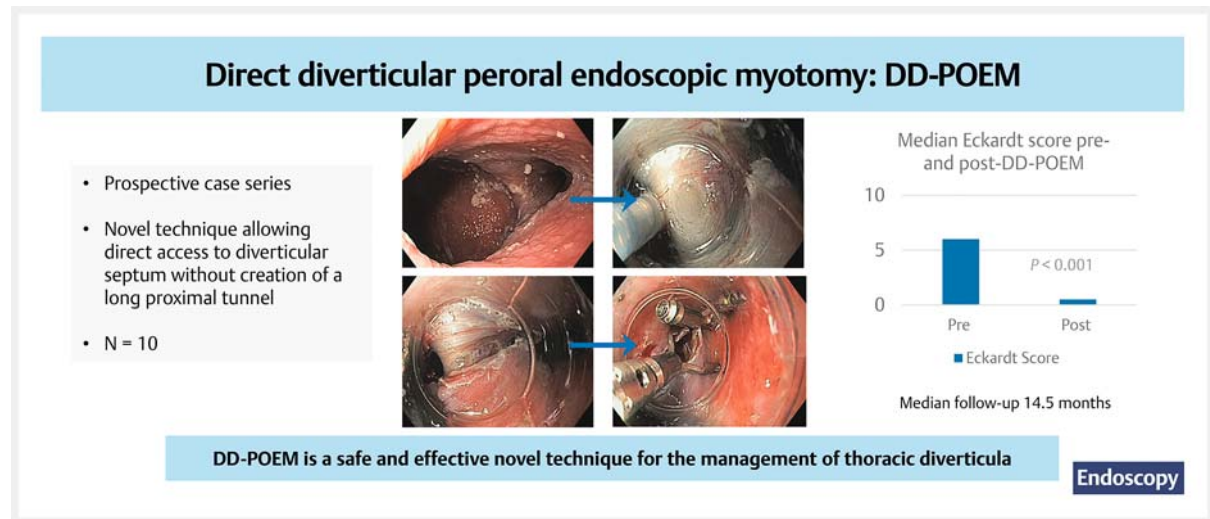


Direct diverticular peroral endoscopic myotomy for the treatment of thoracic esophageal diverticula: technique and outcomes

GRAPHICAL ABSTRACT



Authors

Julia L. Gauci¹, Sunil Gupta^{1,2}, Muhammad Abu Arisha¹, Andrew Tang¹, Timothy O'Sullivan^{1,2}, Anthony Whitfield^{1,2}, Oliver Cronin^{1,2}, Varan Peranathan¹, Clarence Kerrison¹, Eric Y. Lee¹, Nicholas G. Burgess^{1,2}, Michael J. Bourke^{1,2}

Institutions

- 1 Department of Gastroenterology and Hepatology, Westmead Hospital, Sydney, Australia
- 2 Westmead Clinical School of Medicine, The University of Sydney, Sydney, Australia

Corresponding author

Michael J. Bourke, MD, Department of Gastroenterology, Westmead Hospital, Suite 106A, 151 hawkesbury Rd, Westmead, Sydney, NSW 2145, Australia
michael@citywestgastro.com.au

submitted 23.5.2023

accepted after revision 17.8.2023

published online 18.10.2023

Bibliography

Endoscopy 2024; 56: 41–46

DOI 10.1055/a-2182-5853

ISSN 0013-726X

© 2023, Thieme. All rights reserved.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Table 1 s

Supplementary material is available under

<https://doi.org/10.1055/a-2182-5853>

ABSTRACT

Background Diverticular peroral endoscopic myotomy (POEM) is an alternative to surgery for the management of symptomatic thoracic esophageal diverticula. Conventionally, this requires proximal tunnel formation but a direct approach may simplify the technique. Herein, we report the outcomes of direct diverticular-POEM (DD-POEM).

Methods We conducted a single-center prospective observational study evaluating DD-POEM. This involved a direct approach to the diverticulum. Success was defined as an Eckardt score of ≤ 3 without the need for reintervention.

