

Ten Initial Cases of Peroral Endoscopic Myotomy for Treatment of Esophageal Motility Disorders at Okayama University Hospital

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Peroral endoscopic myotomy (POEM) for treatment of esophageal motility disorders has recently been reported to be highly effective and less invasive than other treatment. POEM was recently introduced in Okayama University Hospital under the supervision of a physician from a high-volume center. To verify the safety and efficacy of POEM during its introduction in our institution. We examined 10 cases in whom POEM was performed between January 2016 and April 2017. The patients included 7 men and 3 women, with a median age (range) of 49 years (17-74) and median symptom duration of 6 years (1-21). Seven patients had a straight esophagus, and the remaining 3 had a sigmoid esophagus. According to the Chicago classification, 6 patients were diagnosed with type I achalasia, 2 with type II achalasia, and 2 with distal esophagus spasm. Treatment outcomes and adverse events were evaluated. Treatment success was defined as a >3 decrease in Eckardt score or a score of <3 at the time of discharge. The treatment success rate was 90%, with the average Eckardt score decreasing significantly, from 4.7 to 0.9 ($p < 0.05$). No mucosal perforation, severe infection, mediastinitis, severe bleeding, or gastroesophageal reflux occurred intraoperatively or postoperatively. POEM was introduced to Okayama University Hospital, and the first 10 cases were accomplished safely and effectively under the supervision of an expert physician from a high-volume center.

Key words: achalasia, Eckardt score, peroral endoscopic myotomy (POEM)

Esophageal motility disorders such as achalasia are characterized by the absence of esophageal peristalsis and abnormal relaxation of the lower esophageal sphincter [1, 2]. Most patients present with symptoms such as dysphagia, chest pain, vomiting, and aspiration. The standard treatment for esophageal motility disorders includes endoscopic balloon dilatation and the Heller-Dor procedure. Peroral endoscopic myotomy (POEM) has been reported to have high efficacy with low invasiveness [3]. The popularity of POEM as a

treatment for esophageal motility disorders has increased, and reports of successful cases are common. However, POEM is a novel procedure and is considered difficult and risky for inexperienced institutions or physicians to introduce without instruction from experts. POEM was recently introduced to Okayama University Hospital under the supervision of a physician from a high-volume center. Here, we now report the safety and efficacy of POEM during the introduction period in our institution.

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Materials and Methods

This study examined 10 cases in whom POEM was performed between January 2016 and April 2017. All procedures were performed by Y.S., whose past practice included 20 cases of POEM in 3 years at Showa University Northern Yokohama Hospital, along with Professor Inoue as one of the developers of the procedure. Patient characteristics, treatment outcomes, and adverse events were evaluated. In all cases, endoscopy, high-resolution manometry (HRM), and radiographic examinations were performed before POEM. A blood biochemical examination was performed in each patient to evaluate any association of secondary esophageal motility disorders and achalasia with systemic diseases, and pathological examination of esophageal biopsies was performed for the diagnosis of eosinophilic esophagus and other disorders. HRM was used to distinguish between achalasia and distal esophagus spasm (DES), based on the Chicago classification [4]. Achalasia was diagnosed on the parameter of integrated relaxation pressure (IRP) greater than 15 mmHg, and 100% failed peristalsis or spasm. Type I achalasia shows no contractility and Type II achalasia shows more than 20% panesophageal pressurization, and Type III achalasia shows more than 20 spasms. DES was diagnosed by the parameter of IRP, short distal latency, distal contractile integral and 100% failed peristalsis [5].

Patient characteristics. The patients included 7 men and 3 women, with a median age (range) of 49 years (17-74 years) and symptom duration of 6 years (1-21 years). The mean (range) Eckardt score before POEM was 4.7 (2-8) (Table 1). Seven patients had a straight esophagus, and 3 had sigmoid esophagus. According to the Chicago classification, measurements of esophageal pressure by HRM were used in diagnosing type I achalasia in 6 cases, type II in 2 cases, and DES in 2 cases. Two patients had a history of endo-

scopic balloon dilation (Table 2).

All patients were kept on a liquid diet for 1 day prior to the procedure. Intravenous antibiotics were started the day of the procedure and continued for 2 days. POEM was performed under general anesthesia, with the patient in a supine position. An upper gastrointestinal endoscope equipped with a water jet (Olympus GIF Q260J; Olympus Corp., Tokyo, Japan) was used for the procedure, and a transparent cap with a tapered end (DH-28GR; Fujifilm, Tokyo, Japan) was used in all cases.

