The Performance of Peroral Endoscopic Myotomy in Sigmoid-Type Achalasia

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ABSTRACT

Objective: Sigmoid-type achalasia represents an advanced stage of achalasia characterized by significant dilation and tortuosity of the esophageal lumen. Considering the demonstrated efficacy of peroral endoscopic myotomy (POEM) in treating early-stage achalasia, this procedure may offer an alternative therapeutic approach for sigmoid-type achalasia. This study aimed to assess POEM's feasibility and short-term efficacy in patients with sigmoid-type achalasia.

Materials and Methods: We enrolled 16 consecutive patients with sigmoid-type achalasia (eight with type 1 and eight with type 2). The anticipated outcomes were symptom relief during the 12-month follow-up period (evaluated through a reduction in Eckardt symptom scores), an acceptable incidence of procedure-related adverse events, and a decrease in esophageal diameter and barium height.

Results: POEM was successfully performed in all cases, with a median operative time of 118.50 minutes (range: 52–206 minutes). No serious complications associated with POEM were observed. During the 12-month follow-up period, the median Eckardt symptom score decreased from 6 (2-10) preoperatively to 1 (0-3) ($P = 0.008$). Complications were mucosal injuries (31.25% of cases), pneumoperitoneum (12.5%), and minor bleeding (6.25%), although no interventions were needed.

Conclusion: POEM procedure has exhibited favorable treatment outcomes, showcasing a high clinical success rate in addressing sigmoid-type achalasia. Despite the occurrence of acceptable adverse events, the procedure remains a viable alternative treatment or bridging therapy for sigmoid-type achalasia. Nonetheless, it is crucial to acknowledge that this procedure presents greater challenges in comparison to the treatment of typical achalasia.

Keywords: POEM; achalasia; sigmoid achalasia (Siriraj Med J 2024; 76: 611-619)

INTRODUCTION

Achalasia, a primary esophageal motility disorder, is prevalent worldwide.[1] Sir Thomas Willis first described it in 1674, and Dr. Hertz formally named it in 1915.[2] Histologically, achalasia is characterized by the absence of Auerbach's nerve plexus, resulting in impaired esophageal peristalsis or insufficient lower esophageal sphincter relaxation. Although the etiology remains unclear, recent evidence suggests potential viral infection, autoimmune, and genetic causes.[3] The management of achalasia involves a spectrum of therapeutic modalities. Pharmacological interventions are utilized for patients deemed high-risk, who are unable to undergo procedural interventions. Endoscopic procedures, including botulinum toxin injection or pneumatic balloon dilatation, are offered to patients unable to tolerate the adverse effects of medications

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or general anesthesia. Nevertheless, these interventions often exhibit a notable incidence of early symptom recurrence, thus necessitating surgical intervention as a final recourse. Laparoscopic Heller myotomy with fundoplication stands as the definitive treatment for all presentations and severities of achalasia, contingent upon the patient's ability to withstand the procedural and anesthetic demands.[4] In 2010, Inoue introduced peroral endoscopic myotomy (POEM) for achalasia[5]; this procedure has since gained popularity worldwide due to its favorable outcomes code. In Thailand , POEM was initiated in 2013 supported by Thai Association for Gastrointestinal Endoscopy (TAGE).[6] Sigmoid-type achalasia signifies an advanced stage of the disease typically observed in cases with prolonged durations, often exceeding 10 years. Historically, esophagectomy has been a recourse for this condition; however, it is accompanied by notable morbidity and mortality rates. Presently, Heller myotomy stands as the established standard treatment, albeit recurrent symptoms remain common. POEM has demonstrated favorable outcomes in non-sigmoid achalasia, its efficacy in sigmoid-type achalasia is less substantiated due to limited data. Nevertheless, POEM presents a potential alternative therapeutic approach for sigmoid-type. This study aims to elucidate the treatment outcomes and associated complications of utilizing POEM as an alternative procedure for sigmoid-type achalasia.

