



Review

# Clinical Insights into Zenker's Diverticulum: Anatomy, Pathophysiology, Diagnosis, and Evolving Treatments

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## Abstract

**Background/Objectives:** Zenker's diverticulum (ZD) is a rare but clinically relevant condition. It is a false, pulsion-type diverticulum due to the protrusion of mucosal and submucosal layers through the Killian's Triangle. Its pathogenesis is multifactorial and entails cricopharyngeus muscle dysfunction and age-related tissue degeneration. This review addresses the current evidence regarding the anatomy, pathophysiology, clinical presentation, diagnostic approach, and therapeutic management of ZD. **Methods:** For this literature review, we searched the PubMed and Scopus databases using combinations of keywords relevant to Zenker's diverticulum, including "Zenker's diverticulum," "esophageal diverticula," "diagnosis," "endoscopic treatment," and "surgery". We included articles published in recent decades, with a focus on most recent ones regarding clinical studies, systematic reviews, meta-analyses, and descriptions of new diagnostic and therapeutic techniques. **Results:** Characteristic symptoms comprise progressive dysphagia, regurgitation of undigested food, halitosis, and, in advanced cases, aspiration-related respiratory complications. Diagnosis of ZD is primarily based on barium swallow esophagography and endoscopic evaluation, complemented by other imaging techniques. Current therapeutic options include traditional open surgery and endoscopic procedures, including newer minimally invasive techniques. **Conclusions:** ZD is the most common type of esophageal diverticulum and can have a disabling impact on a patient's quality of life. It is commonly underdiagnosed or misdiagnosed as another condition, and prevalence is expected to increase with the growing population ageing. Improved understanding of its pathophysiology is needed to refine diagnostic and therapeutic strategies and minimize recurrences and risks.



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**Keywords:** esophageal diverticula; diverticulum; Zenker's diverticulum; endoscopy; pharynx; swallowing disorders; dysphagia; esophageal pouch

## 1. Introduction

Zenker's diverticulum (ZD) is a rare condition that still represents both a diagnostic and therapeutic challenge [1]. It consists of the herniation of mucosal and submucosal

layers at the level of the hypopharynx, with a subsequent pouch formation that can retain ingesta [2,3]. This condition typically presents in elderly patients and is clinically significant, as it leads to gradually worsening dysphagia. Over time, this can lead to compromised nutritional status and, in more advanced cases, an increased risk of respiratory complications such as aspiration pneumonia [4–6].

The precise cause of ZD remains a debated subject; however, the prevailing theory suggests that dysfunction of the cricopharyngeus muscle increases intraluminal pressure and contributes to diverticulum formation [4,7,8].

The standard diagnostic approach relies on barium swallow esophagography, although more recently, advances in endoscopic and ultrasonographic techniques have proven to be useful [1,7,9–11]. Therapeutic strategies for ZD have also evolved. Traditional open surgical methods, once considered standard, are now frequently replaced by minimally invasive endoscopic procedures, with improved safety profiles and faster recovery times. Additionally, newer tunneling techniques such as peroral endoscopic myotomy (Z-POEM) have shown promising efficacy and lower recurrence rates, although robust long-term follow-up data are still lacking [12–15].

This work aims to provide an updated and critical overview of the literature regarding the anatomy, pathophysiology, clinical manifestations, diagnostic modalities, and management options for ZD, with an emphasis on recent advances and ongoing challenges in the field.

## 2. Methods

This is a narrative review of the literature. A comprehensive literature search was conducted using the PubMed and Scopus databases to identify studies relevant to ZD. Google Scholar was consulted as a supplementary tool to identify additional recent publications and gray literature not captured by the primary databases. The search strategy combined the following keywords in multiple Boolean combinations: “*Zenker’s diverticulum*”, “*esophageal diverticula*”, “*clinical features*”, “*diagnosis*”, “*endoscopic treatment*”, and “*surgery*”. The search was limited to articles published between 2000 and 2025 to ensure inclusion of both foundational knowledge and the most recent advances. We prioritized and preferentially emphasized more recent evidence (particularly studies and reviews published between 2021 and 2025) when synthesizing results and drawing conclusions. Only studies published in English and available in full text were considered.

Titles and abstracts were screened for relevance, and duplicates were removed. Eligible studies were assessed according to predefined inclusion and exclusion criteria. Inclusion criteria comprised original clinical studies (cohort studies, case series, and case reports) and systematic or narrative reviews, theses, dissertations, and book chapters that specifically addressed anatomy, pathophysiology, clinical presentation, diagnostic methods, or therapeutic approaches to ZD. Exclusion criteria included studies without clinical relevance, studies with unclear methodology or unverifiable data, case reports not highlighting novel or unusual presentations, and non-English publications.

After full-text assessment, 79 publications met the eligibility criteria and were included in the final reference list of this review. Among these, systematic reviews and meta-analyses were prioritized for evidence synthesis, while case reports were retained when they highlighted unusual presentations, rare complications, or novel diagnostic and therapeutic insights. This approach ensured a balanced overview of high-level evidence alongside clinically relevant observations.

The review process followed the methodological rigor typically applied in narrative reviews, aiming to provide an updated and comprehensive overview of current knowledge while acknowledging the limitations inherent to non-systematic designs.

### 3. Historical Background

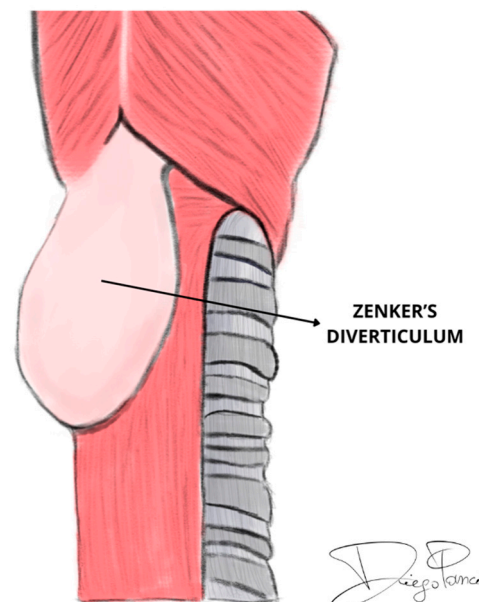
Zenker's diverticulum was first documented in 1769 by Dr. Abraham Ludlow, in a letter addressed to a colleague, reporting his observations following an autopsy. He describes an abnormal sac-like pouch arising from the posterior pharyngeal wall in a patient who, to relieve a presumed stenosis or fibrous tumor, had ingested a glass of mercury as an extreme measure.

