Review Article

Indication for the endoscopic treatment of Zenker's diverticula

María Rita Rodríguez-Luna[1], Margherita Pizzicannella[2], Silvana Perretta[1,2,3]

[1]Research Institute against Digestive Cancer (IRCAD), Strasbourg, France; [2]IHU-Strasbourg, Institute of Image-Guided Surgery, Strasbourg, France; [3]Department of Digestive and Endocrine Surgery, Nouvel Hôpital Civil, Strasbourg University Hospital, Strasbourg, France

Contributions: (I) Conception and design: MR Rodríguez-Luna, M Pizzicannella, S Perretta; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: MR Rodríguez-Luna, M Pizzicannella, S Perretta; (V) Data analysis and interpretation: MR Rodríguez-Luna, M Pizzicannella, S Perretta; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Silvana Perretta. 1 Place de l'Hôpital CEDEX, 67000 Strasbourg, France. Email: silvana.perretta@ircad.fr.

Abstract: Zenker's diverticulum (ZD) is a false pulsion diverticulum located in Killian's triangle. It accounts for about 70% of all esophageal diverticula. ZD incidence is uncommon, and it is mostly present in the elderly population. Although the pathophysiology has not been completely elucidated, an impaired relaxation of the cricopharyngeal muscle (CPM) has been identified as the leading mechanism. For this reason, the current therapeutic modalities are based on CPM myotomy to eliminate diverticular bolus retention, improve bolus flow, relieve outflow obstruction, and mitigate neuromotor impairment. The conventional open approach through a left cervicotomy has been mostly replaced by transoral techniques using either rigid endoscopy or flexible endoscopes. The minimally invasiveness of these techniques allows for reinterventions in case of recurrence. Endoscopic techniques present several advantages in terms of lower risk of adverse events, can be accomplished without the need for general anesthesia and neck hyperextension, and provide for a rapid patient recovery. The recent introduction of cutting-edge technology Z-POEM allows through a direct septal visualization for a complete myotomy, leading to a lower recurrence rate and higher symptoms resolution than endoscopic septotomy. The potential advantages also account for lower complication rates making it a promising technique.

Keywords: Zenker's diverticulum (ZD); transoral endoscopic treatment; cricopharyngeal muscle (CPM); rigid endoscopy; flexible endoscopy; myotomy; Z-POEM

Received: 12 October 2020; Accepted: 02 November 2020; Published: 25 December 2021.
doi: 10.21037/aoe-2020-21
View this article at: http://dx.doi.org/10.21037/aoe-2020-21

Introduction

Zenker's diverticulum (ZD) is a rare disease with an incidence of <1/100,000 cases with a higher prevalence in the elderly population (patients aged between 70 and 80 years) (1), usually with a high comorbidity. It is the most common diverticulum among hypopharyngeal diverticula. The pharyngeal pouch includes the mucosal and the submucosal layers only, hence making it a false pulsion-type diverticulum (2,3). Abraham Ludlow first described ZD in 1,769 during an autopsy. However, it was not until 1877 that the German pathologists von Zenker and von Ziemssen fully described the disease based on a large series of patients, thereby obtaining the eponym (4).

Pathophysiology

ZD occurs in a region of muscle weakness, located between the inferior pharyngeal constrictor and the cricopharyngeal muscle (CPM). This triangular-shaped region is referred to as Killian's triangle (5) (*Figure 1*). Although the pathophysiology has not been completely elucidated, ZD is considered to originate from uncoordinated pharyngeal contractions and upper esophageal sphincter (UES)

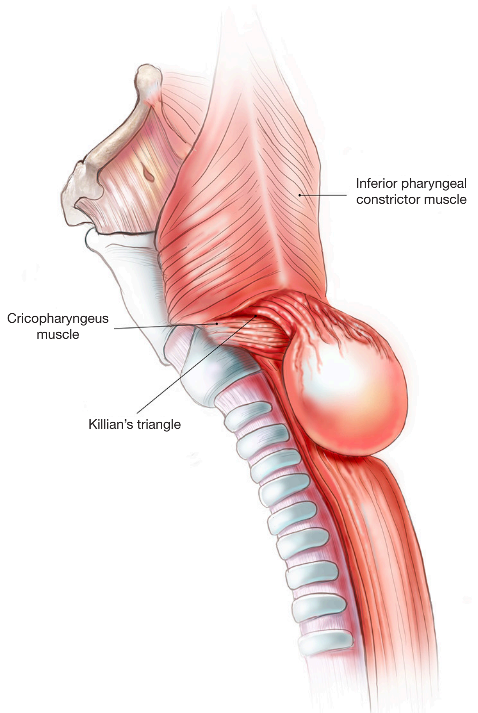

Figure 1 ZD occurring in Killian's triangle which is located between the inferior pharyngeal constrictor and the cricopharyngeal muscle. ZD, Zenker's diverticulum.

dysfunction. The increased hypopharynx intraluminal pressure during swallowing combined with incomplete CPM relaxation and inadequate opening of the UES result in luminal pressurization forcing the mucosa and submucosa to posterior herniation (6). In addition, age-related anatomical and physiological changes such as impaired pharyngeal swallowing phases, decreased cells in Auerbach's plexus, and functional changes such as fibrosis, atrophy, hypertrophy and inflammation may contribute to the higher incidence in the elderly population (7). Additionally, in aged population, numerous swallows requiring bolus clearance can also produce an increased intrabolus pressure, explaining the disease's high incidence in the elderly (8).

Studies have also suggested that gastroesophageal reflux disease can predispose to increased pressure in the UES (9).

Diagnosis

Diagnosis of Zenker diverticula is symptom-driven. The primary leading symptomatology includes dysphagia, regurgitation, halitosis, weight loss, malnutrition, and aspiration pneumonia, which is the most severe adverse event that increases morbidity and considerably affects quality of life (10,11). The diagnosis of ZD is mostly based on barium esophagogram, which is the reference standard. Radiologically, ZD appears as an outpouched sac filled with contrast in the posterior aspect of the pharyngoesophageal junction (*Figure 2*). In 1953 Brombart described ZD classification according to the disease progression from initial to advance stages (12). It consists of 4 types: type I diverticula are only visible during the UES's contraction phase, whereas type IV diverticula are large and resulting in esophageal compression.

