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Esophagus (K Ravi, Section Editor)

Management of Esophageal Diverticula

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Abstract

Purpose of review Esophageal diverticula are outpouchings of the esophageal mucosa that are an uncommon but well-established cause of dysphagia. The purpose of this review is to highlight the endoscopic and surgical management of the various subtypes of esophageal diverticula.

Current findings Both surgical and endoscopic management options exist for the various esophageal diverticula subtypes, including Zenker's diverticulum, Killian–Jamieson diverticulum, mid-esophageal diverticulum, and epiphrenic diverticulum. These treatment options should be considered for patients with symptomatic esophageal diverticula, while asymptomatic patients can be observed without need for intervention. Submucosal myotomy of the muscular septum is a newer promising technique for management of esophageal diverticula that merits further study.

Summary Surgical and endoscopic management of various esophageal diverticula appears to be safe and feasible.The literature on both surgical and endoscopic approaches appears most robust for Zenker's diverticula and is more limited for the other esophageal diverticula given their rarity.

Esophageal diverticula: symptoms, diagnosis, and subtypes

Esophageal diverticula are outpouchings of the esophageal mucosa and an uncommon yet well-established cause of dysphagia. Commonly, esophageal diverticula may be discovered incidentally, and patients may be asymptomatic. When symptoms are present, the most common presenting symptom is dysphagia; however, patients may present with a constellation of symptoms including halitosis, regurgitation, cough, weight loss, malnutrition, hypersalivation, or recurrent episodes of aspiration and pneumonia. Standardized questionnaires such as the 10-item Eating Assessment Tool (EAT-10), Functional Outcome of Swallowing Scale (FOSS), and Reflux Symptom Index (RSI) may be used to assess patient symptoms and monitor them over time and with therapy [1]. A video swallow study and/or esophagram is the most common test to identify an esophageal diverticulum, although other cross-sectional imaging tests such as computed tomography of the chest can also demonstrate these abnormalities. Endoscopic evaluation can be considered for diagnostic confirmation when other diagnostic modalities are inconclusive. Given the association between esophageal diverticula and esophageal motility disorders, esophageal manometry can be considered in cases where an underlying esophageal motility disorder may be suspected.

Esophageal diverticula can be subdivided based on the layers of the esophagus involved (true diverticula vs. pseudodiverticula), primary mechanism behind their formation (pulsion vs. traction), and location. True diverticula include all layers of the esophageal wall (mucosa, submucosa, muscularis propria, and adventitia), while pseudodiverticula only include the mucosa and submucosa [2]. Pulsion diverticula are formed when increased intraluminal pressure results in herniation of the esophageal wall at a point of weakness, while traction diverticula occur when an external process pulls on the esophageal wall resulting in a defect [2]. Pulsion diverticula are sometimes observed in cases of esophageal dysmotility, such as achalasia, where aperistalsis and elevated lower esophageal sphincter pressures can increase intraluminal presssure [2]. Traction diverticula may be seen with mediastinal inflammation, which can extend to involve the esophageal wall. [2]

There are four main types of esophageal diverticula, namely, Zenker's diverticula, Killian–Jamieson diverticula, mid-esophageal diverticula, and epiphrenic diverticula (Table 1). Zenker's and Killian–Jamieson diverticula are both located in the hypopharyngeal region, mid-esophageal diverticula in the middle esophagus, and epiphrenic diverticula in the distal esophagus. In this review, we will discuss endoscopic and surgical management of the various subtypes of esophageal diverticula. In general, such interventions should be considered for patients with symptoms that are attributable to the esophageal diverticula, whereas asymptomatic patients can most often be observed without need for intervention.

