REVIEW ARTICLE

Therapy of Zenker's Diverticulum

Arnd Vogelsang, Brigitte Schumacher, Horst Neuhaus

SUMMARY

Introduction: Zenker's diverticulum is a rare disease, which can cause considerable suffering. The classic presentation is worsening dysphagia. Anatomically there is a loose bulge of the dorsal wall of the hypopharynx. A septum between the diverticulum and the lumen of the esophagus can develop and hamper the passage of food. Therapeutic options include the open diverticular resection in combination with myotomy of the cricopharyngeus muscle, or endoluminal or transoral approaches which merely split the septum by means of rigid or flexible endoscopy.

Methods: Selective review of literature found in Medline.

Results: Significant relief is achievable in more than 90% of cases by one or another approach. Endoluminal methods have lower complication rates but higher recurrence rates.

Discussion: Treatment planning should be interdisciplinary, and take into account individual anatomy and risk factors, as well as local expertise.

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Ludlow originally described what would later be called a Zenker's diverticulum in an autopsy report written in 1764. The lesion was given its current name in 1877, referring to the pathologist Friedrich Albert von Zenker of Erlangen, Germany.

The pathological finding is a saclike outpouching of the mucosa and submucosa of the dorsal wall of the hypopharynx, immediately cranial to the upper esophageal sphincter. This lesion is actually a pseudodiverticulum, because its wall is composed only of the mucosa and submucosa. It arises for two main reasons. There is a weak spot in the muscular wall of the hypopharynx at the site where the diverticulum develops. The dorsal hypopharyngeal musculature is composed of the striated fibers of the inferior pharyngeal constrictor muscle, whose lower portion is also known as the cricopharyngeus muscle. The fibers of this muscle run obliquely in its upper portion and horizontally in its lower portion. Between these two portions, there is a gap of variable size, called Killian's triangle. Dorsal outpouching of the mucosa and submucosa occurs preferentially at this site of least resistance (*figure 1*).

The second reason why Zenker's diverticula come about is elevated pressure in the hypopharynx, which can be demonstrated manometrically (1). This is thought to be due to increased tone in the cricopharyngeus muscle, with insufficient relaxation of the esophageal sphincter lying under it (1, 2). Histopathological studies show that the cricopharyngeus is vulnerable to degenerative changes such as atrophy and fibrosis, which render it less elastic (2). After myotomy of the cricopharyngeus, the manometrically measured bolus pressure in the hypopharynx becomes normal again, and the physiological drop in hypopharyngeal pressure during the act of swallowing is restored (1). The effectiveness of myotomy of the cricopharyngeus as the sole treatment of Zenker's diverticulum has been demonstrated in multiple studies. This indicates that the cricopharyngeus plays a central pathophysiological role in giving rise to the condition (1, 3–5) and suggests that the treatment of Zenker's diverticulum should always include myotomy of the cricopharyngeus, whatever else is done in addition.

Clinical features

The most common symptoms are dysphagia and regurgitation. In the early stage of the condition, dysphagia is usually only for solids; later, there can be dysphagia for food of any consistency, as well as for liquids. Acute symptoms may be present, too, such as the feeling of a bolus of food in the throat, gagging on

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food, and coughing while eating. Rarer symptoms include nocturnal regurgitation of undigested food, hoarseness, and halitosis. There may be severe sequelae, such as loss of up to 20 kg of weight and cachexia, or complications such as recurrent aspiration pneumonia. The retention of orally consumed medications in the diverticulum can render them ineffective. An important psychosocial effect of the condition is that sufferers alter their eating habits and become socially withdrawn. Because of their symptoms, they avoid eating in the company of others. Many affected persons report a significant impairment of their quality of life as the condition progresses.

Zenker's diverticulum usually manifests itself clinically after age 50; among patients undergoing treatment, the peak age is around 70. Often, many years elapse between the onset of symptoms and the treatment. Because patients are usually old when they are treated, they often have significant comorbidities that must be taken into account when the therapeutic alternatives are considered.