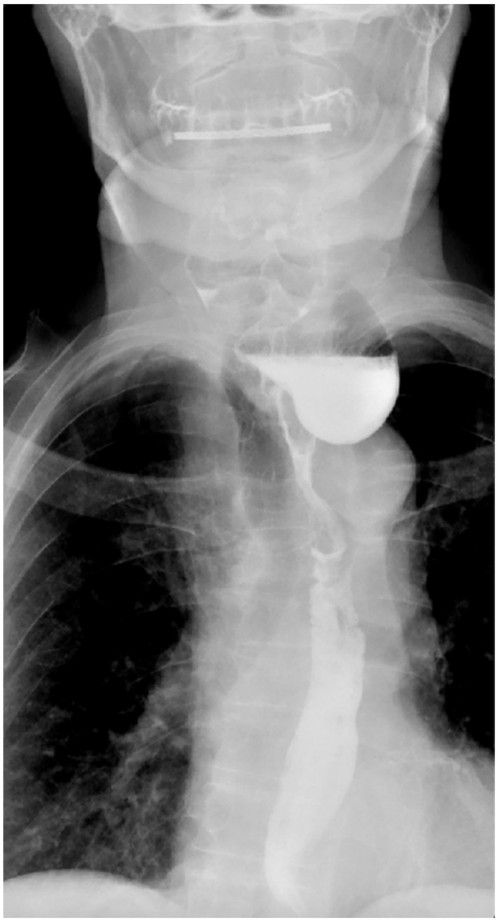

Figure 2 Anterior-posterior view of a barium esophagogram showing contrast within a Zenker's diverticulum.

Small diverticula can be missed out during the radiographic examination due to image superimposition. Dynamic fluoroscopy can improve detection as it allows for patient rotation (13). Esophagogastroduodenoscopy (EGD) provides anatomical information. It is essential before surgical management to rule out malignancy

(0.4% to 1.5% incidence) (14,15). Although esophageal manometry (EM) is not mandatory, it can be used to evaluate pharyngoesophageal motility during swallowing. It can detect a hypertonic UES or any dyskinesia and document maximal pressure in the ZD (16). However, pharyngoesophageal pressure monitoring is complex due to asymmetric sphincter pressures and sphincter movement during swallowing (17) conditioning failure to detect abnormalities in 40% to 60% of patients with ZD (18). Recently, high-resolution manometry (HRM) thanks to high spatial and temporal resolution has improved our ability to capture pharyngeal pressure events demonstrating that the changes occurring at the CPM appear to result in persistent UES pressurization during UES opening, rather than in a high tonic resting pressure (19).

Treatment

Therapeutic management of ZD is guided by two main factors; patient's symptoms and diverticular size. For asymptomatic diverticula <1 cm a conservative treatment is indicated with regular esophagograms during the follow-up (20). Surgical treatment should be addressed to symptomatic patients with or without associated complications with the objective of relieve symptoms and improve quality of life (11). Alarm symptoms that should prompt treatment because of the high risk for developing pulmonary aspiration are coughing while eating, regurgitation of food and choking.

Two main approaches for the ZD management have been described, namely open and transoral (endoscopic) approaches. Historically, ZD was treated with an open neck cervicotomy and diverticula excision, later associated with a CPM myotomy (21,22). The open approach morbidity includes recurrent laryngeal nerve injury in 3%, leak or perforation in 3% and cervical infection in 2% with an overall morbidity of 11%. Yuan *et al.* reported a success rate in symptoms resolution after the open approach of 93–95% and a recurrence rate of 2.9%. However, compared to endoscopic therapy higher morbidity and mortality were reported (11% *vs.* 8.7% and 0.9% *vs.* 0.4% for the open and endoscopic approach respectively) (23).

Nowadays the open surgical approach is no longer the gold standard. With the evolution of endoscopic techniques as well as an improved understanding of the underlying pathophysiology, ZD is mainly treated with transoral endoscopic flexible or rigid techniques due to their cost-effectiveness and lower risk of adverse events as compared to the conventional open approach (9). As a matter of fact, the endoscopic approach has shown its superiority in terms of shorter operative time, shorter length of hospital stay, and a faster oral intake resumption. Additionally, flexible endoscopy is not limited by the diverticula size. Smaller 1–2 cm diverticula are more challenging to treat surgically, as advancing a stapling device into a smaller space can be difficult. The open approach continues to be an efficient option for patients with complex ZD endoscopic exposure, reported in 4.4–18% (24,25) of the procedures, and in selected cases such as patients in whom symptomatology persists after the initial therapy and are suitable for reintervention (26). It could also serve as a therapeutic option in younger and healthy patients who desire lasting symptoms resolution, given the higher success rate and the lower likelihood of recurrence (26).

Rigid endoscopy

First described by Mosher in 1917 (4), this technique is performed by means of a rigid diverticuloscope with CPM myotomy as the key component. The procedure can be performed using electrocautery, also referred as Dolhman technique (27), carbon-dioxide laser therapy (28) or the presently more popular stapling technique (29,30) (*Figure 3*). The stapler-assisted septotomy allows to create a common cavity between the esophagus and ZD through a delta-shaped anastomosis (31). Endoscopic staplers do not staple and cut until the tip. Modifications can be performed by shortening the anvil or lowering the blade to achieve a more complete septum division (2). For the stapling technique, it is recommended that ZD should measure at least 2 cm, although clinical success has been correlated with a diverticular size of >3 cm (16,32). In addition, as reported in the literature, large diverticula can require more than one cartridge to divide the common wall. The use of multiple cartridges is associated with an increased risk of pouch and esophageal perforation (33).

Better outcomes in terms of oral diet resumption, complication rate, length of hospital stay and mortality have been reported for transoral endostapling techniques in the two largest retrospective studies (16,24).

