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Techniques and efficacy of flexible endoscopic therapy of Zenker's diverticulum

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Abstract

Zenker's diverticulum (ZD) is an abnormal hypopharyngeal pouch often presenting with dysphagia. Treatment is often sought with invasive surgical management of the diverticulum being the only mode of definitive therapy. Primarily done by an open transcervical approach in the past, nowadays treatment is usually provided by otolaryngologists using a less invasive trans-oral technique with a rigid endoscope. When first described, this method grew into acceptance quickly due to its similar efficacy and vastly improved safety profile compared to the open transcervical approach. However, the main limitation with this approach is that it may not be suitable for all patients. Nonetheless, progress in the field of natural orifice endoscopic surgery over the last 10-20 years has led to the increase in utilization of the flexible endoscope in the treatment of ZD. Primarily performed by interventional gastroenterologists, this approach overcomes the prior limitation of its surgical counterpart and allows adequate visualization of the diverticulum independent of the patient's body habitus. Additionally, it may be performed without the use of general anesthesia and in an outpatient setting, thus further increasing the utility of this modality, especially in elderly patients with other comorbidities. Today, results in more than 600 patients have been described in various published case series using different techniques and devices demonstrating a high percentage of clinical symptom resolution with low rates of adverse events. In this article, we present our experience with flexible endoscopic therapy of Zenker's diverticulum and highlight the endoscopic technique, outcomes and adverse events related to this minimally invasive modality.

Key words: Zenker's diverticulum; Flexible endoscopy; Natural orifice endoscopic surgery; Per-oral endoscopy; Dysphagia; Cricopharyngeus myotomy; Cricopharyngeus septotomy

Core tip: Definitive therapy for Zenker's diverticulum (ZD) typically includes either diverticulectomy or myotomy/

septotomy of the cricopharyngeus muscle. Previously done as an open transcervical approach by surgeons, treatment has now evolved to include a minimally invasive trans-oral approach with flexible endoscopy performed by gastroenterologists. In this article we highlight our experience with flexible endoscopic therapy of ZD at our institution, describe commonly used flexible endoscopic techniques and devices, and assess efficacy and safety data related to this minimally invasive modality.

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INTRODUCTION

Zenker's diverticulum (ZD) is a pharyngeal outpouching caused by increased intraluminal pressure, in conjunction with an area of inherent weakness in the hypopharynx known as the Killian triangle. This area of vulnerability is formed in between two pharyngoesophageal muscles, the inferior pharyngeal constrictor and the cricopharyngeus. Since the original description of the condition by Ludlow[1] and then Zenker von Zeimssen[2]; the pathophysiology that leads to the ZD has been poorly understood. Currently, the mechanism that leads to increase in luminal pressures causing the ZD is thought to be due to poor upper esophageal sphincter (UES) compliance[3,4].

Characteristic symptoms for ZD include dysphagia, which is the presenting symptom in 80%-90% of patients. Additionally, patients may present with cough, dysphonia, malnutrition and weight loss. Occurrence is not usual in patients under the age of 40 years with incidence most prevalent in males in the seventh or eighth decade of life[5]. The diagnosis of ZD is based on clinical and radiographic findings, with dynamic barium esophagram being the confirmatory study[6]. Surgical intervention involving disruption of the cricopharyngeus by myotomy and/or diverticulectomy is the mainstay of treatment. The open trans-cervical approach that was originally described by Wheeler[7] has now evolved after a sentinel paper published by Dohlman and Mattson[8] to a less invasive trans-oral approach using a rigid endoscope. This technique currently performed by otolaryngologists, is the method of choice due to similar efficacy, reduced patient morbidity and overall shorter hospital stay compared to traditional open transcervical surgery[9].

Indeed, all patients who are diagnosed with ZD would ideally undergo endoscopic therapy as the benefits mentioned previously make this a more favorable choice for patients and clinicians. However, as with all surgical procedures there are several pre-interventional considerations. At the crux of these issues are the needs to visualize the diverticulum trans-orally. Several patient indicators including high body mass index and poor neck flexibility predispose the patient to higher risk of adverse events and procedural failure. As such, an open approach is still used in 15% to 68% of cases[5]. Nevertheless, within the past 20 years the trans-oral approach has progressed with the advent use of a flexible endoscope. Currently performed by interventional gastroenterologists/endoscopists, this method helps overcome the prior concerns of visual limitations while still providing a minimal invasive approach to this complex surgical condition. Several variations to this procedure have been explored and published in recent times, though, lacking comprehensive long-term analysis and comparative effectiveness of these various techniques. In this article we highlight our experience with flexible endoscopic therapy of ZD at our institution, describe commonly used flexible endoscopic techniques and devices, and assess efficacy and safety data related to this minimally invasive modality.

