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Different therapeutic approaches to Zenker diverticulum: A retrospective comparative study between the flexible endoscopic method using needle knife and the rigid endoscopic method using laser in terms of effectiveness, complications and recurrence rates

Dissertation
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Zusammenfassung:

Einleitung:

Unter einem Zenker-Divertikel versteht man eine erworbene Ausstülpung der Mukosa- und Submukosaschichten durch einen dreieckigen Bereich in der Wand des Pharynx zwischen Cricopharyngeus und Thyropharyngeus (Killian´s Dehiszenz/Killian Dreieck) im Bereich des pharyngoösophagealen Übergangs. Es ist der häufigste Typ der ösophagealen Divertikel mit einem Prävalenz zwischen 0,01 bis 0,11% und tritt meistens bei Patienten mittleren und höheren Alters auf (1). Typische Symptome und Komplikationen sind Dysphagie, Aufstoßen, chronische Husten, Halitosis, zervikales Borborygmus, sowie Aspirationspneumonie. Sekundäre Konsequenzen und potentielle Komplikationen sind Ineffektivität von Medikamenten, Unterernährung und Gewichtsverlust (2-6). Eine Therapie ist bei symptomatischen Patienten indiziert und erfordert in Anbetracht der Ätiopathogenese die Myotomie des Musculus cricopharyngeus (7). Diese Myotomie kann durch verschiedene Methoden durchgeführt werden. Es werden hierbei die offene chirurgische Methode, die Myotomie durch eine transorale starre Endoskopie sowie die Myotomie mittels flexibler Endoskopie unterschieden. Die drei Verfahren können die Beseitigung der Abflusshinderung und die Wiederherstellung der Kontinuität am pharyngoösophagealen Übergang durch eine Myotomie mit oder ohne Resektion des Divertikels (Divertikulektomie) oder Divertikulopexie erreichen(8).

Für diese verschiedenen Therapieansätze des Zenker-Divertikels wurden in den letzten Jahren hohe Erfolgsraten berichtet, wobei aufgrund der schwachen und teils widersprüchlichen Datenlage die Frage weitesgehend unbeantwortet geblieben ist, welche der möglichen Methoden primär und im Hinblick auf bestimmte Patientenfaktoren (Alter und Komorbiditäten) genutzt werden sollte. Im Rahmen dieser Studie sollten daher retrospektiv die Ergebnisse der minimalinvasiven Methoden in einem tertiären universitären Zentrum (Klinikum Oldenburg) verglichen werden.

Material und Methoden

Alle Patienten, die im Studienzeitraum von Januar 2009 bis Oktober 2021 im Klinikum Oldenburg (Oldenburg, Deutschland) eine interventionelle Behandlung eines Zenker Divertikels erhielten, wurden eingeschlossen. Verglichen wurden die Ergebnisse der starren endoskopischen Methode mittels Laser, durchgeführt durch die Hals-Nasen-Ohren (HNO) Abteilung, mit den Ergebnissen der flexiblen endoskopischen Methode mittels Nadelmesser, durchgeführt durch die gastroenterologische Abteilung. Die beiden Gruppen wurden hinsichtlich der Wirksamkeit bei der Reduktion oder Beseitigung der Symptome und der Komplikations- und Rezidivraten verglichen. Für die klinische Verbesserung der Symptome definierten wir eine Nachbeobachtungszeit von mindestens drei Monaten. Patienten, die keine Nachsorgetermine in unserem Krankenhaus hatten, wurden per Post mit einem standardisierten Fragebogen kontaktiert, um Symptomlinderung, Rezidiv und Notwendigkeit einer erneuten Intervention zu beurteilen.

Ergebnisse:

Es wurden in diesem Zeitraum bei insgesamt 136 Patienten eine interventionelle Therapie des Zenker Divertikels durchgeführt. 88 Patienten erhielten in der gastroenterologischen Abteilung eine flexible endoskopische Therapie und 48 Patienten in der HNO-Gruppe eine Therapie mittels starrer Endoskopie. Das durchschnittliche Alter in beiden Gruppen betrug 70 Jahre. Zwei Patienten in der HNO-Gruppe erhielten aufgrund des Scheiterns der Platzierung des Laryngoskops eine flexible endoskopische Behandlung durch die gastroenterologische Abteilung. Die durchschnittliche Interventionszeit und der Krankenhausaufenthalt waren in der gastroenterologischen Gruppe kürzer (p-Wert <0,05). Hinsichtlich der Rezidiv- oder Komplikationsrate wurde zwischen den beiden Gruppen keine signifikanten Unterschiede festgestellt. Im Gegensatz hierzu bestanden für die subjektive Verbesserung oder Fehlen von Symptomen (primärer Endpunkt) ein signifikanter Unterschied. 88,7% der Patienten in der gastroenterologischen Gruppe im Vergleich zu 65,5% in der HNO-Gruppe berichteten subjektiv eine Verbesserung oder das Fehlen von Symptomen (p-Wert <0,05).

Schlussfolgerung

Diese Studie legt nahe, dass die flexible endoskopische Methode im Vergleich zur starren endoskopischen Methode eine potenziell effektivere und kürzere Prozedur mit ähnlichen Sicherheitsprofilen bei der Behandlung von Zenker Divertikeln darstellt. Randomisierte Studien sollten durchgeführt werden, um diese retrospektiven Daten zu verifizieren.

Keywords: Zenker diverticulum, Rigid endoscopy, Flexible endoscopy

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Abbreviations

CPM	Cricopharyngeal muscle
ENT	Ear-nose-throat
FE	Flexible endoscopy
FU	Follow UP
UEHPZ	Upper Esophageal High-Pressure Zone
ZD	Zenker diverticulum

Declaration

I affirm that this submission is my original work and, to the best of my knowledge, does not contain any previously published or authored material from another individual. Furthermore, no portion of this work has been used to fulfill the requirement of any other degree or diploma from this university or any other institution of higher education, unless properly acknowledged within the text.

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Parts of this work have been submitted for publication.

1 Introduction

1.1 Esophageal diverticula

A diverticulum in the gastrointestinal tract can be defined as an outpouching of the layers of a hollow organ. It can be congenital (rare) or acquired(9).

Diverticula can be classified in true and false types. A true diverticulum involves an outpouching of the all layers, while a false diverticulum exhibits a weak area in the muscular layer, through which the mucosal and the submucosal layers will protrude(10).

Additionally, diverticula can be classified as pulsion or traction types. The pulsion diverticulum arises from increased intraluminal pressure and it is usually a false diverticulum. The traction diverticulum arises from an extraluminal traction usually from inflammation and it is considered a true diverticulum(11).

Concerning esophageal diverticula, three main localizations can be distinguished. The first one is the most proximal, directly above the upper esophageal sphincter posteriorly known as Zenker's diverticulum. The second localization is in the mid esophagus, which is usually a traction diverticulum secondary to inflammation in the mediastinum. The third one is directly proximal to the lower esophageal sphincter, which is called an epiphrenic diverticulum, usually associated with motility disorders(12-14).

1.2 Zenker's diverticulum

1.2.1 Definition and history of Zenker's diverticulum (ZD)

ZD is an acquired false diverticulum in which the mucosal and submucosal layers directly above the upper esophageal sphincter protrude through a weak muscular area in the Killian's triangle, situated between the thyropharyngeal muscle and the cricopharyngeal muscle.

The first known description of Zenker's diverticulum dates back to 1769 when Ludlow, a surgeon from Great Britain, described it as an autopsy finding(15).

In 1877, pathologists Zenker and von Ziemssen also characterized this pathology, with Zenker further explaining the pathogenesis as being due to increased intraluminal pressure in the esophagus and the presence of a distal restriction. The anatomy of the lesion was described in the early 1900s by Killian, who noted that the outpouching of

the pharyngeal wall occurs dorsally in the midline between the thyropharyngeus muscle above and the cricopharyngeus muscle below(16).

1.2.2 Epidemiology of Zenker's diverticulum

ZD is considered the most common type of esophageal diverticulum, with a prevalence ranging between 0.01 and 0.11% and a typical incidence among middle-aged and elderly population(1). A recent epidemiological study in Finland estimated the incidence to be about 2.9/100 000 Person-years(17). Geographical difference in incidence exists, with ZD being more common in northern Europe(18). Due to the presence of asymptomatic cases, determining the actual incidence is challenging.

ZD is typically diagnosed in Patients in their 60s or 70s, rarely before the fifth decade of life(19). A database review of 3197 patients with ZD in the USA showed that the mean age of diagnosis was 73±12.3 years, with more than half of the patients being males (55%).

1.2.3 Anatomy of Zenker's diverticulum

The Pharynx is approximately 12.5 cm long cone-shaped muscular channel. Its widest part is cranially at the base of the skull with a diameter of about 2.5 cm (nasopharynx), and its narrowest part is caudally at the level of the lower border of C6 vertebra, with a diameter of about 1.3 cm (laryngopharynx). The wall structure of the pharynx consists of the following layers from innermost to outermost: mucosa, submucosa, the pharyngeobasilar fascia, the pharyngeal muscles and the buccopharyngeal fascia.

The muscles of the pharynx are composed of three constrictor muscles (superior, middle, and inferior) located externally, and three additional internal muscles (Stylopharyngeus, Palatopharyngeus, and Salpingopharyngeus).

The constrictor muscles originate separately from distinct origins and overlap each other, leading to their insertions in various cartilages and bones(20).

The superior constrictor muscle originates from pterygomandibular ligament, the pterygoid hammulus and the posterior end of mylohyoid line of the mandible.

The middle constrictor muscle originates from the stylohyoid ligament and the horns of the hyoid bone.

The inferior constrictor muscle consists of two parts. The superior part originates from an oblique line on the thyroid cartilage (thyropharyngeal muscle), inserting into the median pharyngeal raphe. The lower part originates from the cricoid cartilage (cricopharyngeus muscle) and blends with the circular esophageal muscle fibers.

The three constrictor muscles insert posteriorly into a median fibrous pharyngeal raphe(20).

Zenker diverticulum is believed to arise from a gap between the superior and inferior components of the cricopharyngeus muscle(21). This gap is called the Killian triangle. The Cricopharyngeus muscle contributes the area of maximal pressure in the upper esophageal sphincter (UES), with the greatest pressure being directly above the inferior components of the cricopharyngeus muscle(22).

Various theories explain the pathogenesis of Zenker's diverticulum. One controversial theory suggests that it is a pulsion diverticulum originating from increased intraluminal pressure in the upper esophageal sphincter during swallowing. Based on manometric and radiographic studies, it was observed that the Upper Esophageal High-Pressure Zone (UEHPZ) is composed of three parts: cervical esophagus, cricopharyngeal muscle and the inferior constrictor muscles of the pharynx, with evidence suggesting that the cricopharyngeus muscle represents the main muscle of the UEHPZ(23).

Zaninotto et al. studied pharyngo-esophageal function in 12 patients with Zenker's diverticulum before and after undergoing cricopharyngeal myotomy with or without diverticulectomy, using low-compliance, high-frequency manometry. The results were compared to nine healthy volunteers serving as controls. Additionally, computerized morphometry was used to analyze the muscle and connective tissue in the cricopharyngeal muscle, comparing the results with findings from cadavers without a history of dysphagia. Preoperative manometry in patients with ZD revealed insufficient relaxation of the upper esophageal sphincter (UOS), with a mean residual UOS pressure during swallowing of 7.9 mmHg, compared to 0.2 mmHg in controls ($p < 0.001$). Additionally, the pharyngeal intrabolus pressure was increased in Patients with ZD (21 mmHg, range 0-52) compared to controls (9 mmHg, range 0-16) ($p < 0.001$). After myotomy, both parameters showed a significant decrease. Moreover, the study revealed that patients with ZD had fewer muscle fibers in the cricopharyngeus ($p < 0.05$) and a significantly lower muscle-to-connective tissue ratio ($p < 0.05$) compared to controls. This study supports the theory that ZD is a result of increased intrapharyngeal pressure during swallowing due to incomplete relaxation of the cricopharyngeal muscle resulting from localized sclerosis(24).

In addition to the theory of elevated pressure in the upper esophageal sphincter, it is hypothesized that the association with other motility disorders of the esophagus, such as achalasia, can play a role(22). It is also postulated that gastroesophageal reflux

resulting in spasm of the cricopharyngeal muscle plays a role in the pathophysiology of Zenker Diverticulum(25). At last it is accepted that a multifactorial process is associated with the pathogenesis of Zenker's diverticulum(26).

1.2.4 Clinical presentation of Zenker's diverticulum

ZD presents with different symptoms, with dysphagia representing about 80 to 90% of patient complaints. Additional symptoms include halitosis, regurgitation of food, or hoarseness of voice with cervical borborygmi being pathognomonic for ZD(3).

Secondary consequences and potential complications include the inefficacy of medications, malnutrition, and weight loss(2, 3). Cancer development, likely due to the chronic irritation and inflammation from food and fluid retention, has been associated with Zenker's diverticulum, with an incidence of about 0.4 to 1.5%(4-6).

Interestingly Zenker's diverticulum is considered as one of the typical oropharyngeal causes of dysphagia of elderly patients(27).

Dysphagia is classified as oropharyngeal or esophageal. Another type of dysphagia is functional dysphagia, which should be a diagnosis of exclusion(28). Oropharyngeal dysphagia involves disturbance in the complex act of swallowing. Esophageal dysphagia involves disruptions in the passage of fluid or solid food after swallowing. (26, 27)

In the case of oropharyngeal dysphagia, patients typically complain of symptoms in the neck and pharynx, including an inability to swallow. This often results in regurgitation, coughing, and may lead to aspiration. In severe cases, patients may experience difficulty swallowing saliva(26). Other causes of the oropharyngeal dysphagia include(27): Neurological causes like Stroke, Parkinson's disease, cranial nerve palsy or bulbar palsy; and anatomical or muscular causes like myasthenia gravis, oropharyngeal malignancy, cricopharyngeal spasm or a pharyngeal pouch (e.g., ZD).

In the case of esophageal dysphagia, symptoms are localized in the esophagus, with patients complaining of discomfort in the thorax or epigastrium. If the pathology affects the proximal esophagus, patients may feel symptoms in the neck. Unlike oropharyngeal dysphagia, symptoms in esophageal dysphagia are more pronounced with solid food than with fluids. This difference can be a practical method for clinical differentiation between the two types. In some cases, esophageal dysphagia may improve after drinking of fluids(26, 27, 29).

1.2.5 Diagnosis of Zenker's Diverticulum

In cases where clinical features suggest ZD (such as dysphagia, postprandial cough, and regurgitation), a barium swallow can be performed. This procedure helps delineate the cervical pouch or web(30). Zenker's diverticulum can be classified according to the size of the pouch craniocaudally, into small (0-2 cm), intermediate (2-4 cm) or large (4-6 cm) categories(31). Another classification that aids in planning the mode of therapy is Brombart's classification, which divides ZD into four categories based on the longitudinal axis(32):

Stage I A tiny "thorn-like" diverticulum with a longitudinal axis of about 2 to 3 mm
Stage II A "club-like" diverticulum roughly 7 to 8 mm in length.
Stage III The pouch measures more than 10 mm in length without compression of the esophagus.
Stage IV The pouch compresses the esophagus.