Results 10 patients underwent DD-POEM (median age 72 years; interquartile range [IQR] 14.3; male 60% [n=6]). Median diverticulum size was 40 mm (IQR 7.5) and median location was 35 cm from the incisors (IQR 8.3). Five patients (50%) had an underlying dysmotility disorder. The median procedure duration was 60 minutes (IQR 28.8). There were no adverse events. The median hospital stay was 1 day (IQR 0.75). The pre-procedure median Eckardt score of 6 (IQR 4)

significantly improved to 0 (IQR 0.75; $P < 0.001$) at a median follow-up of 14.5 months (IQR 13.8). Success was achieved in all patients.

Conclusions DD-POEM was a safe technique for the management of thoracic esophageal diverticula. Owing to its simplicity and excellent performance it should be further evaluated for the treatment of this disorder.

Introduction

Esophageal diverticula are uncommon, with a prevalence of 0.06%–4% [1]. Although they are often discovered incidentally, they may present with debilitating symptoms such as dysphagia, regurgitation, weight loss, and aspiration [2]. Esophageal diverticula may occur in the upper esophagus (Zenker's diverticulum) or the thoracic portion. Owing to their anatomic location within the mediastinum, the management of thoracic diverticula is considered separately. Thoracic diverticula include mid-esophageal "traction" diverticula, usually secondary to mediastinal inflammation [3], and epiphrenic "pulsion" diverticula, which are often associated with dysmotility, particularly impaired relaxation of the lower esophageal sphincter [4].

Asymptomatic patients with thoracic diverticula typically do not require treatment. Symptomatic patients should undergo high resolution manometry and if present, treatment of the underlying dysmotility disorder will often result in symptom resolution [4]. Traditional management for patients with persistently symptomatic esophageal diverticula is surgical resection; however, resection poses a considerable risk of morbidity and mortality [5].

Flexible endoscopic septum division was developed as a minimally invasive alternative to surgery for the treatment of Zenker's diverticula; however, it is associated with high recurrence rates due to incomplete septotomy, probably as a result of operator fear of inadvertently dividing the esophageal wall [6]. The application of this technique to the treatment of thoracic diverticula was limited by the potential risks of perforation and mediastinitis in this location [7]. Advances in submucosal tunneling techniques led to the development of a promising alternative, diverticular peroral endoscopic myotomy (D-POEM), which would allow complete dissection of the muscular septum while preserving mucosal integrity, thereby reducing the risk of complications and symptom recurrence [8]. However, submucosal tunnel creation is time consuming and associated with a steep learning curve. Furthermore, this cohort of patients have often undergone prior surgical or endoscopic therapy to treat underlying dysmotility, with resulting submucosal fibrosis making third space navigation challenging.

We previously described a novel technique, transmucosal diverticular myotomy, herein referred to as direct diverticular POEM (DD-POEM), which enables direct access to the diverticular septum while still preserving the mucosa, thereby simplifying and shortening the procedure compared with previously outlined techniques [9]. In this article, we describe the clinical outcomes for patients who underwent DD-POEM for symptomatic thoracic diverticula at our center.

Methods

We conducted a single-center prospective observational study of patients undergoing DD-POEM for the treatment of symptomatic thoracic diverticula. Consecutive patients referred to our unit for endoscopic management of persistently symptomatic thoracic diverticula were enrolled between May 2017 and March 2023. Patients had to be aged over 16 years and provide written consent to participate in the study. The diagnosis of thoracic diverticula was based on endoscopic assessment and contrast imaging (barium swallow). All patients underwent high resolution manometry to investigate for the presence of underlying esophageal dysmotility. If dysmotility was diagnosed, patients were only considered for endoscopic treatment of their thoracic diverticula if they remained symptomatic following endoscopic and/or surgical management of the dysmotility disorder. A validated symptom scoring system (Eckardt score) was utilized and calculated prior to and after endoscopic intervention [10]. The study was approved by the Human Research Ethics Committee at Westmead Hospital.

