

REVIEW ARTICLE

Zenker's diverticulum: exploring treatment options

Il diverticolo di Zenker: un excursus sulle differenti opzioni terapeutiche

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SUMMARY

Zenker's diverticulum is an acquired sac-like outpouching of the mucosa and submucosa layers located dorsally at the pharyngoesophageal junction through Killian's dehiscence. It is the most common type of oesophageal diverticula with a reported prevalence ranging between 0.01 to 0.11% and typically occurs in middle-aged and elderly patients. Predominant symptoms are dysphagia and regurgitation. Treatment is recommended for symptomatic patients and considering the aetiopathogenesis of the disease demands myotomy of the cricopharyngeal muscle. Myotomy may be pursued through either open surgical or endoscopic techniques. Management of Zenker's diverticulum has dramatically progressed during past decades. Open surgery with cricopharyngeal myotomy has long been the conventional treatment with satisfactory results, but is associated with high complication rates. Since Zenker's diverticulum mainly affects frail elderly patients, less invasive treatments are indicated. In recent years, endoscopic repair of Zenker's diverticulum has been found to be a viable safe and effective alternative to surgery and gained widespread acceptance. Endoscopic stapled diverticulotomy is generally the preferred approach, but flexible endoscopy is a valuable option, particularly for high-risk patients. The literature is mainly based on retrospective case series or comparative case series, and the optimal treatment modality has not yet been established. The choice between the different approaches depends on local expertise and preferences. Based on retrospective literature results, appropriate technique selection dictated by the size of the diverticulum and the patient's conditions is however desirable.

KEY WORDS: Zenker's diverticulum • Cricopharyngeal muscle • Myotomy • Diverticulectomy • Endoscopic stapling diverticulotomy • Flexible endoscopy

RIASSUNTO

Il diverticolo di Zenker è una estroflexione sacciforme della mucosa e sottomucosa che si sviluppa a livello della parete posteriore della giunzione faringo-esofagea attraverso il triangolo di Killian. Il diverticolo di Zenker è il più frequente tra i diverticoli del tratto gastrointestinale superiore con prevalenza compresa tra 0,1 e 0,11%. Colpisce prevalentemente pazienti di età medio-avanzata. Sintomi prevalenti di presentazione sono la disfagia ed il rigurgito. Il trattamento è indicato per i pazienti sintomatici e, considerando le recenti acquisizioni sulla eziopatogenesi, sottende la miotomia chirurgica o endoscopica del muscolo cricofaringeo. Nel corso delle ultime decadi la gestione del diverticolo di Zenker ha subito una notevole evoluzione. Accanto alla tradizionale exeresi chirurgica, efficace ma gravata da alto tasso di complicanze, si sono affermate altre forme di trattamento meno invasive e maggiormente indicate in pazienti compromessi per età o comorbidità. La sezione del setto sotto guida endoscopica (diverticolotomia) si è dimostrata una sicura ed efficace opzione terapeutica. La diverticolotomia endoscopica con suturatrice meccanica (endostapler) è attualmente la tecnica che prevale, ma una valida alternativa è rappresentata dalla endoscopia flessibile in particolare nei pazienti ad alto rischio. Resta ancora da definire tuttavia quale sia il trattamento ottimale per il diverticolo di Zenker ed attualmente la scelta tra l'una o l'altra tecnica dipende di fatto dalle preferenze e abilità locali. Alla luce dei dati presenti in letteratura, basati esclusivamente su studi retrospettivi, la dimensione del diverticolo e le condizioni cliniche del paziente dovrebbero guidare nella scelta della procedura terapeutica più appropriata.

PAROLE CHIAVE: Diverticolo di Zenker • Muscolo cricofaringeo • Miotomia • Diverticolectomia • Diverticolotomia endoscopica con suturatrice meccanica • Endoscopia flessibile

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Introduction

Zenker's diverticulum (ZD), also known as hypopharyngeal diverticulum, is an acquired sac-like outpouching of the mucosa and submucosa layers originating from the pharyngoesophageal junction. It consists in a typical pulsion diverticulum (false diverticulum) occurring dorsally at the pharyngoesophageal wall through a *locus minoris resistentiae* (the Killian's dehiscence) bounded by the

propulsive oblique inferior pharyngeal constrictor muscle and the transversal fibres of the cricopharyngeal muscle (contributing to the upper oesophageal sphincter) ¹. The first description of Zenker's diverticulum dates back to 1769 by Ludlow ². A century after that report, a German pathologist, Friedrich Albert von Zenker, recognized and further characterized the physiopathology of this peculiar entity, since then deserving the eponym ³.

Although a complete understanding of the pathogenesis of ZD has not yet been reached, it is generally accepted that ZD is the landing place of a disorder of the upper oesophageal sphincter opening. ZD occurs due to increased intraluminal pressure in the oropharynx during swallowing, against an inadequate relaxation of the cricopharyngeal muscle, and subsequent incomplete opening of the UES, causing the protrusion of the mucosa through an area of relative weakness at the dorsal pharyngoesophageal wall ⁴.

