Received: 19 May 2023 | Accepted: 22 March 2024

DOI: 10.1002/ueg2.12586

ORIGINAL ARTICLE

UNITED EUROPEAN GASTROENTEROLOGY ueg journal WILEY

Peroral endoscopic myotomy for hypercontractile (Jackhammer) esophagus: A retrospective multicenter series with long-term follow-up

David Albers[1] | Mana Witt[2] | John E. Pandolfino[3] | Thomas Rösch[2] | Guido Schachschal[2] | Torsten Beyna[4] | Horst Neuhaus[4] | Christian Gerges[4] | Jennis Kandler[4] | Hans-Dieter Allescher[5] | Jan Martinek[6] | Alessandro Repici[7,8] | Alanna Ebigbo[9] | Helmut Messmann[9] | Brigitte Schumacher[1] | Yuki B. Werner[2]

[1]Department of Internal Medicine and Gastroenterology, Elisabeth-Krankenhaus Essen, Essen, Germany

[2]Department of Interdisciplinary Endoscopy, University Hospital Hamburg-Eppendorf, Hamburg, Germany

[3]Division of Gastroenterology and Hepatology, Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA

[4]Department of Internal Medicine and Gastroenterology, Evangelisches Krankenhaus Düsseldorf, Düsseldorf, Germany

[5]Center for Esophageal and Gastrointestinal Motility Disorders, Center for Internal Medicine, Gastroenterology, Hepatology and Metabolism, Klinikum Garmisch-Partenkirchen, Garmisch-Partenkirchen, Germany

[6]Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

[7]Department of Biomedical Sciences, Pieve Emanuele, Humanitas University, Rozzano, Italy

[8]Department of Gastroenterology, Humanitas Research Hospital -IRCCS-, Rozzano, Italy

[9]Department of Gastroenterology, University Hospital Augsburg, Augsburg, Germany

Correspondence

Thomas Rösch, Department of Interdisciplinary Endoscopy, University Hospital Hamburg-Eppendorf, Martinistraße 52, Hamburg 20246, Germany.
Email: t.roesch@uke.de

Abstract

Introduction: Long-term outcome data are limited for non-achalasia esophageal motility disorders treated by peroral endoscopy myotomy (POEM) as a separate group. We investigated a subset of symptomatic patients with hypercontractile esophagus (Jackhammer esophagus).

Methods: Forty two patients (mean age 60.9 years; 57% female, mean Eckardt score 6.2 ± 2.1) treated by primary peroral myotomy for symptomatic Jackhammer esophagus 2012–2018 in seven European centers were retrospectively analyzed; myotomy included the lower esophageal sphincter but did not extend more than 1 cm into the cardia in contrast to POEM for achalasia. Manometry data were re-reviewed by an independent expert. The main outcome was the failure rate defined by retreatment or an Eckardt score >3 after at least two years following POEM.

Results: Despite 100% technical success (mean intervention time 107 ± 48.9 min, mean myotomy length 16.2 ± 3.7 cm), the 2-year success rate was 64.3% in the entire group. In a subgroup analysis, POEM failure rates were significantly different between Jackhammer-patients without ($n = 22$), and with esophagogastric junction outflow obstruction (EGJOO, $n = 20$) (13.6% % vs. 60%, $p = 0.003$) at a follow-up of 46.5 ± 19.0 months. Adverse events occurred in nine cases (21.4%). 14 (33.3%) patients were retreated, two with surgical fundoplication due to reflux. Including retreatments, an improvement in symptom severity was found in 33 (78.6%) at the end of follow-up (Eckardt score ≤3, mean Eckardt change 4.34, $p < 0.001$). EGJOO ($p = 0.01$) and frequency of hypercontractile swallows ($p = 0.02$) were predictors of POEM failure. The development of a pseudodiverticulum was observed in four cases within the subgroup of EGJOO.

Conclusions: Patients with symptomatic Jackhammer without EGJOO benefit from POEM in long-term follow-up. Treatment of Jackhammer with EGJOO, however,

Present addresses
Christian Gerges and Brigitte Schumacher, University Hospital of Essen, Essen, Germany.
Jennis Kandler, University Hospital of Düsseldorf, Düsseldorf, Germany.

remains challenging and probably requires full sphincter myotomy and future studies which should address the pathogenesis of this variant and alternative strategies.

KEYWORDS
adverse events, Eckardt score, esophagogastric junction outflow obstruction (EGJOO), failure, Jackhammer esophagus, lower esophageal sphincter (LES), motility, peroral endoscopic myotomy (POEM)

INTRODUCTION

Hypercontractile esophagus (HE)—commonly called Jackhammer esophagus (JE)—is a rare but clinically relevant non-achalasia spastic disorder that is considered a major disorder of peristalsis in the Chicago Classification (CC).[1,2] Current understanding of its pathophysiology is incomplete. Hypercontraction is supposed to be related to excessive cholinergic excitatory activity and an impaired synchronization of the circular and longitudinal muscle layer.[3,4] Provocative testing using multiple rapid swallows suggests that abnormal neural inhibition plays a further role, but this applies not to all JE-patients.[5] Symptomatic patients with hypercontractile esophagus primarily have dysphagia and chest pain.[1,6,7] Over time, symptoms spontaneously resolve in some patients,[8,9] whereas others show a progression to achalasia subtype III.[10] The determinants of such different clinical presentations are unknown but could be essential for well-founded indications. Overall, HE comprises a heterogeneous group of entities that potentially respond to therapeutic options differently. Especially, the involvement of the lower esophageal sphincter (LES) is still a matter of debate, as esophageal hypercontractility can manifest with or without esophagogastric junction outflow obstruction (EGJOO).[6,7,11] The impact of EGJOO in patients with Jackhammer esophagus on therapeutic interventions is not known.

Treatment options for HE comprise conservative (e.g., calcium channel blockers) as well as endoscopic approaches. Medical therapy has been shown to be inferior to endoscopic interventions (62.6% vs. 79.4%).[12] The latter include botulinum toxin injection or pneumatic dilation, which aim to lower the contractility vigor of the LES, but the optimal treatment approach is unknown.[6,7,12,13] Although successful peroral endoscopic myotomy (POEM) has been associated with increased symptom relief in short-term follow-up, data on long-term clinical outcomes, albeit positive, remains limited to cohort studies with mixed-disease groups including achalasia type III and small sample sizes.[14–28] In this retrospective multicenter study, we aimed to evaluate POEM in patients with Jackhammer esophagus after a minimum follow-up of 2 years.

Key summary

Established knowledge on this subject?

- Patients with non-achalasia esophageal motility disorders benefit from peroral endoscopic myotomy (POEM).

What are the significant and/or new findings of this study?