Diagnostic assessment

The most important diagnostic procedure is the esophageal barium swallow, with imaging at multiple levels. At the level of the sternoclavicular joint, the typical outpouching on the dorsal surface of the esophagus is seen, and the size and position of the diverticulum can be assessed easily (*figure 2*). Many authors use a classification of Zenker's diverticula by their size, measured in the craniocaudal direction: small (up to 2 cm), intermediate (2 to 4 cm), and large (4 to 6 cm).

Esophagogastroduodenoscopy is not necessary to establish the diagnosis, but it should nonetheless be performed after the barium swallow (if it has not already been done as the initial procedure). It serves to exclude other conditions that might also be responsible for the patient's symptoms, e.g., gastroesophageal reflux or esophageal tumors. The endoscope must be introduced with utmost caution and under direct vision, so that the typically slitlike opening to the esophageal lumen at the cranial, ventral edge of the diverticulum can be recognized and entered.

Treatment

Historical development

The surgical excision of a diverticulum through a lateral cervical approach has been described multiple times since 1884. In the 20th century, further techniques such as the division (myotomy) of the cricopharyngeus muscle were developed. The latter is often performed in combination with diverticulum resection to eliminate the causative elevation of pressure in the upper esophageal sphincter (5).

As early as 1917, Mosher divided the muscular bridge between the esophagus and the diverticulum by an endoscopic approach in a small number of patients (6) but had to stop performing this technique because of the associated mortality. In 1960, Dohlmann and

The dorsal hypopharynx with Killian's triangle (left) and a Zenker's diverticulum (right). From: Siewert R: Lehrbuch für Chirurgie, 8th ed., Chap. 7, p. 542, Fig. 7.41, with the kind permission of Professor Siewert, Munich.

Mattson described splitting of the septum by coagulation via rigid transoral endoscopy (7). A modification of this procedure, the so-called stapler technique, was introduced by Collard in 1993: here, the edges of the wound are stapled together at the same time (8). The most recent method of treating Zenker's diverticulum is the division of the septum (mucomyotomy) by using flexible endoscopy with a needle-knife or with argon plasma coagulation (APC). Since the early 1990's, this technique has been increasingly used internationally. The first studies were published in 1995

Figure 2: Anteroposterior x-ray: Barium swallow revealing a Zenker's diverticulum. Lateral x-ray: lateral displacement of the esophageal lumen.

Mucomyotomy with a needle-knife followed by free passage into the esophagus (ZD=Zenker's diverticulum).

FIGURE 3

Figure 4:

A view through the transparent cap: the diverticulum is seen at left, the esophagus with nasogastric tube at right.

by groups from the Netherlands and Brazil (9, 10); further studies with modifications have followed in the last few years (11–18).

Surgical resection of the diverticulum

The operation is performed under general endotracheal anesthesia. An incision is made at the anterior border of the left sternocleidomastoid muscle, and the dissection is carried down ventral to the carotid sheath until the diverticulum is reached where it lies between the esophagus and the cervical spine. Once the neck of the diverticulum has been exposed, the diverticulum is dissected free, picked up, and resected, e.g., with a stapling device. A myotomy of the cricopharyngeus muscle is performed in addition: this muscle is divided from the aboral edge of the diverticular neck caudally over a distance of 3 to 5 cm, without opening the underlying esophageal mucosa. Further, less commonly used options include mobilizing the entire diverticulum cranially and suturing it in place there (diverticulopexy) or invaginating the diverticulum into the esophagus so that an opening of the esophagus itself can be avoided.

Endoluminal treatment with mucomyotomy

The principle underlying this form of treatment is that the septum between the esophageal lumen and the diverticulum should be divided as completely as possible. Because the cricopharyngeus muscle makes up the muscular portion of this "bridge," a myotomy is necessary for this purpose. Once the septum has been split, food can pass unhindered out of the diverticulum, which is now collapsed ventrally, into the esophagus (figure 3).

When mucomyotomy is performed through a rigid endoscope, general endotracheal anesthesia as well as hyperextension of the neck are necessary. A special diverticuloscope, often the so-called Weerda laryngoscope, is used to visualize the partition wall (septum) of the diverticulum. This instrument consists of two branches that can be held at variable angles. One branch is introduced into the esophagus and the other into the diverticulum, and the angle between them is increased until the partition wall is visualized. A rigid endoscope is then used for visualization while the septum is divided with a CO₂ laser or with diathermic scissors.

