Zenker’s diverticulum (ZD) is an outpouching of tissue through the Killian triangle that is believed to be caused by dysfunction of the cricopharyngeal muscle. ZD is a relatively uncommon disorder occurring in the elderly. The predominant symptom of ZD is dysphagia, and the most serious consequence is pulmonary aspiration. Videofluoroscopy confirms the diagnosis. Therapy of symptomatic ZD has evolved from an open surgical approach to less invasive transoral endoscopic techniques. Transoral endoscopic therapy using rigid instruments is performed primarily by otorhinolaryngologists, whereas transoral therapy using flexible endoscopes is performed by surgical endoscopists and gastroenterologists. The common goal of all modalities is severing of the septum between the esophageal lumen and the diverticulum containing the cricopharyngeal muscle. Although flexible endoscopic therapy was described nearly 20 years ago, it has experienced a recent resurgence paralleling the advancements of therapeutic endoscopy in other areas, such as endoscopic submucosal dissection. Direct head-to-head comparisons of rigid and flexible endoscopic therapy are lacking, and each approach has variations in techniques as well as advantages and disadvantages. In this article, we review the pathophysiology and management of patients with ZD with an emphasis on flexible endoscopic therapy.

Keywords: Zenker’s Diverticulum; Flexible Endoscopic Diverticulotomy; Dysphagia.

Zenker’s diverticulum (ZD) is a posterior pharyngoesophageal pouch that forms through pulsion forces in an area of relative hypopharyngeal wall weakness between the oblique fibers of the inferior pharyngeal constrictor and the horizontal fibers of the cricopharyngeus (CP) muscles. Poor upper esophageal sphincter (UES) compliance is the presumed pathophysiologic mechanism of action. This dysfunction creates a high-pressure zone eventuating in increased pulsion forces and subsequent ZD formation. This entity most commonly presents in the elderly and can be associated with a plethora of potential symptoms, of which dysphagia is most common. It has become accepted that unless a myotomy of the CP muscle is performed wholly or as part of therapy for ZD, successful amelioration of symptoms and prevention of recurrence is unlikely.

For decades, the mainstay of treatment for ZD was an open surgical approach through a neck incision with performance of myotomy of the UES and removal or suspension of the diverticulum. Over the past 4 decades, however, alternative and often preferable incisionless transoral approaches have been developed. The literature is rife with endoscopic publications, although the vast majority involves the use of rigid tube instrumentation (rigid endoscopy). Rigid endoscopic therapy became popularized after a landmark study published by Dohlman and Mattson in 1960 and is typically performed by otorhinolaryngologists. Fewer, though increasingly more common, published data are available regarding treatment using flexible endoscopy performed predominately by surgical endoscopists and gastroenterologists. In this manuscript, we focus on the pathophysiology and interventions for ZD.

Pathophysiology

As in any pulsion diverticulum, the major pathogenesis relates to increased intraluminal pressure leading to an outpouching in an area of relative wall weakness when compared with surrounding areas. In ZD, this area of weakness is located in the hypopharynx between 2 strong pharyngoesophageal muscles, the CP and inferior pharyngeal constrictor. This area is known as the triangle of Killian, an area of lower hypopharyngeal wall tone and relatively decreased pressures in the contiguous retropharyngeal space that leads to pouch formation posteriorly (Figure 1). This posterior pouch includes only mucosa and submucosa, thus, a ZD should be considered a pseudodiverticulum. Less clear are the exact forces that contribute to increased luminal pressures initiating and sustaining

