



Peroral endoscopic myotomy as treatment for Zenker's diverticulum (Z-POEM): a multi-center international study

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Abstract

Background Peroral endoscopic myotomy for the treatment of Zenker's diverticulum (Z-POEM) is a novel technique that has been described in several recent reports. This method utilizes the third space (submucosal layer) to create a tunnel to facilitate complete visualization of the septum and hence cutting it entirely. Conventional endoscopic septotomy carries the risk of recurrence due to incomplete visualization of the septum. While surgical correction is a risky and lengthy procedure in old comorbid patients with Zenker's diverticulum. The aim of this study is to assess the efficacy and safety of Z-POEM.

Methods The study enrolled 24 patients diagnosed with Zenker's diverticulum (ZD) who underwent Z-POEM at seven independent endoscopy centers in five different countries.

Results Mean patient age \pm standard deviation (SD) was 74.3 ± 11 years. Most of the patients were males ($n = 20$, 83.3%); four (16.7%) were females. More than 50% of the patients ($n = 14$, 58.3%) had associated comorbidities. The mean size of the diverticula was 4 cm (range 2–7 cm). The Kothari-Haber Score was used to assess clinical symptoms; values ranged from 6 to 14 (median = 9). We achieved 100% technical success with a median procedure time of 61 min and no adverse events. Median hospital stay was 1 day (range 1–5 days). There is a significant reduction in the Kothari-Haber Score after Z-POEM ($P < 0.0001$). Technical success was achieved in 100% of the patients. Clinical success was achieved in 23/24 (95.8%) of the patients with a median follow-up of 10 months (range 6–24 months).

Conclusion Z-POEM is a safe and effective modality for managing ZD.

Keywords Zenker's diverticulum (ZD) · Peroral endoscopic myotomy (POEM) · Third-space endoscopy · Endoscopic diverticulectomy · Dysphagia

Introduction

Zenker's diverticulum (ZD) is a rare disorder characterized by herniation of the mucosa and submucosa through Killian's triangle, a region located between the inferior constrictor and cricopharyngeus muscles [1]. ZD is diagnosed predominantly in elderly males, notably among those

in the seventh decade of life [2]. The precise etiology is unknown, although several studies have suggested that ZD may develop in response to increased hypopharyngeal bolus pressure together with the reduced wall compliance, resulting in a pulsion diverticulum [3, 4]. Symptoms associated with ZD include regurgitation, halitosis, dysphagia, cough and recurrent aspiration [5]. Surgical correction used to be the main stay for treating ZD. However, surgical correction as an invasive procedure is associated with high morbidity and mortality (2.5–46% and 0–2.3%, respectively) largely due to associated comorbidities [6, 7].

Endoscopic intervention is a less invasive alternative management strategy that involves incision through the septum to connect the diverticulum to the esophageal lumen [8]. However, this procedure carries the risk of perforation and

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incomplete cutting of the septum [9]. Lower morbidity and mortality, shorter operative and recovery times, and lower rates of adverse events are the main reasons why endoscopic septotomy is favored over surgical correction, particularly in elderly patients [10]. Multiple studies have reported outcomes associated with endoscopic septotomy; success rates are typically between 56 and 100% with symptoms recurring in 10–35% of patients [11, 12]. The high rate of recurrence had been attributed to incomplete division of the septum [13–15].

Peroral endoscopic myotomy (POEM) was first described for the treatment of achalasia [16]. It is currently used for the treatment of other gastrointestinal diseases including gastroparesis (gastric or G-POEM) and for the removal of submucosal tumors (submucosal tunneling endoscopic resection, or STER) [17]. This technique creates a third space via submucosal tunneling that results in the complete exposure and division of the septum [18, 19].

Recently, POEM has been applied for the treatment of ZD (Z-POEM). Submucosal endoscopy facilitates complete visualization and division of the septum. Initial studies featuring Z-POEM reported promising results [18–23]; technical and clinical success were achieved in more than 90% of patients. Nonetheless, there is very little published data available on this subject.

The main objective of this international study is to evaluate the safety and efficacy of Z-POEM for the management of symptomatic ZD.