In 1877, Zenker provided a detailed description of the condition based on 34 cases, proposing a pulsion mechanism as the underlying pathogenesis. Subsequently, Killian identified the precise anatomical site of origin of the diverticulum [1].

### 4. Anatomy

Zenker's diverticulum is a rare condition, yet it is the most common type of esophageal diverticulum [13,16].

It is a false, pulsional-type diverticulum that arises from the posterior wall of the hypopharynx. It is described as "false" because it involves only the mucosal and submucosal layers [2,3], herniating through a locus minoris resistentiae known as Killian's triangle (KT) [17] (Figure 1).

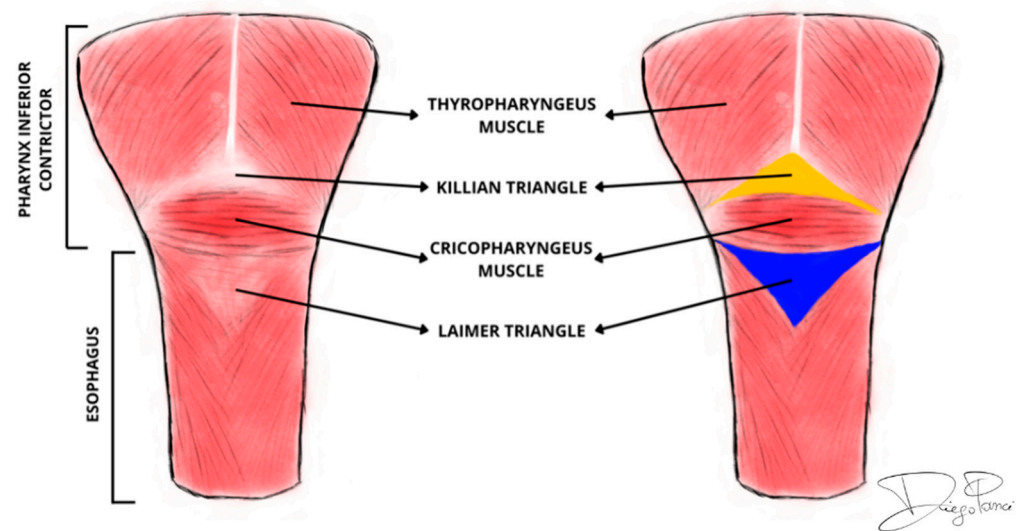


**Figure 1.** Schematic representation of the typical appearance of Zenker's diverticulum. The diverticulum presents as a posterior outpouching of the mucosal and submucosal layers of the hypopharynx's wall, protruding through Killian's triangle, between the thyropharyngeal and cricopharyngeal parts of the inferior constrictor muscle of the pharynx. It typically extends posteriorly and inferiorly, lying between the cervical esophagus and the prevertebral fascia. Illustration by Diego Panci.

This region of anatomical weakness is located between the two portions of the inferior constrictor muscle of the pharynx [17], which differ in origin, insertion, and fiber orientation. The thyropharyngeal portion, with obliquely oriented fibers, originates from the oblique lamina of the thyroid cartilage and inserts onto the median pharyngeal raphe. The cricopharyngeal portion arises from the cricoid cartilage and presents thicker, horizontally oriented fibers [18,19] (Figure 2).

At rest, the esophageal inlet is closed thanks to the synergistic action of the cricopharyngeus muscle (CP) and the proximal circular fibers of the esophageal musculature. These structures functionally constitute the upper esophageal sphincter (UES), which relaxes temporarily during swallowing to let the bolus pass [4]. The CP is composed of striated muscle and approximately 40% elastic connective tissue, which contributes to its baseline

tone, independent of neural input. It is innervated primarily by the pharyngeal plexus (via branches of the vagus and glossopharyngeal nerves), with additional sympathetic contributions from the cranial cervical ganglion [20].



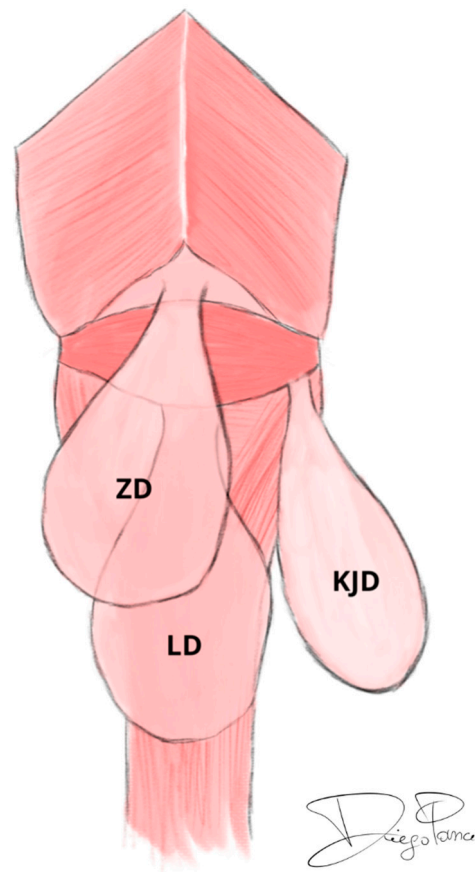
**Figure 2.** Schematic highlighting Killian's triangle (KT) and Laimer's triangle (LT). KT is a triangular area between the oblique fibers of the thyropharyngeus muscle and the transverse fibers of the cricopharyngeus muscle (CP) and is the site for Zenker's diverticulum formation. LT is located inferior to the CP, with the CP forming its superior boundary and the diverging longitudinal muscle fibers of the proximal cervical esophagus defining its lateral borders. Therefore, in this region, the muscular layer is composed exclusively of circular muscle fibers, with an absence of longitudinal ones. This lack of longitudinal fibers results in a localized area of anatomical weakness, predisposing the site to the formation of Laimer's diverticulum. Illustration by Diego Panci.

