Journal of the Canadian Association of Gastroenterology, 2021, 4(3), 110–114
doi: 10.1093/jcag/gwaa018
Original Article
Advance Access publication 12 June 2020

OXFORD

Original Article

The Canadian POEM Experience: The First 50 Patients

Mandip Rai, HonBSc, MD, FRCPC[1], Matthew Woo, BSc, MD, FRCPC[2], Robert Bechara, HonBSc, MD, FRCPC[1,*]

[1]Division of Gastroenterology, Queen's University, Ontario, Canada; [2]Division of Gastroenterology, University of Calgary, Alberta, Canada; Division of Gastroenterology, Queen's University, Ontario, Canada

Correspondence: Robert Bechara, HonBSc, MD, FRCPC, Department of Gastroenterology, Hotel Dieu Hospital, Queen's University, 166 Brock Street Kingston, Ontario K7L 5G2, Canada, e-mail: bechara.robert@gmail.com

Abstract

Background and Aims: Peroral endoscopic myotomy (POEM) has emerged as a less invasive technique for performing myotomy in patients with achalasia. This study aims to assess the safety and efficacy of POEM in a Canadian tertiary care center.

Methods: All consecutive patients who underwent POEM between March 2016 and May 2018 at a tertiary center were included. The primary outcome of the study was clinical success rate of POEM defined as a post-POEM Eckardt score ≤3 at ≥3 months. Adverse events were recorded according to the Clavien-Dindo grading system.

Results: A total of 50 consecutive patients underwent 51 POEM procedures with a mean procedure length of 85.6 ± 29.6 min. Post-POEM Eckardt scores of ≤3 at ≥3 months was achieved in 98% of patients. The incidence of pathologic reflux post-poem was 23%. The median length of hospital stay was 1 day. No major adverse events occurred.

Interpretation: POEM is a safe and effective procedure for the treatment of achalasia. At a median follow-up of 19.5 months, 98% of patients had sustained clinical response (Eckardt score ≤3).

INTRODUCTION

The term *achalasia* has its origins from the Greek word that translates to "failure to relax" and was first described in the 17th century by Sir Thomas Willis (1). It is a disorder of esophageal motility characterized by a loss of enteric neurons resulting in impaired relaxation of the lower esophageal sphincter (LES) and absence of esophageal peristalsis (2). A Canadian population-based study for achalasia revealed a mean incidence and prevalence of 1.63 and 10.8 per 100,000 people (3). The incidence remained constant with a rising prevalence over time as this is a chronic disorder. Patients with achalasia commonly suffer from symptoms of dysphagia, regurgitation of undigested food, respiratory symptoms (nocturnal cough, recurrent aspiration and pneumonia), chest pain and weight loss (4).

There are no current treatments that allow for regeneration of the enteric neurons. Interventions focus primarily on lowering the LES pressure to provide symptom relief and improve quality of life. The first technique for the treatment of achalasia was devised by Sir Thomas Willis and consisted of a forceful passage of a sponge attached to a long, thin whale bone through the lower esophagus. Interventions since then have been refined and include botulinum toxin injection, controlled pneumatic dilatation (PD), laparoscopic Heller myotomy (LHM) and, more recently, peroral endoscopic myotomy (POEM).

POEM has emerged as a minimally invasive endoscopic treatment for achalasia, and the first human case was performed in 2008 by Professor Haruhiro Inoue, and in 2010, he published the first case series of POEM in 17 patients showing excellent results (5). Numerous papers have since demonstrated that POEM is a safe and highly effective treatment for achalasia (6,7).

In this paper, we analyze the outcomes of patients with achalasia undergoing POEM at a single Canadian center. All procedures were done by a single operator who completed a formal 1-year fellowship in Japan at the Showa University Digestive Diseases Center under the guidance of Professor Haruhiro Inoue.

Received: December 26, 2019; Accepted: May 16, 2020

METHODS

Patients

A total of 50 consecutive patients underwent POEM at the Kingston Health Sciences Centre from March 2016 to May 2018. All patients with a diagnosis of achalasia were included. The diagnosis was based on high-resolution esophageal manometry (HRM) using the Chicago classification 3.0 when available (Sandhill, Milwaukee, WI) (8). If HRM was not available, the diagnosis was based on older manometric data and/or endoscopic and radiologic evidence. Prior to POEM, patients also received an esophagogastroduodenoscopy (EGD) and timed barium esophagram (TBE). As a part of post-POEM follow-up, patients underwent repeat EGD, HRM, ambulatory pH testing and timed barium esophagram.