Patients with ZD often present with symptoms of dysphagia and may experience weight loss, raising concerns about malignancy. Therefore, initial investigations should include an esophagogastroduodenoscopy to rule out esophageal cancer and confirm the diagnosis of ZD. The incidence of malignancy in ZD is rare and was described in literature of about 0.4 – 1.5%(4-6). In the case of anticipating a ZD, gastroscopy should be performed cautiously to avoid perforation of the diverticulum. This is especially important due to the difficulty often encountered during intubation of the upper esophagus in these cases.

1.3 Therapy of Zenker's diverticulum

Symptomatic patients with ZD should be offered interventional therapy. Conservative therapy should only be considered if intervention is not feasible due to the patient's general medical condition or if the patient refuses intervention.

Asymptomatic patients with small diverticula occasionally found on diagnostic investigations are not in need of treatment. As here the risk of adverse events due to intervention outweigh the aspiration or cancer risk due to the diverticulum(33).

The aim of treatment in the different modalities is to restore the continuity of the esophagus by removing the functional obstruction caused by the cricopharyngeal muscle through performing a myotomy(8). By doing so, the reservoir diverticulum will

be shallow or may be eliminated, restoring the functional continuity of the esophageal lumen.

1.3.1 Surgical therapy

For the past few decades, surgical management has been widely accepted as the preferred treatment for ZD. This approach aims to restore esophageal continuity by performing a diverticulectomy in conjunction with a cricopharyngeal myotomy. The efficacy of this approach has been demonstrated in numerous studies. Patients are typically placed under General anesthesia in a supine position, with hyperextension of the neck and tilting the head to the right side. A precise longitudinal incision is made along the anterior border of the left sternocleidomastoid muscle revealing the cervical esophagus and the pharynx following careful retraction of the carotid sheath and the sternocleidomastoid muscle laterally. The surgeon then meticulously separates the diverticulum from the surrounding tissue and performs a cricopharyngeal myotomy. The diverticulum can be either resected using a surgical stapler (diverticulectomy) or lifted and attached to the paravertebral fascia (diverticulopexy). In some cases, the pouch may be folded back into the esophageal lumen. This surgical intervention restores the smooth flow of food and liquid through the esophagus(34).

In a literature review by Yong Yuan et al., 41 studies were included, comprising a total of 2826 patients. This review reported an open surgery morbidity rate of 10.5% (297/2826) and a mortality rate of 0.6% (17/2826) in patients treated for ZD. The overall risk of serious complications was relatively low including mediastinitis (0.2%), perforation (3.3%), recurrent laryngeal nerve injury (3.3%), and cervical infection (1.8%). Notably, more than half of the patients underwent a diverticulectomy combined with a cricopharyngeal myotomy(35). Out of the 41 studies in this review, only two studies did not perform a myotomy, reflecting the significance of dividing the cricopharyngeal muscle, which has been increasingly acknowledged by surgeons over the years. This was further emphasized by the study of Helena et al., which objectively measured the opening size of the upper esophageal sphincter before and after the cricomyotomy using video-fluoroscopy. The study demonstrated that incision of the cricopharyngeal muscle helps to normalize the opening size of the upper esophageal sphincter in patients with cricopharyngeal dysfunction(36).

The efficacy of cricopharyngeal myotomy in treating ZD is further supported by the findings of Shaw et al. In their study, they found that the compliance of the upper

esophageal sphincter (UOS), as measured through the hypopharyngeal intrabolus pressure is normalized following the cricomyotomy in patients with ZD(37).
The mean operating time is about 124.0 min, with the patient staying in the hospital for a median of 3 days(38). Oral intake is possible after a median of 1 day(39).
Some authors regard the open transcervical approach as the most effective method for treating small diverticula(40).

1.3.2 Endoluminal diverticulotomy

For decades, the surgical transcervical approach was considered the gold standard in the management of ZD. In 1917 Mosher introduced the endoluminal approach, initially adopted by a minority of ENT surgeons in the following years. Over time, the tools evolved from scissors to CO2 lasers and Argon plasma.
The introduction of the linear Stapler brought about a dramatic change in endoluminal therapy of ZD. With this device, the diverticulum can be cut while simultaneously sealing the cutting edge at the base of the diverticulum. This advancement made this technique safe and secure, even for surgeons concerned about the risk of mediastinitis, establishing the endoluminal stapling approach as an acceptable alternative to the open transcervical method.
Subsequently, endoluminal therapy using flexible endoscopy was introduced, offering the advantage of eliminating the need for hyperextension of the neck and general anesthesia(41).
A very important point to be considered, is the fact that endoluminal therapy is most suitable for large diverticula (Brombart III or IV). Because in that case a complete division of the muscular septum of the cricopharyngeus muscle between the ZD and the esophagus can be achieved. Otherwise, the septum between the two lumens could be too short.
A critical aspect of endoluminal treatment is the cutting of the lower part of the septum. Particularly in large diverticula, as the lowest part of the diverticulum may extend below the septum. If cutting is performed too deeply, reaching the bottom, a perforation into the mediastinum becomes unavoidable. This dilemma leaves the operator balancing between cutting too short, risking recurrence, and cutting too deep, risking mediastinitis.
With most surgeons preferring to be on the side of caution, it is not surprising that the rate of recurrence in the endoluminal method, especially for small diverticula, is higher than with the open transcervical method(42).

Endoluminal therapy using rigid endoscopy

The endoluminal approach using rigid endoscopy to treat ZD was introduced in the 1960s(43). Over the years, instruments and techniques have been developed, leading to the utilization of the microendoscopic method with a double lipped scope and Carbon dioxide laser(43, 44). This endoluminal method with rigid endoscopy is performed under general anesthesia and requires full extension of the neck to expose the diverticulum.

The management of Zenker's Diverticulum using stapler was first introduced by Colard et al. and Martin Hirsch independently in 1993(45, 46).

A recent systematic review and meta-analysis of nine retrospective studies comparing the stapler method with the CO2 laser method has revealed no significant difference between the two methods in terms of efficacy, complications or reintervention rate(47). Other methods that can be used for cutting the septum include electrocautery and Harmonic Ace (Ethicon Endo-surgery, Inc., Cincinnati, Ohio, USA).

A drawback of the stapler technique is that the full length of the pharyngeal pouch is not reached in some patients(48). In a meta-analysis conducted in the UK, 7.7% of procedures were intra-operatively abandoned due to failure to expose the small diverticulum. In the same meta-analysis, good postoperative results were achieved, with over 90% of patients reporting significant improvement or resolution of symptoms. Complications included dental trauma, temporary hoarseness, and sore throat, with 4.8% reported Perforation. One patient died(49).

In another meta-analysis of Yuan et al., which identified 1,060 patients who underwent CO2 laser diverticulotomy from 19 studies, the complication rate reached 9.3%, with a mortality rate of 0.2%. The common reported complications were mediastinitis 1.3%, subcutaneous emphysema 3%, fistula 1.1%, and bleeding 1%. In a follow-up period of 1-3 years, 93% of the patients were completely symptom-free with 3.9% suspected to have recurrence(35).

The rigid endoscopy procedure is done under general anesthesia with hyperextension of the neck. At the beginning, a nasogastric tube is placed and the septum between the diverticulum and the esophagus is exposed using a diverticuloscope (most commonly, Weerda diverticuloscope). The septal wall as well as the diverticulum floor is inspected using an operating microscope. In the CO2 laser method, a CO2 laser device is used to dissect the midline of the muscular septum completely till reaching the adventitial layer without entering the mediastinal fat(48).

A recent study revealed a mean procedure time for the rigid endoscopy of 54 minutes with a mean hospital stay of 4.9 days and adverse events occurring in 30% of patients(50).

Endoluminal therapy using flexible endoscopy

In 1995, flexible endoscopy was first employed in the treatment of ZD, with the same objective as the rigid endoscopy method: to cut the mucosa, submucosa, and muscular septum between the diverticulum and the esophagus(51, 52).

The procedure can be performed under conscious sedation, allowing access to the diverticular septum without the need for the hyperextension of the neck. This represents a significant advantage compared to the rigid endoscopy method, which may be limited by patient characteristics such as Body Mass Index and poor neck flexibility.

Patients are usually positioned in the left lateral position under propofol sedation. Some authors prefer to conduct the procedure under general anesthesia. The diverticulum is initially inspected with the endoscope to ensure that it is free from food debris. It is a common practice to place a nasogastric tube into the stomach to aid orientation during the procedure. Various instruments have been utilized for cutting the diverticular septum including needle papillotome, hook knife, Argon plasma coagulation and monopolar forceps(3). Frequently, a transparent endoscopic cap is applied to enhance visualization and stretch the septum.

In 2003, Evrard et al. introduced a soft diverticuloscope, which can be placed as an overtube over the endoscope. This diverticuloscope features two flaps, which help stabilize and provide tension on the diverticular septum to facilitate the cutting procedure while also protecting the esophageal and diverticular walls(53). It is not uncommon for the procedure to be repeated to gradually cut the septum, with a mean number of repetition ranging from 1 to 3 times as reported in studies(54, 55). To close the cutting defect, one to three clips are routinely applied to reduce the risk of delayed perforation or bleeding(56).

With the introduction of third-space endoscopy, a novel approach (Z-POEM, Zenker PerOral Endoscopic Myotomy) was introduced by Li et al., aiming to fully cut the septum to prevent recurrence after forming a submucosal tunnel to mitigate the risk of perforation(57). In this method, the mucosal roof of the muscular septum is usually left intact. However the efficacy of this procedure is still under investigation, as a recent study revealed a relatively high recurrence rate(50). The European Society of

Gastrointestinal Endoscopy (ESGE) considers this procedure experimental and recommends its performance within the context of research projects(58).

Regarding the evaluation of the efficacy of the flexible endoscopy in the treatment of Zenker's diverticulum, a meta-analysis conducted by Ishaq et al. involving 813 patients, revealed a success rate of 91%, with an adverse event rate of 11.3% and a recurrence rate of 11%(59).

The recurrence of Zenker's diverticulum is not uncommon, irrespective of the treatment approach. Factors predisposing to recurrence in the first 48 months include a diverticulum size of more than 5 cm before treatment, septotomy length of less than 25 mm, as well as diverticulum size of more than 10 mm after treatment(60).

For the treatment of recurrence, a study of flexible endoscopy diverticulotomy conducted by Antonello et al. on 25 patients with recurrence of symptoms is reported. The results were compared to 34 treatment-naïve patients. It was found that the success, recurrence, and complication rates did not show significant differences. The study concluded that the flexible endoscopy method is both safe and effective for treating recurrences(61).

1.4 Research question

There is no consensus on the optimal approach for managing ZD, with many patients undergoing conservative, surgical intervention via the transcervical approach, or endoluminal procedures using either rigid or flexible endoscopy. The choice of management often depends on the medical specialty responsible for diagnosing the patient(17). The European Society of Gastrointestinal Endoscopy (ESGE) has recommended flexible endoscopic treatment as the first-line therapy for ZD with only weak recommendation based on the low quality of evidence(58). Inline, prospective studies comparing surgical approaches (open or using rigid endoscopy) versus the flexible endoscopy approach are mostly lacking.

In our tertiary university institution, we conducted a direct retrospective comparison of all patients treated by the flexible endoscopy method or the rigid endoscopy method using laser technique in the study period from January 1st 2009 to October 27th 2021. The aim of the study was to compare efficacy in terms of clinical improvement, defined as the absence or improvement of symptoms at a minimum of 3 months after the procedure. Secondary outcomes included the safety of the procedures in terms of the

incidence of complications, time to onset of oral consumption, duration of hospital stay, recurrence and reintervention rates.

Hereby, we aimed to draw conclusions regarding the differences between the two methods, enabling us to formulate a statement regarding the first modality of choice for managing patients with symptomatic Zenker’s diverticulum.

2 Materials and Methods

2.1 Study population

This retrospective study included all adult patients who underwent treatment for symptomatic Zenker's Diverticulum either using flexible endoscopy or rigid endoscopy at our tertiary university institution (Klinikum Oldenburg, Oldenburg, Germany). The study period was defined from January 1st 2009 to October 27th 2021.

Identification of eligible patients for the study was conducted using a query in the Clinic patient management program (ClinicWinData, E&L medical systems GmbH, Erlangen) utilizing OPS and ICD-codes.

After identifying the patients to be included in the study, personal data (name and date of birth) were pseudonymized.

Eligible patients (n=136) were divided into two treatment groups. Of these, 88 patients received myotomy by a flexible gastroscope using a needle knife (Gastroenterology group), while 48 patients were treated with rigid endoscopic CO_2 laser myotomy in the operating theater of the otolaryngology department (ENT "Ear-Nose-Throat" group).

Inclusion criteria

All patients treated for symptomatic Zenker's Diverticulum at Klinikum Oldenburg, Oldenburg, Germany between January 1st2009, and October 27th 2021, in either the Gastroenterology department or the otolaryngology department. Age above 18 years.

Exclusion criteria:

Age under 18 years. For the evaluation of the primary endpoint regarding clinical improvement, patients who did not undergo any clinical or endoscopic evaluation after a minimum of 3 months post-procedure were excluded. In cases where no improvement or if a recurrence of symptoms occurred within the defined 3-month period, the clinical follow-up data of these patients were included in the statistical analysis.

2.2 Treatment procedures

2.2.1 Gastroenterology group

In the Gastroenterology group, Initially, between 2009 and 2016, the procedures were performed under conscious sedation. However, following an intraprocedural arterial

bleeding event, a transition was made to performing the procedures under general anaesthesia from 2016 to 2020. After reevaluation of the literature and the own data, the procedure was once again conducted under conscious sedation from 2020 onwards. Consequently, approximately 59% (n=52) of the procedures in the Gastroenterology group were performed under conscious sedation using intravenous propofol.

The patient was positioned in a left lateral position. Following sedation and the application of a mouthpiece to protect the teeth, the gastroscope (Olympus GIF 1TQ160, GIF-HQ190 or GIF-Q180) was introduced through the mouth opening. ZD was meticulously inspected for any debris. A complete esophagogastroduodenoscopy was performed to rule out any other pathology in the upper gastrointestinal tract. Following this, a nasogastric tube was placed into the stomach under endoscopic guidance to prevent perforation of the diverticulum.

A distance cap was placed over the tip of the gastroscope, aiding in stabilization and offering improved visualization of the operative field.

Using a needle papillotome (FUJIFILM medwork 2.8mm), an incision was made in the middle of the diverticular septum, with the goal of stepwise cutting of the mucosa and submucosa to expose the muscle layer (figures 1 and 2). The muscle fibers were cautiously cut to reach the buccopharyngeal fascia. Any bleeding during the procedure is typically managed using coagulation current. The standard settings for the electrosurgical unit (ERBE VIO 200D) were (Effect 2, duration 3, interval 3, coagulation 50W). Upon completion of cutting the muscular septum, the immediate efficacy of therapy was assessed by testing the passage of the gastroscope with the mounted cap in the esophagus and comparing it to pre-therapy passage. The septal defect was typically closed using three to four clips.

Following the procedure, patients were typically transferred to the regular ward. Those who received general anesthesia were monitored in intermediate care unit until they are extubated, and they were usually returned to the regular ward on the same day. Consumption of water and tea was permitted on the same day, while oral nutrition was usually resumed after one to two days.