Zenker's diverticulum

Zenker's diverticulum is a posterior pharyngoesophageal outpouching through Killian's triangle, an area of hypopharyngeal wall weakness between the oblique fibers of the inferior pharyngeal constrictor and horizontal fibers of the cricopharyngeus muscle (Figs. 1 and 2) [3]. Zenker's diverticula are pseudodiverticula that occur due to pulsion in the setting of poor upper esophageal sphincter compliance and dysfunction of the cricopharyngeus muscle [3]. On physical examination, a palpable neck mass may sometimes be present, especially if the pseudodiverticulum is large in size and filled with liquid or solid food. The mainstay of diagnosis is a dynamic video swallow study. As discussed above, treatment of Zenker's diverticulum should only be

Table 1. Characteristics of the various esophageal diverticula subtypes

Esophageal diverticula subtype	Extent of esophageal wall involvement (true diverticula vs. pseudodiverticula)	Primary mechanism (pulsion vs. traction)	Location
Zenker's diverticula	Pseudodiverticula	Pulsion	Hypopharynx
Killian–Jamieson diverticula	Pseudodiverticula	Pulsion	Hypopharynx
Mid-esophageal diverticula	True diverticula	Traction	Mid esophagus
Epiphrenic diverticula	Pseudodiverticula	Pulsion	Distal esophagus

Fig. 1 Esophagram demonstrating a Zenker's diverticulum.

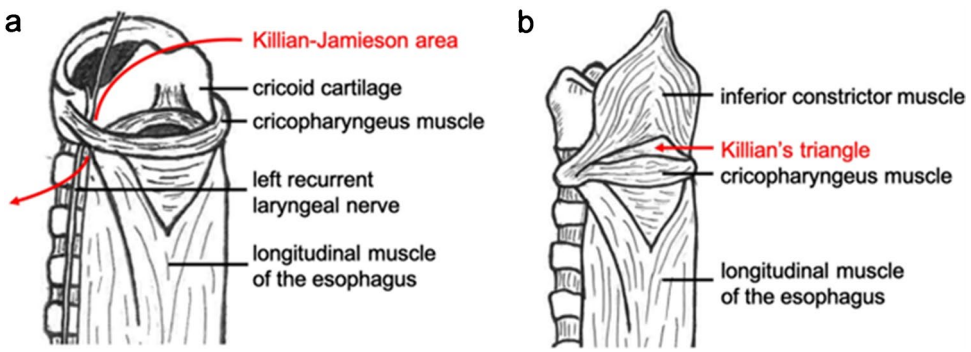

Fig. 2 Anatomic differences between Zenker's and KJ diverticula. This figure was adapted from Saisho, K., Matono, S., and Tanaka, T. et al. Surgery for Killian–Jamieson diverticulum: a report of two cases. *surg case rep* 6, 17 (2020). https://doi.org/10.1186/s40792-020-0789-0. Note: this article is distributed under the terms of the Creative Commons Attribution 4.0 International license (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

offered to patients with attributed symptoms, whereas asymptomatic patients can be observed.

Patients with a symptomatic Zenker's diverticulum may be managed surgically or endoscopically. The open surgical approach involves a myotomy that extends from 2 cm proximal into the inferior pharyngeal constrictor to 5 cm distally through the cricopharyngeus followed by resection of the diverticulum (diverticulectomy), suspension and fixation of the diverticulum to the hypopharyngeal wall (diverticulopexy), or invagination of the diverticulum into the esophagus (diverticular inversion) [3, 4]. For larger pouches, a diverticulectomy is typically performed, whereas for small- to moderate-sized pouches, diverticulopexy with or without cricopharyngeal myotomy may be performed [3]. Open surgical management results in symptom resolution in 90–95% of patients [4]. However, adverse events may include fistula or abscess formation, hematoma, phonation difficulties, and recurrent nerve paralysis. In addition, enteral nutrition with a nasogastric or nasojejunal tube may be needed temporarily following surgery to decrease risk of infection and mediastinitis as the patient recovers from surgery. With the development of endoscopic approaches for the management of Zenker's diverticula as outlined below, the open surgical approach, which requires an open neck dissection, does not appear to have a significant role in the management of this condition at this time.

