blanching of the gastric mucosa visualized in retroversion (> Fig. 2a,b). The distal penetrating vessels were identified as the defining point for the end of the submucosal tunnel on the gastric side. In addition, fluoroscopy was used to confirm the extension of the tunnel for at least 2 cm beyond the GEJ (> Fig. 2c,d).

# Post-POEM management and follow-up

Follow-up was scheduled at 1, 3, 6, and 12 months after POEM. All the patients were prescribed PPIs for a duration of 10 weeks after POEM. PPIs were stopped 2 weeks prior to the first objective assessment of GERD during follow-up at 3 – 4 months. Post-POEM evaluation at 3 months included symptom analysis, timed barium esophagogram, EGD, 24-hour pH study and esophageal manometry.



▶ Fig. 1 Flow diagram depicting the methodology of the current study. POEM, peroral endoscopic myotomy; PPI, proton pump inhibitor; GERD, gastroesophageal reflux disease.



► Fig. 2 Identification of the gastroesophageal junction (GEJ) and assessment of the gastric myotomy: **a** endoscopically by identification of the narrow portion of the tunnel representing the GEJ; **b** fluoroscopically by confirming the position of the endoscope at the GEJ; **c** with endoscopic view of the completed myotomy; **d** by fluoroscopic image confirming an adequate gastric myotomy.

## **Evaluation of GERD**

GERD was evaluated using symptoms (heartburn and regurgitation) at each of the follow-up visits (1, 3, 6, and 12 months). In addition to symptom analysis, EGD and 24-hour pH impedance study were also performed at 3 months. The 24-hour pH study was performed as follows: the pH probe was placed transnasally, which was connected to a pH data acquisition device (ZepHr pH monitor with ComforTEC disposable catheters; Sandhill Scientific, Highlands Ranch, Colorado, USA). A DeMeester score > 14.72 was considered to be indicative of GERD [14].

An EGD was repeated at 1 year to document an objective assessment of the response to PPIs and to detect new cases, if any, of reflux esophagitis. The severity of reflux esophagitis was classified as per the Los Angeles grading for esophagitis (grade A to D) [15].

The following variables were analyzed for their association with GERD: age, sex, body mass index (BMI), type of achalasia, length of myotomy, history of previous treatment, and manometric findings, including IRP and LES pressure.

## Management of post-POEM GERD

All patients with evidence of reflux esophagitis, with or without symptoms, were prescribed a PPI (equivalent to 40 mg panto-prazole or 20 mg rabeprazole) until the next objective evaluation at 1 year after POEM. PPIs were not prescribed in patients with GERD on 24-hour pH study in the absence of symptoms and erosive esophagitis. In patients with either persistence of symptoms or erosive esophagitis on subsequent follow-up (i. e. 6 months or 1 year), double-dose PPIs were prescribed.

Lifestyle interventions, including avoidance of late-night meals, cessation of smoking and alcohol, and head-end elevation of the bed, were advised to all the patients.

## **Definitions**

## Treatment failure

We defined prior treatment failure as patients who had relapsed with symptoms along with objective evidence of stasis on timed barium esophagogram after previous pneumatic dilation (single or multiple sessions) or Heller's myotomy with or without fundoplication.

## **GERD**

We defined GERD as the presence of typical symptoms, including heartburn and regurgitation, in conjunction with objective evidence of GERD in form of a positive pH impedance study or erosive esophagitis.