Treatment options encompass open surgery or transoral rigid or flexible endoscopy and are aimed at eliminating functional outflow obstruction and restore continuity at the pharyngoesophageal junction through myotomy with or without resection of the diverticulum (diverticulectomy) or diverticulopexy ⁵. Changes in treatment modalities during the last decades reflect better understanding of the underlying pathophysiologic mechanism over the years ⁶. The present paper provides a review of the management of ZD. Mostly based on retrospective series, the current literature shows heterogeneous results. In clinical practice, the management and therapeutic approach to ZD is far from being standardized and the optimal treatment option remains unsettled. None of the available studies demonstrates substantial superiority of one technique over another, and the choice between different approaches is made according to local expertise ⁷. Though less-invasive procedures may sometimes be the sole option, for instance in older multi-morbid patients unfit for surgery, the best procedure should be defined according to precise factors ⁷ other than local practice, and a tailored approach based on the size of the diverticulum, patient conditions and ability to withstand surgical complications is advisable ⁷⁻⁹.

Epidemiology, clinical presentation and pathophysiology

Zenker's diverticula typically present in middle-aged adults and elderly individuals, especially during the seventh and eighth decades of life, with a 1.5-fold male predominance. There is a geographical variation in its occurrence, and ZD is more frequent in northern Europe ¹⁰. The estimated annual incidence is 2 per 100,000 with prevalence between 0.01 and 0.11% ¹¹. However, although Zenker's diverticula are the most common type that cause symptoms ⁴, its incidence and prevalence may be underestimated as many diverticula may remain clinically silent, and many elderly patients with small pouches and minimal symptoms may not seek medical advice ¹. As ZD is directly related to aging, the prevalence of ZD is expected to increase due to the increased aging population.

Classical symptoms of Zenker's diverticulum are progressive oropharyngeal dysphagia (usually to solids and liquids), regurgitation (often hours after ingestion) of

undigested food debris due to food entrapment in the diverticulum, pharyngeal stasis of secretion, chronic cough, chronic aspiration, halitosis, sensation of a lump in the throat, hoarseness, whistling and cervical borborygmi ¹. The patient may note food on the pillow upon awakening in the morning. Although small diverticula may not cause symptoms, larger diverticula usually are symptomatic. Both the inability of the sphincter to fully open and the extrinsic compression from the pouch itself are likely to explain the dysphagia experienced by patients ⁴. With very large diverticula, a gurgling swelling in the neck can occasionally be detected on palpation. Secondary consequences and potential complications of ZD include *ab ingestis* pneumonia secondary to aspiration, medication ineffectiveness, malnourishment and unintentional weight loss. Other reported complications of untreated ZD are diverticulitis, peptic ulceration, bleeding, iatrogenic perforations during passage of endoscopes or nasogastric tubes, fistulas and vocal cord paralysis ¹¹.

Cancer, probably a result of chronic irritation and inflammation due to food and liquid stasis, has rarely been reported in association with Zenker diverticula, with an incidence of 0.5% ¹². Malignancy should be suspected if there is a sudden change in the severity of symptoms, such as severely worsening dysphagia or aphagia or development of alarm symptoms (haemoptysis, haematemesis or local pain) ¹³.

A barium swallow study is the mainstay in diagnosis of Zenker's diverticulum, which allows determination of its size and location, but careful endoscopic evaluation is mandatory to rule out malignancy ^{6,12}.

Though it is widely accepted that the primary cause of a Zenker's diverticulum appears to be impaired relaxation of the upper oesophageal sphincter, generating an abnormally increased pharyngeal intrabolus pressure, as corroborated by manometric investigations ¹⁴, ZD is likely to be a multifactorial disorder. The noncompliant cricopharyngeal muscle shows structural changes in terms of histological reduction in muscle component combined with qualitative fibre alterations, increase in fibrotic tissue and significant increase of the collagen to elastin ratio ^{14,15}. The aging process might play a role because of the loss of tissue elasticity and the decrease in muscle tone. Some authors postulate an anatomical predisposition ¹². This belief is reinforced by the evidence of rare familial cases in addition to geographical and racial differences ^{11,12}, and further supported by the results of morphometric and anthropometric studies of the Killian's triangle showing that the dimension of the triangle correlates with anthropometric features ¹⁶. This might account for the geographical variations in incidence of ZD and for its male predominance. Because gastroesophageal reflux contributes to cricopharyngeal dysfunction, a relation between gastro-oesophageal reflux disease and ZD has finally been assumed ¹¹, but never been consistently investigated.

What is the aim of treatment?

The primary therapeutic aim is to create a communicating door between the diverticulum and the oesophageal lumen by transecting the septum to eliminate the diverticulum reservoir, restore outflow continuity at the pharyngo-oesophageal segment allowing clearance of ingested bolus and subsequently relief symptoms and prevent recurrence⁵. Treatment should be reserved for symptomatic patients with or without associated complications^{11 17}, while small asymptomatic diverticula do not need treatment as the risk of severe adverse complications, cancer and aspiration is low⁶.

