Chapter 23
Intramural Surgery Per Oral Endoscopic Myotomy for Zenker's Diverticulum (Z-POEM)

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Zenker's diverticulum (ZD))is an outpouching that occurs within Killian's triangle which constitutes an area of anatomic weakness just above the upper esophageal sphincter. This triangle is formed by the pharyngeal constrictors superiorly and the transversely oriented cricopharyngeus (CP)) inferiorly. High pressures are generated in this space when there is improper relaxation of the cricopharyngeus during swallowing, which can lead to the development of a pulsion-type false

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esophageal diverticulum [1]. Generally, ZD is rare with a prevalence of 0.01–0.11% with most occurring during the fifth to seventh decades of life [1–3]. Patients may describe symptoms largely attributed to trapped food, excess secretions, or air becoming trapped in the diverticulum. Patients may also experience the need to clear their throat periodically or following meals. Additionally, patients may regurgitate undigested food, putting them at risk for aspiration and subsequent pneumonia. The diverticulum may spontaneously empty and cause coughing or belching noises as air is evacuated, also known as esophageal borborygmi. Dysphagia is the most common symptom, which may cause patients to change their diet with notable resultant weight loss. The diagnosis of ZD is established through a thorough history and physical exam followed by imaging studies such as a contrast esophagram or via an upper endoscopy [1, 2].

Historically, treatment of ZD was performed through an open approach with a left cervical incision in order to remove the diverticulum and divide the cricopharyngeus. This approach was associated with a higher rate of complications such as vocal cord paralysis, esophageal leakage, or mediastinitis. The treatment approach to ZD has evolved from an open surgical to a rigid endoscopic approach, and most recently, to a flexible endoscopic approach. Although no prospective randomized trials have been performed to demonstrate the superiority of one approach, based on the morbidity and long hospital stays associated with the open approach, the minimally invasive approach is generally preferred [1, 4]. Flexible endoscopic diverticulotomy was first introduced in 1982 with the first series reported by Mulder and colleagues [5]. This approach was initially intended for patients who were poor surgical candidates unable to tolerate general anesthesia or those with unfavorable anatomy or neck extension for rigid scopes [4]. Over time, minimally invasive approaches became favored as there is a lower associated morbidity in this group of older patients with many pre-existing comorbidities. The minimally invasive approach provides a shorter surgery time, the possibility of performing the procedure without general anesthesia, a shorter hospital

stay, and earlier oral food intake [2]. In both the rigid and flexible endoscopic approach, the main goal is to divide the common wall or septum of the diverticulum to achieve a cricopharyngeal myotomy (Fig. 23.1). This combines the diverticulum with the esophageal lumen which may improve pharyngeal motor function and reduce symptoms of dyspha-

