Practice patterns, techniques, and outcomes of flexible endoscopic myotomy for Zenker's diverticulum: a retrospective multicenter study

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ABSTRACT

Background Flexible endoscopic myotomy has been increasingly performed for Zenker's diverticulum using various endoscopic techniques and devices. The main aims of this study were to assess practice patterns and compare outcomes of endoscopic myotomy for Zenker's diverticulum.

Methods Procedures performed at 12 tertiary endoscopy centers from 1/2012 to 12/2018 were reviewed. Patients (≥ 18 years) with Zenker's diverticulum who had dysphagia and/or regurgitation and underwent endoscopic myotomy were included. Outcomes assessed included technical success, clinical success, and adverse events.

Results 161 patients were included. Traditional endoscopic septotomy was performed most frequently (137/161, 85.1 %) followed by submucosal dissection of the septum and myotomy (24/161, 14.9 %). The hook knife (43/161, 26.7 %) and needle-knife (33/161, 20.5 %) were used most frequently. Overall, technical and clinical success rates were 98.1 % (158/161) and 78.1 % (96/123), respectively. Adverse events were noted in 13 patients (8.1 %). There was no significant difference in technical and clinical success between traditional septotomy and submucosal dissection groups (97.1 % vs. 95.8 %, $P = 0.56$ and 75.2 % vs. 90.9 %, $P = 0.16$, respectively). Clinical success was higher with the hook knife (96.7 %) compared with the needle-knife (76.6 %) and insulated tip knife (47.1 %). Outcomes were similar between centers performing > 20, 11 – 20, and ≤ 10 procedures.

Conclusions Flexible endoscopic myotomy is an effective therapy for Zenker's diverticulum, with a low rate of adverse events. There was no significant difference in outcomes between traditional septotomy and a submucosal dissection approach, or with centers with higher volume, though clinical success was higher with the hook knife.

Introduction

Zenker's diverticulum is a false diverticulum of the mucosa and submucosa at the junction of the hypopharynx and esophagus [1]. Zenker's diverticulum is relatively rare, with a reported prevalence of 0.06 % to 4 % in the United States [2]. It typically affects patients between 65 and 75 years of age, and has a 1.5-fold male predominance [3]. Common symptoms include dysphagia and regurgitation of undigested food.

Treatment options for Zenker's diverticulum include open surgical cricopharyngeal myotomy with or without diverticulectomy, transoral septum division with a rigid esophagoscope, or flexible endoscopic myotomy. Open surgery can be associated with a significant risk of adverse events including mediastinitis, recurrent laryngeal nerve injury, salivary fistula, and esophageal stenosis (4 % – 30 %), with an overall mortality of 1 % – 2 % [4, 5]. Transoral division of the septum using a rigid endoscope has traditionally been considered the "minimally invasive" alternative to open surgical treatment. However, reduced neck mobility and the requirement for general anesthesia can be a contraindication to rigid endoscopy in some patients. This modality also adds to the cost as the procedure needs to be performed in the operating room. In addition, a small (< 2 cm) Zenker's diverticulum can be difficult to treat with a rigid endoscope. As a result, a flexible endoscopic approach for cricopharyngeal myotomy for Zenker's diverticulum was developed and first described by Ishioka et al. [6].

Flexible endoscopic myotomy has been increasingly performed to treat Zenker's diverticulum; however, there is a wide variation in the procedure technique, predominantly related to equipment availability, technical expertise, and endoscopist preference, especially with the recent emergence of newer endoscopic submucosal dissection (ESD) knives and devices. With this in mind, the main aims of this study were to assess practice patterns and outcomes (technical success, clinical success, and adverse events) after endoscopic myotomy for Zenker's diverticulum, and to compare outcomes between various centers by case volume and types of devices used.

Methods

Patient selection and study design

The endoscopy database at 12 high-volume tertiary care endoscopy centers was retrospectively reviewed from January 2012 to December 2018. The study was approved by the institutional review board at each participating site.

Patients who underwent endoscopic myotomy and met the following inclusion criteria were included: age ≥ 18 years; a history of dysphagia and/or regurgitation; objective evidence of Zenker's diverticulum, demonstrated by esophagram and/or upper endoscopy. Exclusion criteria were: patients with esophageal stricture, ring or web; portal hypertension; coagulation disorder (international normalized ratio > 1.5 and/or platelets < 50 000); history of achalasia or other primary esophageal motility disorder; and eosinophilic esophagitis.