According to the current focus on the contribution of cricopharyngeal muscle in the genesis of ZD, treatment imposes myotomy of the cricopharyngeal muscle independently of the additional procedure (creation of a plain oesophagodiverticulostomy, diverticulectomy or suspension diverticulopexy)⁶. Division of cricopharyngeal muscle fibres (even without diverticulectomy) reduces the UES resting pressure and normalizes both UES opening (relaxation) and intrabolus pressure as demonstrated by pharyngo-oesophageal manometry^{4 8 9 15}.

Since both the cricopharyngeal muscle and the upper muscular cuff of the oesophagus appear to be involved in the pathogenesis of ZD, some authors advocate the extension of the myotomy for 2-3 cm into the muscularis propria of the oesophagus below the cricopharyngeal muscle¹⁵. In their opinion, extended myotomy to the oesophageal muscle potentially reduces the risk of recurrence. This raises however doubt as to whether it is associated with an increased risk of mediastinum exposure and perforation or vascular injury, especially in case of huge floating or plunging diverticula.

Treatment options

In the general trend versus less invasive approaches, new techniques and new devices have been implemented, and transoral endoscopic treatment¹⁸ and flexible endoscopy^{19 20} have gained in popularity over open surgery with a concurrent decrease in mortality and morbidity. Treatment procedures for ZD encompass open cricopharyngeal myotomy with diverticulectomy or diverticulopexy or diverticular inversion, myotomy alone²¹, endoscopic staple-assisted oesophagodiverticulostomy^{18 22}, endoscopic CO₂-laser myotomy²³, endoscopic harmonic scalpel diverticulotomy²⁴ and flexible endoscopic diverticulotomy²⁵. As already mentioned, the evolution in surgical and endoscopic treatment reflects the better understanding of underlying mechanisms, and it is a widespread belief that myotomy should always be part of treatment⁶. Diverticulectomy, diverticulopexy or inversion alone without myotomy are no longer acceptable given the high rate of long-term recurrence in the absence of cricopharyngeal myotomy²⁶.

Surgical techniques

The management of patients with pharyngeal pouch may be either conservative (for smaller than 1 cm, asymptomatic diverticula) or surgical through an incision in the neck (open) or mouth (endoscopic). Surgery – either open or minimally invasive – is the main therapeutic approach.

A) Open surgery: Surgical repair of ZD, based on a transcervical access, consists in stapled or hand-sewn diverticulectomy or diverticulopexy or inversion with concurrent cricopharyngeal myotomy or even myotomy alone for small diverticula. The operation is usually performed under general anaesthesia, but can also be performed under local anaesthesia or C5-C6 superselective spinal anaesthesia²⁷. The patient is positioned in a supine position with a small pillow under his shoulders and the head hyperextended and slightly turned to the right side. The left later neck incision is made ventrally to the sternocleidomastoid muscle. Following division of the subcutaneous tissue and platysma, the pharynx and cervical oesophagus are exposed by retracting the sternocleidomastoid and carotid sheath laterally and the larynx and thyroid gland medially. Once the pouch is identified and completely dissected from the surrounding loose connective tissue and the neck of the pouch displayed, transection (myotomy) of the cricopharyngeal muscle and proximal fibres of the oesophageal muscle is performed for a length of about 5 cm on the cervical oesophagus^{27 28}. Following myotomy the ZD is: 1) surgically excised (diverticulectomy) or 2) uplifted and retracted as far as possible towards the prevertebral fascia and suspended as high as possible by suture to the prevertebral fascia or posterior pharyngeal wall (diverticulopexy) with the collar of the sac in a non-dependent position or finally, 3) inverted into the oesophageal lumen and oversewn (diverticulum inversion or invagination)²⁷⁻²⁹. In case of minute diverticula, once the myotomy is performed, the marsupialized diverticulum disappears becoming a part of the freed mucosa²⁸. During the surgical procedure, care must be taken to not injure the following anatomical structures: the recurrent laryngeal nerve running in the tracheoesophageal groove, the external laryngeal nerve that runs deep to the superior thyroid artery, the descending hypoglossal nerve and the cervical cutaneous nerve²⁸. A drain is placed, the subcutaneous space and platysma borders are sutured and the skin incision is closed. The drain is removed after 24 to 48 hours²⁸. Intravenous broad-spectrum antibiotics are usually administered perioperatively and continued for 1 week after surgery²⁹.

All studies of the different open surgical approaches are retrospective, and few are comparative where selection criteria for the choice of treatment are either not stated or unclear. The following surgical algorithm may however be drawn from the available literature: small (1 cm) symptomatic pouches are very likely well suited to myo-

tomy alone, moderate-sized diverticula (1 to 4 cm) are best treated by myotomy with suspension or inversion, and larger pouches probably warrant diverticulectomy with myotomy^{28,30}.