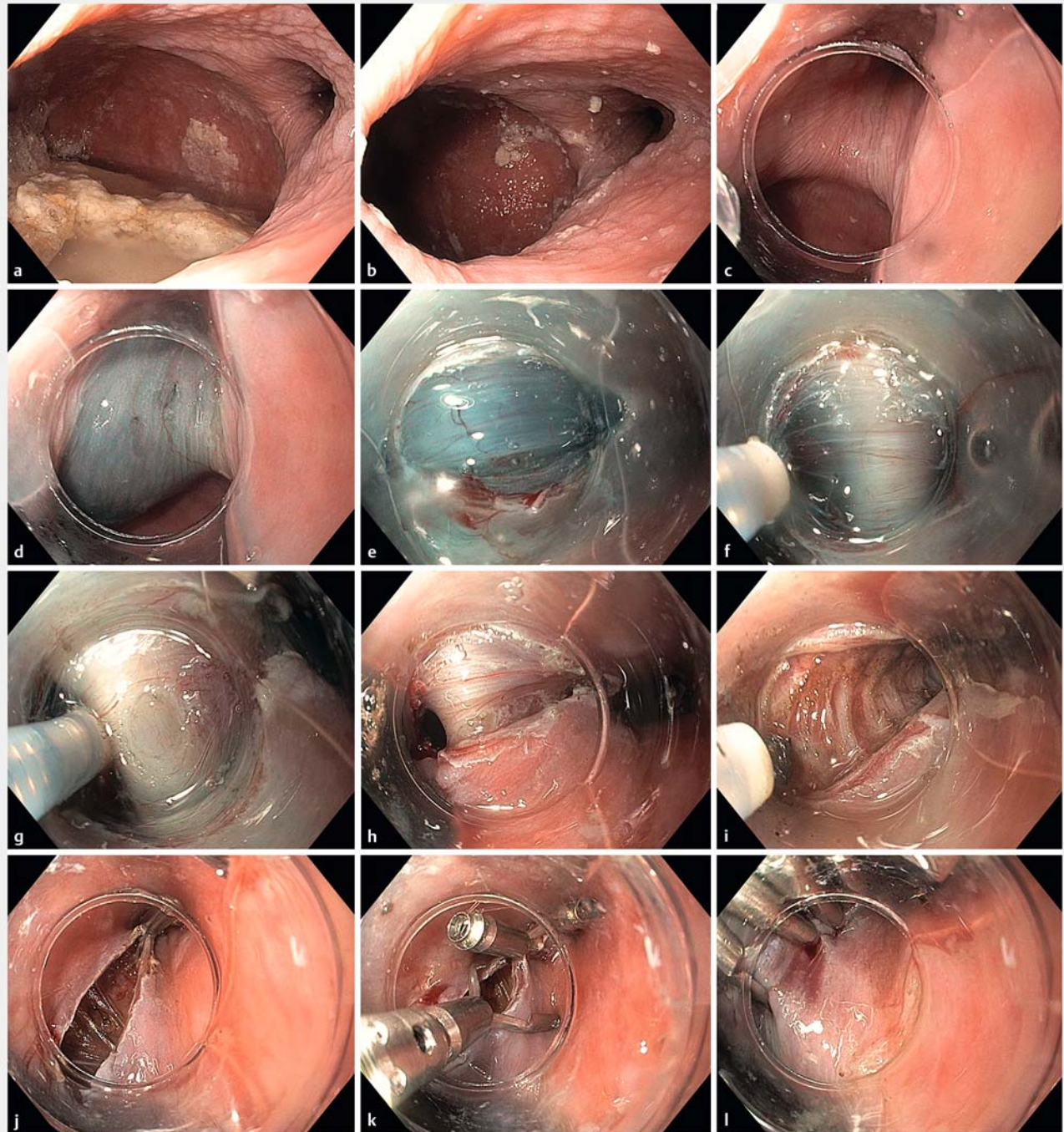
Patients and equipment

All endoscopic procedures were performed by a study investigator (accredited gastroenterologist with interventional endoscopy training and an established tertiary referral practice). Procedures were performed under general anesthesia with endotracheal intubation. A GIF-HQ190 high definition gastroscope (Olympus, Tokyo, Japan) was used. A transparent distal tapered cap (ST Hood; Fujifilm, Tokyo, Japan) was the preferred distal attachment. Carbon dioxide insufflation was used for all cases. A microprocessor-controlled generator (VIO 300D; ERBE, Tübingen, Germany) was used for all cases. Large vessels were avoided and significant intraprocedural bleeding was treated with hemostatic forceps (Coagrasper; Olympus) using soft coagulation (effects 5–7). A triangle tip electrosurgical knife (Olympus Medical Systems, Tokyo, Japan) was used. Minor bleeding was treated with soft coagulation.

DD-POEM procedure

Endoscopic assessment of the diverticulum was conducted using a gastroscope. Any residual food or fluid within the diverticulum was first cleared. DD-POEM was then performed following a four-step process (► **Fig. 1**, ► **Video 1**).

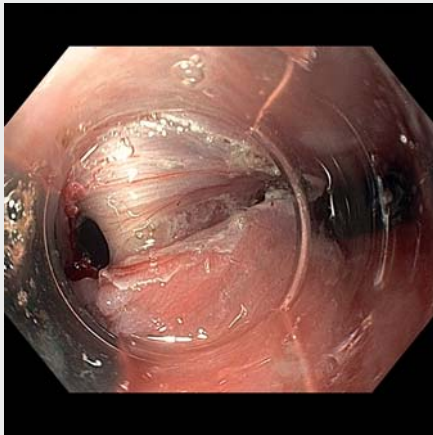
Step 1. Submucosal injection and incision. A submucosal injection of succinylated gelatin with 0.4% indigo carmine and 1:100 000 epinephrine was performed to create a cushion, directly proximal to the diverticular septum. A 2 cm oblique mucosal incision was made above the septum to enter the submucosal plane (Endo Cut Q, effect 2).



