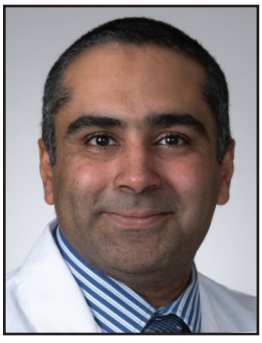
Douglas G. Adler MD, FACG, AGAF, FASGE, Series Editor

Endoscopic Management of Zenker's Diverticulum

Bilal Aslam



Moamen Gabr

Zenker's diverticulum (ZD) is a pharyngeoesophageal pulsion diverticulum which presents in the elderly and contributes to morbidity due to dysphagia and pulmonary aspiration. Open surgery and rigid endoscopy have previously been the primary modalities for therapy, however with a favorable safety profile and similar success rates, flexible endoscopy has become an emerging therapeutic modality in the treatment of ZD. This review seeks to highlight endoscopic techniques and tools in the management of ZD.

INTRODUCTION

Zenker's diverticulum (ZD), first reported by Ludlow in 1769,[1] is a pharyngeoesophageal pouch characterized by posterior herniation through Killian's triangle or Killian dehiscence, anatomically located superior to the cricopharyngeus muscle and inferior to the inferior pharyngeal constrictor muscle (Figure 1). After a detailed case series of pulsion diverticula was published in 1867 by Friedrich Zenker, the entity was eponymized.[2] An uncommon entity with a reported prevalence of 0.01%-0.11%,[3] ZD often presents in the seventh to eighth decade, with a male predominance.[4]

Although the mechanism of development is not entirely clear, diminished upper esophageal sphincter (UES) opening leading to increased intraluminal pressures and subsequent tissue migration through an anatomic defect has been suggested;[5] structural abnormalities of the cricopharyngeus muscle have been implicated as an explanation for the diminished UES relaxation and increased bolus flow pressure.[6] Reported to have an association with GERD,[7] also of unclear mechanism, acid-induced muscle shortening has been proposed as a unifying hypothesis linking the two conditions.[8]

Presentation includes, but is not limited to, dysphagia, post-prandial emesis, regurgitation of food, retention of food and other contents within diverticular space, halitosis, cough, weight loss, malnutrition and pulmonary aspiration. Dysphagia in patients suffering from ZD can manifest as malnutrition[9] reported in 54% of patients in one series. ZD has been associated with the retention of video capsule and subsequent endoscopic retrieval.[10-12] There are also case reports of ZD

Bilal Aslam, MD Moamen Gabr, MD Department of Gastroenterology, University of Kentucky, Lexington, KY

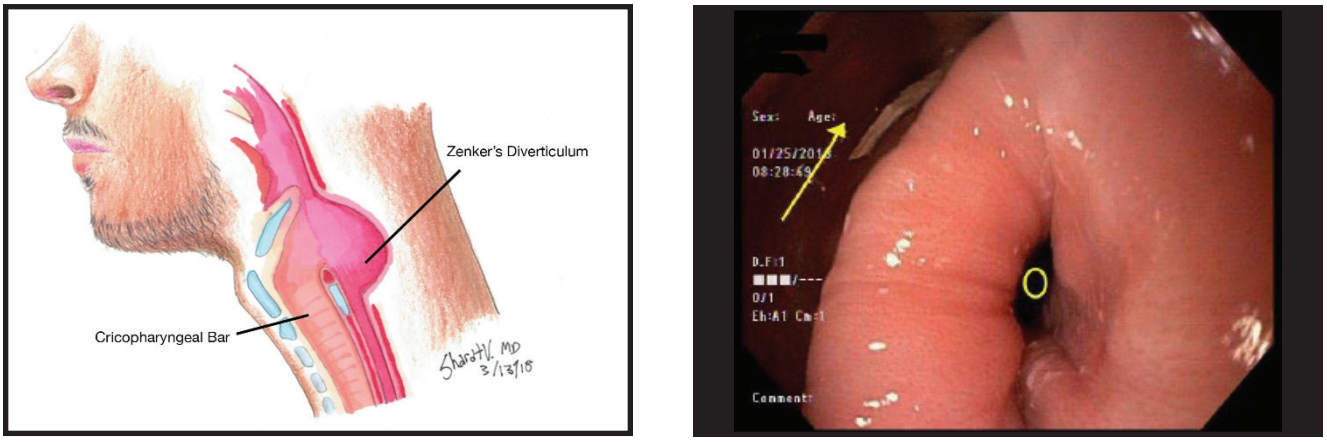


Figure 1. Anatomic depiction of Zenker's diverticulum (left). *Image courtesy of Dr. Sharat Vallurupalli.* Endoscopic representation of ZD; arrow highlighting ZD with yellow circle highlighting esophageal lumen (right).

complicated by the presence of carcinoma within the diverticulum,[13-17] however this is exceedingly rare.

