

## Clinical Evaluation of Repeat Peroral Endoscopic Myotomy for Achalasia

Khan Mustabar<sup>1</sup>, DeZhi He<sup>1</sup>, XiaoTong Wang<sup>1</sup>, Kele Wei<sup>1</sup>,  
1. Hospital of Zhengzhou University, Henan PR China.

Corresponding author

Professor Dr. DeZhi He( PhD)

Email ID: doctorhedezhi@163.com

### Abstract:

**Aim:**The goals of this research are to evaluate the efficacy, safety, and feasibility of repeating the peroral endoscopic myotomy (Re-POEM) procedure for achalasia patients.

**Methods:**Between February 2018 and August 2020, we performed Re-POEM on ten patients with achalasia whose first POEM attempt had failed. What kind of complications occurred, how long patients stayed in the hospital after surgery, how long patients waited for results, how long patients waited for results, how long patients waited for results, how long patients waited for results, how long patients waited for results, how long patients waited for results, how long patients waited for results, how long patients waited for results, how long patients waited for results, what exactly do you have in mind? And/or additional criteria? We statistically assessed the results of our observations of add).

**Results:**All Re-POEM surgeries were technically successful 100% of the time. There were no significant variations in operational time, postoperative fasting time, postoperative hospital stays, or total hospitalisation expense when comparing the current POEM to the original POEM. There were no perforations, pleural effusions, or gas-related complications in either procedure, and the rates of mucosal injury, chest discomfort, fever, and delayed bleeding were similar ( $P>0.05$ ). All patients' Eckardt scores were less than 3 throughout the median 8.5-month (5-28-month) follow-up after Re-POEM. Three individuals developed clinically associated gastroesophageal reflux disease (GERD), with one instance showing reflux esophagitis by gastroscopy. The symptom score ranged from 1.4.

**Conclusions:**When initial POEM has failed and a patient presents with persistent or recurrent dysphagia, re-POEM is a practical, safe, and successful option.

**Keywords:**Achalasia. Peroral endoscopic myotomy. Dysphagia

### Introduction

Achalasia affects 1 in every 100,000 persons every year [1]. Some of the hallmarks of this primary motility disease include a tense lower esophageal sphincter, no peristalsis in the esophagus, and a compromised relaxation response at the time of swallowing. Symptoms such as dysphagia, regurgitation, chest discomfort, and weight loss greatly reduce quality of life in patients with this condition [2]. Peroral endoscopic myotomy (POEM) has risen to prominence as the therapy of

choice for achalasia since Inoue's groundbreaking use of POEM in the clinical treatment of achalasia in 2010 and its following success [3]. Even though POEM has a high success rate in treating achalasia, the therapeutic benefit is not satisfying for some people. If POEM doesn't work, there's not much data to use in making therapy decisions. To conduct this research, we analysed the medical records of individuals with achalasia who had undergone a second POEM surgery after the previous one had failed (Re-POEM).

## **Patients and methods**

### **Patients**

We collected clinical data from patients diagnosed with achalasia using esophagogastroduodenoscopy (EGD), barium swallow, and high-resolution (HR) manometry at the first affiliated Hospital of Zhengzhou University between February 2018 and August 2020. Ten patients with achalasia who had undergone previous POEM procedures that had been unsuccessful were included in this study to have the Re-POEM operation.

### **Preoperative preparation**

High-resolution (HR) manometry, chest enhanced CT, barium swallow and esophagogastroduodenoscopy were performed to diagnose and rule out esophageal cancer, lower esophageal ulcer and other diseases upon admission to the hospital. Performed the blood routine, liver and kidney function, electrolytes, coagulation function, ECG, lung function and other tests to eliminate surgical contraindications. Before undergoing surgery, patients were given information about the potential benefits and drawbacks of the treatment, and all of them signed a written informed consent form. form.