► **Fig. 1** Direct diverticular peroral endoscopic myotomy (DD-POEM) procedure. **a** Endoscopic assessment of the diverticulum was conducted using a gastroscope. **b** Any residual food or fluid within the diverticulum was cleared. **c–l** DD-POEM was then performed following a four-step process. **c–e** Step 1: submucosal injection just above the septum (**c, d**) and oblique mucosal incision to the long axis of the septum (**e**). **f** Step 2: identification of the muscular bridge/septum. **g** Peri-septal dissection to achieve isolation of the septum and adequate exposure under direct vision. **h, i** Step 3: complete myotomy of the muscular septal bridge. **j–l** Step 4: closure of the mucosal incision with through-the-scope clips.

Step 2. Peri-septal submucosal dissection to isolate the muscular bridge. Once the submucosal plane was entered, a submucosal tunnel was created on either side of the septum in order to isolate the septal bridge. Tunnel creation was commenced distal to the mucosal incision just above the septum

(i.e. no tunnel creation proximal to the septum was required). Submucosal dissection was performed using a combination of Dry Cut (effect 4) and preciseSECT (effect 4). Dissection was carried out on the luminal side of the septum and extended ≥ 2 cm below the inferior limit of the diverticulum. This was re-



Video 1 Peri-septal dissection to achieve isolation of the septum and adequate exposure under direct vision prior to complete myotomy of the septal bridge.
Online content viewable at:
<https://doi.org/10.1055/a-2182-5853>

peated on the diverticular side of the septum extending to the base of the diverticulum. The objective was to achieve isolation of the septum and adequate exposure under direct vision.

Step 3. Diverticular myotomy. Full-thickness myotomy of the diverticular septum was carefully performed using Dry Cut (effect 4) and preciseSECT (effect 4). The adventitia was preserved. The myotomy was extended ≥ 2 cm below the inferior aspect of the thoracic diverticulum.