The main aims of the study were: 1) to assess practice patterns with respect to techniques and devices used for endoscopic myotomy of Zenker's diverticulum; 2) to determine outcomes (technical success, clinical success, and adverse events) of endoscopic myotomy for Zenker's diverticulum; and 3) to compare outcomes between various centers by case volume and types of devices used.

Definitions

Technical success was defined as the ability to successfully complete the endoscopic cricopharyngeal myotomy (septotomy). Clinical success was defined as symptom relief (improvement in Eckardt score to < 3, with dysphagia component < 2). Procedure-related adverse events were recorded and categorized according to the published American Society for Gastrointestinal Endoscopy criteria of adverse events [7]: intraprocedural (before completion of endoscopy), post-procedural (within 14 days), and late (after 14 days). Centers were categorized into three groups based on procedure volumes: > 20, 11 – 20, and ≤ 10 procedures.

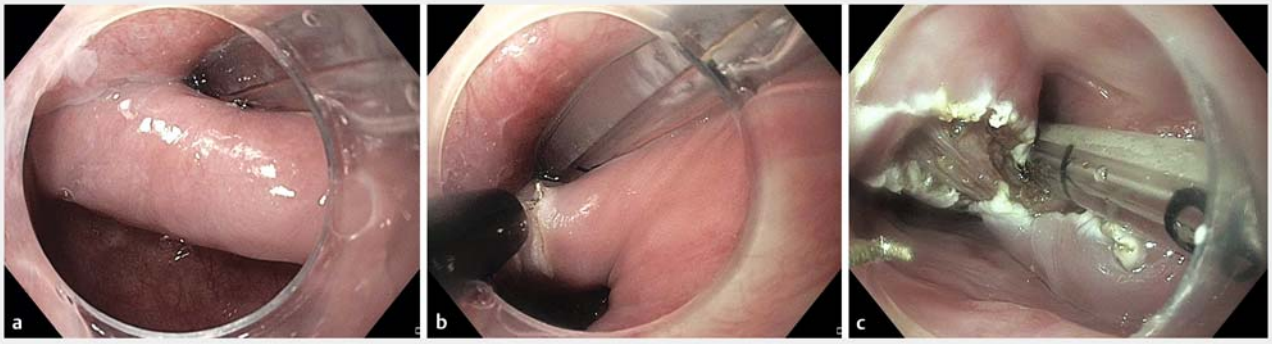
Data collection

Patient demographics, clinical history, radiologic imaging, endoscopy and surgery reports, and pertinent clinical encounters were reviewed. The size of the Zenker's diverticulum was measured based on endoscopy or esophagram. Symptoms (i. e. dysphagia, regurgitation, pain, weight loss) were assessed using the Eckardt score [8]. Weight loss was documented based on weight measurements during clinical encounters.

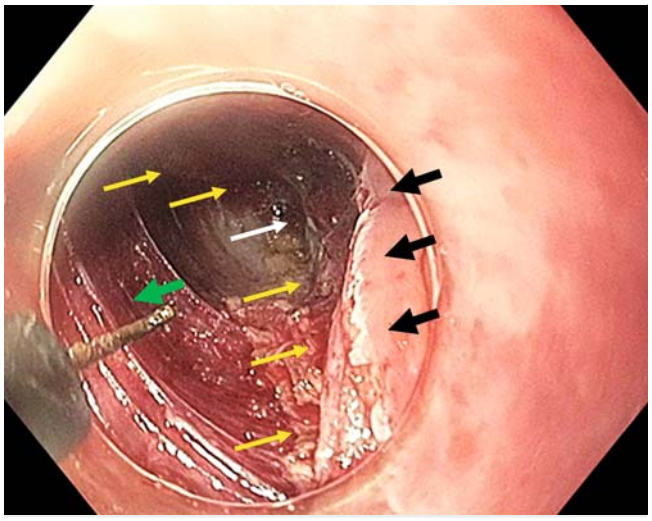
Follow-up data were obtained from clinical encounters and/or phone calls after the procedure to discuss symptoms. In addition, all patients were given the on-call gastroenterology service contact information to call after their procedure in case they developed concerning symptoms. Clinical status updates were obtained by follow-up phone calls for patients who did not have adequate follow-up based on clinical encounters and chart review.