### **Description of POEM procedure**

Each patient was given general anaesthesia before being placed in the lateral decubitus position and intubated with a single-lumen endotracheal tube. The specific methods were as follows: The conventional POEM procedure for achalasia was used after the submucosal injection, and the submucosal tunnel was extended in the direction of the positive site of the lifting sign. If all four walls of the cardia showed a negative mucosal lift sign, submucosal injection was performed 1-2 cm above the cardia, and the site of the lifting sign was chosen as the direction of the submucosal tunnel's extension. Inoue et al. [2, 6] provided a detailed account of the standard POEM approach, which was followed here: To create the tunnel entrance, a TT knife was used to make a 1.5 cm longitudinal mucosal incision. Next, a mixture of glycerol fructose and methylene blue was

submucosally injected 10 cm above the gastroesophageal junction (GEJ). Submucosal tissue was divided from top to bottom to about 2 to 3 centimeters below the gastroesophageal junction, creating a submucosal tunnel. Myotomy began 2 cm distal to the incision and prolonged 2-3 cm below the gastroesophageal junction, completing the third stage of the circular muscle dissection performed under direct endoscopic visualization. With the bleeding stopped and the cardia unobstructed, the mucosal incision was closed with clips [7-8]. The revised POEM consists of four primary steps:

After injecting a mixture of glycerol fructose and methylene blue submucosally from 3 to 5 centimeters under the cardia to the bottom and 8 to 10 centimeters above the gastroesophageal junction, a 1.5-centimeter-long longitudinal mucosal incision was made with a triangle tip (TT) knife to create the tunnel entry. The mucosa was then split in half vertically, about 1 cm from top to bottom, to make a submucosal tunnel. Third, a myotomy was performed below distal to the incision and continued 2-3cm below the gastroesophageal junction, all while observing the procedure through the endoscope. Fourth, the mucosal entrance point must heal shut.

### **Postoperative treatment**

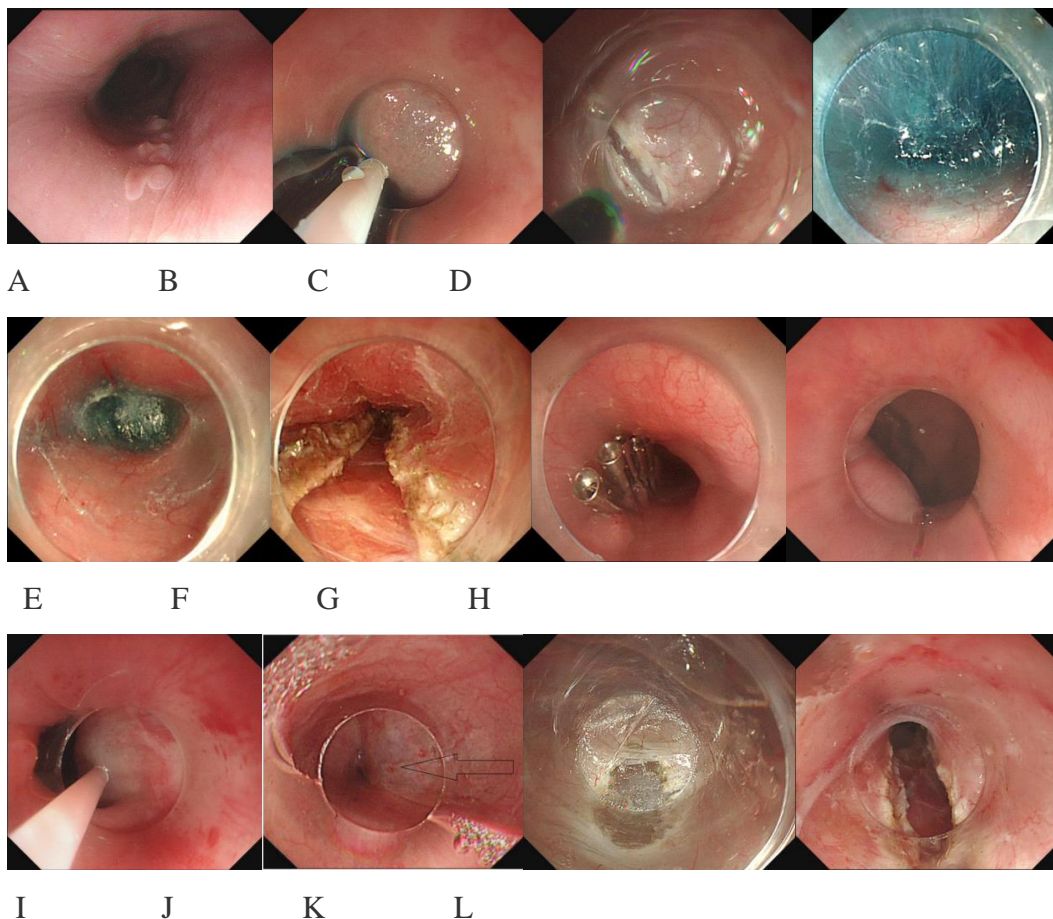
Patients were given total parenteral nutrition treatment, and then the diet was gradually resumed. At the same time, the patient would stay in hospital for 3 days of intravenous prophylactic antibiotics and proton pump inhibitor (PPI) therapy. Patients were followed up regularly by outpatient clinics or by telephone after operation, and Eckardt symptom scores were performed. Upper gastrointestinal barium meal radiography or gastroscopy were performed periodically.