THE UNIVERSITY OF FLORIDA (UF) EXPERIENCE

Aims and outcomes

The aim of this study was to assess the efficacy and safety of patients undergoing flexible endoscopic treatment of ZD. Efficacy was defined by: (1) technical success of endoscopic therapy; and (2) improvement in dysphagia score. Safety was characterized by the lack of development of intra-procedural or post-procedural adverse events (AE).

Definitions

Technical success: Procedural technical success was defined as the ability to successfully perform flexible endoscopic cricopharyngeus myotomy.

Dysphagia score: A score range (0-4) was used to quantify dysphagia prior to and after endoscopic treatment[10].

Adverse events: Endoscopic adverse events were assessed based on previously established criteria by the American Society of Gastrointestinal Endoscopy (ASGE)[11].

Methods and techniques

This study was approved by the University of Florida Institutional Review Board (IRB). Our electronic endoscopy database was queried from January 2006 through June 2014 for patients who were referred to a single interventional endoscopist for flexible endoscopic treatment of ZD. Diagnosis of ZD was made with either barium esophagram, computed tomography or direct endoscopic visualization.

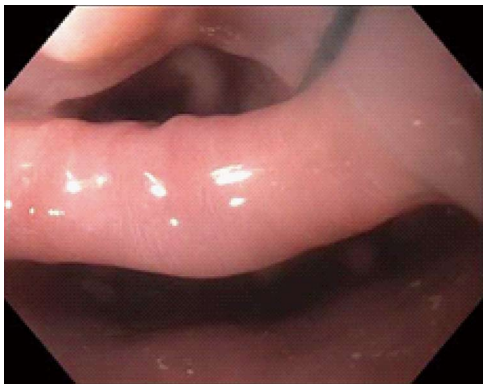

Figure 1 Endoscopic appearance of Zenker's diverticulum (esophageal lumen with guidewire is above the Zenker's diverticulum); note the cricopharyngeus septum separating the Zenker's diverticulum from the esophagus.

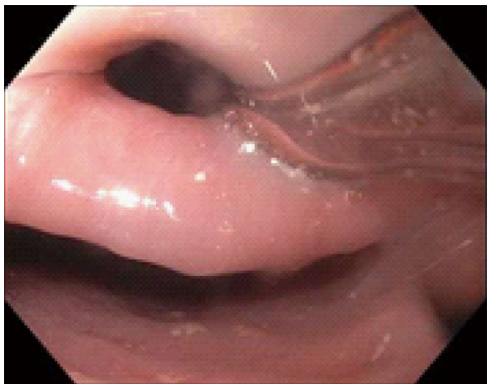

Figure 2 Nasogastric tube in true lumen of the esophagus.

General anesthesia was used per anesthesiologist recommendations and prophylactic antibiotics were typically not given. The procedure was begun after general endoscopic evaluation of the ZD (Figure 1), stomach and duodenum. A nasogastric or orogastric tube (Figure 2) was then placed over a guidewire for improving visualization of the diverticulum and protection of the anterior esophageal wall during myotomy. A needle knife was then used to perform the myotomy (Figure 3) exposing the transverse fibers of the cricopharyngeus. Following the procedure, all patients were then admitted overnight for observation and gradual advance of their diet.

Results

A total of 8 patients [50% male, mean age 72.4 years (range 58-88)] underwent technically successful flexible endoscopic myotomy of their ZD. One endoscopic treatment session was performed per patient and all patients noted improvement in their dysphagia symptoms after therapy. The mean pre-procedure dysphagia score was 2.6 (range 2-4) and post-procedure dysphagia score was 0.4 (range 0-2). There were no AE and mean follow-up time was 5.8 mo (range 0-17). Two patients with mild residual dysphagia did not wish to undergo a repeat procedure or other interventions.

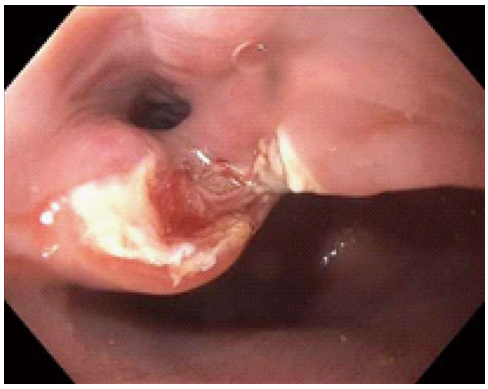

Figure 3 Cricopharyngeus myotomy.