B) Rigid endoscopy: Though ZD can affect young adults as well, it is primarily a disease of the elderly, often affected by significant comorbidities and a minimally-invasive endoscopic approach avoiding the need for a neck incision, thus offering potential advantages. The rationale is that a septum containing the cricopharyngeal muscle divides the diverticulum sac from the oesophagus. By endoscopically dividing this party wall, the cricopharyngeal muscle is divided, and the diverticulum is marsupialized and becomes a unique cavity with the oesophagus, eliminating food entrapment and relieving the outflow obstruction. A number of endoscopic options to section the septum using operating laryngoscopes and laparoscopic instruments are available that are characterised by shorter operative time, reduced hospital stay, quicker resumption of oral intake and lower complication rates; moreover, they are as effective as open surgery.

B1) Endoscopic stapling diverticulotomy: In 1993, Collard¹⁸ in Belgium, and simultaneously Martin Hirsch³¹ in England, proposed a transoral single-stage cut and suture technique using a laparoscopic stapler introduced through a rigid endoscope, namely the bivalved Karl Storz Weerda diverticuloscope. The patient is positioned supine with the neck fully extended. The procedure requires general anaesthesia with orotracheal intubation. The bivalved laryngoscope in the closed position is carefully introduced into the oesophageal inlet under direct vision or better under video endoscopic monitoring. The diverticuloscope is then slowly withdrawn and with the opened self-retracting valves accommodated to expose the party wall between the diverticulum and the oesophageal lumen so that the anterior blade of the diverticuloscope is placed inside the oesophagus while the posterior blade intubates the diverticulum. The diverticuloscope is advanced until the bottom of the diverticulum is exposed. The common wall and the cricopharyngeus are set between the two lips of the diverticuloscope. An endoscopic linear stapler is introduced through the diverticuloscope down to the septum so that the cartridge blade is in the oesophagus and the anvil blade in the diverticulum. The diverticulostomy is created by simultaneously cutting and sealing together the anterior wall of the ZD and the posterior wall of the oesophagus with a double (or triple) row of staples along the cutting edges with minor leakage, perforation, mediastinitis or bleeding rates^{32,33}. Care must be taken to avoid diverticular perforation while placing the stapler. Attention must be paid in proper selection of patients to avoid leaving a significant residual septum in smaller diverticula (which may lead to persistent symptoms) given the non-functional protruding end of the stapler³². The fact that the stapler anvil extends beyond the end of the

staples and the staples extend beyond the razor cut entails that the stapler leaves some residual pouch, usually about 1.5 cm³³. The technique is consequently not indicated for diverticula smaller than 3 cm. However, the end of the stapling device can be trimmed to reduce the length of its non-functional distal tip and to subsequently allow advancement of the blade to the bottom of the diverticulum³⁴. The use of retraction sutures (with an Endostitch suturing device) through the lateral edges of the common wall to provide proximal tension on the cricopharyngeal bar and easier delivery of the septum fully into the jaws of the endoscopic stapling device has been successfully described³⁵⁻³⁷. Endoscopic staple-assisted oesophagodi-diverticulostomy has gained widespread acceptance and is often considered the first-line choice for treatment of ZD. The technique has become the most frequent surgical intervention for pharyngeal pouch performed in ENT practice in UK³⁸.

B2) Endoscopic carbon dioxide laser diverticulostomy: Endoscopic CO₂ laser-assisted diverticulostomy, first introduced in 1981 by van Overbeek¹², is a sutureless technique where the septum is divided by CO₂ laser. The principle of the laser endoscopic technique is to perform a full-length mucosal incision and complete myotomy of the common wall that separates the diverticulum from the oesophagus. The procedure is performed under general anaesthesia with endotracheal intubation. Once the diverticuloscope is accommodated and the tissue bridge is properly exposed, an operating microscope with a 400 mm lens and attached CO₂ laser micromanipulator is focused on the common wall visualized through the diverticuloscope. Using the laser at 5 to 10 Watts in continuous mode, the spur is transected at the midline down to the bottom of the diverticulum, with care taken not to leave residual common wall. The cricopharyngeal muscle fibres appear as they retract laterally during division^{39,40}. Visualization of targeted tissue through the microscope and the precise laser beam control enabled by the micromanipulator device allow excellent exposure and the precision required to section the common wall down to the bottom of the diverticulum sac without the view being impaired by instruments^{39,41}. Carbon dioxide laser endoscopic diverticulotomy can also be achieved with thinner diverticulosopes than those required for the stapler-assisted technique, keeping a good view of the diverticular threshold⁴⁰. Microendoscopic laser techniques seem suitable to treat small-moderate sized diverticula or as a complementary technique in addition to endoscopic stapling when the pouch is considered too small to be (further) cut by the stapler^{17,39,42}. With regard to concerns over less secure mucosal closure achieved with this sutureless technique, the CO₂ laser has a high-energy, high-focus beam providing high cutting power while minimizing lateral thermal tissue damage, arguably ensuring rapid healing and mucosal coverage of cut surfaces^{39,41,42}. Peretti et al.⁴³ have interestingly reported on endoscopic CO₂ laser cri-

copharyngeal myectomy for medium-sized ZD. The partial myectomy of the posterior part of the cricopharyngeal muscle is achieved by entirely sectioning the posterior part of the muscle itself, following two vertical paramedian lines, and then removing the in-between portion of the muscle fibres up to the external fascial layer.

