Dysphagia (2022) 37:84–92
https://doi.org/10.1007/s00455-021-10252-0

ORIGINAL ARTICLE

Per Oral Endoscopic Myotomy for the Management of Large Esophageal Diverticula (D-POEM): Safe and Effective Modality for Complete Septotomy

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Received: 18 July 2020 / Accepted: 13 January 2021 / Published online: 3 February 2021

Abstract

With the advent of the technique of sub-mucosal tunnelling, peroral endoscopic myotomy (POEM) has been used for the treatment of esophageal diverticulum, which otherwise is a recurring problem with conventional flexible endoscopic treatment due to incompleteness of septotomy. This study reports our experience of the use of diverticular POEM (D-POEM) technique in the management of large esophageal diverticulum. This is a retrospective study of prospectively maintained database including all consecutive patients with symptomatic esophageal diverticulum presenting at a tertiary care academic center. D-POEM was performed using the technique of submucosal tunnelling and septotomy. Besides baseline parameters, technical success, clinical success, size of diverticula, procedure time, complications and symptom recurrence on follow up were noted. A total of five patients (4 males; median age 72) were included with an average Charlson comorbidity index of 3.2 ± 0.8. Of them, three had Zenker's while two had epiphrenic diverticulum. The median symptom duration was 12 months with a mean diverticulum size of 68.8 ± 1.9 mm. The mean procedure time was 64.80 ± 12.6 min. with a mean septotomy/myotomy length of 79.44 ± 12.2 mm. Minor adverse events were noted intra-procedure in two cases. Clinical success achieved in all cases with a significant mean dysphagia score reduction from 2.20 to 0.20 post procedure ($p = 0.011$). On a median follow up of 280 days (range 98–330), none had recurrence of symptoms. Our data highlighted that complete septotomy by D-POEM technique can be achieved for the management of large esophageal diverticulum and is safe and effective.

Keywords Esophageal diverticulum · Zenker's · Epiphrenic diverticulum · Per oral endoscopic myotomy · Diverticular POEM

Introduction

Esophageal diverticula entails a rare condition wherein outpouching of the esophageal wall may lead to symptoms in the form of dysphagia, regurgitation and occasionally chest pain or aspiration pneumonia [1]. It can be located either in the pharyngeal esophagus (Zenker's diverticulum), mid-esophagus (Rokitansky diverticulum) or distal esophagus (epiphrenic diverticulum). The key step in the management of symptomatic cases is septotomy allowing the esophageal and diverticular lumens to converge. Earlier, surgical treatment used to be the primary modality with a success rate of 80–100%, but with high morbidity and mortality rates (30 and 3% respectively) [2, 3]. With the advent of flexible endoscopic treatment, the adverse events rate was lower (~ 15%), but with reported lower success rates (56–100%) and higher recurrence rates of up to 35% [4–7]. This high recurrence rate was attributed to inadequate septotomy as the distal end of the diverticulum cannot be precisely gauged from the luminal view.

Using the recent technique of submucosal space creation, per oral endoscopic myotomy (POEM) have been successfully used for the management of various conditions such as achalasia, gastroparesis and subepithelial tumors [8]. This

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technique has recently been used for performing septotomy in the management of esophageal diverticula termed as diverticular per oral endoscopic myotomy (D-POEM) [9]. Data on the outcome of this modality is limited with only one large multicentre study [10] and the technique is still evolving.

We present here the technical nuances, difficulties and outcome of D-POEM performed on symptomatic large Zenker's (ZD) and epiphrenic (ED) diverticula cases in a tertiary care centre.

Materials and Methods

This is a retrospective review of our prospectively maintained database of patients who had undergone D-POEM for symptomatic ZD or ED at a tertiary care academic center between July 2019 and February 2020. The study was approved by the institutional ethics committee. Consecutive patients who underwent D-POEM were diagnosed based on imaging studies such as barium esophagogram and/or CT scan and confirmed by esophagogastroduodenoscopy (EGD). Besides the patient demographics, symptomatology of the patients in the form of dysphagia, halitosis, vomiting and weight loss were noted. Dysphagia was quantified as per the Dakkak and Bennnett score (zero, no dysphagia; one, dysphagia to solids; two, dysphagia to semisolids; three, dysphagia to liquids; four, complete dysphagia) [11]. The dysphagia scores were noted pre-procedure and on follow-up, either on clinical visit or phone calls. The other parameters noted included location and size of diverticula, Charlson comorbidity index [12], procedure time, length of hospital stay, number of repeat procedures and symptom recurrence.