Description of procedure

Preprocedure testing included barium esophagram and diagnostic upper endoscopy to confirm the diagnosis and rule out alternative and coexisting conditions. Endoscopic treatment of Zenker's diverticulum is based on division of the muscle septum (▶ **Fig. 1a**) between the diverticulum and the esophageal lumen to create a common channel. This can be accomplished by either 1) directly cutting the septum (▶ **Fig. 1b,c**) including the overlying mucosa, submucosa, and muscle (traditional flexible endoscopic septotomy/myotomy), or 2) by submucosal dissection on the septum followed by muscle incision (▶ **Fig. 2**), similarly to the technique previously reported by Kedia et al. [9]. In this technique, a submucosal injection and incision is made directly on the septum, and the submucosa is accessed and dissected. The muscle fibers are then identified and are cut to the level of the base of the diverticulum. Septotomy is thus completed. This is different from submucosal tunneling endoscopic septum division (ST-ESD/Z-POEM) where injection and incision are performed at a point proximal to the septum and submucosal tunneling is performed in the caudal direction towards the septum and on both sides of the septum prior to subsequent



▶ **Fig. 1** Traditional flexible endoscopic septotomy/myotomy for Zenker's diverticulum. **a** Endoscopic view showing Zenker's diverticulum at the bottom and an orogastric tube in the esophageal lumen at the top. The septum is clearly seen in the middle. **b** Start of myotomy with a hook knife. **c** Hook knife myotomy extended distally.



▶ **Fig. 2** Endoscopic submucosal dissection on the septum and myotomy for Zenker's diverticulum. The Zenker's diverticulum (not seen) is to the right of the photo with black arrows pointing to the mucosa on the diverticular side. The yellow arrows show the septum, cut to the base of the diverticulum (white arrow). The green arrow points to esophageal submucosa on the left.

myotomy. Identification of the septum may be easier with the submucosal dissection technique compared with Z-POEM, where it is sometimes difficult to identify the septum, as tunneling begins proximally and is directed caudally towards the general direction on the septum. In addition, closure of the mucosal incision following submucosal dissection on the septum is likely to be easier as the site is on the septum rather than the more difficult location proximally (which may be closer to the upper esophageal sphincter) in a Z-POEM.

An orogastric or nasogastric tube may be used to maintain orientation during myotomy and to protect the contralateral esophageal wall from inadvertent injury. A transparent distal attachment cap is often used to improve visualization and increase endoscope stability during myotomy. A plastic overtube, which enables localization and stabilization of the Zenker's diverticulum septum, modified for this purpose by cutting two semicircular shaped areas at the distal tip, has also been described to facilitate endoscopic myotomy.

A variety of ESD tools have been used to perform myotomy, including a biliary needle-knife, insulated tip knife (Olympus America, Center Valley, Pennsylvania, USA), HybridKnife (ERBE, Marietta, Georgia, USA), HookKnife (Olympus America), stag beetle (SB) knife (Olympus America), and Clutch-Cutter knife (Fujifilm Medical Systems USA, Wayne, New Jersey, USA). Hemostatic clips can be placed prophylactically after myotomy to prevent delayed bleeding and perforation, but the location and number of clips placed varies greatly. This study assessed the use of these various techniques, accessories, and devices for endoscopic Zenker's diverticulum myotomy at the study centers.

Statistical analysis

Numerical variables were reported as mean (standard deviation [SD]) or as a median (range) when they followed a normal or skewed distribution, respectively. Categorical variables were summarized as frequency and percentage. The two myotomy techniques (traditional flexible endoscopic myotomy, and endoscopic submucosal dissection on the septum followed by myotomy) were compared. We hypothesized that there would be no significant difference in outcomes (technical success, clinical success, and adverse events) between the traditional myotomy and submucosal dissection groups. Chi-squared and Fisher's exact tests were used to compare the outcomes between types of myotomy performed, volume of cases per center, and type of knife used. A subgroup analysis was performed to report clinical outcomes after excluding patients who underwent prior surgery for treatment of Zenker's diverticulum. A univariate and multivariate regression analysis was also performed to study the effect of procedure-related factors on adverse events. The following variables were included: orogastric/nasogastric tube, distal attachment cap, overtube use, routine clip placement, intraprocedural antibiotics, and routine antibiotic use after the procedure. A P value of <0.05 was considered statistically significant. Data were analyzed using SPSS ver-

▶ **Table 1** Patient characteristics.