## Statistical analysis

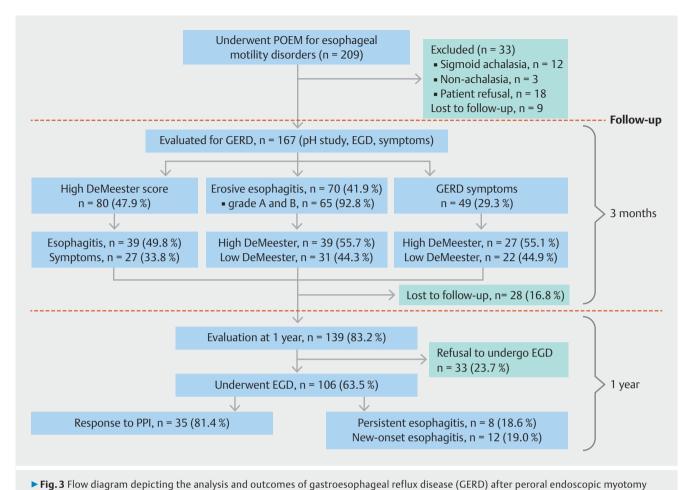
The data were analyzed and compared between the groups of patients with and without reflux after the POEM procedure. The data were presented as median (range) or mean (standard deviation [SD]). A Student's paired *t* test was used to analyze continuous variables and a chi-squared test for categorical variables. *P* values of <0.05 were considered to be statistically significant. Multiple logistic regression was performed using the stepwise method irrespective of the significance on univariate analysis to avoid errors of multiple comparisons and identify important predictors of outcome that could have been missed while analyzing each outcome separately. The data were analyzed using MedCalc for Windows, version 12.2.1.0 (MedCalc Software, Ostend, Belgium).

# Results

A total of 209 adult patients underwent POEM for esophageal motility disorders during the study period (December 2016 to January 2018). Of these, 12 patients had sigmoid achalasia, 18 did not agree to complete evaluation of GERD, three had non-achalasia spastic esophageal disorders, and nine were lost to follow-up. Objective evaluation of GERD was available at 3 months on 167 patients with idiopathic non-sigmoid achalasia (86.1%) ( Fig. 3).

# Demographics of study patients

Overall, 167 patients (52.7% men; mean (SD) age 41 (14.42) years) underwent a complete evaluation for GERD. The majority of the patients were treatment naïve (118 [70.7%]) and had type II (64.7%) or type I (25.8%) achalasia. Pneumatic dilation, used in



(POEM). EGD, esophagogastroduodenoscopy; PPI, proton pump inhibitor.

40/49 patients (81.6%) was the main modality of management in patients with a history of prior treatment. Other baseline characteristics including Eckardt score and pre-POEM esophageal manometry parameters have been outlined in > Table 1.

# Intraprocedural variables

POEM was performed via an anterior and posterior route in 106 (63.5%) and 61 patients (36.5%), respectively. The mean (SD) length of esophageal myotomy was 7.62 (2.99) cm and gastric myotomy 2.94 (0.45) cm (> Table 1).

# **Analysis of GERD**

Erosive esophagitis and reflux on 24-hour pH study were found in 41.9% and 47.9% of patients, respectively. The majority of the subjects (92.9%) had mild erosive esophagitis (LA grade A or B). The incidence of erosive esophagitis was not significantly different in patients with high (>14.72) or normal (<14.72) DeMeester scores (48.8% vs. 35.6%; *P*=0.12). Symptomatic GERD was detected in 29.3% of patients. There was no significant difference in the incidence of symptoms in patients with high and normal DeMeester scores (33.8% vs. 25.3%; *P*=0.24) (▶ **Table 2**).

The achalasia subtypes, pre-procedural patient-related variables (age, sex, and BMI), parameters of esophageal manometry (LES pressure and IRP), intraprocedural variables (length and or-

ientation of myotomy) were not significantly different between patients in the high and low DeMeester groups (> Table 2).

# Logistic regression analysis of factors effecting GERD

On logistic regression analysis, the patient-related factors including BMI, age, sex, and type of achalasia did not significantly impact on the prevalence of GERD after POEM. The technique of POEM, including the length of myotomy (esophageal or gastric) and orientation of myotomy (anterior vs. posterior), also did not affect the incidence of post-POEM GERD (Table 3).