Outcome measurements

The primary outcome of the study was clinical success rate of POEM defined as a post-POEM Eckardt score ≤3 at ≥3 months. Secondary outcomes included operative time, adverse events, in-hospital length of stay, change in integrated relaxation pressure (IRP), prevalence and incidence of pathologic reflux, and reduction in barium column height on TBE at 1 min.

POEM procedures

Prior to POEM, all patients consumed liquids for 1–5 days depending on the degree of stasis noted on the TBE. All patients were given prophylactic intravenous antibiotics and intravenous proton-pump inhibitor (PPI) 15–30 min before initiation of POEM. All procedures were performed in the operating room under general anesthetic with endotracheal intubation and subglottic secretion drainage to minimize the risk of microaspiration (9).

After clearance of any residual esophageal contents and endotracheal intubation, the following landmarks were identified: upper esophageal sphincter, trachea, left main bronchus, aortic arch, spine, lower esophageal sphincter, and proximal extent of spastic contractions. Once the landmarks were identified, the area of submucosal entry, tunnel and myotomy were planned based on prior examination of the manometry, TBE, clinical history of chest pain, degree and location of lumen tortuosity, and proximal location of spastic contractions. The various stages of POEM were performed as described previously (10). In brief, submucosal injection with saline with indigo carmine was performed with subsequent incision and tunnel formation with the triangle tip knife (KD-640L, Olympus Medical Systems, Tokyo, Japan). The tunnel was then advanced 2–3 cm into the stomach and the myotomy performed. After confirming an adequate myotomy and hemostasis, 80 mg of tobramycin in 20 mL of saline was instilled into the tunnel, and the mucosal incision was closed with four to six hemostatic clips (Figure 1). After the procedure was completed, a POEM Difficulty Score (ranging from 0 to 10) was assigned as previously described in the literature (11).

Patients were admitted post-procedure and continued fasting until the following day. EGD was performed on post-POEM day 1. At the time of the endoscopy, an intraprocedural esophagram was also performed. Patients were subsequently initiated on a clear fluid diet which was advanced to a regular diet by post-POEM day 4. Patients were discharged post-POEM day 1 if they had a normal EGD and contrast esophagram as well as tolerated a liquid diet. Medications prescribed on discharge included a 3- to 5-day course of antibiotics, 12–24 weeks of twice daily proton-pump inhibitor, viscous lidocaine as needed and 2 weeks of sucralfate suspension. Follow-up EGD, a 24-hour pH (off PPI), manometry and TBE were performed between 4 and 6 months post-POEM. If patients were diagnosed with conclusive pathological reflux at follow-up as per the Lyon Consensus, they were maintained on PPI indefinitely.

Adverse Events

Adverse events were categorized according to the Clavien-Dindo classification that includes mucosal injury, mucosal perforation, submucosal hematoma, bleeding, mediastinal emphysema, pneumothorax, pneumoperitoneum, pneumonia and incomplete incision closure, and were noted as per the Clinical practice guidelines for peroral endoscopic myotomy (12,13). Major adverse events were defined as Clavien-Dindo classification Grade IIIb–V. Minor adverse events were defined as Clavien-Dindo classification Grade I–IIIa.

Statistical Analysis

Data are presented as frequencies and percentages, means (± standard deviation) or median (range) where appropriate. The pre-/post-Eckardt scores and pre-/post-IRP scores were compared using the nonparametric Wilcoxon signed-rank test. *P* values <0.05 were considered significant. All calculations were conducted in SPSS v23 (IBM, New York, United States).

RESULTS

In total, 50 patients underwent 51 POEM procedures between March 2016 and May 2018. Clinical and demographic data are shown in Table 1. Seventeen (34%) patients had type III achalasia and 25 (50%) patients had prior treatments, including 10 (20%) who underwent prior myotomy (surgical or endoscopic). The median pre-POEM IRP was 29 mmHg (4–53).