Chang *et al.* (34) asserted these results in a review that included studies during a twelve year period [1990–2002]. Authors reported better outcomes for the transoral endostapling compared to the open transcervical approach in terms of morbidity (2.6% versus 11.8%), mortality (0.3% versus 1.6%), hospital stay (1.8 versus 7.6 days) and oral

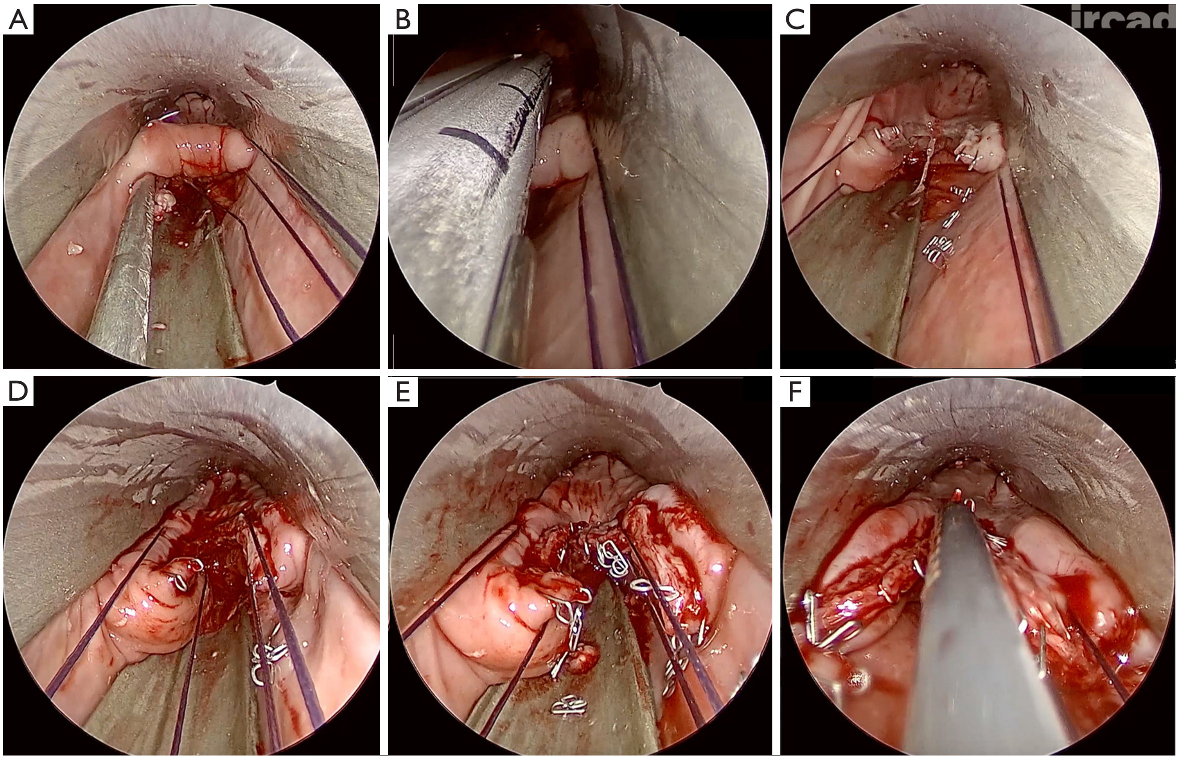

Figure 3 Rigid endoscopic stapled technique. (A) Sutures are placed for adequate traction; (B) endoscopic stapler [Endo GIA™, Medtronic, (Mansfield, MA) placement]; (C) endoscopic view once the first stapler has been fired; (D) sutures are placed before the stapler is fired for the second time; (E) endoscopic view after the stapler has been fired for the second time (the complete septum transection can be observed); (F) division of the last adhesions with a hook.

diet resumption (1 versus 4.5). Overall comparable efficacy in symptoms resolution (94% versus 95%) was reported among the studies.

The rigid endoscopic stapling technique has a complication rate of 7% accounting for dental injury (2%) and perforation (2%), while the reported recurrence rate is 10% (17). The ultrasonic scalpel (Ultracision®, Ethicon EndoSurgery, Cincinnati, Ohio) (35), the vessel-sealing system (LigaSure™, Medtronic, Mansfield, MA) (36), and the carbon dioxide laser have been proposed as alternatives to the stapler for septum transection (37). Unlike the stapler-assisted technique, the use of these tools can potentially leave unsealed edges during transection, leading to leakage and mediastinitis. Outcomes after myotomy with ultrasonic dissection device are scarce, the mean complication rate of 8%, with 2% of mediastinitis and an overall symptom resolution rate of 93% have been reported. Results were similar compared to carbon dioxide laser technique (17).

To introduce a rigid diverticuloscope, neck hyperextension is mandatory and is correlated with technical success. Neck hyperextension can be burdensome for older patients with poor neck flexibility. In addition, inadequate jaw opening and upper teeth protrusion can make difficult the insertion of the rigid diverticuloscope. These cumbersome conditions can lead to a higher risk of adverse events and force to conversion (38). This procedure is generally not indicated in small diverticula (<3 cm).

Flexible endoscopy

The flexible endoscopic treatment of ZD with septotomy was introduced in 1995 by Mulder (39) and Ishioka (40). It was rapidly adopted due to its reproducibility, safety, and efficacy. This technique has been previously applied to poor surgical candidates with anatomical conditions which made difficult to achieve an adequate exposure under rigid esophagoscopy. As a matter of fact, it can be performed without neck hyperextension. An obvious advantage of the flexible endoscopic technique lies in the fact that it does