B3) Harmonic scalpel: More recently, using the Weerda diverticuloscope with the patient under general endotracheal anaesthesia, the section of the party wall between the diverticulum and the oesophagus has been achieved using a harmonic scalpel (Harmonic Ace). The harmonic scalpel, or Ultracision (Ethicon Endo-Surgery, Cincinnati, Ohio), is used in laparoscopic surgery to simultaneously cut and coagulate tissues with minimal thermal spread to adjacent tissues. The harmonic scalpel blade operates ultrasonically, causing protein denaturation such that vessels are sealed and tamponaded while providing adequate and effective timely haemostasis. This sutureless technique has been shifted to ZD repair as an additional tool for performing a cricopharyngeal myotomy with success and minimal complications. In particular, diverticulostomy with the ultrasonic scalpel has proved effective for small ZD (≤ 2 cm). The smaller diameter of the harmonic scalpel allows it to be manoeuvred and positioned within small diverticula. In addition, the harmonic scalpel's cutting surface extends to its distal tip, allowing it to perform endoscopic oesophagodiverticulostomy in patients with shallow pouches that could not be adequately treated with the stapling device^{24,44-46}. The use of the harmonic scalpel technique with a soft diverticuloscope has recently been described⁴⁶.

Freehand, cap-assisted or diverticuloscope-assisted flexible endoscopy

In addition to surgical techniques, evolution in flexible endoscopy paved the way for its use in the treatment of ZD. In 1995, two landmark papers^{19,20} indicated that flexible endoscopy was a possible option for ZD. Flexible endoscopy shares the same principles as rigid endoscopy: the septum between the diverticulum and the oesophagus contains the cricopharyngeal muscle, while by dividing the septum and creating a common cavity a myotomy is automatically added⁶. High-risk elderly patients are expected to benefit the most from flexible endoscopic diverticulotomy¹¹. The procedure can be safely performed in the endoscopy suite, in the inpatient or outpatient setting, does not require general anaesthesia and is rapid and effective^{25,47}. Some centres offer this option to all ZD patients⁴⁷, although most authors recommend reserving it for a subset of selected patients, especially highly morbid patients and older individuals who are poor surgical candidates with head and neck anatomy that make rigid endoscopic access difficult^{11,17}. The technique can be either "freehand" or combined with a variety of different accessories (hood, cap, overtube) to obtain a better exposure of the

septum, stabilize the position and protect the oesophageal and diverticular wall against thermal injury⁴⁸⁻⁵⁷. Patients are placed in a left lateral decubitus position, either in conscious sedation or under general anaesthesia with propofol or endotracheal intubation according to local practice^{47,53}. Antibiotic prophylaxis is not routinely administered. The procedure is usually done with a standard flexible endoscope and starts with initial endoscopic examination with suction of possible retained material from the diverticulum. A standard large bore (16-18 Fr) nasogastric tube is generally inserted (over a guidewire) in the oesophagus for the aforementioned purpose. Transparent caps or oblique-end hoods attached to the tip of the flexible endoscope can further stabilize the position⁵⁴⁻⁵⁶. A novel device for exposing, stretching and fixing the septum, and optimizing the operative field is the soft diverticuloscope (ZD overtube; Cook Endoscopy, Winston-Salem, North Carolina, USA)⁵². This double duck-billed transparent soft-rubber overtube has two distal flaps of 40 mm and 30 mm that respectively protect the anterior oesophageal and posterior diverticular wall. The overtube is advanced over the endoscope up to a black marker indicating the average distance (16 cm) between the septum and teeth line. Under endoscopic vision the septum is displayed and the position of the overtube can be further adjusted⁵³. Once the septum is properly exposed, different cutting methods can be applied. Incision can be done using needle-knives, monopolar forceps, argon plasma coagulation or a hook-knife⁵⁵⁻⁵⁸. With the needle-knife, the predominant cutting technique, the septum is divided through blended current or pure coagulation current. The incision is caudally directed by moving the tip of the endoscope, hence the tip of the needle, from the middle at the top of the septum towards the basis of the ZD recess, indifferently from the inside of the diverticulum towards the posterior oesophageal wall or in the opposite direction^{50-54,56}. The wound edges of the ZD spur separate immediately after incision. The incision has to be cautiously balanced to prevent mediastinal perforations due to excessive incision (beyond the inferior border of the diverticulum) and to be complete (not too short)¹¹. An incomplete cricopharyngeal myotomy may account for the higher recurrence rates associated with flexible endoscopy. Ideally, ZD should be reduced to < 1 cm left⁴⁸. Bleeding at the site of incision can be locally controlled. Some endoscopists routinely place one or more metal endoclips at the incision basis to secure the oesophageal and diverticula margins, thereby preventing microperforations^{25,53}. Concerns over perforation risks associated with a sutureless section have led some authors to adopt a clip-assisted (clip and cut) technique where, prior to dissection with a needle-knife in the middle, two endoclips are placed on either side of the ZD bridge⁵⁹. Several authors describe limited incisions in a single session in short-term repeat procedures, and reserving one-session diverticulotomy for small diverticula¹¹.

