

An international study on the use of peroral endoscopic myotomy (POEM) in the management of esophageal diverticula: the first multicenter D-POEM experience

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ABSTRACT

Background The aim of this study is to report a novel, multicenter experience with the diverticular peroral endoscopic myotomy (D-POEM) technique in the management of esophageal diverticula.

Methods This is a multicenter, international, retrospective study involving three centers. D-POEM was performed using the principles of submucosal endoscopy.

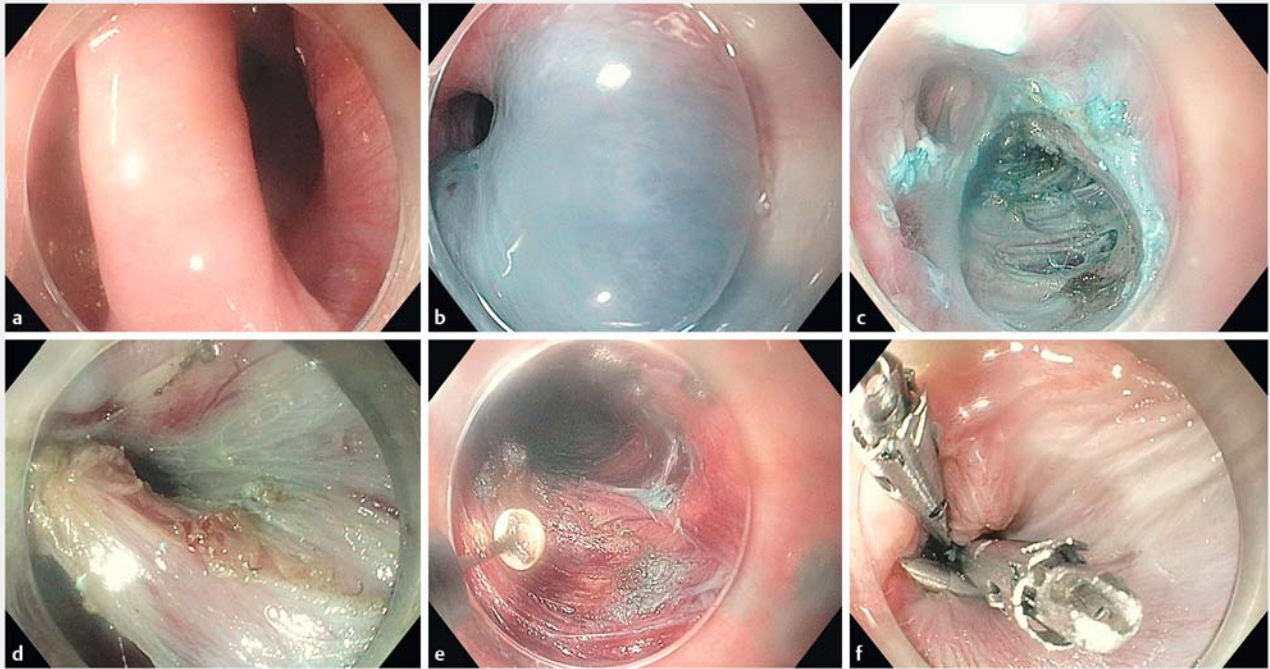
Results A total of 11 patients with an esophageal diverticulum (Zenker's 7, mid-esophagus 1, epiphrenic 3) were included. The mean size of the esophageal diverticula was 34.5 mm. The overall technical success rate of D-POEM was 90.9%, with a mean procedure time of 63.2 minutes. There were no adverse events. Clinical success was achieved in 100% (10/10), with a decrease in mean dysphagia score from 2.7 to 0.1 ($P < 0.001$) during a median follow-up of 145 days (interquartile range 126–273).

Conclusion Endoscopic management of esophageal diverticula using the novel technique of D-POEM appears promising. This first case series on D-POEM suggests that the procedure is feasible, safe, and effective in the management of esophageal diverticula. D-POEM offers the distinct advantage of ensuring a complete septotomy. Larger studies are needed to confirm these intriguing results.