The primary outcome measure was clinical success defined as resolution of dysphagia symptoms post-procedure without the need for repeat intervention during follow-up. Secondary endpoints included technical success (defined as completion of procedure), adverse events with severity grading as per the American Society for Gastrointestinal Endoscopy lexicon [13], mucosal injury (type I and II) [14], insufflation related events such as subcutaneous emphysema, capno-thorax and capno-peritoneum requiring intervention.

Procedural Technique

One day prior to the procedure all patients were kept nil per oral and an EGD was done to thoroughly clean the diverticulum, esophagus and stomach of any debris using sterile saline solution. All patients received intravenous antibiotic as per institution protocol. Anti-fungal was prescribed for a week prior to the procedure, if there was evidence of candidiasis on the initial screening EGD. All the procedures were performed under general anesthesia with endotracheal intubation with patient lying in supine position. A preprocedural written informed consent was taken from all the patients.

Procedural Steps

The steps follow the basics of a standard POEM procedure with modifications. The principle is to create a submucosal tunnel after entering upstream of the septum, complete septotomy of the muscular septum/bar and closure of the mucosal entry point (videos 1 and 2). A schematic representation of the steps for ZD is illustrated in Fig. 1. Similar principle holds true for ED as well.

A high-definition upper gastrointestinal endoscope (GIF-HQ 190; Olympus, Center Valley, PA) fitted with transparent distal attachment (D-201-11804, Olympus, Tokyo, Japan) was used for all cases.

Creation of Mucosal Elevation for Entry A mucosal bleb was created by injecting 15–20 ml solution, consisting of 1% indigo carmine and 0.9% saline, around 1–2 cm proximal to the diverticulum and along the septum. For larger diverticulum where the esophageal lumen is completely chinked, sub-mucosal bleb was created on the visible septum, rather than 1–2 cm proximal.

Submucosal Entry and Creation of Tunnel on Both Sides of the Septum With the help of triangular tip knife having water-jet facility (TTJ knife, KD-645L, Olympus, Tokyo, Japan) using ENDO Cut Q mode ((ERBE, Tubingen, Germany; duration one, interval six and effect three) a longitudinal incision of 3–4 cm was given over the mucosal elevation (Figs. 2b, 3b). The apical and lateral edges were undermined with the help of spray coagulation (50 W; effect two) and entry into the submucosal space was achieved. Submucosal tunnel was created and extended with the help of submucosal injection (Figs. 2c, 3c) and spray coagulation till the thick diverticular septum was identified (Figs. 2d, 3d). Thereon, the tunnel was continued on both sides of the septum, keeping the spray towards the septum to avoid mucosal injury that can occur on either side of the septum (on one side is the mucosa of the diverticulum while on the other side it is of the esophagus). The tunnel was completed on the diverticular side till its base and on the esophageal side it was extended 1–2 cm beyond the base.

For larger diverticulum, where the bleb was created on the septum, incision was given over the bleb and on encountering the septum, the initial fibers were dissected to facilitate tunneling on the esophageal side.