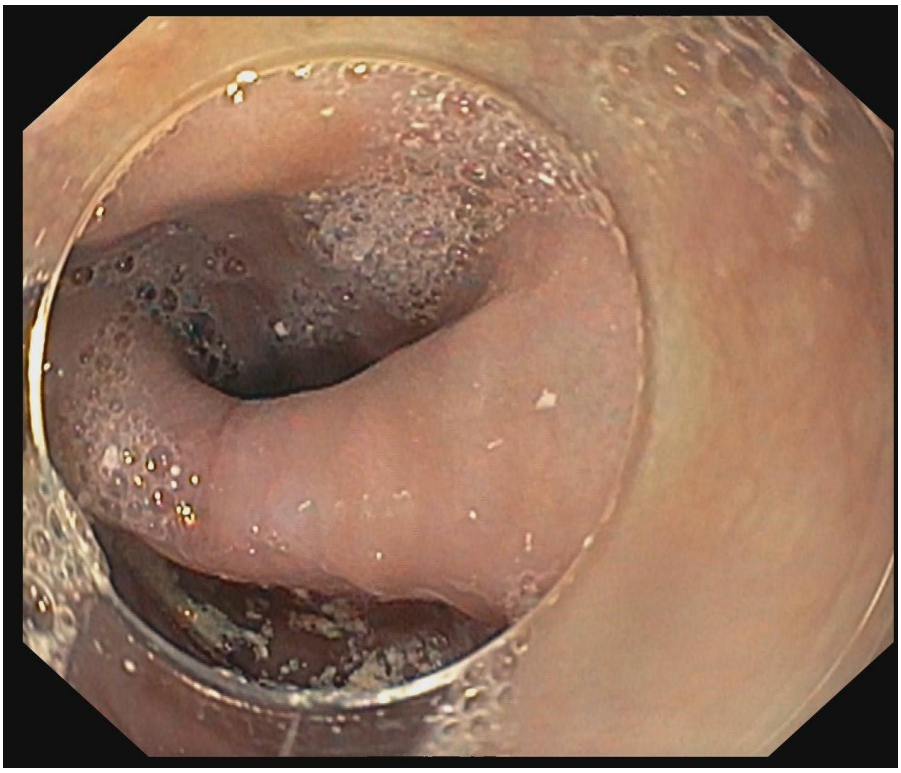

Figure 1: endoscopic view of Zenker's diverticulum (ZD) during treatment.

This endoscopic image illustrates a key intra-procedural step in the management of Zenker's diverticulum. The septum of the diverticulum is clearly visualized and stabilized using a mounted cap, facilitating precise endoscopic intervention. The image highlights the anatomical distinction between the diverticular pouch (lower portion), where residual food debris is still present, and the true lumen of the esophagus (upper portion). The presence of food residue underscores the functional impairment associated with ZD, reinforcing the need for effective therapeutic intervention.

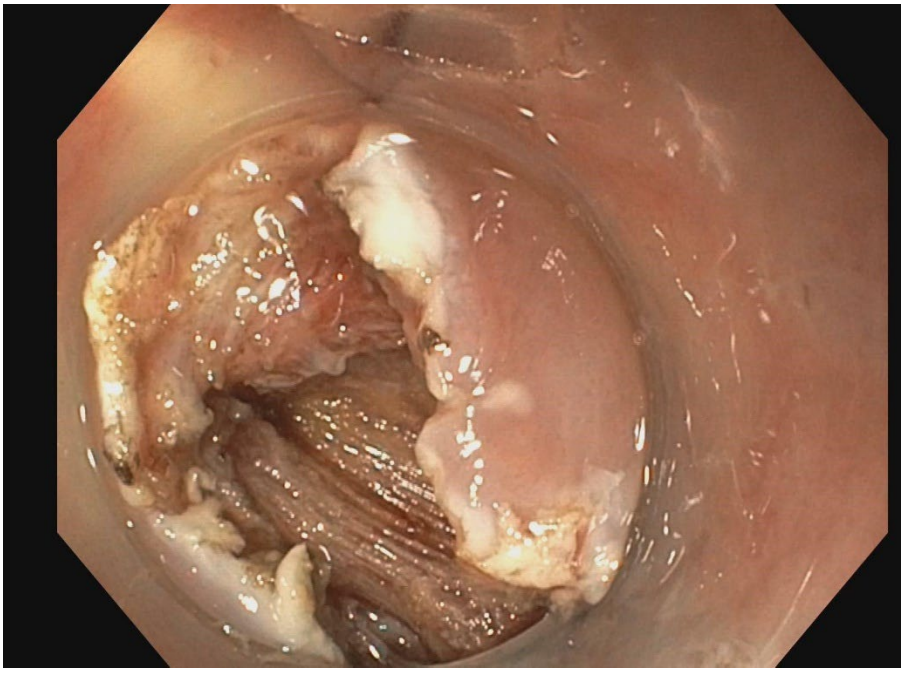

Figure 2: Post-dissection view of the Zenker's diverticulum septum.

This endoscopic image demonstrates the post-dissection appearance of the Zenker's diverticulum (ZD) septum following a stepwise myotomy. After sequential cutting of the mucosa and submucosa, the underlying muscle fibers are clearly exposed. The partially incised septum reveals deeper muscular layers and connective tissue, indicating the progression of the myotomy.

2.2.2 ENT group

In the rigid endoscopy group, all procedures were performed under general anesthesia with endotracheal intubation in the operating theatre. The patient was placed in a supine position with the head tilted backwards through neck extension. After inserting a mouthpiece to protect the teeth, a Weerda diverticuloscope was introduced to expose the septum of the Zenker diverticulum. A moist sponge was placed in the esophagus to protect the esophageal mucosa. The ZD was thoroughly inspected and cleaned from any food debris. An operating microscope was utilized to apply CO2 laser waves (4 to 6-Watt super pulse). The muscle fibers of the septum were incised until the appearance of the buccopharyngeal fascia. Any bleeding was coagulated. At the conclusion of the operation, a nasogastric tube was inserted. Following extubation, the patient was typically returned to the regular ward on the same day. Prophylactic antibiotics were usually administered and continued for approximately 5 days after the procedure. Enteral nutrition via the nasogastric tube was typically administered for 4 to 5 days, after which oral nutrition was permitted.

2.3 Data collection

We collected the following data from the clinical information system, including discharge letters and procedure reports, using the Medico program and Clinic Windata program:

- Age in years
- Gender
- The presence of any previous intervention
- Technical success
- Endotracheal intubation
- Duration of intervention in minutes
- Complications (major and minor)
- Mortality
- Duration of stay in the hospital in days

- Time to resumption of oral intake in days
- Recurrence of the diverticulum
- Reintervention for recurrence
- Final clinical improvement

2.4 Data analysis

The aim of the study was to compare efficacy in terms of clinical improvement, defined as the absence or improvement of symptoms at a minimum of 3 months after the procedure between the two treatment groups. Secondary outcomes included the safety of the procedures in terms of the incidence of complications, time to onset of oral consumption, duration of hospital stay, recurrence and reintervention rates.

Primary Endpoint:

- The primary aim of the study was to compare efficacy in terms of clinical improvement, defined as the absence or improvement of symptoms at a minimum of 3 months after the procedure between the two treatment groups.

Secondary Endpoints:

- Secondary outcomes included the safety of the procedures, assessed by the incidence of complications.
- Additional secondary endpoints were the time to onset of oral intake, duration of hospital stay, recurrence rate, and reintervention rate.

2.5 Regression Analysis

Univariate regression analysis was performed for clinically relevant variables, e.g. clinical improvement after therapy, recurrence and reintervention. Multivariable regression analyses were used with a stepwise forward model to determine risk factors for the occurrence of the three parameters above in which all univariate significant variables were included. At each step, variables were chosen based on p-values and a p-value threshold of 0.1 was used to set a limit on the total number of variables included in the final model. Results were given as odds ratios, 95% confidence intervals and p-values. P-values of less than 0.05 were considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics 29.0 (IBM Corp., Armonk, New York, USA).

Due to incomplete data on diverticulum depth within the ENT group, regression analysis was limited to the Gastroenterology cohort. As a result, it remains uncertain whether these findings are applicable to the ENT group.

2.6 Calculations, statistics and presentations

Graphical presentations, standard deviation calculations, and median computations were performed using IBM SPSS Statistics (Version 29.0.0.0 (241)). A p-value < 0.05 was considered statistically significant. The thesis was processed using Microsoft Word 2016 MSO.

Data are presented as means ± standard deviation (SD) for continuous variables and as frequencies and percentages for categorical variables. Continuous variables were compared using the Mann-Whitney U test, while categorical variables related to patient characteristics and procedural parameters were analyzed using the Fisher's Exact Test and the Fisher-Freeman-Halton Test. Results are reported as odds ratios (OR), 95% confidence intervals (CI), and p-values. Statistical analyses were conducted using IBM SPSS Statistics 29.0.

2.7 Ethic approval

The study was conducted in accordance to the Standards set in the Declaration of Helsinki 1964 and its later amendments, and it was approved by the local ethic committee (Number 2022-018).

3 Results

As outlined above, we conducted a retrospective study on all patients treated in the time period from January 1st 2009 to October 27th 2021 for ZD in our tertiary university center. We compared the flexible endoscopy method performed in 88 patients and the rigid endoscopy method using laser technique involving 48 patients in this time period. We compared efficacy in terms of clinical improvement, defined as the absence or improvement of symptoms at a minimum of 3 months after the procedure. Secondary outcomes included the safety of the procedures in terms of the incidence of complications, time to onset of oral consumption, duration of hospital stay, recurrence and reintervention rates.

3.1 Patients' characteristics

In the flexible endoscopy group, data were obtained from 88 patients who underwent therapy for Zenker's Diverticulum between January 2009 and October 2021, with 46 of them being males. For the ENT group, data were collected from 48 patients during the same period, including 32 males. Thus, the gender distribution for both groups was 78 males and 58 females. The mean age of patients in both groups was 70 years, ranging from 43 to 93 years. There was no significant difference in age distribution between the two groups, with a mean age of 70 years in the Gastroenterology group and a mean age of 68 years in the ENT group. Among female patients, the mean age was 75 years, while among males, it was 66 years.

The most common group comprised patients aged between 70 and 89 years, totaling 79 patients.

Table 1: Patient demographic

Comparison of the median age with the interquartile range, and gender distribution between the two study groups. IQR = interquartile range.

	Total (n=136)	Gastro (n=88)	ENT (n=48)
Male sex (%)	78 (57.35%)	46 (52.27%)	32 (66.66%)
Age, median [IQR]	71 [64; 77.5]	72 [65; 78]	70 [63; 76]

3.2 Previous Interventions

The majority of patients in both groups (n=129) did not have any previous intervention. In the Gastroenterology group, six patients had undergone previous interventions: four

had previous ENT therapy, one had undergone previous flexible endoscopy intervention, and one had undergone open surgical therapy.

In the ENT group, one patient had a previous intervention in the same department one year prior, and due to recurrence of symptoms, a reintervention was performed in the ENT department. Subsequently, a final intervention was conducted for this patient in the Gastroenterology department due to persistence of complaints.

Table 2: Proportion of previous interventions

Comparison of whether patients in each group received a pre-intervention before the main procedure. For those who received a pre-intervention, the type of intervention is detailed.

Parameters	Total (n=136)	Gastro (n=88)	ENT (n=48)
No previous interventions	129 (94.85%)	82 (93.18%)	47 (97.9%)
Endoscopic preintervention	1 (0.7%)	1 (1.1%)	0 (0.0%)
ENT preintervention	5 (3.6%)	4 (4.5%)	1 (2.1%)
Surgical preintervention	1 (0.7%)	1 (1.1%)	0 (0.0%)

3.3 Technical success of the interventions

The intervention was successfully completed in all patients in the Gastroenterology group. However, in the ENT group, two patients experienced treatment failure. The first patient had stiffness in the cervical vertebrae, which hindered achieving adequate neck reclination. Consequently, the procedure was performed in the Gastroenterology department using flexible endoscopy. In the second patient, intubation of the esophagus with esophagoscope was not feasible due to muscular stenosis caused by the Zenker diverticulum. This patient was subsequently referred to the Gastroenterology department, where the procedure was conducted using flexible endoscopy.

3.4 Duration of the intervention

Regarding the duration of intervention (figure 3 and table 3), we observed a difference between the two groups ($p = 0.004$, Mann-Whitney U test). In the Gastroenterology group, the mean duration was 30.8 minutes (Std. deviation 12.67), while the median duration was 27 minutes which is 7 minutes shorter than 33 minutes in the ENT group (95% CI = [2.0, 13.0]). The shortest duration of intervention, 12 minutes, was recorded in the Gastroenterology group, while in the ENT group, the shortest duration of

intervention was 15 minutes (measured from the start of the diverticuloscope application). The mean duration in the ENT group was 39.74 minutes (Std. Deviation 17.11). The median duration in the ENT group was 35.50 minutes.

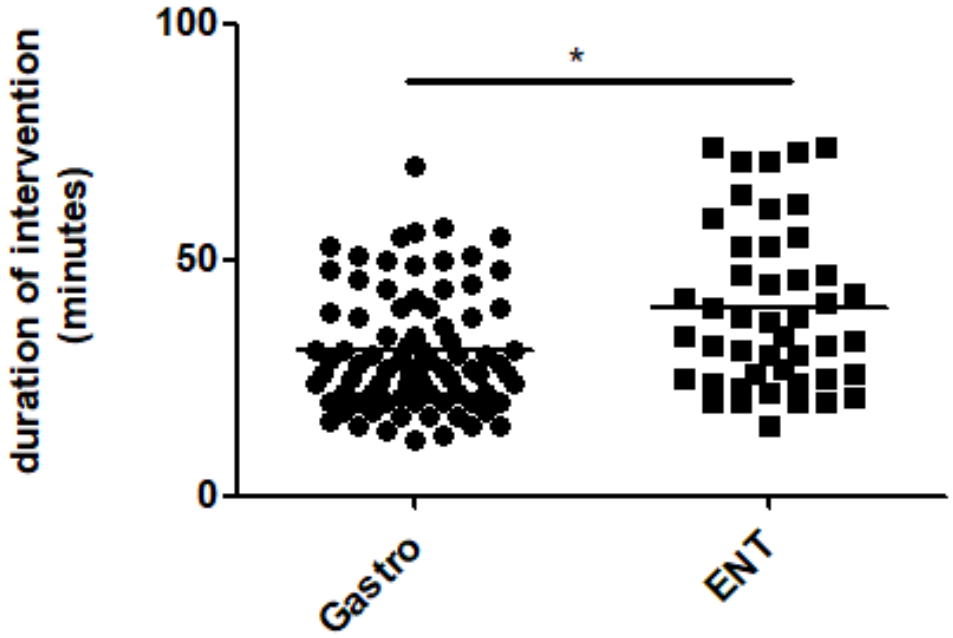

Figure 3: Duration of intervention

The diagram compares the duration of intervention between the two study groups. The distribution indicates that the Gastroenterology group had a shorter duration of intervention. * indicates a statistically significant p-value (p = 0.004, Mann-Whitney U test).