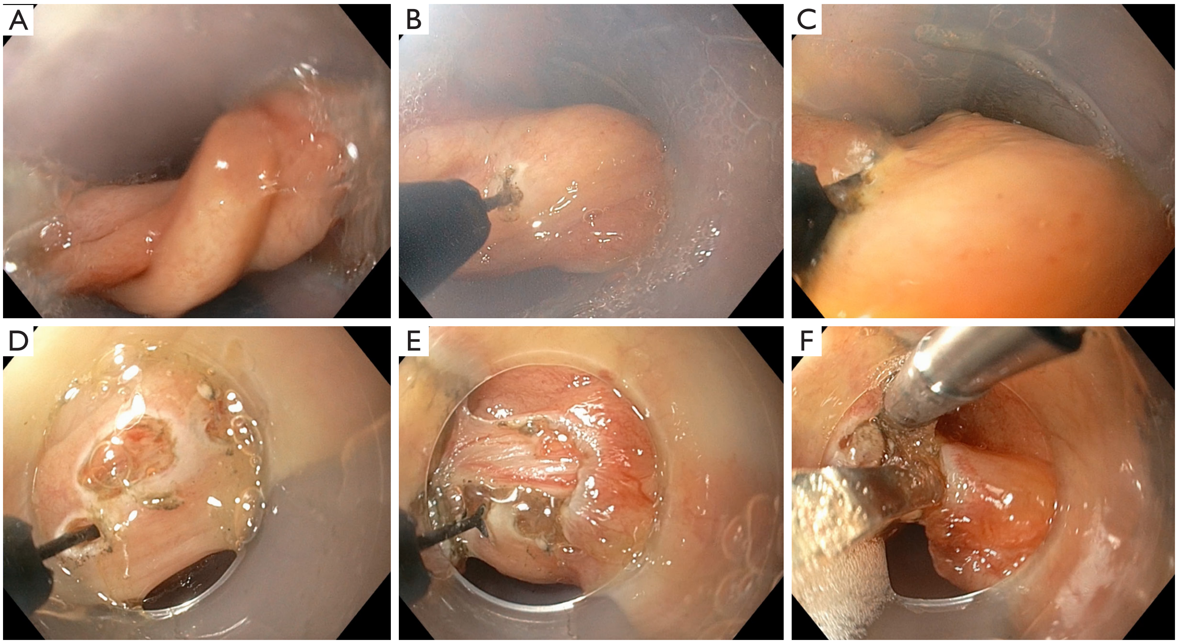

Figure 4 Flexible endoscopy. Diverticuloscope-assisted myotomy. (A) ZD septum identification after the introduction of a soft diverticuloscope (Zenker's Diverticulum Overtube; Cook Endoscopy, Winston-Salem, MA, USA); (B) beginning of the septotomy with the Triangle-Tip Electrosurgical Knife (KD-640L, Olympus); (C) progression of the septotomy; (D) transparent cap used to enhance visualization of the CPM fibers; (E) distal septal division; (F) clips (Instinct™ Endoscopic Clips, Cook Medical, Bloomington, IN, USA) placement at the distal end of the septotomy. ZD, Zenker's diverticulum; CPM, cricopharyngeal muscle.

not depend on the diverticula size. Since small diverticula (1 to 2 cm) are challenging when treated surgically or by transoral stapling technique, flexible endoscopy is considered the first-line therapy in ZD <30 mm. Flexible endoscopy can be performed under conscious sedation, without requiring general anesthesia and neck overextension which are required for open or rigid endoscopic approaches. Nevertheless aspiration is a concern and many surgeons prefer general anesthesia to secure airway protection as the procedure is performed in close proximity to the vocal cords.

The objectives of the procedure are similar to rigid endoscopy and open techniques, namely CPM myotomy, and septum reduction to less than 1 cm (20). To enhance septal exposure, the tip of the gastroscope is fitted with a transparent cap (41). Like any other therapeutic endoscopic procedures, the use of carbon dioxide is warranted due to the potential micro-perforation. A nasogastric tube can be placed to delimitate the anterior esophageal wall intraoperatively. A soft diverticuloscope (Zenker's diverticulum Overtube; Cook Endoscopy, Winston-Salem, North Carolina, United States) can be used to enhance exposure. Similarly to the rigid diverticuloscope, the soft diverticuloscope has two distal flaps (40 and 30 mm), which help to protect the posterior diverticular wall and the anterior esophageal wall. It carries a black marking indicator to measure the distance from the teeth line to the septum (16 cm). It is inserted by means of a stiff guidewire. The long valve (40 mm) is positioned in the esophagus and the short valve (30 mm) in the diverticulum (*Figure 4A*).

The septum is commonly divided in a proximal-to-distal fashion using a needle knife, a Triangle Tip Electrosurgical Knife or the hook knife especially used for endoscopic submucosal dissection (ESD) (*Figure 4B,C,D,E*). Other means of division include argon plasma coagulation, bipolar or monopolar forceps, or instruments passed alongside the endoscope, such as ultrasonic and stapling devices (9,42). Currently the optimal cutting technique remains unknown since comparative trials have not been conducted. The most commonly used system is the hook knife (43).

Once the septotomy has been completed, endoscopic clips are placed to secure the distal edge of the incision to prevent any delayed perforation and bleeding (*Figure 4F*) (38).

Due to the potential risk of mediastinal perforation, some authors have adopted a limited septotomy, which consists in a short myotomy of the common wall (1). However, this approach leads to higher recurrence rates, requiring reintervention (20).

To prevent recurrence, other groups have used an extended myotomy into the esophageal wall for 5 to 10 mm beyond the diverticular tip. This extended approach reduced the dysphagia rate from 12% with the standard technique to less than 5% (2).

The ability to correctly visualize the septum may vary depending on the devices used. Costamagna *et al.* compared two different techniques for flexible needle-knife diverticulotomy, i.e., the cap-assisted versus the diverticuloscope-assisted technique. The cap-assisted group showed significantly longer operative times and a higher complication rate of 32% versus 0% in the diverticuloscope-assisted group. A higher recurrence rate during the follow-up period (3 to 60 months) was also observed in the cap-assisted group compared to the diverticuloscope-assisted group (29% *vs.* 9%, respectively) (44).

Another technical modification to enhance visualization of the septum is the "open window" technique. This technique consists in removing a 5 mm piece of square-shaped mucosa, which is closed with clips after myotomy completion (45).