There are two types of endoscopic management options for Zenker's diverticula, namely, rigid and flexible; both of which work by severing the cricopharyngeal muscle [3, 5]. Both the rigid and flexible endoscopic options are great options for management of Zenker's diverticula. The rigid endoscopic transoral approach involves passage of a rigid diverticuloscope, either the Dohlman or Weerda type, and dividing the common wall (Fig. 3) [6]. Rigid endoscopic management was first described more than a century ago by Mosher in 1917 [6]. This approach can be successful using different techniques including electrocautery (Dohlman technique, first reported in 1960 [7]), carbon dioxide laser therapy (reported by van Overbeek [8] in 1984), and more recently and now most commonly linear stapling (reported by Collard in 1993 [9]). This procedure is typically performed by otolaryngologists under general anesthesia and requires neck

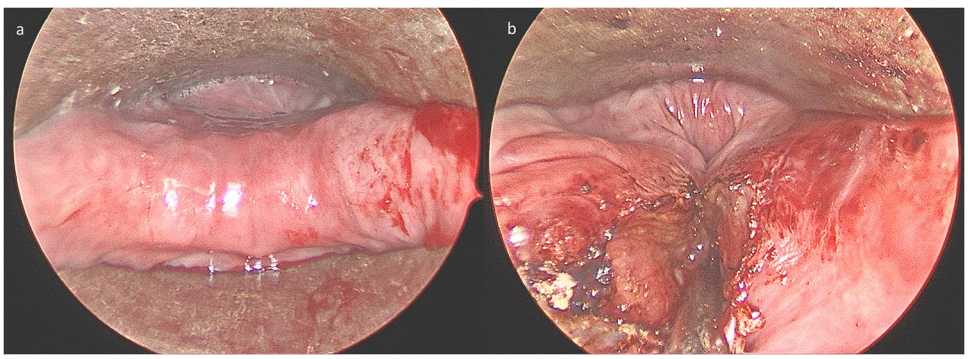

Fig. 3 Rigid endoscopic management of Zenker's diverticulum demonstrating the **A** preoperative anatomy and **B** postoperative anatomy. Images courtesy of Dr. Dale C. Ekbom, Mayo Clinic.

hyperextension for visualization. As such, patients with altered anatomy of the head and neck such as cervical kyphosis or fixation or large tongue may not be good candidates [6]. Careful patient selection is critical as up to 6% of patients fail attempted rigid endoscopic treatment despite pre-procedure screening and subsequently require open surgical or flexible endoscopic management [6]. The rates of clinical success, as defined by symptom resolution, with the rigid transoral approach generally exceed 90%. [3]

The flexible endoscopic transoral cricopharyngeal myotomy is a newer technique and performed by dividing the septum using a needle knife sphincterotome or endoscopic submucosal dissection knife to achieve complete transection of the cricopharyngeus (Video 1) [3, 10]. The first case series on the use of flexible endoscopic diverticulotomy was by Ishioka et al. [11] and Mulder et al. [12] in 1995. In a systematic review and meta-analysis on the use of flexible endoscopic septum division for Zenker's diverticula consisting of 20 studies with 813 patients, the pooled clinical success, adverse events, and recurrence rates were 91, 11, and 11%, respectively. [13] A newer systematic review and meta-analysis on the same approach for Zenker's diverticula with 13 studies and 589 patients found pooled immediate symptomatic response, overall adverse event, and overall recurrence rates of 88, 13, and 14%, respectively. [14] In this study, the rates of adverse events were greater when the diverticulum size was 4 cm or greater compared to less than 4 cm (17% vs. 7% respectively) [14]. A single-center study on cap-assisted endoscopic septotomy showed an early clinical success of 96% with adverse events in 4% [15•]. However, 31% had a recurrence at a mean of 9 months and 95% were managed with a second endoscopic septotomy [15•]. At a mean follow-up of 5.5 years, 95% were asymptomatic after a mean of 1.3 procedures [15•]. Among the endoscopic techniques, this has the most available literature and avoids need for creating a submucosal tunnel, a technique not widely available. However, recurrence rates may be somewhat higher theoretically than other endoscopic techniques due to incomplete myotomy, as this technique does not easily allow for assessment and visualization of myotomy completeness. [10]