POEM was successfully completed in all patients. The mean myotomy length was 16.5 cm (13.7 cm in the esophagus and 2.8 cm in the cardia) and the incision was closed with a median of 5 clips (range 4–8). The mean operative time was 85.6 minutes (range 45–180) (Table 2). All patients had an EGD and contrast study performed the next day and there were no instances of esophageal leak. Patients were discharged after

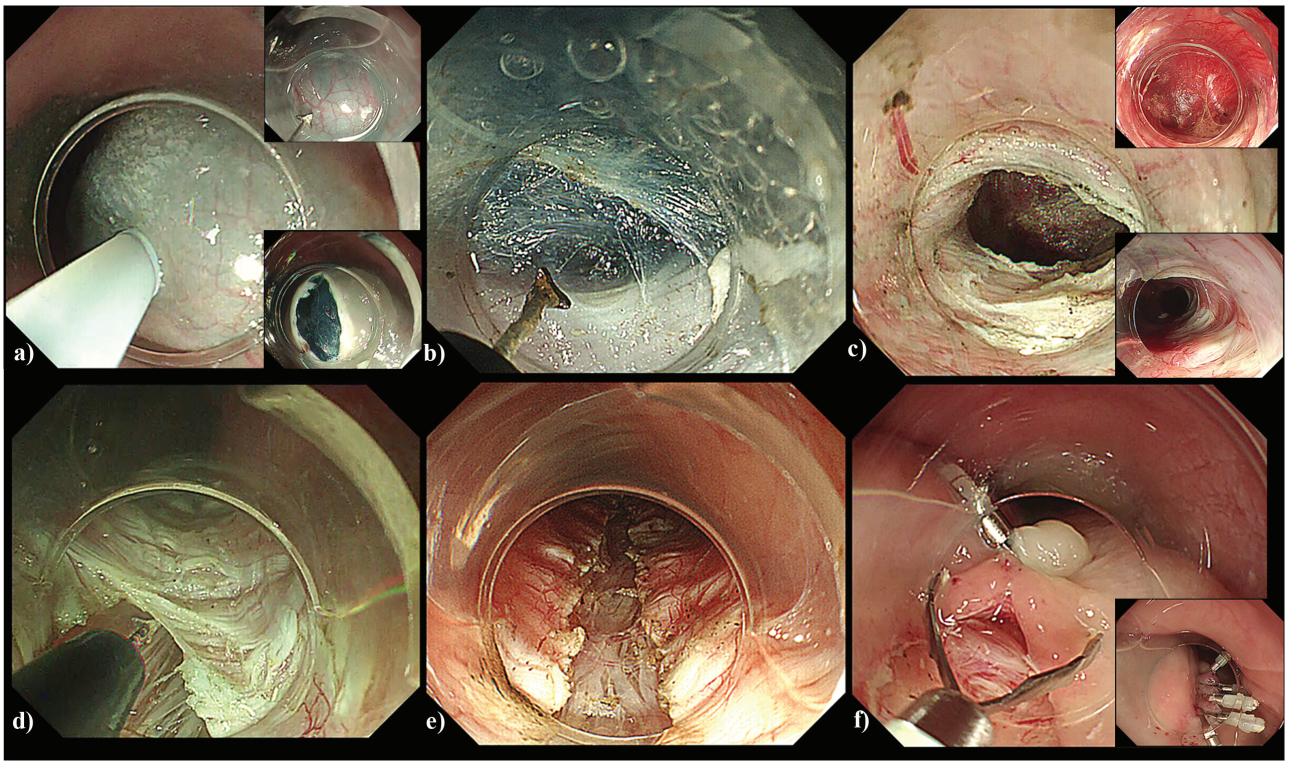

Figure 1. Stages of POEM. (a) Injection and mucosal incision, (b) submucosal tunneling, (c) completed tunnel, view from just above the lower esophageal sphincter (main), gastric side (right upper) and esophageal side (right lower) (d) myotomy, (e[1]) completed myotomy (f) closure with hemostatic clips.

a median of 1 day (range 1–2). There were no major adverse events and one minor adverse event of a 1-cm submucosal hematoma for which the patient was asymptomatic and did not result in any clinical sequela.

Forty-nine (98%) patients met the prespecified primary outcome of a post-POEM Eckardt score of ≤3 at ≥3 months. The median improvement [in Eckardt] was 6 (Wilcoxon signed ranks $P < 0.005$) (Table 3). Thirty-four patients successfully underwent follow-up HRM and the median improvement in IRP was 15 (range −3 to 41, Wilcoxcon signed ranks $P < 0.005$). Eighteen patients had follow-up TBE and 12 had a reduction in 50% of the barium column at 1 min. Clinical, radiographic, endoscopic or functional follow-up occurred at a median 19.5 months (range 5–38).