MATERIALS AND METHODS

There are no absolute contraindications for POEM in patients diagnosed with achalasia, as it can be performed for all types of the condition. Sigmoid achalasia is diagnosed clinically with the aid of high-resolution manometry (HRM) or imaging studies. The study initially commenced as a retrospective investigation, involving the review of medical record data between 2014 and 2017. Subsequently, it transitioned into a prospective cohort study, continuing until 2022 under Institutional Review Board (IRB) approval, with strict adherence to the initial protocol. The enrollment criteria for patients were as follows: (1) being aged 18 years or older; (2) Having received a confirmed diagnosis of achalasia, which was based on clinical symptoms and further supported by diagnostic procedures such as EGD, BE, or HRM; (3) possessing a tortuous-shaped esophagus with or without a diameter exceeding 6 cm, as determined by an esophagogram or CT scan[7,8]; and (4) having undergone the POEM procedure between January 2014 and July 2022. Furthermore, patients with severe comorbidities rendering them unsuitable for peroral endoscopic myotomy (POEM) or anesthesia, those with malignant diseases, pseudo-achalasia, uncorrected coagulopathy, or those lacking adequate data for review, were excluded from the analysis.

The data were collected and analyzed in an anonymous format. Due to the cohort study nature of data collection and the impossibility of personal identification, signed patient consent forms were not necessary. This research received approval from the Siriraj Institutional Review Board (IRB) under protocol no. 394/2560(EC2), COAno. Si 599/2017.

Preoperative evaluations

The preoperative evaluations primarily employed 3 procedures: the Eckardt symptom scoring system[9], timed barium esophagography, and or high-resolution manometry. A CT scan served as an optional fourth method for select patients, as detailed below.

Eckardt symptom score

The Eckardt symptom scoring system was used to subjectively evaluate achalasia symptoms. This system measured 4 items: weight loss, dysphagia frequency, regurgitation frequency, and chest pain occurrence. Each item was assessed on a scale of 0–3, resulting in a total possible score of 12; higher overall scores indicated more severe disease.

Timed barium esophagography (TBE)

TBE helps predict treatment outcomes and recurrence rates.[10] TBE is similar to the barium swallow test but includes specific modifications. Notably, multiple sequential films are taken at predetermined intervals following a single swallow of a fixed volume of a barium suspension with a particular density. In our study, TBE was performed using a 200-ml oral bolus of low-density barium, with radiographs captured at 1, 2, and 5 minutes post-swallowing. Sigmoid-type achalasia was classified based on the degree of tortuosity of the esophageal lumen (revealed by the barium swallow), the diameter of the dilation, and the height of the esophagus.

High Resolution Manometry (HRM)

HRM using ManoScan™ (Medtronic company) was conducted using a standard technique, and the results were interpreted according to the Chicago Classification version 4.0 of esophageal pressure topography.[11] HRM is considered the gold standard for diagnosing achalasia cardia. However, the dilation and tortuosity of a sigmoid esophagus are readily demonstrated on an esophagogram or esophagogastroscopy. Manometry typically reveals incomplete or absent lower esophageal sphincter relaxation

in response to swallowing, a high median integrated relaxing pressure (> 15 mmHg), and an aperistalsis pattern. Achalasia type was also classified under HRM as Chicago classification.

Computerized Tomography scan (CT)

This study exclusively employed computed tomography (CT) scans for cases manifesting a notably tortuous esophagus, necessitating a comprehensive evaluation of its structure. CT scans quantified the extent of esophageal dilation and tortuosity, the latter assessed via the positioning of the lumen in axial CT images. Sigmoid-type achalasia was categorized into two subtypes following the classification system proposed by Inoue et al.[5] In sigmoid type 1 (S1), the esophagus exhibited marked dilation and tortuosity, featuring a single visible lumen on any CT slice. Conversely, sigmoid type 2 (S2) entailed highly dilated and tortuous esophagus, occasionally displaying a double lumen on CT slices or BE. [Fig 5]. CT scans also facilitated the assessment of adjacent anatomical structures, aiding in the exclusion of other pathologies and providing orientation information