Myotomy was performed on the posterior wall (5 o'clock position) of the esophagus as follows. In step 1, a submucosal injection was performed (Fig. 1A). In step 2, an incision of a few millimeters was made to allow entry into the submucosal tunnel. In step 3, a submucosal tunnel was created by dissecting the fibers with a triangular tip knife (Triangle Tip Knife, KD-640 L; Olympus Corp.) and using spray coagulation (Fig. 1B). In step 4, the tunnel was extended across the gastroesophageal junction for at least 2 cm. In step 5, in the circular rather than longitudinal muscle, myotomy was performed at the proximal esophagus and gastroesophageal junction (Fig. 1C). In step 6, the end-point was determined using another ultrathin scope. With an additional ultrathin endoscope in place in the stomach, the main endoscope was placed closer to the anal side in the submucosal tunnel. Then, the light of the main scope was observed with an additional ultrathin scope to confirm that the muscle layer incision was sufficient [6] (Fig. 1D). Finally, in step 7, the mucosal incision was closed using endoclips (EZ Clip, HX-610-090 L; Olympus Corp.) from the distal to the proximal end (Fig. 1E). Treatment success was defined as a >3 decrease in Eckardt score (Table 1) or a score of <3 at the time of discharge after POEM. The study was approved by the local ethics review committee (approval No. 2018) and registered in the University Hospital

Table 1 Eckardt score

Symptom	Score			
	0	1	2	3
Dysphagia	None	Occasional	Daily	With every meal
Regurgitation	None	Occasional	Daily	With every meal
Chest pain	None	Occasional	Daily	Several times a day
Weight loss (kg)	0	< 5	5~10	> 10

Table 2 Characteristics of patients performed POEM at Okayama University Hospital from January 2016 to April 2017.

No.	Age	Gender	Past history	Past treatment	Duration of symptoms (year)	Chicago classification	X-ray examination
1	39	M	none	none	4	I	Straight (Spindle)
2	22	M	lung abscess	none	1	I	Straight (Flask)
3	46	M	appendicitis	none	5	I	Sigmoid
4	59	F	breast cancer	none	1	II	Straight (Spindle)
5	74	M	angina pectoris, diabetes, hypertension hyperurisemia, appendicitis	none	6	DES	Straight (Spindle)
6	50	F	appendicitis	pneumotic dilation	21	I	Sigmoid
7	38	M	depression	none	7	I	Straight (Spindle)
8	67	M	ureter stone	none	4	DES	Straight (Spindle)
9	74	M	none	none	8	II	Straight (Spindle)
10	17	F	none	pneumotic dilation	4	I	Sigmoid

DES, distal esophagus spasm.