The absence of an anchoring raphe allows the CP to descend, moving away from the upper constrictor muscles, while the esophagus shortens longitudinally. This increases the KT size, creating a predisposition for diverticulum formation [21]. In most cases, ZD extends towards the left side, probably due to the natural curvature of the cervical esophagus or to an asymmetrical thickness of the left and right walls of the KT [1]. Less frequently, ZD is located laterally or posterolaterally along the esophageal wall. Rarely, double diverticula have also been reported in this region [8].

Zenker's diverticulum, Killian–Jamieson's diverticulum (KJD), and Laimer's diverticulum (LD) are the three principal variants of pharyngoesophageal diverticula, arising in areas of anatomical weakness [22].

Killian–Jamieson's diverticulum develops in the Killian–Jamieson's area, a triangular space located laterally and inferior to KT, immediately beneath the CP and lateral to the cervical esophagus [23].

Similarly, LD originates between the CP and the longitudinal fibers of the proximal esophagus. The main difference from KJD is that LD is located posteriorly and along the midline, and it is covered only by the circular fibers of the esophagus, lying beneath the CP [24] (Figure 3).



**Figure 3.** Schematic showing the three main pharyngoesophageal diverticula: Zenker’s diverticulum (ZD), Killian–Jamieson’s diverticulum (KJD), and Laimer’s diverticulum (LD). ZD arises from Killian’s triangle, a midline area between the thyropharyngeus and cricopharyngeus muscles (CP). KJD develops in the eponymous area, lateral and inferior to Killian’s triangle, beneath the CP and lateral to the cervical esophagus. LD forms posteriorly along the midline, between the CP and the longitudinal esophageal fibers, covered only by circular muscle fibers beneath the CP. Illustration by Diego Panci.

### 5. Classification and Staging

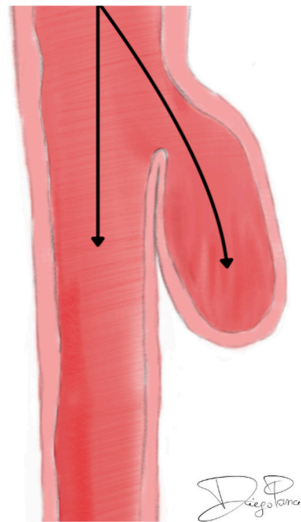
Zenker’s diverticulum can reach a length of up to 15 cm, although such dimensions are extremely rare; in fact, in most cases, its length does not exceed 4 cm [8].

The most common shape presents the fundus located inferiorly and the entrance superiorly, with a high risk of ingesta retention, as food follows an alternative pathway [8] (Figure 4).

The Morton, Van Overbeek, and Lahey staging systems are commonly used to classify ZD based on diverticular size and severity, which are assessed radiographically using barium swallow esophagography with videofluoroscopy [25] (Table 1).

**Table 1.** ZD Classification and Staging.

Classification	Small	Intermediate	Large
MORTON-BARTNEY	<2 cm	2–4 cm	>4 cm
VAN OVERBEEK-GROOTE	Shorter than 1 cervical vertebra	—	Longer than 3 cervical vertebrae
LAHEY	Stage 1: Minimal mucosal protrusion	Stage 2: Clearly defined sac, pharynx, and esophagus still in line	Stage 3: Large, advanced diverticulum: diverticular sac large enough to push the esophagus anteriorly



**Figure 4.** Schematic of a sagittal section of the proximal esophagus illustrating the lumen of Zenker's diverticulum (ZD) and its orifice. The image demonstrates the normal passage of the bolus through the esophageal lumen alongside the abnormal entry of food material into the diverticular sac, which is then temporarily retained within the pouch, contributing to the most common signs and symptoms of ZD. Illustration by Diego Panci.

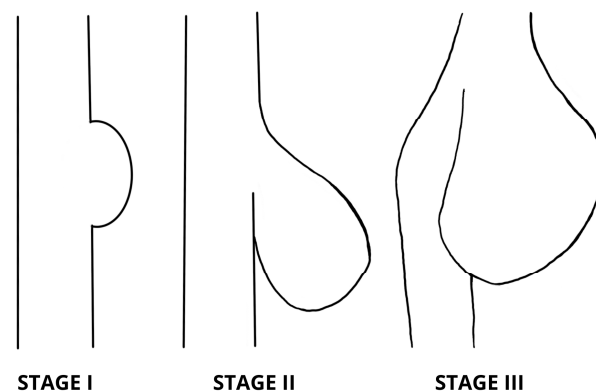
Staging helps determine the most appropriate therapeutic approach and the patient's prognosis [25].

The Morton–Bartley classification divides diverticula into three categories: small (less than 2 cm), medium (between 2 cm and 4 cm), and large (greater than 4 cm) [26].

The Van Overbeek and Groote classification is based on a comparison between the length of the diverticulum and the cervical vertebrae visible on radiographs. According to this classification, small diverticula are shorter than one vertebra, while large ones are longer than three vertebrae [27].

The Lahey classification is one of the most widely used and divides ZD into the following stages:

- Stage I: A small mucosal protrusion, limited in size, is observed.
- Stage II: A defined sac is visible, but the esophagus and hypopharynx are still aligned without obvious distortions.
- Stage III: The diverticulum is clearly visible and the hypopharynx aligns with it, while the esophagus is pushed forward, showing an indented deformation [25] (Figure 5).



**Figure 5.** Stylized illustration of Lahey's classification stages of the diverticulum. Stage I shows a small mucosal protrusion with limited size. Stage II presents a defined sac, while the esophagus and hypopharynx remain aligned without distortion. Stage III depicts a prominent diverticulum causing anterior displacement and deformation of the esophagus relative to the hypopharynx. Illustration by Diego Panci.