Step 4. Closure of the mucosal incision. The first clip was placed on the inferior aspect of the wound, without involving the wound, to raise an uninvolved mucosal mound. This inverts the raised edges of the incision into the lumen. The remainder of the defect was then closed using small (11 mm) through-the-scope clips (Lockado; CK Surgitech, Arundel, Australia). It is important not to use large clips because this may result in too much mucosa being dragged into the wound, which can result in jagged, uneven, and incomplete closure.

The procedure time was recorded as the time taken to complete all of the steps involved in DD-POEM (i. e. from the start of submucosal injection to final clip placement). The presence or absence of submucosal fibrosis was recorded.

Post DD-POEM management and follow-up

Following the procedure, patients were fasted and admitted to hospital overnight. They received intravenous fluids and a single dose of intravenous antibiotics (ceftriaxone and metronidazole). The following morning, they were clinically reviewed and, if well, were started on clear fluids. They were discharged home once afebrile, pain-free, and tolerating a liquid diet. Patients were advised to gradually advance their diet as follows: free fluids from Day 2, soft diet from Day 3, and then liberalize their diet as tolerated from Day 5. All patients were prescribed proton pump inhibitors twice daily for 2 months, then as required. Follow-up encounters, either clinical review or standardized

phone interviews, were conducted at 2 weeks, and 6, 12, 18, and 24 months.

Outcomes

An excellent clinical outcome was defined as an Eckardt score of ≤ 3 without the need for reintervention. Technical outcomes, including procedure duration, hospital length of stay, and adverse events, were systematically recorded. Technical success was defined as completion of all the steps involved in DD-POEM and complete division of the muscular bridge.

Statistical analysis

SPSS version 27.0 (IBM Corp., Armonk, New York, USA) was used for data analysis. Continuous variables were reported as means and SDs or medians and interquartile ranges (IQRs), as appropriate. Categorical data were expressed as frequencies (%). Chi-squared tests were used to test for association between categorical variables. A *P* value of < 0.05 was used to determine statistical significance.

Results

Between May 2017 and March 2023, 10 patients underwent DD-POEM (median age 72 years [IQR 14.3]), the majority of whom were male ($n = 6$; 60%) (see **Table 1 s** in the online-only Supplementary material). The most common indication for referral was regurgitation, with all patients reporting this symptom at least daily, followed by dysphagia, which was reported in 9/10 patients (90%).

Esophageal diverticula were a median of 40 mm in maximum dimension (IQR 7.5) and located a median of 35 cm from the incisors (range 25–42 cm; IQR 8.3) (**Table 1 s**). Six (60%) were located at the 3 o'clock position, and the remaining 4 (40%) were situated at the 9 o'clock position. The majority were epiphrenic diverticula ($n = 7$; 70%), and the remaining three esophageal diverticula (30%) were situated in the mid-esophagus. The latter cases were not associated with dysmotility.

Five patients (50%) were diagnosed with an esophageal dysmotility disorder, all of whom underwent endoscopic and/or surgical treatment prior to referral for diverticulotomy (**Table 1 s**). Of these patients, one with Type I achalasia underwent conventional POEM, whereas 2/4 patients diagnosed with non-achalasia esophageal motility disorder had previously undergone lower esophageal sphincter-preserving POEM. Two patients (20%) underwent prior laparoscopic myotomy, diverticulectomy, and fundoplication at different centers; both experienced a staple-line leak postoperatively.

DD-POEM was performed in all cases with no technical difficulties. The median duration of DD-POEM was 60 minutes (IQR 28.8). A median of 7 clips (IQR 3.3) were needed for closure of the mucosal incision. Submucosal fibrosis was noted in five patients (50%), all of whom had undergone prior endoscopic or surgical intervention. There were no significant intraprocedural or delayed complications. The median hospital length of stay was 1 day (IQR 0.75). The pre-procedure median Eckardt score was 6 (IQR 4); this significantly improved to 0 (IQR 0.75; $P < 0.001$) at a median follow-up of 14.5 months (IQR 13.8).

An excellent clinical response was achieved in all 10 patients (100%). No patients developed recurrence of their symptoms and no cases of reintervention were recorded during the follow-up period.