POEM equipment and procedure

All procedures in each patient were performed by the same endoscopist, who is an expert in peroral endoscopic myotomy (POEM), having completed more than the established learning curve threshold of >20 cases.[12] The procedure of this study was performed in the same manner as the *standard POEM equipment and procedure* described previously by Phalanusitthepha et al.[12], which included the following details: The operation began with the patient lying in the supine position with the abdomen exposed under general anesthesia. A forward-viewing endoscope with an outer diameter of 9.8 mm, designed for routine upper gastrointestinal screening, was used with a transparent distal cap attachment (DH-28GR, Fujifilm). The procedure was performed under low-flow carbon dioxide insufflation to prevent air embolism. A mucosal incision was made with a triangular-tip knife after mucosal injection using a mixture of 0.9% normal saline with 0.3% indigo carmine dye. Submucosal tunneling was performed with the same knife until the achieved gastric area, about 2-3 cm below the EGJ, was reached for complete submucosal tunneling creation, and the length of the submucosal tunnel was created just slightly longer than the myotomy length. Next, the myotomy was performed only on the circular muscle, and the longitudinal muscle was spared; the length of the myotomy was performed with the standard POEM. Depending on the severe tortuosity of the esophagus, the myotomy location (anterior or posterior) was selected depending on the anatomy of sigmoid achalasia, which varied in each patient. While the procedure was performed, coagulating forceps (Coagrasper, FD-411QR; Olympus) connected to an electrosurgical energy generator, specifically a VIO 300D electrogenerator (ERBE), were used for hemostasis and to coagulate large vessels. For the final closure of the mucosal entry site, hemostatic clips (EZ-CLIP, HX-110QR; DF Olympus) were applied to avoid the leakage of esophageal content into the mediastinum.

Postoperative care

During the immediate postoperative period, chest X-rays and plain abdominal X-rays were conducted to ensure the detection of any possible complications, such as nonclinical pneumomediastinum, pneumothorax, and pneumoperitoneum, even in asymptomatic patients. Patients were also fasted for at least 16 hours, with intravenous antibiotic infusions and appropriate pain relief administered as needed.

Outcome measurements

The primary endpoint of the study was clinical success, defined as achieving an Eckardt score of less than 3 at one month post-procedure. Secondary outcomes encompassed achieving technical success, defined as the completion of gastric and esophageal myotomy within a single-stage procedure, along with the evaluation of operative details and perioperative complications. Eckardt scores were assessed before and after the POEM procedure at 1, 3, 6, and 12 months. Recurrent symptoms were defined as Eckardt scores exceeding 3. Additionally, esophageal diameter and barium height were measured pre- and post-POEM via BE or TBE; in the case of TBE, the value used for comparison is the 5-minute value. Post-procedure gastroesophageal reflux disease (GERD) symptoms were also thoroughly evaluated.

Follow-up

Medical records were reviewed to assess patient follow-up at intervals of 1, 3, 6, and 12 months, focusing on the evaluation of clinical symptoms and Eckardt symptom scores. A timed barium esophagogram was conducted at the 1-month mark. Esophagogastroduodenoscopy and high-resolution manometry (HRM) were carried out during the 12-month sessions.

Statistical analysis

Data with and without normal distribution were presented as mean ± SD or median (range), respectively. Wilcoxon's signed-rank test was used to compare non-

normal varaibles between pre- and post-treatment. Friedman's test was employed to test the change in non-normal variables among 5 different time points with Bonferroni's correction for pairwise comparisons. Fisher's exact test was applied to determine factors related to advrerse event. Two-sided p-values less than 0.05 were considered statistical significance. IBM SPSS 29.0 (Chicago, IL, USA) was employed.

RESULTS

The data were collected between January 2014 (when POEM was first performed at Siriraj Hospital) and July 2022. The study recruited 16 patients; their demographic data are detailed in Table 1. There were 8 men and 8 women, with a mean age of 43.13 ± 14.15 years old. Their disease courses varied from 9.31 ± 3.42 years. Eight patients had been diagnosed with S1 achalasia; the remaining eight had S2 achalasia. Among these 16 patients, 5 individuals had previously undergone other procedures. Specifically, one patient had undergone a biopsy in the EGJ area, one had received pneumatic dilation treatment, two had undergone Heller myotomy, and one had received both pneumatic dilation and Heller myotomy treatments. All cases underwent HRM examination, but due to the significant tortuosity of the esophageal tube, a complete examination could only be successfully performed in 2 cases, allowing for accurate interpretation. Among these cases, one was classified as Chicago type I, and the other as type II. The median Eckardt score was 6, and the average esophageal diameter was approximately 6.49 cm. The average height of the barium column at 5 min of TBE was 7.15 cm (Table 1).