## 6. Pathogenesis

At the level of KT, whose size can vary from person to person, the bolus must pass from the relatively wide hypopharynx to the narrower esophageal inlet. It is thought that the formation of the diverticulum is attributable to inadequate relaxation of the UES and, therefore, to CP dysfunction (CPD): the bolus, thus, encounters abnormal resistance, leading to an increase in hypopharyngeal pressure, which can cause, over time, the herniation of the mucosa and submucosa at the KT. This phenomenon is often associated with esophageal motility disorders, the most common of which is achalasia [4,7].

This relation has been confirmed using High-Resolution Manometry (HRM). This technique became available at the beginning of this century, overcoming the limits of traditional manometry. High-Resolution Manometry can compensate for UES movements during swallowing, is quick enough to record striate fiber contractions, and can capture the asymmetrical distribution of pressures. In patients with ZD, HRM highlights how the pharynx maintains normal contractile capacity and adequate pressure gradients, while recording increased residual pressures at the UES, indicative of incomplete opening of it due to a CPD. Some patients show elevated pharyngeal pressures as a possible compensatory mechanism. These data explain the effectiveness of cricopharyngeal myotomy in improving dysphagia [28,29].

Since ZD mainly affects the elderly, age-related tissue degeneration is believed to contribute to its onset: [30] with aging, the CP can become hypertonic, obstructing the normal passage of the bolus [11]. Cricopharyngeus muscle hypertrophy is due to a combination of fibrosis of the connective component and loss of elasticity of muscle fibers [31].

Cricopharyngeus Muscle Dysfunction can also be a consequence of various neurological and systemic conditions, including cerebrovascular disease, Parkinson's disease, and amyotrophic lateral sclerosis. In addition, supratentorial lesions secondary to ischemic stroke can cause its onset [32].

Gastroesophageal reflux, which induces cramps in the CP, may contribute to its pathogenesis [8]. It is also hypothesized that acid damage to the esophageal mucosa leads to longitudinal shortening of the esophagus, which weakens the KT area, promoting herniation of the mucosa and submucosa, thus leading to the formation of ZD [21].

A congenital muscular weakness of the UES and individual anatomical variants of the KT area can predispose to ZD development. Patients with a long neck can present a wider KT and, therefore, a higher risk of ZD onset [4,8].

Once the pouch is excised, it usually shows a multilayered squamous epithelial lining, and the submucosa often presents fibrous tissue surrounding it.

Exceptionally rare histologic variants have also been reported: a case of an ulcerated pocket with submucosal infiltration by plasma cells, lymphocytes, and eosinophils has been described [27].

## 7. Clinical Features

### 7.1. Symptoms Overview

Most frequent symptoms include dysphagia, undigested food regurgitation, halitosis due to the fermentation of food material stagnating in the diverticulum, sensation of a foreign body in the throat, chronic cough, and involuntary weight loss. [4,5,33]. Symptoms tend to intensify, and large diverticula can lead to malnutrition [27].

Bleeding represents a rare complication of ZD; these patients usually present with hematemesis or hemoptysis, often complicating the diagnosis. Most of these patients are treated with open surgery, but in some reported cases, an endoscopic management of the bleeding has been successfully achieved [34].

The possibility of squamous cell carcinoma arising within a ZD should be considered in case of sudden symptoms intensification, particularly progressive dysphagia, pain, hemoptysis, or marked regurgitation of food; a rare but reported phenomenon in the literature [35].

### 7.2. Dysphagia

Dysphagia is broadly defined as “difficulty in swallowing” according to the ICD-10 (International Statistical Classification of Diseases and Related Health Problems 10th Revision). Oropharyngeal dysphagia specifically involves dysfunction of the oral and pharyngeal phases and is commonly evaluated through safety and efficacy impairments [36]. The European Society for Swallowing Disorders defines dysphagia as a dysfunction of one or more components of the swallowing apparatus—from the oral cavity to the esophagus and its sphincters—typically caused by anatomical or structural abnormalities [37].

In ZD, dysphagia results from both the persistent CPD and from the presence of the diverticulum itself, which retains ingested food and liquids and compresses the cervical esophagus. Both mechanisms disrupt bolus transit and compromise esophageal emptying, contributing collectively to the swallowing impairment [38–40].

In ZD’s early stages, dysphagia may occur only when swallowing solid foods, but, as the diverticulum increases in size, difficulty swallowing may extend to foods of any consistency, including liquids [1].

Signs, including aspiration, regurgitation, and weight loss, are common across all disorders that cause dysphagia. Common symptoms include coughing, choking, voice change, globus, prolonged meals, fatigue, dietary restriction, and reduced eating pleasure [36].

### 7.3. Consequences of Retention of Ingested Material in Zenker’s Diverticulum

Most of the other recurrent symptoms present because the diverticular pouch retains ingested material and intermittently communicates with the pharyngo-esophageal lumen during swallowing, promoting stasis, fermentation, and micro-aspiration of ingested material with several clinical consequences. Fermentation of stagnant food and liquids often leads to halitosis and an unpleasant taste [7,11,25,41]. The accumulated contents may be regurgitated spontaneously or during swallowing, posing both social and nutritional challenges; regurgitation can be assessed on endoscopic examination [2,39,41].

In some cases, aspirated material can enter the airway, resulting in aspiration events and placing patients at risk for aspiration pneumonia (pulmonary infection due to ab ingestis). It develops when upper gastrointestinal secretions reach the lungs in amounts sufficient to overwhelm protective mechanisms. Even small volumes can trigger pneumonia if the bacterial load is high [11,42].

Foreign bodies, such as oral tablet formulations, can be trapped in the diverticulum, compromising the effectiveness of therapy and increasing the risk of ulceration and bleeding [43].

### 7.4. Key Clinical Signs

Signs and symptoms of ZD may be present for weeks or even years before a diagnosis is made. In advanced cases, as the pouch enlarges, patients may develop systemic manifestations such as weight loss, malnutrition, and, in some instances, emaciation [11,40,44].

More specific findings include cervical borborygmi, described as a rumbling sound over the anterior neck that is almost pathognomonic of ZD, especially when associated with a palpable swelling in the cervical region. On palpation of such a swelling, compression may elicit a characteristic gurgling sound known as Boyce’s sign, which corresponds to the splash-like noise generated by fluid and air shifting within the diverticular

pouch. Boyce's sign is relatively specific and—when observed together with compatible symptoms—strongly points to ZD [22,45].