Forty-eight patients (96%) had follow-up endoscopy and 35 (70%) patients had ambulatory pH at the time of last clinical follow-up. The prevalence and incidence of pathologic reflux at follow-up was 30% and 23%, respectively. There were no instances of stricture or Barrett's esophagus.

Interpretation

The clinical success rate was 98% for our primary clinical outcome of an Eckardt score of ≤3 at ≥3 months. At a median follow-up of 19.5 months, 98% of patients had a sustained clinical benefit with an Eckardt score of ≤3. The safety profile of POEM was excellent with no minor or major adverse events. One patient initially had treatment success at 3 months, but had recurrence of symptoms with an Eckardt score of 4 at 14 months. This patient had a prior Heller myotomy and no further treatment was planned. Another patient with an Eckardt score of 8 at 3 months after POEM successfully underwent a second anterior POEM and achieved an Eckardt of 1 that was maintained at 15-month follow-up.

Our clinical success rate is comparable with other studies (6,14–19). Longer term studies have shown that POEM has a durable response with a slight decrease over time. In a retrospective study by Ngamruengphong et al. (6), there was a clinical success rate of 98%, 98% and 91% at follow-up of 6, 12 and >24 months, respectively. Nabi et al. (7) showed a clinical success rate at 1, 2 and 3 years of 94%, 91% and 90%, respectively. Inoue et al. (14) reported success rates of 91.3%, 91.0% and 88.5% at 2 months, 1–2 years and 3 years. Li et al. (20) published single-center results from China with one of the largest follow-up periods and it showed success rates at 1, 2, 3, 4 and 5 years of 94.2%, 92.2%, 91.1%, 88.6% and 87.1%, respectively. Based on the current literature, we expect some degree of symptom recurrence and overall treatment failure (Eckardt score>3) over time. This will be examined in future studies.

Our study included many complex achalasia patients. In total, 50% of patients had prior treatment for achalasia with 20% having previous pneumatic dilation and 20% having a prior myotomy. Our data suggest that POEM is a safe and effective

Table 1. Patient demographics

Total patients (Male:Female)	50 (28 male:22 female)
Age (years) [mean, SD]	53.2±18.8
BMI (kg/m^2) [mean, SD]	28.4±7.4
American Society of Anesthesiologists (ASA) class [median, range]	3 (1–4)
Duration of symptoms (months) [median, range]	60.0 (10–720)
Charlson comorbidity index [median, range]	1 (0–7)
Achalasia subtype (*n*, %)	
Type I	6 (12.0%)
Type II	22 (44.0%)
Type III	17 (34.0%)
Unclassified	5 (10.0%)
Sigmoid esophageal morphology (*n*, %)	8 (16.0%)
Patient with prior treatments (%)	25 (50.0%)
Pneumatic	10 (20%)
Botulinum toxin	8 (16.0%)
Myotomy	10 (20.0%)
Integrated relaxation pressure, IRP (mmHg) [median, range]	29.0 (4.0–53.0)
Previous GERD (*n*)	4 (8%)

Table 2. Operative findings during peroral endoscopy myotomy

Operative time (min) [mean, SD]	85.6 ± 29.6
Myotomy length (cm) [mean, SD]	16.5 ± 3.3
Esophageal (cm) [mean, SD]	13.7 ± 3.6
Gastric (cm) [mean, SD]	2.8 ± 1.1
Efficiency (min/cm myotomy) [mean, SD]	5.4 ± 2.3
Clips (*n*) [median, range]	5 (4–8)
Major Complications (*n*) [Clavien-Dindo grade IIIb – V]	0
Minor complications [Clavien-Dindo grade I–IIIa]	1
Length of stay (days) [median, range]	1 (1–2)
POEM Difficulty Score [median, range]	2 (0–6)

