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Original Article

Role of Rapid Drink Challenge During Esophageal High-resolution Manometry in Predicting Outcome of Peroral Endoscopic Myotomy in Patients With Achalasia

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Background/Aims
Peroral endoscopy myotomy (POEM) is effective to treat achalasia. We aim to determine POEM effect on esophageal function and search for predictive factors of response to POEM and co-occurrence of gastroesophageal reflux disease (GERD).

Methods
A total of 64 untreated achalasia patients who underwent high-resolution manometry (HRM) before and 3 months after POEM were retrospectively included. Response to treatment was defined as an Eckardt score < 3. Reflux symptoms and patient's satisfaction were evaluated. Data were compared using paired *t* test, Chi-square test or log rank test.

Results
The 2-year success rate in response to POEM was 90%. All responders reported being satisfied while only 33% of non-responders did ($P < 0.001$) and 64% of patients with reflux symptoms were satisfied versus 96% of those without ($P = 0.009$). On HRM, the integrated relaxation pressure and the contractile pattern changed significantly after POEM but were not predictive of response. Between pre and post POEM HRM, a decrease in maximal esophageal pressurization during rapid drink challenge (RDC) was associated with a better response rate than an increase of pressurization (91% vs 50%, $P = 0.004$). As evidenced by pH monitoring performed after POEM, GERD was pathological or borderline in 50% of patients (18/36) while only 19% (11/59) reported clinically significant reflux symptoms. On post POEM HRM, maximal esophageal pressurization during RDC was lower in patients with pathological or borderline GERD compared to those without ($P = 0.054$).

Conclusions
Esophageal HRM parameters changed significantly after POEM. Maximal esophageal pressurization during RDC may be useful to predict outcome.
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Key Words
Esophageal achalasia; Gastroesophageal reflux; Manometry; Myotomy

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Introduction

Esophageal achalasia is a rare primary esophageal motor disorder characterized by impaired relaxation of the esophagogastric junction (EGJ) and absence of normal esophageal peristalsis.[1] This condition is responsible for symptom occurrence such as dysphagia, regurgitation, chest pain, and weight loss.

Esophageal high-resolution manometry (HRM) is the gold standard for achalasia diagnosis.[2,3] To evaluate EGJ relaxation during swallowing, integrated relaxation pressure (IRP) is used. In achalasia, IRP is above the upper normal limit. Three clinically relevant subtypes of achalasia are described in the Chicago classification version 3.0 based on the pattern of esophageal body contractility.[4] This classification is not only descriptive, but also useful to predict treatment outcome.[2,5] Several studies showed that type II achalasia is not only the most frequent type of achalasia (2/3 of patients) but also the one associated with the best response to treatment while type III has the worst response rate.[2,5-7]

To date, there is no available therapy for restoring normal esophageal function. Treatment remains palliative and aims at alleviating EGJ obstruction. This requires disruption of the lower esophageal sphincter (LES; one component of the EGJ). This has been traditionally performed by botulinum toxin injection, balloon dilation or surgical myotomy. Pneumatic dilation and laparoscopic Heller myotomy are considered as the most effective therapies.[1,8] A European randomized trial demonstrated that after 5 years of follow-up, pneumatic dilation and laparoscopic Heller myotomy had comparable success rates (82% and 84% respectively).[9]

Peroral endoscopic myotomy (POEM) is a promising method to treat achalasia.[10] Many studies demonstrated good short-term outcome.[11-14] However, occurrence of gastroesophageal reflux disease (GERD) has been described in as much as 60% of patients.[15,16]

Reduction of EGJ relaxation pressure is frequently observed after achalasia treatment and up to half of the patients may show partial recovery of peristalsis.[17] These changes in esophageal function, mainly described after pneumatic dilation and surgical myotomy, were not systematically associated with improvement in symptoms.[18,19] So far, the changes induced by POEM and their impact on outcome have not yet been described in large series. Therefore the present study aim to determine the effect of first-line POEM treatment on esophageal function, as defined by HRM, and search for predictive factors of response to treatment and occurrence of GERD symptoms.

Materials and Methods

Patients

Patients with achalasia and referred for POEM were recruited retrospectively in 2 centers from 2012 to 2016. Patients were included if they had achalasia and if an esophageal HRM was performed before and after POEM. The diagnosis of achalasia was based on HRM with an abnormal integrated relaxation pressure (> 15 mmHg) before POEM. Patients with normal median IRP (< 15 mmHg) and 100% of absent contractions on HRM could be included if they were symptomatic and had complementary examinations (upper gastrointestinal endoscopy, endoscopic ultrasonography, barium esophagogram, and/or impedance planimetry [EndoFLIP]) in favor of achalasia.[20] Exclusion criteria were endoscopic (pneumatic dilation and botulinum toxin injection) or surgical treatment (Heller myotomy) prior to POEM, inability to pass a catheter through the EGJ during HRM, and absence of Eckardt score recording 3 months after POEM.