### 7.5. Symptoms Assessment Tools

Currently, there is no universally accepted scoring system for assessing the symptoms of ZD. However, several tools have been used: the Dakkak and Bennett score mainly considers dysphagia; the Eckardt score, designed for achalasia, considers dysphagia, regurgitation, chest pain, and weight loss; the broader Kothari–Haber score also considers coughing and hoarseness. Of these, only the Kothari–Haber score is validated for ZD [3,46].

Several subjective assessment tools have been described in the literature to analyze the symptoms associated with ZD. The Eating Assessment Tool (EAT-10) has been used to quantify dysphagia in patients with ZD, providing a simple and validated measure of reported symptoms. It is a self-assessment questionnaire consisting of 10 questions. Each question is rated on a scale from 0 (no problem) to 4 (severe problem), for a maximum total score of 40. A score  $\geq 3$  is considered abnormal. The tool has shown excellent internal consistency and high test-retest reliability [47].

The SWAL-QOL questionnaire, developed to assess swallowing-related quality of life, was used to measure perceived benefits after endoscopic treatment of the diverticulum. In addition, the MD Anderson Dysphagia Inventory (MDADI) was used to assess the impact of dysphagia on daily life, supporting a patient-centered approach to managing the disorder [47–49].

## 8. Epidemiology

Zenker's diverticulum is a rare condition; however, it accounts for between 70% and 75% of all esophageal diverticula [11]. Most patients are diagnosed after the age of 60, often over 75, with a male predominance of approximately 1.5:1 [50]. However, cases in children have also been documented [51].

The estimated prevalence is between 0.01% and 0.11% of the general population (approximately 10–110 cases per 100,000 inhabitants) [25].

The geographical distribution shows a higher frequency in northern European countries, the United States, and Canada, while the condition is rare in Asian countries such as Japan and Indonesia [25].

These geographical differences in the incidence of the condition could be explained by individual anatomical variations that affect the size of the KT: individuals with longer necks can have a larger KT than those with shorter necks [4]. However, the global prevalence may be underestimated, as many asymptomatic diverticula are not diagnosed [3].

## 9. Diagnosis

### 9.1. Diagnostic Evaluation

The diagnosis of ZD requires a combination of clinical evaluation, radiological imaging, and endoscopic evaluation [2].

Barium esophagography is considered the gold standard for diagnosing ZD. This imaging technique offers clear visualization of the diverticulum, typically highlighted as a posterior protrusion at the CP. Continuous dynamic fluoroscopy allows for assessment of the size and functionality of the UES, facilitating the identification of small diverticula and the recognition of any aspiration risks [2,40].

The examination is performed in lateral and anteroposterior projection while the patient is seated after the administration of several boluses of liquid and dense barium, to investigate the presence and the features of the ZD: its position and measures, diverticulum neck width, and swallowing functionality. Additionally, it is important to assess

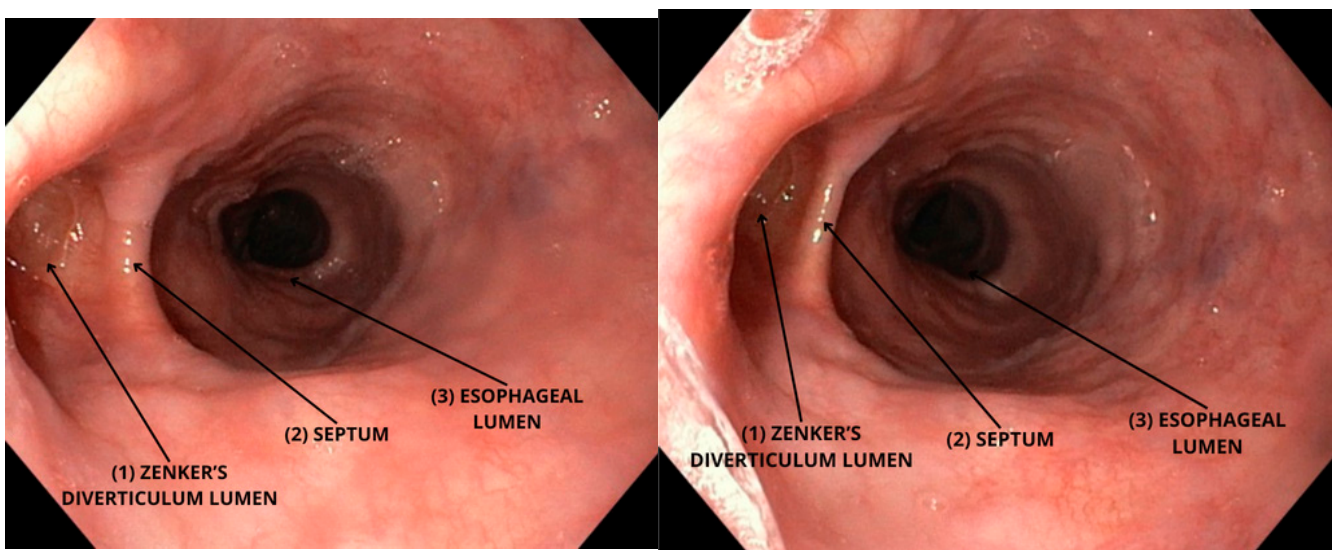
contrast agent accumulation, regurgitation, aspiration events, and its mass effect on the adjacent esophagus.

To analyze ZD, a framerate of 3–4 frames per second is recommended as a pragmatic balance between adequate temporal resolution and minimizing radiation exposure. In selected cases, higher frame rates (e.g., 30 fps) may be required for detailed functional evaluation. Furthermore, it is advisable to extend the examination to the lower esophagus, the stomach, and the duodenum to exclude other comorbidities like hiatal hernia or reflux esophagitis [1,9,52].