Patients and methods

This is an international, multi-center, retrospective study that included patients treated at seven centers in five countries, including Costa Rica, Egypt, Lebanon, Mexico, and Turkey. The study enrolled patients with ZD who underwent Z-POEM between January 2018 and December 2019. The diagnosis of ZD was based on results of a barium swallow test and/or computerized tomography (CT) scan that were confirmed endoscopically. Data collected for each enrolled patient included disease duration, specific clinical symptoms, history of previous interventions, size of the diverticulum, intra-operative details, intra- and post-procedural adverse events, and duration of hospital stay and follow-up. Patient symptoms were evaluated using the Kothari-Haber Score. This scoring system is specific for ZD and is based on seven parameters, including dysphagia, weight loss, regurgitation, halitosis, cough, hoarseness, and pneumonia [24]; this scoring system (minimum 0 and maximum 16 points) is unique as it does not focus on dysphagia alone, but considers it in conjunction with other symptoms that are closely associated with ZD (Table 1). Adverse events were graded

Table 1 Kothari-Haber Score for Zenker's diverticulum

Symptoms	Score
1. Weight loss (over 1-year)	
(a) 1–10 lbs	1
(b) 10–20 lbs	2
(c) > 20 lbs	3
2. Difficulty swallowing	
(a) Solid	1
(b) Semi-solid	2
(c) Solid + liquid	3
3. Regurgitation (oropharyngeal symptom)	
(a) Occasional	1
(b) Daily	2
4. Halitosis (oropharyngeal symptom)	
(a) Occasional	1
(b) Daily	2
5. Cough (respiratory symptom)	
(a) Occasional	1
(b) Daily	2
6. Hoarseness (respiratory symptom)	
(a) Occasional	1
(b) Daily	2
7. Pneumonia	
(a) No	0
(b) Yes	2

based on their severity according to the American Society for Gastrointestinal Endoscopy lexicon [25].

Z-POEM: technical aspects

All patients signed informed consent prior to the procedure. Patients were placed in a supine position under general anesthesia. High definition diagnostic or therapeutic gastroscopes with auxiliary water channels were used for this procedure (GIF-HQ 190/GIF-1TH 190 Olympus or Fujinon 760 Z). A transparent cap was fitted to the tip of the gastroscope. Carbon dioxide (CO₂) insufflation was used throughout the entire procedure. Electrosurgical settings included Endo Cut Q (effect 3, duration 3) and soft coagulation (60 W, effect 4) or SWIFT coagulation (50 W, effect 2; Erbe, Tübingen, Germany). Sterile 0.9% saline mixed with 1% methylene blue was used for injection. Different types of knives were used based on the discretion of the endoscopists, as well as local availability and expertise. Knives used for tunneling include the Triangle tip knife (TT, KD-640-L; Olympus), the Hybrid Knife (I-type, ERBE, Germany) or the Flush Knife (BTS-Fujinon). Knives used for septotomy include the Insulated Tip knife (IT, KD-610L; Olympus), the Hybrid Knife (O-type, ERBE, Germany), the Hook Knife (KD-620LR; Olympus), or the Clutch Cutter Knife (DP2618DT, Fujinon).

Coagulation forceps (FD-410 LR, Olympus) were used when large blood vessels were encountered or to counteract bleeding that could not be stopped with the knife.

Z-POEM steps

Z-POEM was carried out using six specific steps (Fig. 1): (Supplementary Video).

Step 1: Creation of the submucosal bleb just proximal to the septum.

Step 2: Creation of a tunnel opening of ~ 1 cm in length.

Step 3: Dissection on the esophageal and diverticular sides of the septum to achieve complete exposure.

Step 4: Complete division of the septum.

Step 5: Extension of the myotomy by 1 cm into the esophageal muscle to ensure complete division of the septum.

Step 6: Closure of the tunnel opening using endoclips after examination to rule out any mucosal injuries. Short clips are preferred to avoid foreign body sensation.

All patients were admitted to the hospital for observation after completion of Z-POEM. All patients were kept NPO for 24 h after the procedure; prophylactic antibiotics (third-generation cephalosporins) were administered for 3 days.