Table 3. Clinical Outcomes

Follow-up (months), median (range)	19.5 (5–38)
Pre-Eckardt, median (range)	7.5 (4–12)
Post-Eckardt, median (range)	1 (0–4)
Reduction in Eckardt, median (range)	6 (1–12)
Post-POEM Eckardt ≤3 (%) at 3 months	49 (98.0%)
Reflux esophagitis total (%)	
No esophagitis	35 (70%)
LA grade A	4 (8.0%)
LA grade B	6 (12.0%)
LA grade C	3 (6.0%)
LA grade D	0 (0.0%)
Pathological reflux as per the Lyon Consensus (*n*, %)	13 (30.2%)
Post POEM IRP ≤15 (%)	29 (85.3%)
TBE with >50% reduction (1 min) (%)	12 (66.7%)

procedure even after previous treatment failure. Safety has been demonstrated in other studies as well. In the prior mentioned studies by Ngamruengphong et al., Nabi et al. and Li et al., 39.5%, 46% and 34% had prior treatment. In another large study that looked at treatment-naïve patients and prior treatment failure patients undergoing POEM, success at 3 years was 81.1% versus 76.3% with similar safety results (21). In contrast, higher rates of treatment failure and complications including perforations have been shown in patients with prior interventions undergoing LHM (22).

Post-POEM reflux rates vary as there is inconsistency in definitions used in studies. A large systematic review reported rates of abnormal acid exposure with pH monitoring of 39.0% (95% CI, 24.5–55.8%) after POEM and 16.8% (95% CI, 10.2–26.4%) after LHM. The rate of esophagitis after POEM was 29.4% (95% CI, 18.5–43.3%) and 7.6% (95% CI, 4.1–13.7%) after LHM.

Stasis can be misdiagnosed as pathologic reflux disease if 24-h pH studies are not manually reviewed (23–25). A manual review of a subset of patients after their POEM procedure who had a 24-h pH study demonstrated that 42% had episodes of a slow decrease in pH suggestive of stasis (26). In the current study, we applied the Lyon Consensus to diagnose patients with GERD. Pathologic reflux was seen in 30% of patients. Furthermore, four patients with previous Heller myotomy had pathologic reflux prior to the POEM, making the incidence of GERD post-POEM 23%. Of the 13 patients that met criteria for GERD based on the Lyon criteria, 11 had acid exposure times (AET) >6% on 24-hour pH testing off PPI with no esophagitis, LA Grade A or LA Grade B esophagitis on endoscopy. One patient had LA Grade C esophagitis on endoscopy with a normal pH study. One patient had LA Grade C esophagitis with AET >6% on 24-h pH testing. Four of the 13 patients who met criteria for GERD were asymptomatic.

Seven patients in our study who had LA Grade A or B esophagitis had a normal 24-h pH study. Interestingly, on further review, five out of these seven patients had what appeared to be esophagitis noted only in the area overlying the tunnel created during the POEM procedure. Four out of five of these patients had resolution of the esophagitis on follow-up EGD despite being off PPI. It is speculated that the mucosa overlying the area of the tunnel may be more sensitive to acid or these changes that appear endoscopically as esophagitis are unrelated to acid and may be mild ischemic changes as a result of dissection of the

submucosal vessels supplying the overlying mucosa. The exact significance and underlying etiology of this finding remains to be elucidated. However, these changes may result in the inappropriate diagnosis of reflux esophagitis if only endoscopy is used as the diagnostic tool.

Limitations to our study include a relatively short follow-up period and not all patients completed all follow-up investigations due to logistical difficulties for out of town patients and patient preference. Patients had their repeat EGD, manometry and pH studies on separate days for the most part. Ideally these would be done at the same time serially in follow-up.

To date, this is the largest published Canadian experience with POEM. We have demonstrated that POEM is a safe and effective treatment for achalasia regardless of treatment history. The long-term Canadian data regarding durability of treatment success will be further investigated and is likely to follow that of the international experience and we expect overall good durability of symptom control.

Funding

No funding was received to complete this study.

Conflict of interest: R.B. is a consultant of Olympus Corporation.