Abbreviations used in this paper: AEs, adverse events; CP, cricopharyngeus; UES, upper esophageal sphincter; ZD, Zenker’s diverticulum.
this dehiscence. Difficulty in effectively studying this area results in part from the challenges of accurate manometric measurements due to asymmetry of the sphincter pressure and a wide range of sphincter movement during swallowing. Video fluoroscopy is valuable (Supplementary Video 1), particularly for diagnosis; but precise determination of abnormal function is limited by variations in quality and interpretation of these studies. Nevertheless, through these studies, the most likely mechanism proposed for the increased forces is decreased compliance of the UES with failure to open completely.4 This failure to achieve adequate diameter for effective bolus clearance leads to a subsequent increase in the hypopharyngeal pressure gradient. Data further supporting this hypothesis are the finding of a marked increase in fibroadipose tissue replacement of muscle and normal connective tissue compromising sphincteric elasticity, sphincter opening, and the generation of an elevated pressure gradient in the hypopharynx. It should be noted that this change in compliance is not equivalent to a change in UES pressure, a phenomenon that has been inconsistently demonstrated. Several other contributing factors to a pharyngoesophageal pouch appear likely as well. For example, an increase in intrabolus pressure has been well documented because of the stiffness of the CP and hypopharynx. Furthermore, as the diverticulum enlarges, it may compress the pharyngoesophageal segment as well as increase stiffness and the intrabolus pressure. Increased intrabolus pressure is also increased in older patients who perform multiple swallows to achieve bolus clearance. Finally, incoordination of pharyngeal contraction and UES opening has also been variably demonstrated by some investigators.  

**Demographics, Symptoms, and Diagnosis**

ZD usually occurs between the seventh and eighth decades of life and rarely before the age of 40 years.6–8 This anomaly occurs with aging, specifically changes in fibrosis and muscle necrosis in the UES. It occurs predominantly in men, and the overall prevalence of ZD among the general population is believed to be between 0.01% and 0.11%.9 The incidence varies based on region, being more common in Northern than Southern Europe. It has been described more frequently in the United States, Canada, and Australia than in Japan and Indonesia.10 It is unclear if these differences in prevalence reflect differences in longevity or anatomical differences between geographic areas.11 In the United Kingdom, the incidence of ZD is about 2 per 100,000 people per year.12 Notably, these data reflect symptomatic patients, so the number of asymptomatic patients with ZD is unknown. Symptoms may be present for weeks to years before a diagnosis is made.5 Although a plethora of symptoms have been ascribed to ZD, 80% to 90% of patients complain of dysphagia. There are 2 mechanisms by which the diverticulum may cause dysphagia: incomplete opening of the UES and extrinsic compression of the cervical esophagus by the diverticulum itself. Cervical borborygmus, particularly in the presence of a palpable lump in the neck, is almost pathognomonic of ZD. As the pouch enlarges and dysphagia increases, symptoms become more severe with resultant weight loss and malnutrition. A sudden increase in the severity of dysphagia and regurgitation and/or development of alarm symptoms, such as local pain and hemoptysis or hematemesis, may signal the presence of ulceration13 or squamous cell carcinoma within the ZD, which has an incidence of 0.4% to 1.5%.14–16 Hoarseness/dysphonia, cough, and aspiration pneumonia have been described in 30% to 40% of patients.17,18 It is unclear whether this is caused by direct aspiration of diverticulum contents or pharyngeal pooling of contents with overflow.19 Regurgitation of undigested foods and halitosis may occur because of stasis of food in the pouch. In some patients, pills may become lodged in the diverticulum leading to decreased efficacy of medications and potentially to ulceration and bleeding. Gastroenterologists should be aware of the possibility of entrapment of a video capsule within a ZD.9,10 Gastrointestinal bleeding from a ZD has also been described and can be managed endoscopically in these patients.21,22

Other pathologies described in association with ZD include laryngocele, leiomyoma, polymyositis, cervical esophageal web, carotid body tumor, anterior cervical fusion, stenosis of the upper esophagus, hiatus hernia,
and gastroesophageal reflux. There is no clear evidence of causation by these additional lesions, but it is important to note that additional causes of dysphagia might be present in patients with ZD.

Radiography as the Primary Means of Diagnosis of ZD

The radiologic features of ZD are well known. Esophagography is necessary to confirm the diagnosis of ZD (Figure 2A and B); however, dynamic continuous fluoroscopy is preferred (Supplementary Video 1) because static images may be insufficient in patients with small diverticulum. Additionally, evidence of overflow and aspiration can be seen. Differentiation from the less common, and smaller, Killian-Jamieson diverticulum that arises from the proximal anterolateral cervical esophagus and lies inferior to the CP muscle is important. Although Killian-Jamieson diverticula may be treated endoscopically, it is unclear if the efficacy and safety are the same as with ZD, as the recurrent laryngeal nerve runs close to the base of the diverticulum.