More recently, Zenker's diverticulum peroral endoscopic myotomy (Z-POEM) (Video 2) was described with an aim to decrease the perforation rate associated with flexible endoscopic septum division, as that involves a full-thickness incision including mucosal and muscular fibers that form the diverticular septum [16]. The perforation rate with the flexible endoscopic septum division was reported to be as high as 6.5% [13]. Submucosal tunneling endoscopic septum division (aka Z-POEM) was developed using the principles of esophageal POEM and potentially allows for improved visualization of the cricopharyngeus and complete division of the cricopharyngeus to the base of the diverticulum [16]. This technique requires creation of a submucosal lift followed by mucosal incision at the tunnel entry, submucosal tunnelling between the mucosal and muscular layers, septum division, and closure of the mucosal incision with hemostatic clips [16]. This technique, while technically challenging, may allow for a more complete myotomy as the muscular layer is fully exposed and therefore may be associated with a lower recurrence rate. [10]

The results of a systematic review and meta-analysis on the use of Z-POEM for Zenker's diverticulum consisting of 11 studies with 357 patients yielded an overall pooled technical success rate of 96% and pooled clinical success rate of 93% with an adverse event rate of 12% and recurrence rate of 11% [17••]. While the clinical success for Z-POEM was higher than flexible endoscopic cricopharyngeal septotomy (relative risk 1.11, $p < 0.01$), there were no differences in technical success, adverse events, or recurrence [17••]. In a multicenter international retrospective study on 10 centers with 75 patients with mean size of Zenker's diverticula 31.3 mm, the overall technical success rate was 97% and clinical success rate was 92% [18•]. The adverse event rate was 7% with 1 patient having mild bleeding treated conservatively, and 4 perforations [18•]. The mean dysphagia score (Dakkak and Bennett score) decreased from 1.96 to 0.25 ($p < 0.01$), and only 1 patient reported recurrent symptoms at 12 months. [18•] The mean procedure time and length of hospital stay were 52 min and 1.8 days, respectively. [18•] In totality, the available data suggest that Z-POEM is an effective therapeutic option for patients with symptomatic Zenker's diverticulum.

In addition to its effectiveness as a primary intervention, Z-POEM appears feasible and effective after failed prior surgical or endoscopic interventions [20]. In a study on 32 patients with failed prior interventions, Z-POEM had a technical success of 94% and clinical success of 97% with a significant reduction in the median dysphagia score from 2 to 0 over a median follow-up of 166 days. [21•] Extensive fibrosis was noted in 59%, and 4 adverse events (13%) were noted including 2 inadvertent mucosotomies and 2 leaks. [21•]

Some advantages of Z-POEM over flexible endoscopic cricopharyngeal myotomy include 1) improved visualization and procedural control as the muscle can be better isolated and base of the diverticulum more easily identified, 2) less bleeding compared to flexible endoscopic cricopharyngeal myotomy, 3) preservation of the mucosa which may prevent infection or leak, and 4) rapid dietary advancement after procedural intervention. In a retrospective international study evaluating outcomes with Z-POEM versus flexible endoscopic cricopharyngeal septotomy, the former had a lower adverse event rate of 10% versus 31% ($p = 0.02$) [22•]. Some disadvantages include the tight working space very high in the esophagus, which can increase the technical difficulty of this approach. Additionally, Z-POEM may not be the optimal approach for large diverticula. While it may be the best flexible endoscopic approach, it has potential to be a two-stage procedure for such cases. The decision to choose between Z-POEM and flexible endoscopic approach is based largely on endoscopist preference and discretion rather than on the size of the diverticulum.

Killian–Jamieson diverticulum

Killian–Jamieson diverticulum is a proximal, anterolateral cervical esophageal outpouching through the Killian–Jamieson triangle that lies inferior to the cricopharyngeus muscle, superior to the circular muscle of the esophagus, and lateral to the longitudinal muscle (Fig. 2) [3, 23]. Unlike Zenker's diverticulum, which involves the posterior wall and is located above the

cricopharyngeus, Killian–Jamieson diverticulum involves the anterolateral wall and is located below the cricopharyngeus. Similar to Zenker's diverticulum, however, Killian–Jamieson diverticula are pseudodiverticulum, most commonly unilateral although sometimes these may also be bilateral. They present with symptoms similar to Zenker's diverticulum, although there is decreased aspiration risk given that this diverticulum is located below the upper esophageal sphincter.