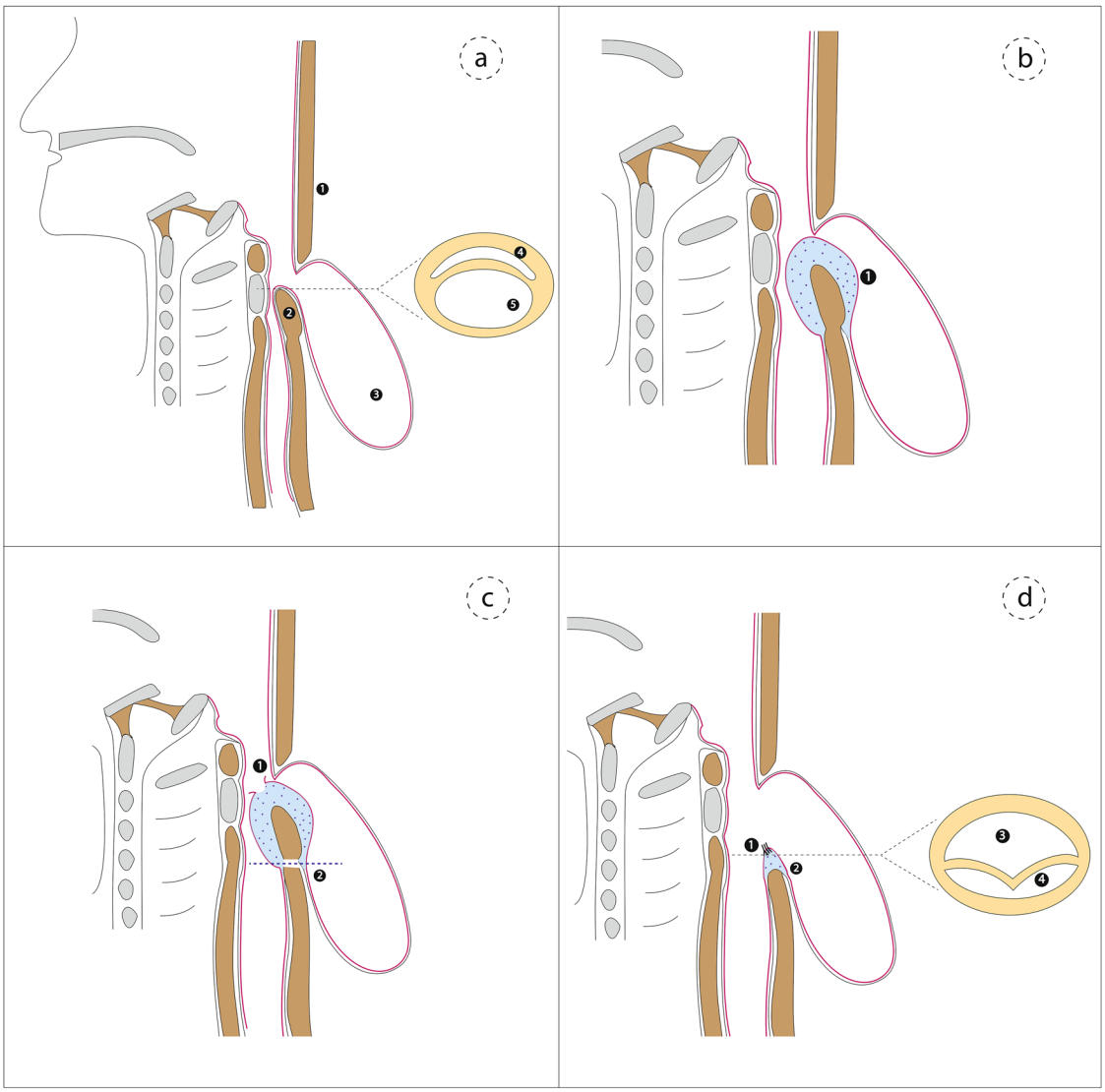

Fig. 1 Schematic representation of the steps of D-POEM: **a** the anatomy of Zenker's diverticulum with cross-sectional view as seen on esophagogastroduodenoscopy (*1* inferior pharyngeal constrictor muscle; *2* cricopharyngeal muscle; *3* diverticulum; *4* compressed esophageal lumen; *5* diverticular lumen); **b** Creation of the submucosal space with injection of saline and indigo carmine (1); **c** entry into the submucosal tunnel and septotomy (*1* mucosal entry point; *2* extent of septotomy); **d** post-septotomy status with cross-sectional view as seen on esophagogastroduodenoscopy (*1* clip closure of the mucosal entry point; *2* redundant mucosal fold; *3* widened esophageal lumen; *4* residual mucosal part of the diverticulum)