- Heterogenity in patients with hypercontractile/Jackhammer esophagus influences the treatment outcome.
- Esophagogastric junction outflow obstruction is an independent risk factor for POEM failure if the cut is not extended distally into the cardia, as in achalasia.
- Repeat interventions maintain symptom improvement over time compared to baseline in failure cases.

METHODS

Study population and method of analysis

This observational cohort study in seven European centers was approved by the local ethics committee at each participating center (Hamburg Chamber of Physician reference number PV 5775). Patients who underwent POEM (as primary myotomy technique) for non-achalasia spastic motility disorder up to November 2018 (study inclusion endpoint) were included based on initial chart review.

A *motility review committee* (YW, TR) headed by an external expert (JP) reviewed the diagnosis and manometric tests of all eligible patients (n = 86; see also Figure S1). After review, the following groups were formed;

a. All patients with hypercontractile (Jackhammer) esophagus, according to the Chicago Classification v3.0,[2] were included in the study and analyzed except patients with an Eckardt Score ≤3, a surgical history (fundoplication), and/or previous myotomy. We subdivided the patients into two groups based on their high-resolution manometric results pre-POEM:
   a) We defined Jackhammer esophagus as ≥20% hypercontractile swallows with a distal contractile integral (DCI) >8000 mmHg s cm and an integrated relaxation pressure (IRP) of ≤15 mmHg.
   b) We used the definition of Jackhammer esophagus with an EGJOO in patients with ≥20% hypercontractile swallows with a DCI >8000 mmHg s cm and an elevated IRP of >15 mmHg in the absence of an anatomical abnormality. In the updated Chicago classification, the correct definition would be EGJOO with hypercontractile features (Jackhammer esophagus).

b. We further classified patients with Jackhammer esophagus into a third group. Although the reviewed manometric test pre-POEM did not meet the criteria of ≥20% hypercontractile swallows, but the diagnosis was reasonable as these patients were under treatment, changed manometric patterns spontaneously, or were tested conventionally.

All patient information was anonymized for analysis. Part of the data of five cases from Essen[22] and seven from Hamburg[29] were previously reported in a different context, partially only with regard to adverse events (AE) that occurred with the POEM technique.[29]

POEM workup, POEM procedure and follow-up

The pre-procedural symptom severity was assessed by the Eckardt symptom score (0–12) as reported elsewhere.[30–32] All patients underwent pre-procedural high-resolution manometry (HRM) performed under local anesthesia to exclude normal motility and to define the extent of hypercontractility in the tubular esophagus. A calibrated solid-state manometric catheter with 4.2- or 3.7-mm diameter and closely spaced circumferential pressure sensors at 1 cm intervals over 36 cm (Medtronic GmbH, or Standard Instruments GmbH) was placed transnasally in order to provide simultaneous recording from the hypopharynx to the stomach. The swallow protocol included baseline recording and ten 5-mL swallows in a supine position using water or saline, each swallow time separated by 30-s intervals.

All POEM procedures were performed by interventional gastroenterologists with extensive experience.[29,32,33] Myotomy was started at the most proximal point of the hypercontractile segments determined by prior HRM using a tailored approach and measured on endoscopy (cm from LES upwards), and circular myotomy was performed in all patients continuously down to the LES, which was included, but usually not extended into more than 1 cm into the cardia.

A double dose of proton-pump inhibitor (PPI) was administered postprocedural and continued for two weeks and prolonged when indicated due to heartburn. Re-evaluation of clinical symptoms, including reflux and endoscopy, was performed 1–6 months following the POEM procedure, 12–24 months, and after 24 months. A HRM was routinely recommended in cases of symptom persistence or recurrence.

Technical success was defined as the successful completion of the POEM procedure. AE were primarily defined as any deviation of the standard course during or following the POEM procedure[29]; severity was then graded according to 2010 ASGE guidelines[34] and the more recent AGREE classification.[35]

A *clinical treatment failure* was defined as an Eckardt Symptom score greater than three at the last follow-up evaluation or additional interventional treatment during follow-up.

The *overall clinical improvement* was defined as an Eckardt Symptom score equal to or less than three at the last follow-up evaluation regardless of any additional interventional treatment during follow-up.

Statistical analysis

Continuous data are reported as mean with standard deviation (SD) or median with interquartile range (IQR, first and third quartiles). Categorial variables are expressed as counts and proportions. Continuous variables were checked for normal distribution using the Shapiro–Wilk test. A comparison between study groups was done using the Fisher's Exact Test for categorial and the Student's *t*-test, Mann-Whitney-*U*-test, or Wilcoxon-test for continuous variables. We used a multivariate logistic regression model, which was chosen of the goodness of fit, including age, sex, and baseline variables that differed significantly in the univariate analyses to identify the independent predictors of failure cases. Two-sided *p*-values less than 0.05 were considered significant. *p* values were reported without correction for multiple testing. Data analysis was performed using the statistical software package R, version 4.0.5 (R Foundation for Statistical Computing).[36]

RESULTS

Of 1658 patients treated with POEM until November 2018 in the seven centers, a total of 53 patients were treated for symptomatic hypercontractile (Jackhammer) esophagus. Figure S1 shows the study flow chart: 42 patients with the unequivocal diagnosis of Jackhammer esophagus, including two subgroups with or without EGJOO, were included in our analysis after re-review of manometry.

Study population

Baseline characteristics of the study patients and the two subgroups are summarized in Table 1. In the total group (n = 42), the mean Eckardt symptom score was 6.2 ± 2.1, mainly due to dysphagia (2.2 ± 0.7) and chest pain (1.8 ± 1.0). Medical or interventional endoscopic treatment was performed in 42.9% of patients before POEM, and one-third took daily PPI at baseline. HRM differences between the two subgroups are also outlined in Table 1; the mean IRP and the mean number of hypercontractile swallows were significantly different.

A third group (group 3) consisted of eight patients. Their re-reviewed manometric findings prior to POEM did not meet the criteria confirming a hypercontractile motility pattern as defined before, although these patients were symptomatic (four female, mean age 48.8 ± 8.6 years, mean Eckardt score 5.8 ± 2.7, mean IRP 10.7 ± 4.1 mmHg, mean DCI 4304 ± 2304 mmHg s cm) and the written report of the index manometry suspected a Jackhammer esophagus. Seven of these eight patients have already undergone

TABLE 1 Baseline patient characteristics.