According to French law, this type of retrospective analysis of data, obtained during the clinical evaluation of patients, does not require ethical board review. Patients were informed that their clinical data could be used for clinical research, after anonymization. They had the possibility to sign a document indicating their refusal to participate, in which case their files were not used for the study.

High-resolution Manometry Procedure and Analysis

Esophageal HRM (Manoscan; Medtronic, Duluth, GA, USA) was performed before and 3 months after POEM. In our centers HRM was routinely performed after POEM as part of the patient's work-up. The protocol consisted in a 30-second baseline recording without swallowing, followed by ten 5-mL water swallows in the supine position, and a rapid drink challenge (RDC) test (200 mL free drinking) in the seated position.

HRM studies were retrospectively reviewed by 1 single expert (S.R.), unaware of POEM outcome, using Manoview software (Medtronic). The following parameters were analyzed: EGJ resting pressure, median IRP for ten 5-mL swallows, percentage of 5-mL swallows associated with pan-esophageal pressurization, percentage of 5-mL swallows associated with esophageal contraction as defined by the Chicago classification version 3.0.[4] IRP, maximal esophageal pressurization,[21] and occurrence of pan-esophageal pressurization and esophageal shortening were measured during RDC as well.[22] On the HRM performed before POEM, 3 subtypes of

achalasia were determined based on the Chicago classification; if the criteria of the Chicago classification were not fulfilled for the contractile pattern, a subtype of incomplete form of achalasia (achalasia variant) was defined (abnormal IRP and at least 1 intact or ineffective or fragmented esophageal contraction and less than 20% of premature contractions). After POEM, the median IRP of the ten 5-mL water swallows was calculated and the esophageal body contractility was characterized according to the Chicago classification as failed, weak, premature, fragmented, or intact. Finally the esophageal length was measured between the distal border of the upper esophageal sphincter and the proximal border of the EGJ at 30-mmHg isobaric contour before and after POEM (Fig. 1). On the post POEM HRM, the manometric length of the myotomy was estimated based on the distance between the upper border of the EGJ and the 30-mmHg isobaric contour of esophageal contractions, when present. The pressurization in the zone of the myotomy was considered significant if it occurred for at least 20% of swallows (Fig. 1B).

Peroral Endoscopic Myotomy Procedure

Recommended diet was only clear liquid intakes on the day before POEM procedure. Sedated and intubated, patients were placed in the supine position. An esophageal endoscopy was first performed to clean the lumen and to remove residual food. A high-definition endoscope (Olympus 190; Olympus, Tokyo, Japan), fitted with transparent caps, was used and the procedure was performed under CO_2 insufflation. POEM was carried out as described by Inoue et al.[10] Using 10 mL to 15 mL of a mixture of 0.2 mg/mL indigo carmine and 0.9% saline, a submucosal lift was created 10 cm above the EGJ on the anterior or posterior mucosa. This was done to perform a longitudinal mucosal incision in order to introduce the scope into the submucosal space. A submucosal tunnel was then created using Dual Knife (Olympus) or water jet knife Nestis (Nestis SAS, Lyon, France) and extended 2 cm to 3 cm distally to the EGJ. After tunneling, a Hook Knife (Olympus) was used allowing a selective circular myotomy. Hemostasis was performed using hot biopsy forceps. The length of esophageal myotomy was about 6 cm to 8 cm above the EGJ and 2 cm below. The endoscopist reported the approximate length of the myotomy in the patient's chart. No physiological measurement (such as EndoFLIP) was performed during the POEM procedure. Finally, endoscopic clips were used to close the mucosal entry site of the tunnel avoiding any contamination by esophageal contents.