To overcome the drawbacks of the previously mentioned endoscopic modalities, and to reduce recurrence, a submucosal tunneling technique similar to the one used in per-oral endoscopic myotomy (POEM) for achalasia has been reported. It is referred as Z-POEM (POEM for Zenker's diverticulum) (46) or STESD (Submucosal Tunneling Endoscopic Septum Division) (47). This submucosal tunneling technique allows for a complete exposure and visualization of the septum, which is divided selectively, sparing the overlying mucosa (48). The advantages of this approach include a more profound resolution of symptoms and a lower recurrence rate due to a more precise septum transection. A lower leakage rate has also been described since the site in the mucosal entry is closed with endoscopic clips (47).

The technical steps are comparable to those described for POEM. After septum visualization (*Figure 5A*), a mucosal lift and incision are carried out (*Figure 5B,C*); then a submucosal tunnel (*Figure 5D*) on both sides of the septum is created, extended 1 to 2 cm distally to the diverticulum's base. A complete septum division is obtained under endoscopic control in order to prevent from any unintentional injury (*Figures 5E,F,G,H*). The mucosal incision site is finally closed with several endoscopic clips (*Figure 5I*).

A mucosal incision with muscular interruption also known as the "MIMI" approach has been proposed as a modification of the Z-POEM. MIMI allows a direct access to the septum, reducing the need for the submucosal tunnel. In this technique, a methylene blue dye is injected into the submucosa directly on the CPM. A longitudinal incision of 1 to 1.5 cm is made on the mucosal septum. The submucosa is dissected bluntly on both sides of the CPM with the aid of the cap. The CPM is transected transversely until the base and the mucosal entry point is sealed with clips (49). A small retrospective cohort study which compared the MIMI technique (19 patients) versus non-tunneled flexible endoscopy (7 patients with conventional endoscopic septotomy) reported an 89.5% rate of clinical success in the MIMI group versus 100% in the non-tunneled group (P=0.101). The dysphagia score improved in the MIMI group as compared to the non-tunneled group (mean dysphagia scores from 1.74 to 0.39, P=0.0018, and 1.29 to 0.71, P=0.129, respectively). There was one major complication that required open surgical repair due to pharyngeal perforation in a patient with a small ZD in the MIMI group. Recurrence occurred in 11.7% of MIMI patients and 42.9% of non-tunneled flexible endoscopic patients (P=0.096) (49).

Outcomes following endoscopic transoral myotomy

Outcomes following transoral approaches have been extensively analyzed. The success rate of rigid endoscopy (90–100%) is comparable to the conventional open approach (80–100%) (9). A meta-analysis published in 2016 with including 11 articles compared the surgical approach with the endoscopic treatment (50). The most common endoscopic techniques included endoscopic stapling diverticulotomy (30), carbon dioxide laser (51), and electrocautery (52). After a pooled analysis, the endoscopic treatment was found superior in terms of shorter procedure times and lengths of hospital stay, earlier oral diet resumption, and lower complication rates. The surgical group presented a lower rate of recurrence (SMD 0.08, 95% CI: 0.03, 0.13). The high heterogeneity in the recurrence rate of the endoscopic group ranged from 3% to 32%, and this could be explained by the vast variety of septotomy techniques used.

Another relevant meta-analysis of 115 studies (mostly retrospective case series) which compared adverse events