	All	Jackhammer without EGJOO	Jackhammer with EGJOO	*p*-Value
Patients	42	22 (52.4)	20 (47.5)	
Age, years	60.9 ± 13.1	59.1 ± 13.4	62.9 ± 12.8	0.36
Female, %	24 (57.1)	10 (45.5)	14 (70.0)	0.10
BMI, kg/m^2	26.4 ± 5.9	26.7 ± 7.2	26.1 ± 4.3	0.76
Eckardt symptom score	6.2 ± 2.1	6.2 ± 1.8	6.2 ± 2.4	0.92
Dysphagia	2.2 ± 0.7	2.2 ± 0.8	2.2 ± 0.7	0.90
Regurgitation	1.5 ± 0.9	1.4 ± 1.0	1.6 ± 0.9	0.51
Chest pain	1.8 ± 1.0	1.9 ± 1.0	1.7 ± 1.0	0.49
Weight loss	0.7 ± 1.1	0.6 ± 1.0	0.7 ± 1.1	0.85
Symptom duration, months	36 [12;75]	36 [16;84]	18 [12;66]	0.22
Previous treatment				
Medical therapy (calcium-channel blocker)	11 (26.2)	6 (27.3)	5 (25.0)	1
Pneumatic dilation	4 (9.5)	1 (4.6)	3 (15.0)	1
Botulinum toxin injection	10 (23.8)	7 (31.8)	3 (0.2)	0.50
Gastroesophageal reflux disease				
Symptoms				
Heartburn	15 (38.5)	5 (25.0)	10 (52.6)	0.20
Medical therapy (PPI)				
Intermittent	6 (14.3)	4 (18.2)	2 (10.0)	0.60
Daily	14 (33.3)	5 (22.7)	9 (45.0)	0.40
Endoscopy				
Refluxesophagitis LA grade A/B	9 (21.4)	6 (27.3)	3 (15.0)	0.50
Barrett-esophagus	Nil			
Hernia (EGD or HMR)	18 (42.9)	8 (36.4)	10 (50)	0.50
High-resolution manometry				
Number of hypercontractile swallows	*N* = 4 [3;8]	*N* = 3 [2;7]	*N* = 6 [3;8]	**0.015**
Length of hypercontractile segment from LES, cm	13.9 ± 3.8	14.5 ± 5.0	13.2 ± 1.5	0.28
Maximal DCI, mmHg s cm	18,584.9 ± 10,905.2	17,759.7 ± 10,265.3	19,492.6 ± 11,768.5	0.62
Mean DCI, mmHg s cm	9744.7 ± 8430.8	8177.5 ± 4248.5	11,468.6 ± 11,289.7	0.23
Multi-peaked contraction	34 (82.9)	17 (77.3)	17 (89.5)	0.40
Integrated relaxation pressure, mmHg	15.7 ± 8.5	9.3 ± 4.8	22.8 ± 5.3	**<0.001**

Note: Variables are mean and standard deviation, median [first; third quartile] or *n* (%). Bold values indicate *p* values <0.05.

Abbreviations: BMI, body mass index; DCI, distal contraction integral; EGD, esophagogastroduodenoscopy; EGJOO, esophagogastric junction outflow obstruction; HRM, high-resolution manometry; LA, Los Angeles classification; LES, lower esophageal sphincter; PPI, proton-pump inhibitor.

medical (*n* = 5) and/or endoscopic treatment (*n* = 7) before being referred to POEM. In this group of excluded patients, long-term clinical success was achieved in 3 (37.5%) patients after a mean follow-up of 41.8 ± 15.4 months (mean Eckardt score 3.8 ± 2.8, mean GIQLI 104.7 ± 20.3). Two out of the remaining failed patients were retreated with repeat POEM or botulinum injection.

Procedures, technical success and adverse events

Table 2 shows the procedural data, including the frequency and grade of AE. Jackhammer patients without EGJOO received a slightly shorter myotomy and had significantly fewer periprocedural events (4.6% vs. 35%, *p* = 0.02). AE are detailed in Tables S1 and S2; no

TABLE 2 Procedural data.

	All	Jackhammer without EGJOO	Jackhammer with EGJOO	*p*-Value
Patients	42	22	20	
Procedure time, min	107.4 ± 48.9	107.5 ± 45.5	107.4 ± 53.5	1
Myotomy length, cm	16.2 ± 3.7	15.5 ± 4.1	17.0 ± 3.1	0.20
Transcutaneous capnoperitoneum puncture	18 (42.9)	9 (40.9)	9 (45.0)	1
Technical success	42 (100)	22 (100)	20 (100)	1
Events				
Intraprocedural events	8 (19.0)	1 (4.6)	7 (35.0)	**0.02**
Post-procedure (in-hospital)	7 (16.6)	4 (18.2)	3 (10.0)	1
Fever >38.0°C	7 (17.1)	4 (19.1)	3 (15.0)	1
Adverse events, severity[a]				
Severe	0	0	0	
Moderate	8 (19.0)	3 (13.6)	5 (25.0)	0.45
Mild	1 (2.4)	1 (4.5)	0	1
Hospitalization time, days	4.8 ± 2.5	4.9 ± 3.0	4.8 ± 1.9	0.85
	Pre | post	**Pre | post**		**Pre | post**
Hemoglobin, g/L	13.6 | 12.6	13.7 | 12.6		13.5 | 12.6
White cell count, 10^9/L	7.8 | 11.0	8.3 | 11.4		7.2 | 10.5
C-reactive protein, mg/L	4.7 | 79.4	5.0 | 76.1		4.3 | 82.9

Note: Variables are mean and standard deviation or *n* (%). Bold values indicate *p* values <0.05.

Abbreviation: EGJOO, esophagogastric junction outflow obstruction.

[a]According to 2010 ASGE definitions (see Ref. 29), details in Table S1.

severe AE occurred, but the rate of moderate and mild AE was 21.4% ($n = 9$) overall.

Clinical results

After a mean follow-up of 46.5 ± 19.0 months, 27 (64.3%) Jackhammer patients (*groups 1 and 2*) still benefitted from the POEM procedure (Table 3). Three patients (all were older than 75 years) died during follow-up at 24, 70, and 72 months unrelated to the POEM procedure. Comparing the two groups, only 3 of 22 (13.6%) patients without EGJOO had a recurrence of symptoms, whereas 12 of 20 (60%) patients with EGJOO failed due to persistent or recurrent symptoms in 4 and 6 cases, and due to severe gastroesophageal reflux in two further cases during follow-up ($p = 0.003$, Figure 1a, Table 3). Further treatments for the initial failures are described in the Supporting Information S1.

An overall clinical improvement of the symptom severity over time was observed in 33 (78.6%) of 42 patients. These patients reported an Eckardt symptom score ≤3 at latest follow-up. The mean Eckardt symptom score was reduced to 1.7 ± 2.2 (mean Eckardt change 4.34, $p < 0.001$; Figure 1b) at the end of follow-up (37.9 ± 20.4 months after the last reintervention) with the inclusion of all retreatment effects.

In this cohort of 42 patients (groups 1 and 2), multivariate analyses identified a hypercontractile (Jackhammer) esophagus with EGJOO (odds ratio: 12.9; $p = 0.01$) and an increased number of hypercontractile swallows on HRM at baseline ($n = 6$ vs. $n = 3$, odds ratio: 71.1; $p = 0.02$) as independent risk factors for the development of failure following POEM.