Surgical and endoscopic management of Killian–Jamieson diverticulum have been described, generally in case reports or small cases series given the rarity of this diagnosis with approximately 68 cases described in the literature to date [24]. The approach to surgical intervention is similar to that for Zenker's diverticulum, consisting of diverticulectomy or diverticulopexy with or without cricopharyngeal and esophageal myotomy [25]. Diverticulopexy may be a better option for high-risk patients compared to diverticulectomy, as it is associated with a lower risk of suture line or staple line leakage and allows for earlier peroral feeding [25]. Endoscopic management options include transmural septum division and submucosal tunneling diverticulotomy (POEM) [23, 26, 27]. The endoscopic submucosal tunnelling diverticulotomy, compared to endoscopic direct diverticulotomy, offers a theoretical advantage of creating a more complete septotomy and lower risk of laryngeal nerve injury or leak [28]. In a retrospective study on 13 patients with Killian–Jamieson diverticulum that underwent endoscopic diverticulotomy with median follow-up of 33 months, the clinical success rate was 92% [28]. Surgeons and endoscopists should note that the recurrent laryngeal nerve enters the pharynx near the base of the diverticulum and recognize the importance of this anatomical structure to avoid potential adverse events.

Mid-esophageal diverticulum

Unlike the aforementioned diverticula, which are pseudodiverticula developed via pulsion and located in the pharynx or upper esophagus,

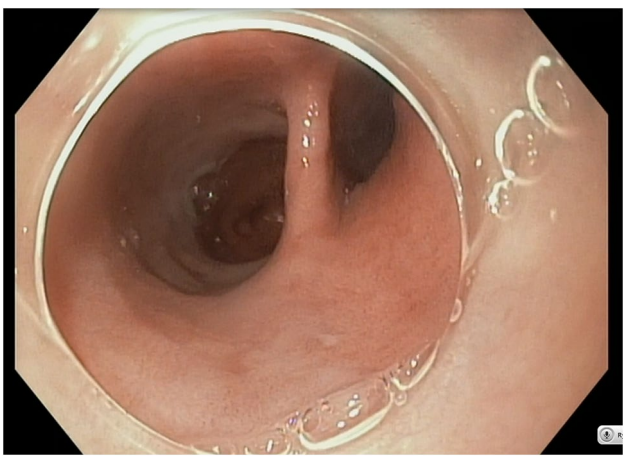

Fig. 4 Endoscopic visualization of a mid-esophageal diverticulum.

mid-esophageal diverticula are true diverticula developed via traction, and as its name suggests, located in the mid-esophagus (Fig. 4). Mid-esophageal diverticula are thought to develop due to mediastinal disease processes that result in inflammation and subsequent retraction of the esophageal wall segments. Some commonly described etiologies include infections such as tuberculosis and histoplasmosis, and neoplasms such as lymphoma, lung malignancies, and esophageal cancer [29–31]. Occasionally, mid-esophageal diverticula can be of the pulsion subtype occurring secondary to an esophageal motility disorder [32]. Surgical intervention remains the mainstay of treatment for mid-esophageal diverticula, although endoscopic septum division and POEM approaches have been described [33–36]. Care must be taken with septum division, however, given lack of a hypertrophic muscular wall. Additionally, the underlying mediastinal inflammatory process requires concomitant evaluation and treatment.

Epiphrenic diverticulum

Epiphrenic diverticulum are typically located in the distal esophagus and are considered pulsion-type diverticula that often develop due to an esophageal motility disorder (Fig. 5) [37]. While its overall prevalence is low (0.2–0.8%), an underlying esophageal motility disorder is present in more than 60% of cases, most commonly achalasia [38]. Historically, the management of these diverticula has been surgical, requiring diverticulectomy, myotomy, and partial fundoplication [39, 40]. The goal of the myotomy is to decrease recurrence of the diverticulum, while the goal of fundoplication is to decrease significant gastroesophageal reflux [40]. In a single-center study with 27 patients that underwent surgery for primary epiphrenic diverticulum over a 12-year period, 90% of patients reported excellent satisfaction and morbidity was seen in 3 patients. [41]