Table 3: Duration of intervention

Comparison of the mean duration of intervention between the Gastroenterology and the ENT groups, showing shorter duration in the Gastroenterology group (p=0.004). [1]*p* <0.05 as considered significant. [2]Mann-Whitney U test.

Intervention type	Mean duration of intervention in minutes (range)	*p* value[1]
Gastroenterology	30.8 (12 – 70)	0.004[2]
ENT	39.7 (15 – 74)	

3.5 Complications

In the Gastroenterology group, we observed complications in 9 patients (10.2%), while in the ENT group, the complication rate was 2 patients (4.2%), as shown in table 5. However, we did not detect a statistically significant difference between the two groups (p = 0.327 Fisher's exact test).

In the Gastroenterology group, a total of nine complications were documented, including two perforations and two cases of emphysema, all of which were interpreted as major complications. The remaining five complications consisted of bleeding and fever. One of the patients with perforation died.

In the ENT group, two complications were reported. The first was a perforation, which was managed using sponge-vacuum therapy and the placement of a metal stent. The second complication was hoarseness of voice due to recurrent laryngeal nerve paresis.

Table 4: Complication rates

Summary of the complication rates of the two study groups. Although there are differences in the complication rates, the p-value of 0.327 was not statistically significant. [1]*p* <0.05 was considered significant. [2]Fisher´s exact test.

Parameters	Gastro	ENT	*p* value[1]
Complications	9 / 10.2%	2 / 4.2%	0.327[2]
Major complications	4 / 4.5%	1 / 2.1%	
Minor complications	5 / 5.6%	1 / 2.1%	
No Complications	79 / 89.8%	46 / 95.8%	
Total	88 / 100%	48 / 100%	

3.6 Resumption of oral intake

In terms of the number of days until resumption of oral intake postoperatively, we observed a difference between the two groups (p = < 0.001, Mann-Whitney U test). In the Gastroenterology group, the median duration was two days shorter than in the ENT group (95%-CI = [2.0, 3.0]).

Table 5: Resumption of oral intake

Comparison of mean time to resumption of oral intake between the Gastroenterology and the ENT groups, showing a faster resumption in the Gastroenterology group. Mean time to resumption of oral intake in days with standard deviation (p < 0.001). [1]*p* <0.05 was considered significant. [2]Mann-Whitney U test.

Intervention type	resumption of oral intake in days (SD)	*p* value[1]
Gastroenterology	1.9 (1.04)	< 0.001[2]
ENT	4.5 (3.25)	

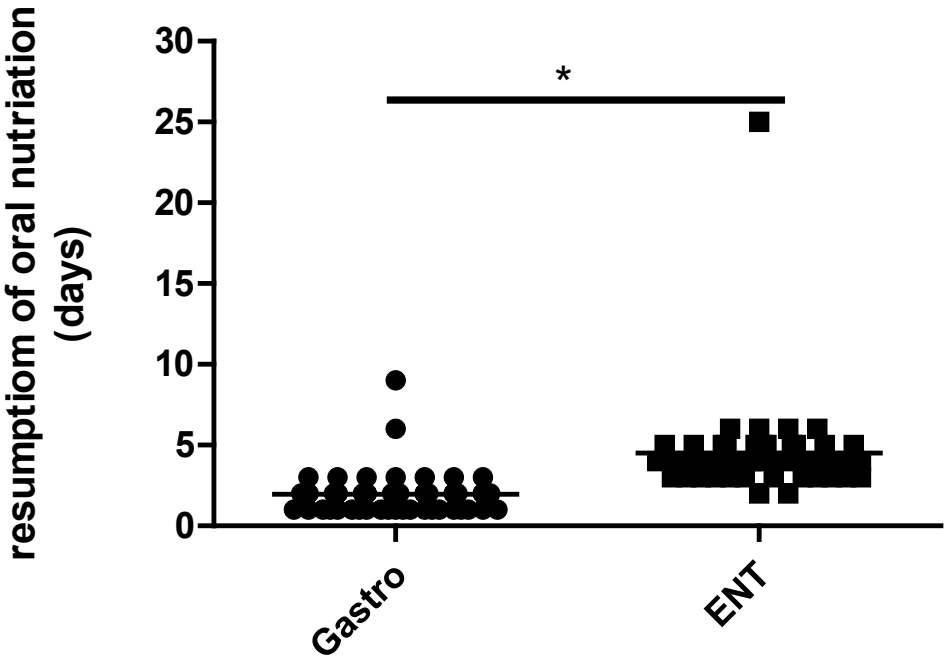

Figure 4: Time of resumption of oral intake

The diagram compares the duration in days till resumption of oral intake between the two study groups. The distribution indicates that the Gastroenterology group had a shorter duration till resumption of oral intake with a statistically significant p-value ($p < 0.001$, Mann-Whitney U test).

3.7 Length of hospital stay

There was a significant difference between the two groups regarding the duration of hospital stay in days ($p = <0.001$, Mann-Whitney U test) (figure 5 and table 6). In the Gastroenterology group, the median number of days was 2 days shorter than in the ENT group (95% CI = [1.0, 2.0]).

Table 6: Duration of hospital stay

Comparison of mean hospital stay duration in days (with standard deviation) between the Gastroenterology and ENT groups, showing a shorter stay in the Gastroenterology group ($p < 0.001$). . [1]*p* <0.05 was considered significant. [2]Mann-Whitney U test.

Intervention type	Mean duration of stay in days (SD)	*p* value[1]
Gastroenterology	5.4 (2.29)	<0.001[2]
ENT	7.5 (4.8)	

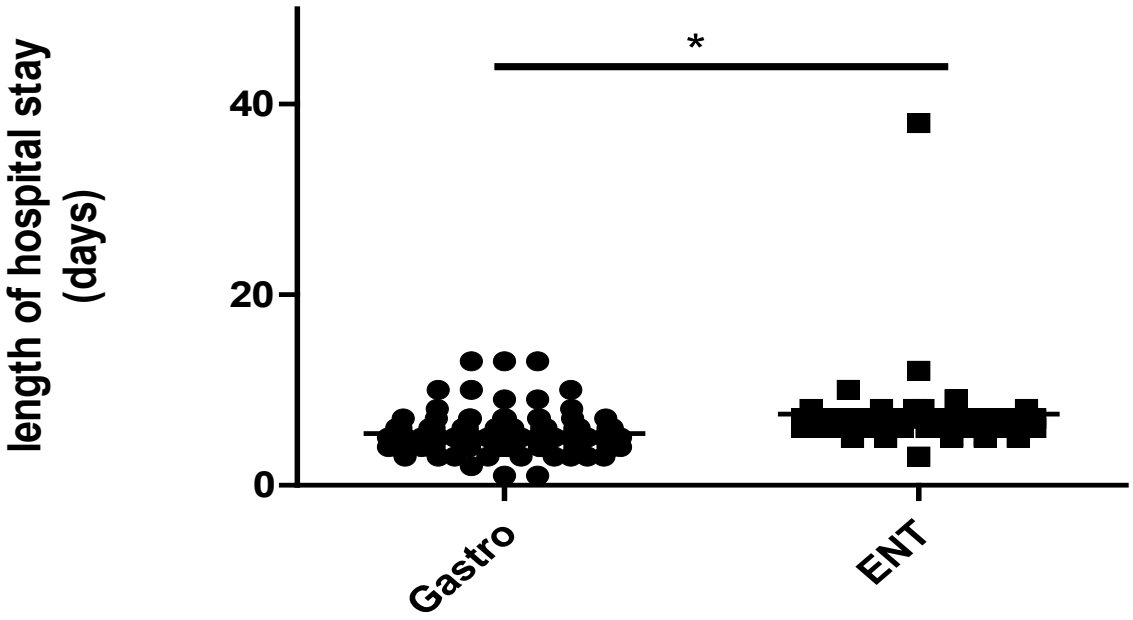

Figure 5: Duration of hospital stay

The diagram compares the duration of hospital stay in days between the two study groups. The distribution indicates that the Gastroenterology group had a shorter hospital stay with a statistically significant p-value ($p < 0.001$, Mann-Whitney U test).

3.8 Follow-Up Data

The assessment of the clinical improvement was based on patient-reported feedback after the final procedure or the objective endoscopic findings, even if the patient had to receive more than one intervention.

To assess the necessity of multiple interventions to achieve clinical improvement, a separate analysis regarding recurrence and reintervention rate was conducted.

In the ENT group, we managed to collect follow-up data for clinical evaluation from 29 out of 48 patients (60%) within a minimum period of 3 months. The longest follow-up period was 12 years. The clinical evaluation for the ENT group primarily relied on a questionnaire sent to each patient by post, inquiring about their pre-operative complaints and whether they improved, worsened, or remained the same post-operatively. To prevent outliers, the two patients in the ENT group who did not receive therapy due to inability to expose the diverticulum, were excluded from the statistical analysis regarding follow-up results, recurrence, duration of intervention, and duration of hospital stay.

In the Gastroenterology group, follow-up data were obtained from 61 out of 88 patients (69.3%) within a minimum period of three months. In cases with lost follow-up data,

where there was no improvement or recurrence of symptoms within three months, the data were included in the analysis. The longest follow-up period was 8 years.

3.8.1 Symptoms

In the Gastroenterology group, 54 out of 61 patients (88.5 %) reported improvement or absence of symptoms after the final intervention. Six patients (9.8%) did not notice any difference of symptoms, while one patient (1.6%) experienced worsening of symptoms due to a complication of perforation, attributed to a wide septum of ZD (figure 6).

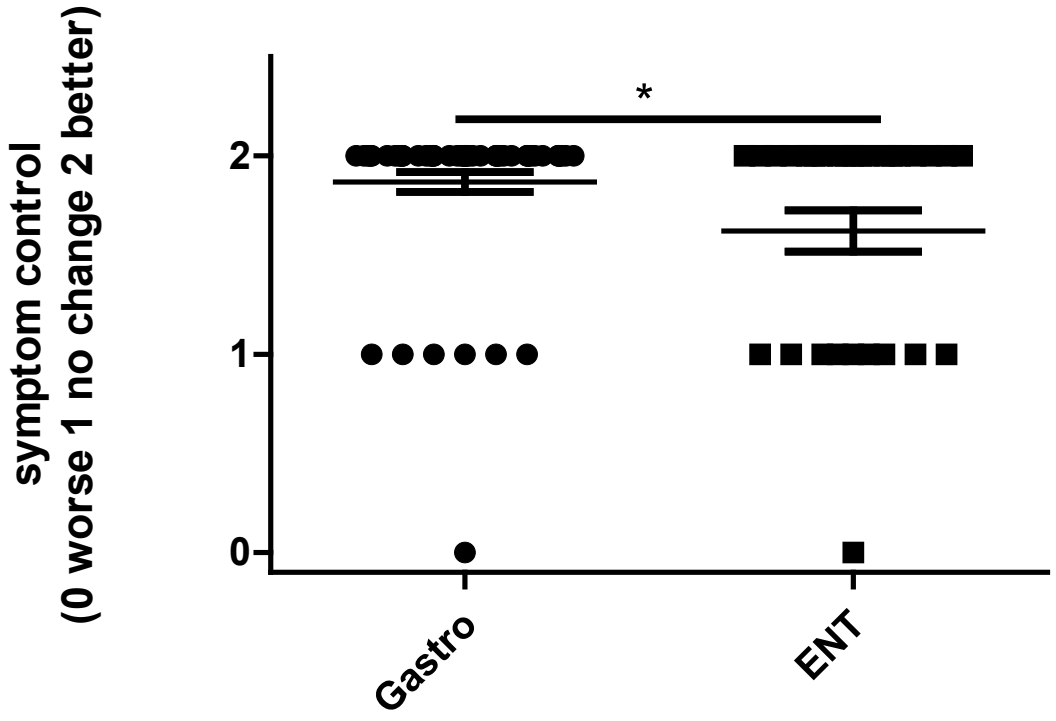

Figure 6: Symptom control after intervention

The chart shows symptom follow-up data as a percentage after the final intervention in the two groups, with the y-axis indicating the percentage of patients. This visualization allows for a clear comparison of symptom outcomes across both groups following treatment.

For the ENT group, 19 out of 29 patients (65.5%) reported improvement of symptoms, while nine patients (31.0%) did not notice any difference postoperatively. One patient (3.4%) experienced worsening of symptoms, which was attributed to a small residual Zenker diverticulum identified during gastroscopy. Whether this residual diverticulum was responsible for the symptoms or if the symptoms were related to motility disorders remained unclear. We observed a statistical difference between the two intervention groups (p = 0.015 Fisher-Freeman-Halton).

3.8.2 Recurrence rate after the initial procedure

After a follow-up period of at least three months, we collected clinical data indicating recurrence of Zenker diverticulum, either through the persistence of symptoms or through endoscopic evaluation, in the two groups. Patients experiencing recurrence of symptoms within a period of less than three months were not excluded from the analysis. Data was available from 61 (69.3%) patients in the Gastroenterology group and from 29 (60%) patients in the ENT group. Among the Gastroenterology group, 21 (34.4%) patients were documented to have recurrence of Zenker's Diverticulum symptoms. Comparable numbers of 9 (32.1%) patients in the ENT group reported recurrence of symptoms. No statistical difference was observed between the two groups (p = 1.00 Fisher's exact Test).

Table 7: Recurrence rate

Comparison of recurrence rates after the first procedure between the Gastroenterology and ENT groups, showing no significant difference between the groups (p = 1.0). [1]p <0.05 was considered significant. [2]Fisher's exact test.

Intervention type	No recurrence	Recurrence	Total	p value[1]
Gastroenterology	40 / 65.6%	21 / 34.4%	61 / 100%	1.0[2]
ENT	19 / 67.9%	9 / 32.1%	28 / 100%	
Total	59 / 66.3%	30 / 33.7%	89 / 100%	

3.8.3 Reintervention rate

We collected data for patients requiring reintervention due to recurrence or persistence of symptoms after the first procedure. In the Gastroenterology group, data were available for 61 patients, with 18 patients (29.5%) undergoing reintervention for managing ZD. For the ENT group, we obtained data from 29 patients, with 4 patients (13.8%) receiving reintervention. We did not observe a statistical difference between the two groups (p = 0.123).

Table 8: Reintervention rate

Comparison of reintervention rates after the first procedure between the Gastroenterology and ENT groups, showing no significant difference between the groups (p = 0.123). [1]*p* <0.05 was considered significant. [2]Fisher's exact test.

Intervention type	No reintervention	Reintervention	Total	*p* value[1]
Gastroenterology	43 (70.5%)	18 (29.5%)	61 (100%)	0.123[2]
ENT	25 (86.2%)	4 (13.8%)	29 (100.0%)	
Total	68 (74.7%)	22 (24.4%)	90 (100.0%)	

3.9 Regression analysis

3.9.1 Clinical improvement

In this regression analysis as highlighted in table 9 and 10, we aimed to identify factors potentially associated with clinical improvement following endoscopic therapy. Both univariable (Table 9) and multivariable logistic regression analyses (Table 10) were performed to explore the influence of various clinical parameters. The outcome of interest was defined as clinical improvement after therapy.

Table 9: Logistic univariable regression analysis - clinical improvement

Logistic univariable regression analysis of variables potentially influencing clinical improvement after endoscopic therapy (dependent variable). Results were given as odds ratios, 95% confidence intervals and p-values (statistical significance: * p<0.05).