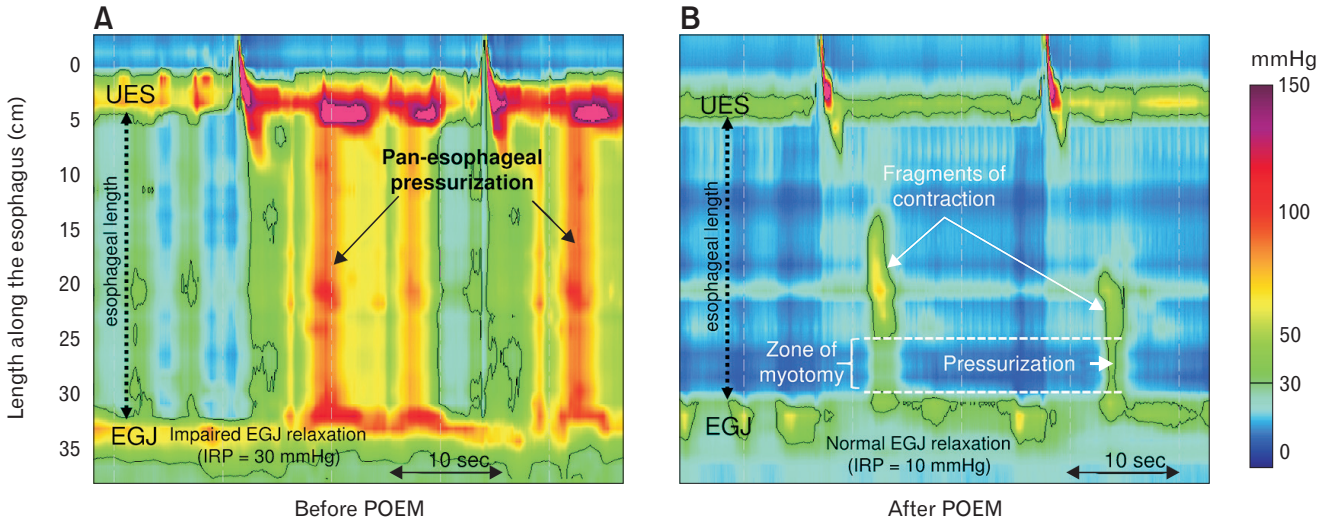


Figure 1. Example of esophageal high-resolution manometry (HRM) before (A) and after (B) peroral endoscopic myotomy (POEM). Before POEM, HRM was typical of type II achalasia with impaired esophagogastric junction (EGJ) relaxation (integrated relaxation pressure [IRP] > 15 mmHg), absence of esophageal contraction and pan-esophageal pressurization. After POEM, a fragmented esophageal contraction is observed with a normalization of IRP (< 15 mmHg). The zone of myotomy is visible as a distal defect between the esophageal contraction and the EGJ. After the second swallow, pressurization is observed in the zone of the myotomy. The esophageal length is measured from the distal border of the upper esophageal sphincter (UES) to the proximal border of the EGJ defined at the 30-mmHg isobaric contour during a period without swallowing and at the end of the expiration (vertical arrows). The fragmented contraction might indicate an incomplete myotomy.

Follow-up and Response to Treatment

Three months after POEM, patients underwent esophageal HRM and clinical evaluation. Patients' charts were reviewed to obtain follow-up data. During follow-up evaluation, systematic questionnaires were used: Eckardt score,[23] GERD questionnaire (GERD-Q),[24] and a simple question to evaluate overall satisfaction ("Are you satisfied with the results of the treatment?"). Treatment with POEM was considered successful if the Eckardt score was less than 3 points. GERD symptoms were considered as significant if the total score of the first 2 items of the GERD-Q (heartburn frequency and regurgitation frequency) was 4 or more. Patient's charts were also searched for post POEM upper gastrointestinal endoscopy, esophageal pH monitoring, and proton pump inhibitor (PPI) treatment.

Statistical Methods

Quantitative data are expressed as median (interquartile range) and qualitative data as percentage unless otherwise mentioned. Continuous variables before and after POEM were compared using non-parametric tests (Mann Whitney or Kruskal Wallis tests) while categorical data were compared using the chi-square test. Success rates were evaluated using the Kaplan-Meier method starting from the date of POEM to that of re-treatment or last clinical visit. Response curves were compared using the log-rank test. A P-value of < 0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 64 patients were included in the present study (Fig. 2). Their characteristics before treatment are presented in Table 1. All patients but one had an Eckardt score ≥ 3 before treatment. The

Table 1. Baseline Characteristics of Patients

Characteristics	n = 64
Age (yr)	55 (19-83)
Gender	
Male	38 (59)
Female	26 (41)
Body mass index (kg/m²)	24.8 (16.8-40.0)
Center	
Lyon	56 (87)
Bordeaux	8 (13)
Achalasia subtypes	
Type I	5 (8)
Type II	44 (69)
Type III	8 (12)
Incomplete form of achalasia[a]	7 (11)

[a]Incomplete form of achalasia is defined by the manometric diagnosis of esophagogastric junction (EGJ) outflow obstruction, according to the Chicago classification version 3.0, that is an impaired EGJ relaxation (median integrated relaxation pressure > 15 mmHg) without the criteria for type I, II, or III achalasia. The patients of this group had complementary examinations in favor of achalasia, leading to the diagnosis of an incomplete form of achalasia.
Data are presented as median (range) or number (%).