Introduction

Esophageal diverticula are rare outpouchings of the esophagus with a prevalence of up to 3% based on radiological and endoscopic studies [1, 2]. Zenker's diverticulum is the most common type of esophageal diverticulum. Flexible endoscopic modalities for Zenker's diverticulum can be performed with the patient under moderate sedation without the need for neck hyperextension and consist mainly of performing septotomy using a variety of instruments (e. g. endoscopic submucosal dissection knives). The reported clinical success rates range between 56% and 100%, and adverse events occur in an average of 15% of procedures. Importantly, the median clinical recurrence is 10.5%; however, recurrence rates up to 35% have been reported [1, 3–8]. The relatively high recurrence rate has been attributed to incomplete septotomy as it is virtually impossible to accurately delineate the bottom of the septum [9].

The submucosal space has been successfully utilized for the performance of endoscopic myotomy during peroral endoscopic myotomy (POEM). Theoretically, POEM could be an optimal technique for the performance of Zenker's myotomy (septotomy) as submucosal tunneling enables complete exposure and division of the septum. This may result in reduction and potentially elimination of the risk of symptom recurrence. Until recently, only limited case reports had described the use of POEM for the treatment of esophageal diverticula [10–14]. The aim of this paper is to report a novel, multicenter experience with the diverticular POEM (D-POEM) technique in the management of esophageal diverticula.



► Fig. 1 Endoscopic images of diverticular peroral endoscopic myotomy (D-POEM) in a patient with a symptomatic Zenker's diverticulum. **a** An upper gastrointestinal endoscope fitted with a 4-mm clear cap was advanced to the site of the Zenker's diverticulum. **b** A submucosal bleb was created proximally to the Zenker's diverticulum in the posterior hypopharynx. **c** A 1.5-cm mucosal incision was made using the triangle tip knife. **d** A submucosal tunnel was created, which was then extended to both the end of the diverticulum and the proximal esophagus. **e** A septotomy was performed using the insulated tip knife initially and then the triangle tip knife as the esophageal tunnel widened. **f** The mucosal incision was then completely closed using clips.

Methods

This international, multicenter, retrospective study involved three tertiary hospitals: two in the USA and one in Asia. Consecutive patients with symptomatic esophageal diverticula who underwent flexible endoscopic septotomy using the POEM technique between January 2014 and December 2017 were included. Esophageal diverticula were diagnosed on imaging studies, including barium esophagram and/or computed tomography (CT), and confirmed by endoscopy. Dysphagia score was quantified according to the Dakkak and Bennett score (0, no dysphagia; 1, dysphagia to solids; 2, dysphagia to semi-solids; 3, dysphagia to liquids; 4, complete dysphagia) [15]. Patients with <30 days of follow-up and those with esophageal diverticula in the setting of esophageal motility disorders (e.g. achalasia) were excluded.

Patients were identified using center-specific endoscopic or billing databases. Electronic records were reviewed to capture the following variables: demographics; esophageal diverticula location and size; symptoms; Charlson comorbidity index (CCI) [16]; imaging findings; prior surgical interventions; reason for denied surgery when applicable; technical success; procedure time; type of anesthesia; length of hospital stay (LOS); number of repeat procedures; clinical success; symptom recurrence at 30, 60, and 90 days; need for surgery; adverse events graded according to the American Society for Gastrointestinal Endos-

copy (ASGE) lexicon [17]; and duration of follow-up. The retrospective review of data was approved by each Institutional Review Board (IRB).