References

1. Willis T. Pharmaceutice Rationalis Sive Diatribe de Medicamentorum Operationibus in Human Corpore. London, UK: Hagae Comitis; 1674.
2. Boeckxstaens GE, Zaninotto G, Richter JE. Achalasia. Lancet 2014;383(9911):83–93.
3. Sadowski DC, Ackah F, Jiang B, et al. Achalasia: incidence, prevalence and survival. A population-based study. Neurogastroenterol Motil 2010;22(9):e256–61.
4. O'Neill OM, Johnston BT, Coleman HG. Achalasia: a review of clinical diagnosis, epidemiology, treatment and outcomes. World J Gastroenterol 2013;19(35):5806–12.
5. Inoue H, Minami H, Kobayashi Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy 2010;42(4):265–71.
6. Ngamruengphong S, Inoue H, Chiu PW, et al. Long-term outcomes of per-oral endoscopic myotomy in patients with achalasia with a minimum follow-up of 2 years: an international multicenter study. Gastrointest Endosc 2017;85(5):927–933.e2.
7. Nabi Z, Ramchandani M, Chavan R, et al. Per-oral endoscopic myotomy for achalasia cardia: outcomes in over 400 consecutive patients. Endosc Int Open 2017;5(5):E331–9.
8. Kahrilas PJ, Bredenoord AJ, Fox M, et al.; International High Resolution Manometry Working Group. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil 2015;27(2):160–74.
9. Smulders K, van der Hoeven H, Weers-Pothoff I, et al. A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation. Chest 2002;121(3):858–62.
10. Bechara R, Inoue H. POEM, the prototypical "New NOTES" procedure and first successful NOTES procedure. Gastrointest Endosc Clin N Am 2016;26(2):237–55.
11. Bechara R, Woo M, Hookey L, Chung W, Grimes K, Onimaru M, et al. Peroral endoscopic myotomy for complex achalasia and the POEM difficulty score. Digest Endosc 2019;31(2):148–55.
12. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240(2):205–13.
13. Inoue H, Shiwaku H, Iwakiri K, et al. Clinical practice guidelines for peroral endoscopic myotomy. Dig Endosc 2018;30(5):563–79.
14. Inoue H, Sato H, Ikeda H, et al. Per-oral endoscopic myotomy: a series of 500 patients. J Am Coll Surg 2015;221(2):256–64.
15. Sharata AM, Dunst CM, Pescarus R, et al. Peroral endoscopic myotomy (POEM) for esophageal primary motility disorders: analysis of 100 consecutive patients. J Gastrointest Surg 2015;19(1):161–70; discussion 170.
16. Ramchandani M, Nageshwar Reddy D, Darisetty S, et al. Peroral endoscopic myotomy for achalasia cardia: treatment analysis and follow up of over 200 consecutive patients at a single center. Dig Endosc 2016;28(1):19–26.
17. Familiari P, Gigante G, Marchese M, et al. Peroral endoscopic myotomy for esophageal achalasia: outcomes of the First 100 patients with short-term follow-up. Ann Surg 2016;263(1):82–7.
18. Werner YB, Costamagna G, Swanström LL, et al. Clinical response to peroral endoscopic myotomy in patients with idiopathic achalasia at a minimum follow-up of 2 years. Gut 2016;65(6):899–906.
19. Shiwaku H, Inoue H, Yamashita K, et al. Peroral endoscopic myotomy for esophageal achalasia: outcomes of the first over 100 patients with short-term follow-up. Surg Endosc 2016;30(11):4817–26.
20. Li QL, Wu QN, Zhang XC, et al. Outcomes of per-oral endoscopic myotomy for treatment of esophageal achalasia with a median follow-up of 49 months. Gastrointest Endosc 2018;87(6):1405–1412.e3.
21. Nabi Z, Ramchandani M, Chavan R, et al. Peroral endoscopic myotomy in treatment-naïve achalasia patients versus prior treatment failure cases. Endoscopy 2018;50(4):358–70.
22. Smith CD, Stival A, Howell DL, et al. Endoscopic therapy for achalasia before Heller myotomy results in worse outcomes than heller myotomy alone. Ann Surg 2006;243(5):579–84; discussion 584–6.
23. Crookes PF, Corkill S, DeMeester TR. Gastroesophageal reflux in achalasia. When is reflux really reflux? Dig Dis Sci 1997;42(7):1354–61.
24. Smart HL, Foster PN, Evans DF, et al. Twenty four hour oesophageal acidity in achalasia before and after pneumatic dilatation. Gut 1987;28(7):883–7.
25. Novais PA, Lemme EM. 24-h pH monitoring patterns and clinical response after achalasia treatment with pneumatic dilation or laparoscopic Heller myotomy. Aliment Pharmacol Ther 2010;32(10):1257–65.
26. Woo M, Rai M, Canning S, Chakraborty A, Bechara R. An anaylsis of objective pH testing in post-POEM achalasia patients. Presented at: ACG 2018 Annual Scientific Meeting Abstracts. Philadelphia, PA: American College of Gastroenterology. 2018.