An important modification involves the use of a stapling device that is introduced under endoscopic vision. Once this device (e.g., an Endo-GIA 30 stapler) is in position, the diverticular septum is divided while the V-shaped edges of the wound are simultaneously stapled. The theoretical advantage of this technique is the lower risk of perforation and bleeding through simultaneous wound closure by stapling. Multiple applications of the stapler are necessary for large diverticula.

Mucomyotomy via flexible endoscopy is performed through a video gastroscope with the patient in the left lateral position. The patient is not intubated, but is given analgesia and sedation (midazolam/disoprivan/pethidine).

Before the procedure, a nasogastric feeding tube is placed over a guide wire. This tube enables better orientation during the procedure and also stabilizes the esophageal wall (figure 3). A transparent cap is applied to the tip of the endoscope to give a wider view of the septum.

The endoscope is then introduced up to the septum (figure 4) and the latter is divided with a needle-knife or an APC probe introduced through the working channel of the endoscope, in the midline, from cranial to caudal, till just above the bottom of the diverticulum (figures 5 and 6). Optionally, the wound edges can be closed with metal clips. In case the symptoms persist or recur because of a residual septum, the procedure can be repeated.

Results

Nearly all of the published studies on the different treatment modalities for Zenker's diverticulum are retrospective studies of evidence grades IIB and III (case-control studies, non-randomized). They provide information on results and complications.

In a few non-randomized studies, surgical techniques were compared with each other and with rigid endoscopy; no comparative study encompassing all three methods has been performed to date. The average age of the patients in all of these studies was about 70 years. Few of the publications mention drop-out rates, but it seems likely that patients undergoing open surgical treatment were carefully selected from the initial patient pool.

The literature search for this review article was performed by searching the Medline database for the terms "Zenker," "Zenker's diverticulum," and "Zenker and therapy." The authors considered all studies that included at least 10 patients treated with a clearly defined method and in which the long-term results were reported and the complication rates clearly presented.

Table 1 contains an overview of the studies on the various types of treatment that were obtained by our literature search. The relevant studies for each type of treatment are listed and described.

Surgical treatment

(Diverticulum resection/diverticulopexy/myotomy)

An analysis of 10 studies published since 1990 (19–25, e10, e11) with at least 30 patients in each study yielded a rate of symptomatic improvement of up to 94%, with up to 91% of patients being free of symptoms after the procedure. The recurrence rate was up to 7.5% with a single outlying value of 16% in one study (20). Serious complications such as mediastinitis, pneumonia, and severe hemorrhage occurred in as many as 7.5% of cases in some of the studies. Fistula formation, stenosis, recurrent laryngeal nerve palsy, and wound infections occurred in up to 25% of the patients. In three studies, there was mortality ranging from 1.2% to 3.4% (19, 24, e11).

Mucomyotomy with a rigid endoscope

In a meta-analysis of seven studies on CO₂ and stapler treatment, the symptoms markedly improved in up to 96% of patients, while a completely asymptomatic state was achieved in up to 90% (e1–e7). The recurrence rate ranged as high as 15.4%. The less serious complications were dental injury, transient vocal cord paresis, hemorrhage, fistula formation, cervical abscesses, cervical emphysema, aspiration pneumonia, and perforations that could be managed conservatively. More serious complications occurred in 3.8% of the patients in one study and consisted of two cases of hemorrhage that had to be treated by open surgery (e2). Stapler treatment was not possible in as many as 13% of the patients in the stapler group because of their individual anatomical situation.

Sen et al. (e8) reviewed the results of 29 studies of endoscopic stapling technique (ESD) comprising a total of 576 patients. 53% to 100% of the patients in each study were completely relieved of their symptoms, while the rate of conversion to an open transcervical approach because of a difficult anatomical situation

Figure 5: Division of the septum with the needle-knife: the diverticulum is seen below, the esophagus with nasogastric tube above.

Figure 6: Three months after treatment: complete mucomyotomy with collapse of the diverticulum at 5 o'clock.

ranged from 0% to 30%. The average length of hospital stay was 2.3 days. The rate of complications ranged from 0% to 17%; 2.6% of patients in the overall collective had serious complications (14 perforations), and there were two deaths, yielding a mortality of 0.43%. Most of the perforations necessitated an immediate conversion of the procedure to open surgical treatment.