All 16 patients underwent POEM successfully. The median operative time was 118.50 (52-206) minutes, while the average myotomy length was 9.19 ± 2.5 cm. The median length of hospital stay was 3 days (Table 2). The lengths of the esophagogastric junction and the myotomy were measured using incisors as a landmark. After the procedure, four patients developed GERD symptoms, all of whom had mild symptoms that resolved with medication; however, in the EGD follow-up, reflux esophagitis was not found. The technical success rate was 100%, consistent with the clinical success rate at 1 month. However, at 12 months, one patient (6.25%) experienced recurrent symptoms. (Table 3).

Several adverse event were noted, ranging from mild to moderate according to the ASGE severity guideline.[13] In 5 cases (31.25%), mucosal injuries were caused by the tip of the esophagogastroscope cap and dual knife; one injury occurred in the fundus and esophagogastric junction zone, while the others were in the esophagogastric junction zone. However, the mucosal defects were securely closed using endoscopic hemoclips , and there was no need for further intervention. No cases of pneumothorax occurred. One patient (6.25%) experienced minor bleeding at the posterior pharynx, which stopped spontaneously without the need for additional intervention. Pneumoperitoneum occurred in 2 patients (12.50%). In these cases, the air in the peritoneal cavity was released intraoperatively via a 20-gauge needle puncture. There were no reoperations or mortality postoperatively, and none of the patients required any intervention related to achalasia (Table 5).

The median preoperative Eckardt symptom score was 6 (2-10). By the 1, 3, 6 and 12-month follow-ups, the symptom scores had dropped to 1(0-3), 1(0-2), 1(0-4) and 1(0-3), respectively (P = 0.008) (Table 4) (Fig 1). Pairwsie comparisons showed significant difference in Eckardt score between pre and post 1, 3 month. Before the POEM procedure, the maximal dilatation of the esophagus was 6.49 cm on average, but 1 months afterward, the means were 4.4 cm (P = 0.003) (Table 4) (Fig 2). While esophageal height at 5 min of TBE was 7.15 cm before the procedure, the height decreased to 5 cm at the 1-month follow-ups (Table 4) (Fig 3).

The adverse event was found in S1(4) and S2 (4) cases equally (Table 5). The patient who had previous procedures tend to have complications more than those with no previous procedure, but not statically significant (P=0.282). In the S1 group, adverse event tended to develop in patients who had undergone previous procedures. However, in the S2 group, patients experienced adverse events at a consistent rate, rateregardless of their history of previous procedures, but the difference was not statically significant (P=0.143) (Table 5).

The association between operative time and adverse events. Although no statistically significant correlation was found, it is worth noting that adverse events tended to occur more frequently with longer operative times (Table 5).

DISCUSSION

For sigmoid-type achalasia, Faccani et al.[14] recommended using transhiatal esophagectomy as the standard treatment for patients aged less than 55 years who have severe mucosal inflammation or moderate to severe dysplasia. However, esophagectomy for achalasia has a morbidity rate of 50% and a mortality rate of 3%.[15] By comparison, in a study by Panchanatheeswaran et al.[16] involving 8 patients with sigmoid-shaped esophagus who underwent laparoscopic Heller myotomies, all patients experienced improvements in their dysphagia and regurgitation symptoms. Thus, laparoscopic Heller myotomy remains

TABLE 1. Demographic data of 16 patients.

Sex, Male/ Female : n	8/8
Age (years)	
Mean ± SD	43.13 ± 14.15
Median (range)	40 (23-70)
Disease course (years) : mean ± SD	9.31 ± 3.42
Type of sigmoid achalasia	
S1	8
S2	8
Previous intervention : n (%)	5 (31.25%)
Biopsy	1 (6.25%)
Endoscopic pneumatic dilatation	1 (6.25%)
Heller myotomy	2 (12.50%)
Endoscopic pneumatic dilatation and Heller myotomy	1 (6.25%)
Chicago classification : n (%)	
Type I	1 (6.25%)
Type II	1 (6.25%)
Type III	0
Cannot be evaluated due to severe tortuous	14 (87.50%)
Eckardt symptom scores: median (range)	6 (2-10)
Esophageal dilatation, mean ± SD (cm)	6.49 ± 2.43
Barium height, mean ± SD (cm)	7.15 ± 3.76

TABLE 2. Operative details of POEM procedure and complications.

Operative data	
Operation time, median (range), mins	118.5 (52-206)
Myotomy length mean ± SD, cm	9.19 ± 2.50
Length of hospital stay median (range), days	3 (2-10)

TABLE 3. Treatment outcome.