Cases, n	161
Age, mean (range), years	73.5 (46 – 101)
Sex, n (%)	
▪ Male	86 (53.4)
▪ Female	75 (46.6)
Zenker's diverticulum size, mean (range), cm	2.7 (0.5 – 7.0)
Eckardt score, mean (SD)	3.9 (2.4)
ASA class, median (range)	2 (1 – 4)
Prior treatment, n (%)	36 (22.4)
▪ Endoscopic myotomy	16 (9.9)
▪ Transcervical surgery	6 (3.7)
▪ Endoscopic dilation	9 (5.6)
▪ Surgical transoral myotomy	8 (5.0)

SD, standard deviation; ASA, American Society of Anesthesiologists.

▶ **Table 2** Endoscopic myotomy procedure characteristics (n = 161).

Orogastric or nasogastric tube, n (%)	56 (34.8)
Standard distal attachment cap, n (%)	130 (80.7)
Modified overtube, n (%)	39 (24.2)
Technique, n (%)	
▪ Traditional flexible endoscopic myotomy	137 (85.1)
▪ ESD on septum and myotomy	24 (14.9)
Routine use of clips	
▪ Cases, n (%)	89 (55.3)
▪ Number of clips, median (range)	2 (1 – 7)
Antibiotics, n (%)	
▪ Intraprocedure	88 (54.7)
▪ Post-procedure	81 (50.3)
Total procedure time, mean (range), minutes	54.1 (13 – 168)

ESD, endoscopic submucosal dissection.

sion 21.0 (IBM Corp., Armonk, New York, USA) by an experienced biostatistician.

Results

A total of 161 patients (mean age 73.5 years; 53.4 % male) were included from 12 tertiary care endoscopy centers (▶ **Table 1**). Mean Eckardt score on presentation was 3.9 (SD 2.4). The mean Zenker's diverticulum size was 2.7 cm (range 0.5 – 7.0 cm).

A total of 22.4 % (36/161) of patients had undergone prior treatment for Zenker's diverticulum including transcervical surgery in 6 patients, transoral rigid endoscopic myotomy in 8 patients, flexible endoscopic myotomy in 16 patients, and endoscopic dilation in 9 patients, with 3 patients undergoing more than one treatment modality.

The median American Society of Anesthesiologists (ASA) class of study patients was 2 (range 1 – 4). The majority of patients underwent general anesthesia for the procedure (93.8 %), although three centers had a total of 10 patients who underwent monitored anesthesia care for ASA class II (2 patients) and III (8 patients).

Techniques for endoscopic myotomy

Traditional flexible endoscopic myotomy (septotomy) was performed most frequently (137/161, 85.1 %). The endoscopic submucosal dissection technique on the septum followed by myotomy was only used in a minority of cases (24/161, 14.9 %) (▶ **Table 2**).

Accessories for myotomy

An orogastric or nasogastric tube was placed in 56 patients (34.8 %) during the procedure before myotomy (▶ **Table 2**). A standard distal attachment cap was used in the majority of patients (130/161, 80.7 %). A modified overtube was used in 39 patients (24.2 %).

The type of endoscopy knife used is summarized in ▶ **Table 3**. The hook knife was used most frequently (43/161, 26.7 %), followed by the needle-knife (33/161, 20.5 %) and insulated tip knife (29/161, 18.0 %) (▶ **Table 3**). Most centers used only one particular knife for all cases, whereas some centers used a combination of two knives.

Clips were placed after myotomy in 89 patients (55.3 %) (▶ **Table 2**). A median of 2 clips were placed (range 1 – 7). Intraprocedural antibiotics were given to 88 patients (54.7 %), and antibiotics were given post-procedure in 81 patients (50.3 %), ranging from 2 to 7 days. After the procedure, 36.6 % patients (59/161) were discharged on the same day. Post-procedure esophagram was performed in 67 patients (41.6 %), on the day after the procedure and before discharge in patients who were admitted. The mean total procedure time was 54.1 minutes (SD 78.9, median 52, range 13 – 168).