Mucomyotomy with a flexible endoscope

The results of this technique have been published to date in 10 studies containing a total of 388 patients (table 2) (9–18). Marked improvement of symptoms was achieved in 84% to 96% of the patients in each of the studies, while in three of the studies total relief of symptoms could be achieved in 39% to 100% of patients (11, 12, 15). One to three sessions were needed to produce these results. The recurrence rate ranged from 3% to 35%; in most cases of recurrence, total relief of symptoms was achieved by repeated treatment.

A serious complication occurred only in a single patient in one of the studies who developed mediastinitis followed by sepsis and a prolonged recovery (12). All of the remaining complications were mild and occurred at rates ranging from 2% to 23% (table 2). They included mild hemorrhage, fever, cutaneous

TABLE 1

Results of different types of treatment

Type of treatment	Surgical	CO ₂ /stapler	Endoluminal Stapler only	Endoluminal Flexible
No. of studies; Reference no. Year	10; 15–24 1955–1999	7; e1–e7 1999–2004	29; e8 1993–2003	10; 9–18 1995–2007
No. of patients	1532	456	576	388
Follow-up (years)	3.8	2.0	2.1	1.3
Recurrences (%)	3.6–7	3.9–15.4	0–32	3.3–35
Symptomatic improvement (%)	84–94	80–96	(N.A.)	93–96
Total relief of symptoms (%)	82–91	53–90	53–100	39–100
Complications (%)				
– mild	7.4–25	3.9–20	0–17	2–23
– severe	3.9–7.5	0–3.8	0–2.6	0–3
Mortality (%)	1.2–3.4*	0	0–0.4	0

* in 3 studies

or mediastinal emphysema, and pneumonia. The overall mortality in all of the studies combined was zero.

In our study (15), we treated 31 patients with needle-knife mucomyotomy and graded them very precisely afterward on a specifically developed dysphagia scale. Ten patients (32%) needed repeated procedures. After an average of 2.2 years of follow-up, 12 patients (39%) were asymptomatic, while 14 (45%) had mild or moderate residual symptoms. Four patients (13%) had marked symptoms and desired repeated treatment, while one patient (3%) chose to undergo surgery.

Overview

Three different treatment concepts are currently available for symptomatic Zenker's diverticulum: open surgery and treatment via rigid or flexible endoscopy. All three of these methods improve dysphagia with success rates above 90%. The figures with respect to total relief of symptoms also seem to be comparable, although the published data are less than fully informative because a dysphagia score has generally not been used and because the results have usually been reported retrospectively. A further limitation arises from the variable length of follow-up; currently, the shortest follow-up times have been reported for treatment via flexible endoscopy.

Open surgical treatment has the highest complication rate because it is the most invasive of the three methods. This fact is clinically relevant because of the comorbidity that is often present in this generally older patient group. A further disadvantage is the longer length of hospital stay and recovery compared to endoluminal treatment. On the other hand, the advantages of open surgery are also a function of its radicality, namely, its reliably good results and the rare need to perform the procedure a second time.

Another supposed advantage of resective treatment, in view of the very rare occurrence (0.4%) of malignant neoplasia in a Zenker's diverticulum that has been present for many years (19) is, in the authors' view, not really an advantage at all. Careful endoscopic examination reveals malignant changes in the diverticulum; moreover, once endoscopic treatment has been performed, the most likely cause of the development of carcinoma (pressure and stasis in the diverticulum) has been eliminated. Nonetheless, this matter should be discussed with the patient before the treatment is decided upon.

The rigid endoscopic approach is well established, particularly in Europe. Its advantages include a short hospital stay, particularly after stapler esophagodiverticulostomy, as well as low rates of complications and recurrences. A meta-analysis (e8), however, revealed a rate of serious complications up to 3.8%, with a 0.43% mortality. Less serious complications occurred about as frequently as after flexible endoscopy and mainly consisted of local problems such as dental injury, vocal cord paresis, and fistulae. General endotracheal anesthesia is necessary for this procedure, as it is for the others. In some patients (about 13%), the procedure must be converted to open surgery for anatomical reasons such as lack of hyperextensibility of the neck, inability to open the jaws wide enough, or a small diverticulum (< 2 cm). The patient must be aware of this possibility and consent to it before the procedure is performed.