Discussion

Thoracic diverticula are uncommon and usually detected incidentally [1]. However, when symptomatic, they can significantly impact quality of life and may result in complications such as aspiration and nutritional failure [2]. Epiphrenic diverticula are often associated with a hypercontractile dysmotility disorder and symptoms usually resolve upon treatment of the underlying spastic condition [2, 11]. A small cohort of these patients are treatment refractory and require further intervention to treat the diverticulum. We report the first case series of DD-POEM, demonstrating that this novel technique is safe, simple, and effective, with excellent clinical and technical success in all patients, no recurrence, and no adverse events.

DD-POEM involves the creation of a dissection plane within the submucosal space on both sides of the septum. As a result, the endoscopist is able to view the muscular bridge in its entirety, enabling complete septotomy to be achieved with confidence. An excellent clinical outcome was achieved in all 10 patients (100%), which was sustained over a median follow-up period of 14.5 months. In addition, our technique allows for the preservation of the mucosal lining, reducing the risk of mediastinal complications. The main innovation of DD-POEM lies in performing a mucosal incision just above the septum, without creating a long, proximal tunnel, making the technique more precise. Technical success (i. e. completion of all steps in DD-POEM and complete septotomy) was achieved in 100% of patients, despite 50% of our cohort having undergone previous endoscopic and/or surgical interventions. This approach was demonstrated to be safe, with no intra- or post-procedural complications, and was associated with a short hospital stay (median 1 day). Moreover, our technique was efficient, with a median procedure time of 60 minutes, which is shorter than published reports for alternative endoscopic techniques [12, 13].

The current standard of care for patients with persistently symptomatic thoracic diverticula is surgery, which typically involves laparoscopic myotomy, diverticulectomy, and fundoplication [5]. A meta-analysis of 25 studies (n=511) involving surgical treatment of thoracic diverticula revealed a pooled treatment success rate, morbidity, and mortality of 88.5%, 21.1%, and 5.9%, respectively. Staple line leaks are particularly problematic, occurring in as many as 13.3% of patients and often necessitating reoperation [14]. In our series, both patients who underwent surgical diverticulectomy prior to referral to our unit suffered a postoperative leak, which resulted in prolonged and complicated inpatient admissions.

Flexible endoscopic septum division, developed as a minimally invasive alternative for the management of Zenker's diverticula, has a reported technical success rate of 91% and an adverse event rate of 11.3% [6]. The main limitation of this technique is the inability to visualize the distal end of the mus-

cular septum while performing myotomy. This results in high rates of recurrence (up to 30%), most likely due to incomplete septotomy, which often requires reintervention [15]. Furthermore, operators are reluctant to apply this technique to the treatment of thoracic diverticula owing to the potential for perforation in the mediastinal space [16]. To overcome this problem, submucosal tunneling techniques, collectively termed diverticular POEM (or D-POEM), have been applied to the management of esophageal diverticula [17]. Working within the submucosal space allows the base of the septum to be accurately identified and safely divided. A recent meta-analysis comparing D-POEM with flexible endoscopic septum division in the management of Zenker's diverticulum revealed that the clinical success of D-POEM was significantly greater (risk ratio [RR] 1.13, 95%CI 1.05–1.22), although interestingly there was no significant difference in the technical success rates (RR 0.99, 95%CI 0.95–1.02) or adverse event rate (RR 0.77, 95%CI 0.26–2.30); the procedure time and length of hospital stay were also comparable [7]. However, the management of Zenker's diverticula is not readily applicable to thoracic diverticula; the thoracic location presents unique endoscopic challenges and an increased risk of mediastinal complications.