Technical and clinical success of treatment options

Treatment of ZD has dramatically evolved over the past years. An external surgical approach has for long been the conventional treatment modality with satisfactory clinical success rates ranging between 80-100%¹⁷. The Mayo Clinic reported excellent or good outcome in 93% of 888 patients treated with open surgery²¹, but complication and mortality rates are not negligible and have been reported to be as high as 30% and 3%, respectively^{60 61}. Major complications (requiring intensive medical treatment, blood transfusion, surgery or intensive care unit admission) include pharyngocutaneous fistulas, parapharyngeal abscess, mediastinitis, perforation, pneumomediastinum, oesophageal stricture, wound infection, significant bleeding requiring operative revision, vocal cord paralysis, aspiration pneumonia, and death. Minor complications consist of transient recurrent laryngeal nerve paralysis, postoperative fever and temporary subcutaneous emphysema suggestive of microperforation. In a literature review by Zbaren et al.⁶², mediastinitis and stenosis were reported in up to 9.5% and 7.1%, respectively, of external approach cases. Cutaneous fistulas and recurrent laryngeal nerve paralysis were described in 19% and 12.9%, respectively. Among the available transcervical modalities, only diverticulectomy removes the pouch allowing histopathological examination of the diverticulum sac¹. However, this technique is associated with a higher risk of pharyngocutaneous fistula (up to 30%), transient or permanent recurrent nerve paralysis, and oesophageal strictures. Some authors suggest therefore diverticulum inversion as an effective, less traumatic and less complicated surgical treatment modality²⁹. However, after either inversion or suspension of the sac, no further inspection of the diverticulum mucosa is possible for early detection of malignancy, and this has to be kept in mind in case of larger long-standing diverticula in which the risk of malignant degeneration is reported to be higher^{62 63}. As already mentioned about the aetiology of the disease, myotomy is a crucial part of the ZD treatment whatever the attitude towards the pouch is. Although very effective at mid-term, ZD resection without myotomy predisposes to the development of postoperative salivary fistula and to long-term recurrence of the pouch, probably due to persistence of high intrapharyngeal pressure against the posterior pharyngeal wall²⁶. Data reported in the relevant literature indicate recurrence in 3-19% of diverticular resections, 6-15% of cases with diverticulum inversion, and up to 7% for diverticular suspension²⁹. According to the available literature, lacking in high quality comparative studies, the choice between transcervical surgical options may be best dictated by the size of the ZD in the context of the patient's conditions. Diverticulectomy is advisable for ZD larger than 5-6 cm and in younger patients given

the risk, though low, of malignant degeneration, while diverticulum inversion or suspension are suitable to small-moderate sized (up to 4 cm) diverticula, and patients with small, but symptomatic, pouches can be adequately managed with myotomy alone^{17 28-30 65}.

As already pointed out, since ZD affects frail elderly patients, who are more often than not poor surgical candidates, less invasive treatments are desirable. The first attempt in 1917 to introduce an endoscopic approach was promptly abandoned due to high complications and mortality rates. An endoscopic approach for the treatment of ZD was again attempted in 1960 with satisfactory results, but due to concerns over possible leak with mediastinitis surgeons were reluctant and the endoscopic technique did not gain acceptance⁶⁶. It was not until 1993 that a rigid endoscopic approach with endostapler was definitively introduced and became increasingly popular^{34 35}. Endoscopic stapling of pharyngeal pouch is less invasive, very safe and effective, and has become, as supported by the abundant literature, the first-line surgical treatment with clinical success rates that favourably compare with open surgery¹⁷. Large studies demonstrated endostapling to be effective in 90-100% of cases⁵, with acceptable persistent symptomatic relief during long-term follow-up²⁷. Myotomy, the crucial aspect of ZD treatment, is unavoidably a part of the procedure. Endoscopic stapler-assisted diverticuloesophagostomy has a lower rate of major complications (fistula, iatrogenic perforation and mediastinitis, persistent recurrent laryngeal nerve injury) up to 4% on average, with < 1% mortality. Minor adverse events include sore throat, gingival or mucosal tear, dental injury, transient vocal cord palsy, subcutaneous emphysema and foreign body sensation or stenosis due to staples⁶⁷. Antibiotics are not routinely given nor is a NGT routinely inserted. The distinct advantages of endostapling over standard open-neck technique encompass, as reported in several series^{27 60 68 69} and in a recent meta-analysis involving 585 patients⁷⁰, the absence of skin incision, shorter operative time, minimal or absent post-operative pain, quicker resumption of oral intake (within 24 hours), reduced hospital stay calculated from the day of operation until discharge (24-48 hours), resulting in lower total hospital charges, as well as a lower rate of overall complications. An additional advantage lies in case of repeat procedures, for persistent or recurrent symptoms, that can successfully be carried out through a transoral approach (rigid or flexible), while an open approach may pose a major technical challenge²⁷. Review of the literature highlights mean recurrence rates of about 6% (range 0-22%) consistent with the mean recurrence rate of 5% reported for external approaches⁶⁸. The above-mentioned meta-analysis⁷⁰ reports a clinical success rate in terms of resolved or significantly improved symptoms of 91% with a recurrence rate as high as 12.8% and a technical success rate in 92% of cases. This relatively high level