Manometric follow-up

A manometric follow-up was available in 29 of the 42 patients (69%), with a reduction of the maximal (mean change: 16,358.0 mmHg s cm) and mean DCI (mean change: 9691 mmHg s cm) were documented; the mean IRP was reduced from 15.7 ± 8.5 to 11.9 ± 7.7 mmHg (Table S3).

Details of retreatment of initial failures

Fourteen of 15 failed patients were retreated, 6 (14.3%) patients received more than one additional treatment during follow-up.

TABLE 3 Main treatment outcomes.

	All	Jackhammer without EGJOO	Jackhammer with EGJOO	*p*-Value
Patients	42	22	20	
Mean FU time	46.5 ± 19.0	48.7 ± 20.6	45.4 ± 8.0	0.44
Eckardt symptom score	1.7 ± 2.2	1.2 ± 2.1	2.2 ± 2.3	0.16
Success	27 (64.3)	19 (86.4)	8 (40.0)	
Failure	15 (35.7)	3 (13.6)	12 (60.0)	**0.003**
Early failure caused by persistent symptoms	4 (9.5)	-	4 (20.0)	0.50
Late failure caused by symptom recurrence	9 (21.4)	3 (13.6)	6 (30.0)	0.20
Failure caused by GERD	2 (4.8)	-	2 (10.0)	0.22
Additional treatment	14 (33.3)	3 (13.6)	11 (55.0)	**0.008**
One additional treatment	9 (21.4)	1 (4.5)	8 (40.0)	**0.008**
Two additional treatments	3 (7.1)	1 (4.5)	2 (10.0)	0.60
>2 additional treatments	2 (4.8)	1 (4.5)	1 (5.0)	1
Retreatment due to persistence or recurrence	12 (28.6)	3 (13.6)	9 (45.0)	**0.04**
GERD treatment	2 (4.8)	-	2 (10.0)	0.22
Initial retreatment therapy				
Pneumatic dilation	5 (11.9)	1 (4.5)	4 (20.0)	0.14
Botulinum toxin injection	2 (4.8)	-	2 (10.0)	0.22
Combined dilation and botulinum injection	3 (7.1)	2 (9.0)	1 (5.0)	1
Re-POEM	2 (4.8)	-	2 (10.0)	0.22
Surgery for GERD	2 (4.8)	-	2 (10.0)	0.22
Second retreatment therapy				
Re-combined dilation and botulinum injection	1 (2.4)	-	1 (5.0)	0.48
Endoscopic stent implantation following combined dilation and botulinum injection	1 (2.4)	1 (4.5)	-	1
Re-POEM following botulinum injection	2 (4.8)	-	2 (10.0)	0.22
Surgery (esophagectomy) following surgical GERD therapy	1 (2.4)	-	1 (5.0)	0.48
Further retreatment therapy				
Surgery (LHM) following endoscopic stent implantation	1 (2.4)	1 (4.5)	-	1
Dilatation, botulinum, re-re-POEM following botox and re-POEM	1 (2.4)	-	1 (5.0)	0.48

Note: Variables are mean and standard deviation, or *n* (%). Bold values indicate *p* values <0.05.

Abbreviations: EGJOO, esophagogastric junction outflow obstruction; FU, follow-up; GERD, gastroesophageal reflux disease; LHM, laparoscopic Heller myotomy; POEM, peroral endoscopic myotomy.

Alternative strategies were used as the initial failure treatment: A surgical partial fundoplication was performed in the two cases of post-POEM gastroesophageal reflux-associated failures. In one case it has been combined with a hiatoplasty without a further re-myotomy, the other was re-myotomized at the same procedure according to a laparoscopic Heller myotomy (LHM). A re-fundoplication was recommended in the one case two years later, and esophagectomy following LHM was performed in the other case after 3.75 years. Two patients underwent a repeat POEM; pneumatic dilation was conducted in five patients as monotherapy and in three patients combined with the injection of botulinum toxin. One patient with a failed combined dilation and botulinum injection therapy followed by an unsuccessful endoscopic stent implantation, was referred for surgery (LHM). A sole botulinum injection was performed in two patients; both were retreated with re-POEM in their further course (at 8 and 25 months after the botulinum injection) (Table 3). Overall, four patients (all with EGJOO) underwent a repeat POEM therapy during follow-up. Three patients underwent surgery, respectively.

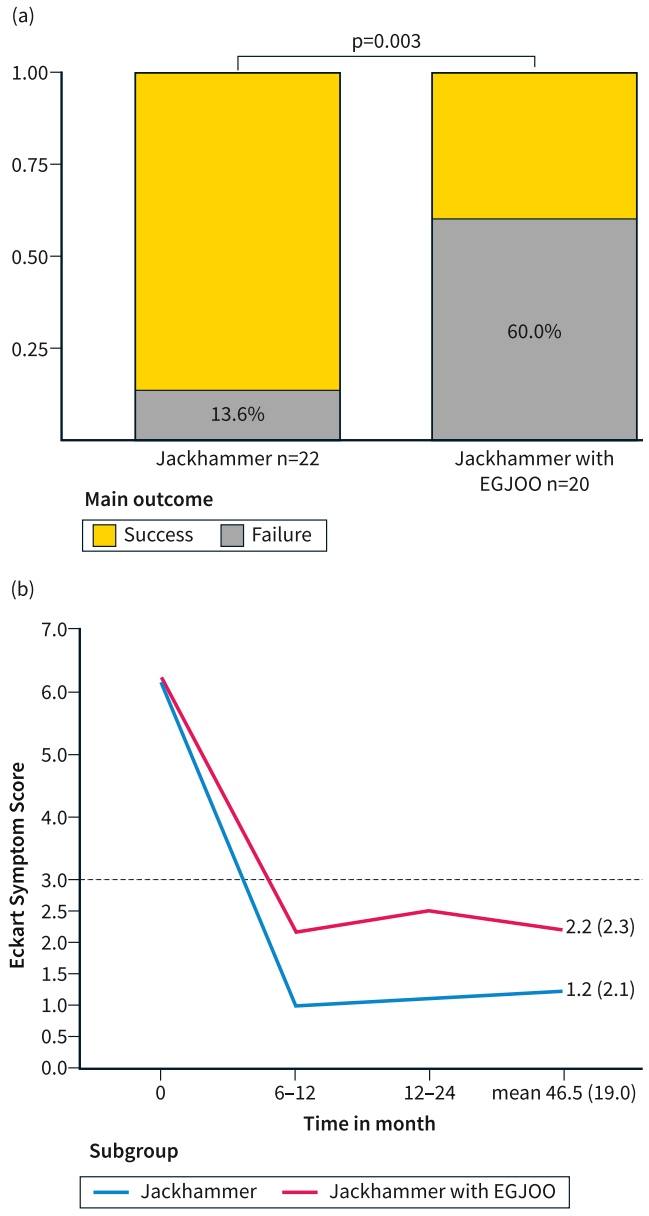

FIGURE 1 Comparison of the two groups of Jackhammer esophagus without and with EGJOO: Failure rates at mean follow-up (46.5 ± 19.0 months) (a) and Eckardt-symptom-score over time among the study groups (b). EGJOO, esophagogastric outflow obstruction.