	Number (%)
GERD symptom	4 (25)
Reflux esophagitis (EDG at 12 month)	0
Technical success	16 (100)
Clinical success at 1 month	16 (100)
Recurrent symptom at 12 month	1 (6.3)

TABLE 4. Pre-POEM and post-POEM Eckardt symptom scores, esophageal dilatations, and Barium height.

	Pre	Post 1 month	Post 3 month	Post-6 month	Post 12 month	*p*-value
Eckardt symptom scores#	6 (2-10)	1 (0-3)	1(0-2)	1 (0-4)	1 (0-3)	*0.008*
Esophageal dilatation, cm*	6.49 ± 2.43	4.4 ± 1.46	-	-	-	*0.003*
Barium height, cm*	7.15 ± 3.76	5 ± 3.52	-	-	-	*0.066*

#Median (range), *Mean ± SD

TABLE 5. Complication and Factor related to adverse event.

(a) Complications	Number (%)
Mucosal injury	5 (31.25)
Mild*	4
Moderated*	1
Pneumoperitoneum	
Mild*	2 (12.50)
Bleeding	
Moderated*	1 (6.2)

(b) Factor related to adverse event		n	AE: Number (%)	*P*-value
Type	**Previous procedure**			
S1	Yes	3	3	
	No	5	1	*0.143*
S2	Yes	2	1	
	No	6	3	
Previous procedure				
Yes		5	4	*0.282*
No		11	4	
Operative time (min)				
≤120		8	2 (25%)	*0.132*
>120		8	6 (75%)	

* ASGE severity grading system

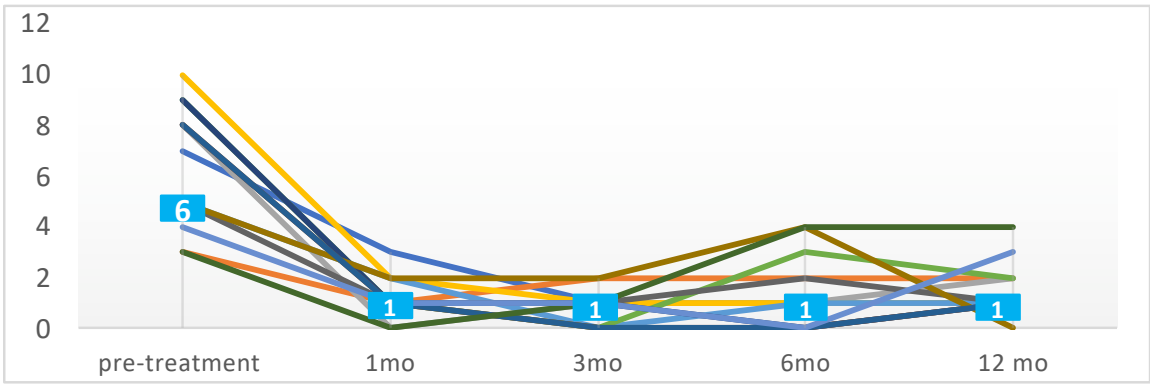


Fig 1. The median of the Eckardt score at pre and post POEM, each point of follow up (1, 3, 6, 12 month)