Parameter	OR	95% CI	p value
Age	0.979	0.895-1.071	0.645
Male gender	1.179	0.239-5.809	0.840
Depth of diverticulum	0.981	0.908-1.059	0.619
Complication	**0.136**	**0.023-0.789**	**0.026** *
Reintervention	0.269	0.053-1.356	0.112

Table 10: Logistic multivariable regiossion analysis - clinical improvement

Logistic multivariable regression analysis of variables potentially influencing clinical improvement after endoscopic therapy (dependent variable). Results were given as odds ratios, 95% confidence intervals and p-values (statistical significance: * p<0.05).

Parameter	OR	95% CI	p-value
Complication	**0.116**	**0.018-0.739**	**0.023** *

Among the variables analyzed, the occurrence of complications emerged as the only statistically significant factor in both univariable and multivariable analyses. In the univariable model, the presence of complications was associated with a significantly reduced likelihood of clinical improvement (OR 0.136, 95% CI 0.023–0.789, $p = 0.026$). This association remained significant after adjusting for other variables in the multivariable model (OR 0.116, 95% CI 0.018–0.739, $p = 0.023$).

Other variables, including age, gender, depth of the diverticulum, and the need for reintervention, did not show statistically significant associations with clinical improvement in this cohort. Age and diverticulum depth had odds ratios close to 1.0, indicating minimal or no effect, and wide confidence intervals suggested uncertainty around their estimates. Similarly, male gender and reintervention showed no meaningful influence on the likelihood of clinical improvement.

3.9.2 Recurrence

This analysis aimed to identify clinical and procedural factors associated with recurrence after the initial endoscopic therapy (tables 11 and 12). Using both univariable (table 11) and multivariable logistic regression models (table 12), we investigated the potential influence of patient demographics and treatment-related variables on the likelihood of recurrence.

Among the variables examined, two factors - depth of the diverticulum and the occurrence of complications - were significantly associated with recurrence in both univariable and multivariable analyses.

Table 11: Logistic univariable regression analysis - recurrence

Logistic univariable regression analysis of variables potentially influencing recurrence after endoscopic therapy (dependent variable). Results were given as odds ratios, 95% confidence intervals and p-values (statistical significance: * p<0.05).

Parameter	OR	95% CI	p value
Age	1.009	0.952-1.070	0.761
Male gender	2.045	0.659-6.353	0.216
Previous intervention	0.000	0.000	0.999
Depth of diverticulum	**1.071**	**1.009-1.137**	**0.024** *
Complication	**5.937**	**1.041-33.853**	**0.045** *

Table 12: Logistic multivariable regiossion analysis - recurrence

Logistic multivariable regression analysis of variables potentially influencing recurrence after endoscopic therapy (dependent variable). Results were given as odds ratios, 95% confidence intervals and p-values (statistical significance: * p<0.05).

Parameter	OR	95% CI	p value
Depth of diverticulum	**1.078**	**1.013-1.147**	**0.018** *
Complication	**7.473**	**1.148-48.663**	**0.035** *

A greater diverticulum depth was independently associated with an increased risk of recurrence after the initial endoscopic therapy. In the univariable analysis, the odds ratio was 1.071 (95% CI: 1.009–1.137, $p = 0.024$), and this effect remained significant in the multivariable model (OR 1.078, 95% CI: 1.013–1.147, $p = 0.018$).

Additionally, the presence of complications during or after the procedure was significantly associated with higher recurrence rates after the initial flexible endoscopic therapy. The univariable analysis revealed an odds ratio of 5.937 (95% CI: 1.041–33.853, $p = 0.045$), which increased to 7.473 (95% CI: 1.148–48.663, $p = 0.035$) after adjusting for other variables in the multivariable model.

Other variables, including age, gender, and previous intervention, did not show a statistically significant association with recurrence.

3.9.3 Reintervention

This analysis aimed to identify predictors of reintervention after endoscopic therapy, with a particular focus on patient and procedural characteristics. Using logistic regression models, we evaluated both univariable (table 13) and multivariable (table 14) associations between several variables and the need for repeat intervention.

Table 13: Logistic univariable regression analysis - reintervention

Logistic univariable regression analysis of variables potentially influencing reintervention after endoscopic therapy (dependent variable). Results were given as odds ratios, 95% confidence intervals and p-values (statistical significance: * p<0.05).

Parameter	OR	95% CI	p value
Age	1.026	0.962-1.094	0.437
Male gender	3.043	0.861-10.756	0.084
Previous intervention	0.000	0.000	0.999
Depth of diverticulum	**1.088**	**1.091-1.161**	**0.012***
Complication	2.786	0.613-12.667	0.185

Table 14: Logistic multivariable regiossion analysis - reintervention

Logistic multivariable regression analysis of variables potentially influencing reintervention after endoscopic therapy (dependent variable). Results were given as odds ratios, 95% confidence intervals and p-values (statistical significance: * p<0.05).

Parameter	OR	95% CI	p value
Depth of diverticulum	**1.088**	**1.091-1.161**	**0.012***

Among all factors analyzed, depth of the diverticulum was the only variable significantly associated with reintervention in both univariable and multivariable models. The odds ratio was 1.088 (95% CI: 1.019–1.161, $p = 0.012$) in both analyses, indicating that with increasing diverticulum depth, the likelihood of requiring a subsequent intervention increases significantly.

Although not statistically significant, male gender demonstrated a trend toward increased risk of reintervention (OR 3.043, 95% CI: 0.861–10.756, $p = 0.084$).

Other variables, including age, complications, and previous intervention, did not show statistically significant associations with the need for reintervention.

3.10 Summary of the clinical outcome of the procedures

We present here a flow chart for the Patients with Zenker Diverticulum included in the study from January 2009 to October 2021, followed by table representations of the study results regarding the different secondary Endpoints.

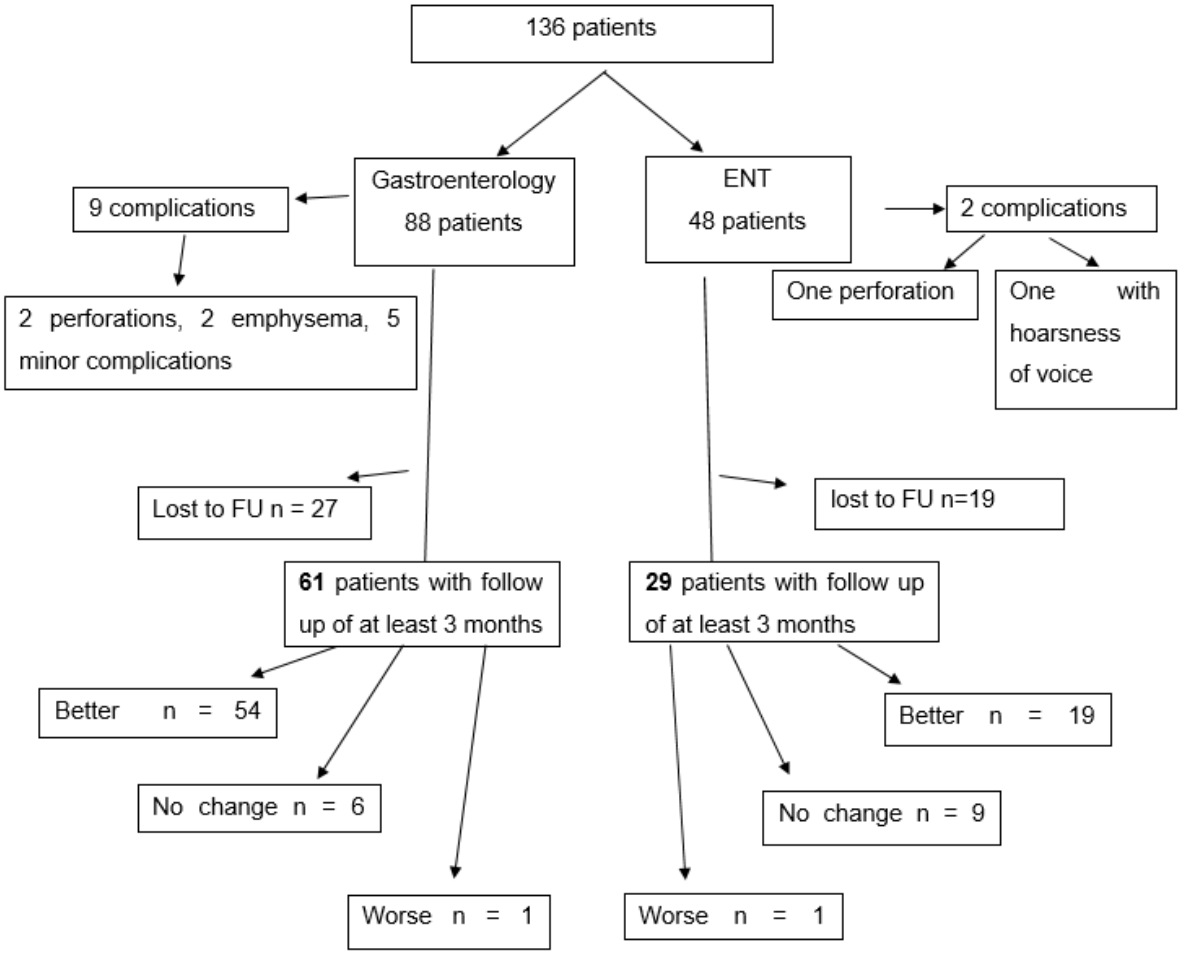

Figure 7: Flow chart of the results of the study

The flow chart provides an overview of patient distribution and outcomes for the two therapeutic interventions. It shows the total number of patients included in the study, along with the number of patients lost to follow-up and those who experienced complications. Additionally, the chart represents the efficacy of each procedure, illustrated by symptom follow-up data, allowing for a visual comparison of therapeutic success and challenges between the two interventions.

Table 15: Summary of the outcome of the study groups

Summary of the outcome parameters for both study groups.[1]*p* <0.05 was considered significant. [2]Mann-Whitney U test. [3]Fisher's exact test. [4]Mann-Whitney U test. [5]Fisher-Freeman-Halton

Parameters	Gastro group	ENT group	*p*-value[1]
Mean age in years	70	68	
Gender	52.27% males	66.66% males	
Previous intervention	6.8%	2.08%	
Technical success	100%	95.83%	
Endotracheal intubation	36 (41%)	48 (100%)	
Mean duration of intervention in minutes (range)	**30 (12-70)**	**39 (15-74)**	***p* < 0.004[2]**
Complications	**9 (10.2%)**	**2 (4.2%)**	***p* = 0.327[3]**
Mortality	1	0	
Mean duration of hospital stay in days (Std. Deviation)	**5.4 (2.29) Range (1-13)**	**7.5 (4.8) Range (3-38)**	***p* < 0.001[4]**
Mean time to resumption of oral intake in days (Std. Deviation)	**1.9 (1.04) Range (1-9)**	**4.5 (3.25) Range (2-25)**	***p* < 0.001[4]**
Recurrence of the diverticulum	21 (34.4%)	9 (32.1%)	*p* = 1.00[3]
Reintervention for recurrence	18 (29.5%)	4 (13.8%)	*p* = 0.123[3]
Final clinical improvement	**54 (88.5%)**	**19 (65.5%)**	***p* = 0.015[5]**

4 Discussion

There are different therapeutic approaches for the management of Zenker's Diverticulum including open surgical approaches, rigid endoscopic procedures, and minimally invasive techniques using flexible endoscopy. Unfortunately, there is no standardized therapeutic option, meaning that the type of therapy a patient receives largely depends on the expertise and department where the diagnosis is made.

Given this variability, we aimed to leverage the relatively high number of cases treated in our institution, either in the Gastroenterology department using the flexible endoscopy or in the ENT department using rigid endoscopy and CO2 Laser, to clarify the advantages and disadvantages of each procedure, considering clinical improvement, recurrence, and complication rates.

We collected data from 136 patients treated for Zenker's Diverticulum at our institution (Klinikum Oldenburg, Oldenburg Germany) between January 1st of 2009, and October 27th of 2021. Of these, 88 patients (46 males, median age 70 years) underwent treatment in the Gastroenterology group using flexible endoscopy, while 48 patients (32 males, median age 68 years) were treated in the ENT group using rigid endoscopy and CO2 laser.

Consistent with previous studies indicating Zenker's diverticulum as a disease of the elderly population(1), the most frequent age group in our study was between 70 and 89 years (n = 79). This underscores the necessity for minimally invasive and effective procedure for this patient demographic, which often suffers from other comorbidities and especially reduced neck mobility.

Notably, less than half of the patients in the Gastroenterology group (41%, n = 36) underwent the procedure with endotracheal intubation, compared to all patients in the ENT group (100%, n = 48) who underwent the procedure under general anesthesia with endotracheal intubation. This highlights a potential advantage of flexible endoscopy for patients, particularly if reintervention due to symptom recurrence is necessary.

However, by omitting endotracheal intubation, there is a risk of aspiration, especially in cases of bleeding or regurgitation of diverticulum contents. Our study observed one patient experiencing intraprocedural arterial bleeding with aspiration, prompting the gastroenterologist initially to shift toward using general anesthesia in the flexible endoscopy group for a short period of this study. Ultimately, the decision to avoid

endotracheal intubation rests with the experienced gastroenterologist, who must assess the benefit-risk ratio for each patient.

The procedure was successfully performed in all patients in the Gastroenterology group using flexible endoscopy. In the ENT-group, hyperextension of the neck posed a challenge for one patient with cervical vertebral stiffness, leading to referral to the Gastroenterology group for performing the procedure using flexible endoscopy. Another patient in the ENT group had muscular stiffness in the upper esophageal sphincter caused by the diverticular septum, resulting in unsuccessful exposure of the diverticulum using esophagoscope (pediatric or adult) or diverticuloscope. The procedure was successfully performed using flexible endoscopy in the Gastroenterology department.

The technical challenges associated with rigid endoscopic diverticulotomy have been well-documented in the literature and are often attributed to anatomical limitations that can impede adequate exposure and access. A literature review conducted by Dzeletovic et al. (22), which analyzed 11 studies published between 1995 and 2010, reported conversion rates from rigid endoscopy to an open surgical approach as high as 30% in one study with a small cohort (n = 23) (62). Notably, the largest study included in that review (n = 102) demonstrated a substantially lower conversion rate of 4% (63), suggesting that while technical difficulties are not uncommon, they may vary significantly depending on patient selection, operator and institutional expertise.

Our findings are consistent with the lower end of the reported conversion spectrum. In our ENT cohort, 2 out of 48 patients (4%) required a change in operative strategy, switching to flexible endoscopic diverticulotomy following unsuccessful attempts with the rigid technique. This rate mirrors the conversion figure reported in the largest cohort of the aforementioned review and underscores the practical limitations occasionally encountered with rigid endoscopy.

The primary factors contributing to these technical failures are anatomical in nature. Specifically, conditions such as pronounced dental overbite, cervical spine rigidity due to kyphosis, limited neck extension, and restricted oral aperture can compromise the feasibility of rigid diverticuloscope placement and maneuverability (7). These anatomic constraints can not only prolong the procedure but also increase the risk of intraoperative complications, making patient selection a critical determinant of procedural success.

