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Original Article

Clinical Results of Peroral Endoscopic Myotomy in Patients with Achalasia, Esophageal Diverticular Disease, and Refractory Gastroparesis: A Single-Center Experience

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Abstract

Objective: Peroral endoscopic myotomy has been accepted as a new and minimally invasive treatment for primary esophageal motility diseases, esophageal diverticula, and refractory gastroparesis. This study reports the long-term results related to successful outcomes after peroral endoscopic myotomy.

Methods: Patients who underwent peroral endoscopic myotomy for achalasia, esophageal diverticulum, and delayed gastric emptying between January 2018 and March 2022 were included. The data were scanned retrospectively. Gastroscopy, esophagography, and high-resolution manometry were performed on the achalasia patients included in the study. The disorders were classified according to the Chicago classification. 2 of the patients were diagnosed with type III, 6 with type II, and 9 with type I achalasia. The Eckardt score was used to evaluate patients with dysphagia. Peroral endoscopic myotomy with division of septum was performed in 2 patients. Endoscopic pyloromyotomy was performed in 2 patients with a diagnosis of refractory gastroparesis. The refractory gastroparesis patients were diagnosed by preprocedural history, Gastroparesis Cardinal Symptom Index score (>20), physical examination, gastroscopy, abdominal tomography, and solid–liquid gastric excretory scintigraphy.

Results: In patients with achalasia with a follow-up of more than 3 years after peroral endoscopic myotomy, the Eckardt scores improved significantly compared with the preprocedure scores (score of 2.1 ± 1.4 3 years after peroral endoscopic myotomy and 7.1 ± 2.0 before the procedure, $P < .001$). The 14 (82%) patients with achalasia showed symptomatic improvement according to the Eckardt score after follow-up (Eckardt B3). None of the patients with symptomatic improvement developed symptoms that required reintervention. In 2 patients with esophageal diverticula, there was a decrease in the complaint of food entrapment in the chest. In patients with diverticula with a follow-up of more than 3 years, the Eckardt scores improved significantly from baseline before the procedure (2.4 ± 1.2 preprocedure and 7.3 ± 1.9 at 3 years postprocedure $P < .001$). One of the 2 patients with refractory gastroparesis had an improvement of >50% in the Gastroparesis Cardinal Symptom Index score. The other patient did not show any symptomatic improvement.

Conclusion: Peroral endoscopic myotomy, peroral endoscopic myotomy with division of septum, and gastric peroral endoscopic myotomy are safe and effective treatment options in patients with achalasia, esophageal diverticulum, and refractory gastroparesis, respectively.

Keywords: Acalazia, D-POEM, endoscopy, esophageal diverticulum, G-POEM, gastroparasia, POEM

INTRODUCTION

Achalasia is a primary motility disorder of the esophagus. It is the most common primary esophageal motility disorder. Although the etiology of achalasia is not fully known, there are studies showing that it is most commonly caused by immune-mediated neuronal loss in the myenteric plexus. Achalasia is a disease characterized by the development of dysphagia and chest pain as a result of the lack of primary peristalsis in the esophagus with the relaxation of the lower esophageal sphincter (LES) after swallowing.[1] The aim of achalasia treatment is to reduce the resistance to food in the esophagus by reducing pressure in the LES, which has an important role in the pathophysiology of the disease and to ensure the passage of food into the stomach. Therefore, the main treatment in achalasia is the dissection of the muscle layer that causes resistance in the LES. Peroral endoscopic myotomy (POEM)— a new treatment modality for dissecting the muscle sheet to reduce resistance)—is an alternative treatment for achalasia and other esophageal motility disorders. POEM, first performed by Inoue in 2008, is performed entirely endoscopically across the esophagogastric junction (EGJ). By creating a controlled surgical myotomy, it provides superiority over both laparoscopic Heller myotomy (LHM) and pneumatic dilatation (PD).[2]