Outcomes

The procedure was technically successful in 158/161 patients (98.1 %). Follow-up was available for 123 patients. Mean Eckardt score improved from 3.9 (SD 2.4) to 0.88 (SD 1.37) after endoscopic myotomy at a mean follow-up of 5.7 (SD 7.5) months. The mean dysphagia component of the Eckardt score improved from 2.2 to 0.5 after the endoscopic myotomy.

The overall clinical success rate was 78.1 % (96/123). The technical success rate was 97.1 % (133/137) in the traditional myotomy group (95 % confidence interval [CI] 96.5 % – 100 %) and 95.8 % (23/24) in submucosal dissection group (95 %CI 87.2 % – 100 %; $P = 0.56$) (▶ **Table 4**). The clinical success rate was higher (90.9 %, 95 %CI 77.9 % – 100 %) in the submucosal dissection group compared with the traditional myotomy group (75.2 %, 95 %CI 66.7 % – 83.8 %) but did not reach statisti-

▶ **Table 3** Devices used for endoscopic myotomy for Zenker's diverticulum.

Device for endoscopic myotomy	No. of patients (%)		Total n = 161
	Traditional flexible endoscopic septotomy/ myotomy n = 137 (85.1 %)	ESD on septum and myotomy n = 24 (14.9 %)	
Hook knife	30 (21.9)	13 (54.2)	43 (26.7)
Needle-knife	33 (24.1)	0	33 (20.5)
Insulated tip knife	29 (21.2)	0	29 (18.0)
Insulated tip knife + hook knife	16 (11.7)	0	16 (9.9)
HybridKnife	3 (2.2)	5 (20.8)	8 (5.0)
SB Junior Knife	5 (3.6)	3 (12.5)	8 (5.0)
SB Knife	6 (4.4)	2 (8.3)	8 (5.0)
Clutch-Cutter	5 (3.6)	0	5 (3.1)
Hook knife + needle-knife	4 (2.9)	0	4 (2.5)
DualKnife	2 (1.5)	1 (4.2)	3 (1.9)
Needle-knife + triangle-tipped knife	2 (1.5)	0	2 (1.2)
Triangle-tipped knife	1 (0.7)	0	1 (0.6)
SB Junior + Insulated tip knife	1 (0.7)	0	1 (0.6)

ESD, endoscopic submucosal dissection.

▶ **Table 4** Procedure outcomes.

Outcomes, n/N (%)	Traditional flexible endoscopic septotomy/ myotomy	ESD on septum and myotomy	*P* value
Technical success	133/137 (97.1)	23/24 (95.8)	0.56
Clinical success	76/101 (75.2)	20/22 (90.9)	0.16
Adverse events	9/137 (6.6)	4/24 (16.7)	0.11
Repeat intervention	23/137 (16.8)	2/24 (8.3)	0.54

ESD, endoscopic submucosal dissection.

cal significance (P = 0.16). The clinical success rate was significantly higher in the hook knife group (96.7 %) compared with needle-knife (78.6 %) and Insulated tip knife (47.1 %) groups (P < 0.001). However, the technical success rate was similar between the three knives used (96.7 % for hook knife, 100 % for needle-knife and insulated tip knives) (▶ **Table 5**).

Clinical success rates were statistically similar (P = 0.29) between centers categorized according to case volumes: > 20 cases (76.8 %), 11 – 20 cases (72.7 %), and ≤ 10 cases (90.5 %). Similarly, technical success rates were not statistically different (P = 0.30) between the three groups: > 20 cases (98.8 %), 11 – 20 cases (95.7 %), and ≤ 10 cases (100 %) (▶ **Table 5**).

In a subgroup analysis after excluding patients with prior surgical treatment for Zenker's diverticulum, technical success rate was 98.6 % (145/147) and the clinical success rate was 78.2 % (86/110), which were similar to the main cohort.

A repeat intervention for recurrent symptoms was required in 25/161 patients (15.5 %). These included endoscopic myotomy in 15 patients, endoscopic dilations in 4 patients, transcervical surgery in 3 patients, and rigid transoral myotomy in 3 patients.

