

Zenker's diverticulum: endoscopic treatment with or without diverticulotome

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Abstract

Zenker's diverticulum is defined as a diverticulum located in the posterior esophageal wall, just above the cricopharyngeal muscle. Most patients experience symptoms in this area after the age of 60. In the past, the standard treatment was surgical diverticulotomy, but endoscopic treatment was introduced over 20 years ago. For more than 15 years, overtubes are introduced to facilitate the procedure, but their use is not been widely established in our country. Therefore, this study aims to evaluate whether endoscopic diverticulotomy with the use of this device is easier (faster) than the standard method. **Materials and methods:** A prospective study was conducted to establish which of the two endoscopic methods to treat Zenker's diverticulum (ZD) made the septum incision time shorter. The time count was done using video recording and started when the probe—standard method (SM)—or the overtube (MD) were placed, as this is the exact moment when septum cutting begins. The count stopped when the cut was finalized. **Results:** A total of 20 patients were treated from January 2015 to December 2018. Zenker's diverticulum diagnosis was achieved by endoscopy and esophagogram to classify the size of the tumor. The average age of the patients was 61 years (46-85). Ten patients were assigned to each group. Symptoms resolved in 7 patients of the SM group, compared to 9 in the MD group. The three patients who did not respond to the treatment were classified as stage II in the functional outcome swallowing scale at 18 months of follow-up. The average time of the procedure was 32 (25-45) minutes in the SM group and 12 (7-15) minutes in the MD group ($p < 0.001$). **Conclusions:** ZD myotomy with flexible endoscopy using an overtube has potential benefits in terms of shorter operative times, shorter post-operative stays, and an earlier reintroduction of food. From a technical point of view, this method allows for better exposure of the septum, which facilitates cutting. However, more extensive studies are needed to confirm these results.

Keywords

Dysphagia, Zenker, endoscopic diverticulotomy, diverticulotome, complications.

INTRODUCTION

Zenker's diverticulum is a pulsion diverticulum that, due to its critical location, causes dysphagia. Since it prevents proper nutrition and triggers symptoms such as regurgitation, chronic cough, and weight loss, it has a direct negative

impact on the patients' quality of life. This condition is also associated with other complications, the most severe being recurrent aspiration, which results in recurrent pneumonias and, consequently, a high rate of morbidity and mortality (1). The anatomical region where it is located is called *the Killian triangle*, which is in the posterior wall of the

hypopharynx, between the inferior pharyngeal constrictor muscle and the transverse fibers of the cricopharyngeal muscle (**Figure 1**) (2). Zenker's diverticulum was named after the German pathologist Friedrich Albert von Zenker, who, together with von Ziemssen, reported 23 cases at the University of Erlangen in 1878 and defined it as "a hernia of the posterior hypopharyngeal membrane proximal to the upper sphincter of the esophagus". However, it should be noted that it was first described in 1769 by Dr. Abraham Ludlow, and not by Dr. Zenker (3, 4).

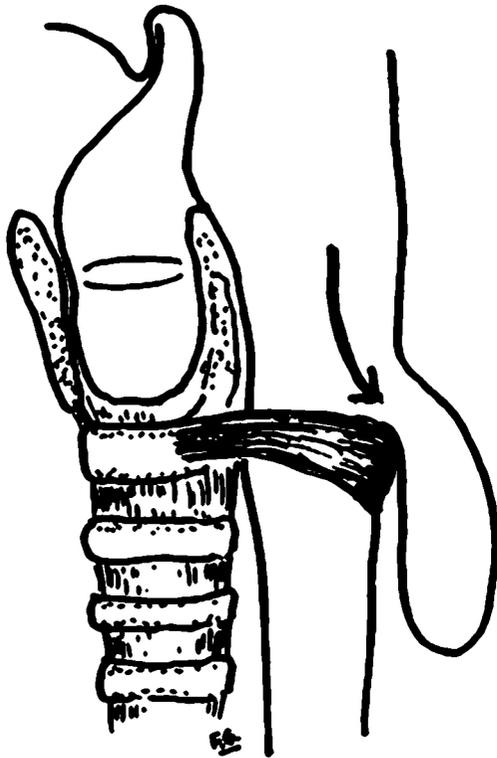


Figure 1. Anatomical representation of Zenker's diverticulum. Adapted from (4)