of recurrence may reflect incomplete sectioning of the fibres of the septum by the stapler. Determining the point at which stapler division of the septum should end is a critical issue, as a division that is too shallow will lead to persisting symptoms, while a division that is too deep increases the risks of perforation with mediastinitis. The same circumstance accounts for the high long-term recurrence rates recorded by Bonavina et al.²⁷ in the subgroup of patients treated for small (< 3 cm) diverticula, when recurrence rates were stratified according to ZD size. In small diverticula, a portion of the septum may remain undivided. Diverticula smaller than 3 cm represent a formal contraindication to an endosurgical approach because too shallow to properly accommodate the anvil of the stapler and allow complete transection of the septum; recurrence may occur in > 35% of patients. Endoscopic stapling diverticulotomy is better suited to medium-sized diverticula (3-5 cm)⁹ in accordance with the existing literature. On the other hand, diverticula longer than 6 cm represent a relative contraindication to endoscopic treatment as the residual pouch may be too large to allow easy clearance of the common cavity upon swallowing⁷¹. Moreover open surgical diverticulectomy with myotomy provides radicality, eliminating any theoretical risk of carcinoma, and this has to be borne in mind when considering the potential of malignant evolution in residual pouches after endoscopic treatment⁷². Despite early reports over higher complication rates with endoscopic CO2 laser⁷³ and ultrasonic cutting⁷⁴ in the management of ZD, some authors suggest a possible complementary role of these techniques for dividing the residual septum when endostapling fails to be complete or when introduction of a stapling gun results in poor access or a poor surgical view^{44 70 75}. After rigid endoscopic or surgical treatment, a persistent septum or a residual pouch can still be evident on barium swallow examination. Persistent symptoms may be due to other underlying swallowing abnormalities and/or inadequate myotomy without any correlation between the size of the residual pouch and symptomatic recurrence. There is general agreement in the literature that the assessment of treatment outcome and the need for further treatment has to be clinically prompted by patient's symptoms^{1 17}. Rigid endoscopy is not always technically feasible and may require conversion to open surgery in about 5% of cases. A recent review of the literature reports technical success rates ranging from 70% to 100%¹⁷. The main reasons for technical failure are impossible or inadequate exposure of the diverticulum due to the patient's anatomy such as retrognathia, teeth protrusion, rigid cervical kyphosis, insufficient neck motility, inability to hyperextend the neck or to open the mouth wide. Moreover, rigid endoscopy requires general anaesthesia with endotracheal intubation, and not all patients are fit for surgery or able to withstand general anaesthesia. Last but not least, in addition to anatomical or clinical

considerations, smaller or very deep diverticula are not amenable to rigid endoscopy since those conditions impair accommodation of the rigid diverticuloscope and stapler in the pouch. In case of small diverticula, the anvil of the stapler cannot be properly placed and cricopharyngeal muscle cannot adequately be resected. Other factors predictive of success or failure are short necks, decreased hyomental distance, large osteophytes, obesity, redundant mucosa^{6 11 17 76 77} and the radiological characteristics of the diverticulum⁷⁸.

In the general trend towards a minimalist approach, flexible endoscopy is an attractive alternative and may overcome some of the technical limitations of open surgery and rigid endoscopy, as well as some of the constraints related to ZD size and the patient's conditions. Flexible endoscopy is usually performed in the endoscopic unit, under conscious sedation with midazolam and/or opiates, and is optimal for frail elderly patients, unfit for surgery, who are most likely to benefit from a brief procedure without the need for general anaesthesia and for neck hyperextension⁴⁷. As for rigid endoscopy, flexible endoscopic treatment focuses on releasing the cricopharyngeal spasm by performing a cricopharyngeal myotomy and restoring the outflow continuity. Assuming no complications, it allows a rapid (normally after 24 hr) oral diet resumption and fast hospital discharge (usually 12-48 hr in an inpatient setting and 6 hours in the outpatient setting) with success and complication rates similar to endostapling. In case of symptom persistence or recurrence the procedure is safely and easily repeatable. In a recent retrospective paper⁷⁹ assessing flexible endoscopy versus endostapler the authors reported similar outcomes in terms of hospital stay, dysphagia symptom score improvement and complication rates, but a significantly longer procedure time for endostapling versus flexible endoscopy. Several case series published since 1995 demonstrate the efficacy and safety of flexible endoscopy with clinical success rates ranging from 56% to 100%^{19 47-59}. The lower clinical success rate of 56% reported in one series⁵³ is very likely due to the fact that clinical remission was assessed according to the presence or absence of a pool of symptoms and not only dysphagia. When considering the sole series in which success is defined according to dysphagia, clinical success rises to 84-100%^{19 48 49 51 52 54-57}. Moreover in some cases outcome was assessed after one treatment session^{52 53 57}, while in other series it was determined after multiple treatment sessions^{19 48-50 55 56 58}. Unlike rigid endoscopy, and in particular endostapling, the technique of flexible ZD septotomy is neither univocal nor standardized. As already mentioned, different cutting techniques exist that can be variably combined with different accessories. The optimal cutting technique is unknown as prospective randomized trials are lacking and the choice is mainly based on the endoscopist's personal experience and preferences. The needle-knife, even if more difficult to master without ad-