Complete Septal Division Septotomy was performed using insulated tip knife (ITknife 2™, KD-611L, Olympus, Tokyo, Japan) with the same settings as described above for ENDO Cut Q mode (ERBE, Tubingen, Germany) (Figs. 2e, 3e). The advantage of ITknife2 is that the insulated tip prevents injury to the mucosa of the esophageal side when the knife is hooked on to the septum with tip towards the esophageal mucosa as cutting in this orientation can sometimes be a little bit blind especially in very large diverticula. The septum was completely dissected down till the base and was extended 1–2 cm further over the esophageal side to ensure completeness of the septotomy (Figs. 2f, 3f). For ED, the dissection was continued into the esophageal side to release the lower esophageal sphincter (LES) as well. Adequacy of the septotomy during the procedure was assessed by the evident widening of the visible esophageal lumen diameter (Fig. 3g), reduced septal demarcation and easy passage of the scope through the esophageal lumen.

Hemostasis and Closure During and on completion of the procedure any blood vessel encountered or accidentally injured was tackled with either spray coagulation when small or with the help of hemostatic forceps (Coagrasper, Olympus, Tokyo, Japan) with soft coagulation mode

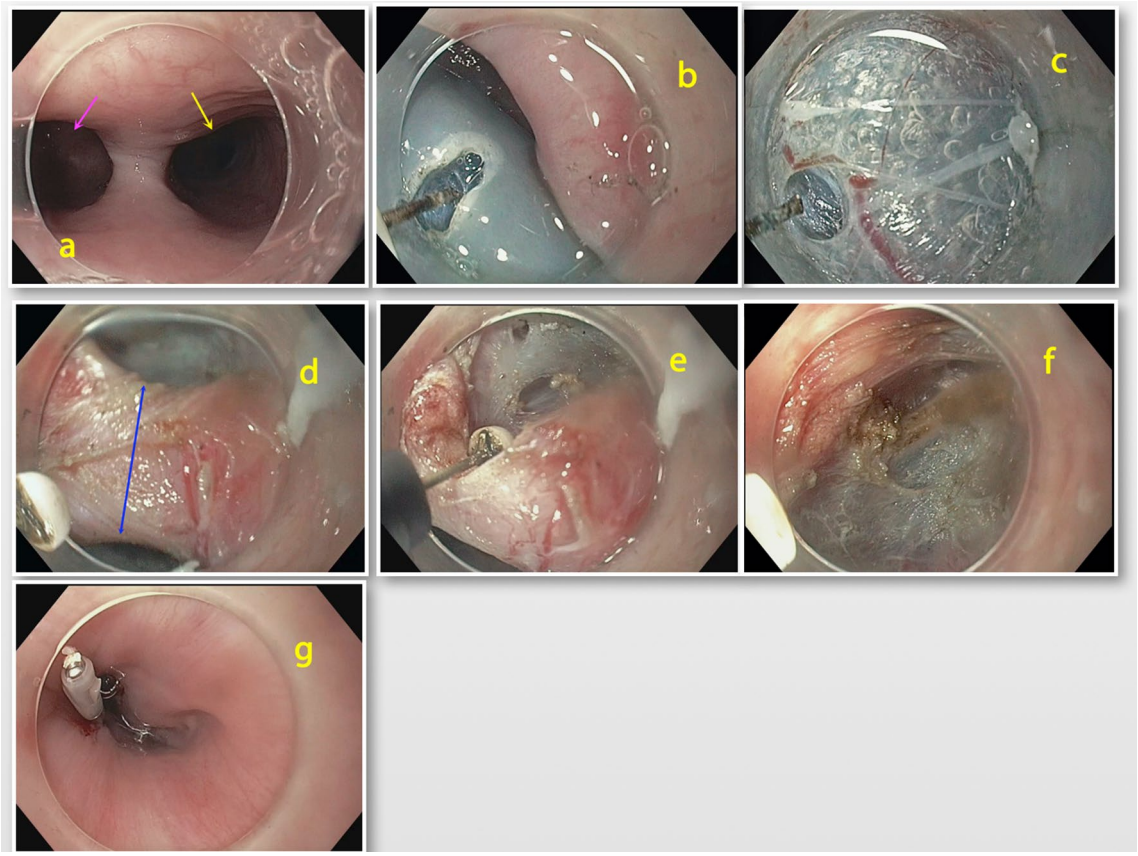

Fig. 2 Sequential steps of D-POEM for Zenker's diverticulum: **a** endoscopic view showing the esophageal (yellow arrow) and diverticular (pink arrow) lumen; **b** sub-mucosal injection followed by incision with TTJ knife; **c** submucosal dissection and tunnelling; **d** muscular septum identified (blue arrow); **e** septotomy using IT-Knife; **f** complete septotomy performed; **g** closure of mucosal incision site with clips

(ERBE, Tubingen, Germany, Watt-80, effect-4) when large. The esophageal mucosa was inspected for any evidence of mucosal injury and tackled accordingly. The mucosal incision was then closed with the help of hemoclips (EZ clip long, Olympus, Japan) (Figs. 2g, 3h).

Post-procedure

Post-operative, patients were observed in the ICU for 24 h and if no untoward event occurred during observation, they were shifted in the general ward. After ruling out any leak on water soluble contrast study, soft diet was started on post-operative day 2. In the absence of any post-operative adverse event in the form of bleeding, fever, chest pain, abdominal pain or vomiting, patients were discharged on day 3 of the procedure. Patients were kept on routine oral broad spectrum-antibiotics for 5–7 days. All were prescribed oral PPI for 4 weeks.

Follow Up

Patients were followed up after 4 weeks for relief of symptoms or recurrence. In cases of recurrence of symptoms, further work-up such as barium swallow study and follow-up EGD were advised. Further follow-up by clinic visit or over phone calls were done at 3, 6, 9 and 12 months.

Statistical Analysis

The analysis was performed using SPSS 21.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used as appropriate. Continuous data was expressed as either median with interquartile range or mean with standard deviation. A p value of < 0.05 was considered as significant.