Various radiologic correlations to ZD progression and predictors to therapy have been described. The little-known Brombart classification scheme seen on esophagography defines 4 types of ZD with the original concept of progression from one stage to another. In this schema, type 1 diverticula are only visible during the contraction phase of the UES, whereas type IV lesions are large and lead to compression on the esophagus. Although this has not been established, the scheme has been used to assess the response to therapy. In one study, Brombart III–IV diverticula were managed significantly more commonly with rigid endoscopic procedures than open procedures. Postprocedural residual diverticulum and filling with contrast were strongly associated with prolonged dysphagia in the early postoperative period but failed to correlate significantly with symptomatic recurrence.

In another study, pouch neck length, soft tissue plane between the pouch and the esophagus, diameter of the pouch opening, and the maximum diameter of the pouch were measured. A favorable outcome was predicted by a higher ratio of pouch neck diameter to soft tissue plane and predicts the need for a shorter myotomy. A closer apposition of the diverticulum to the proximal esophageal wall is expected to improve the technical ease of dividing the common septum containing the CP muscle.

ZD may also be diagnosed by transcutaneous ultrasonography. During ingestion of water, an increase in the lesion’s size, a reduction in the definition of the margins, and heterogeneous echogenicity of the lesion’s contents are seen. The importance of ultrasound findings is the differentiation of a ZD from a thyroid mass. Ultrasoundography as a diagnostic modality for ZD may also be useful in elderly patients who cannot tolerate barium esophagography and in those with a neck mass on physical examination. In the future, neck ultrasonography may be used for assessing the UES. A recent study identified the normal diameters of the closed UES, the mean duration of opening, and the mean duration of displacement in the anterior and lateral directions. As this idea is further developed, it may allow us to detect abnormalities at the level of the UES that correlate with ZD.

Surgical Considerations

The UES is composed of the posterior surface of the thyroid and cricoid cartilage and 3 muscles: inferior pharyngeal constrictor, CP, and cervical esophagus. Of these 3 muscles, the CP provides for the dominant portion of UES function. It forms a muscular sling around the upper esophagus between the two sides of the cricoid cartilage and extends posteriorly to mesh with the inferior pharyngeal constrictor. The average length of the CP is 1.9 cm in men and 1.6 cm in women. Two sets of CP muscle fibers have been identified: the horizontally
oriented fibers, which occlude the esophageal introitus, and an oblique band of fibers, which are responsible for the propulsion of the bolus. As a result of this anatomic relationship, ZD forms posteriorly on the left side in a majority of cases. This is important not only for the determination of the neck incision site but because endoluminal therapy dictates the division of the common wall between the diverticulum and the esophageal lumen. The diverticulum may be posterior, posterolateral, or lateral (pharyngocele); but the most commonly encountered type is the posterior pulsion diverticulum. The size of the diverticulum may also vary considerably. In early stages, a diverticulum of ≤1 cm may occur. On the other hand, ZD as large as 6 cm have been reported Rarely, a ZD may be bilobed, in which case the dominant lobe is drained.

Open Approach

With an open approach, an external neck incision is performed. This incision is performed along the anterior border of the sternocleidomastoid muscle, usually on the left side given the propensity of the pouch to emerge in this location. Through this incision, the diverticulum may be easily exposed. Contiguous tissue is dissected away to achieve adequate visualization of the neck of the diverticulum just below the transversely crossing fibers of the inferior pharyngeal constrictor and the horizontally crossing fibers of the CP muscle. A myotomy is performed approximately 2 cm proximally into the constrictor to 5 cm distally through the CP and into the proximal esophagus. The pouch may be treated by 3 techniques: inversion, -pexy, or resection. A larger pouch (>5 cm) is typically excised with closure of the opening by a linear stapling device. Moderate-sized diverticulum can be treated with combined diverticulopexy and CP myotomy, whereas a smaller diverticulum is more frequently treated with suspension or CP myotomy alone. A contrast swallow is performed postoperatively to exclude a leak. Oral feedings may be initiated the day after surgery. Potential adverse events (AEs) of open surgery include fistula formation, abscess, hematoma, recurrent nerve paralysis, difficulties in phonation, and Horner syndrome.