TECHNICAL ASPECTS

Since landmark studies by Mulder[12] and Ishioka[13], the use of flexible endoscopy to treat ZD has come into many centers as an additional minimally invasive modality for management. Described by radiographic and manometric studies by Cook[3], pathogenesis of this abnormality seems to be related to poor UES compliance leading to increase swallowing pressures and in turn a Killian's dehiscence. As such, the mainstay of treatment has been ablation or division of the cricopharyngeus "septum" (cricopharyngeus myotomy or septotomy) and there have been many variations in the way this myotomy is performed. Additionally, most institutions have employed tools aiding to secure and expose the septum such as the diverticuloscope and clear cap assisted devices. Currently, 19 case series/analyses[10,12-29] have been published describing flexible endoscopic therapy in over 600 patients with ZD (Table 1).

Pre-operative assesment

Typically, symptomatic patients undergo barium esophagram and index upper endoscopy for diagnosis of ZD. One of the advantages of flexible endoscopic therapy for ZD is the ability to perform the procedure without general anesthesia in many cases. This allows patients who are not ideal candidates for endotracheal intubation to undergo either moderate sedation (conscious sedation/CS) or deep sedation/monitored anesthesia care (MAC). In published studies (Table 2) where mode of anesthesia was mentioned, greater than half of all patients underwent endoscopic procedures with either CS or MAC, without mention of intraoperative adverse events related to airway compromise. Nevertheless, some authors[26] still insist in using general anesthesia to protect the airway in case of bleeding at the UES and since the improved muscle relaxation provides greater safety assurance when manipulating the endoscope.

Table 1 Published cases for flexible endoscopic therapy of Zenker's diverticulum

Ref.	Total patients (n = 678)	Age (range)	Device for myotomy	Assist device	Pre-procedure dysphagia score	Post-procedure dysphagia score	Clinical symptom resolution rate	Adverse events	Recurrences	Followup (range)
Mulder *et al*[12]	20	Mean 82 (41-100)	FC	None	NA	NA	85%	0%	0	Mean 7 (1-18)
Ishioka *et al*[13]	42	Mean 68 (46-102)	NK	None	NA	NA	93%	5%	7	Mean 38 (12-96)
Hashiba *et al*[14]	47	(58-81)	NK	None	NA	0 or 1	96%	14.9%	0	(0-12)
Mulder *et al*[15]	125	Median 77 (41-100)	APC	None	NA	NA	100%	20%	NA	NA
Sakai *et al*[16]	10	(67-87)	NK	Cap	1.8	0	100%	0%	0	(2-12)
Evrard *et al*[17]	31	Median 78	NK	DS			93%	13%	9	Median 12.5
Costamagna *et al*[18]	28	Median 66 (47-86)	NK	Cap	NA	NA	43%	32%	4	Median 36 (9-60)
Costamagna *et al*[18]	11	Median 70 (63-84)	NK	DS	NA	NA	91%	0%	1	Median 6.5 (3-15)
Rabenstein *et al*[19]	41	Mean 73	APC	Cap	NA	NA	95%	19.5%	5	Mean 16
Christiaens *et al*[10]	21	Median 77.5 (52-89)	FC	Cap	1.5	0	100%	3%	2	Median 22.4
Volgelsang *et al*[20]	31	Median 69 (52-92)	NK	Cap	NA	NA	100%	23%	10	Mean 26
Manner *et al*[21]	8	Mean 66	APC	Cap	NA	NA	NA	37.5%	NA	NA
Tang *et al*[22]	6	Mean 71 (48-91)	NK	Endo Clips	NA	NA	100%	0%	0	NA
Al-Kadi *et al*[23]	18	Mean 80 (68-91)	NK	None	(2-4)	NA	87.5%	5.5%	NA	Mean 27.5
Case *et al*[24]	22	Median 85	NK	None	NA	NA	100%	32%	4	Mean 12.7
Repici *et al*[25]	32	Mean 74.8 (58-92)	HK	Cap	2.96	0.62	NA	6.25%	3	Mean 23.9 (12-48)
Hondo *et al*[26]	5	Median 69.6 (59-83)	HS	DS	2	0.20	NA	0%	0	Mean 1
Huberty *et al*[27]	150	Median 73 (42-94)	NK	DS	1.88	0.34	90.3%	2.2%	31	Median 43 (13-121)
Ramchandani *et al*[28]	3	Mean 79	SB-K	DS	NA	NA	100%	0%	0	NA
Manno *et al*[29]	19	Median 74 (46-84)	IT-K	DS	NA	NA	100%	0%	2	Median 27
Perbtani (current study)	8	72.4	NK	None	2.6	0.4	100%	0%	2	Mean 5.8 (1-17)

NK: Needle knife; IT-K: Insulated tip knife; SB-K: Stag beetle knife; HK: Hook knife; HS: Harmonic scalpel; FC: Forceps coagulation; APC: Argon plasma coagulation; DS: Diverticuloscope; NA: Not available.