Gastroparesis is a gastric motility disorder of unknown etiology that occurs in uncontrolled diabetics and after vagotomy. Treatment options for gastroparesis are limited. It is a chronic disease that causes eating problems with increased morbidity secondary to wasting of the patient. Furthermore, gastroparesis causes frequent hospitalization of the patient and increased need for nutritional support.[3] Stomach fundus anomalies, antrum and antroduodenal coordination, pyloric dysfunction, and abnormal small intestine motility are held responsible for the pathophysiology of gastroparesis.[4] Disruption of gastric motility and increased pyloric pressure are 2 important components of gastroparesis. The effects of current medical treatments are limited, and the potential for side effects is quite high. For this reason, the gastric peroral endoscopic myotomy (G-POEM) method, which facilitates gastric emptying by reducing pyloric resistance by pyloromyotomy, is a promising treatment method.[5]

Esophageal diverticular disease is extremely rare and occurs in the pharyngeal esophagus, middle esophagus, or distal esophagus. The prevalence of esophageal diverticular disease is approximately 0.06%–4%, as estimated on the basis of radiological and endoscopic studies.[6] The treatment of esophageal diverticulum is through septotomy, which can be achieved in several ways as follows: open surgery, rigid endoscopy, or flexible endoscopy. More recently, POEM has gained acceptance[2] with advances in endoscopic techniques and instrumentation.

In this study, we aimed to report the long-term results of various types of POEM, which is 1 of the new treatment modalities.

METHODS

Patients who underwent POEM owing to achalasia, esophageal diverticulum, and gastroparesis between January 2018 and March 2022 were included in the study. The data were scanned retrospectively. The study was carried out with the approval of Inonu University Health Sciences Non-Interventional Clinical Research ethics committee (Date: April 12, 2022, No: 2022/3359). Gastroscopy, esophagography, and high-resolution manometry (HRM) were performed on achalasia patients included in the study. The disorder was classified according to the Chicago classification. 2 of the patients were diagnosed with type III, 6 with type II, and 9 with type 1 achalasia. A detailed history, physical examination, and Eckardt score[7] were evaluated in all the patients before the procedure. Patients with a history of surgery for achalasia were not included in the study. Other treatment options such as balloon dilatation and surgery were offered to the patients for the treatment of achalasia. Those who preferred POEM were included. In 2 patients, endoscopy revealed large esophageal diverticula. The Eckardt score was used to evaluate patients with diverticula. Peroral endoscopic myotomy with division of septum (D-POEM) was performed in 2 patients. A preprocedural history, physical examination, Eckardt score, thoracic tomography, and gastroscopy were performed on patients with diverticular disease. The diverticulum was in the distal esophagus. G-POEM was performed in 2 patients with a diagnosis of refractory gastroparesis. The refractory gastroparesis patients were diagnosed by preprocedural history, Gastroparesis Cardinal Symptom Index (GCSI) score (>20)[3], physical examination, gastroscopy, abdominal tomography, and solid–liquid gastric excretory scintigraphy.

Physiological and Anatomical Evaluation After the Procedure

Manometric examination was not performed in achalasia patients after the procedure. Postprocedure evaluation of the patients was performed 6 months later as per their symptoms and endoscopy results. The evaluation of patients with esophageal diverticula was performed 6 months later by endoscopy and esophagography. The Los Angeles classification (LA A, B, C) was used to assess the achalasia patients in the 6 months and 3 years follow-up endoscopic assessment; the detection rates of LA A, B, an C were 18%, 16%, and 1% and 8%, 3%, and 0% at 6 months and 3 years, respectively.

Three months after G-POEM, the gastric emptying scintigraphy results and gastric emptying function were evaluated, and the patients' symptoms were assessed by GCSI at 1 month and 3 months after the procedure and every 6 months thereafter. After the initial endoscopic follow-up was done within 3 months after G-POEM, it was done at 1-year intervals to detect potential reflux.

POEM

The POEM technique has been explained in detail before. We applied it similarly to the technique first performed by Inoue.[2] POEM is performed under general anesthesia with endotracheal intubation. A high-resolution gastroscope with CO_2 insufflation is used. A transparent cap should be attached to the end of the gastroscope. Upper endoscopy is performed, and after entering the stomach, the scope is slowly pulled up and a bleb is created by submucosal injection at the 4–5 o'clock level with a posterior approach from the appropriate place according to the achalasia type. A longitudinal incision is made in the mucosa above the injection and guided through the mucosotomy and into the submucosal space. A longitudinal submucosal tunnel is then created, ending 3–4 cm beyond the EGJ at the point marked by the methylene blue injection. A selective myotomy of the muscle layer is then performed, starting 3–4 cm below the mucosectomy site and 2–3 cm distal to the EGJ. After the myotomy is completed, the mucosectomy area is closed using endoscopic clips.