Long-term sequelae: Reflux and diverticula/blown-out-myotomy

Following POEM, heartburn was observed in 27 out of 41 (65.9%) patients, and more than half of the patients (53.7%) took PPI daily at the end of follow-up. The rate of reflux esophagitis, overall 25%, was similar compared to the baseline data (Tables S1 and S3).

Formation of a *pseudodiverticulum* in the distal esophagus was observed in 4 patients (9.5%) within 9 months post-POEM, all belonging to the study group of Jackhammer patients with EGJOO, that is, 20% (4/20) in this subgroup. Figure 2 shows the typical findings in one of these patients. Three patients remained symptomatic at 1, 3, and 6 months following POEM. Two patients had residual contractile activity above the myotomy and an incomplete myotomy distally, clearly demonstrated by HRM. They were retreated with POEM as the sole strategy at 12 months post-POEM, and surgery at 17 months after initial endoscopic retreatment (combined PD/botulinum at 1 month-FU followed by stent implantation at 9 months-FU), respectively. Graded pneumatic dilation (30/35 mm diameter) at 8 and 9 months-FU has sustainably improved symptoms in one patient, although an incomplete myotomy was not proven by HRM. Instead, a small hiatal hernia was present. The fourth patient had no complaints throughout his follow-up (60 months). Manometric findings at 3 months follow-up showed no contractile activity; a small hernia was at most only present.

DISCUSSION

This multicenter study retrospectively investigated the long-term effect of POEM in patients with symptomatic hypercontractile (Jackhammer) esophagus. The key findings are (i) POEM success rates were significantly lower in patients with EGJ outflow obstruction (40% vs. 86%), (ii) beneficial long-term clinical improvement can be achieved in the majority of the Jackhammer patients with 78% overall success after a mean follow up 46.5 months, regardless of any additional therapy, (iii) the POEM procedure was more demanding in patients with than without EGJ outflow obstruction, that affected the safety and the outcome, (iv) predictors of POEM failure included the presence of EGJ outflow obstruction and frequency of hypercontractile swallows, and (v) the formation of pseudodiverticulum post-POEM was notably observed in some patients with EGJ outflow obstruction.

All of these findings are subject to additional considerations. The first issue is the role of EGJ outflow obstruction in the setting of the Jackhammer esophagus. There is quite some heterogeneity in manometrical findings: Different studies report on the involvement of the LES in patients with HE with somewhat different results. The study by Herregods et al. observed an association between dysphagia and the participation of the LES.[37] In contrast, Kahn et al. suggested no distinction in outcome and symptom-scoring for LES-independent and LES-dependent patient subgroups.[38] Nevertheless, the study by Roman et al. showed a significantly higher IRP in non-multipeaked HE than in a multipeaked cohort.[39] A recent multicentre study[7] and a meta-analysis[12] found that an EGJOO occurred in HE patients in 10% and 24.1% of cases, respectively. The current iteration of the CC[1] does not recommend subdividing HE based on involvement of the LES due to a lack of evidence for clinical differences between these groups. But the participation of the LES may be crucial for therapeutic considerations.

Although this is a retrospective multicenter series without study-specific standardization of technique, all centers performed LES myotomy in these cases. However, they usually did so without the 2–3 cm extension into the cardia, as standard in achalasia,

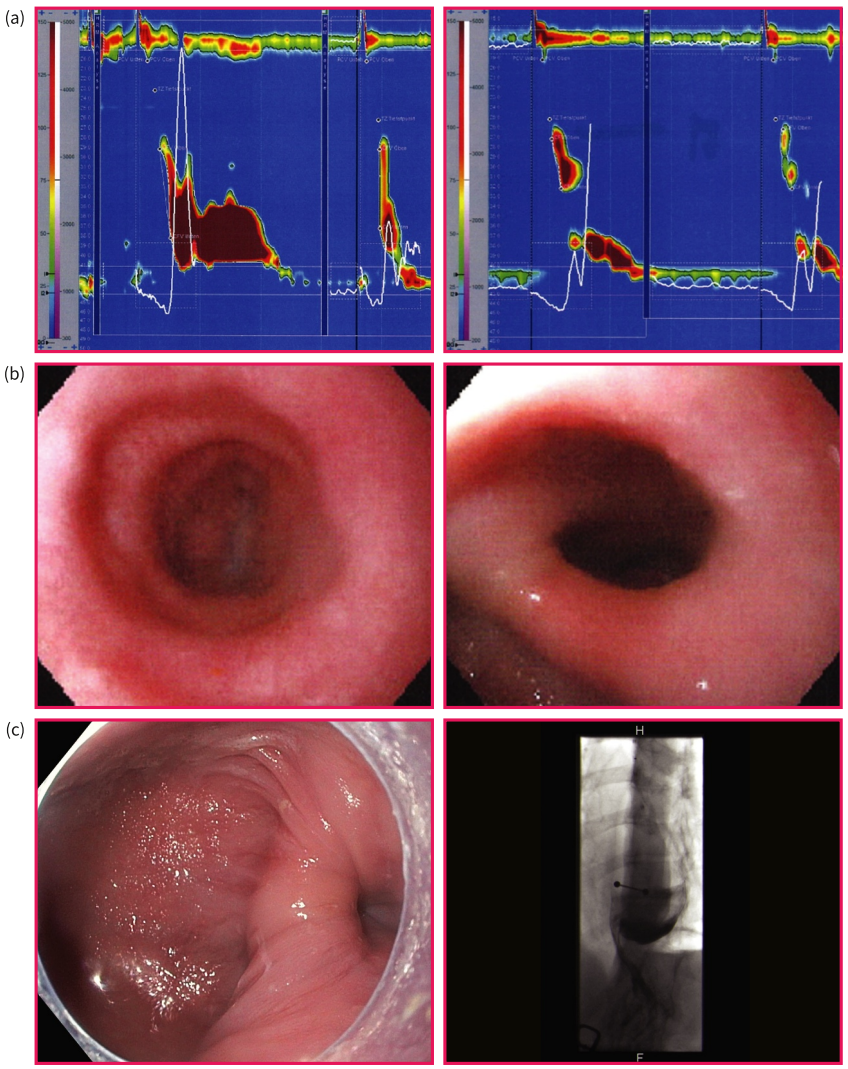

FIGURE 2 Development of a pseudodoverticulum following POEM in a Jackhammer patient with EGJOO. (a) In contrast to pre-POEM, the HRM control at 3 month FU that shows residual contractility above the area of myotomy and in the distal part corresponding to an incomplete myotomy. (b) The esophagus was undilated at baseline, whereas the 3 month control suggests a slight edge in the distal esophagus. (c) Endoscopy and esophagogram clearly show the progression of the pseudodiverticulum or blown-out myotomy at 12 month follow-up. This patient underwent repeat POEM. EGJOO, esophagogastric junction outflow obstruction; FU, follow-up; HRM, high-resolution manometry; POEM, peroral endoscopic myotomy.