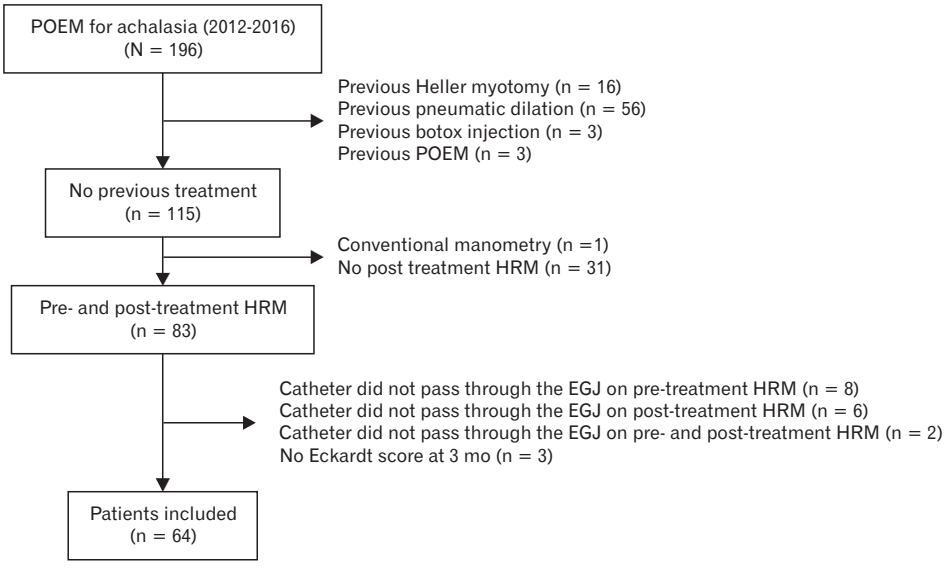


Figure 2. Patients' flow chart. One hundred and ninety-six peroral endoscopic myotomies (POEM) were performed during the studied period and 64 patients with achalasia, without previous treatment, and with pre- and post-treatment high-resolution manometry (HRM) were included. Patients with incomplete data (catheter not passed through the esophagogastric junction (EGJ) or absent Eckardt score at 3 months) were excluded.

Table 2. Clinical and Manometry Characteristics Before Peroral Endoscopic Myotomy, 3 Months After and at Last Follow-up Visit

Characteristics	Baseline (before POEM)	3 months after POEM	Last follow-up
Total Eckardt score	6 (2-11)	1 (0-5)[a]	1 (0-7)[a]
Sub scores			
Dysphagia	2 (0-3)	1 (0-3)[a]	0 (0-3)[a]
Regurgitation	2 (0-3)	0 (0-2)[a]	0 (0-3)[a]
Chest pain	0 (0-3)	0 (0-1)[a]	0 (0-2)[a]
Weight loss	0 (0-3)	0 (0-1)[a]	0 (0-2)[a]
High-resolution manometry			
EGJ resting pressure (mmHg)	25.9 (4.4-78.4)	6.1 (0-25)[a]	
Median IRP (mmHg)	22.3 (4.7-55.0)	7.2 (0.0-21.7)[a]	
Percentage of single 5 mL swallows with pan-esophageal pressurization	65 (0-100)	0 (0-80)[a]	
Rapid drink challenge[b]			
Pan-esophageal pressurization	40 (83)	5 (8)[a]	
Esophageal shortening	20 (31)	4 (7)[a]	
IRP during RDC (mmHg)	18.6 (0.1-48.8)	4.5 (0.0-38.6)[a]	
Maximal esophageal pressurization (mmHg)	50 (12-132)	19 (2-47)[a]	

[a]$P < 0.001$ vs baseline.

[b]Rapid drink challenge available in 48 patients before peroral endoscopic myotomy (POEM) and 56 after POEM.
EGJ, esophagogastric junction; IRP, integrated relaxation pressure; RDC, rapid drink challenge.
Data are presented as median (range) or number (%).

patient with an initial Eckardt score < 3 was treated because of daily dysphagia, without regurgitation, pain, or weight loss, which explains the low baseline score observed. Baseline HRM parameters are described in Table 2. Before POEM, 12 patients had a baseline IRP below 15 mmHg and 100% absent esophageal contractions with or without pan-esophageal pressurization.

Effects of Peroral Endoscopic Myotomy on Esophageal Function Assessed With High-resolution Manometry

An esophageal HRM was performed within a median delay of 2.7 months (range: 1.2-8.1) after POEM. Overall, a significant decrease in EGJ resting pressure ($P < 0.001$) and median IRP ($P < 0.001$) were observed after treatment (Table 2). After POEM, median IRP was within the normal range (< 15 mmHg) in 59 patients (92%) and above the normal range in 5 patients (8%; Table 2). Post POEM esophageal contractility was absent in 22 (34%) patients, ineffective in 28 (44%), fragmented in 2 (3%), premature in 10 (16%), and intact in 2 (3%). Contractility was more frequently absent in patients who had Type I achalasia before POEM while contractility was present in 61% of patients with Type II, 88% with Type III, and 100% with incomplete forms of achalasia (Fig. 3) ($P < 0.001$). A distal pressure defect at the level of the myotomy (Fig. 1) was observed between a fragment of esophageal contraction and the EGJ in 47 patients; the median length of this defect was 5.5 cm (range: 1.5-13.0). When a distal defect was identifiable, a distal pressurization occurred in this zone for at least 20% of the swallows in 19 cases (40%). Changes in esophageal length before and after POEM differed among patients: at least 1 cm longer after POEM in 45% of patients; at least 1 cm shorter in 20%; and no significant change in 35%.