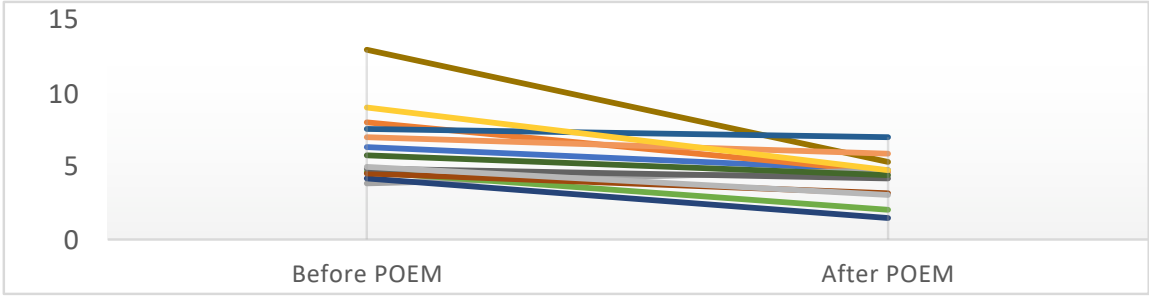


Fig 2. The mean of esophageal diameter before and after POEM 1 month follow-up

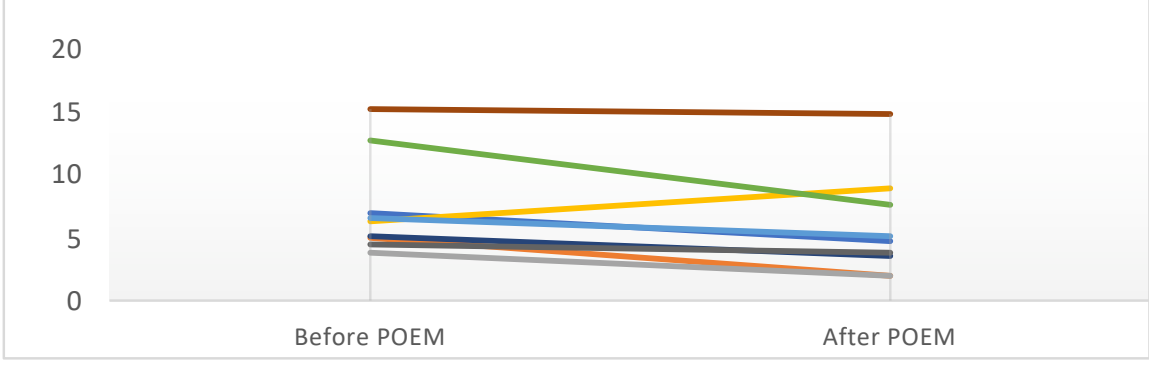


Fig 3. The mean of barium height before and after POEM 1 month follow-up

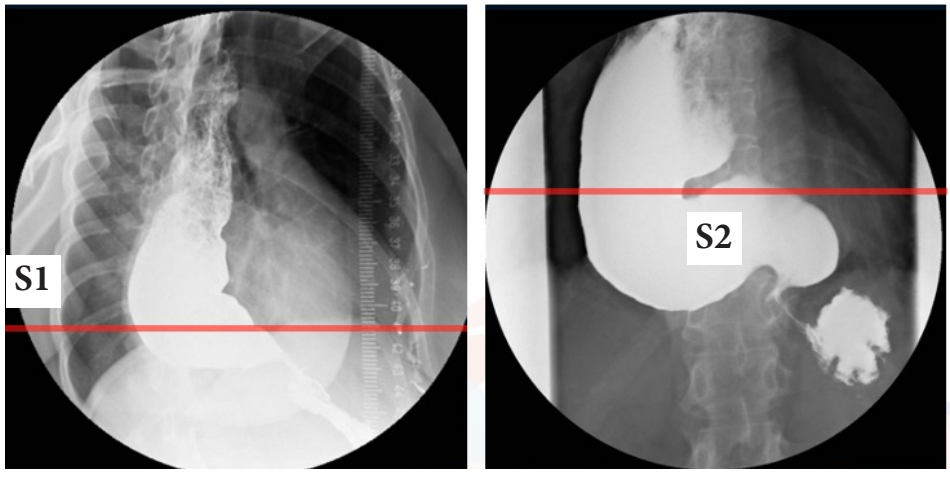


Fig 5. sigmoid type (S1, S2)

the standard operative treatment for achalasia, and it can be performed for sigmoid-type achalasia.

POEM involves minimally invasive surgery to treat achalasia, and its effectiveness has been supported by numerous studies.[5,17,18] In cases of sigmoid-type achalasia, the objective of using the POEM treatment is to reduce morbidity and mortality. Unlike its role with non-sigmoid types of achalasia, POEM for sigmoid-type achalasia focuses on relieving the outflow tract obstruction caused by aperistalsis of the esophagus. A sigmoid-shaped esophagus has tortuous acute angulations and is highly dilated, making it difficult for an endoscopist to control the scope. Before the POEM procedure is executed, retained food particles in the esophagus must be removed. Mucosal inflammation is typically generalized from the proximal site of the esophagus to the esophagogastric junction due to the stasis of food particles and the presence of candida esophagitis. The fibrosis found in the submucosal space makes it challenging to create a submucosal tunnel and can cause mucosal perforations. If a patient exhibits evidence of esophageal candidiasis, an antifungal drug should be administered. When the submucosal tunnel is created near the esophagogastric junction, the angulation of the esophagus and inflammation can result in a false submucosal tract. The endoscopist must therefore exercise caution to avoid mucosal injuries, or else the scope might enter the peritoneal cavity; this is especially the case with S2 achalasia, when even greater care is needed.