including type III. It can thus only be speculated whether such an extension would have improved the results in this subgroup, as it is suggested by the subgroup's high rate of post-POEM pseudodiverticula (20%) as supported by a small case series.[16] Furthermore, retreatment of these EGJOO cases with other achalasia therapies raised success rates to almost 80% within the limited retreatment follow-up available. Therefore, we cannot know whether these cases represent different disease states or varying degrees of severity or differences in anatomy. Another point is that spontaneous symptom resolution is described in HE patients,[9] so these types of patients in our cohort could not have benefitted from the intervention. How large the proportion of these patients is cannot be estimated but should be equally distributed in our study subgroups.

In the literature summarized in Table 4, most (but not all) papers, most of which reported on a mixed patient collective, extended myotomy 2–3 into the cardia, although none did subdifferentiate between the different groups (Table S4). Nevertheless, we suggest extending myotomy as in type III achalasia, at least in cases with Jackhammer and distal outflow obstruction.

On the other hand, there seem to be more factors than just distal outflow obstruction. Higher frequencies of hypercontractile swallows (another significant factor in the multivariate analysis) may represent a more severe degree of disease. They might also lead to a more difficult and complex procedure that, in consequence, may be prone to an incomplete myotomy or increased post-POEM fibrosis.

In the literature, as mentioned, success and complication rates of POEM for spastic disorders are primarily described in mixed series

TABLE 4 Results of case reports/case series of adult patients with Jackhammer esophagus focusing on papers with non-achalasia motility disorders.

Author	Jackhammer cases	All non-achalasia spast. disorders	Achalasia type III	F-up	Results for Jackhammer (if reported separately)
Ko et al. 2014[14]	*N* = 1	0	0	3 months	Improvement
Khashab et al. 2015[15]	*N* = 10	*N* = 9	*N* = 54	8 months	No separate analysis
Bechara et al. 2016[16]	*N* = 4	0	0	3 months	1 failure (no LES cut)
Kandulski et al. 2016[17]	*N* = 1	0	0	6 months	Recurrence
Dawod et al. 2017[18]	*N* = 1	0	0	1 month	Significant improvement
Khashab et al. 2018[19]	*N* = 18	*N* = 32	0	9 months	No separate analysis of Jackhammer
Filicori et al. 2019[20]	0	*N* = 40[a]	0	48 months	90% improvement in Eckardt, no separate analysis
Choi et al. 2019[21]	*N* = 2	0	0	6/12 months	All good
Albers et al. 2018[22]	*N* = 6	0	*N* = 7	15 months	No separate analysis
Bernardot et al. 2020[23]	*N* = 13	*N* = 17	*N* = 30	6 months	No separate analysis (all NAMS together)
Nabi et al. 2021[24]	*N* = 10	*N* = 11	*N* = 53	47 months[b]	83% success "at short-term f-up"
Nakamura et al. 2021[25,c]	*N* = 1	0	*N* = 9	2 years	No separate analysis of Jackhammer case
Canakis et al. 2002[26]	*N* = 13	0	0	16 months	92% success rate (Eckardt 1.5)
Estremera et al. 2022[27]	*N* = 0	*N* = 7	0	10–44 months	Eckardt improvement in all cases
Hosaka et al. 2022[28]	*N* = 21	0	0	n.r.	76% of those with f-up (n.r.) improved[d]

Abbreviations: Eckardt, Eckardt symptom score; f-up, follow-up; LES, lower esophageal sphincter; NAMS, non-achalasia motility disorder; n.r., not reported.

[a]Consisting of 15 hypercontractile esophagi (no further definition), 11 distal esophageal spasms and 14 esophagogastric outflow obstructions.

[b]Only available for 57% of cases, not further specified.

[c]Patients >75 years of age.

[d]Only 21/87 treated by POEM; 13 received no therapy, 10 resolved spontaneously.

with low numbers, short follow-up, and/or no detailed analyses of specific subgroups, especially of non-achalasia motility disorders (Summary in Table 4[14–28] or in meta-analyses[12,40,41]). It appears, however, that most of these papers did not report results for Jackhammer esophagus separately or in detail in manometric analysis, so there were usually analyzed together with other non-achalasia motility disorders or even together with achalasia type III (see Table 4). Only one study reporting on the subgroup of Jackhammer patients had a follow-up longer than one year, although some/most patients did not seem to have reached the stated follow-up of 48 months.[24] Another series with long-term follow-up (47 months) included 15 patients with HE but reported the results combined with other non-achalasia motility disorders.[20]

Another issue is the relatively high rate of AE, mostly graded moderate or mild according to ASGE definition,[34] or the AGREE classification[35] (see Table 2, and details in Tables S1 and S2). Notably, more intraprocedural events were observed in patients with EGJOO. In terms of our observation of late AEs, blown-out myotomy was noted in four patients and is consistent with the model and clinical description observed in treated achalasia patients by Triggs et al.[42] in two cases. Despite complete myotomy, the presence of hiatal hernia may have caused the problem in the other two patients.

The focus on the first event (clinical treatment failure) is the standard measure in POEM trials to report the effect of POEM treatment, entitled as success rate.[31,32] Hypercontractile motility disorders are mostly chronic diseases and may remain a progressive condition. Therefore, we were also interested in exploring the POEM effect across the last reported Eckardt Symptom score in comparison to baseline regardless of any repeated treatment, or period of discomfort during follow-up (defined as overall clinical improvement). These data may reflect both, the effect of POEM treatment and disease burden over time.

Natural limitations of retrospective and multicenter studies as in our series are well known: The POEM technique was not precisely and study-specifically standardized, although, even prospectively, the length of myotomy would have required some sophisticated additional methodology. Also, patient symptom documentation may have varied as well as follow-up tests were not consistently performed, which we share with all other case series. However, the reassessment of findings by an international expert involved in the introduction and further development of the Chicago classification (JP) may be a significant advantage of our paper.

Despite these limitations, we conclude that in patients with hypercontractile (Jackhammer) esophagus, the presence of EGJOO

faces a higher risk of POEM failure. It seems that the limited myotomy, which was performed in the study patients, did not prevent symptom recurrence. It is therefore suggested to add conventional myotomy up to 2–3 cm into the cardia as in patients with achalasia type III. These data highlight the need for future studies within this patient group, as heterogeneity of their motility pattern exists.