Taken together, these observations emphasize the importance of pre-procedural anatomical assessment when considering rigid endoscopic approaches for Zenker's diverticulum. In cases where unfavourable anatomy is identified, flexible endoscopy may serve as a more suitable first-line intervention, thereby reducing the need for intraoperative conversion and associated morbidity.

Regarding previous interventions, managing patients with recurrent or persistent symptoms after prior interventions for Zenker diverticulum is challenging.

In our study, six patients in the Gastroenterology group had previous interventions (one surgical, four using rigid endoscopy, and one endoscopic). Follow-up data on symptom improvement after reintervention were available for only three of these patients, who reported symptom improvement. Regarding the complications, one patient experienced arterial bleeding during the reintervention.

In the ENT group, one patient had undergone two previous interventions in the same department within the prior three years. The procedure was repeated using rigid endoscopy and CO2 laser, resulting in perforation, which was managed with sponge therapy. Due to recurrence of symptoms, the patient ultimately underwent intervention in the Gastroenterology group using flexible endoscopy.

While the number of patients with previous intervention is small, we can still argue that these patients are of higher risks of complications and that the flexible endoscopy method is suitable for challenging cases with prior interventions, aligning with the recommendations of the ESGE guidelines (weak recommendation, low quality of evidence, level of agreement 100%)(58).

Regarding the overall complication rate, no statistically significant difference was observed between the two treatment groups ($p = 0.327$, Fisher's exact test). In the Gastroenterology group, nine adverse events were documented, corresponding to a complication rate of 10.2%. This finding is consistent with the results reported in a comprehensive meta-analysis conducted by Ishaq et al., which included 20 studies published between 1995 and 2015 and encompassed a total of 813 patients undergoing flexible endoscopic diverticulotomy (59).

The meta-analysis by Ishaq et al. revealed a pooled adverse event rate of 11.3%, although individual studies showed a wide variability, with complication rates ranging from 5% to 36%. The most frequently reported complication was perforation, occurring in 28 patients across the included studies. Other notable adverse events included bleeding (n = 24), emphysema (n = 16), fever (n = 15), pneumonia (n = 3), and, more

rarely, neck abscess (n = 1). These findings illustrate the heterogeneous nature of complications associated with flexible endoscopic techniques and highlight the importance of both procedural expertise and perioperative care in minimizing risk.

Interestingly, a meta-regression analysis performed within the same study aimed to identify potential predictors of adverse event rates showed that factors such as the choice of endoscopic device, the size of the diverticulum, and the use of sedation were not found to significantly influence the incidence of complications. This suggests that procedural safety is likely influenced by other variables, such as operator experience, institutional protocols, or patient-specific anatomical and physiological factors.

Our results align closely with these findings, reinforcing the notion that while flexible endoscopic diverticulotomy is generally safe, a non-negligible risk of complications remains. Awareness of this risk, combined with standardized perioperative protocols and appropriate case selection, is essential to ensure optimal patient outcomes.

In our study, of the nine complications in the Gastroenterology group, four were considered major. Two patients experienced perforations, with one detected intraprocedural through prolapse of mediastinal fat. The myotomy was closed using four clips, and subsequent CT-thorax revealed mediastinal emphysema. The patient was managed conservatively with antibiotics, and his clinical course until discharge was uneventful.

The second patient was a 77-year-old multimorbid patient with COPD and malnutrition due to Zenker’s diverticulum. During the septum cutting with the needle Papillotome, a relatively larger perforation emerged. The defect was closed using a large OVESCO-Clip, which was later removed using a special cutter. Subsequent follow-up endoscopy demonstrated closure of the defect. However, the patient’s clinical condition deteriorated, leading to respiratory insufficiency and eventual death. It remains uncertain whether the cause of death was directly related to the diverticulotomy procedure or to the patient’s pre-existing compromised clinical condition.

The other two major complications in the Gastroenterology group included patients with emphysema, who were conservatively managed with antibiotics and had an uneventful clinical course. The remaining five minor complications in this group consisted of minor bleedings and fever.

In the ENT group of our study, two postoperative complications were documented, resulting in a complication rate of 4.2%. This rate is notably lower compared to that reported in previously published large-scale studies. For instance, a meta-analysis

conducted by Yuan et al. reviewed data from 1,060 patients across 91 studies who had undergone carbon dioxide (CO_2) laser diverticulotomy. The authors reported an overall complication rate of 9.3%, identifying emphysema (1.3%; 14/1,060), bleeding (1.0%; 11/1,060), mediastinitis (1.3%; 14/1,060), and fistula formation (1.1%; 12/1,060) as the most frequently observed adverse events 1.1%, 12/1060) (35). These findings highlight the potential risks associated with the procedure, despite its widespread acceptance as a minimally invasive therapeutic option for Zenker's diverticulum.

In addition, Hoffmann et al.(64) presented a retrospective single-center analysis of 103 patients treated with rigid endoscopic CO_2 laser diverticulotomy at the Department of Otolaryngology, Christian-Albrechts-University in Kiel, Germany. Their study reported a complication rate below 4% (4/103), with the nature of complications including one case of mediastinal leakage, one suspected case of mediastinitis, and two instances of dental injury. These findings suggest that while the procedure is generally considered safe, complications may still arise, particularly in complex or repeat interventions.

In our current series, the two documented complications warrant further discussion. The first case involved a patient with a history of two prior rigid endoscopic diverticulotomy procedures. During the third intervention, the procedure was complicated by an iatrogenic perforation with subsequent development of mediastinitis. This serious complication was effectively managed using endoscopic vacuum-assisted closure therapy (EndoSponge), demonstrating the feasibility of minimally invasive management even in the context of severe complications. The second case involved a patient who reported persistent hoarseness following the intervention. Clinical evaluation raised suspicion of a recurrent laryngeal nerve paresis, a rare but recognized complication following endoscopic treatment of Zenker's diverticulum, particularly when manipulation near the cricopharyngeal region is extensive.

Taken together, our findings support the growing body of evidence suggesting that rigid endoscopic CO_2 laser diverticulotomy can be performed with a relatively low complication rate. However, caution is warranted in patients undergoing repeat procedures, as the risk of adverse events, including perforation and nerve injury, may be elevated in this subgroup. Early recognition and prompt management of complications are critical to ensuring optimal outcomes.

A comparative analysis was conducted to evaluate the procedural durations between the two intervention groups—rigid endoscopic diverticulotomy performed by the ENT

team and flexible endoscopic diverticulotomy conducted by the Gastroenterology team. The comparison revealed a statistically significant difference in procedure times between the two groups ($p = 0.004$, Mann–Whitney U test). Specifically, the median duration of the intervention was found to be 7 minutes shorter in the flexible endoscopy group compared to the rigid endoscopy group.

For consistency and accuracy in measuring procedure times, the start of the intervention was defined as the point of introduction of the diverticuloscope in the ENT group and the point of gastroscope insertion in the Gastroenterology group. This standardized timepoint allowed for a direct and clinically meaningful comparison between the two procedural approaches, accounting for the technical setup unique to each method.

The shorter duration observed in the flexible endoscopy group may reflect inherent differences in procedural complexity, required setup, and the ease of access to the target anatomical site. In contrast, rigid endoscopy often necessitates a more extensive setup, including the insertion and correct positioning of the diverticuloscope, which can be technically challenging, particularly in patients with limited cervical mobility or anatomical variations.

These findings suggest a potential procedural efficiency advantage associated with the flexible endoscopic technique, which may have implications for both operating room logistics and patient safety.

4.1 Clinical outcome

To assess the efficacy of the two treatment modalities, the primary endpoint of the study was defined as the clinical outcome following the final intervention, irrespective of the number of procedures required to achieve symptom resolution. Clinical success was evaluated based on either subjective patient-reported outcomes or objective findings observed during follow-up endoscopy. Outcomes were categorized into three groups: improvement, no change, or deterioration.

Upon analysis, a statistically significant difference was observed in the primary outcome between the two groups. In the Gastroenterology (flexible endoscopy) cohort, 88.5% of patients reported symptom improvement or complete resolution at a minimum of three months post-intervention, compared to 65.5% in the ENT (rigid endoscopy) cohort ($p = 0.015$, Fisher–Freeman–Halton test). These findings suggest superior clinical efficacy associated with the flexible endoscopic approach.

The observed efficacy of flexible endoscopy is further supported by a recent retrospective, multicenter cohort study conducted across six tertiary referral centers in Germany. This study included 327 patients treated with flexible endoscopic techniques between 2003 and 2024 and reported a high clinical success rate of 97.4%, with a symptomatic recurrence rate necessitating re-admission in 16.7% of cases (65).

Despite the higher overall success rate in the flexible endoscopy group in our study, it is noteworthy that recurrence rates following the initial intervention were slightly higher in the Gastroenterology group (34.4%) compared to the ENT group (32.1%), though this difference was not statistically significant ($p = 1.0$). Similarly, the reintervention rate was higher in the Gastroenterology group (29.5%) versus the ENT group (13.8%), again without reaching statistical significance ($p = 0.123$).

These findings suggest that while flexible endoscopic treatment is highly effective in achieving symptom resolution, it may be associated with a higher likelihood of requiring multiple procedures to attain a satisfactory clinical outcome. Given the minimally invasive nature, low morbidity, and procedural feasibility of flexible endoscopy, the necessity for reintervention should be considered an acceptable aspect of the treatment course rather than a limitation.

A retrospective study published by the Mayo Clinic in February 2023 evaluated the outcomes of 75 patients who underwent flexible endoscopic myotomy for Zenker’s diverticulum. The authors reported a recurrence rate of approximately 20%, with 26.7% of those experiencing recurrence successfully managed through repeat endoscopic interventions. Notably, younger age was identified as a significant predictor of recurrence ($p < 0.01$) (66).

These findings are consistent with several other studies that have reported relatively high recurrence rates following flexible endoscopic treatment. A single-center study conducted in Augsburg, Germany, assessed 46 patients treated with flexible endoscopy for Zenker’s diverticulum. The initial clinical success rate was 100%; however, symptom recurrence was observed in 30% of patients within a mean follow-up period of 4.4 months. These patients required an average of 1.39 additional endoscopic sessions per patient, achieving clinical outcomes comparable to those who did not experience recurrence. Identified risk factors for symptom recurrence in this cohort included younger age, male gender, larger diverticulum size, and longer duration of symptoms prior to intervention (67).

In the context of our study, the mean follow-up period used to assess the primary endpoint following the final intervention was 30.8 months. This relatively extended observation period allows for a robust evaluation of long-term outcomes and recurrence, aligning with follow-up durations considered representative in the literature for capturing late symptom relapse.

The elevated recurrence rate associated with flexible endoscopy must be interpreted in light of its procedural advantages. The technique avoids the need for endotracheal intubation and is generally well-tolerated, even in older or multimorbid patients. These features make it an especially practical option for repeated interventions in cases of recurrence, thereby reinforcing its role as a safe and effective first-line and repeat treatment modality for Zenker's diverticulum.

This comparison between the two different methods for management of Zenker's Diverticulum was able to present a difference in the efficacy of therapy between the flexible endoscopy method and the rigid endoscopy method using Laser, with more patients in the flexible endoscopy group benefiting from improvement of symptoms after undergoing a relatively minimally invasive and shorter procedure, mostly without the need for endotracheal intubation and general anesthesia. This makes it preferable, especially for the target population of elderly multimorbid patients, without a significant increased risk of complications.

4.2 Regression analysis

Clinical improvement in regression analysis

In the regression analysis conducted within the Gastroenterology group, the occurrence of complications emerged as the only variable significantly associated with clinical improvement. In the univariable model, complications were linked to a markedly reduced likelihood of improvement (OR 0.136, 95% CI 0.023–0.789, p = 0.026). This association remained significant in the multivariable model after adjustment for potential confounders (OR 0.116, 95% CI 0.018–0.739, p = 0.023). These findings suggest that procedural or post-procedural complications may substantially compromise therapeutic success. This underscores the importance of meticulous technique, vigilant intra- and post-procedural monitoring, and prompt management of adverse events to optimize clinical outcomes. The consistency of this finding across both regression models strengthens the validity of the association and positions

complications as a critical determinant of clinical improvement following endoscopic therapy.

Interestingly, a review of the current literature did not identify any studies that directly reported an association between complications and diminished clinical improvement following flexible endoscopic septotomy for Zenker's diverticulum. Most published series describe a generally low rate of adverse events, with minor complications—such as limited bleeding, superficial mucosal injury, or localized subcutaneous emphysema—rarely leading to lasting clinical impact. For example, in a large prospective series by Repici et al., early clinical success exceeded 96% despite the occurrence of a small number of complications, all of which were managed conservatively without long-term sequelae (68).

While diverticulum size did not reach statistical significance as a predictor of clinical improvement in our analysis, the literature presents a more nuanced picture. A prospective study by Costamagna et al. (n = 89) identified large pouch size (≥50 mm) as an independent predictor of clinical failure, with a hazard ratio of approximately 11 at six months. In that cohort, patients with larger diverticula had significantly lower long-term success unless a sufficiently deep septal division was achieved (60).

Conversely, other studies suggest that within the commonly encountered range of Zenker diverticulum sizes, size alone does not preclude successful endoscopic treatment. A recent multicenter study from the UK (n = 126) found no statistically significant association between pouch size and clinical success (OR ~0.99, $p = 0.50$) in their logistic regression model. Importantly, no specific size threshold was identified as predictive of treatment failure, supporting the efficacy of flexible endoscopic therapy across a broad range of anatomical presentations when performed in specialized centers (69).

These findings collectively indicate that while complications appear to negatively influence clinical improvement in our cohort, such an association has not been widely reported elsewhere. This may reflect differences in sample size, complication severity, or management protocols across studies. Further prospective investigations with standardized complication grading and outcome measures may help clarify the clinical relevance of adverse events in this context.

Recurrence after the initial flexible endoscopy in regression analysis

This regression analysis sought to identify both clinical and procedural factors that influence the risk of recurrence after initial flexible endoscopic therapy for Zenker's

diverticulum. Using univariable and multivariable logistic regression models, we assessed the impact of patient demographics and treatment-related variables on recurrence outcomes.

It is worth noting that recurrence here refers to the need for multiple intervention to reach the clinical efficacy and to be differentiated from the clinical improvement after the last intervention.

Among all variables examined, diverticulum depth and the occurrence of complications were the only factors that demonstrated a statistically significant association with recurrence in both analytical models.

These findings suggest that deeper diverticula may pose technical challenges for complete septal division or may carry a higher risk of incomplete myotomy, thereby predisposing patients to symptom recurrence following the initial procedure.

In addition, the presence of intra- or post-procedural complications was significantly associated with increased recurrence rates. This emphasizes the potential long-term consequences of procedural complications on therapeutic durability and highlights the need for meticulous operative technique and vigilant postoperative care to mitigate these risks.

Other evaluated parameters, including age, gender, and history of prior intervention, did not show a statistically significant association with recurrence in this cohort. These findings are consistent with previous literature suggesting that while demographic factors may influence treatment selection or tolerance, they are not independent predictors of long-term outcomes.