Contrast Computed Tomography (CT) scan of the neck/chest is described in recent literature as a complementary imaging modality rather than a first-line diagnostic test: CT can delineate diverticular size, its relationship to adjacent neck and mediastinal structures, detect complications (e.g., inflammation, perforation or abscess), and can be especially valuable in complex or atypical presentations or preoperative planning; however, dynamic contrast swallow (barium esophagography) remains the principal diagnostic study to demonstrate the pouch itself, with CT used when additional anatomic detail or complication exclusion is required [22,53].

In ultrasound diagnostics, ZD can be mistaken for a thyroid nodule or other lesion, with the risk of unnecessary biopsies [54]. Swallow contrast-enhanced ultrasound (Swallow-CEUS) is an alternative ultrasound technique that involves the extravascular administration of ultrasound contrast agents. It has the advantages of no radiation and bedside applicability; therefore, it has the potential to become a preferred diagnostic tool for confirming ZD, particularly in cases where conventional ultrasound raises suspicion [10].

Esophagogastroduodenoscopy is useful for assessing the conditions of the diverticulum and planning any surgical procedures [8] (Figure 6).



**Figure 6. Endoscopic Visualization of the Zenker's diverticulum Access.** These endoscopic images distinctly delineate the anatomical relationship crucial for transoral diverticulectomy. The central, darker lumen represents the true esophageal orifice (3), while immediately adjacent, typically along the posterior or left posterior wall, the wide ostium of the Zenker's diverticulum (1) is clearly visible. The mucosal fold or septum (2) separating the two lumina is readily apparent, representing the cricopharyngeal bar or common wall that serves as the primary target for endoscopic intervention. The clear visualization of both the esophageal lumen and the diverticular pouch inlet is essential for accurate orientation and safe execution of the procedure. Images courtesy of Professor Giovanni Tomasello, MD, from his personal archive.

During the examination, it is crucial to be particularly cautious when inserting the endoscope; if it advances too quickly, a small ZD can easily go unidentified. Furthermore, esophageal intubation performed without adequate direct visualization of the esophageal tract can result in accidental insertion of the instrument into the diverticulum, with a consequent risk of perforation [55].

This procedure is also useful for ruling out the presence of malignant tumors or other underlying causes of the patient's symptoms. In cases of suspected neoplasia, a CT scan may also be indicated [1].

## 9.2. Differential Diagnosis

The differential diagnosis of ZD includes several structural, neoplastic, reflux-related, motility, and neurogenic conditions with overlapping clinical manifestations [7,56].

### 9.2.1. Other Esophageal Diverticula

The differences between Zenker's, Killian–Jamieson's, and Laimer's diverticula have already been discussed in the 'Anatomy' section.

Mid-esophageal and epiphrenic diverticula are etiologically and topographically distinct from ZD, typically located in the middle or distal esophagus and often associated with motility disorders or mediastinal inflammation; their identification relies on barium swallow or CT mapping, and manometry is recommended when distal pathology is suspected [7].

### 9.2.2. Achalasia

Achalasia is a primary esophageal motility disorder characterized by impaired relaxation of the lower esophageal sphincter (LES) and absent or abnormal peristalsis of the esophageal body, which can mimic symptoms of ZD, especially dysphagia and regurgitation; however, certain clinical, endoscopic, radiologic, and manometric features allow their differentiation [57]. Radiologic contrast studies in achalasia typically show a "bird's beak" narrowing at the esophagogastric junction and esophageal dilatation, while barium swallow for ZD shows a pouch above the UES. HRM confirms achalasia by showing incomplete LES relaxation, plus aperistalsis; such motility features are absent in ZD [28,40,58,59].

### 9.2.3. Gastroesophageal Reflux Disease and Laryngopharyngeal Reflux

Gastroesophageal reflux disease and laryngopharyngeal reflux can mimic or contribute to pharyngeal symptoms, complicating the diagnostic distinction from ZD. Reflux-related complaints, such as globus, chronic throat clearing, cough, and hoarseness, are non-specific and overlap with other pharyngoesophageal disorders [7,60].

Endoscopy can demonstrate objective reflux findings when erosive esophagitis or Barrett's mucosa are present, but a normal examination does not exclude reflux as the primary cause of symptoms [61,62].

For patients with persistent or predominantly extra-esophageal symptoms, ambulatory impedance-pH monitoring is recommended, as it can quantify both acid and non-acid events and define their proximal extent [63].

Hypopharyngeal multichannel intraluminal impedance-pH has been validated as a diagnostic method to confirm pharyngeal acid reflux episodes, demonstrating good accuracy and reproducibility in distinguishing true reflux events from artifacts or swallows [64].

### 9.2.4. Benign Peptic or Radiation Strictures

Benign peptic or radiation strictures and Schatzki rings are differentiated from ZD by the pattern of obstruction: strictures produce a concentric or short-segment luminal

narrowing on endoscopy and barium study without a posterior outpouching and are commonly associated with reflux-related mucosal injury or prior radiation history [65].

#### 9.2.5. Extrinsic Neck Lesions

Extrinsic neck lesions, such as thyroid nodules or pharyngoesophageal collections, can mimic a diverticular pouch; in such cases, high-resolution cervical ultrasound, contrast-enhanced swallow-ultrasound, or CT demonstrates a lesion distinct from the esophageal lumen, differentiating it from a pharyngoesophageal diverticulum that fills with oral contrast [66,67].

#### 9.2.6. Neurogenic Dysphagia

Neurogenic dysphagia due to conditions such as stroke, Parkinson's disease, or motor neuron disease presents as impaired oropharyngeal swallow function; clinical bedside screening, flexible endoscopic swallowing study, or videofluoroscopic swallow study, together with neurological assessment, reveals aspiration, pharyngeal residue, and ineffective bolus propulsion, distinguishing these disorders from ZD [7,68].

#### 9.2.7. Malignant Transformation

Malignancy arising within a ZD is rare but clinically significant. Advanced age, male sex, chronicity of the condition, and increased diverticulum size are considered potential risk factors for malignant transformation. Clinical features that may suggest the presence of malignancy include worsening dysphagia, unexplained weight loss, blood-stained regurgitated contents, regurgitation of tumor fragments, painful swallowing, melena, hematemesis, and hemoptysis. Early-stage cancers, such as carcinoma in situ or small lesions, may escape detection through standard imaging or endoscopic evaluation. In such cases, removal of the pouch and complete histopathologic examination of the resected specimen is often the only way to definitively diagnose malignancy [69,70].