Procedural technique

Prior to performing the procedure various steps are essential to ensure safety in performing the myotomy: (1) Placement of a nasogastric (NG) or orogastric (OG) tube is a common practice that has been introduced with two potential benefits: First, it allows enhanced visualization of the esophageal lumen and diverticulum, and secondly it protects the anterior esophageal wall from injury from instruments used during myotomy; (2) Accessories to improve visualization: Sakai *et al*[16] originally described the use of an assist or accessory device during ZD therapy to stabilize and visualize the septum. A transparent oblique-end hood was used at the tip of the endoscope that extended distally. This in turn served to prevent closure of the upper esophageal sphincter thus allowing for better visualization of the tissue bridge between the esophagus and the diverticulum. Similarly, clear mucosectomy caps[19] have been used with similar intentions. In 2003 Evrard *et al*[17] described the use of a soft diverticuloscope as an adjunct that served a similar function as the clear cap device. The diverticuloscope is placed as an overtube on the endoscope and contains two distal flaps that serve to straddle the septum and safeguard the anterior esophageal and posterior diverticular walls. At this point the instrument used to divide the septum is introduced either alongside or through a channel within the endoscope. In review of the published cases, only one study looked at outcomes between accessories. Costamagna *et al*[18] documented lower complication rates and procedural time with the diverticuloscope *vs* using a clear cap. However, it is worth noting that the diverticuloscope is only commercially available in Canada and Europe.

In performing the cricopharyngeus myotomy the optimal instrument for ablation remains debatable. Moreover, due to the lack of prospective comparative trials the device chosen is often dependent on prior training and preference of the endoscopist. The most commonly used device is the needle knife as is our

Table 2 Modes of sedation used *n* (%)

Sedation type	Patients (*n* = 678)
Conscious sedation	352 (52)
Monitored anesthesia care	60 (9)
General anesthesia	77 (11)
Not reported	189 (28)

practice, followed by argon plasma coagulation (APC) and forceps coagulation (Table 3). This is notably different amongst otolaryngologists, where either carbon dioxide laser or a stapler-assisted device is most frequently employed[30]. When using the needle knife the tip of the instrument is placed at the center of the septum where coagulation, blended or alternating current can be used[16,18,20]. The division through the septum occurs in craniocaudal motion, which exposes the transverse fibers of the cricopharyngeal muscle. The incision should not extend past the inferior portion of the diverticulum, as risk for perforation significantly increases. Length of the myotomy has been described safely up to 5-10 mm from the bottom of the ZD[16,26,27] with endoclips placed by some endoscopists[18] distally for prophylaxis against microperforations.

Emerging techniques: Recent advances in natural orifice translumenal endoscopic surgery (NOTES) have given rise to novel myotomy techniques including per oral endoscopic myotomy (POEM)[31]. Similarly, endoscopic submucosal dissection (ESD) techniques have recently been reported[32] to extend its application to aid in cricopharyngeal myotomies. In this small case series, a modified clear cap overtube was created to secure the diverticular wall while indigo carmine solution was injected into the septum. A submucosal bleb or lift was then created which served to increase exposure of the cricopharyngeal muscle fibers and theoretically enabling a safer and more complete myotomy. Although this variation of flexible endoscopic treatment of ZD is in it's infancy, this study highlights the continual innovative modifications being made to optimize clinical outcome, reduce recurrence rate and sidestep technical hurdles faced by its predecessor.

Post-operative care

In the post-operative period patients have been discharged as outpatients after as short as 6 h as long as there were no apparent adverse events[20]. However, in most cases, patients are hospitalized for 24-48 h with gradual progression of their diet 12 h post-operatively. Post-procedural radiologic studies remain institution dependent. The development of perforations is a concern but there is a low sensitivity for detection of microperforations using this method. Additionally, little correlation has been seen between radiographic findings and patient symptoms[6,33]. We endorse imaging only if there is a clinical suspicion for perforation.