Follow-up and study outcomes

Patient follow-up occurred at fixed intervals of 6, 12, 18, and 24 months. Follow-up included assessments of clinical symptoms (Kothari-Haber Score) and barium studies. Technical success was defined as full completion of the procedure as outlined above [22]; clinical success was defined as complete or near-complete resolution of symptoms (i.e.,

a Kothari-Haber Score < 2) [24]. Recurrence was defined as Kothari-Haber Score of 3 or more [24].

Statistical analysis

Data were analyzed using the SPSS version 20 for Windows 2010. Numerical data are presented as the mean (SD) for normally distributed data or median (IQR) for abnormally distributed data. Categorical data are presented as number (percent). Paired *t* test or related samples-Wilcoxon signed rank tests were used to compare pre- and post-procedure results. *P* values < 0.05 were considered to represent statistical significance.

Results

Twenty-four patients (mean age 74.3 ± 11 years, range 54–98 years, including 20 males and 4 females) underwent Z-POEM during the defined study period. All procedures were performed by endoscopists who are experienced with POEM and third-space endoscopy procedures (minimum 50 POEM procedures). Fourteen (58.3%) patients had associated comorbidities, including hypertension; only 8 (33.3%) of the patients reported no associated comorbidities. American Society of Anesthesiologists (ASA) physical status classification of the patients ranged from I to IV. The median size of the diverticula was 4 cm (range 2–7 cm). Prior history of endoscopic intervention was noted in 3 (12.5%) patients (Table 2). The median baseline Kothari-Haber Score was 9 (range 6–14) (Fig. 2).

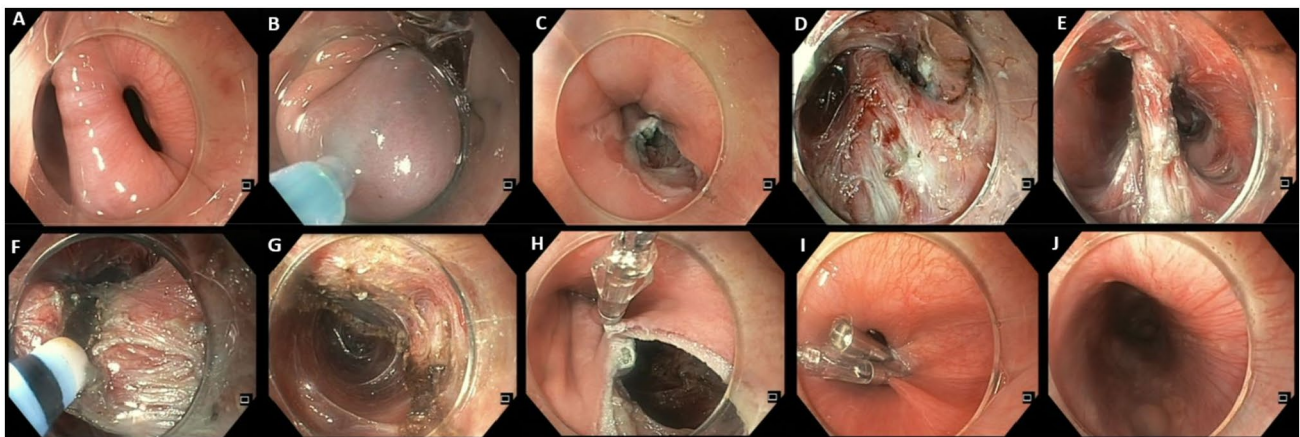


Fig. 1 Steps of peroral endoscopic myotomy for Zenker's diverticulum (Z-POEM). **a** The septum is visualized with the narrow esophageal lumen on the right side and the wider diverticular lumen on the left; **b** a submucosal blue bleb is formed in response to local injection of saline mixed with methylene blue; **c** opening of the tunnel. **d** Start of dissection in the tunnel and initial exposure of the septum; **e** com-

plete dissection of the submucosa on either side of the septum; **f** incision at the septum; **g** extension of the myotomy into the esophageal muscles; **h** deployment of the first clip at a point adjacent to the tunnel opening; **i** complete closure of the tunnel opening with endoclips; **j** visualization of the wide esophageal lumen