The published experience of D-POEM in the thoracic esophagus is limited to a few small case series, with mostly short follow-up periods [8, 12, 18–21]. The largest case series (n=13) [12] reported clinical success, technical success, and adverse events rates of 84.6%, 92.3%, and 30.4%, respectively, and median hospital stay of 3 days (range 3–5 days), all of which are inferior to our findings. Complications included capnoperitoneum, mucosal injury, and a delayed leak [12]. The only case of technical failure in the latter cohort was as a result of submucosal fibrosis [12]. Five (50%) of our cohort had documented submucosal fibrosis, which did not preclude a successful outcome. This group had a mean procedure duration of 70 minutes (range 40–120 minutes); our median procedure time was shorter, at 60 minutes [12]. Other case studies report mean procedure times ranging from 36 minutes to 63.2 minutes [8, 18, 19]. These series included epiphrenic diverticula only, whereas our cohort included complex patients who had undergone multiple interventions prior to referral, as well as three patients with mid-esophageal diverticula, which are notoriously challenging and underrepresented in the literature. The duration of hospital stay was much lower in our group, with a median of 1 day compared with 3.2–8.8 days in the published case series of D-POEM for thoracic diverticula [8, 12, 18–21].

DD-POEM provides similar advantages to D-POEM by dissecting within the submucosal space while preserving mucosal integrity. Our technique differs by obviating the need for creation of a proximal tunnel, which is time consuming, involves a steeper learning curve, and is potentially responsible for the higher adverse event rates and longer inpatient hospital stay demonstrated in D-POEM. Our excellent clinical and technical success rates suggest that long tunnel creation is of no additional benefit in the context of endoscopic diverticular myotomy. Furthermore, we suspect that eliminating proximal tunnel creation reduces the risk of incurring mucosal injury, a reported complication with D-POEM [12], which was not observed in our

group. This is supported by large multicenter data showing that tunnel creation during conventional POEM was associated with inadvertent mucosotomy (2.8%) and bleeding (0.3%) [22]. Although underreported in the literature, there is a recognized risk of disorientation during tunnel creation that may result in missing the diverticular septum altogether. This reflects the imprecision of the long tunnel technique. Precision in medicine is increasingly recognized as an essential pillar for the provision of high quality patient care [23]. We postulate that direct access to the septum is of particular benefit in the management of thoracic diverticula, which are more challenging than Zenker's diverticula not only due to their anatomical location but also as a result of their pathophysiology. A proportion of patients will have already undergone endoscopic or surgical interventions to treat dysmotility, which in our experience was associated with significant scarring and submucosal fibrosis, making tunneling especially challenging and time intensive.

Our study is limited by its small size and involvement of a single tertiary center. As previously stated, thoracic diverticula are rare, even more so when selecting those patients who require treatment due to persistent symptoms. The cohort was recruited over a 5-year period in a high volume tertiary center where POEM procedures are performed on a weekly basis. Recruiting large cohorts would take several years, which would not keep up with the rate of technical advances in third space endoscopy. Owing to their rarity and requirement for subspecialized treatment skills, these cases should only be tackled by operators with significant experience in third space endoscopy.

Conclusion

DD-POEM is a novel third space technique, which allows for safe and effective treatment of thoracic diverticula. Further studies validating our results are needed. However, given the challenges of obtaining large cohort studies with long-term follow-up and the unacceptable complication rates associated with surgery, we propose that DD-POEM should potentially be considered as standard of care for the management of symptomatic thoracic diverticula.

Competing interests

The authors declare that they have no conflict of interest.