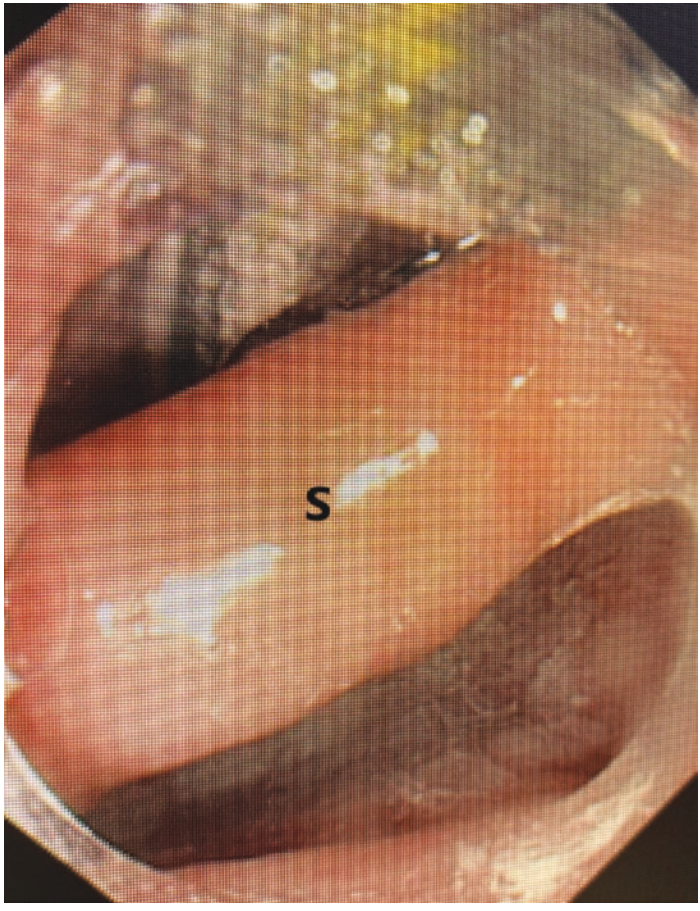

FIGURE 23.1 Septum (S) created between the true esophageal lumen and the false diverticulum containing an NGT and colorful wire to improve visualization

gia and regurgitation [4]. When performed by an experienced surgeon or gastroenterologist, patients experience between an 85 and 100% long-term success rate with regard to symptomatic relief [1, 4]. Patients not experiencing relief can undergo a revised minimally invasive approach or an open approach [1].

With the advent of new accessories and techniques, endoscopic options for treatment of ZD include but are not limited to endoscopic stapling, CO_2 laser, and submucosal tunneling with the use of various devices including argon plasma coagulation, needle knife, monopolar or bipolar forceps, hook knife, clutch cutter, stag beetle knife, or harmonic scalpel [2]. By using the principle behind per oral endoscopic myotomy (POEM) for treatment of achalasia, Li and colleagues first described the per oral endoscopic myotomy for Zenker's diverticulum (Z-POEM)) [6]. It was initially developed to decrease the risk of perforation with flexible endoscopic techniques which have been reported as high as 6.5% [7]. In addition, this tunneling technique may decrease the risk of diverticulum recurrence, which is notably higher compared to an open repair. Various tunneling techniques have been described, including Zenker's per oral endoscopic myotomy (Z-POEM), submucosal tunneling endoscopic septum division (STESD), or mucosal incision with muscular interruption (MIMI), which will be described further below.

General Technical Principles

The patient is taken to the operating room or endoscopic suite where the procedure is to be performed. After informed consent is obtained, anesthesia is provided. General anesthesia may be used to improve the ease of the procedure for the patient and the proceduralist. It is recommended for general anesthesia to be administered using rapid sequence intubation (RSI) due to the high risk of aspirating contents of the diverticulum [4]. Alternatively, if the patient cannot tolerate general anesthesia or if the proceduralist prefers, the proce-

dure may be performed under conscious sedation with monitoring by the anesthesia team. Antibiotic prophylaxis is administered. The patient is either placed in the left lateral decubitus or supine position. Carbon dioxide insufflation is used throughout the procedure due to its rapid absorption by the soft tissues and to minimize any postoperative subcutaneous emphysema. Initially, a standard upper gastrointestinal (GI) endoscopy is performed to evaluate the septotomy with an Olympus GIF-HQ190 gastroscope (Olympus Co., Japan) with a 2.8-mm working channel. Any residual food in the diverticulum should be removed if able. A transparent cap or a diverticuloscope may be used on the endoscope to assist with the procedure. A beveled (or non-beveled) silicone-based endoscopic cap (Barrx™ RFA Cleaning Cap, Covidien, Mansfield, MA) may be used [8]. The bevel may assist with exposure by pulling the flap away from the working area. Alternatively, a soft, flexible diverticuloscope (Cook Medical, Indiana, USA) may be used and is placed over the endoscope and advanced to 20 cm from the incisors in order to straddle the common wall between the true esophageal lumen and the diverticulum. The short blade is placed into the diverticulum and the long blade into the esophagus. A nasogastric tube or visible colorful wire (Jagwire™, Boston Scientific, MA) can also be used to reference the true esophageal lumen, which may not be easily visible during the procedure.

Flexible Endoscopic Septum Division

In the flexible endoscopic septum division (FESD) technique, once the septum is exposed, the diverticular septum is cut using various available endoscopic devices. The cutting device is used to create a mucosotomy over the cricopharyngeus muscle and carried down until the septum is completely divided [9]. The use of a Dual Knife (Olympus Co., Japan, with the following electrocautery settings: Endocut I mode, effect 1, soft coag effect 2; generator VIO® 300D; ERBE, Tubingen, Germany) has been described [10]. A midline inci-

sion is performed from the esophageal lumen toward the diverticulum with a medium length of 1.5 cm. Once the myotomy is complete the mucosa is closed with a series of endoscopic metallic clips (Resolution 360 Clips, Boston Scientific, Marlborough, MA) [10]. The endoscope is passed into the esophagus to assess for resistance.