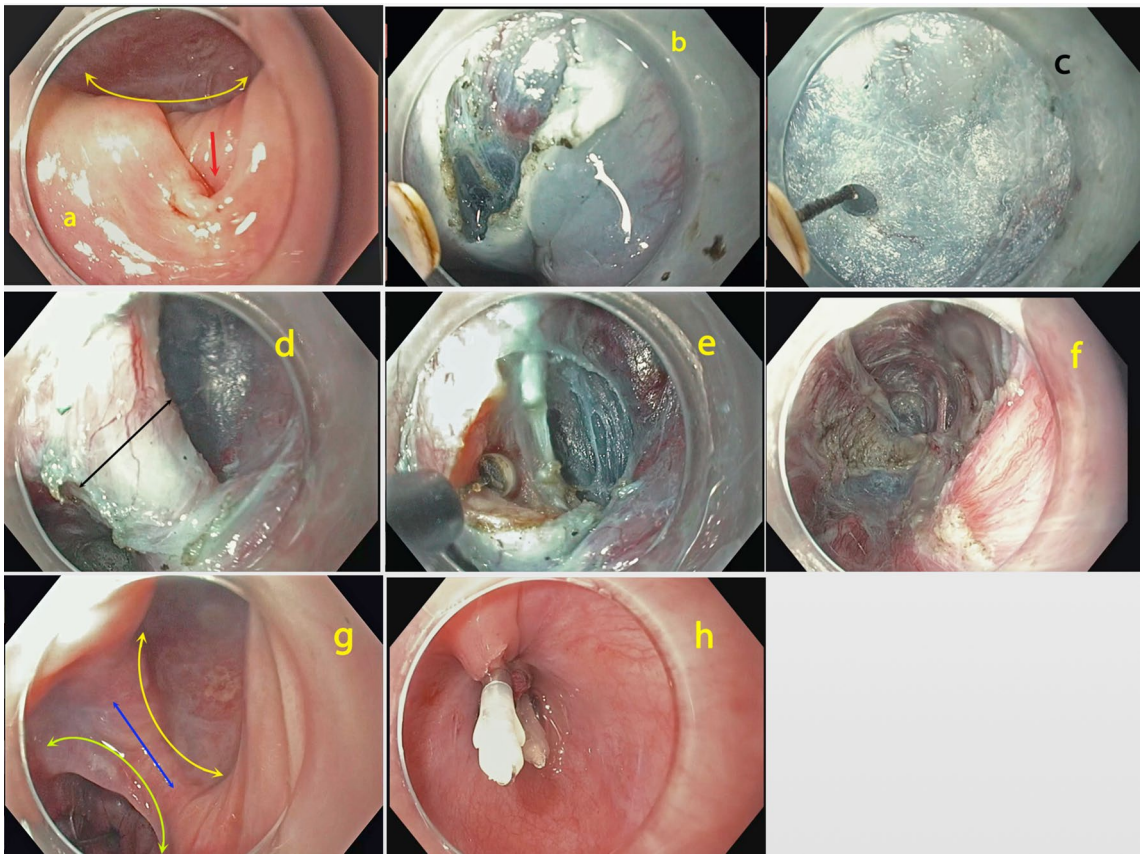

Fig. 3 Sequential steps of D-POEM for epiphrenic diverticulum: **a** endoscopic view showing the compressed esophageal (red arrow) opening and diverticular (yellow arrow) lumen; **b** sub-mucosal injection followed by incision with TTJ knife; **c** submucosal dissection and tunnelling; **d** muscular septum identified (black arrow); **e** septotomy using IT-Knife; **f** complete septotomy performed; **g** post-septotomy status (yellow arrow—residual diverticular lumen; blue arrow-mucosal residual bridge; green arrow-widened esophageal lumen); **h** closure of mucosal incision site with clips

Results

This study included five patients [4 males; median age 72 (range 49–74)] (Table 1) with an average Charlson comorbidity index of 3.2 ± 0.8. Out of them, three patients had ZD while two had ED. The median duration of symptoms was 12 months (IQR 47) with the commonest symptom being dysphagia (all cases). One patient of ZD complained more of reflux than dysphagia. Halitosis was noted in 3/5 (60%), weight loss in 2/5 (40%) and vomiting in 3/5 (60%). The baseline mean dysphagia score was 2.20 ± 0.8, with two patients having dysphagia score of 2 (40%) and two with dysphagia score of 3(40%). The mean diverticulum size was 68.8 ± 1.9 mm.

Procedure Characteristics and Outcomes