The occurrence of pressurization was significantly reduced after both single swallows ($P < 0.001$) and RDC ($P < 0.001$; Table 2).

Clinical Response to Peroral Endoscopic Myotomy and Reflux Symptoms Occurrence

Based on the Eckardt score, POEM procedure was successful in 87.5% of patients at 3 months. The last follow-up visit was performed within a median duration of 21 months (range: 3-57) after POEM (Fig. 4). Between baseline and last follow-up, the Eckardt score decreased significantly ($P < 0.001$; Table 2) and POEM was successful in 84% of patients. Among the 10 patients (16%) considered as failures at last follow-up visits, one patient had a myositis, 2 patients underwent a second POEM (at 14 months and 18 months, respectively), and 7 patients did not receive further treatment (Fig. 4). Success rate was 92% at 12 months and 90% at 24 months (Fig. 5).

Last follow-up GERD-Q scores were available for 59 patients.

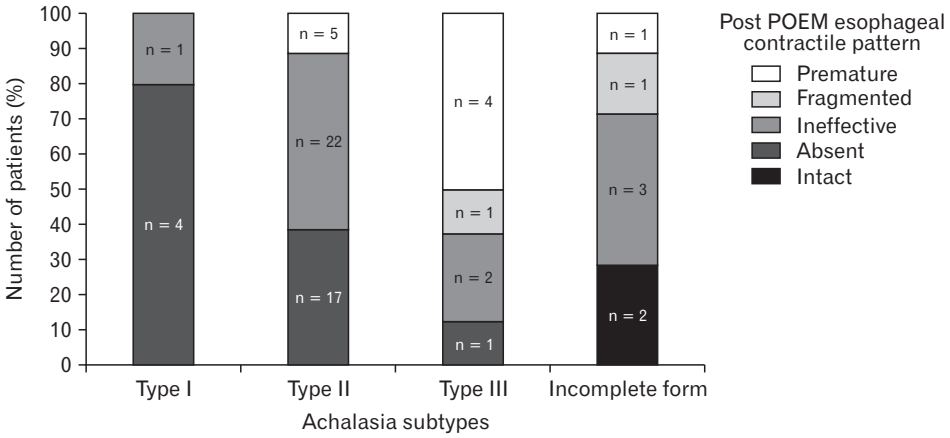


Figure 3. Post-treatment esophageal body contractility according to pre-treatment achalasia subtypes. Esophageal contraction was absent in 80% of patients with type I achalasia treated with peroral endoscopic myotomy (POEM). Esophageal contractility (intact, ineffective, fragmented, or premature) was present in most patients with type II, type III or incomplete form of achalasia (89%, 88%, and 100%).

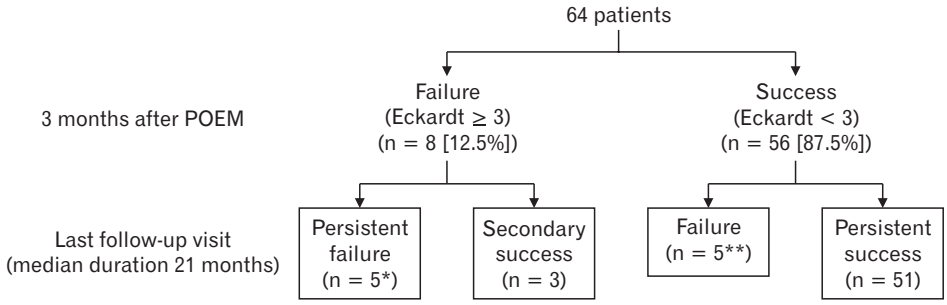


Figure 4. Response to treatment is presented at 3 months and during the last follow-up visit (median duration after peroral endoscopic myotomy [POEM]: 21 months [range 3.4-57.3]). Five patients with a negative response at 3 months were persistent non-responders at the last follow-up visit; 1 had myositis, 1 underwent second POEM, 14 months after the first one, and 3 did not receive any further treatment. Five patients with a positive response at 3 months presented recurrent symptoms at the last follow-up visit: 1 underwent a second POEM, 18 months after the first one, and 4 did not receive any further treatment. *One myositis: 1 second POEM at 14 months; 3 follow-up without treatment. **One second POEM at 18 months; 4 follow-up without re-treatment.