Outcome Following Open Surgical Approach

In a recent comprehensive review of the surgical literature of ZD1 of more than 2800 patients from 41 studies, overall morbidity occurred in 11%, including recurrent laryngeal nerve injury in 3%, leak or perforation in 3%, and cervical infection in 2%. Open surgery resolves symptoms in 90% to 95% of patients.

Endoscopic Approaches

There are 2 types of endoscopic therapies for ZD: rigid and flexible. The common goal of both approaches is to sever the CP muscle (Figure 3).
Rigid Transoral Approach Technique

The transoral approach to a ZD was developed to circumvent the relatively high frequency of AEs and mortality associated with the open approach. Although some of these AEs are caused by the frailty of the elderly population who tend to develop a pharyngeal diverticulum, some, such as fistulae and infection, are not. These are surgically related because of leakage at the suture line and an inadvertent breach of the mucosa. A transoral approach lessens these risks by avoiding an incision, using less operating time, and, in some cases, without needing general anesthesia.

The myotomy is performed by passing a rigid diverticuloscope (Figure 4) and dividing the common wall. The methods to divide the common wall have evolved from electrocautery, known as the Dohlman technique, to carbon-dioxide-laser therapy to the now more commonly performed stapling. Fewer reports have emerged on the use of harmonic scalpels to perform diverticulotomy. This device uses ultrasonic energy to coagulate the septal tissue prior to division.

Outcome Following Rigid Transoral Approach

Outcomes following the above approaches were recently comprehensively reviewed. Using the Dohlman technique in nearly 500 patients, a mean complication rate of 8% was seen, with mediastinitis in 2%. However, in some series, complication rates as high as 18% were seen. Overall improvement in symptoms occurred in 93%. Results are similar using the carbon-dioxide-laser technique. The stapling technique cuts the septum and seals without causing tissue damage. Resolution is achieved in approximately 90%, with recurrence in 10%. In a review of more than 1800 patients, the complication rate was 7%, which included dental injury in 2% and a perforation rate of about 2%. Other AEs may include sore throat and gingival/mucosal laceration. The early data for harmonic scalpel use appear equally promising.

It should be noted that radiographic evidence of a refractory septum and/or residual diverticulum does not correlate with symptom persistence or recurrence after intervention with a rigid endoscopic approach.

Decisions Regarding Choice of Open Surgical or Rigid Transoral Approach

The most important decision in the management of ZD is whether to use an open or transoral approach. Several factors need to be considered. The first is whether clear visualization of the diverticulum can be achieved endoscopically. Although this may not be clear until transoral visualization is attempted, preoperative patient characteristics are predictive of a lack of success. For example, in one study, rigid endoscopy was significantly less successful in patients with short necks, decreased hyomental distance, and/or a high body mass index. A second key factor favoring an open approach is insufficient protection of the diverticulum sac by the dorsal esophageal wall (in patients with small diverticula without a clearly defined shelf). In other words, unless the medial wall of the diverticular sac is adhesed and fibrosed against the esophageal wall, cutting through this wall to create a common channel results in frank perforation. Similarly in patients with a small diverticulum where cricopharyngeal myotomy is performed solely, an open approach is often necessary. Finally, in patients who require additional surgery, such as diverticulectomy, diverticulopexy, or inversion of the diverticulum, an open operation is needed. Indications for an open approach include primary therapy or secondary therapy in the event of a failed endoscopic approach, which occurs in 16% to 68% of patients. Clearly, physician expertise in the transoral approach influences this variability to a large degree.

Flexible Endoscopic Approach

Transoral endoscopic therapy using a rigid endoscope cannot be performed in all patients. An open approach is required in 15% to 68% of cases when inadequate rigid endoscopic exposure of the diverticulum occurs from upper teeth protrusion, inadequate jaw opening, or insufficient neck mobility. Additionally, the risk of perforation is increased with insertion of a rigid diverticuloscope when there is insufficient protection of a small diverticulum sac by the dorsal esophageal wall.