From a pathophysiological perspective, it is a pulsion diverticulum caused by an increase of intraluminal pressure, resulting in mucosal and submucosal prolapse (hence the term pseudodiverticulum) in Killian's triangle, where a normally low wall tone is associated with relatively low pressures in the adjacent retropharyngeal space, leading to diverticulum formation in the posterior part (**Figure 1**). However, it is not yet clear what are the forces contributing to the increase in luminal pressures, so manometric measurement is considered a challenge due to the asymmetry of the sphincter pressure and its wide range of motion (5, 6). Zenker's diverticulum is a rare disorder (with incidence rates ranging from 0.01% to 0.11% in the general popula-

tion), but its true incidence rate is difficult to determine due to variations in the severity of symptoms, although it is more prevalent in men between the seventh and eighth decades of life (6, 7). Dysphagia is the cardinal symptom, and two causal mechanisms are known: incomplete opening of the upper esophageal sphincter and extrinsic compression of the cervical esophagus by the diverticulum itself. From a clinical standpoint, cervical borborygmi, particularly in the presence of a palpable mass in the neck, is almost pathognomonic of Zenker's diverticulum, although it is not a frequent finding (8). Warning signs such as local pain and hemoptysis or hematemesis may indicate ulceration or squamous cell carcinoma within Zenker's diverticulum, with an incidence rate between 0.4% and 1.5% (6, 9).

Videofluoroscopic swallowing study is useful for its diagnosis because it provides information on size and location of the diverticulum and sometimes mucosal lesions in the diverticular pouch can be identified (10, 11). In addition, it allows making a differential diagnosis of the less common and smaller Killian-Jamieson diverticulum, which occurs in the anterolateral wall of the proximal esophagus and below the cricopharyngeal muscle (12). Although useful, the diagnostic performance of modified barium swallow is conditioned by variations in quality of its execution and interpretation. Performing upper gastrointestinal endoscopy is necessary to rule out the presence of squamous cell carcinoma (13) and is essential to describe the anatomy of the diverticulum and, therefore, guide the therapeutic strategy.

Several classification systems based on size and morphology have been proposed, including the Brombart classification (**Table 1**) (14) and the Morton/Bartley classification (**Table 2**) (15).

Table 1. Brombart classification (size and morphology of diverticula) (14)

Stage	Definition
I	Longitudinal axis 2–3 mm, "thorn-like diverticulum"
II	Longitudinal axis of 7–8 mm, "club-like diverticulum"
III	Caudally oriented axis of >1 cm in length
IV	Compression of the esophagus

Taken from: Mantsopoulos K et al. EUR Arch Otorhinolaryngol. 2014;271(3):583-8.

Surgical treatment has been described since the 19th century, with an approach to hernia treatment. Cricopharyngeal myotomy was only recently (over the last decades) implemented and, more recently, endoscopic septotomy has been recognized as a fundamental technique in correcting Zenker's diverticulum, showing improvement in relation

to food retention (liquids and solids) and suppression of all or the vast majority of symptoms after being performed (15). However, both open and endoscopic transcervical approaches are associated with potential complications and risks that are less frequent with the endoscopic technique, which is why the latter is the first option for treatment, considering that these patients are usually malnourished, older, and almost always present with associated comorbidities, which significantly increases surgical risk (16-18).

Table 2. Morton/Bartley Classification (Size) (15)

Stage	Definition
I	< 2 cm
II	2-4 cm
III	> 4 cm

Taken from: Miller FR, Taylor C. Zenker's Diverticulum: Endoscopic Surgical Management Options. Clin Surg. 2017;2:1422.

MATERIALS AND METHODS

A prospective study comparing two endoscopic methods to treat Zenker's diverticulum was conducted to know which method allows shorter septum incision times, resulting in a shorter procedure (surgical and anesthetic time) and reduced risk of morbidity and mortality.

Secondary objectives of the study included the evaluation of symptom resolution according to the functional outcome swallowing scale (FOSS), which was assessed before and after the procedure, as well as the evaluation of the resolution of major complications such as bleeding (requiring transfusion support or endoscopic reintervention for control), perforation, and recurrence of symptoms with an average follow-up of 18 months.