Perioperative Management

A contrast esophagram was done on the first postoperative day. If no leakage was observed, a liquid diet was started, and if everything was progressing as expected, the patients were discharged within 3 days. They were then allowed to gradually switch to a soft food diet for 2 weeks. The patients included in this study were not routinely given proton pump inhibitors (PPI) in the early period after the procedure.

Follow-up Symptoms and Physiological Evaluation

All the achalasia patients were re-evaluated by performing upper endoscopy and reassessment of symptoms using the Eckardt score at 6 months postoperatively. For patients with reflux symptoms, it was recommended to start antisecretory therapy to prevent distal esophageal acid exposure. Symptomatic "success" was defined as having an Eckardt score of B3 and not requiring reinvasive intervention for persistent or recurrent symptoms. Patients who indicated reflux were recommended to have upper endoscopy again 5 years after POEM. Esophagitis classification was performed according to the LA classification.

An esophagram was also performed in patients with esophageal diverticulum. Symptomatic "success" was defined as having current Eckardt score B3 and not requiring reintervention for persistent or recurrent symptoms, which is consistent with previous studies. A liquid diet was started in those who did not have leakage. Patients without complaints were discharged in 3 days. Semisolid foods were introduced within 2 weeks. Patients without chest pain and chest tightness were accepted as treatment success. Upper endoscopy was performed 1 month later.

Contrast-enhanced stomach radiographs were taken to control leakage in 2 patients with refractory gastroparesis. Three days later, a liquid diet was started. The patients were discharged on the sixth and eighth days.

Statistical Analysis

The Statistical Package for Social Sciences (IBM SPSS Corp., Armonk, NY, USA), version 22.0 for Windows computer package program was used for statistical analysis of research data. In the descriptive statistics section, the categorical variables are presented as numbers and percentages, and the continuous variables are presented as mean ± standard deviation and median (minimum–maximum value). Comparisons were made for continuous variables using the independent or paired t-test where appropriate. A two-tailed *P* value < 0.05 was used to determine the statistical significance in all the results. It is presented as mean ± standard deviation unless otherwise stated.

RESULTS

Preoperative Patient Characteristics and Perioperative Outcomes

Twenty-one patients who underwent POEM between January 2018 and February 2022 were included in the study. The POEM procedure was performed by a single gastroenterologist, and these patients represent the first cases in the endoscopist's institutional experience. Thirteen (62%) of the patients were women, and their mean age was 46 (36–65 years). Preoperative diagnosis was achalasia type I in 9 patients, achalasia type II in 6 patients, achalasia type III in 2 patients, esophageal diverticulum in 2 patients, and refractory gastroparesis in 2 patients.

The median processing time of the POEM procedure in achalasia patients was 76 min (range 35–185 min). The median hospital stay was 4 days (range 3–10 days), and 14 patients (67%) were discharged on the third day after POEM. One patient had transmural hemorrhage in the esophagus 1 day after the procedure, and the patient recovered spontaneously within 3 days. Mild fluid passage was observed from the clip site in 3 patients. In these patients, re-endoscopy was performed, and the incision sites were closed with new clips. Mucosal injury occurred in 1 patient during the procedure. Mucosal damage was successfully treated with clips in the same session.

Table 1. Changes in scores for each of the mean Eckardt symptom components before and after the procedure.