Submucosal Tunneling Technique: Z-POEM [Q]

The first description of the Z-POEM technique involved four major steps: (1) Mucosal incision, (2) submucosal tunneling, (3) septum division, (4) mucosal closure. This differs from the FESD technique whereby the whole septum is directly divided [4]. Once the septum is visualized and in center view, the submucosa overlying the cricopharyngeus muscle is injected with 3–5 mL of a mixture of saline, epinephrine, and methylene blue (or 1% indigo carmine) (Fig. 23.2). The methylene blue may also be injected into a syringe of pre-packaged Orise gel© (Boston Scientific, Marlborough, MA) to darken the solution which can then be used for the submucosal injection. This dye is used as needed throughout the procedure. Once a submucosal bleb is created, a mucosotomy is performed over the middle of the septum with any of various tools as previously mentioned. The use of a HybridKnife and VIO® 300D generator with setting EndoCut Q 3-1-1 has been described (Erbe USA, Marietta, GA). The endoscope is inserted into the submucosal space and the space is dissected in a proximal to distal direction with the HybridKnife (setting forced Coag/Effect 2/50W) on both sides of the septum past the diverticulum and onto the circular and longitudinal fibers of the esophagus. Next, a myotomy of the entire length of the cricopharyngeus is performed using the HybridKnife with setting (EndoCut Q 3-1-1) [4]. The endoscope is withdrawn from the submucosa into the esophagus. Once hemostasis is confirmed, the mucosal defect is closed with Endoclips (Resolution 360 Clips, Boston Scientific, Marlborough, MA).

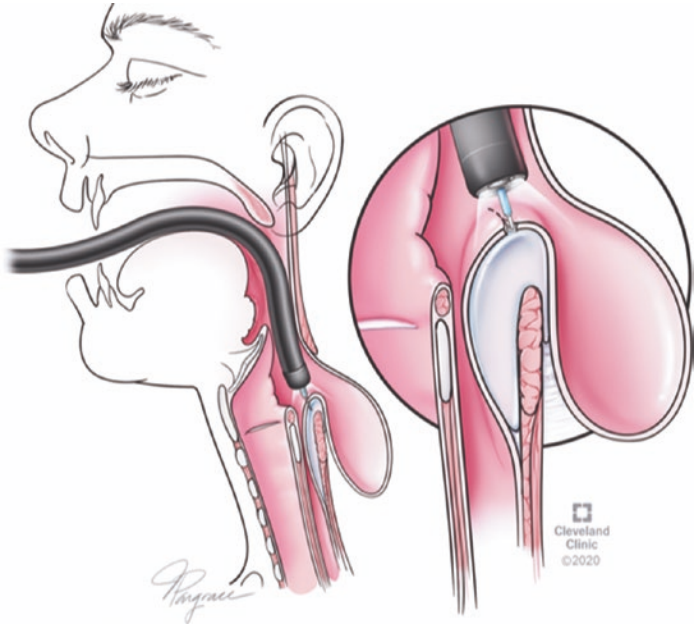

FIGURE 23.2 Submucosal bleb created with an endoscopic injection needle

For difficult mucosal closures, the endoscopic overstitch suture device (Apollo Endosurgery, Austin, TX) can be employed. The nasogastric tube and/or guidewire is removed and the endoscope is passed into the esophagus to assess for any residual resistance at the cricopharyngeus.