# Response to antireflux therapy

At 1 year, 139 patients (83.2%) were available for follow-up and 106 of them (63.5%) underwent EGD, including 43 of the patients (61.4%) with reflux esophagitis and 63 of those (65.0%) without evidence of esophagitis at 3 months. Complete resolution of esophagitis was documented in 35 patients (81.4%) after PPI therapy. Persistent esophagitis was found in eight patients (18.6%). Of these, two patients were not compliant with PPI therapy, while six had persistent or residual erosive esophagitis (grade A 4; grade B 2) on regular once a day PPI therapy. Among the 63 patients without reflux esophagitis on initial EGD at 3 months, reflux esophagitis was diagnosed in an additional 12 patients (grade A 9; grade B 3) at 1 year. A high De-

➤ **Table 1** Baseline demographics, esophageal manometry findings, and details of the peroral endoscopic myotomy (POEM) procedure in the 167 study subjects.

Age, mean (SD), years	41 (14.42)						
Sex, female, n (%)	79 (47.3%)						
Body mass index, mean (SD), kg/m <sup>2</sup>	22.2 (3.89)						
Type of Achalasia, n (%)							
Type I	43 (25.8%)						
<ul> <li>Type II</li> </ul>	108 (64.7%)						
Type III	11 (6.6%)						
<ul> <li>Unknown</li> </ul>	5 (3.0%)						
Previous therapy, n (%)							
<ul><li>None</li></ul>	118 (70.7%)						
Pneumatic dilation	40 (24.0%)						
Botox injection	2 (1.2%)						
<ul> <li>Pneumatic dilation + Botox injection</li> </ul>	1 (0.6%)						
<ul> <li>Heller's myotomy</li> </ul>	6 (3.6%)						
Baseline Eckardt score, mean (SD)	6.93 (1.50)						
Pre-POEM manometry, mean (SD)							
4-s integrated relaxation pressure, mmHg	26.4 (12.99)						
<ul> <li>LES pressure, mmHg</li> </ul>	35.42 (14.73)						
Characteristics of POEM procedure							
Length of myotomy, mean (SD), cm							
Total	10.58 (3.07)						
<ul> <li>Esophageal myotomy</li> </ul>	7.62 (2.99)						
Gastric myotomy	2.94 (0.455)						
Orientation of myotomy, n (%)							
<ul> <li>Anterior</li> </ul>	106 (63.5%)						
• Posterior 61 (36.5							
SD, standard deviation; LES, lower esophageal sphincter.							

Meester score was previously documented at 3 months in eight of these patients (grade A 5; grade B 3) (**Fig. 3**).

# Discussion

In this study, we found that the incidence of GERD is high (48%) after POEM in Indian patients with idiopathic achalasia. There are no intraprocedural or patient-related factors that influence the occurrence of GERD after POEM.

The efficacy of POEM has been unequivocally proven in multiple studies with short- and medium-term follow-up [2,3,16]. However, recent reports indicate that the incidence of GERD may be higher after POEM compared with Heller's myotomy and pneumatic dilation [17-20]. The emergence of reports of peptic stricture and Barrett's esophagus after POEM highlight

▶ Table 2 Comparison of patient- and technique-related factors in patients with and without gastroesophageal reflux after undergoing peroral endoscopic myotomy (POEM).