### **Data collection**

Data on patients' demographics, surgical outcomes, operative times, complication rates, hospital stays, costs, and follow-up were compiled. The failure of POEM treatment was defined as persistent or recurrent symptoms within 3 years after operation, and the Eckardt score was  $\geq 4$  [9]. The time of POEM operation was recorded as the time from mucosal incision to mucosal closure.

### **Statistical analysis**

We ran the numbers via SPSS22.0, a statistical programme. Mean SD was used to summarise the normally distributed data for the measurements (SD). Quantitative data was compared using the paired t-test, while qualitative data was compared using the McNamara Chi-square test. Statistical significance was found at the P 0.05 level.



The standard POEM: A: Scar after initial POEM; B: Submucosal injection; C: Mucosal incision; D、E: Establishment of submucosal tunnel; F: Circular muscle dissection; H: Obvious relaxation of cardia after Re-POEM.

The modified POEM: I、J: One-time submucosal injected from 3-5 cm under cardia to bottom until 8~10cm above the gastroesophageal junction; K、L: Direct incision of the muscular layer after the establishment of a short tunnel.

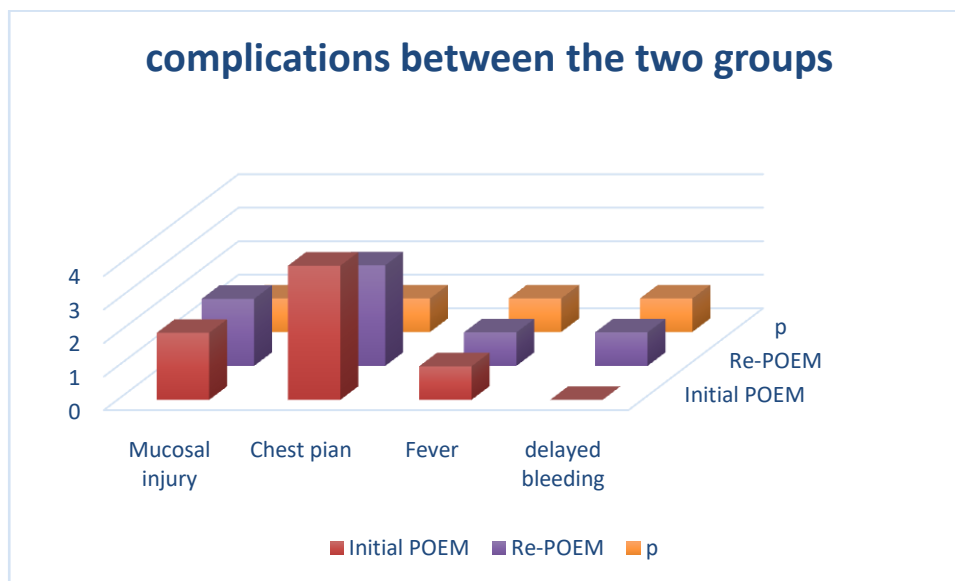
## Results

### Patient characteristics

There were 10 patients altogether, 9 men and 1 woman, with a mean age of 28 (16-60). After surgery, all patients continued to experience discomfort including dysphagia. The average Eckardt score was 5.6, below average (4 -8). Two patients had additional balloon dilations following their first POEM operation, although this did not clearly alleviate their symptoms. At an average of 14.3 months (5-29) following their initial POEM, all patients (6 with conventional POEM and 4 with modified POEM) got therapy with Re-POEM.