Endoscopic Mucosal Incision and Muscle Interruption (MIMI)

In the mucosal incision and muscle interruption (MIMI) technique, a solution of blue dye as previously described is injected directly into the submucosa overlying the cricopharyngeal septum, in comparison to the Z-POEM technique whereby the injection and overlying incision are made in the

hypopharynx and a submucosal tunnel is created to reach the septum. A 1–1.5 cm longitudinal incision is made in the mucosa overlying the cricopharyngeus with a triangle-tip (TT) knife (KD-640L, Olympus, Tokyo, Japan) on cutting current (Endocut effect 2-1-2) (Fig. 23.3). Using ERBE Vio 300 electrosurgical generator (ERBE, Tübingen, Germany), the submucosa on both sides of the cricopharyngeal septum are dissected bluntly with the endoscopic cap and the TT knife using coagulation current (Spray coagulation, 50 W, effect 2) until the base of the diverticular septum is clearly identified (Figs. 23.4 and 23.5). The cricopharyngeus muscle is then

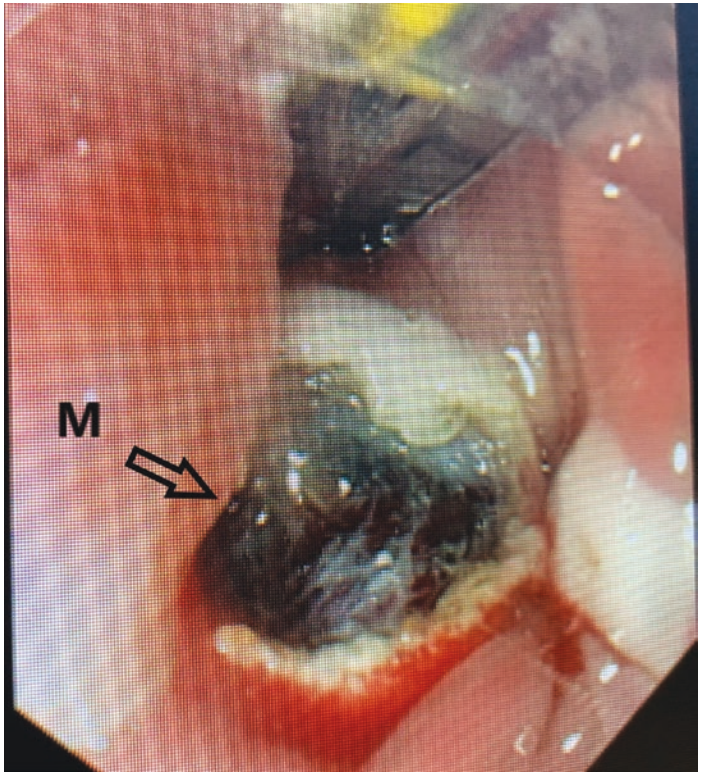

Figure 23.3 Mucosotomy (M) created along the septum

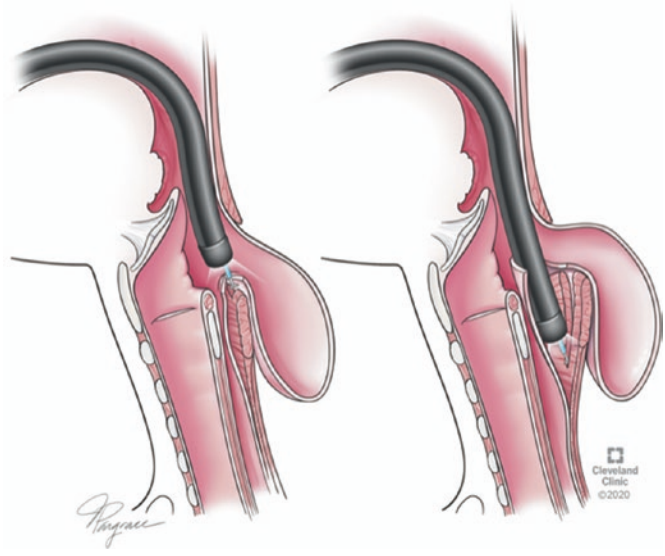

FIGURE 23.4 Creation of mucosotomy and submucosal tunnel

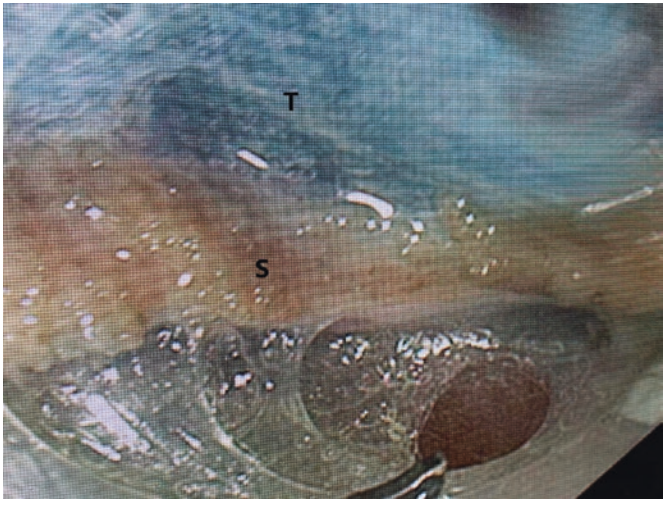

FIGURE 23.5 Demonstration of submucosal flaps with septum in the center and tunnel (T)

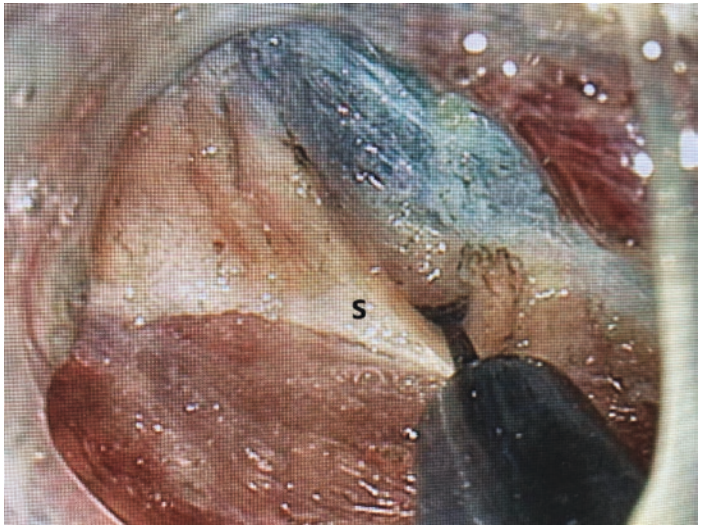

FIGURE 23.6 Cricopharyngeal myotomy