Adverse events

Overall, procedure-related adverse events were seen in 13/161 patients (8.1 %, 95 %CI 3.8 % – 12.3 %) (▶ **Table 6**). All procedure-related adverse events were intraprocedural or post-procedural within 14 days. No severe adverse events were recorded. There were no late adverse events. Adverse event rate was higher in the submucosal dissection group (16.7 %, 95 %CI 0 % – 20.3 %) compared with the traditional myotomy group (6.6 %, 95 %CI 3.4 % – 12.6 %) but did not reach statistical significance (P = 0.11) (▶ **Table 4**). Perforations were seen in seven patients (4.3 %): two were treated with an over-the-scope clip, one re-

▶ **Table 5** Comparison of outcomes by type of knife used and case volume.

Outcomes, n/N (%)	Type of knife			*P* value	Case volume per center			*P* value
	Hook knife	Needle-knife	Insulated tip		>20	11–20	≤10	
Technical success	42/43 (97.7)	33/33 (100)	29/29 (100)	0.48	79/80 (98.8)	44/46 (95.7)	35/35 (100)	0.30
Clinical success	29/30 (96.7)	22/28 (78.6)	8/17 (47.1)	<0.001	53/69 (76.8)	24/33 (72.7)	19/21 (90.5)	0.29
Adverse events	2/43 (4.7)	2/33 (6.1)	3/29 (10.3)	0.63	9/80 (11.3)	3/46 (6.5)	1/35 (2.9)	0.28

▶ **Table 6** Adverse events.

Adverse events	No. of patients		
	Traditional flexible endoscopic septotomy/ myotomy (n=137)	ESD on septum and myotomy (n=24)	Total (n=161)
Perforations (all at site of septotomy), n	4	3	7
Bleeding, n	1	0	1
Others, n	4	1	5
Total, n (%)	9 (6.6)	4 (16.7)	13/161 (8.1); P = 0.11

ESD, endoscopic submucosal dissection.

quired repeat endoscopy for clip placement due to a leak seen on post-procedure esophogram, and four contained perforations noted on barium esophogram within 24 hours and were managed medically. Bleeding requiring a blood transfusion was recorded for one patient (0.6%). Five post-procedural adverse events were noted including three emergency department visits for pain, one admission for dehydration, and one patient required repeat endoscopy for dysphagia, which required clip removal. Intraprocedural bleeding treated with endoscopic thermal therapy using spray coagulation and/or coagrasper during the procedure was seen in 14 patients (8.7%) and was not considered as an adverse event. Hemostatic clip and epinephrine injection were used as adjunctive therapy in two of these patients.

Adverse event rates were compared by volume of cases per center, and by type of knives used. Overall, there was no statistically significant difference in adverse event rates (P =0.28) according to case volume: >20 cases (11.3%), 11–20 cases (6.5%), and ≤10 cases (2.9%) (▶ **Table 5**). Similarly, there was no statistically significant difference (P=0.63) in adverse events between type of knives used: hook knife (4.7%), needle-knife (6.1%), and insulated tip knife (10.3%) (▶ **Table 5**).

In the subgroup analysis after excluding patients with prior surgical treatment for Zenker's diverticulum, the adverse event rate was 8.2% (12/147), which was similar to the overall procedure-related adverse event rate.

In the multivariate regression analysis, none of the procedure-related factors was found to significantly affect the adverse events outcome. The factors included in the regression model were: orogastric/nasogastric tube (odds ratio [OR] 1.20, 95%CI 0.39–3.80; P=0.72), standard distal cap (OR 1.05, 95% CI 0.25–4.48; P =0.95), overtube use (OR 1.06, 95%CI 0.29–3.85; P =0.93), routine clip use (OR 0.51, 95%CI 0.16–1.59; P =0.23), intraprocedural antibiotic use (OR 0.51, 95%CI 0.16–1.57; P=0.24), and routine antibiotic use (OR 0.59, 95%CI 0.91–1.84; P =0.37).