ACKNOWLEDGMENTS

We thank the Hamburger Foundation für Wissenschaften, Entwicklung und Kultur Helmut und Hannelore Greve (Hamburg, Germany) and the Dr. med. Carl-August Skröder Foundation (Hamburg, Germany) for their generous support of our POEM research.

Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST STATEMENT

There were no conflicts of interest for any of the authors in relation to the study topic.

DATA AVAILABILITY STATEMENT

Data are available in pseudonymized form upon request.

ORCID

David Albers https://orcid.org/0000-0003-1507-4590
Thomas Rösch https://orcid.org/0000-0003-2270-2495
Christian Gerges https://orcid.org/0000-0001-8271-1102

REFERENCES

1. Yadlapati R, Kahrilas PJ, Fox MR, Bredenoord AJ, Prakash Gyawali C, Roman S, et al. Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0(©). Neuro Gastroenterol Motil. 2020;33(1):e14058. https://doi.org/10.1111/nmo.14058
2. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, Smout AJPM, et al. The Chicago Classification of esophageal motility disorders, v3.0. Neuro Gastroenterol Motil. 2015;27(2):160–74. https://doi.org/10.1111/nmo.12477
3. Jung HY, Puckett JL, Bhalla V, Rojas-Feria M, Bhargava V, Liu J, et al. Asynchrony between the circular and the longitudinal muscle contraction in patients with nutcracker esophagus. Gastroenterology. 2005;128(5):1179–86. https://doi.org/10.1053/j.gastro.2005.02.002
4. Korsapati H, Bhargava V, Mittal RK. Reversal of asynchrony between circular and longitudinal muscle contraction in nutcracker esophagus by atropine. Gastroenterology. 2008;135(3):796–802. https://doi.org/10.1053/j.gastro.2008.05.082
5. Mauro A, Quader F, Tolone S, Savarino E, De Bortoli N, Franchina M, et al. Provocative testing in patients with jackhammer esophagus: evidence for altered neural control. Am J Physiol Gastrointest Liver Physiol. 2019;316(3):G397–403. https://doi.org/10.1152/ajpgi.00342.2018
6. de Bortoli N, Gyawali PC, Roman S, Tolone S, Sifrim D, Tutuian R, et al. Hypercontractile esophagus from pathophysiology to management: proceedings of the pisa symposium. Am J Gastroenterol. 2021;116(2):263–73. https://doi.org/10.14309/ajg.0000000000001061
7. Philonenko S, Roman S, Zerbib F, Gourcerol G, Gault N, Ropert A, et al. Jackhammer esophagus: clinical presentation, manometric diagnosis, and therapeutic results - results from a multicenter French cohort. Neuro Gastroenterol Motil. 2020;32:e13918. https://doi.org/10.1111/nmo.13918
8. Mion F, Marjoux S, Subtil F, Pioche M, Rivory J, Roman S, et al. Botulinum toxin for the treatment of hypercontractile esophagus: results of a double-blind randomized sham-controlled study. Neuro Gastroenterol Motil. 2019;31(5):e13587. https://doi.org/10.1111/nmo.13587
9. Schupack D, Katzka DA, Geno DM, Ravi K. The clinical significance of esophagogastric junction outflow obstruction and hypercontractile esophagus in high resolution esophageal manometry. Neuro Gastroenterol Motil. 2017;29(10):1–9. https://doi.org/10.1111/nmo.13105
10. Huang L, Pimentel M, Rezaie A. Do Jackhammer contractions lead to achalasia? A longitudinal study. Neuro Gastroenterol Motil. 2017;29(3):e12953. https://doi.org/10.1111/nmo.12953
11. Quader F, Mauro A, Savarino E, Tolone S, de Bortoli N, Franchina M, et al. Jackhammer esophagus with and without esophagogastroc junction outflow obstruction demonstrates altered neural control resembling type 3 achalasia. Neuro Gastroenterol Motil. 2019;31(9):e13678. https://doi.org/10.1111/nmo.13678
12. Wahba G, Bouin M. Jackhammer esophagus: a meta-analysis of patient demographics, disease presentation, high-resolution manometry data, and treatment outcomes. Neuro Gastroenterol Motil. 2020;32(11):e13870. https://doi.org/10.1111/nmo.13870
13. Vanuytsel T, Bisschops R, Farré R, Pauwels A, Holvoet L, Arts J, et al. Botulinum toxin reduces Dysphagia in patients with nonachalasia primary esophageal motility disorders. Clin Gastroenterol Hepatol. 2013;11(9):1115–21.e2. https://doi.org/10.1016/j.cgh.2013.03.021
14. Ko WJ, Lee BM, Park WY, Kim JN, Cho JH, Lee TH, et al. Jackhammer esophagus treated by a peroral endoscopic myotomy. Korean J Gastroenterol. 2014;64(6):370–4. https://doi.org/10.4166/kjg.2014.64.6.370
15. Khashab MA, Messallam AA, Onimaru M, Teitelbaum EN, Ujiki MB, Gitelis ME, et al. International multicenter experience with peroral endoscopic myotomy for the treatment of spastic esophageal disorders refractory to medical therapy (with video). Gastrointest Endosc. 2015;81(5):1170–7. https://doi.org/10.1016/j.gie.2014.10.011
16. Bechara R, Ikeda H, Inoue H. Peroral endoscopic myotomy for Jackhammer esophagus: to cut or not to cut the lower esophageal sphincter. Endosc Int Open. 2016;4(05):E585–8. https://doi.org/10.1055/s-0042-105204
17. Kandulski A, Fuchs KH, Weigt J, Malfertheiner P. Jackhammer esophagus: high-resolution manometry and therapeutic approach using peroral endoscopic myotomy (POEM). Dis Esophagus. 2016;29:695–6. https://doi.org/10.1111/dote.12182
18. Dawod E, Saumoy M, Xu MM, Kahaleh M. Peroral endoscopic myotomy (POEM) in Jackhammer esophagus: a trick of the trade. Endoscopy. 2017;49(10):E254e255. https://doi.org/10.1055/s-0043-115887
19. Khashab MA, Familiari P, Draganov PV, Aridi HD, Cho JY, Ujiki M, et al. Peroral endoscopic myotomy is effective and safe in non-achalasia esophageal motility disorders: an international multicenter study. Endosc Int Open. 2018;6(08):E1031e1036. https://doi.org/10.1055/a-0625-6288
20. Filicori F, Dunst CM, Sharata A, Abdelmoaty WF, Zihni AM, Reavis KM, et al. Long-term outcomes following POEM for non-achalasia motility disorders of the esophagus. Surg Endosc. 2019;33(5):1632–9. https://doi.org/10.1007/s00464-018-6438-z
21. Choi YI, Kim KO, Park DK, Chung JW, Kwon KA. Clinical outcomes and safety of high-resolution manometry guided superficial partial circular muscle myotomy in per-oral endoscopic myotomy for Jackhammer esophagus: two cases report. World J Clin Cases. 2019;7(16):2322–9. https://doi.org/10.12998/wjcc.v7.i16.2322