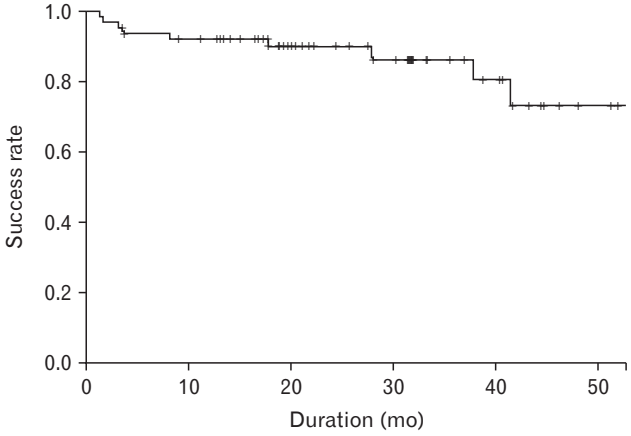
Eleven patients (19%) reported typical reflux symptoms at least twice a week (total score of the first 2 items of GERD-Q score ≥ 4). The same 59 patients answered the question about overall satisfaction. Among them, 6 were not satisfied and had an Eckardt score ≥ 3. For the other 53 patients who were satisfied, 50 had an Eckardt score < 3, and the 3 remainders an Eckardt score of 3. A significantly higher proportion of patients without reflux symptoms (46/48 patients [96%]) were satisfied with the results of the treatment compared to those with reflux symptoms (7/11 patients [64%], $P = 0.009$).

Clinical and Manometric Predictive Factors of Response

Clinical and manometric factors are presented according to the clinical response in Table 3. No center effect was observed (2-year success rate of 89% and 100%, respectively, $P = 0.392$). There was a trend for patients who failed to respond to POEM to more frequently reported GERD symptoms and receive PPI therapy than those for whom POEM was successful (Table 3).

Pre POEM Chicago classification type did not predict patient outcome. The clinical response was not significantly associated with the post POEM contractility pattern either ($P = 0.122$). Interestingly the post POEM median IRP was normal for the 10 patients considered as failures.

RDC was available before and after POEM in 44 patients. The maximal esophageal pressurization measured during RDC decreased after POEM in 40 patients (91%). The POEM success rate was significantly associated with a decrease in maximal esophageal pressurization (2-year success rate of 91% in patients with decreased pressurization vs 50% in patients without decreased pressurization, $P = 0.004$). Decreased maximal pressurization between pre and post POEM RDC had a sensitivity of 94% to predict success, a specificity of 33%, a positive predictive value of 89%, and a



	12 mo	24 mo	36 mo	48 mo
Success rate (%)	92%	90%	86%	73%
Patients at risk	53	27	15	4

Figure 5. Positive response rate after peroral endoscopic myotomy procedure according to the Kaplan-Meier survival curve. At 12 months, the success rate was 92% for 53 patients at risk. At 24 months the success rate was 90% for 27 patients at risk.

negative predictive value of 50%.

The median length of the post POEM distal pressure defect observed on HRM did not significantly differ between patients with successful (5.5 cm [range: 2.0-13.0 cm]) or failed (5.8 cm [range: 1.5-10 cm], $P = 0.651$) POEM treatments, nor did the occurrence of pressurization in this zone of defect (36% in success group vs 63% in failure group, $P = 0.621$).

Clinical and Manometric Predictive Factors of Gastroesophageal Reflux Disease Occurrence

Esophageal pH monitoring was performed off PPI in 36 patients within a median delay of 2 months (range: 1-39 months) after POEM. The esophageal acid exposure time (AET) was greater than 6% in 13 patients (36% of patients who underwent pH monitoring), leading to a diagnosis of pathological GERD according to the Lyon consensus.[25] The diagnosis of GERD was borderline (AET between 4% and 6%) in 5 patients and GERD was absent (AET < 4%) in 18 patients (50%). Significantly more patients with pathological or borderline diagnosis of GERD (47%) were on daily PPI treatment compared to those with no GERD (6%, $P = 0.013$). Post POEM HRM measurements showed that pathological or borderline GERD patients exhibited significantly lower maximal esophageal pressure during RDC (10 mmHg [range: 2-47 mmHg]) than patients with no GERD (23 mmHg [range: 10-42 mmHg], $P = 0.054$) as well as significantly longer esophageal length (24.8 cm [range: 19.8-27.7 cm]) compared to the no GERD patients (22.6 cm [range: 19.9-27.4 cm], $P = 0.015$). No other manometric parameters were significantly associated with pH monitoring results.

At the end of the follow-up period, clinically significant reflux symptoms were reported by 20% of patients (2/10) with a diagnosis of pathological GERD (AET > 6%) on pH monitoring, 20% (1/5) of those with a borderline GERD (AET 4-6%) and 12% (2/17) of those with a normal AET ($P = 0.815$). The percentage of POEM success was not significantly different between GERD status groups, identified by pH monitoring, with an observed success rate of 77% in patients with pathological GERD, 100% in patients with borderline GERD, and 89% in patients without GERD, ($P = 0.398$).