y (POEIVI).							
No reflux (normal DeMeester score) (n = 87)	Reflux present (high DeMeester score) (n =	P value					
42.2 (14.45)	40.01 (14.38)	0.31					
37 (42.5)	42 (52.5)	0.63					
22.8 (3.83)	21.5 (3.86)	0.07					
23 (26.4%)	20 (25.0%)						
56 (63.4%)	52 (65.0%)						
5 (5.7%)	6 (7.5%)						
23 (26.4%)	26 (32.5%)						
Pre-POEM manometry, mean (SD)							
27.42 (15.52)	24.68 (9.33)	0.68					
36.45 (14.47)	34.67 (14.93)	0.50					
Length and orientation of myotomy							
10.43 (3.28)	10.74 (2.83)	0.27					
7.52 (3.20)	7.74 (2.76)	0.36					
2.89 (0.45)	3.0 (0.45)	0.36					
%)							
57 (64.77%)	49 (62.03%)						
31 (35.23%)	30 (37.97%)						
0.61 (0.733)	0.70 (0.80)	0.53					
ın (SD)							
14.33 (7.15)	15.02 (7.74)	0.68					
8.90 (4.35)	9.19 (4.78)	0.79					
22 (25.3%)	27 (33.8%)	0.24					
31 (35.6%)	39 (48.8%)	0.12					
16 (18.4%)	18 (22.5%)						
10 (10.4%)	.0 (22.370)						
13 (14.9%)	18 (22.5%)						
` '							
13 (14.9%)	18 (22.5%)						
	(normal DeMeester score) (n = 87)  42.2 (14.45) 37 (42.5) 22.8 (3.83)  23 (26.4%) 56 (63.4%) 5 (5.7%) 23 (26.4%) n (SD)  27.42 (15.52) 36.45 (14.47) yotomy 10.43 (3.28)  7.52 (3.20) 2.89 (0.45)  %) 57 (64.77%) 31 (35.23%) n (SD) 14.33 (7.15) 8.90 (4.35) 22 (25.3%)	No reflux (normal DeMeester score) (n = 87)  42.2 (14.45) 42.5 42 (52.5) 22.8 (3.83)  23 (26.4%) 20 (25.0%) 56 (63.4%) 52 (65.0%) 5 (5.7%) 6 (7.5%) 23 (26.4%) 26 (32.5%)  n (SD)  27.42 (14.47) yotomy 10.43 (3.28) 10.74 (2.83)  7.52 (3.20) 7.74 (2.76) 2.89 (0.45) 30 (37.97%)  10.61 (0.733) 0.70 (0.80)  n (SD)  14.33 (7.15) 15.02 (7.74) 8.90 (4.35) 9.19 (4.78) 22 (25.3%) 27 (33.8%)					

SD, standard deviation; IRP, integrated relaxation pressure; LES, lower esophageal sphincter; PPI, proton pump inhibitor.

▶ **Table 3** Logistic regression analysis of risk factors for gastroesophageal reflux after peroral endoscopic myotomy (POEM).

	Univariat	te analysis		Multivariate analy	Multivariate analysis		
	OR	95 %CI	P value	Adjusted OR (for age and sex)	95%CI	P valu	
Age (<41 vs. >41 years)	1.31	0.71 – 2.40	0.38	0.74	0.35 – 1.55	0.43	
Male	1.00	Reference		1.00			
Female	0.63	0.34-1.17	0.15	0.67	0.42 – 1.49	0.71	
Median BMI (<22.2 vs. >22.2 kg/m²)	1.31	0.71-2.42	0.37	0.67	0.32 – 1.41	0.29	
<b>Type of achalasia</b> Type I and III				0.66	0.32 – 1.42	0.31	
Туре II	1	Reference		1	Reference		
Previous therapy Yes/No	1.09	0.56 - 2.14	0.78	1.21	0.53 – 2.76	0.64	
Pre-POEM manometry							
Median IRP (>24.6 vs. <24.6 mmHg)	1.16	0.61-2.19	0.64	1.14	0.51 – 2.55	0.74	
LES pressure, mmHg				0.96	0.44-2.09	0.93	
Median length and orientation of myot	omy						
Esophageal (>7.0 vs. <7.0 cm)	1.31	0.71 – 2.46	0.38	1.12	0.51 – 2.44	0.77	
Gastric (>3.0 vs. <3.0 cm)	2.32	0.68-8.18	0.17	1.67	0.52 – 5.37	0.39	
Anterior myotomy	0.89	0.47 – 1.66	0.71	1.14	0.51 – 2.44	0.74	
Posterior myotomy	1.00	Reference		1.00	Reference		
Post-POEM Eckardt score (> 1 vs. ≤ 1)	1.21	0.65 - 2.22	0.38	1.35	0.64-2.86	0.43	
Post-POEM manometry							
Median IRP (>8.4 vs. <8.4 mmHg)	1.07	0.57 – 2.01	0.82	0.79	0.35 – 1.80	0.59	
LES pressure, mmHg				1.37	0.60 - 3.12	0.44	

the importance of evaluation and management of GERD in these patients [12,21].