A recent review by Jin Xu et al.[19] demonstrated an overall clinical success rate of 90.4%. Additionally, several studies reported adverse events ranging from 3% to 13%[19,20], a range similar to our findings. Our study also showed a high clinical success rate (100%), which may be attributed to the technical success leading to clinical success. Hence, this result may suggest that POEM yields a favorable outcome comparable to that observed in non-sigmoid-type achalasia. However, it is imperative to note that POEM for the treatment of sigmoid-type achalasia presents significantly greater technical challenges than in non-sigmoid achalasia. In the 12-month follow-up, only one case of recurrent symptoms was identified. The factors contributing to recurrent symptoms were not clearly discerned, representing a limitation of this study. This limitation arises due to the small sample size, precluding definitive conclusions regarding this factor.

The POEM procedure took 118.50 minutes (52–206), longer than the typical operative time for non-sigmoid types of achalasia.[21] In our study, mucosal injuries occurred in 5 patients (31.25%), higher than the frequency observed for non-sigmoid types[22], this might be attributed to the severe tortuosity and significant dilation of the esophagus, which are inherent characteristics of the disease, resulting in a more challenging surgical procedure compared to the non-sigmoid type. This study suggests a propensity for perioperative adverse events in S2 and previous procedure cases. However, statistical significance was not attained, and due to the restricted number of cases, definitive conclusions on this matter cannot be reached. Nonetheless, in consideration of the outcomes, despite persistent esophageal lumen dilation, the mean esophageal diameter decreased by 4 cm twelve months postoperatively. Improvement in dysphagia symptoms was evident through lower Eckardt symptom scores, with a mean reduction of 3. As the morphological changes to the esophagus may be irreversible, symptom relief, weight gain, and manometry outcomes should be the main criteria to evaluate the clinical success of treatment with POEM.

In addition to other limitations of this study, it is important to acknowledge that the lower esophageal sphincter was not assessed in all patients due to the severely tortuous esophagus, which hindered the appropriate placement of the probe.[23] Regarding the adverse events observed in this study, the analysis suggests that cases more likely to experience adverse events are those with S2-type achalasia, in which the esophagus exhibits severe tortuosity and significant dilation, as well as cases with prior interventions leading to fibrosis, making the surgical plane difficult and challenging. The data show that the adverse event of POEM in sigmoid-type achalasia is more than in non-sigmoid type achalasia, which is the same reason as previously described.[19,20] However, due to the limited statistical significance of the numerical data, the small sample size, and the short-term follow-up, the impact may not be statistically significant. Notably, this disease is extremely rare, and this series may represent the largest compilation to date. Gathering more patient data is crucial for further understanding.

CONCLUSION

The POEM procedure is feasible for treating sigmoid-type achalasia, with a high rate of clinical success, even in the presence of acceptable adverse events. Therefore, it can be considered as a viable alternative treatment or bridging therapy for patients with sigmoid-type achalasia. However, it is important to note that POEM is technically more challenging than the treatment of typical achalasia. Nevertheless, esophagectomy may remain the only option for many patients with a sigmoid esophagus or for those in whom myotomy or other treatment modalities have failed. There is a need for a large, multicenter study, possibly a randomized controlled trial, to provide definitive data

on the roles of various treatment options for managing this condition.

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Conflicts of Interest

There is no conflict of interest in publishing this article.

DISCLOSURE

A portion of the results from the current study was presented at the academic conference International Digestive Endoscopy Network(IDEN), which took place on June 8-10, 2023 in Korea, and the abstract was published in the proceedings.

Author Contributions

Conceptualization : C.P. ; Datacollection : S.M., J.W. ; Formal analysis : T.S., S.M. ; Funding acquisition : none ; Investigation : C.P., M.M., S.L., T.S. ; Methodology : C.P., M.M., S.L., ; Project admistration : C.P., S.M. ; Resources : C.P. ; Supervision : V.C., T.A., A.M. ; Visualization : V.C., T.A., A.M. ; Writing- original draft : J.W., S.M. ; Writing-review &editing : S.M., T.S. All authors have read and agreed to the final version of the manuscript.

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