Taken together, these results underscore the importance of anatomical characteristics - particularly diverticulum depth - and procedural safety as central determinants of long-term success following flexible endoscopic treatment. Strategies to optimize procedural technique, minimize complications, and tailor treatment to individual anatomy may help to reduce recurrence rates and improve clinical durability.

Future prospective studies with larger sample sizes and extended follow-up are warranted to validate these observations and further refine predictive models for recurrence, ultimately informing patient selection and procedural planning.

Reintervention in regression analysis

This regression analysis aimed to identify clinical and procedural predictors associated with the need for reintervention after flexible endoscopic treatment of Zenker’s diverticulum.

Among the variables examined, diverticulum depth was the only factor significantly associated with reintervention in both univariable and multivariable analyses. indicating that with increasing diverticulum depth, the probability of requiring additional treatment significantly increases. This suggests that deeper diverticula may pose greater technical challenges during the initial procedure, increasing the risk of incomplete septal division and residual symptoms that necessitate further intervention.

Although not reaching statistical significance, male gender showed a trend toward increased likelihood of reintervention. While this association did not meet the conventional threshold for significance, it may warrant further exploration in larger, adequately powered cohorts to determine whether anatomical or physiological sex-related differences influence procedural outcomes.

These findings highlight the critical role of anatomical factors, particularly diverticulum depth, in influencing long-term procedural success. They underscore the need for careful pre-procedural evaluation and tailored treatment strategies, especially in patients with deep diverticula who may be at increased risk for suboptimal initial outcomes and repeat procedures.

Future research involving larger study populations, prospective designs, and standardized follow-up protocols is needed to confirm these findings and to develop evidence-based strategies aimed at minimizing the need for reintervention in this patient population.

4.3 Study limitations

Despite the valuable insights provided by this study, several limitations must be acknowledged to appropriately contextualize the findings and guide future research.

First, the study experienced a relatively high rate of loss to follow-up, which may have led to some selection bias. In the ENT group, clinical outcome data were obtained from only 29 of the 48 patients, and in the Gastroenterology group, from 61 of the 88 patients. The resulting follow-up rates - 60.4% and 69.3%, respectively - limit the representativeness of the analyzed population. Patients lost to follow-up may have had different clinical outcomes compared to those who responded, potentially skewing the efficacy and complication rates reported.

Second, the retrospective nature of the study imposes inherent methodological constraints. Data were collected from existing medical records rather than through prospective design, limiting the ability to control for confounding variables or ensure

consistency in documentation. Retrospective studies are prone to various biases, including selection bias, information bias, and recall bias, all of which can impact the validity and reproducibility of the results. Additionally, the lack of standardized protocols for follow-up assessments may have contributed to inconsistencies in reporting patient outcomes.

Third, a key variable - diverticulum size or depth - was not uniformly documented across the study population. Specifically, measurements of diverticulum depth were absent for all patients in the ENT cohort and for a considerable portion of those in the Gastroenterology group. Given that diverticulum size is a potentially important predictor of procedural difficulty, treatment response, and risk of recurrence, the absence of this data represents a significant limitation. It reduces the ability to perform subgroup analyses or adjust for this variable in outcome comparisons.

However, this also reflects the clinical practice since in most of the patients radiological confirmation and measurement of the diverticulum is not necessary for planing and conductions of the procedure

Furthermore, the reliance on patient-reported outcomes or subjective endoscopic impressions to assess treatment success introduces variability in endpoint determination. While such assessments are common in clinical practice, the absence of a standardized symptom scoring system or objective outcome criteria may have affected the accuracy of outcome classification.

Lastly, the study was conducted in a single-center setting, which may limit the generalizability of the findings to broader patient populations or different clinical environments. Institutional experience, procedural volume, and equipment availability may differ across centers, influencing both clinical outcomes and complication rates.

In future research, a prospective, multicenter study design with standardized follow-up protocols and comprehensive data collection, including anatomical characteristics such as diverticulum size, would provide stronger evidence and allow for more robust subgroup analysis. Despite these limitations, the current study contributes meaningful preliminary data and highlights clinically relevant differences between rigid and flexible endoscopic approaches for the management of Zenker’s diverticulum.

5 Summary and conclusion

In summary, the lack of standardized therapeutic approach to Zenker's diverticulum highlights the importance of this study in comparing the two commonly used approaches: the rigid endoscopy method using laser and the flexible endoscopy method.

With the inclusion of 136 patients treated in our institution in two different departments, we aimed to compare the two methods in terms of efficacy in resolving symptoms, as well as comparing complications and recurrence rates.

Notably, the flexible endoscopy method predominantly done in the Gastroenterology department showed favorable outcomes. The intervention was successfully performed in all patients; with most patients sedated using propofol without the need for general anesthesia, which represents a potential advantage and adds to patient comfort.

There was no significant difference in the complication rates between the two groups, with the flexible endoscopy demonstrating slightly shorter duration of intervention with higher rates of clinical improvement and resolution of symptoms during follow-up. This finding supports the flexible endoscopy method as a preferable option, especially for the elderly multimorbid patients.

The study also highlighted the technical difficulties in performing the rigid endoscopy method due to anatomical differences, particularly in cases of previous intervention. In these cases, the flexible endoscopy method represents a suitable option in treating patients with history of failed rigid endoscopy intervention.

In conclusion, we anticipate that this study will provide valuable insights to help orient medical professionals in choosing the optimal intervention for managing Zenker's diverticulum. We consider the flexible endoscopy method a valuable minimally invasive procedure with a relatively low risk, which makes it suitable for a substantial number of elderly patients. Other considerations should refine the treatment option according to patient characteristics. Further research is warranted to elaborate on the treatment of choice for Zenker's diverticulum.

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7 Acknowledgement

I extend my deepest gratitude to Prof. Alexander Arlt und Dr. Christian Meinhardt for their exceptional supervision, invaluable guidance, support, insightful advice, and meticulous corrections throughout my research.

I am deeply thankful to Prof. Hans Seifert and Prof. Florian Hoppe for their crucial assistance in the collection and organization of the data.

Lastly, I would like to express my heartfelt appreciation to my wife, daughters, and my parents for their unwavering presence, support, assistance, love, and encouragement.

8 Lebenslauf

Der Lebenslauf wurde aus Gründen des Datenschutzes in der elektronischen Fassung dieser Dissertation nicht dargestellt.

9 Attachment

9.1 Questionnaire and consent for the gastroenterology group

Universitätsklinik für Innere Medizin- Gastroenterologie, Hepatologie, Stoffwechselmedizin, Nieren- und Hochdruckerkrankungen, Klinikum Oldenburg, Rahel-Straus-Str. 10, 26133 Oldenburg

Adresse des Pat.
Xxxxxxxxxxxxxxx
Xxxxxxxxxxxxxxx
Patienteninformationsbogen
Informationsschrift für Patientinnen und Patienten

Oldenburg den .....

Sehr geehrte Frau / Herr .....,

am xx.xx.xxxx haben Sie eine Schwellendurchtrennung im Rahmen einer Magenspiegelung zur Behandlung eines Zenker-Divertikels (Aussackung in der Speiseröhre) in der Univeristätsklinik für Gastroenterologie im Klinikum Oldenburg erhalten.

Wir möchten Sie nun einladen an der Studie ***"Therapeutische Optionen des Zenker-Divertikels. Eine retrospektive Vergleichstudie zwischen der flexiblen endoskopischen- und chirurgischen starren endoskopischen Therapien von Effektivität, Komplikations- und Rezidivraten, sowie wirtschaftlichen Aspekte"*** teilzunehmen. Mit Ihrer Teilnahme können Sie zu einer weiteren Verbesserung der Technik beitragen. Bitte lesen Sie sich die folgenden Informationen sorgfältig durch. Sie können dann entscheiden, ob Sie teilnehmen möchten.

Hintergrund der Studie:
Das Zenker-Divertikel kann sowohl chirurgisch als auch endoskopisch im Rahmen einer Magenspiegelung behandelt werden. Für beiden Methoden konnten in den letzten Jahren hohe Erfolgsraten nachgewiesen werden. Es gibt jedoch kaum suffiziente Vergleichstudien zwischen der unterschiedlichen Methoden der Zenkerspaltung.
Aufgrund dieser teils auch widersprüchlichen Datenlage soll nun im Rahmen dieser interdisziplinären Studie der Universitätsklinik für Innere Medizin / Gastroenterologie und Klinik für HNO unter Schirmherrschaft der Carl von Ossietzky Universität Oldenburg ein Vergleich der beiden genannten Methoden erfolgen.

Zielsetzung: Vergleich der Zenkerspaltung (Zenker-Divertikulotomie) zwischen der starren Endoskopie und der flexibelen Endoskopie in den Endpunkten:

- Besserung der Beschwerden und Gewichtsverlauf
- Wiederauftreten der Beschwerden (Rezidivhäufigkeit, Langzeitverlauf)
- Kosten

- Komplikationen

Wie läuft die Studie ab?
Es erfolgt eine Datenerhebung der bereits durchgeführten Therapien. Diese Art von Studie wird auch retrospektive Analyse genannt. Teilnehmende Kliniken sind:

- Die Universitätsklinik für Gastroenterologie
- Klinik für Hals- Nasen- und Ohrenkrankheiten

Wir bitten hiermit um Ihre Einwilligung, um Ihre bei uns gespeicherten Daten zu verwenden. Die Teilnahme an dieser Studie ist freiwillig. Sie können jederzeit durch mündliche oder schriftliche Mitteilung an Herrn Mohamed Ihre Einwilligung zurückziehen und müssen dafür keine Gründe nennen. Die Ablehnung der Teilnahme hat keine nachteiligen Folgen für Sie.

Habe ich einen persönlichen Nutzen?
Es ist nicht zu erwarten, dass Sie selbst aus Ihre Teilnahme direkt gesundheitlichen Nutzen ziehen, Die Ergebnisse dieser Studie werden jedoch für die Planung von Maßnahmen und Handlungen von ÄrztInnen herangezogen, um zukünftig eine optimale Unterstützung zu gewährleisten und dadurch die Lebensqualität der Betroffenen zu verbessern. Die Teilnahme an dieser Studie bringt ebenso keine Risiken für Sie.

Datenschutz:
Wir versichern Ihnen, dass Ihre Unterlagen vertraulich und pseudonym behandelt werden und keine Rückschlüsse auf Ihre Person zulassen. Der Zugang zu Ihren Daten, die nur zu wissenschaftlichen Zwecken verwendet werden, obliegt ausschließlich Herrn Mohamed und Dr. Meinhardt, die der Schweigepflicht unterliegen. Ihr Name wird an keiner Stelle im Forschungsmaterial erscheinen. Das gilt auch für eine etwaige Veröffentlichung der Forschungsergebnisse. Auf Wunsch wird Sie Herr Mohamed gerne nach Ende der Studie über die Ergebnisse der Untersuchung informieren.

Anbei erhalten Sie einen Fragebogen, ein Einwilligungsformular und einen Briefumschlag. Sind Sie damit einverstanden und möchten unsere Studie unterstützen dann brauchen Sie nur die Einwilligung zu unterschreiben, den Fragenbogen auszufüllen und beide an uns im Briefumschlag zurückzuschicken. Nehmen Sie sich bitte für die Antwort ausreichend Zeit, eine Briefmarke brauchen Sie nicht!
Im Falle dass die betroffene Person gestorben ist oder eigenständig nicht antworten oder unterschreiben kann bitten wir die Angehörigen, wenn möglich, die u.g. Fragen zu beantworten und das Einwilligungsformular zu unterschreiben.

Wir hoffen auf Ihre Unterstützung und bedanken uns herzlich im Voraus.

Mit freundlichen Grüßen

Univ. -Prof. Dr. Alexander Arlt
Klinikdirektor der Universitätsklinik für Innere Medizin – Gastroenterologie, Hepatologie, Stoffwechselmedizin, Nieren und Hochdruckerkrankungen
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und Hochdruckerkrankungen
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z.H. Herrn Moustafa Mohamed
Rahel-Straus-Straße 10
26133 Oldenburg

Informationsblatt und Einwilligungserklärung von Herrn/Frau xxx Geb. xx.xx.xxxx
(Für Ihre Unterlagen)

Fragebogen:

1- Wie hat der o.g. Eingriff Ihre Beschwerden (Schluckstörung, Aufstoßen, Husten, Mundgeruch, etc.) beeinflusst? Die Beschwerden waren nach dem Eingriff:

□ gebessert □ gleichgeblieben □ verschlechtert

2- Ist ein Wiederauftreten des Zenker-Divertikels (Aussackung in der Speiseröhre) bei Ihnen nach dem Eingriff festgestellt worden?

□ ja □ nein

3- Mussten nach dem o.g. Eingriff weitere operative Maßnahmen durchgeführt werden zur Behandlung Ihrer Beschwerden?

□ ja □ nein

Einwilligung:

Ich habe die Informationsschrift gelesen. Ich stimme der Teilnahme an der Studie freiwillig zu. Für meine Entscheidung hatte ich ausreichend Zeit. Ein Exemplar der Informationsschrift und der Einwilligungserklärung habe ich erhalten.

Datenschutz:

Mir ist bekannt, dass bei dieser Studie personenbezogene Daten verarbeitet werden sollen. Die Verarbeitung der Daten erfolgt nach gesetzlichen Bestimmungen und setzt gemäß Art. 6 Abs. 1 lit. aus der Datenschutz-Grundverordnung folgende Einwilligungserkälrung voraus:

Ich wurde darüber aufgeklärt und stimme freiwillig zu, dass meine in der Studie erhobenen Daten, insbosendere Angaben über meine Gesundheit, zu den in der Informationsschrift beschriebenen Zwecken in pseudonymisierter Form aufgezeichnet, ausgewertet und ggf. auch in pseudonymisierter Form an Universitäten etc. Weitergegeben werden können, u.U. auch in Länder mit geringeren Anforderungen an den Datencschutz als in der Europäischen Union. Dritte erhalten keinen Einblick in

personenbezogene Unterlagen. Bei der Veröffentlichung von Ergebnissen der Studie wird mein Name ebenfalls nicht genannt. Die personenbezogenen Daten werden anonymisiert, sobald dies nach dem Forschungszweck möglich ist. Die Daten werden nach der Studienabschluss 10 Jahre bewahrt. Mir ist bekannt, dass diese Einwilligung jederzeit schriftlich oder mündlich ohne Angabe von Gründen widerrufen werden kann, ohne dass mir dadurch Nachteile entstehen. Die Rechtmäßigkeit der bis zum Widerruf erfolgten Datenverarbeitung wird davon nicht berührt. In diesem Fall kann ich entscheiden, ob die von mir erhobenen Daten gelöscht werden sollen oder weiterhin für die Zwecke der Studie verwendet werden dürfen.

Ich bin mit der Erhebung, Verarbeitung, Speicherung und Weitergabe meiner personenbezogenen Daten (der personenbezogenen Daten meiner Angehörigen / meines Angehörigen) entsprechend der Beschreibungen zum oben bezeichneten Forschungsvorhaben einverstanden.
Eine Kopie der Informationsschrift und dieser Einwilligungserklärung habe ich erhalten.