Symptoms	Before the procedure	3 years after the procedure
Eckardt score (range 0–12)	7.1 ± 2.0	2.1 ± 1.4[a]
Dysphagia (range 0–3)	2.2 ± 0.8	1.2 ± 1.0[a]
Regurgitation (range 0–3)	1.8 ± 1.1	0.8 ± 0.5[a]
Chest pain (range 0–3)	1.6 ± 1.2	0.5 ± 0.9[a]
Weight loss (range 0–3)	1.8 ± 1.5	0 ± 0[a]

There was a significant reduction for each symptom. [a]*P* < .001

In 2 patients with a diagnosis of esophageal diverticulum, the diverticulum was localized to the distal esophagus with epiphrenic and pulsion diverticulum types. The median processing time for D-POEM was 34 min (30–80 min). The median hospital stay was 4 days (3–5 days).

The median procedure time for G-POEM in refractory gastroparesis was 67 min (range 62–72 min). The median hospital stay was 7 days (range 6–8 days), and 1 patient (50%) was discharged on the sixth postoperative day. When 1 patient had abdominal pain on the second day, endoscopy was performed and closed with new clips.

Symptomatic Outcomes and Reinterventions

The patients were evaluated for their preprocedural symptom scores, and the mean follow-up period was 40 months (36–41 months). The Eckardt scores of patients with achalasia with a follow-up period longer than 3 years improved significantly compared with the preprocedure scores (2.1 ± 1.4 preprocedure and 7.1 ± 2.0 at the third year postprocedure). Fourteen achalasia patients (82%) had symptomatic success at follow-up (Eckardt B3), and none of the patients required reintervention for persistent or recurrent symptoms. Table 1 shows the change in the Eckardt score for each symptom, and Table 2 shows the change in the total Eckardt scores by diagnosis subtype. Significant improvement occurred in all 4 symptoms in the Eckardt scoring system.

In 2 patients with esophageal diverticula, there was a decrease in the complaint of entrapment in the chest. The resent symptom scores were evaluated in patients with a median follow-up range of 38 months (range 36–40 months). In patients with diverticula with a follow-up of more than 3 years, the Eckardt scores improved significantly from baseline before the procedure (2.4 ± 1.2 preprocedure vs 7.3 ± 1.9, *P* < .001 at 3 years postprocedure). Two patients (85%) had symptomatic success at current follow-up (Eckardt B3), and none developed symptoms that required reintervention for persistent or recurrent symptoms. When endoscopy was performed on these patients, it was observed that the diverticulum improved. Table 2 shows the changes in the total Eckardt scores by the diagnosis subtype. Significant improvement occurred in all 4 symptoms in the Eckardt scoring system.

One of the 2 patients with refractory gastroparesis had an improvement of >50% in the GCSI score. When endoscopy was performed on the patient, it was observed that the pylorus was open, and no residual food was observed in the stomach after 8 h of fasting. In gastric emptying scintigraphy performed with liquid and solid food, T½ > 180 min before the procedure at 0, 30, 60, 90, and 120 min decreased to 88 min after the procedure. The other patient did not show any symptomatic improvement. In endoscopic evaluation, the pylorus was partially open,

Table 2. Comparison of mean Eckardt scores before and after the procedure after 3-year follow-up of 3 diseases

		Average Eckardt score				Gastric discharge scintigraphy (/minute)		GCSI	
Diagnosis	Patient	Before the procedure	Third year	Symptomatic successa	Reprocess for recurrent or persistent symptoms	Before the procedure	Sixth month	Before the procedure	Postprocedure
Achalasia Type I	9	6.5	1.6[b]	80	0				
Achalasia Type II	6	6.8	1.8[b]	76	0				
Achalasia Type III	2	8.2	2.4[b]	62	0				
Esophageal diverticulum	2	7.2	2.2[b]	85	0				
Refractory gastroparesis	1			59	0	>180	88[b]	24	10[b]
	1			26	0	>180	>180	27	20

[a]Symptomatic success was defined as an Eckardt score of B3 after the procedure and when there was no need for reintervention for persistent or recurrent symptoms; it was also considered as part of the rate of improvement in the GCSI index in patients with refractory gasroparesis
[b]*P* < .01 before the procedure vs after the procedure
GCSI, Gastroparesis Cardinal Symptom Index

and residual food was observed in the stomach after 8 h of fasting. In gastric emptying scintigraphy performed with liquid and solid food, T½>180 min before the procedure was measured at 0, 30, 60, 90, and 120 min, whereas it was measured T½>180 min after the procedure.