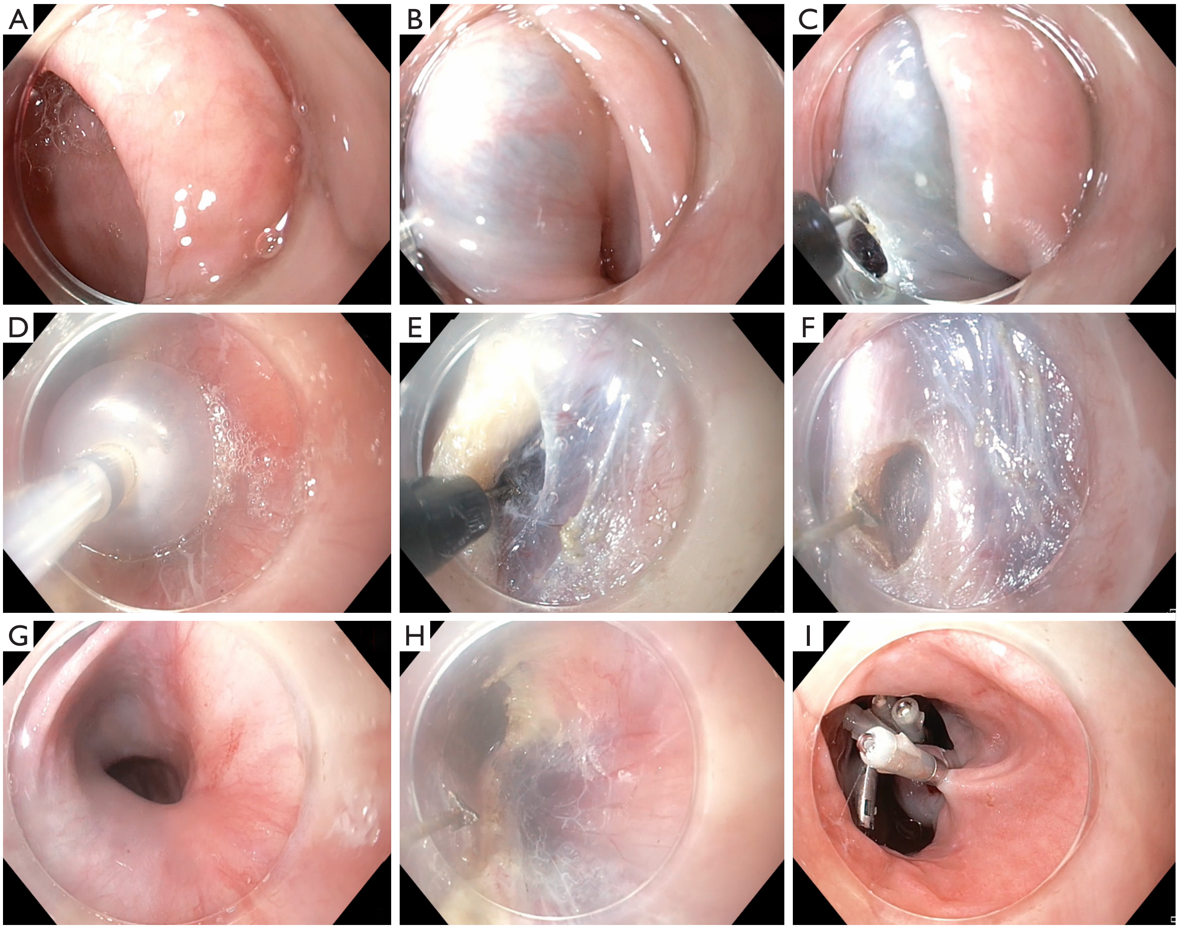

Figure 5 Z-POEM technique. (A) Septum identification; (B) submucosal space injection of methylene blue 2 cm above the ZD septum using a standard injection catheter (23G Interject, Boston Scientific, Natick, Massachusetts, USA); (C) 15 mm mucosotomy with the Triangle-Tip Electrosurgical Knife (KD-640L, Olympus); (D) introduction of a 15 mm stone extraction balloon (Olympus, Singapore) to create the submucosal space; (E) beginning of the myotomy; (F) CPM myotomy progression; (G) revision of the esophageal mucosa; (H) endoscopic view of the complete myotomy; (I) mucosal entry site sealed with Instinct™ endoscopic clips (Cook Medical, Bloomington, IN, USA). ZD, Zenker's diverticulum; CPM, cricopharyngeal muscle.

after rigid endoscopy and flexible endoscopy therapies reported a similar rate of mortality, infection, and perforation in the rigid and the flexible groups. However, bleeding and recurrence were more likely after flexible endoscopy (20% *vs.* <10% and 4% *vs.* 0% respectively) (53). The results are probably explained by the stapling technique used in the rigid endoscopic approach which allows for a complete septal division with sealed edges.

The evidence of flexible endoscopic myotomy is scant and mostly derived from case series (18 case series with 650 patients) in which the long-term follow-up is missing. Additionally, there is a lack of consensus on the definition of recurrence (17). The reported clinical resolution of 90% does not reflect the long-term follow-up recurrence. Evidence has shown that the best clinical success for flexible endoscopy is correlated with a small diverticular size (54). Recently Perbtani *et al.* (55) published a review of all the patients presenting a ZD who underwent a flexible endoscopic treatment. In terms of morbidity authors described an incidence of 11.8%. The most frequent complication were microperforations mostly treated conservatively. Only four cases presented macroscopic perforations detected either during the intervention or with subsequent oral contrast leak. All the macroperforation were managed successfully with endoscopic clipping. Six patients presented with intraoperative bleeding and it was treated with epinephrine, endoscopic clips or electrocautery. Only one patient presented post-operative bleeding which was managed with epinephrine injection. The most common reported sign of infection was fever requiring antibiotic therapy. Mortality was reported only in one patient of the series because of pulmonary embolism.

Long-term outcomes of flexible endoscopy were evaluated by Costamagna *et al.* in an intention-to-treat analysis on 89 patients. The clinical success rate was 69% at 6 months and only 46% at 48 months after flexible endoscopic myotomy (using the diverticuloscope-assisted technique). Authors also described the prognostic variables associated with clinical success. These variables include ZD length of ≤25 mm at 6 and 48 months, ZD size before treatment of ≥5 cm at 6 and 24 months, and ZD size after treatment of ≥10 mm at 48 months (54). Bresteau *et al.* reported a similar recurrence rate of 34% after a mean follow-up of 23 months (56).

The high recurrence rate (~50%) after flexible endoscopy can be explained by incomplete septotomy due to poor visualization or resulting from the concern related to risk of mediastinal perforation. The submucosal tunneling technique was developed to overcome this limitation. The current clinical evidence on Z-POEM is still scarce and limited mostly to case series reports (46,57,58). Recently, the first multicenter international retrospective trial evaluated the use of Z-POEM in 75 patients with symptomatic ZD, with a mean age of 73.3±1.2, and a mean Charlson Comorbidity Index of 4±0.2. Mean procedure time was 52.4±2.9 minutes. Adverse outcomes occurred in 6.7% of cases. One bleeding, managed conservatively, and 4 perforations were observed (1 severe and 3 moderate as reported by American Society for Gastrointestinal Endoscopy lexicon) (59). The severe perforation required intensive care unit monitoring and was self-resolved afterwards. The other 3 moderate perforations were treated as follows: two with cyanoacrylate glue, and one with endoscopic clipping. The overall mean hospital stay was 1.8±0.2 days. The overall technical success rate was 97.3% (73/75) while clinical success was achieved in 92% of patients with a decrease in the mean dysphagia score from 1.96 to 0.25 (P<0.0001). Two failures were described due to the lack of septum location and failure to create the tunnel. At 12 months of follow-up, only one patient presented dysphagia recurrence and was treated with repeated endoscopic diverticulotomy (60).

Stronger clinical evidence will come from the ZIPPY trial, a prospective, international, multicenter, double-blind, randomized study, with the aim to compare the short-term and long-term clinical outcomes of Z-POEM versus flexible endoscopic septotomy which will start in 2021 (61).

Conclusions

Rigid and flexible transoral approaches have become the first-line therapy of ZD management, replacing the traditional open approach, due to the consistent superiority in terms of faster oral intake resumption, shorter operative times and shorter length of hospital stay. Submucosal tunneling techniques comparable to the POEM for achalasia have been recently implemented in the algorithm of management showing potential advantages such as lower risk of perforation and recurrence. This movement toward a flexible approach would benefit from the standardization of the available techniques and instrument refinement.

Acknowledgments

The authors would like to thank Guy Temporal and Christopher Burel for their assistance in medical English proofreading and Catherine Cers for illustrations.
Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editors (Dania Nachira and Venanzio Porziella) for the series “Management of Esophageal Perforations and Injuries and Other Benign Diseases” published in *Annals of Esophagus*. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/aoe-2020-21). The series “Management of Esophageal Perforations and Injuries and Other Benign Diseases” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of this work in ensuring that questions related to the accuracy or integrity of any part of this work are appropriately investigated and resolved.