There is a variety of techniques and methods to perform flexible endoscopic transoral cricopharyngeal myotomy. The septum (CP muscle) is commonly divided using a needle knife (normally used for endoscopic retrograde cholangiopancreatography use) or cutting devices designed for endoscopic submucosal dissection (ESD), such as a hook knife (Figure 5A–C). Other methods used to divide the septum include monopolar and bipolar forceps, argon plasma coagulation, harmonic scalpels and stapling devices, the latter two of which are passed alongside the endoscope and not through the flexible endoscope channel. The optimal cutting technique remains elusive as comparative trials in this arena are lacking. Some therapeutic endoscopists advocate for the use of a soft diverticuloscope to stabilize the septum, improve visualization, and further guide the instrument of incision. This accessory is positioned such that it straddles the septum with stabilizing flanges within the upper esophageal lumen and within the ZD, although it is not available in the United States. Other accessories used to enhance visualization include transparent hoods or caps attached to the tip of the endoscope, generally reserved for endoscopic mucosal resection. When the soft diverticuloscope is not used, the preprocedural placement of a nasogastric tube is a frequent maneuver and has a dual benefit. The tube acts as an incisional
guide while also serving as a method to deliver enteral nutrition in the event of a procedural AE, such as perforation. If placed nasally, the use of a small-caliber endoscope is used to perform transnasal endoscopy and avoid transfer of the guidewire. A small hole is cut in the tip of the nasogastric tube to allow wire passage. Blind passage of a nasogastric tube is not recommended.

The transoral flexible endoscopic approach to ZD was first described nearly 20 years ago.\textsuperscript{42,43} Since then several series have been published that highlight a variety of efficacious technical applications and an acceptable safety profile. This technique successfully reduces cricopharyngeal sphincter pressure\textsuperscript{44} and has been shown to be comparable to the use of a rigid transoral diverticuloscope in terms of efficacy and safety.\textsuperscript{45} Nonetheless, flexible transoral cricopharyngeal myotomy is not commonly performed in the United States. The advantages of a flexible endoscopic approach are the flexibility and smaller endoscope diameter, which are especially useful for patients with poor neck extension and/or limited jaw retraction. Additionally, this technique can also be performed without the use of general anesthesia. Flexible endoscopic intervention may be most suitable for elderly patients with comorbid medical conditions limiting surgical intervention. In rare instances, patient comorbidities limit even flexible endoscopic diverticulectomy. Injection of botulinum toxin into the diverticular apex has been described in a small series of 2 patients with satisfactory outcomes.\textsuperscript{46}

**Outcome of Flexible Endoscopic Cricopharyngeal Myotomy**

At the time of this writing, 18 case series have been published regarding the use of flexible endoscopic therapy for the treatment of ZD (Table 1).\textsuperscript{32,38,47–62} The available studies comprise nearly 650 patients. The available data suggest that adequate treatment can be provided in 1 to 2 treatment sessions with a high rate of clinical resolution and a low rate of diverticular recurrence or persistence. The majority of the included studies report a clinical resolution rate of >90%, whereas the recurrence or persistence of clinical symptoms appears to be <20%; however, no formal definitions of clinical success exist. We believe clinical success should be based solely on improvement in symptoms and not on radiographic or endoscopic findings. The difficulty arises in regard to diversity of symptoms, which can be attributed to ZD. An additional limitation of many flexible endoscopic series is the lack of clinical follow-up. Of the 18 available studies, the length of postprocedural follow-up was not reported in nearly one-third of the studies. AEs following flexible endoscopic therapy range from inconsequential to life threatening. In our appraisal of the available studies, we identified a median overall AE rate of 6% (range 0%–38%) in the 16 studies with available data. Bleeding is the most common intraprocedural event occurring in a minority of cases (<5%). This can generally be controlled endoscopically using a variety of electrocautery devices or endoclips. Postprocedural throat pain is nearly uniform and often requires narcotic medications. Uncomplicated subcutaneous emphysema may represent microperforation; however, this finding does not appear to be associated with increased recurrence or persistence of clinical symptoms.
## Table 1. Reported Literature of ZD Using Flexible Endoscopy

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<th>Author/year</th>
<th>Number of patients</th>
<th>Median or mean age (y)</th>
<th>NGT guide</th>
<th>Accessory device</th>
<th>Incision device</th>
<th>Adverse event rate (%)</th>
<th>Number of procedures (mean)</th>
<th>Diverticulum recurrence rate (%)</th>
<th>Clinical resolution rate (%)</th>
<th>Median or mean follow-up (mo)</th>
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APC, argon plasma coagulation; N/A, not available; NGT, nasogastric tube.