The current literature depicts contrasting results with regards to the incidence and risk factors for GERD after POEM, possibly due to selection bias (>Table 4). In addition, the response of post-POEM GERD to PPI therapy has not been previously evaluated. In one of the largest multicenter studies [6], objective evaluation of post-POEM GERD (by pH study) was performed in only 60% of the subjects. In another study, only 68/112 patients were analyzed for GERD after POEM. Of note, the symptoms of GERD were significantly less severe in those who did not return for objective evaluation of GERD [12]. This suggests that symptomatic patients are more likely to be evaluated for GERD; therefore, the true incidence of post-POEM GERD cannot be quantified by analyzing a selected group of patients. We attempted to address this concern and analyzed consecutive patients who underwent POEM for achalasia.

In the current study, the majority of the patients (86%) underwent objective evaluation for GERD using EGD and 24-hour pH impedance analysis. About half of the patients had GERD

(high DeMeester score) on pH study. Erosive esophagitis (mostly grade A or B) was detected in 42% of patients; however, symptoms of reflux were evident in fewer patients (29%). Only one-third of the patients with a high DeMeester score were symptomatic for GERD, suggesting that the majority of the patients with reflux were detected incidentally. Our results are in concordance with a recent multicenter study by Kumbhari et al. [6], where a high DeMeester score, reflux esophagitis, and asymptomatic GERD were found in 57.8%, 23.2%, and 60.1% of patients, respectively. In other studies, the incidence of symptomatic GERD and reflux esophagitis have been found to be 18%–40% and 20%–60%, respectively (> Table 4).

The second major finding of our study was a lack of association between patient-related factors, like age, sex, BMI, type of achalasia, and the incidence of GERD. Similarly, the technique of POEM (anterior vs. posterior), length of myotomy, and post-POEM esophageal manometry parameters, such as IRP and LES pressure, did not influence the occurrence of post-POEM GERD. In order to substantiate the findings in the current study and reduce the margin of error, we performed a multivariate analysis,

▶ Table 4 Studies depicting the objective evaluation of gastroesophageal reflux after peroral endoscopic myotomy (POEM).

	n	, 3 1	Percentage of subjects with GERD on basis of:			Predictors of GERD
		country	symptoms	reflux esophagitis (percentage under- going endoscopy)	24-hour pH study (percentage under- going pH testing)	
Sharata et al. 2015 [11]	100	Retrospective, USA	Heartburn 8%; regurgitation 10%	27.4% (73%)	38.2% (68%)	Not reported
Hungness et al. 2016 [12]	115	Retrospective, USA	28% (GERD-Q>7)	25% (61%)	45% (20%)	Hiatus hernia, BMI > 35 kg/m²
Shiwaku et al. 2016 [9]	105	Prospective, Japan	Not reported	60 % - grade A 44 %	13%	IRP
Familiari et al. 2016 [7]	103	Retrospective, Italy	Heartburn 18.4%	20.4% - grade A 8.7%	50.5%	IRP
Wang et al. 2016 [10]	56	Retrospective, China	23.2%	21.4%	44.6%	Low IRP, full-thickness myotomy
Jones et al. 2016 [8]	43	Retrospective, USA	28% (GERD-HRQL, GERSS)	Not reported	58% (60%)	Not reported
Kumbhari et al. 2017 [6]	282	Retrospective, multicenter	39.9%	23% (83%) - grade A 11.6%	57.8%	Female sex
Current study	167	Retrospective, India	29.3%	41.9% - grade A 20.4%	47.9%	No factors