DISCUSSION

Our study revealed that POEM for achalasia, esophageal diverticulum, and refractory gastroparesis provided long-term permanent symptomatic relief in 82%, 100%, and 50% of patients, respectively, without the need for reintervention. It was observed that the present symptoms of the patients improved significantly at 3 years compared with the baseline values before the procedure.

Werner et al redetected achalasia symptoms in the follow-up of 3 achalasia patients who had symptomatic improvement after POEM. Although early reports after POEM showed improvement in symptoms in 90%–95% of patients, it was reported that this rate decreased partially to 79%–92% in long-term follow-ups.[8] Symptom recurrences are seen after LHM and PD. In the European achalasia study, patients were randomized to either LHM or PD, with success rates of 90% and 86% after 2 years, respectively.[9] The results of our study add to the growing evidence suggesting that POEM outcomes result in equivalent treatment efficacy and resilience when compared with current standard treatments for the treatment of achalasia.

One of the important concerns after POEM is the development of iatrogenic gastroesophageal reflux (GER). The incidence of GER after POEM is between 30% and 40% according to pH meters and endoscopic methods. The rate of GER development after LHM and partial funduplication was found to be between 21% and 42%.[10] Our incidence of GER after POEM was 35% at 6 months and 11% at 3 years in endoscopic controls. A Barrett esophagus did not occur in any of these patients. These patients were successfully treated with PPI. No surgery was performed for GER. After POEM, patients should be monitored for GER and managed with medical and surgical treatments.

The treatment of a diverticulum is diverticulotomy with rigid endoscope, septotomy, surgical diverticulotomy, and D-POEM; the use of D-POEM has recently increased.[11] Both technical and clinical success rates are high in D-POEM (92%–100%). There are studies calculating an average processing time of 36 min. The Eckard scores showed an improvement of 2.7%. In our study, a significant improvement was observed in the Eckardt score postprocedure compared with the scores preprocedure. Our processing time is 34 min on average. Symptomatic improvement was found to be 85%. D-POEM stands out as an alternative treatment to surgery and rigid endoscopy in patients with esophageal diverticula.

Refractory gastroparesis is a condition characterized by delayed gastric emptying without an organic cause.[12] The precise pathogenesis of gastroparesis includes autonomic neuropathy, gastric hypersensitivity, vagal nerve dysfunction impairing relaxation of the pylorus, loss of neuronal nitric oxide synthase expression, and loss of Interstitial cells of Cajal (ICCs).[13] Gastroparesis treatment is aimed at correcting the causes in the pathogenesis. Pharmacotherapy in the form of prokinetic and selective motilin and ghrelin agonists are the main elements in the treatment of gastroparesis. However, though the effectiveness of drug therapy is limited, its side-effect profile is quite high.[14] Recently, treatment has been aimed at eliminating the spasm of the muscle in the pyloric canal, which is 1 of the important elements in its pathogenesis. These treatments include botulinum toxin injection, endoscopic transpyloric stent placement, and laparoscopic pyloroplasty. G-POEM was developed to eliminate spasms in the pylorus. G-POEM is emerging as a promising treatment modality in the treatment of gastroparesis. Gonzalez et al found success rates of 79% and 70% for the 3- and 6-month periods, respectively.[15] Although the technical success rate was 100% in our study, 59% success was achieved in GCSI in 1 patient. In the gastric emptying scintigraphy of the same patient, it was reduced to 88 min and the patient was relieved. There is need for more case volume to be able to comment on this issue.

The limitations of our study are the small number of patients, absence of HRM after POEM, and not using funduplication in combination with POEM. The low number of cases with refractory gastroparesis is also another limitation in our study.

In conclusion, POEM should be used as an appropriate treatment in the treatment of achalasia. G-POEM in patients with refractory gastroparesis and D-POEM in patients with esophageal diverticulum seem to be the promising treatment options.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İnönü University (Date: April 12, 2022, Decision No: 2022/3359).

Informed Consent: Written informed consent was not obtained from the patients because it was a retrospective analysis and the ethics committee did not consider it necessary in this study.

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