22. Albers D, Frieling T, Dakkak D, Kuhlbusch-Zicklam R, Töx U, Gittinger M, et al. Peroral endoscopic myotomy (POEM) is effective in treatment of noncardiac chest pain caused by hypercontractile esophageal motility disorders: results of the POEM-HYPE-Study. Z Gastroenterol. 2018;56(11):1337–42. https://doi.org/10.1055/a-0668-2605
23. Bernardot L, Roman S, Barret M, Vitton V, Wallenhorst T, Pioche M, et al. Efficacy of per-oral endoscopic myotomy for the treatment of non-achalasia esophageal motor disorders. Surg Endosc. 2020;34(12):5508–15. https://doi.org/10.1007/s00464-019-07348-y
24. Nabi Z, Chavan R, Ramchandani M, Basha J, Jagtap N, Karyampudi A, et al. Long-term outcomes of per-oral endoscopic myotomy in spastic esophageal motility disorders: a large, single-center study. J Clin Gastroenterol. 2021;55(7):594–601. https://doi.org/10.1097/mcg.0000000000001395
25. Nakamura J, Hikichi T, Hashimoto M, Takasumi M, Kato T, Kobashi R, et al. Efficacy and safety of peroral endoscopic myotomy for esophageal achalasia and achalasia-related diseases in patients aged 75 Years and over. Healthc (Basel). 2021;9(12):1668. https://doi.org/10.3390/healthcare9121668
26. Canakis A, Xie G, Kim RE. Peroral endoscopic myotomy is an effective treatment option for managing jackhammer esophagus: a single center experience. J Clin Gastroenterol. 2023;57(6):569–73.
27. Estremera-Arévalo F, González G, Areste I, et al. Outcomes of per-oral endoscopic myotomy in patients with spastic esophageal motility disorders not fulfilling Chicago Classification criteria. Rev Esp Enferm Dig. 2022:114(11):641–7.
28. Hosaka H, Kawami N, Manabe N, Kuribayashi S, Sato H, Funaki Y, et al. Clinical presentation and therapeutic outcome of patients with jackhammer esophagus-a multicenter cohort study in Japan. Esophagus. 2022;19(3):393–400. https://doi.org/10.1007/s10388-022-00916-7
29. Werner YB, von Renteln D, Noder T, Schachschal G, Denzer UW, Groth S, et al. Early adverse events of per-oral endoscopic myotomy. Gastrointest Endosc. 2017;85(4):708–718e2. https://doi.org/10.1016/j.gie.2016.08.033
30. Eckardt VF, Aignherr C, Bernhard G. Predictors of outcome in patients with achalasia treated by pneumatic dilation. Gastroenterology. 1992;103(6):1732–8. https://doi.org/10.1016/0016-5085(92)91428-7
31. Ponds FA, Fockens P, Lei A, Neuhaus H, Beyna T, Kandler J, Frieling T, et al. Effect of peroral endoscopic myotomy vs pneumatic dilation on symptom severity and treatment outcomes among treatment-naive patients with achalasia. A randomized clinical trial. JAMA. 2019;322(2):134–44. https://doi.org/10.1001/jama.2019.8859
32. Werner YB, Hakanson B, Martinek J, Repici A, von Rahden BH, Bredenoord AJ, et al. Endoscopic or surgical myotomy in patients with idiopathic achalasia. N Engl J Med. 2019;381(23):2219–29. https://doi.org/10.1056/nejmoa1905380
33. Von Renteln D, Fuchs KH, Fockens P, Bauerfeind P, Vassiliou MC, Werner YB, et al. Peroral endoscopic myotomy for the treatment of achalasia: an international prospective multicenter study. Gastroenterology. 2013;145(2):309–11.e1-3. https://doi.org/10.1053/j.gastro.2013.04.057
34. Cotton PB, Eisen GM, Aabakken L, Baron TH, Hutter MM, Jacobson BC, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc. 2010;71(3):446–54. https://doi.org/10.1016/j.gie.2009.10.027
35. Nass KJ, Zwager LW, van der Vlugt M, Dekker E, Bossuyt PM, Ravindran S, et al. Novel classification for adverse events in GI endoscopy: the AGREE classification. Gastrointest Endosc. 2022;95(6):1078–85.e8. https://doi.org/10.1016/j.gie.2021.11.038
36. Team RC. A language and environment for statistical computing. Vienna: Foundation for Statistical Computing; 2021. https://www.R-project.org/
37. Herregods TV, Smout AJ, Ooi JL, Sifrim D, Bredenoord AJ. Jackhammer esophagus: observations on a European cohort. Neuro Gastroenterol Motil. 2017;29(4). https://doi.org/10.1111/nmo.12975
38. Kahn A, Al-Qaisi MT, Obeid RA, Katzka DA, Ravi KM, Ramirez FC, et al. Clinical features and long-term outcomes of lower esophageal sphincter-dependent and lower esophageal sphincter-independent Jackhammer esophagus. Neuro Gastroenterol Motil. 2019;31(2):e13507. https://doi.org/10.1111/nmo.13507
39. Roman S, Pandolfino JE, Chen J, Boris L, Luger D, Kahrilas PJ. Phenotypes and clinical context of hypercontractility in high-resolution esophageal pressure topography (EPT). Am J Gastroenterol. 2012;107(1):37–45. https://doi.org/10.1038/ajg.2011.313
40. Chandan S, Mohan BP, Chandan OC, Jha LK, Mashiana HS, Hewlett AT, et al. Clinical efficacy of per-oral endoscopic myotomy (POEM) for spastic esophageal disorders: a systematic review and meta-analysis. Surg Endosc. 2020;34(2):707–18. https://doi.org/10.1007/s00464-019-06819-6
41. Khan MA, Kumbhari V, Ngamruengphong S, Ismail A, Chen YI, Chavez YH, et al. Is POEM the answer for management of spastic esophageal disorders? A systematic review and meta-analysis. Dig Dis Sci. 2017;62(1):35–44. https://doi.org/10.1007/s10620-016-4373-1
42. Triggs JR, Krause AJ, Carlson DA, Donnan EN, Campagna RA, Jain AS, et al. Blown-out myotomy: an adverse event of laparoscopic Heller myotomy and peroral endoscopic myotomy for achalasia. Gastrointest Endosc. 2021;93(4):861–8.e1. https://doi.org/10.1016/j.gie.2020.07.041

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Albers D, Witt M, Pandolfino JE, Rösch T, Schachschal G, Beyna T, et al. Peroral endoscopic myotomy for hypercontractile (Jackhammer) esophagus: a retrospective multicenter series with long-term follow-up. United European Gastroenterol J. 2024;12(7):930–40. https://doi.org/10.1002/ueg2.12586