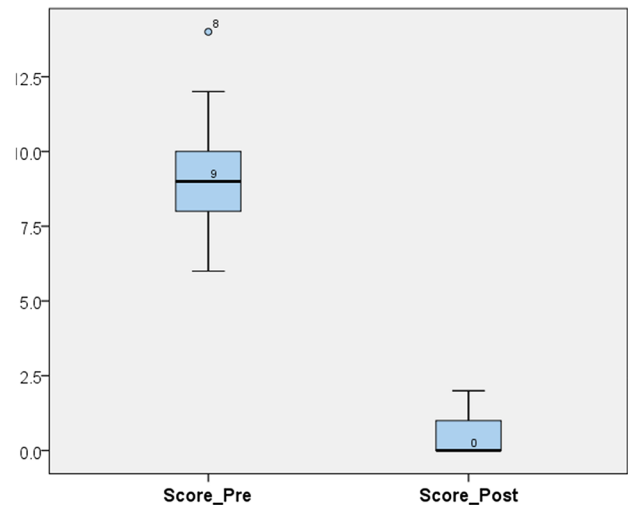
Table 2 Demographic data of the patients (total = 24)

Age (years)	
Range	54–98
Mean (SD)	74.3 (11)
Gender (number, %)	
Male	20 (83.3%)
Female	4 (16.7%)
Comorbidities (number, %)	
No	10 (41.7%)
Hypertension	5 (20.8%)
Hypertension and diabetes	3 (12.5%)
Hypertension and renal impairment	1 (4.2%)
Hypertension and CAD	1 (4.2%)
CAD	1 (4.2%)
AF	1 (4.2%)
COPD	1 (4.2%)
Congestive heart failure and AF	1 (4.2%)
ASA PS classification (number, %)	
ASA I	10 (41.7%)
ASA II	9 (37.5%)
ASA III	4 (16.7%)
ASA IV	1 (4.2%)
Disease duration (years)	
Range	1–15
Median (IQR)	2 (2)
Diverticulum size (cm)	
Range	2–7
Median (IQR)	4 (2)
Previous therapies (number, %)	
Surgery	0 (0%)
Endoscopic	3 (12.5%)
Kothari-Haber Score (pre-procedure)	
Range	6–14
Median (IQR)	9 (3)

ASA American Society of Anesthesiologists, AF atrial fibrillation, CAD coronary artery disease, COPD chronic obstructive pulmonary disease, IQR interquartile range, PS physical status, SD standard deviation

Procedure details

The median procedure time was 61 min (range 32–210 min). Technical success was achieved in all 24 cases (100%). On average, four endoclips were used in each procedure. No adverse events were encountered. Subcutaneous emphysema was detected in 5 (20.8%) patients. Median hospital stay was 1 day (range 1–5 days). Clinical success was achieved in 23 patients (95.8%; Table 3) with a median post-procedure Kothari-Haber Score of 0 (range 0–2; Fig. 2). There is a significant decrease in the Kothari-Haber Score when comparing pre- and post-procedure results ($P < 0.0001$; Table 4). Median follow-up time was 10 months (range 6–24 months);

**Fig. 2** Box plots featuring Kothari-Haber Scores before and after the procedure**Table 3** Procedure details and follow-up

Procedure time (min)	
Range	32–210
Median (IQR)	61 (75)
Number of clips used	
Range	3–7
Median (IQR)	4.5 (2)
Technical success (number, %)	24 (100%)
Adverse events (number, %)	
Bleeding	0 (0%)
Perforation	0 (0%)
Surgical emphysema	5 (20.8%)
Hospital stay (days)	
Range	1–5
Median (IQR)	1 (2)
Follow-up period (months)	
Range	6–24
Median (IQR)	10 (11)
Kothari-Haber Score (post-procedure)	
Range	0–3
Median (IQR)	0 (1)
Clinical success (number, %)	23/24 (95.8%)

IQR interquartile range

Table 4 Pre- and post-Z-POEM Kothari-Haber Score

Variables	Pre-Z-POEM Median (IQR)	Post-Z-POEM Median (IQR)	P value
Kothari-Haber Score	9 (3)	0 (1)	< 0.0001

during this period, only one patient experienced symptoms with a Kothari-Haber Score of 3 at 6 months post-procedure. Of note, this patient presented with a 7 cm diverticulum and a Kothari-Haber Score of 9 prior to the procedure; he reported that he is satisfied with the current level of symptoms and as such required no further intervention. Eleven patients (45.8%) remained in follow-up for more than 12 months with no recurrence of clinical symptoms.