Procedure technique

All patients were placed in the supine or left lateral position under general anesthesia with endotracheal intubation. A high definition standard flexible upper gastrointestinal endoscope (GIF-HQ 190/GIF-H180], Olympus, Center Valley, Pennsylvania, USA; or EG2990i/EG2990k, Pentax Medical Corp., Montvale, New Jersey, USA) fitted with a clear cap was used in all patients. The flexible endoscope was carefully advanced across the narrow and thin hypopharynx and into the esophagus. The entire esophagus was examined (**► Fig. 1**). After the initial examination, a thorough cleaning of the esophageal lumen and the diverticulum was performed using sterile 0.9% saline. Intravenous antibiotics were administered to the patients as per institutional protocol. Carbon dioxide (CO₂) on low flow setting was used during all procedures.

A mucosal bleb was created by injecting a combination of 1% indigo carmine, dilute epinephrine, and 0.9% sterile saline into the submucosa 1–2 cm proximally to the diverticular septum. A 1-cm incision, serving as the tunnel entry, was then created with a triangle tip knife (KD 640L, Olympus) using dry cut mode at 50 W, effect 3 (ERBE, Tübingen, Germany). The submucosal fibers were dissected with spray coagula-

tion (40W, effect 2) and the endoscope was passed into the submucosal space with the aid of the clear cap. A submucosal tunnel was then created using spray coagulation and injection of indigo carmine solution until the diverticular septum was identified. When large vessels were identified, these were treated using the Coagrasper (Olympus) in soft coagulation mode at 80W, effect 5. The tunnel was then extended on both sides of the septum, the diverticular side and the esophageal side. Tunneling was continued until the bottom of the diverticulum was reached. This was easily identified by the absence of posterior muscle fibers. The septum was thus entirely exposed.

Septotomy was then performed using the insulated tip knife (KD-610L, Olympus) and EndoCut Q, current at 50W, effect 2. Under direct endoscopic view, the muscle fibers of the septum were completely dissected down to the bottom of the diverticulum. The myotomy was extended to include approximately 1 cm of the proximal esophagus to ensure complete septotomy.

The esophageal mucosa was then examined for any evidence of perforation or laceration followed by incision closure using endoscopic clips. The fist clip was deployed at the most distal end of the incision border to facilitate approximation. The subsequent clips were applied in the proximal direction until complete closure was achieved [18].

Post-procedure, all patients in the US centers were routinely admitted overnight for observation and kept nil per os. At the Asian center, the patients were routinely admitted for 3–5 days post-procedure. Intravenous prophylactic antiemetics and broad-spectrum antibiotics were prescribed as per institutional protocol. A contrast esophagram was routinely obtained on the following morning and soft diet was commenced if no leak was present in the US centers. Routine imaging studies were not obtained at the Asian center. Patients were provided with routine broad-spectrum antibiotics for 5–7 days and remained on soft diet for 1–2 weeks, followed by commencement of normal diet. Patients were given clinic follow-up appointments in 2–4 weeks to assess clinical response and delayed post-procedure complications.

Outcomes

The primary endpoint was clinical success, defined as complete or near-complete resolution of dysphagia (Dakkak and Bennett score of 0 or 1), without the need for repeat endoscopic or surgical intervention during follow-up. Secondary endpoints included: the rate of technical success (defined as completion of all steps of diverticular POEM, including complete septotomy); adverse events, with severity graded per the ASGE lexicon [17]; dysphagia recurrence (defined as recurrence of dysphagia with Dakkak and Bennett score of 2 or more, or requiring repeat endoscopic or surgical intervention).

Statistical analysis

The Fisher's exact test for categorical variables was used to analyze the clinical outcomes and adverse event rates. Continuous variables were reported as mean and standard deviation (SD), or median and range, where appropriate. Dysphagia score was analyzed as a continuous variable. A level of significance of $P <$

0.05 was adopted for all inferential testing. The analysis was performed using STATA software, version 13 (Stata Corp LLC, College Station, Texas, USA).