Patients who underwent diverticulotomy were clinically tested for dysphagia to solids or liquids, cough, regurgitation, globus pharyngeus, aspiration, weight loss, and need for supplemental nutrition, among others. A pre- and post-procedure FOSS score was established using the methodology for calculating this score described by Salassa (**Table 3**)

Table 3. Functional outcome swallowing scale (19)

Stage	Criteria
0	- Normal and asymptomatic physiological function.
I	- Normal physiological function (defined by no or minimal dietary modification and no aspiration), but with episodic or daily symptoms of dysphagia, such as reflux symptoms, globus pharyngeus, odynophagia, repetitive swallowing, difficulty chewing, minor oral incompetence (drooling) and feeling that food sticks in the throat or esophagus.
II	- Compensated abnormal function manifested by major dietary changes or extended mealtime (longer than one third of the time considered to be the usual time for the patient). - No weight loss, absent or occasional cough, absent or occasional mild aspiration (defined as aspiration cleared with a cough and limited to the subglottis, determined by barium swallow or video fiberoptic evaluation). - Stage I symptoms may be present. Patients in this stage are stable in terms of nutrition and respiratory status, but swallowing behavior is modified.
III	- Decompensated abnormal function due to weight loss of 10% or less of body weight over 6 months due to dysphagia, frequent coughing, gagging, or aspiration during meals. - Aspiration may be mild (as defined by stage II) or moderate (defined as silent or limited to the trachea). - Patients in this stage are not stable in terms of nutrition or respiratory status. No lung complications have occurred, but the patient is at risk of developing them.
IV	- Severely decompensated abnormal function defined as by weight loss of more than 10% of body weight over 6 months due to dysphagia or severe aspiration (defined as occurring below the trachea or any bronchopulmonary complications). - Non-oral feeding (> 50% of nutrition). - Patients in this stage are almost completely unable to swallow and can do it safely only under strictly defined conditions that do not meet their nutritional needs.
V	- Non-oral feeding for all nutrition. - Patients in this stage present with complete swallowing failure. - They are different from stage IV patients in that they cannot swallow anything safely.

Taken from: Salassa J. Dig Dis. 1999;17(4):230-4.

(19, 20). Only FOSS stage II, III, IV, and V patients were considered, and a videofluoroscopic swallowing study was performed as a confirmatory diagnostic method using Brombart classification stages II, III, and IV (**Table 1**) (21). To ensure a periodic balance in the number of subjects allocated to either of the two endoscopic diverticulotomy procedures (with or without diverticulum overtube), patients were randomized in blocks, also known as permuted block randomization. The procedure was timed from the moment the probe was placed in position in the usual method or after the diverticulum overtube was placed in the method that used this accessory (overtube method), since this is the moment when the septum is cut, until the cut was completed (video recording). The details of how the procedure was performed in each group are described below.

Standard method

The procedure is performed under general anesthesia with the patient in a left lateral decubitus position. Adequate endoscopic exposure of the septum that separates the diverticulum from the esophageal lumen is a key element. It is usually accomplished by inserting a nasogastric tube (NGT), which is left in place during the procedure. The NGT protects the contralateral esophageal wall from thermal injury during septum transection. The endoscope is placed *with a short cap* and the septum of the diverticulum is cut with a pointed papillotome. After completing the cut, a hemoclip is placed at the vertex of the cut to prevent perforation of the mediastinum.

Method with diverticulum overtube

Dr. Deviere built a plastic diverticulum overtube (**Figure 2**) with two flaps: a long one that is placed in the esophagus and a short one that is placed in the diverticulum and exposes the septum, which is cut with the needle papillotome; the NGT and the cap are not needed, and the clip is placed at the end of the procedure (**Figure 3**). The diverticulum overtube may also be made in an endoscopy unit using a colonic or enteroscopy overtube (**Figure 4**); it should be noted that the flap left in the esophagus (the long flap) is 3 cm long and the one left in the diverticulum is 2 cm long.

RESULTS

A total of 20 patients treated from January 2015 to December 2018 were included. In all of them, the main symptom was dysphagia to solids and liquids. Zenker's diverticulum diagnosis was achieved by initial endoscopy, and an esophagogram was performed to classify the size of the tumor. Patients' average age was 61 years (46-85 years),



Figure 2. Diverticulum overtube designed by Dr. Deviere.



Figure 3. Zenker's diverticulum with an overtube clearly separating the septum, which has been cut with a pointed scalpel.