The overall technical success rate was 100%. The mean procedure time was 64.80 ± 12.6 min. The mean septotomy/myotomy length was 79.44 ± 12.2 mm. Adverse events occurred in two cases, one with subcutaneous emphysema and another with type I mucosal injury. Both were managed conservatively. The mean length of hospital stay was 3.20 ± 0.37 days.

Clinical success was achieved in all the cases with a significant mean dysphagia score reduction from 2.20 in the pre-procedure stage to 0.20 in the post-operative phase ($p = 0.011$). The median length of follow up was 280 days (range 98–330). None of the patients had recurrence of symptoms and did not require further intervention till the last follow-up.

Discussion

Zenker's (ZD) or epiphrenic (ED) diverticula are rare disorders of the esophagus and when symptomatic can lead to dysphagia, regurgitation or chest pain. Although endoscopic and radiological studies report a prevalence of around 3% [15, 16], true prevalence is difficult to gauge

Table 1 Characteristics of the patients and procedure details

	Age/sex	Duration of symptoms (months)	Co-morbidities	Type of diverticulum	Dysphagia score (pre-procedure)	Dysphagia score (post-procedure)	Diverticulum size (mm)	Septotomy length (mm)	Procedure time (mins)	Adverse events
1	49/M	8	HbsAg positive	ZD	2	0	60	70	52	–
2	74/F	60	Diabetes	ZD	1	0	71	80	83	–
3	67/M	48	Hypertension, CVA	ZD	2	1	80	80	71	Subcutaneous emphysema
4	72/M	6	Hyperthyroidism, CVA	ED	3	0	41	60	55	–
5	72/M	12	SLE	ED	3	0	92	100	63	Type I mucosal injury