Results

A total of 11 patients (mean age 76.2 years [SD 11.7]; seven women) were included, with an average CCI of 3.8 (SD 1.7; range 0–5). One patient had undergone prior open surgical treatment for Zenker's diverticulum followed by symptom recurrence 5 years later. One patient was denied surgery because of comorbid conditions.

The location of the esophageal diverticula was proximal (Zenker's diverticulum) in 63.6% (7/11), mid-esophageal 9.1% (1/11), and epiphrenic 27.3% (3/11). The mean size of the esophageal diverticula was 34.5 mm (SD 16.5; range 10–53). The main indication for D-POEM was dysphagia in 81.8% (9/11) and regurgitation in 18.2% (2/11).

Procedure characteristics

The overall technical success rate of D-POEM was 90.9% (10/11). Technical success for Zenker's diverticulum was 85.7% (6/7), 100% (1/1) for mid-esophageal esophageal diverticula, and 100% (3/3) for epiphrenic esophageal diverticula. In one patient with a Zenker's diverticulum, D-POEM was attempted but was unsuccessful because of inability to visualize the septum fully. Repeat intervention was declined by the patient.

The mean procedure time was 63.2 minutes (SD 10.3; range 25–113). There were no adverse events encountered during any of the procedures. The mean LOS was 4.1 days (SD 3.8). The mean LOS for patients at the Asian center was 8.75 days (SD 0.85) owing to the local management protocols. In contrast, the mean LOS at the two US centers was 1.4 days (SD 0.2).

Clinical endpoints and adverse events

Clinical success was achieved in 100% (10/10) of patients who underwent successful D-POEM during a median follow-up of 145 days (interquartile range 126–273). The mean dysphagia score decreased from 2.7 to 0.1 ($P < 0.001$). No patients required repeat endoscopic intervention following successful index septotomy during follow-up.

Discussion

The D-POEM technique for the treatment of esophageal diverticula has only been reported in limited case reports [10–14]. This technique is unique in that, through the creation of submucosal tunneling, the cricopharyngeus muscle or the diverticular septum can be methodically exposed, allowing for careful complete septotomy under direct endoscopic visualization, which thereby circumvents the uncertainties encountered in the previously mentioned endoscopic modalities.

The current study is the first series to describe the use of the D-POEM technique for the treatment of symptomatic esophageal diverticula. Our study suggests that D-POEM is safe and feasible, even in elderly patients with pre-existing comorbid conditions or those with prior failed open surgery, and is asso-

ciated with good short-term outcomes. The index endoscopy technical success rate was 90.9% (10/11), with clinical success attained in all patients who underwent successful D-POEM.

Nonetheless, the study has several limitations. Firstly, this is a retrospective study, which carries inherent limitations, including variable follow-up and no standardized algorithm of management across the multiple centers. Also, although this is the first reported case series on D-POEM, the sample size remains small. In addition, only tertiary centers were involved, which limits its generalizability to other centers with less experience. Finally, the follow-up duration is short and the risk of long-term symptom recurrence cannot be inferred. D-POEM is however a new technique and this crucial information will be reported in future studies with long-term follow-up.

In conclusion, in this international, multicenter study, our preliminary data suggest that the novel D-POEM technique is safe and effective in the treatment of symptomatic esophageal diverticula.

Competing interests

Kenneth Chang provides consultancy for and receives educational grants from Cook Medical, Olympus, and Medtronic. Vivek Kumbhari is a consultant for ReShape Lifesciences, Apollo Endosurgery, Boston Scientific, and Medtronic. Vikesh K. Singh is a consultant for Abbvie, Novo Nordisk, and Ariel and is an advisory board participant for Nordmark. Marcia Canto is a consultant for Pentax and the recipient of a research grant from C2 Therapeutics. Anthony N. Kalloo is a founding member and equity holder in Apollo Endosurgery. Mouen Khashab is a consultant for Boston Scientific, Olympus, and Medtronic and is on the medical advisory board for Boston Scientific and Olympus. The remaining authors have nothing to disclose.

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