Discussion

Prior to the recent development of Z-POEM, treatment strategies for ZD included only two options, including an open surgical procedure via a left cervical incision or conventional endoscopic septotomy [2, 26, 27]. There is a limited data available on comparing these two methods [28]. Surgery has a reported high risk of morbidity and mortality in this elderly patient population, notably those with the typical associated comorbidities [6, 7]. Meanwhile, conventional endoscopic septotomy and complete myotomy of the septum significantly increases the risk of perforation [29].

In the past few years, several groups reported the use of Z-POEM to manage ZD; these publications were primarily case reports and case series [19–21]. Z-POEM is a novel technique that represents an extended application of third-space endoscopy that facilitates complete visualization of the diverticular septum. This new modality provides a solution to the problem of managing ZD in elderly patients unfit for surgery. One single multi-center study evaluated safety and efficacy Z-POEM in a cohort of 75 patients [22]; this publication reports a technical success rate of 97.3% and clinical success rate of 92%.

Our study is an international multi-center study that featured patients who were treated at seven independent endoscopy centers in five countries. All facilities were tertiary centers with experience in POEM and third-space endoscopy procedures. Our results suggest that Z-POEM is a flexible procedure with no apparent age limit; this procedure performed successfully in one patient who was 98 years old. Z-POEM is also suitable for patients with multiple comorbidities, including those with a history of prior intervention or those with large diverticula (7 cm; Table 2), both perceived as contributing factors associated with recurrence or failure [30, 31]. This procedure does not impose limitations on the endoscopists; Z-POEM can be performed using either diagnostic or therapeutic endoscopes and accommodates a variety of knives that can be selected based on local preferences and experience.

Z-POEM also presents economic advantages due to the short intra-operative time (median 61 min) and short hospital stay (median of 1 day). In this study, Z-POEM was technically feasible (technical success at 100%) which is

consistent with published data [19–22]. Indeed, the use of D-POEM for the management of numerous types of esophageal diverticula has been considered in literature; one recent study achieved technical and clinical success rates of 100% and 86%, respectively [23].

In this study, Kothari-Haber Score was used to assess clinical success in our patient cohort; this scoring system is composed of seven clinical parameters including, but not focusing only on dysphagia. Kothari-Haber Score is specific for Zenker's diverticulum rather than Eckardt score used in other studies, which is well known for achalasia. Using this scoring system, our clinical success rate was 95.8% with median follow-up of 10 months. One patient had a score of 3 at the 6-month follow-up visit; of note, his baseline score was 9 prior to the procedure. However, this patient was satisfied with the clinical outcome and required no further intervention. Further studies may be needed, as it may be necessary to revise the definition of failure according to Kothari-Haber Score. From the few publications available about Z-POEM, it could be concluded that Z-POEM is indicated in symptomatic Zenker's diverticulum with Kothari-Haber Score > 3, in patients unfit for surgery or in recurrence after prior intervention.

Conclusion

Z-POEM is a safe, effective, and ingenious solution for the management of ZD that successfully overcomes the risk of surgery and the drawbacks of conventional endoscopic septotomy.

Limitations of this study

Retrospective analysis and the lack of long-term follow-up are the main limitations of this study. Wider prospective studies are needed for true evaluation of Z-POEM and comparing it with other modalities.

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Compliance with ethical standards

Ethical Statement This study had been approved from the ethical committee of the gastroenterology division of the internal medicine department in the faculty of medicine of Cairo University.


Conflict of interest Mouen A. Khaskab: consultant and medical advisory board for Olympus and Boston Scientific; consultant for Medtronic. All other authors have no conflicts of interest or financial ties to disclose.

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