Taking into account the clinical evaluation at the end of the follow-up, POEM success tended to be more frequent in patients without significant reflux symptoms (90%) compared to those with clinical symptoms of reflux (63%, $P = 0.053$). As expected the consumption of PPI was significantly more frequent in patients reporting reflux symptoms (82% of patients on daily or on demand PPI therapy) than for those without symptoms (23%, $P = 0.001$). None of the clinical or manometric parameters were associated with the occurrence of reflux symptoms.

Discussion

The present series confirms the clinical efficacy of POEM in achalasia patients. The 2-year success rate (as defined with the Eckardt score) is 90%, significant reflux symptoms are reported by only 19% of the patients with a median follow up of 21 months, and pathological or borderline GERD is observed on pH monitoring in 50% of patients. Based on esophageal HRM, POEM is associated with a significant decrease in EGJ resting and relaxation pressures in all patients, and a partial restoration of esophageal contractility for more than half of the patients. Pre and post POEM manometric parameters measured after the standard protocol of 10 single swallows were not significantly associated with outcome, contrary to the RDC during HRM.

Similarly to Heller myotomy and pneumatic dilatation, POEM improves esophageal function by decreasing the EGJ pressures and restoring esophageal contractility in some cases.[17,26-29] In the present series, these modifications were not predictive of clinical response. For instance, all patients with a persistent elevated IRP had good outcome while all patients with poor outcome had an IRP within the normal range on the post POEM HRM. Similarly, pan-esoph-

Table 3. Predictive factors of Peroral Endoscopic Myotomy Response at the Last Follow-up Visit

Predictive factors	Success (n = 54)	Failure (n = 10)	*P*-value
Age (yr)	59 (19-83)	47 (30-83)	0.174
Male	32 (59)	6 (60)	0.897
Baseline body mass index (kg/m^2)	24.6 (14.2-40.0)	22.8 (18.4-30.2)	0.500
Baseline Eckardt score	6 (2-11)	7 (4-11)	0.537
GERD-Q score (heartburn, regurgitation) ≥ 4[a]	7 (14)	4 (44)	0.060
Use of proton pump inhibitors[a]			0.048
Never	36 (72)	3 (30)	
Occasionally	6 (12)	0	
Every day	8 (16)	6 (60)	
Baseline high-resolution manometry			
EGJ resting pressure (mmHg)	26.4 (4.4-78.4)	23.9 (10.1-57.6)	0.737
IRP (mmHg)	22.9 (4.7-55.0)	19.0 (6.1-43.0)	0.370
Achalasia subtype			0.734
Type I	4 (80)	1 (20)	
Type II	39 (87)	5 (13)	
Type III	6 (75)	2 (25)	
Incomplete form of achalasia	5 (71)	2 (29)	
Patients with at least 20% of swallows with pan-esophageal pressurization	45 (83)	7 (70)	0.997
Results of RDC[b]			
Pan-esophageal pressurization	37 (88)	3 (50)	0.125
Esophageal shortening	19 (45)	1 (17)	0.261
IRP during RDC (mmHg)	20.9 (0.4-48.8)	18.3 (0.1-26.3)	0.371
Maximal esophageal pressurization (mmHg)	50 (17-132)	47 (12-87)	0.389
Post POEM high resolution manometry			
EGJ resting pressure (mmHg)	6.1 (0.0-25.0)	6.1 (1.5-24.8)	0.554
IRP (mmHg)	7.0 (0.0-21.7)	6.4 (2.1-13.3)	0.817
Median IRP > 15 mmHg	5 (9)	0 (0)	0.384
Patients with at least 20% of swallows with pan-esophageal pressurization	13 (24)	2 (20)	0.642
Results of RDC[c]			
Pan-esophageal pressurization	4 (9)	1 (11)	0.868
Esophageal shortening	2 (4)	2 (22)	0.055
IRP during RDC (mmHg)	4.5 (0.0-38.6)	4.6 (0.0-12.0)	0.701
Maximal esophageal pressurization (mmHg)	16 (2-47)	26 (10-31)	0.168
Decrease of maximal pressurization (mmHg)	36 (−10-107)	11 (−19-58)	0.119

[a]Data available for 59 patients.
[b]Rapid drink challenge (RDC) available for 48 patients.
[c]RDC available for 56 patients.
EGJ, esophagogastric junction; IRP, integrated relaxation pressure; GERD-Q, gastroesophageal reflux disease questionnaire.
Data are presented as median (range) or number (%).