Mucomyotomy via flexible endoscopy, like the other techniques, yields a high success rate. The percentage of patients that are totally relieved of their symptoms varies markedly from one series to another and depends in part on the precision of questioning. The low percentage of complete relief (39%) that the authors of the present review found in our own clinical series, as compared to

TABLE 2

Results of flexible endoscopic mucomyotomy

Author	Patients	Sessions	Complications	Follow-up (months)	Results
Mulder (9)	20	3	None	6.7	All patients symptomatically improved
Ishioka (10)	42	1.8	Mild: 4.7%	38	93% without dysphagia, 7.2% improved, 7% recurrence
Hashiba (13)	47	2.2	Mild: 15%	1-12	96% markedly improved, 4% minimally improved
Mulder (14)	125	1.8	Mild: 19.2%	Not stated	Better in all cases, though some patients still had symptoms
Sakai (11)	10	1	None	2-12	All patients with grade 0 dysphagia
Evrard (12)	30	1	Severe: 3 % Mild: 10 %	13	93% total relief 3.3% improved, 3.3% recurrence
Vogelsang (15)	31	1.4	Mild: 23 %	26	39% total relief; 45% markedly improved; 16% unsatisfactory or no improvement
Christiaens (16)	21	1.1	Mild: 2,1 %	3	90% grade 0 dysphagia; 10% grade 1 dysphagia
Rabenstein (17)	34	3	Mild: 20 %	16	15% recurrence with need for repeated treatment
Costamagna (18)	28	1.1	Mild: 23 %	36	29% total relief or with mild residual symptoms; 71% "incomplete response"

the figures in other clinical series, is probably due to our use of a specially developed scoring system (numerical analog scale) to rate dysphagia.

Serious complications are rare in flexible endoscopy. A serious complication occurred in only one patient in a single study (complication rate in that study, 3%; perforation with mediastinitis).

Less serious complications, such as mild hemorrhage and cutaneous or mediastinal emphysema, are more common, while no mortality has occurred with this procedure to date in any of the published series. The fear that it would lead to perforation with mediastinitis has turned out not to be justified. The cutaneous and mediastinal emphysema that occur in some patients are explicable as being due to the egress of air through microscopic tissue openings during coughing or forcible insufflation of air. These conditions rarely cause symptoms and generally resolve rapidly and spontaneously.

The advantages of flexible mucomyotomy are the possibility of performing it under analgesia and sedation (without general endotracheal anesthesia) and the low complication rate associated with its minimal invasiveness. On the other hand, a disadvantage is that it has had, at least until now, a higher recurrence rate than the other techniques and must, therefore, more often be followed by a repeat of the procedure, which can generally be performed without difficulty in the outpatient setting or during a one- to two-day stay in the hospital. A recurrence, in this context, is defined as the reappearance of symptoms, regardless of whether there is any radiologically demonstrable residual or recurrent diverticulum, because these findings are poorly correlated with the clinical symptoms (e9).

In summary, the current state of the published data does not reveal any single one of the various techniques that are available to be clearly superior to the others.

Flexible endoscopic mucomyotomy, because of its lesser invasiveness and low complication rate, appears to be a particularly promising technique. This is especially true because patients with Zenker's diverticulum tend to be old and to suffer from other diseases in addition, making them more vulnerable to any complications that might occur. On the other hand, its major disadvantage is a higher rate of repeated procedures. In the authors' department, repeated procedures have become a less frequent problem as our patient numbers and experience have increased, yet it should also be borne in mind that repeated procedures can generally be carried out easily and safely, if necessary. Prospective studies would be desirable for all of the various treatment methods that are available. These should include data about complication rates and should also assess the long-term improvement of dysphagia with a validated scoring system. In our own center, we are currently carrying out a randomized, controlled trial comparing argon plasma coagulation with needle-knife incision in flexible endoscopic mucomyotomy.

Conflict of interest statement

The authors state that they have no conflict of interest as defined by the guidelines of the International Committee of Medical Journal Editors.

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