Figure 4. Diverticulum overtube designed in our unit.

there was only one woman (curiously, the youngest patient, 46 years). Ten patients were assigned to each group. The average size of the diverticulum was 3.5 cm (2.5-7.0; stage III according to the Brombart classification), which was similar in both groups. Participants were assessed using the FOSS and were as stages II-III patients. Symptoms were resolved in 7 patients in the standard method group vs. 9 in the diverticulum overtube method group (stage 0 of the FOSS, minimum follow-up time: 18 months). The three

patients who did not respond to the standard treatment method were classified as stage II according to the FOSS at 18 months of follow-up. One patient in the standard method group presented emphysema as a complication, but no perforation was evident and was treated conservatively; two experienced bleeding and required the use of the coagulation clamp with adequate control. No complications were reported in the diverticulum overtube method group, and only one patient reported odynophagia 15 days after the procedure was carried out; when endoscopy was done, it was discovered that the hemoclip remained in place but impacted against the contralateral wall, so it was removed, and the patient's condition improved immediately. The average time of the procedure was 32 (25-45) minutes in the standard method group versus 12 (7-15) minutes in the overtube method group ($p < 0.001$).

DISCUSSION

Zenker's diverticulum generally occurs between the seventh and eighth decades of life and it rarely does before the age of 40 (6, 22). Its estimated annual incidence is 2 per 100 000 inhabitants, and its onset is associated with aging, affecting men predominantly. Its prevalence in the general population ranges between 0.01 % and 0.11 % and varies depending on the geographical region; for example, it is more common in northern Europe than in southern Europe and its occurrence frequency in the United States, Canada, and Australia is higher, but lower in Japan and Indonesia. However, these data only include symptomatic cases, so the number of patients with asymptomatic Zenker's diverticulum is unknown to date (6, 23). Before a diagnosis is made, symptoms can be present for weeks or years. Although it has been linked to a wide range of symptoms, 80% to 90% of patients complain of dysphagia, regurgitation, halitosis, esophageal mass sensation, persistent cough, odynophagia, throat clearing, and aspiration pneumonia (22). It can also be an incidental finding in many cases, as it was the case in 17% of our patients, or patients can go to the emergency room with a foreign body, as it happened in 5% of our cases (22).

Given its widespread availability, modified barium swallow with lateral views of the hypopharynx is the most suitable diagnostic study for confirming the diagnosis of Zenker's diverticulum. However, dynamic continuous fluoroscopy is preferred (where available) because static imaging may be inadequate in patients with small diverticula. In addition, videofluoroscopic swallowing study allows assessing the presence of regurgitation and aspiration, as well as differentiating the Killian-Jamieson diverticulum (since it is unclear if the efficacy and safety of endoscopic treatment in these patients are comparable to those in patients with Zenker's diverticulum) (23-25).

The Brombart classification allows classifying diverticulum involvement based on the results of these types of imaging studies (**Table 1**). However, the usual scenario is a patient who complains of dysphagia and is taken to upper gastrointestinal tract endoscopy. Due to the increased risk of perforation during the procedure, it is important to have a high level of suspicion of Zenker's diverticulum in older adult patients who report complains of dysphagia (26).

Therapeutic measures for this condition have been described since the 19th century. They are similar to those used for hernia treatment in that they include mobilization and removal of the diverticular pouch, with or without defect closure, or endoluminal inversion. Cricopharyngeal myotomy (current technique) was introduced later. Its approach may be transoral with self-contained sutures or more invasive, by lateral cervicotomy with or without cricopharyngeal myotomy; however, the latter is associated with complications such as mediastinitis, infection of the superficial operative site, recurrent laryngeal nerve palsy, and development fistulas, and is no longer used (27, 28). The main disadvantages of surgical resection are a higher rate of complications, such as recurrent laryngeal nerve palsy or hematoma, and longer hospital stay; however, up to 90% of patients have been confirmed to be symptom-free after undergoing surgical procedure (29).