divided along its length with the TT knife using coagulation current or Endocut with the settings as above until the base of the septum is clearly divided (Fig. 23.6). The esophagus is examined for any signs of perforation or hemorrhage and the tunnel is closed with endoscopic clips. The endoscope is passed into the esophagus to assess for any residual resistance at the cricopharyngeus [8] (Fig. 23.7).

Postoperative Care

Once the patient has recovered from anesthesia, they may initially be kept *nil* per os (NPO) with maintenance fluids on the day of the procedure. They are subsequently placed on a pureed or soft diet for two weeks to prevent dislodgement of the endoscopic clips. Patients may be either discharged home the same day or kept overnight for observation based on the individual surgeon's comfort and preference. Some may choose to perform a follow-up esophagram before diet

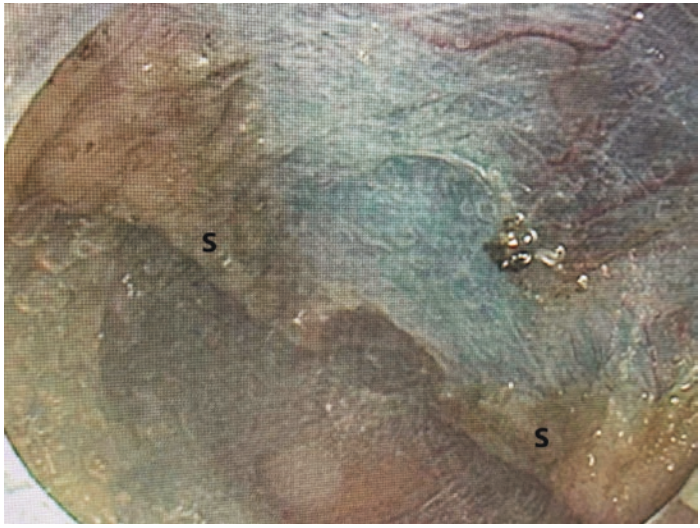

FIGURE 23.7 Submucosal tunnel view after complete myotomy

advancement, particularly if there is clinical concern for complication or perforation such as the presence of crepitus. Patients are discharged home when clinically stable and able to tolerate oral intake [8]. Additionally, the individual surgeon may opt to continue antibiotics for up to 7 days postoperatively [11]. There is no clear evidence suggesting that postoperative esophagram or prolonged antibiotic use is correlated with improved clinical outcomes.