M male, *F* female, *CVA* cerebrovascular accident, *SLE* systemic lupus erythematosus, *ZD* Zenker's diverticulum, *ED* epiphrenic diverticulum

as only symptomatic patients are evaluated. While ZD is the commonest type (~70%) with an estimated prevalence of 0.01–0.11% [5], ED have an estimated prevalence of 0.015% [17]. Initially, the management of choice for both the conditions was surgical [7, 18]. However, these patients are usually elderly with multiple co-morbidities and the operative risk is high with morbidity of 30% and mortality of 3% [7]. The first report of the technique of flexible endoscopic septum division (FESD) was described by Mulder and Ishioka, in 1995 [19, 20]. The goal of this technique is to achieve partial myotomy of the cricopharyngeal muscle and release the intra-luminal "pressure". The technique has evolved over the years with the use of various devices starting from needle knife to hook knife, Stag Beetle (SB) knife (Sumitomo Bakelite Co., Japan) to the recent Clutch Cutter Knife (Fujifilm, Tokyo, Japan) [21]. The pooled success rate of FESD, in a recent meta-analysis, is 91%, with adverse rates of 11.6% and recurrence rates of 11% [5]. The use of submucosal tunnelling for a systematic and complete septum dissection is a new addition to the armamentarium for the endoscopic management of such esophageal diverticula.

Per oral endoscopic myotomy (POEM) using the principle of submucosal tunnelling is an established technique for the management of achalasia [22]. The initial reports of the use of this technique for the management of ZD [9, 23] and ED [24, 25] were promising. Since then, limited data exists on the use of this technique of POEM for the management of diverticula. It has various nomenclature such as Z-POEM (for Zenker's diverticulum), E-POEM (for epiphrenic diverticulum) or a common term D-POEM (for diverticular POEM). We present here our case series of five such large symptomatic esophageal diverticula (three cases of ZD and two of ED) managed with D-POEM with a mean diverticular size of (68.8 ± 1.9) mm. with 100% technical success and clinical success till last follow-up.

The advantage of D-POEM over the conventional FESD is the completeness of the myotomy. Due to the risk of leakage and mediastinitis (4.8%), endoscopists tend to do incomplete/partial myotomy during FESD, with higher recurrence rate (12.8%) and failure rate (7.7%) [26]. D-POEM, on the other hand, allows complete delineation of the septum in the submucosal tunnel resulting in complete dissection of the septum. In fact, Costagmagna et al. had demonstrated that at 6 months, the prognostic variables for failure of FESD are septotomy length of ≤ 25 mm and diverticular size ≥ 50 mm [27]. Thus, larger the diverticulum and shorter the myotomy, higher is the risk for recurrence. ZD occurs due to the dysfunction of the cricopharyngeal muscle and hence, this might not be applicable for non-Zenkers' diverticulum. Previous studies had reported of the use of this technique in a mean diverticular size of 3–4 cm [10, 28, 29] and did not systematically

Table 2 Major studies using D-POEM for management of esophageal diverticula

	No. of cases	Diverticulum size (mean)	Technical/clinical success	Serious adverse events (%)	Follow up (mean/median)	Recurrence
Yang et al. [29] (USA)	7 ZD 1 Mid esophagus 3 ED	34.5 mm	90.9%/100%	0	145 days	0
Yang et al. [10] (multicenter)	75 ZD	31.3 ± 1.6 mm	97.3%/92%	5.3	291.5 days	One patient
Maydeo et al. [32] (India)	20 ZD 5 ED	–	100%/86%	0	12 months	–
Klnoshita et al. [35] (Japan)	14 ED with achalasia	26.5 mm	100%/–	7.1	3 months	–
Basile et al. [36] (France)	7 mid/lower esophagus	–	100%/85%	0	3 months	–
Zeng et al. [28] (China)	2 ZD 5 mid-esophagus 3 ED	–	100%/90%	10	11 months	0
Current study	3 ZD 2 ED	68.8 ± 1.9 mm	100%/100%	0%	9 months	0