GERD, gastroesophageal reflux disease; GERD-Q, GERD questionnaire; BMI, body mass index; IRP, integrated relaxation pressure; GERD-HRQL, GERD health-related quality of life; GERSS, GERD symptom scale.

even though no significant factors were identified on univariate analysis. Several randomized trials have confirmed that the orientation of the myotomy does not influence the incidence of GERD after POEM [22–24]. Similarly, a high BMI was not associated with an increased incidence of post-POEM GERD in a recent study [25]. More recently, Tanaka and colleagues evaluated a novel technique for POEM to preserve the oblique muscle fibers and prevent GERD [26]. Reflux esophagitis of grade B and higher severity was significantly less frequent in the group treated with the new technique (31.3 % vs. 58.1 %; P=0.02). In our study, we did not specifically record and analyze the technique of gastric myotomy and its impact on GERD.

In addition to the incidence and risk factors for post-POEM GERD, we also analyzed the outcome of PPI therapy at 1 year after POEM. Although, the resolution of reflux esophagitis was documented in the majority of the patients, several new cases of erosive esophagitis were detected. Most of these patients (67%) had mild esophagitis (grade A and B) and had had a high DeMeester score at 3 months. Therefore, increased esophageal acid exposure in the absence of endoscopic evidence of esophagitis may not be innocuous and close follow-up is required. In addition, non-compliance with PPI therapy was documented in nearly a quarter of patients. Because most of the patients with post-POEM GERD (70%) are asymptomatic, ensuring compliance with PPI therapy may be especially challenging in these patients.

There are several implications of our study. First, in contrast to the prevalence of GERD in the general population, post-POEM GERD is highly prevalent in Asian patients, similar to that reported in Western studies [27]. Therefore, it is important to convey the risk of GERD and discuss alternative treatment options with patients before contemplating POEM. Second, poor correlation between symptoms and the presence of GERD signifies the importance of universal screening for GERD, irrespective of the presence of symptoms. Third, the occurrence of GERD is not dependent on the technique of POEM. Consequently, novel strategies need to be explored for the prevention of post-POEM GERD in future studies [28–31]. Last, the response to PPIs appears adequate in the majority of the patients who are compliant with them. However, surveillance endoscopy may be required, especially in patients with increased esophageal acid exposure, to look for new cases of reflux esophagitis. Long-term follow-up studies are required to enlighten our knowledge in this group of patients.

The strengths of our study are its large sample size, the objective evaluation of GERD, and a reduced likelihood of selection bias owing to the inclusion of consecutive patients who underwent POEM. The objective documentation of response to PPIs and the clinical significance of increased esophageal acid exposure in the absence of symptoms have not been discussed in previous studies. However, certain drawbacks are noteworthy. About one-third of the patients could not be objectively evaluated for GERD at 1-year follow-up. As a consequence, the response to PPI therapy may have been marginally underestimated or overestimated. We did not use the double-scope method to confirm the gastric extent of the myotomy. An excessive myotomy (>4cm) on the gastric side has been proposed as one of the risk factors for post-POEM reflux [32]. Instead, we

used the "two penetrating vessels" technique and fluoroscopy to define the gastric extent of the myotomy. These techniques have been previously evaluated for estimating the adequacy of gastric myotomy [33,34]. Although, a marginal error is possible using these methods, they are unlikely to grossly over- or underestimate the length of the gastric myotomy.

In conclusion, the incidence of GERD is high after POEM and this risk should be conveyed to the patients. Patient characteristics, orientation of the myotomy, and post-POEM IRP do not correlate with the development of GERD. The majority of patients develop mild erosive esophagitis and respond well to PPI therapy.

# **Competing interests**

The authors declare that they have no conflict of interest.

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