Endoscopic treatment of Zenker's diverticulum has progressed steadily. Dr. Mosher was the first to use a rigid endoscope and separate the pouch from the esophageal wall in 1917 (with the occurrence of a complication due to mediastinitis). Subsequently, in 1932, the technique was modified by Seiffert, although Dohman and Matson were successful in performing diverticulotomies via endoscopy. In 1982, Van Overbeek added the use of carbon dioxide (CO₂) laser to the technique and, in 1993, Collard et al., in Belgium, and Martin-Hirsch and Newbegin, in the United Kingdom, independently reported the performance of a diverticulotomy using mechanical sutures (28, 30, 31). The main advantages of flexible endoscopy, compared to surgical treatment options, are that it is safer, patients have shorter hospital stays (some may even be ambulatory), the overall success rate is of up to 90%, and symptom recurrence occurs in only 10.5% of patients (32). The overall complication and mortality rates from flexible endoscopic Zenker's diverticulotomy are 15% and 0%, respectively, and the most common complications are cervical emphysema (5.7 % do not need to be treated if there is no extravasation of medium), perforation (4.0 % usually resolve with clip placement), and bleeding (3.1 % are usually controlled during the same procedure) (33-36).

The use of peroral endoscopic myotomy (POEM) has been recently described in the management of Zenker's diverticulum (Z-POEM), with a clinical success rate of 92% and a per-

foration rate of 5.5% (37). This technique has gained popularity in recent years, and its potential advantage over standard endoscopic septotomy is complete septum division, which reduces the risk of symptom recurrence. However, it should be noted that in the case of post-Z-POEM recurrence (theoretically lower), the management strategy is still unknown, especially given the possibility of subsequent submucosal fibrosis. These aspects should be considered when selecting patients; however, this method plays a leading and critical role today and in the near future (37, 38).

Table 4 shows the endoscopic series published so far compared to ours. It should be noted that our series is small, but significant to our context. Despite this, the success of the procedure and the low complication rate reported here are consistent with what is currently reported. It is worth noting that although many authors perform this endoscopic procedure under sedation, we believe that it should always be performed under general anesthesia as it is better to have the patient completely immobile, since there is a potential risk of bleeding. Therefore, protecting the airway is recommended due to the risk of aspiration, which can be minimized in the initial phase by using coagulation current in the electro-surgical unit. Another useful measure consists of using an endoscopic laser scalpel (hook knife, triangle, ceramic tip, among others) instead of a pre-cut papillotome because it is very thin and often binds to the tissue, requiring regular removal and reinsertion for cleaning. Another suggestion is to use a ceramic-tipped papillotome in the initial phase to support the septum and avoid esophageal wall perforation.

As shown in our study, the experience with endoscopic diverticulotomy using the diverticulum overtube has been highly satisfactory and resulted in a procedure that requires a significantly shorter time to be performed, which, in the context of this group of patients, who are usually considered to be at high surgical risk (due to age, comorbidities, nutritional status and increased fragility), makes a significant difference in their postoperative recovery, without affecting the procedure results in terms of symptom recurrence (39, 40). The mean procedure time in the standard method group was 32 (25-45) minutes versus only 12 (7-15) minutes in the overtube method group ($p < 0.001$), with no major variations in terms of complications or symptoms recurrence, and with comparable results to the cases series published in the literature. However, the proven safety of the method proposed here should be assessed prospectively in subsequent studies with larger sample sizes that allow performing a higher number of procedures to be evaluated.

CONCLUSION

Myotomy of Zenker's diverticulum with flexible endoscopy using a diverticulum overtube has potential benefits in terms of shorter surgical times, shorter post-operative stays, and earlier food reintroduction. Technically, this method allows for a better exposure of the septum, which facilitates transection, although studies conducted in larger samples are required to validate these results.

Table 4. Experience with endoscopic diverticulotomy. Report of working groups

First author	Year	n	Post-Op Diet, hour	Complications		Recurrence		Hospital stay, hours	Follow-up time
				Number	%	N	%		
Ishioka (41)	1995	42	NA	2/42	5	3/42	7,1	NA	38 months
Hashiba (42)	1999	47	24	7/47	14	2/47	4	Outpatient	1 day to 1 year
Sakai (43)	2001	10	48 h	0	NA	0	NA	NA	2 to 12 months
de la Morena (44)	2005	3	48h	0	NA	0	NA	48	15 months
Vogelsang (45)	2006	31	NA	7/31	23	10/31	32	NA	26 months
Costamagna (46)	2007	39	NA	9/39	23	9/39	23	72 h	36 months
Al Kadi (3)	2010	18	24 h	1/18	6	2/18	11	24-48 h	27,5 months
Gómez (4)	2010	9	12 h	1/9	11	1/9	11	24 h	25 months
Gómez	2018	20	12 h	2:20	10	2	10	24 h	18 months

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