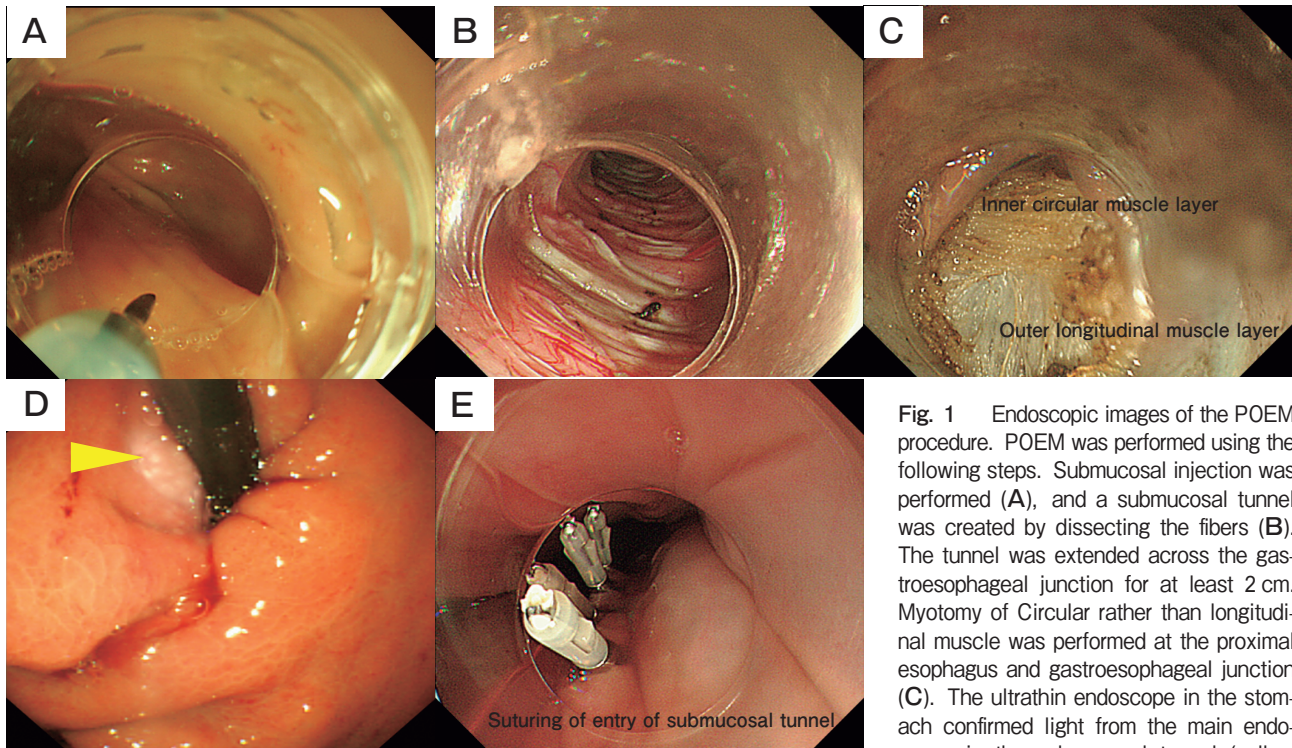


Fig. 1 Endoscopic images of the POEM procedure. POEM was performed using the following steps. Submucosal injection was performed (A), and a submucosal tunnel was created by dissecting the fibers (B). The tunnel was extended across the gastroesophageal junction for at least 2 cm. Myotomy of Circular rather than longitudinal muscle was performed at the proximal esophagus and gastroesophageal junction (C). The ultrathin endoscope in the stomach confirmed light from the main endoscope in the submucosal tunnel (yellow arrow) (D). The mucosal incision was closed from the distal to the proximal end of the incision (E).

Medical Network Clinical Trials Registry (reference No. UMIN 000016126).

Results

The mean Eckardt score (range) was 4.7 (2-8) before POEM and 0.9 (0-4; $p < 0.05$) after POEM. The success rate was 90% at the time of discharge. The median procedure time was 82 min (45-110 min). The median total myotomy length was 11.1 cm (4-17 cm), with median esophageal and gastric myotomy lengths of 9.6 cm (3-16 cm) and 1.5 cm (0-2 cm), respectively. Postoperative hospital stay was 4.3 days (4-6 day). Blood transfusions were not necessary in all cases.

In the present study, there were no adverse events, including mucosal perforation, mediastinitis, severe pne-umomediastinum, severe pneumothorax, postoperative bleeding, or gastroesophageal reflux disease (GERD), during or after POEM (Table 3).

Discussion

This study examined the results of the first 10 cases of POEM during the introduction period in our institution. This was the first use of POEM in the Chugoku and Shikoku regions in Japan. Every case was performed in an operating room and under anesthesia. As this was the first use of this operative technique in our hospital, we consulted Professor Inoue in advance regarding the devices and systems needed. We formed a POEM team (Y.S., K.Y., and R.K.), and the initial surgeon was Y.S. in all 10 cases. Professor Inoue pro-

vided verbal advice while standing behind the initial surgeon. We found that the POEM procedure, especially the decision of the position for submucosal entry, differs in each case, because abnormal, significantly strong, or corkscrew-like peristalsis is different in each patient. The decision of the position of the submucosal entry and the extent of myotomy can be informed by pre-operative endoscopic and radiographic findings, but is ultimately decided during the procedure. It is difficult for a beginner to determine whether abnormal peristalsis is present or not, and even more difficult to determine the optimal site of submucosal entry. Therefore, guidance by Professor Inoue during POEM was essential. Having performed a total of 30 cases, including 10 at our hospital, the operator (Y.S.) is now able to proceed without guidance.

The success rate of POEM in the present study was 90% at the time of discharge, comparable to that found by the International Per Oral Endoscopic Myotomy Survey (2013), which examined the success rate and safety of POEM [7]. Costamagna *et al.* reported that POEM was technically feasible in 10 of 11 (91%) patients, and clinical success, defined as Eckardt ≤ 3 at 1 month, was obtained in all 10 treated patients [8]. Hungness *et al.* reported similar treatment success in 16 of 18 patients (89%) who underwent POEM, with Eckardt scores ≤ 3 and significant reductions in lower esophageal sphincter pressure and barium column height [9]. In the present study, only one case, No. 5, had not obtained sufficient therapeutic effect at discharge to be considered a success. POEM was performed while the patient remained on aspirin. One day

Table 3 Result of performed POEM at Okayama University Hospital from January 2016 to April 2017.