More recently, the development of submucosal endoscopy has provided an endoscopic option. The endoscopic approach includes esophageal POEM combined with septotomy; however, data for this approach is limited to case reports [37]. The two types of POEM approaches that have been described for such diverticula include salvage POEM (S-POEM) and diverticular POEM (D-POEM). In S-POEM [42], a submucosal endoscopic myotomy is performed on the wall opposite the diverticulum, while in D-POEM, a submucosal tunnel is used to expose the diverticular septum and then septotomy is performed [33]. When an underlying esophageal motility disorder is present, this should also be addressed.

Esophageal diverticulum and malignancy

As esophageal diverticula are rare, it is difficult to determine the prevalence of other rare associated conditions (i.e., malignancies). Nonetheless, esophageal diverticula have been associated with cancer in case reports and small cases

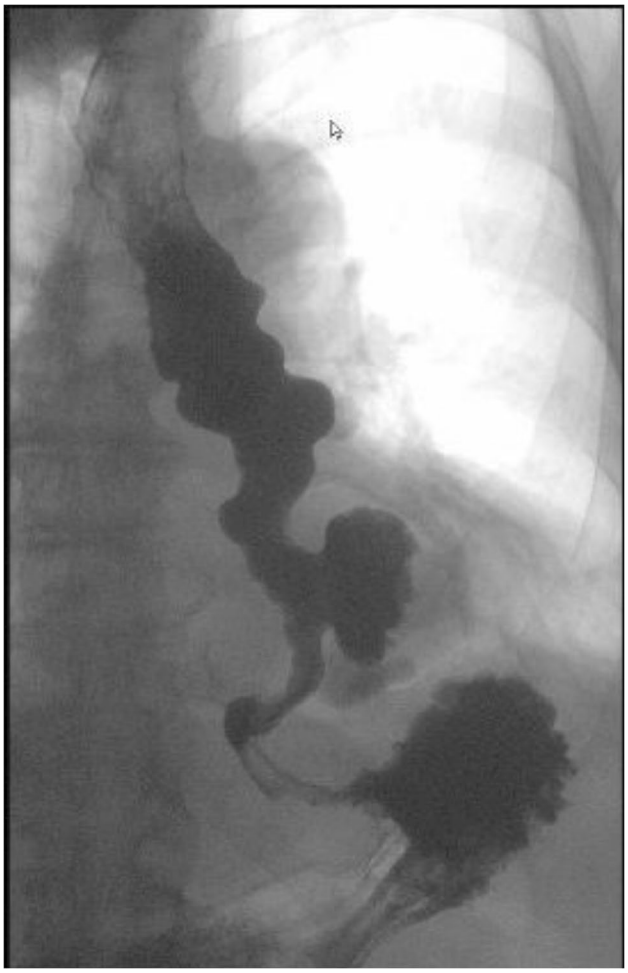

Fig. 5 Esophagram demonstrating an epiphrenic diverticulum.

series although the overall incidence appears to be very low [43]. The incidence of cancer in a diverticulum is estimated at 0.3–7% for pharyngoesophageal diverticula, 1.8% for mid-esophageal, and 0.6% for epiphrenic [43]. Risk factors include old age, male gender, long-standing history, and larger size of diverticulum.43 As such, when assessing a patient with an esophageal diverticulum, alarm symptoms should be elicited, such as hematemesis, melena, unintentional weight loss, and rapid progression of symptoms.

Conclusion

Surgical and endoscopic management of various esophageal diverticula appears to be safe and feasible. There exist limited endoscopic options for mid-esophageal diverticulum. Submucosal myotomy of the muscular septum

with or without distal esophageal myotomy appears to be promising, but this technique has been reported only in case reports and small case series and merits additional study.

Declarations

Conflict of Interest
Ryan J. Law is a consultant for Olympus America, Medtronic, and ConMed and receives royalties from UpToDate. Amrit K. Kamboj has no disclosures.

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Papers of particular interest, published recently, have been highlighted as:
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•• Of major importance

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