References

- [1] Onwugbufor MT, Obirizeze AC, Ortega G et al. Surgical management of esophageal diverticulum: a review of the Nationwide Inpatient Sample database. *J Surg Res* 2013; 184: 120–125
- [2] Ferreira LE, Simmons DT, Baron TH. Zenker's diverticula: pathophysiology, clinical presentation, and flexible endoscopic management. *Dis Esophagus* 2008; 21: 1–8
- [3] Hadi U, Rameh C. Giant midesophageal diverticulum presenting as food impaction: case report and review of the literature. *Am J Otolaryngol* 2007; 28: 122–125
- [4] Herbella FA, Patti MG. Modern pathophysiology and treatment of esophageal diverticula. *Langenbecks Arch Surg* 2012; 397: 29–35
- [5] Zaninotto G, Portale G, Costantini M et al. Therapeutic strategies for epiphrenic diverticula: systematic review. *World J Surg* 2011; 35: 1447–1453
- [6] Ishaq S, Hassan C, Antonello A et al. Flexible endoscopic treatment for Zenker's diverticulum: a systematic review and meta-analysis. *Gastrointest Endosc* 2016; 83: 1076–1089
- [7] Mandavdhare HS, Praveen Kumar M, Jha D et al. Diverticular per oral endoscopic myotomy (DPOEM) for esophageal diverticular disease: a systematic review and meta-analysis. *Esophagus* 2021; 18: 436–450
- [8] Li X, Zhang W, Yang J et al. Safety and efficacy of submucosal tunneling endoscopic septum division for epiphrenic diverticula. *Endoscopy* 2019; 51: 1141–1145
- [9] Sidhu M, Tate DJ, Bourke MJ. Transmucosal diverticular myotomy for the treatment of oesophageal diverticula associated with spastic motility disorders. *Gut* 2020; 69: 1552–1554
- [10] Eckardt VF. Clinical presentations and complications of achalasia. *Gastrointest Endosc Clin N Am* 2001; 11: 281–292
- [11] Demeter M, Ďuriček M, Vorčák M et al. S-POEM in treatment of achalasia and esophageal epiphrenic diverticula – single center experience. *Scand J Gastroenterol* 2020; 55: 509–514
- [12] Nabi Z, Chavan R, Asif S et al. Per-oral endoscopic myotomy with division of septum (D-POEM) in epiphrenic esophageal diverticula: outcomes at a median follow-up of two years. *Dysphagia* 2022; 37: 839–847
- [13] Facciorusso A, Ramai D, Ichkhanian Y et al. Peroral endoscopic myotomy for the treatment of esophageal diverticula: a systematic review and meta-analysis. *J Clin Gastroenterol* 2022; 56: 853–862
- [14] Chan DSY, Foliaki A, Lewis WG et al. Systematic review and meta-analysis of surgical treatment of non-zenker's oesophageal diverticula. *J Gastrointest Surg* 2017; 21: 1067–1075
- [15] Sakai P. Endoscopic myotomy of Zenker's diverticulum: lessons from 3 decades of experience. *Gastrointest Endosc* 2016; 83: 774–775
- [16] Aiolfi A, Scolari F, Saino G et al. Current status of minimally invasive endoscopic management for Zenker diverticulum. *World J Gastrointest Endosc* 2015; 7: 87–93
- [17] Li QL, Chen WF, Zhang XC et al. Submucosal tunneling endoscopic septum division: a novel technique for treating Zenker's diverticulum. *Gastroenterology* 2016; 151: 1071–1074
- [18] Maydeo A, Patil GK, Dalal A. Operative technical tricks and 12-month outcomes of diverticular peroral endoscopic myotomy (D-POEM) in patients with symptomatic esophageal diverticula. *Endoscopy* 2019; 51: 1136–1140
- [19] Yang J, Zeng X, Yuan X et al. An international study on the use of peroral endoscopic myotomy (POEM) in the management of esophageal diverticula: the first multicenter D-POEM experience. *Endoscopy* 2019; 51: 346–349
- [20] Basile P, Gonzalez JM, Le Mouel JP et al. Per-oral endoscopic myotomy with septotomy for the treatment of distal esophageal diverticula (D-POEM). *Surg Endosc* 2020; 34: 2321–2325
- [21] Zeng X, Bai S, Zhang Y et al. Peroral endoscopic myotomy for the treatment of esophageal diverticulum: an experience in China. *Surg Endosc* 2021; 35: 1990–1996
- [22] Haito-Chavez Y, Inoue H, Beard K et al. Comprehensive analysis of adverse events associated with per oral endoscopic myotomy in 1826 patients: an international multicenter study. *Am J Gastroenterol* 2017; 112: 1267–1276
- [23] Collins FS, Varmus H. A new initiative on precision medicine. *N Eng J Med* 2015; 372: 793–795