ageal pressurization after single swallows, which could be an indirect marker of EGJ obstruction, was not associated with the clinical response. Several studies have previously shown the limitations of post treatment esophageal manometry to predict clinical symptoms in patients with achalasia.[17-19,30] Measuring EGJ distensibility using EndoFLIP may be more relevant than EGJ pressure or IRP in patients previously treated for achalasia. Indeed, decreased EGJ distensibility was significantly associated with persistent or recurrent dysphagia in patients previously treated with pneumatic dilation or Heller myotomy. This was not the case for elevated IRP or EGJ pressure.[18,19]

The improvement of esophageal body contractility after acha-

lasia treatment has been reported previously.[17,31,32] Recent data suggested that esophageal body contractility may be present before treatment but not visible due to pan-esophageal pressurization. The esophageal contractility not seen in HRM could be detected in patients with achalasia before any treatment using the EndoFLIP.[33] The present study is one of the first to assess the role of post treatment esophageal body contractility in predicting POEM outcome, and failed to demonstrate a relationship between the presence of esophageal contractility and clinical response or GERD occurrence.

Performing provocative tests during HRM, such as RDC, may be of interest to depict abnormalities not seen with the standard protocol of ten 5-mL swallows.[34] These might be helpful to identify significant EGJ obstruction.[21,35] Measuring the maximal esophageal pressurization, as proposed by Ponds et al,[21] allowed observation that the decrease in maximal pressurization between pre and post POEM RDC was associated with better clinical outcome. Indeed, patients who failed to show a decrease in maximal esophageal pressurization during RDC after POEM, were mainly patients who failed to respond to POEM. Interestingly, the same authors demonstrated that esophageal pressurization during RDC positively correlated to barium height on timed barium esophagogram (TBE) in achalasia patients, regardless of treatment.[21] Barium height on TBE is known to be predictive of outcome, when measured after treatment.[36] Therefore, the results presented herein suggest that maximal esophageal pressurization during RDC may be used as an alternative to TBE to predict outcome after POEM. As TBE was not systematically performed in the present study, this hypothesis could not be confirmed.

To predict outcome after achalasia treatment, investigation of new parameters on HRM was performed. For that purpose, evaluation of the changes in esophageal length before and after POEM was undertaken on the hypothesis that length changes may be related to changes in contraction of the longitudinal muscle layer. These changes were, however, not correlated with clinical response. Evaluation of the length of the distal defect observed on post POEM HRM, corresponding to the myotomy, was also performed. No relationship was found between the length of this defect or the pressurization occurring within this defect and the outcome.

The main complication of POEM may be the occurrence of GERD[29,37] and thus the risk of long-term complications such as Barrett's mucosa and esophageal adenocarcinoma. A recent meta-analysis suggested a higher proportion of GERD after POEM than after Heller myotomy.[38] Herein, half of the patients underwent an esophageal pH monitoring which allowed pathological or borderline GERD to be confirmed in half of them. Interestingly, these patients had a lower maximal esophageal pressurization on RDC than patients without GERD on post POEM HRM. A higher pressurization may indicate a higher EGJ obstruction leading to a stronger anti-reflux barrier and less probability of GERD occurrence. As previously reported, the diagnosis of GERD made by pH monitoring was not correlated with reflux symptoms.[39,40] However, using the GERD-Q score after achalasia treatment, the present study found a proportion of clinically significant reflux symptoms similar to that reported by Hungness et al.[11] According to results herein, patient satisfaction seems to be determined by the absence of clinically significant reflux symptoms as well as the success to POEM evaluated by the Eckardt score. However, the objective pH monitoring of GERD had no such link with patient satisfaction. The systematic administration of PPI following a positive pH monitoring is certainly an important confounding factor that may explain the lack of correlation between symptoms and pH monitoring. Another explanation might be the difficulty of pH monitoring interpretation in the context of achalasia.

The present study has several limitations. The retrospective design, and the short follow-up period limit the strength of the conclusions. Despite the inclusion of a substantial number of patients from 2 academic centers, only 10 patients were considered as POEM failure within a median follow-up time of 21 months. Due to the recent introduction of POEM in clinical practice, most of the studies assessing POEM outcome have a similar short term follow-up. However, the success rate observed herein is in accordance with the literature. It is important to note that 4 operators performed the POEM procedure, their experience was similar, and we failed to find a center effect. Although the Eckardt score is easy to use and has been shown to have a fair reliability in achalasia,[41] it may not be perfect to assess outcome. Indeed, despite post treatment improvement, patients may exhibit some degree of dysphagia and regurgitation leading to an elevated score. Further, besides the Eckardt score, we used a subjective assessment of patient's satisfaction. Interestingly this patient's subjective assessment perfectly correlated with response as defined with the Eckardt score.

In conclusion, POEM is an effective treatment for achalasia, at least in the short term. RDC during HRM before and after POEM may be of interest to predict clinical outcome. Large prospective studies are required to confirm the yield of RDC to evaluate achalasia patients after treatment.

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