_____	_____
Vor- und Nachname (in Druckschrift)	Ort, Datum, Unterschrift

Universitätsklinik für Innere Medizin-Gastroenterologie,
Hepatologie, Stoffwechselmedizin, Nieren
und Hochdruckerkrankungen
Klinikum Oldenburg
z.H. Herrn Moustafa Mohamed
Rahel-Straus-Straße 10
26133 Oldenburg

Informationsblatt und Einwilligungserklärung von Herrn/Frau xxx Geb. xx.xx.xxxx

(Bitte in dem beigefügten Briefumschlag an uns zurückschicken, oder per Fax an 0441 403 xxxx, oder per Mail an: mohamed.moustafa@klinikum-oldenburg.de **)**

Fragebogen:

1. Wie hat der o.g. Eingriff Ihre Beschwerden (Schluckstörung, Aufstoßen, Husten, Mundgeruch, etc.) beeinflusst? Die Beschwerden waren nach dem Eingriff:

□ gebessert □ gleichgeblieben □ verschlechtert

2. Ist ein Wiederauftreten des Zenker-Divertikels (Aussackung in der Speiseröhre) bei Ihnen nach dem Eingriff festgestellt worden?

□ ja □ nein

3. Mussten nach dem o.g. Eingriff weitere operative Maßnahmen durchgeführt werden zur Behandlung Ihrer Beschwerden?

□ ja □ nein

Einwilligung:

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Datenschutz:

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Ich wurde darüber aufgeklärt und stimme freiwillig zu, dass meine in der Studie erhobenen Daten, insbosendere Angaben über meine Gesundheit, zu den in der Informationsschrift beschriebenen Zwecken in pseudonymisierter Form aufgezeichnet, ausgewertet und ggf. auch in pseudonymisierter Form an Universitäten etc. Weitergegeben werden können, u.U. auch in Länder mit geringeren Anforderungen an den Datencschutz als in der Europäischen Union. Dritte erhalten keinen Einblick in personenbezogene Unterlagen. Bei der Veröffentlichung von Ergebnissen der Studie wird mein Name

ebenfalls nicht genannt. Die personenbezogenen Daten werden anonymisiert, sobald dies nach dem Forschungszweck möglich ist. Die Daten werden nach der Studienabschluss 10 Jahre bewahrt. Mir ist bekannt, dass diese Einwilligung jederzeit schriftlich oder mündlich ohne Angabe von Gründen widerrufen werden kann, ohne dass mir dadurch Nachteile entstehen. Die Rechtmäßigkeit der bis zum Widerruf erfolgten Datenverarbeitung wird davon nicht berührt. In diesem Fall kann ich entscheiden, ob die von mir erhobenen Daten gelöscht werden sollen oder weiterhin für die Zwecke der Studie verwendet werden dürfen.

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Eine Kopie der Informationsschrift und dieser Einwilligungserklärung habe ich erhalten.

_____	_____
Vor- und Nachname (in Druckschrift)	Ort, Datum, Unterschrift

9.2 Questionnaire and consent for the ENT group

Klinik für HNO, Klinikum Oldenburg, Rahel-Straus-Str. 10, 26133 Oldenburg
Adresse des Pat.
Xxxxxxxxxxxxxxx
Xxxxxxxxxxxxxxx

Patienteninformationsbogen
Informationsschrift für Patientinnen und Patienten

Oldenburg den .....

Sehr geehrte Frau / Herr .....,

am xx.xx.xxxx haben Sie eine laserchirurgische Schwellendurchtrennung zur Behandlung eines Zenker-Divertikels (Aussackung in der Speiseröhre) in der HNO Klinik im Klinikum Oldenburg erhalten.

Wir möchten Sie nun einladen an der Studie ***"Therapeutische Optionen des Zenker-Divertikels. Eine retrospektive Vergleichstudie zwischen der flexiblen endoskopischen- und chirurgischen starren endoskopischen Therapien von Effektivität, Komplikations- und Rezidivraten, sowie wirtschaftlichen Aspekte"*** teilzunehmen. Mit Ihrer Teilnahme können Sie zu einer weiteren Verbesserung der Technik beitragen. Bitte lesen Sie sich die folgenden Informationen sorgfältig durch. Sie können dann entscheiden, ob Sie teilnehmen möchten.

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Aufgrund dieser teils auch widersprüchlichen Datenlage soll nun im Rahmen dieser interdisziplinären Studie der Universitätsklinik für Innere Medizin / Gastroenterologie und Klinik für HNO unter Schirmherrschaft der Carl von Ossietzky Universität Oldenburg ein Vergleich der beiden genannten Methoden erfolgen.

Zielsetzung: Vergleich der Zenkerspaltung (Zenker-Divertikulotomie) zwischen der starren Endoskopie und der flexibelen Endoskopie in den Endpunkten:

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- Wiederauftreten der Beschwerden (Rezidivhäufigkeit, Langzeitverlauf)
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Habe ich einen persönlichen Nutzen?

Es ist nicht zu erwarten, dass Sie selbst aus Ihre Teilnahme direkt gesundheitlichen Nutzen ziehen, Die Ergebnisse dieser Studie werden jedoch für die Planung von Maßnahmen und Handlungen von ÄrztInnen herangezogen, um zukünftig eine optimale Unterstützung zu gewährleisten und dadurch die Lebensqualität der Betroffenen zu verbessern. Die Teilnahme an dieser Studie bringt ebenso keine Risiken für Sie.

Datenschutz:

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Wir hoffen auf Ihre Unterstützung und bedanken uns herzlich im Voraus.

Mit freundlichen Grüßen

Prof. Dr. Florian Hoppe
Klinikdirektor der Klinik für Hals- Nasen- Ohrenheilkunde und plastische Chirurgie
Klinikum Oldenburg

Univ. -Prof. Dr. Alexander Arlt
Klinikdirektor der Universitätsklinik für Innere Medizin – Gastroenterologie, Hepatologie, Stoffwechselmedizin, Nieren und Hochdruckerkrankungen
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(Für Ihre Unterlagen)

Fragebogen:

4- Wie hat der o.g. Eingriff Ihre Beschwerden (Schluckstörung, Aufstoßen, Husten, Mundgeruch, etc.) beeinflusst? Die Beschwerden waren nach dem Eingriff:
□ gebessert □ gleichgeblieben □ verschlechtert

5- Ist ein Wiederauftreten des Zenker-Divertikels (Aussackung in der Speiseröhre) bei Ihnen nach dem Eingriff festgestellt worden?
□ ja □ nein

6- Mussten nach dem o.g. Eingriff weitere operative Maßnahmen durchgeführt werden zur Behandlung Ihrer Beschwerden?
□ ja □ nein

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Datenschutz:

Mir ist bekannt, dass bei dieser Studie personenbezogene Daten verarbeitet werden sollen. Die Verarbeitung der Daten erfolgt nach gesetzlichen Bestimmungen und setzt gemäß Art. 6 Abs. 1 lit. aus der Datenschutz-Grundverordnung folgende Einwilligungserkälrung voraus:
Ich wurde darüber aufgeklärt und stimme freiwillig zu, dass meine in der Studie erhobenen Daten, insbosendere Angaben über meine Gesundheit, zu den in der Informationsschrift beschriebenen Zwecken in pseudonymisierter Form aufgezeichnet, ausgewertet und ggf. auch in pseudonymisierter Form an Universitäten etc. Weitergegeben werden können, u.U. auch in Länder mit geringeren Anforderungen an den Datencschutz als in der Europäischen Union. Dritte erhalten keinen Einblick in personenbezogene Unterlagen. Bei der Veröffentlichung von Ergebnissen der Studie wird mein Name ebenfalls nicht genannt. Die personenbezogenen Daten werden anonymisiert, sobald dies nach dem Forschungszweck möglich ist. Die Daten werden nach der Studienabschluss 10 Jahre bewahrt. Mir ist

bekannt, dass diese Einwilligung jederzeit schriftlich oder mündlich ohne Angabe von Gründen widerrufen werden kann, ohne dass mir dadurch Nachteile entstehen. Die Rechtmäßigkeit der bis zum Widerruf erfolgten Datenverarbeitung wird davon nicht berührt. In diesem Fall kann ich entscheiden, ob die von mir erhobenen Daten gelöscht werden sollen oder weiterhin für die Zwecke der Studie verwendet werden dürfen.

Ich bin mit der Erhebung, Verarbeitung, Speicherung und Weitergabe meiner personenbezogenen Daten (der personenbezogenen Daten meiner Angehörigen / meines Angehörigen) entsprechend der Beschreibungen zum oben bezeichneten Forschungsvorhaben einverstanden.
Eine Kopie der Informationsschrift und dieser Einwilligungserklärung habe ich erhalten.

_____	_____
Vor- und Nachname (in Druckschrift)	Ort, Datum, Unterschrift

Klinik für HNO und plastische Chirurgie
Klinikum Oldenburg
z.H. Herrn Ahmad Ibrahim
Rahel-Straus-Straße 10
26133 Oldenburg

Informationsblatt und Einwilligungserklärung von Herrn/Frau xxx Geb. xx.xx.xxxx

(Bitte in dem beigefügten Briefumschlag an uns zurückschicken, oder per Fax an 0441 403 xxxx, oder per Mail an: ibrahim.ahmad@klinikum-oldenburg.de **)**

Fragebogen:

4. Wie hat der o.g. Eingriff Ihre Beschwerden (Schluckstörung, Aufstoßen, Husten, Mundgeruch, etc.) beeinflusst? Die Beschwerden waren nach dem Eingriff:
   □ gebessert □ gleichgeblieben □ verschlechtert

5. Ist ein Wiederauftreten des Zenker-Divertikels (Aussackung in der Speiseröhre) bei Ihnen nach dem Eingriff festgestellt worden?
   □ ja □ nein

6. Mussten nach dem o.g. Eingriff weitere operative Maßnahmen durchgeführt werden zur Behandlung Ihrer Beschwerden?
   □ ja □ nein

Einwilligung:

Ich habe die Informationsschrift gelesen. Ich stimme der Teilnahme an der Studie freiwillig zu. Für meine Entscheidung hatte ich ausreichend Zeit. Ein Exemplar der Informationsschrift und der Einwilligungserklärung habe ich erhalten.

Datenschutz:

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Forschungszweck möglich ist. Die Daten werden nach der Studienabschluss 10 Jahre bewahrt. Mir ist bekannt, dass diese Einwilligung jederzeit schriftlich oder mündlich ohne Angabe von Gründen widerrufen werden kann, ohne dass mir dadurch Nachteile entstehen. Die Rechtmäßigkeit der bis zum Widerruf erfolgten Datenverarbeitung wird davon nicht berührt. In diesem Fall kann ich entscheiden, ob die von mir erhobenen Daten gelöscht werden sollen oder weiterhin für die Zwecke der Studie verwendet werden dürfen.

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Eine Kopie der Informationsschrift und dieser Einwilligungserklärung habe ich erhalten.

_____	_____
Vor- und Nachname (in Druckschrift)	Ort, Datum, Unterschrift

9.3 Ethical approval

Carl von Ossietzky Universität Oldenburg / 26111 Oldenburg

Klinikum Oldenburg AöR
Universitätsklinik für Innere Medizin - Gastroenterologie
Herr Moustafa Mohamed
Rahel-Straus-Straße 10
26133 Oldenburg

per E-Mail: **mohamed.moustafa@klinikum-oldenburg.de**

Titel: Therapeutische Optionen des Zenker-Divertikels: Eine retrospektive Vergleichsstudie zwischen den flexiblen endoskopischen und chirurgischen Therapie von Effektivität, Komplikations- und Rezidivraten sowie wirtschaftlichen Aspekten

Antragsteller: Moustafa Mohamed

Unser Zeichen: 2022-018 (bitte stets angeben)

Beratung gem. §15 BO ÄKN

Sehr geehrter Herr Mohamed,

Ihr Antrag vom 31.01.2022, eingegangen am 02.02.2022, hat mir als Vorsitzender der medizinischen Ethikkommission zur berufsrechtlichen Beratung vorgelegen.

Nach § 4 Absatz VI unserer Verfahrensregelung ist der Vorsitzende im Einzelfall ermächtigt, zur Beschleunigung und Vereinfachung des Verfahrens allein oder im Einvernehmen mit einem Mitglied oder mehreren unter Einbeziehung der Geschäftsstelle zu entscheiden.

Die medizinische Ethikkommission hat keine Bedenken gegen die Durchführung der o. g. Studie.

Hinweis:

- **Bitte involvieren Sie die Datenschutzbeauftragte des Klinikums Oldenburg.**

Carl von Ossietzky
Universität
Oldenburg

Fakultät VI - Medizin und Gesundheits-wissenschaften

Medizinische Ethikkommission
- Geschäftsstelle -

TELEFONDURCHWAHL
+49 (0)441 798 3109

FAX
+49 (0)441 798 4745

E-MAIL
med.ethikkommission@uni-oldenburg.de

VORSITZENDER
Prof. Dr. med. Frank Griesinger

JURISTIN
Ass. jur. Carola Alvarez Castillo

OLDENBURG, 07.02.2022

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Bitte beachten Sie noch folgende Punkte:

- Die Ethikkommission erwartet, dass ihr ohne Aufforderung ein Abschlussbericht mit dem beigelegten **Formular B** übermittelt wird.
- Unabhängig davon ist die Ethikkommission unaufgefordert und zeitnah über alle Änderungen am Prüfplan, sowie den in diesem Antrag vorgelegten Dokumenten unaufgefordert und unverzüglich zu unterrichten. Ihr sind unaufgefordert alle schweren unerwünschten Ereignisse mitzuteilen, soweit sie im Zuständigkeitsbereich der Ethikkommission aufgetreten sind.
- Die ethische medizinische und juristische Verantwortung des Studienleiters und des an der Studie beteiligten medizinischen und wissenschaftlichen Personal bleibt entsprechend der Beratungsfunktion der medizinischen Ethikkommission durch diese Stellungnahme unberührt.
- Die Ethikkommission kann dieses Votum jederzeit zurückziehen oder ändern. Dies wird dem Antragsteller mitgeteilt.
- Bitte machen Sie dieses Votum und die der Begutachtung zugrundeliegenden Dokumente allen beteiligten Ärztinnen und Ärzten und Wissenschaftlerinnen und Wissenschaftlern zugänglich.

An der Beratung und Beschlussfassung haben keine Kommissionsmitglieder teilgenommen, die selbst an dem Forschungsvorhaben mitwirken oder deren Interessen davon berührt werden.

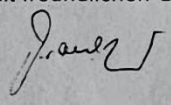
Wir bitten um Mitteilung der teilnehmenden Ärztinnen und Ärzte im Zuständigkeitsbereich der Universität Oldenburg, sobald diese bekannt sind bzw. sofern im Verlauf weitere Ärztinnen und Ärzte hinzukommen.

Wir möchten darauf hinweisen, dass die Stellungnahme der medizinischen Ethikkommission und die studienrelevante Korrespondenz an alle teilnehmenden Ärztinnen und Ärzte weiterzuleiten ist.

Bitte informieren Sie die Ethikkommission unter Nutzung des beigefügten Formulars A über den Beginn der Rekrutierung an Ihrem Studienzentrum.

Wir wünschen Ihnen bei der Durchführung Ihrer Studie viel Erfolg.

Mit freundlichen Grüßen



Prof. Frank Griesinger
Vorsitzender der medizinischen Ethikkommission