Discussion

Endoscopic treatment of Zenker's diverticulum has evolved as newer endoscopic accessories have become more readily available, and as advanced endoscopists become more comfortable with submucosal endoscopy and myotomy. Since the initial description of the endoscopic technique for Zenker's myotomy by Ishioka et al. [6], multiple reports have been published demonstrating the use of newer devices for endoscopic septotomy, as these accessories have become commercially available for performing newer endoscopic procedures such as ESD. Ishaq et al. performed a systematic review and meta-analysis including 27 studies and 813 patients. The overall technical success rate was 91%, adverse event rate was 11.3%, and recurrence rate was 11% [10]. Most studies have used a traditional needle-knife myotomy technique but recent reports describe the use of more advanced accessories and techniques. The use of a scissor-type knife and HybridKnife have recently been described for endoscopic myotomy [11–13]. In view of these recent advances in the management of Zenker's diverticulum, we conducted this multicenter study to assess practice patterns, techniques, accessories, and outcomes of endoscopic myotomy for Zenker's diverticulum.

This study represents a multicenter collaborative effort to report current practice patterns and outcomes associated with

endoscopic myotomy for Zenker's diverticulum. The overall technical success rate was 98.1 % and the clinical success rate was 78.1 %, which are consistent with previously published studies. Recurrent or residual Zenker's diverticulum requiring a repeat procedure was required in 15.5 % of patients in our study. In a subgroup analysis of patients after excluding those with prior surgery for treatment of Zenker's diverticulum, the clinical outcomes were similar to the main cohort, suggesting that prior surgery did not significantly affect the outcomes associated with subsequent endoscopic myotomy.

The knife used for myotomy varied between different centers. The hook knife and needle-knife were used most frequently in this study. The needle-knife was traditionally used for myotomy before newer devices became available. The main disadvantages of the needle-knife include lack of precise control during cutting and concern for perforation resulting from inadvertent deeper incision. The hook knife may present an advantage over the needle-knife owing to its bent tip design, which can be used to hook and pull the muscle fibers for a more precise cut. Previous studies have shown a >90 % success rate and modest rate of adverse events (6 %–8 %) with the hook knife [14, 15]. The insulated tip knife has a ceramic insulated tip that, theoretically, reduces the risk of deep injury and perforation during myotomy. However, the lower clinical success (47.1 %) despite a high technical success (100 %) with the insulated tip knife may reflect incomplete myotomy with this device, possibly due to the ceramic ball tip, which may result in a small residual septum. Scissor-type knives including the SB knife [16, 17] and Clutch-Cutter knife [18] are recent additions to the submucosal dissection armamentarium. These devices have an internal cutting surface with an insulated tip and insulated exterior surface, which potentially reduces the risk of inadvertent perforation and injury to adjacent structures, while increasing the accuracy of myotomy, as the muscle fibers can be grasped within the cutting surface. Finally, the HybridKnife can be useful in the submucosal tunneling method by reducing the time taken for device exchange between injection needle and the knife. In our study cohort, the clinical success rate was significantly higher in procedures that used the hook knife for myotomy compared with the needle-knife or insulated tip knife. This may be related to more accurate myotomy with the hook knife, as the muscle fibers can be "hooked" and pulled towards the endoscope, possibly ensuring a more complete and safer myotomy to the base of the diverticulum. In addition, earlier cases may have been performed with the needle-knife and subsequent cases with the hook knife, possibly suggesting that experience may have favored the clinical success achieved with the hook knife. Hence, larger prospective studies are needed to confirm this finding before the hook knife can be recommended as a standard device for myotomy for Zenker's diverticulum.

Interestingly, the clinical outcomes and safety profile were similar between centers with different case volumes. A learning curve effect is likely to exist with endoscopic myotomy for Zenker's diverticulum and should reflect improvement in clinical outcomes with increasing number of cases. However, the centers and endoscopists who participated in the study were seasoned experts in complex endoscopy, and hence this effect may not have been seen in our study.

The technique used for myotomy also varied significantly in our study. Directly cutting the septum including the overlying mucosa, submucosa, and muscle (traditional flexible endoscopic septotomy/myotomy) was most commonly used, though a small proportion of patients underwent submucosal dissection on the septum followed by myotomy, with statistically similar efficacy and safety outcomes. Recent reports have described two techniques: 1) a double incision and "myectomy" technique for removal of the muscle septum, which may reduce the recurrence rate [19]; 2) submucosal tunneling and selectively cutting the muscle septum while leaving overlying mucosa intact (called ST-ESD or Z-POEM), similarly to peroral endoscopic myotomy (POEM) for achalasia [20]. However, these approaches were not used in our study population probably because they are more recent developments.