Table 3 Devices used for cricopharyngeus myotomy *n* (%)

Device for myotomy	Patients (*n* = 678)
Needle knife	404 (59.6)
APC	174 (25.7)
Forceps coagulation	41 (6)
Hook knife	32 (4.7)
Insulated tip knife	19 (2.9)
Harmonic scalpel	5 (0.7)
Stag beetle knife	3 (0.4)

OUTCOMES

Multiple centers have reported their results of the flexible endoscopic approach to ZD therapy since it's original description in 1995. There have been 19 reported case series that have been published consisting of 670 patients (Table 1). However, due to the subjective manner in which procedural outcome is determined in these series, it is difficult to gauge true objective clinical success. Often, success is based on patient symptoms and not on objective data. Moreover, there are no guidelines or studies that suggest if endoscopic or radiologic surveillance would be beneficial. To improve upon this aspect some centers have instituted using a dysphagia score[10]. The scale ranges from 0-4 as follows: 0: no dysphagia; 1: dysphagia to solids; 2: dysphagia to semi solids; 3: dysphagia to liquids; 4: patient cannot swallow saliva. A score of this manner provides an objective measurement of outcome as is routinely used at our center and in this study as well. In studies where dysphagia score was used, the average pre- and post-treatment dysphagia score was 2.1 (range 1.8-4) and 0.26 (range 0-0.6) respectively. More routinely reported is the clinical resolution rate (CRR). This is commonly described as a symptom improvement either immediately or 2-4 wk post-procedurally. Of the available studies the reported CRR was over 90% (Table 1) and patients with persistent symptoms typically underwent either a repeat procedure or were referred to otolaryngologists for surgical management. Recurrence rate (RR) for symptoms was near 15% from the available data with an average follow-up time of 20 mo. However, follow-up period was not mentioned in nearly a quarter of the reports and is commonly seen as a shortcoming when reporting outcomes for this procedure.

ADVERSE EVENTS

Adverse events (AE) for the flexible endoscopic therapy of ZD have been well reported since first being described. However, due to the lack of standardization there remains heterogeneity of how accounted complications are reported and designated. In the 678 patients that have been reported to undergo the flexible endoscopic procedures, including our current study, 80 patients (11.8%) were reported to

Table 4 Published adverse events after flexible endoscopic therapy of Zenker's diverticulum *n* (%)

Adverse events	80/678 (11.8%)
Micro perforations	52/678 (7.7)
Cervical emphysema	1
Mediastinal emphysema	5
Subcutaneous emphysema	25
Unspecified	21
Macro perforations	4/678 (0.6)
Bleeding	9/678 (1.3)
Infection	12/678 (1.8)
Fever	10
Pneumonia	1
Neck abscess	1
Death	1/678 (0.1)
Adverse events, not otherwise specified	2/678 (0.3)

have AE (Table 4), the most common being micro-perforations, which encompasses greater than half of reported complications. These are described as the patient developing either: cervical, subcutaneous or mediastinal emphysema. Most of these documented by various radiographic studies, had inconsequential medical outcomes and were treated conservatively with or without antibiotics[34]. Macroscopic perforations, the more morbid AE, were only reported in 4 cases. These perforations were seen either during endoscopic visualization or by oral contrast extravasation and were typically managed with endoscopic clipping without any long-term sequelae being reported. Bleeding occurred in 6 of the reported cases, mostly intra-procedural and treated with epinephrine injection, endoclips or electrocautery. Prolonged post-procedural bleeding has only been recorded in 1 case[14] with hemostasis achieved with endoscopic injection of epinephrine. Fever was reported as the most common presentation of infections reported in published cases. Patients were usually treated with antibiotics if specific organ involvement was apparent or for fever lasting more than 24 h. If fever persisted and a focus of infection was not found, then appropriate testing to rule out perforation or mediastinitis is essential[35]. Patient mortality is infrequent, with only one case being reported[15] due to pulmonary embolism. At our institution, similar to previously published series from other centers, we did not encounter any procedural adverse events. However, as mentioned earlier, accurate reporting of AE is likely best achieved in prospective studies using objective predetermined criteria as suggested by the ASGE[11].

CONCLUSION

Flexible endoscopy therapy appears to be a minimally invasive option for the treatment of ZD with several studies showing favorable clinical outcomes and an adequate safety profile. Future efforts should include prospective trials with further standardization of technical aspects, comparison of endoscopic devices and accessories, and report of long-term clinical outcomes with this technique.

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