References

1. Mariette C. Zenker's pharyngo-esophageal diverticulum: Diverticulectomy and diverticulopexy. J Visc Surg 2014;151:145-9.
2. Beard K, Swanström LL. Zenker's diverticulum: Flexible versus rigid repair. J Thorac Dis 2017;9:S154-S162.
3. Smith CD. Esophageal Strictures and Diverticula. Surg Clin North Am 2015;95:669-81.
4. Simić AP, Gurski RR, Pesko PM. The story beyond the Zenker's pouch. Acta Chir Iugosl 2009;56:9-16
5. Jain D, Sharma A, Shah M, et al. Efficacy and Safety of Flexible Endoscopic Management of Zenker's Diverticulum. J Clin Gastroenterol 2018;52:369-85.
6. Dzeletovic I, Ekbom DC, Baron TH. Flexible endoscopic and surgical management of Zenker's diverticulum. Expert Rev Gastroenterol Hepatol 2012;6:449-65; quiz 466.
7. Plant RL. Anatomy and physiology of swallowing in adults and geriatrics. Otolaryngol Clin North Am 1998;31:477-88.
8. Kahrilas PJ, Logemann JA, Lin S, et al. Pharyngeal clearance during swallowing: A combined manometric and videofluoroscopic study. Gastroenterology 1992;103:128-36.
9. Ishaq S, Sultan H, Siau K, et al. New and emerging techniques for endoscopic treatment of Zenker's diverticulum: State-of-the-art review. Dig Endosc 2018;30:449-60.
10. Siboni S, Asti E, Sozzi M, et al. Respiratory Symptoms and Complications of Zenker Diverticulum: Effect of Trans-Oral Septum Stapling. J Gastrointest Surg 2017;21:1391-5.
11. Colpaert C, Vanderveken OM, Wouters K, et al. Changes in Swallowing-related Quality of Life After Endoscopic Treatment For Zenker's Diverticulum Using SWAL-QOL Questionnaire. Dysphagia 2017;32:339-44.
12. Brombart M. Zenker's pharyngo-esophageal diverticulum; pathogenic considerations on radiological studies on 26 cases (23 cases in initial stage). J Belge Radiol 1953;36:166-97.
13. Minovi CM, Minovi A, Dost P. Suture of the mucosa after the endoscopic LASER mucomyotomy of Zenker's diverticulum. Eur Arch Otorhinolaryngol 2015;272:2947-52.
14. Brücher BL, Sarbia M, Oestreicher E, et al. Squamous cell carcinoma and Zenker diverticulum. Dis Esophagus 2007;20:75-8.
15. Valenza V, Perotti G, Di Giuda D, et al. Scintigraphic evaluation of Zenker's diverticulum. Eur J Nucl Med Mol Imaging 2003;30:1657-64.
16. Rizzetto C, Zaninotto G, Costantini M, et al. Zenker's diverticula: Feasibility of a tailored approach based on diverticulum size. J Gastrointest Surg 2008;12:2057-64; discussion 2064-5.
17. Law R, Katzka DA, Baron TH. Zenker's Diverticulum. Clin Gastroenterol Hepatol 2014;12:1773-82.
18. Zaninotto G, Costantini M, Boccù C, et al. Functional and morphological study of the cricopharyngeal muscle in patients with Zenker's diverticulum. Br J Surg 1996;83:1263-7.
19. Rosen SP, Jones CA, Hoffman MR, et al. Pressure abnormalities in patients with Zenker's diverticulum using pharyngeal high-resolution manometry. Laryngoscope Investig Otolaryngol 2020;5:708-17.
20. Bizzotto A, Iacopini F, Landi R, et al. Zenker's diverticulum: exploring treatment options. Acta Otorhinolaryngol Ital 2013;33:219-29.
21. Payne WS. The treatment of pharyngoesophageal diverticulum: the simple and complex. Hepatogastroenterology 1992;39:109-14.
22. Aly A, Devitt PG, Jamieson GG. Evolution of surgical treatment for pharyngeal pouch. Br J Surg 2004;91:657-64.
23. Yuan Y, Zhao YF, Hu Y, et al. Surgical treatment of Zenker's Diverticulum. Dig Surg 2013;30:207-18.
24. Bonavina L, Bona D, Abraham M, et al. Long-term results of endosurgical and open surgical approach for Zenker diverticulum. World J Gastroenterol 2007;13:2586-9.
25. Calavas L, Brenet E, Rivory J, et al. Zenker diverticulum treatment: retrospective comparison of flexible endoscopic window technique and surgical approaches. Surg Endosc 2021;35:3744-52.
26. Johnson CM, Postma GN. Zenker Diverticulum--Which Surgical Approach Is Superior? JAMA Otolaryngol Head Neck Surg 2016;142:401-3.
27. Dohlman G, Mattsson O. The Endoscopic Operation for Hypopharyngeal Diverticula: A Roentgencinematographic Study. AMA Arch Otolaryngol 1960;71:744-52.