The number and location of clips used after myotomy varied significantly and is likely to represent endoscopists' preference, especially with newer devices used for myotomy. However, the routine use of clips after endoscopic myotomy was not associated with reduced risk of adverse events in the multivariate analysis.

The main strengths of our study include a multicenter design with a large number of patients, which allowed us to understand differences in the endoscopic technique and devices currently used to perform endoscopic myotomy for Zenker's diverticulum across the USA, and also to provide an assessment of technical and clinical success, and adverse events. Although there is variation in practice across various sites, none of the procedure-related factors (orogastric/nasogastric tube, distal attachment cap, overtube use, routine clip placement, intraprocedural antibiotics, and routine antibiotic use after the procedure) were found to significantly affect adverse events. Furthermore, our study assessed outcomes based on the type of knife used and case volume per study center, neither of which has been previously reported.

There are several limitations of this study. First, the study was retrospective in design with limited clinical follow-up, as follow-up was not available for all patients. This is likely to be related to the procedures being performed at tertiary referral centers, to which elderly patients travel for advanced medical care but are likely to be followed up locally after their procedures. Second, the myotomy technique and devices used have changed over time and it is not possible to assess all approaches in subgroup analyses. However, this study is an attempt to report those variations, and we have included data from subgroup analyses, where possible, in order to study the impact of practice patterns on clinical outcomes. Third, the study did not assess cost implications associated with the endoscopic tools, devices, and technique used for myotomy. Fourth, we also acknowledge that the small number of patients in the subgroup analyses comparing outcomes by type of myotomy technique, type of knife, and center volume is another limitation, which may reduce the generalization of our findings. Furthermore, statistical significance may not necessarily imply clinical significance and vice versa, especially given the small sample size of

the cohort. However, Zenker's diverticulum is a rare disease and only a limited number of endoscopic myotomy procedures are performed, even at tertiary care centers. Fifth, clinical success was defined by improvement in Eckardt score, which has been typically used for achalasia. This is a limitation of the retrospective analysis given the inability to obtain data regarding dysphagia to specific type of foods (solids, soft solids, liquids), which may be more relevant to Zenker's diverticulum. Instead, mean pre- and post-procedure improvements in Eckardt score and dysphagia component are provided. Finally, it is possible that there is a learning curve for endoscopic myotomy for Zenker's diverticulum, which may have affected the clinical outcomes in the submucosal dissection group. However, all endoscopists included in the study were experienced in ESD and routinely performed POEM and ESD procedures. Further studies should aim to compare traditional septotomy (directly cutting the septum including the overlying mucosa, submucosa, and muscle) with newer techniques such as myectomy [19] and with submucosal tunneling techniques (Z-POEM) for endoscopic treatment of Zenker's diverticulum. This should address the additional cost of newer more expensive accessories, time needed to perform more elaborate tunneling techniques, and the perceived potential benefit of a more complete septotomy that may reduce or eliminate recurrence. The application of these newer techniques for complete septotomy, especially in the elderly population where Zenker's diverticulum is most commonly seen, is also not known.

In conclusion, flexible endoscopic myotomy is an effective therapy for Zenker's diverticulum, with a low rate of procedure-related adverse events. A wide variation was seen in the practice patterns regarding devices used and techniques applied. There was no significant difference in outcomes related to myotomy technique (traditional septotomy vs. submucosal dissection) or case volume. Clinical success was significantly higher with the hook knife compared with the insulation tip knife or needle-knife.

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Competing interests

Dr. Diehl is a consultant/speaker for Boston Scientific, Lumendi, US Endoscopy/Steris, Olympus, Pentax, Cook Medical, GI supply, Medtronic, and Merit Endotek. Dr. Draganov is a consultant for Boston Scientific, Olympus, Cook Endoscopy, and Microtek. Dr. Jamil is a consultant/speaker for Aries Pharmaceutical. Dr. Khara is a consultant for Olympus. Dr. Law is a consultant for Olympus and has received royalties from UpToDate. Dr. Thaker is a consultant for Boston Scientific. Dr. Thosani is a consultant for Boston Scientific, Medtronic, Pentax, and Endogastric Solutions, and has received royalties from UpToDate. Dr. Yang is a consultant for Boston Scientific, Lumendi, and US Endoscopy. Dr. Wagh is a consultant for Boston Scientific, Olympus, and Medtronic. All the other authors declare that they have no conflicts of interest.

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