## 10. Treatment

The choice of the correct treatment for the ZD is mainly based on the patient's symptoms and the diverticulum's dimensions. Conservative treatment is recommended for asymptomatic diverticula, smaller than 1 cm; however, careful follow-up is essential to monitor for symptom development or complications. Symptomatic patients, with or without associated complications, need surgical treatment to relieve symptoms and improve the quality of life [71].

All surgical procedures necessarily require a cricopharyngeal myotomy [72].

Open surgical approaches have historically been the standard in ZD treatment and are associated with high technical success (reported range 80–100%); however, recurrence has been described in up to 19% of cases, and these procedures are burdened by higher morbidity and mortality compared to endoscopic techniques [14]. The procedure involves exposing the diverticulum through a neck incision, followed by the CP myotomy to relieve the obstruction to bolus transit. The diverticulum can then be excised (diverticulectomy), suspended by fixation to the prevertebral fascia with non-absorbable sutures (diverticulopexy), or inverted into the esophageal lumen and subsequently sutured. Rare and major complications include pharyngocutaneous fistulas, parapharyngeal abscesses, mediastinitis, and vocal cord paralysis [2,72]. Minor complications, such as transient paralysis of the recurrent laryngeal nerve, post-operative fever, and subcutaneous emphysema, are more common and affect up to 10–15% of patients [2].

Over the past two decades, rigid endoscopic septotomy (RES) with a suturing device has gained a prominent role in ZD treatment, thanks to its less invasive nature compared to open surgery. However, RES shows significant limitations: difficult access in elderly

patients with cervical deformity or reduced neck mobility, lower technical precision, risk of incomplete septotomy in case of thicker septa, and significant complications with the need to resort to open techniques. To overcome these issues, a variety of alternative endoscopic techniques have become widespread in recent years, including flexible endoscopy, laser-assisted septotomy, and other non-stapler approaches, which are considered valid options in appropriately selected patients [31].

Flexible endoscopy septotomy (FES) allows for a complete sectioning of the septum regardless of its thickness, does not require cervical hyperextension, and is more suitable for elderly patients or those with anatomical limitations. Recurrence and complication rates are comparable to those of RES, but with a better accessibility and reliability profile [14,73].

Endoscopic submucosal tunneling techniques (ESTT), such as peroral endoscopic myotomy for ZD (Z-POEM), which are increasingly widely used, appear to be safe and comparable to FES in terms of clinical success in mid-term follow-up, when performed by an expert endoscopist. Using a flexible endoscope, an incision is made in the mucosa above the diverticular septum, and a small submucosal tunnel is created. Within this tunnel, the muscular septum is dissected in a controlled and complete manner. At the end, the mucosal incision is closed with endoscopic clips [12,74]. Anyway, the Z-POEM technique is very complex and requires specific equipment and advanced endoscopic skills, restricting its applicability to specialized centers [2].

Endoscopic management of ZD recurrences, after surgery or stapling, is particularly challenging. The main addressed risks are perforation and persistent dysphagia; in fact, the staple-on-staple effect can cause dangerous and unpredictable scarring [48,75]. In a study conducted by Antonello et al. [75] on 25 patients who had post-surgical recurrences, 84% showed remission of symptoms, suggesting that flexible endoscopy is a viable alternative to surgery even in postoperative recurrences [75].

## 11. Prognosis

The prognosis of patients affected by ZD varies depending on the chosen treatment [15]. Esophageal comorbidities may lead to poor symptomatic improvement; therefore, preoperative workup of other esophageal disorders is recommended [76].

In a prospective study, conducted by Howell et al. [15], 147 patients with ZD were included (mean age was 68.7 years). Of these, 109 underwent endoscopic treatment and 38 underwent open surgery. After treatment, 88% of patients reported an improvement of >50% in their EAT-10 score, 81% reported an improvement of >75%, and 66% a complete improvement. The median improvement of the EAT-10 score (interquartile range, IQR) was of 93.3% (IQR 72, 100) for endoscopy and 100% (IQR 92.3, 100) for open surgery ( $p = 0.05$ ). The endoscopic approach demonstrated a slightly more favorable safety and efficacy profile (intraoperative complications in 3.7% vs. 7.9%). The median follow-up (IQR) was 86 days for the endoscopy and 97.5 days for open surgery [15].

In a study of 144 patients treated between 2014 and 2019 across three centers in southern France, Rudler et al. [77] compared the clinical efficacy of surgery (97%), RES (79%), and FES (90%), as well as the clinical outcomes. In addition, RES presented a significantly lower rate of technical success. Both endoscopic methods guarantee quicker procedures and reduce recovery time compared to open surgery, but FES offers a better balance between safety and efficacy, resulting in being the preferred choice, especially in fragile patients [77].

A British multicentric study, conducted by Norton et al. [14], involving 126 patients, compared outcomes of FES and RES with those of the endoscopic submucosal tunneling technique (ESTT) Z-POEM: FES and Z-POEM achieved 100% technical success, while RES achieved 80%. After a mean follow-up of 11 months, clinical success was similar

among the groups: 85.3% for RES, 74.1% for FES, and 83.7% for Z-POEM, with lower recurrence rates for Z-POEM (8.3%) compared to RES and FES. Intraoperative complications were comparable across all groups. RES failures often required open surgery, with worse outcomes. Therefore, flexible endoscopic techniques, including Z-POEM, are safe and effective for the treatment of ZD and should be the first-line treatment in specialized centers, reserving open surgery for more complex cases [14].

A recent systematic review and meta-analysis of nine studies, reported by Delgado et al. [16], confirmed the effectiveness of endoscopic techniques in the treatment of ZD by comparing ESTTs, such as Z-POEM, with FES. Out of a total of 759 patients, ESTT showed a higher probability of clinical success and a tendency toward lower recurrence, while maintaining results comparable to FES in terms of technical success, duration of surgery, hospital stay, and complications. These results suggest that ESTT is an effective and safe strategy, confirming its growing role in the minimally invasive treatment of ZD [16].