*For this case series of 3 patients, only 1 case used an NGT and 1 case used a diverticuloscope.
not mandate surgical intervention and may occur in asymptomatic patients. Clinically relevant and potentially the most severe AE is perforation, which can be documented by extravasation of oral water-soluble contrast (Supplementary Video 2). Fortunately, this is relatively uncommon when flexible endoscopic therapy is performed by skilled endoscopists. A recent review by Dzetovic et al\textsuperscript{13} identified a median rate of perforation and/or leak of 4% (range, 0%–27%). Unfortunately, the definition and reporting of AEs have not been standardized, and we strongly recommend the use of a standardized lexicon\textsuperscript{65} so that meaningful comparisons between and within disciplines can be made.

Who Should Be Performing Flexible Endoscopic Cricopharyngeal Myotomy?

Issues pertinent to reluctance of gastroenterologists to performing ZD therapy likely include referral patterns, procedural risks, medicolegal issues, and the complex nature of the procedure. However, the techniques used are now increasingly practiced during many other advanced therapeutic endoscopic procedures.\textsuperscript{3}

There is still no consensus on the technical details when ZD therapy is performed using a flexible endoscope. One cannot underestimate the technical expertise involved in this treatment. We believe endoscopists with training in advanced endoscopy and experience in advanced endoscopic techniques, especially in the use of electrocautery devices, ESD, and possibly endoscopic retrograde cholangiopancreatography (because the use of needle-knife therapy is common), should perform ZD therapy. Some authors have noted an average of 60 minutes required to perform flexible cricopharyngeal myotomy.\textsuperscript{3}

Endoscopic cricopharyngeal myotomy shares common techniques and tools that can be borrowed from those used to perform ESD and per oral endoscopic myotomy.\textsuperscript{3} With advancements and increased utilization of these techniques, experienced therapeutic endoscopists are poised to perform transoral flexible endoscopic therapy of ZD.

Selected expert therapeutic endoscopists may carefully consider developing and offering this therapy for their patients. For those advanced endoscopists planning to incorporate this technique into clinical practice, we recommend utilizing animal models to gain familiarity with the procedure. An animal model using domestic pigs has been previously described in the literature.\textsuperscript{65} Pigs are ideal because of a normal anatomic pharyngeal pouch that resembles a ZD and permits diverticulotomy using the devices described above.

Conclusions

The principles in the diagnosis and treatment of ZD have held fast for decades. There are some new insights into the pathophysiology that explain the development of this pouch as a result of the aging process: most importantly, fibrosis and loss of compliance of the CP. What is new and exciting is the development of transoral treatments for ZD, particularly the flexible endoscopic approach, which now enables endoscopists to become a treatment provider for this problem. Multiple studies using the flexible endoscopic approach have demonstrated equal efficacy to the traditional open and rigid tube oral approach with a low incidence of AEs and a high level of success. Nevertheless, this procedure requires a formidable endoscopic skill, sound knowledge of neck anatomy, and an understanding of the basic surgical principles and contraindications to this approach that necessitate open access for diverticular repair.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of Clinical Gastroenterology and Hepatology at www.cghjournal.org, and at http://dx.doi.org/10.1016/j.cgh.2013.09.016.

References


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Conflicts of interest
The authors disclose no conflicts.
1. Zenker’s diverticulum
   a. typically occurs in males in the 7th or 8th decade of life
   b. a classical symptom is nasal regurgitation when swallowing liquids
   c. cervical borgorgmus is almos pathognomonic for ZD
   d. has an incidence of squamous cell carcinoma within the ZD of 0.4% to 1.5%

True or False

2. Videofluoroscopy is superior to standard barium swallow for diagnosis of ZD

3. Patient’s with Zenker’s diverticulum almost universally have high UES pressures

4. Zenker’s diverticulum arises in an area of weakness located in the anterior pharyngeal muscles

5. The main mechanism leading to the formation of a Zenker’s diverticulum is decreased compliance and increased fibrosis of the UES with failure to open completely when swallowing

6. Open surgical approach to ZD includes identification and resection of the diverticulum with no additional intervention

7. Open surgical approach or rigid endoscopy approaches to ZD result in >90% symptom resolution