No.	Age	Gender	Eckardt score		Operating time (minutes)	Postoperative hospital stay (days)	Length of submucosal tunnel (cm)	Total myotomy length (cm)
			Before POEM	After POEM				
1	39	M	5	0	95	4	13	12
2	22	M	3	0	80	4	6	4
3	46	M	2	2	110	6	10	8
4	59	F	8	1	95	4	16	15
5	74	M	5	4	90	5	20	16
6	50	F	6	1	90	4	9	8
7	38	M	7	1	60	4	11	9
8	67	M	2	0	70	4	15	15
9	74	M	6	0	85	4	18	17
10	17	F	3	0	45	4	9	7

after POEM, a transient submucosal hematoma developed including transient dysphagia. This patient's Eckardt score was still high, at 4, at the time of discharge. After 6 months, his Eckardt score was 0 and he has required no further treatment. In other words, after 6 months, the success rate of 10 patients enrolled at our hospital was 100%.

Although POEM was originally developed as a treatment for achalasia, recently, there have been several reports on POEM for DES; they stated that POEM has a high therapeutic effect for DES as well [10, 11]. In the present study, although only a few cases of achalasia and DES (No. 5 and No. 8) were examined, we obtained 100% therapeutic effect equally for achalasia and DES. Therefore, we consider that POEM is equally effective for achalasia and DES.

Regarding adverse events, in general, POEM is only performed on the circular muscle and not the longitudinal muscle. However, the external longitudinal muscle is very thin, and splits naturally with pressure from the endoscopic carbon dioxide supply. Therefore, the mediastinum is usually seen through the muscle fibers [12]. In almost all POEM cases, the tissue of the mediastinum was observed from the submucosal tunnel with an endoscope. However, this means penetration from one germfree space to another germfree space (submucosal and mediastinum). Therefore, it is completely different from the concept of gastrointestinal perforation as an adverse event, such as that occurring during ESD, when an external space (the gastrointestinal lumen) makes contact with a germ-free space. Unless the mucosal layer is damaged, there is no risk of causing mediastinitis at all in POEM, as long as the entry of the submucosal tunnel is well clipped. Therefore, perforation during POEM as an adverse event means mucosal perforation. A previous study reported a rate of perforation and mucosal damage of 0-7% [13]. Even if perforation of the mucosal layer is recognized during the procedure, clip closure of the perforated lesion of the mucosal layer will be effective in many cases.

The incidence of a gas-related adverse event, minor pneumomediastinum, immediately after POEM, was 100%. However, this was without clinical significance or need for special treatment, and should not be considered an adverse event. This phenomenon should be considered similar to the pneumomediastinum seen after thoracoscopic surgery. Therefore, in POEM, the only gas-related adverse events are severe pneumome-

diastinum or severe pneumothorax, with need for additional treatment, such as thoracic drainage. Major bleeding occurs infrequently during the procedure, probably because few vessels are encountered in the submucosal tunnel. Almost all bleeding can be treated by endoscopic coagulation. GERD occurs frequently and is a logical consequence of the treatment, although it can be easily treated with a proton-pump inhibitor and is not considered an adverse event. Delayed bleeding was previously reported in 1.1% of POEM patients [14]. In the present study, the intraoperative and post-operative adverse events were consistent with those in other reports. There were no cases of perforation, mucosal damage, severe bleeding, severe infection, or mediastinitis. Since we introduced POEM 17 months ago all patients remain alive and show no recurrence of symptoms, including GERD or chest pain.

The reasons for the positive results in the present study were as follows. First, the initial operator had trained at Showa University Northern Yokohama Hospital. POEM is unlike other endoscopic procedures with myotomy performed using endoscopy alone. It is necessary for the initial operator to have sufficient training at an institution performing POEM. Second, Professor Inoue was consulted and provided advice for each of the 10 initial POEM cases performed in our hospital. We were able to adhere to the POEM protocol because real-time advice was provided during surgery. It was also necessary to consult Dr. Inoue to determine whether the patients were candidates for POEM. Third, and most important, it is essential to thoroughly explain the POEM procedure to doctors in the departments of gastrointestinal surgery and anesthesia. We believe that an endoscopist should not independently attempt POEM. A safe technique and successful procedure requires close cooperation with other departments.

In conclusion, POEM was introduced at Okayama University Hospital and the first 10 cases were performed safely and effectively under the supervision of an expert physician from a high-volume center.

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