The other seven studies, carried out by Papaefthymiou et al. [13], involving 747 patients, comparing the technical success of Z-POEM with alternative techniques, resulted in high values for both (97.4% for Z-POEM vs. 95.8% for alternative techniques), with a higher clinical success for Z-POEM (odds ratio: 2.14; 95% confidence interval: 1.42–3.2); similar reintervention and complications rates but with fewer perforation cases. The subgroup analysis confirmed better clinical results than both flexible and rigid diverticulectomy. Nevertheless, the low quality of evidence requires further studies to confirm these results and guide therapeutic choices for ZD treatment. [13]

Table 2 provides a descriptive overview of the main treatment options for ZD. The reported characteristics are derived from heterogeneous studies cited in the text and are intended to aid interpretation rather than to serve as a direct comparative analysis (Table 2).

**Table 2.** Overview of treatment options for Zenker’s diverticulum.

Technique	Typical Indications	Technical Success	Main Considerations on Clinical Outcomes	Major Advantages	Limitations/Risks
Open Surgery	Symptomatic ZD, complex cases, failed endoscopy	Reported as high	Effective symptom relief; recurrence in up to 19%	Definitive treatment, allows diverticulectomy/diverticulopexy or inversion	Invasive; higher morbidity and mortality; postoperative complications
RES <sup>1</sup>	Selected patients with suitable anatomy	Variable across studies	Generally associated with shorter recovery than open surgery; technical failures may require conversion to open surgery	Less invasive than open surgery	Limited in elderly or patients with reduced neck mobility; incomplete septotomy in thick septa
FES <sup>2</sup>	Elderly patients, patients with anatomical limitations, postoperative recurrences	Reported as consistently high	Effective symptom relief; good accessibility; suitable for fragile patients	No cervical hyperextension; complete septum sectioning; good reliability	Requires endoscopic expertise; risk of perforation and recurrence
Z-POEM <sup>3</sup> /ESTT <sup>4</sup>	Complex septa, recurrences, specialized centers	Reported as consistently high	Controlled and complete myotomy; low recurrence; safe in expert hands	Minimally invasive	Technically demanding, requires advanced endoscopic skills and specialized equipment, limited availability

<sup>1</sup> RES: Rigid Endoscopic Septotomy; <sup>2</sup> FES: Flexible Endoscopic Septotomy; <sup>3</sup> Z-POEM: Peroral Endoscopic Myotomy for Zenker’s diverticulum; <sup>4</sup> ESTT: Endoscopic Submucosal Tunneling Technique.

## 12. Discussion

### 12.1. Current Challenges

Zenker's diverticulum should be considered a dynamic disorder arising from pathophysiological mechanisms, rather than a fixed anatomical defect, and can severely affect quality of life.

A structural predisposition (KT) interacts with impaired UES compliance, aging, neurological disease, and reflux, creating a chronic imbalance that culminates in diverticulum formation [1,4,8].

This broader perspective shifts treatment away from a purely surgical act toward multimodal strategies aiming to restore effective swallowing, minimize perioperative risk, and manage recurrence-promoting factors such as neuromuscular dysfunction, reflux, or hiatal hernia [21,76].

### 12.2. Evidence Gaps

Endoscopic management has become central but remains debated. Flexible septotomy is safer and more accessible for elderly or fragile patients [77], while tunneling techniques (Z-POEM) achieve more complete myotomy with higher clinical success and lower recurrence [13,14,16,74]. Yet evidence is limited: most studies are retrospective, heterogeneous, and short-term, reflecting the recent adoption of Z-POEM. Durability and optimal patient selection remain uncertain [2,13,77,78]. Based on current evidence, FES appears to be the endoscopic workhorse due to its favorable safety-accessibility balance, while Z-POEM emerges as the most promising technique for achieving a complete myotomy and minimizing recurrences in expert centers.

### 12.3. Future Perspectives

Priorities for research and clinical practice include the following:

- **Diagnostics:** standardize functional assessment with HRM, high frame-rate videofluoroscopy, and swallow-CEUS to better characterize cricopharyngeal dynamics and aspiration risk [1,2,9,28,29].
- **Evidence quality:** conduct prospective, multicenter trials with  $\geq 2$ –5 years of follow-up using validated, ZD-specific symptom and QoL instruments [47,49] to define comparative effectiveness [13].
- **Patient profile:** systematically integrate frailty and comorbidity into treatment planning, acknowledging the elderly demographic and the risks of aspiration, malnutrition, and peri-procedural complications [15,40].
- **Technique refinement:** optimize endoscopic methods to enhance safety, reproducibility, and accessibility across different centers [2].

## 13. Conclusions

Zenker's diverticulum is a multifactorial condition with increasing clinical relevance in aging populations. Advances in functional and imaging diagnostics are reshaping how patients are selected and how outcomes are predicted.

Recent evidence confirms tunneling endoscopy techniques, particularly Z-POEM, as a safe and effective first-line procedure to be applied in specialized centers. However, current evidence is constrained by retrospective design, heterogeneous endpoints, and short follow-up.

Conducting long-term validation studies, implementing standardized diagnostic pathways, and focusing on translational research to explore recurrence risk are now essential to move to a systemic, patient-centered approach.

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## Abbreviations

The following abbreviations are used in this manuscript, listed in alphabetical order for clarity:

CP	Cricopharyngeus Muscle
CPD	Cricopharyngeus Muscle Dysfunction
CT	Computed Tomography
EAT-10	Eating Assessment Tool
ESTT	Endoscopic Submucosal Tunneling Technique
FES	Flexible Endoscopic Septotomy
HRM	High-Resolution Manometry
KJD	Killian–Jamieson’s Diverticulum
KT	Killian’s Triangle
LD	Laimer’s Diverticulum
LES	Lower Esophageal Sphincter
RES	Rigid Endoscopic Septotomy
Swallow-CEUS	Swallow contrast-enhanced ultrasound
UES	Upper esophageal sphincter
Z-POEM	Peroral Endoscopic Myotomy for Zenker’s diverticulum
ZD	Zenker’s diverticulum

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