Outcomes

Partially due to the rarity of ZD, studies evaluating the appropriate management options and treatment outcomes are largely published as case series or retrospective observational studies. Systematic reviews and meta-analysis suggest endoscopic approaches have shorter recovery time with lower perioperative morbidity, however, not enough evidence is available to support one approach over the other [12–15].

Earlier studies in the endoscopic management of ZD employed techniques such as endoscopic staplers and $C0_2$ lasers. Such studies demonstrated regurgitation and dysphagia improvement in 96% and 86% of patients enrolled with a 12% rate of complications and 18% rate of recurrence treated mostly endoscopically [16].

A study evaluating the aforementioned FESD approach involving 31 patients demonstrated symptomatic relief in all patients with a 70% decrease in the diverticulum size. Three patients had intraprocedural hemorrhage managed endoscopically and five developed a recurrence treated with subsequent endoscopic approach. Overall, the technique was found to be safe and effective [10]. A subsequent meta-analysis confirmed the safety and efficacy of FESD. Twenty studies were included and the results demonstrated pooled success, adverse events, and recurrent rates of 91%, 11.3%, and 11%, respectively [9].

Despite heterogeneity particularly in instrumentation of flexible endoscopic cricopharyngotomy, multiple meta-analyses have demonstrated comparable outcomes to open or rigid endoscopic approaches [13]. A meta-analysis including 115 studies, of which twenty-nine were flexible endoscopic studies, demonstrated no difference in mortality, infection, or perforation. Bleeding and recurrence, however, were more likely after flexible endoscopic repair compared to rigid endoscopic repair. Flexible endoscopy has the advantage of not requiring neck hyperextension, which may be a limiting factor in this patient population. The data for flexible endoscopic approaches overall demonstrates high rates of technical success and clinical response with low complications and recurrence. In a review by Jain and colleagues [17], 997 patients from 23 studies who underwent flexible endoscopic cricopharyngotomy for ZD, a composite technical success rate of 99.4% and clinical success rate of 87.9% were noted. A composite failure and recurrence rate of 10.0% and 13.6%, respectively, were noted. Close to half of the failure and recurrence groups were managed with repeat endoscopic intervention [17]. The study also evaluated the use of diver-

ticuloscope versus cap which demonstrated comparable success rate. The use of a diverticuloscope resulted in higher clinical success rate compared to cap usage (86.8% vs. 75.4%). However, use of the diverticuloscope had twice the risk of symptom recurrence (16.5% vs. 9.5%) but a lower perforation rate than cap usage (2.3% vs. 10.3%). Bleeding and perforation occurred in 6.6% and 5.3%, respectively, with most managed nonoperatively and 0.9% of the perforations requiring invasive management. The study demonstrated the same safety and efficacy of ZD treatment regardless of diverticulum size or prior treatment [17].

A variety of instruments have been implemented in the endoscopic treatment of ZD. A meta-analysis specifically evaluating the use of the needle knife technique included thirteen studies. Overall complication, bleeding, and perforation rates were 13%, 5%, and 7%, respectively. Recurrence occurred at a rate of 14%. Diverticula greater than 4 cm demonstrated pooled adverse event rates of 17%, while diverticulum less than 4 cm had pooled adverse event rates of 7%. Further studies are needed to evaluate if any specific instruments or tools improve outcomes in the management of ZD [18].

As a novel procedure, the data behind Z-POEM is largely presented in the form of case reports generally demonstrating the overall safety and efficacy of the procedures. Smaller case studies involving 5 patients demonstrated Z-POEM can be safely performed entirely endoscopically with little associated pain or complication rates with short-term follow-up having excellent functional and symptomatic results [M]. A multi-institutional study by Yang and colleagues included 75 patients and reported overall technical and clinical success rate of 97.3% and 92%, respectively. In two patients, the septum was unable to be located due to failure in tunneling [19]. Adverse events were noted in 6.7% of patients. A recent meta-analysis evaluated the management of all esophageal diverticula. In analyzing the patients that had ZD treated with Z-POEM, the pooled rates for technical success were 95%. Adverse events were noted at a rate of 6% [20].