## Surgery and complications

All patients underwent successful re-POEM surgeries without complications, and circular myotomy was performed routinely. Fasting time was ( $2.4 \pm 1.075$ ) days (1-4 d), hospital stay was ( $4.90 \pm 2.514$ ) days (2-11 d), and the total time for the reoperation was ( $46.10 \pm 19.593$ ) minutes (29-91 min). There were no statistically significant variations in surgical time, postoperative fasting time, postoperative hospital length of stay (LOS), or overall hospitalisation cost when comparing the current POEM to the original POEM (Table 1). Patients receiving Re-POEM experienced the following five complications: Two patients experienced intraoperative tunnel mucosal injury, which was repaired with a titanium clip; two others experienced post-sternal pain, which was alleviated gradually with symptomatic treatment; one patient experienced post-sternal pain and fever following surgery. Trace evidence of delayed bleeding was found via gastroscopy. Under endoscopic guidance, hemostasis was accomplished by means of electrocoagulation. Comparable rates of mucosal injury, chest discomfort, fever, and delayed bleeding were also observed between the two procedures, although no perforations, pleural effusions, or gas-related problems occurred in table 2.

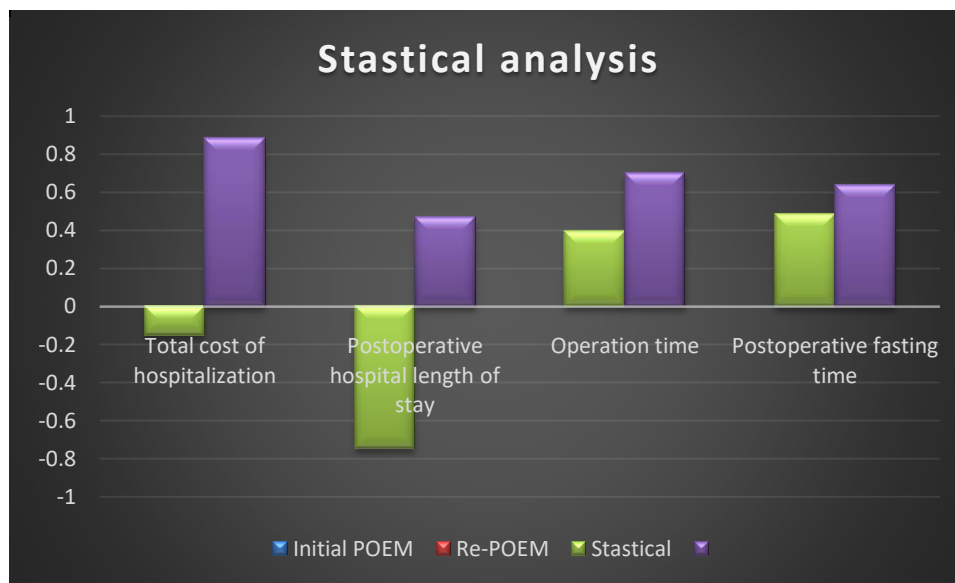


## Follow-up

All patients treated with Re-POEM had Eckardt scores of 3 at a median follow-up of 8.5 months (5-28 months; range, 0-36 months) (1-3). Three individuals experienced symptoms of gastroesophageal reflux illness, and one case was confirmed by gastroscopy to have reflux esophagitis.

**Table.1.** Indexes of observational similarity between the two groups

	Total cost of hospitalization (\$)	Postoperative hospital length of stay (d)	Operation time (min)	Postoperative fasting time(d)
Initial POEM	3577.034±473.848	4.70±1.494	48.10±14.533	2.60±0.843
Re-POEM	3588.992±626.317	4.90±2.514	46.10±19.593	2.4±1.075
Statistic quantity	-0.057	-0.242	0.270	0.514
P	0.955	0.814	0.794	0.619



**Table.2.** Comparison of difficulties between the two groups

		Re-POEM							
		Mucosal injury		Chest pain		Fever		delayed bleeding	
		(n)		(n)		(n)		(n)	
		+	-	+	-	+	-	+	-
Initial	+	1	1	1	2	0	1	0	0
POEM	-	1	7	2	5	1	8	1	9
	P	1.000		1.000		1.000		1.000	