28. Knegt PP, de Jong PC, van der Schans EJ. Endoscopic Treatment of the Hypopharyngeal Diverticulum with the CO 2 Laser. Endoscopy 1985;17:205-6.
29. Koay CB. The role of endoscopic stapling diverticulotomy in recurrent pharyngeal pouch. J Laryngol Otol 1998;112:954-5.
30. Collard JM, Otte JB, Kestens PJ. Endoscopic stapling technique of esophagodiverticulostomy for Zenker's diverticulum. Ann Thorac Surg 1993;56:573-6.
31. Philippsen LP, Weisberger EC, Whiteman TS, et al. Endoscopic stapled diverticulotomy: Treatment of choice for Zenker's diverticulum. Laryngoscope 2000;110:1283-6.
32. Gutschow CA, Hamoir M, Rombaux P, et al. Management of pharyngoesophageal (Zenker's) diverticulum: Which technique? Ann Thorac Surg 2002;74:1677-82; discussion 1682-3.
33. Roth JA, Sigston E, Vallance N. Endoscopic stapling of pharyngeal pouch: A 10-year review of single versus multiple staple rows. Otolaryngol Head Neck Surg 2009;140:245-9.
34. Chang CY, Payyapilli RJ, Scher RL. Endoscopic staple diverticulostomy for Zenker's diverticulum: Review of literature and experience in 159 consecutive cases. Laryngoscope 2003;113:957-65.
35. Whited C, Lee WT, Scher R. Evaluation of endoscopic harmonic diverticulostomy. Laryngoscope 2012;122:1297-300.
36. Nielsen HUK, Trolle W, Rubek N, et al. New technique using LigaSure for endoscopic mucomyotomy of Zenker's diverticulum: Diverticulotomy made easier. Laryngoscope 2014;124:2039-42.
37. Papaspyrou G, Schick B, Papaspyrou S, et al. Laser surgery for Zenker's diverticulum: European combined study. Eur Arch Otorhinolaryngol 2016;273:183-8.
38. Baron TH. Endoscopic Management of Zenker Diverticula. Gastroenterol Hepatol (N Y) 2017;13:242-4.
39. Mulder CJJ, den Hartog G, Robijn RJ, et al. Flexible Endoscopic Treatment of Zenker's Diverticulum: a New Approach. Endoscopy 1995;27:438-42.
40. Ishioka S, Sakai P, Maluf Filho F, et al. Endoscopic Incision of Zenker's Diverticula. Endoscopy 1995;27:433-7.
41. Sakai P, Ishioka S, Maluf-Filho F, et al. Endoscopic treatment of Zenker's diverticulum with an oblique-end hood attached to the endoscope. Gastrointest Endosc 2001;54:760-3.
42. Wilmsen J, Baumbach R, Stüker D, et al. New flexible endoscopic controlled stapler technique for the treatment of Zenker's diverticulum: A case series. World J Gastroenterol 2017;23:3084-91.
43. Mittal C, Diehl D, Draganov P, et al. Practice patterns, techniques, and outcomes of flexible endoscopic myotomy for Zenker's diverticulum: a retrospective multicenter study. Endoscopy 2021;53:346-53.
44. Costamagna G, Iacopini F, Tringali A, et al. Flexible endoscopic Zenker's diverticulotomy: cap-assisted technique vs. diverticuloscope-assisted technique. Endoscopy 2007;39:146-52.
45. Rivory J, Almahayawi A, Roman S, et al. Endoscopic Zenker diverticulotomy using the window technique: a technical trick to improve the field of view. Endoscopy 2016;48:E63-E64.
46. Ebrahim A, Leeds SG, Clothier JS, et al. Zenker's diverticulum treated via per-oral endoscopic myotomy. Proc (Bayl Univ Med Cent) 2020;33:233-4.
47. Li QL, Chen WF, Zhang XC, et al. Submucosal Tunneling Endoscopic Septum Division: A Novel Technique for Treating Zenker's Diverticulum. Gastroenterology 2016;151:1071-4.
48. Khashab MA, Pasricha PJ. Conquering the third space: Challenges and opportunities for diagnostic and therapeutic endoscopy. Gastrointest Endosc 2013;77:146-8.
49. Klingler MJ, Landreneau JP, Strong AT, et al. Endoscopic mucosal incision and muscle interruption (MIMI) for the treatment of Zenker's diverticulum. Surg Endosc 2021;35:3896-904.
50. Albers DV, Kondo A, Bernardo W, et al. Endoscopic versus surgical approach in the treatment of Zenker's diverticulum: systematic review and meta-analysis. Endosc Int Open 2016;4:E678-86.
51. Nyrop M. Endoscopic CO2 Laser Therapy of Zenker'S Diverticulum--Experience from 61 Patients. Acta Otolaryngol Suppl 2000;543:232-4.
52. Von Doersten PG, Byl FM. Endoscopic Zenker's diverticulotomy (Dohlman procedure): Forty cases reviewed. Otolaryngol Head Neck Surg 1997;116:209-12.
53. Crawley B, Dehom S, Tamares S, et al. Adverse Events after Rigid and Flexible Endoscopic Repair of Zenker's Diverticula: A Systematic Review and Meta-analysis. Otolaryngol Head Neck Surg 2019;161:388-400.
54. Costamagna G, Iacopini F, Bizzotto A, et al. Prognostic variables for the clinical success of flexible endoscopic septotomy of Zenker's diverticulum. Gastrointest Endosc 2016;83:765-73.
55. Perbtani Y. Techniques and efficacy of flexible endoscopic therapy of Zenker's diverticulum. World J Gastrointest

Endosc 2015;7:206.
56. Bresteau C, Barret M, Guillaumot MA, et al. Do we still need a diverticuloscope for the flexible endoscopic septotomy of Zenker's diverticulum? J Gastroenterol Hepatol 2020;35:630-3.
57. Hernández Mondragón OV, Solórzano Pineda MO, Blancas Valencia JM. Zenker's diverticulum: Submucosal tunneling endoscopic septum division (Z-POEM). Dig Endosc 2018;30:124-4.
58. Balassone V, Pizzicannella M, Biasutto D, et al. Submucosal per-oral endoscopic myotomy for a large Zenker's diverticulum with use of a hydrodissector knife and an over-the-scope clip closure. VideoGIE 2018;3:373-4.
59. Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010;71:446-54.
60. Yang J, Novak S, Ujiki M, et al. An international study on the use of peroral endoscopic myotomy in the management of Zenker's diverticulum. Gastrointest Endosc 2020;91:163-8.
61. Kaminski MF, Budnicka-Borkowicz A. Comparison of Zenker's Diverticulum Treatment Using Peroral Endoscopic Myotomy and Flexible Endoscopy Septotomy. (ZIPPY). In: August 14, 2020. Available online: https://clinicaltrials.gov/ct2/show/NCT04514042?cond=zenker+diverticulum&draw=2&rank=4. Accessed 28 Aug 2020.

doi: 10.21037/aoe-2020-21
Cite this article as: Rodríguez-Luna MR, Pizzicannella M, Perretta S. Indication for the endoscopic treatment of Zenker's diverticula. Ann Esophagus 2021;4:38.