In a new variation to the Z-POEM, Klingler and colleagues describe the aforementioned MIMI approach whereby the mucosal incision is made directly over the diverticulum. This technique may theoretically decrease the risk of technical failure in the tunneled approach in not being able to identify the septum after tunneling as previously described [19]. Nineteen patients undergoing the MIMI approach and seven patients undergoing the non-tunneled approach were included. The mean ZD size was larger in the MIMI group compared to the non-tunneled group (2.8 cm vs. 1.9 cm, $p = 0.03$). Clinical success was achieved in 89.5% MIMI patients and 100% in non-tunneled patients with no significant differences in the two groups. Dysphagia scores improved in both groups; however, this difference was only significant in the MIMI group ($p \leq 0.001$). Recurrence occurred in 2/17 (11.7%) MIMI patients and 3/7 (42.9%) non-tunneled patients ($p = 0.094$). One patient with a very small (<2 cm) ZD suffered a perforation requiring open surgery in the MIMI approach. Overall, this novel approach was found to be safe and effective, but care should be taken with this approach in patients with a small ZD or a prominent cricopharyngeal bar [19].

Recurrence after treatment of ZD is not infrequent and generally occurs at a frequency of 11–14% [9,17]. Recurrences have been managed with open surgery and repeat endoscopic treatments; however, the optimal approach is not clearly understood. The matter of managing these recurrences with Z-POEM was investigated by Sanaei and colleagues [21]. Thirty-two patients with persistent or recurrent symptoms after prior endoscopic and/or surgical interventions for ZD were included. In this group, Z-POEM was technically successful in all but two patients (93.8%) with clinical success in 96.7%. A reduction in the median dysphagia score from 2 to 0 ($p < 0.001$) was noted. Four adverse events (12.5%) including two inadvertent mucosotomies and two leaks on postoperative esophagram were noted [21].

Future Developments

The management of Zenker's Diverticulum, as in many aspects of surgery, has evolved to be progressively less invasive. With the new era of robotic endoscopy, there may be a role in the management of ZD in the future [22]. The repertoire of tools used in endoscopy is also constantly evolving. A variety of endoscopic options may be implemented in the treatment of ZD with newer technologies being developed or refashioned for use in the treatment of ZD. One particular study evaluated the use of needle knife versus bipolar forceps on pig models. The bipolar forceps were found to be safe and effective with a theoretical added benefit of bonding the mucoso-muscular tissue edges, therefore, potentially decreasing the risk of subsequent perforation. Future studies in human models are necessary to delineate the added benefit [23].

It is thought that the flexible endoscopic approach may not be suitable for diverticula that are too large or too small. In a study evaluating prognostic variables for clinical success in flexible endoscopic septotomy for ZD, it was found that septotomy length less than 2.5 cm or ZD size greater than or equal to 5 cm were independent predictors of failure to achieve symptom relief. For very large diverticulum, open surgery has historically still been the main consideration, however, as described by Wong and Ujiki [4], endoscopic diverticulopexy is a potential alternative to be further studied and evaluated. This approach was completed on a patient with a pre-treatment 6.2 cm ZD that returned with recurrence of dysphagia. A dual-lumen scope and overstitch device with 2-0 DemeLENE sutures (DemeTECH, Miami, FL) were used. The apex of the diverticulum was identified, grasped with a helix device, brought into the jaws of the device, and then brought into the true lumen of the esophagus. It was then pexied to the lateral wall of the esophagus. This was repeated until the entire diverticulum was attached to the lateral wall. Fluoroscopy confirmed no lumenal obstruction,

perforation, or bleeding. As the technology continues to develop, the potential endoscopic options to manage diagnoses such as ZD will continue to evolve to improve patient outcomes while minimizing patient risk.

Ultimately, endoscopic cricopharyngeal myotomy has been found to be a safe and efficacious procedure with favorable outcomes for the treatment of Zenker's diverticulum [24]. Given the variability in instrumentation and techniques across different centers, large-scale prospective studies using standardized techniques with long-term follow-up are needed to better delineate optimal interventions in the treatment of ZD.

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