ditional devices⁴⁷, is the most frequently used cutting device often in combination with a cap^{53,56}, hood^{54,55} or soft diverticuloscope^{52,53} to achieve a more stabilized position and optimal view of the operative field. There are no significant differences in clinical outcomes with the use of one or other accessory. Flexible endoscopy is associated in the available literature with a clinical recurrence rate of 20%¹¹. The incision must not extend beyond the inferior border of the diverticulum as this may cause mediastinal perforation, but a transection that is too short may lead to incomplete cricopharyngeal myotomy and subsequently account for the higher clinical recurrence rates reported for flexible endoscopy. The depth of septotomy is a major technical issue. Unfortunately, when the incision is made from up to down the inferior border may be difficult to endoscopically define, and there are no objective parameters or reliable anatomical landmarks (except for muscular fibres) to guide the endoscopist. This prompted Repici et al.⁵⁷ to expand the use of the hook-knife, from endoscopic mucosal dissection, to ZD septal dissection and assess its safety and efficacy. The direction of the incision is inverted, from the bottom to the top. The cut appears to be more controlled and precise, reducing the risk of unintentional blunted dissection and perforations. The authors reported 1 perforation out of 35 treatments (2.8%) and a very good clinical remission rate (up to 93%). While the technical advantage should correspond to a reduced risk of perforation, the small sample size and short follow-up time did not allow for definitive conclusions. With regard to complication rates, perforations ranging from mediastinitis or cervical abscesses to microperforation (presenting as self-limited subcutaneous cervical emphysema) and bleeding have been reported in 0-27% (median 4%) and 0-10% of cases, respectively¹⁷. Other possible complications of flexible endoscopic treatment of ZD are transient fever with leukocytosis, throat pain, and sedation-related adverse events. Although routinely performed by some authors, post-procedural water-soluble contrast studies have limited sensitivity for detection of small perforations and do not correlate with symptomatic response to endoscopic therapy or with recurrences¹¹. Flexible endoscopy is an appealing safe and effective minimally-invasive treatment option for ZD, with good clinical outcome, acceptable recurrence, and complication rates. The most suitable candidates are older and high-risk patients who are unfit for surgery, even though some authors extend the indication to all symptomatic patients referred for treatment.

When comparing the technical and clinical results from the available literature on ZD treatment, it should be critically pointed out that a direct comparison between studies and results may be inappropriate because data are neither

homogenous nor standardized with regard to multiple variables. Of note in this regard: symptoms collection (dysphagia, dysphagia plus regurgitation, a pool of symptoms), symptom assessment (objective dysphagia scores, subjective grading of symptoms relief and satisfaction), choice of one or other technique (sequential, diverticulum size, clinical conditions, local policy), definition of clinical success (total disappearance of symptoms, disappearance plus improvement), success and recurrence measurements (after one session or multiple sessions), and the variable length of follow-up (the shortest follow-up schedules being reported for treatment via flexible endoscopy in contrast with the more recent series of transorally treated patients and with a historical cohort of surgically treated patients).

None of the available studies, based on retrospective case series, unequivocally demonstrates the substantial superiority of one treatment modality over another, and although rigid endoscopy is the preferred and most frequent approach, the choice between different options depends on local expertise and preferences.

Conclusions

The present paper provides an overview of the literature for the main surgical and endoscopic treatment modalities for ZD. Many treatment alternatives exist, reflecting the fact that none has gained proven superiority. All approaches have been shown to work in the hands of experienced surgeons, otolaryngologists, and gastrointestinal endoscopists, and the optimal treatment policy remains highly debated.

There are no randomized studies comparing the different surgical and endoscopic approaches, few are comparative, and selection criteria for the choice of treatment are either not stated or unclear. The large number of retrospective case series does not allow the possibility to draw firm conclusions, although some general indications have emerged. In particular, small-medium (up to 5 cm) sized diverticula are best treated endoscopically, with ZD up to 3 cm best amenable by flexible endoscopy, while very large diverticula may still benefit from open surgical excision, especially in younger, good surgical candidates. Repeat procedures, in case of treatment failure or symptomatic recurrence, can easily and successfully be achieved through flexible or rigid endoscopy.

Randomized comparative trials of the general approaches to treatment are long overdue, but are hardly feasible. The low prevalence of the disease, the minimum number needed to treat and the highly concentrated local expertise, would make it difficult to enrol and randomize candidates between the various treatment options.

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