### Discussion

The pathogenesis of achalasia is not completely understood. Therefore, most available treatments for achalasia are palliative and aimed to relieve lower esophageal sphincter outflow obstruction,

reduce LES pressure, improve esophageal emptying, relieve symptoms of patients and improve quality of life[10]. The minimally invasive procedure known as peroral endoscopic myotomy combines tunnel endoscopy with surgical myotomy. Although POEM has a good track record of success and is generally well tolerated, there are still some individuals who experience symptoms even after POEM that do not go away or return. Hungness, E. S., et al. reported an overall rate of failure of 8 % in 115 patients who underwent POEM. At present, there are few reports on the further choice of therapy after initial POEM failure. Then, this study conducted a preliminary comparative analysis of the feasibility of Re-POEM for achalasia after initial POEM failure.

The Eckardt symptom scoring system is a method to diagnose and evaluate the severity of achalasia based on the four major clinical symptoms and frequency of occurrence: dysphagia, reflux, chest pain, and weight loss. Therefore, postoperative Eckardt score is a commonly used index for surgical evaluation. In this study, all the 10 patients were followed up for 5 to 28 months with Eckardt score  $\leq 3$  and no recurrent symptoms. Compared with the initial POEM, there was no significant difference in the total cost of hospitalization, postoperative hospital length of stay, operative time and postoperative fasting time, and the incidence of complications was similar. The reason is that the tunnel of the Re-POEM was established on the opposite side of the initial POEM, which perfectly avoided the submucosal adhesion caused by the initial tunnel establishment. Furthermore, the clinical efficacy and the incidence of adverse events of the myotomy were similar with selecting different sites to establish a tunnel for myotomy, so the outcome of the Re-POEM is similar to that of the initial POEM [12].

The reason of initial POEM failure in achalasia may be related to the insufficient length of the myotomy below the EGJ. The length of the myotomy is conventionally 8-10cm, and should be at least 2cm below the EGJ to ensure clinical efficacy. The average myotomy length in this study was 9.3 cm, with a median of 2.7 cm below the EGJ. There was a total of 10 patients analysed in this study; 9 of them were men, who had a greater failure rate, which is in line with the findings reported by Froukje B.van Hoeij et al [13]. Therefore, males can be used as a predictor of recurrence after POEM in patients with achalasia.

Regarding the safety of the operation, there was 1 case of delayed bleeding in the Re-POEM. The patient developed severe chest pain and fever after the operation, and was given analgesic and anti-infective treatment with poor effect. Gastroscopy confirmed that delayed bleeding occurred in the tunnel, electrocoagulation was used to stop bleeding. Postoperative delayed bleeding is a rare operation-related complication of achalasia, which may be related to the improper treatment of exposed blood vessels in the surgical wound. It often occurs in the tunnel and often shows severe

chest pain in the early stage. When the pressure in the tunnel breaks through the tunnel cavity, patients will have gastrointestinal bleeding such as hematemesis and black stool in a short period time, and the prognosis is good after hemostasis under gastroscopy. Endoscopic preventive hemostasis of visible vessels during operation can reduce the risk of delayed bleeding [14].

The most common long-term consequence following Re-POEM is gastroesophageal reflux disease (GERD). This is because POEM reduces symptoms by damaging the LES, which in turn affects the LES's anti-reflux barrier and causes GERD. Furthermore, Fraukje A. Ponds et al. [15] discovered that the bulk of postoperative reflux symptoms in achalasia are not attributable to gastro esophageal acid reflux but rather to the great sensitivity of the esophagus to chemical and mechanical stimulation. Therefore, it is important to not only reduce acid production but also improve esophageal clearance as part of the treatment for clinically associated gastroesophageal reflux disease following POEM. As a result, patients who have undergone initial POEM for achalasia and now come with either persistent or recurrent dysphagia [19, 20] may benefit from undergoing Re-POEM, which appears to be a safe, viable, and beneficial treatment. The study's limited sample size and retrospective design are, however, limitations. Follow-up information is limited, thus future research will benefit from large-scale multi-center investigations.

### **Compliance with ethical standards**

### **Conflict of interest**

There are no conflicts of interest in this study.

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