ZD Zenker's diverticulum, *ED* epiphrenic diverticulum

report of the septotomy length. In our study, the mean diverticular size was 68.8 ± 1.9 mm with a septotomy/myotomy length of 79.44 ± 12.2 mm and no recurrence at a median follow up of 9 months. Thus, our study is the first proof of concept for establishing the benefit of D-POEM in large diverticula with a more complete (longer) septotomy as had been highlighted by Costamagna et al. [27]

In ZD or ED, patients present with symptoms secondary to functional obstruction of the lumen. ED is often associated with concomitant motility disorders (~ 75%) [30]. Hence, HRM is advocated in these cases or sometimes the evidence comes from the barium studies. With the use of D-POEM, the septal muscle can be easily dissected to its base and extended to the LES, as was done in the current study. In fact, this technique when used in a case of achalasia with ED is known as salvage POEM (S-POEM), first described by Sato et al.[31] The largest series of POEM with ED of 14 cases, with a median ED diameter of 29 mm, reported a 71.4% reflux esophagitis rate with 7.1% having GERD symptoms. None of the two cases, in the current study had GERD at 6-month follow-up.

The key step in the technique of D-POEM for ED is to locate the septum. This can be attained by making the entry point 1–2 cm proximal to the diverticulum and along the septum. This ensures that on incision and entering the submucosal space we directly encounter the septum rather than getting lost. The other strategy would be to inject some undiluted indigo carmine into the base of the septum. This acts as bluish tinged beacon during navigation in the tunnel [32]. The limiting factor for D-POEM in ZD is the working space in pharynx, which is too less for the endoscopist's comfort and adds to the difficulty. Larger diverticulum poses bigger challenge. This can be overcome by creating the submucosal bleb on the septum, rather than 1–2 cm proximal, and give incision. On encountering the fleshy septum, the initial fibers can be dissected and submucosal injection given and dissected to create enough space for the submucosal entry. Another strategy could be the hybrid strategy which is a combination of standard septotomy and submucosal tunneling [33]. Closure after D-POEM in ZD can be challenging and gentle closing clips with shorter shafts can be beneficial.

The technique of D-POEM is still evolving and hence is still recommended as an experimental or research modality of treatment for ZD [34]. A recent large multi-centre study of 75 patients showed a clinical success of 92% at 12-month follow-up [10]. The significant studies (≥ 5 cases) of D-POEM and their outcomes are outlined in Table 2. Compared to other major studies, the current study entails cases with larger diverticular size (68.8 ± 1.9 mm). We systematically noted the septotomy/myotomy length (mean—8.0 cm) and hence objectively ensured adequate septotomy length which is a predictive factor for clinical success or recurrence [27]. In fact, measuring the intra-procedure septotomy length can be taken as more objective marker of adequateness of septotomy, keeping the pre-procedure diverticular size in mind.

Although promising as it may appear, D-POEM do have its glitches. While dissecting the cricopharyngeal muscle, the buccopharyngeal fascia lying posteriorly can get breached resulting in perforation [37]. Working in a narrow area, this can become challenging. Moreover, since the mucosa is kept intact in D-POEM, compared to FESD, the excess mucosa can lead to "mucosal blowout" or regurgitation symptoms. This may later require mucosectomy. While conventional FESD does not require general anaesthesia, D-POEM does require and that can be dicey as the patients tend to be elderly with multiple co-morbidities.

This study has established the benefit of sub-mucosal tunnelling method as a more effective technique for ensuring complete and long septotomy in symptomatic large diverticula with acceptable adverse events. The limitations of the study include small sample size and retrospective data. The study was carried out in a tertiary care centre and hence lacks generalisability. Moreover, although the study had 9-month follow-up, longer follow up is needed to assess long-term recurrence. Larger studies with comparative RCTs would be needed before this modality can be recommended as standard modality of choice. With the availability of more robust data, D-POEM may be considered as first line therapy in the future for ZD/ED in expert centres for these poor surgical risk elderly patients with multiple comorbidities.

In conclusion, D-POEM is a safe and effective technique for the management of large symptomatic ZD and ED ensuring a more complete septotomy and thus better outcome.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00455-021-10252-0.

Acknowledgements Dr JS and Dr HSM has contributed equally for the work

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest.

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