The most common modality for diagnosis is a barium-contrasted study (i.e. barium esophagram/barium swallow, videoflouroscopy/modified barium swallow) (Figure 2), with outpouching most prominently characterized on lateral projections;[18] there is also a role for cross-sectional imaging and endoscopy. There are limited reports of characterizing ZD on ultrasound,[19-22] however this has no role in initial diagnostic workup. Validated scoring tools for the assessment of dysphagia (SWAL-QOL, Dakkak-Bennet) have been reported and used for evaluating pre and post intervention status.[23,24]

The mainstay of treatment was previously open surgical correction and endoscopic management with rigid endoscope, but advances in flexible endoscopic tools and techniques have brought flexible endoscopic management to the forefront over the past two decades. This review seeks to highlight endoscopic techniques and tools in the management of ZD.

Management

Although there are no specific guidelines for treatment, intervention should be reserved for symptomatic patients only. The current treatment modalities are open surgery (including diverticulectomy, diverticulopexy, diverticular inversion, myotomy), rigid endoscopy (electrocautery, CO2 laser, stapler, Harmonic scalpel) and flexible endoscopy. As previously reported, the rate of successful management of ZD is comparable between the three established modalities, however adverse effects including mortality are significantly lower in the flexible endoscopic approach.[25] Rigid endoscopy and flexible endoscopy share similar outcome profiles, but flexible endoscopy does not require general anesthesia or neck hyperextension.

The first flexible endoscopic therapy for ZD was reported in 1995.[26] The mainstay of therapy has focused on the division of the cricopharyngeal muscle through an endoscopic myotomy resulting in obliteration of the diverticular cavity and improvement of dysphagia; with many accessories (APC, bipolar forceps, clutch cutter, hood, hook knife, needle knife, stag beetle knife, transparent cap) and new techniques (Z-POEM) at endoscopists' disposal, flexible endoscopic approaches are numerous and effective for treatment of ZD.

Flexible Endoscopic Septum Division:

Flexible endoscopic septum division (FESD) (Figure 3) is the incision of the mucosal layer and myotomy, partial or complete, of the cricopharyngeal muscle resulting in septum division. In a recent meta-analysis[27] FESD reported overall good outcomes with pooled success of 91%, pooled adverse event (AE) rate of 11.3% and pooled recurrence rate of 11%. As there is no standardization to FESD, there is wide heterogeneity among studies and numerous approaches to septum division. Most endoscopic approaches to FESD are multi-modal with combination of accessories

(continued on page 39)

(continued from page 35)

or techniques employed. The blind pouch of the diverticulum increases perforation risk, as it can be confused for the esophageal lumen, most often highlighted during endoscopic retrograde cholangiopancreatography (ERCP).[28]

The introduction of transparent caps or soft rubber duck-billed diverticuloscope (Cook Medical, Winston-Salem, NC) has improved visualization and endoscopic outcomes.[29] The diverticuloscope and cap devices allow for improved visualization, through exposure and fixation of the septum, and aiding in the separation of fibers with gentle spreading pressure. When compared to caps, diverticuloscope use is associated with fewer AE, decreased procedure time, and superior symptom remission,[29] however the overtube system unfortunately is not currently approved by the United States Food and Drug Administration, and its use is reported only in case series from Canada and Europe.

Widely reported,[30-34] the use of a Savary guide wire with nasogastric (NG) tube placement delineates the esophagus from ZD orifice and protects the anterior wall of the septum during myotomy. There is also reported variation across the literature regarding the use of closure clips at the end of the procedure and antibiotics given prior to and after endoscopic treatment.

Post-intervention care lacks a standardized approach but primarily consists of hospital observation, soft diet, and barium contrasted studies to evaluate for perforation.[30,32,34,35] Rates of AE (perforation/cervical emphysema, hemorrhage) vary with FESD, however overall remain relatively low,[27] and are predominantly managed with a conservative approach**.** There are varying rates of symptom recurrence, with most being amenable to repeat FESD having reasonable outcomes**.**

Septum Division Techniques

Needle Knife

Ishioka et al. reported the first FESD in 1995; intervention was carried out with Needle-Knife (NK) and noted improvement in all patients within the series (N=23).[30] Subsequent studies[29,31,32,34-37] detailed effectiveness of NK in the endoscopic management of ZD. Costamagna et al. evaluated prognostic variables for FESD success and reported on short and long-term success (6 and 48 months respectively) having a correlation with septotomy length and size of ZD.[38] The criticism of NK approach is the concern for perforation risk. Hesitancy to extend septotomy length due to lack of direct visualization may contribute to recurrence rates**.**

Hook Knife

The Hook Knife (Olympus Corporation, Center Valley, PA,USA) first reported by Recipe at al.,[39] showed clinical efficacy in septal myotomy; this finding has been reproduced in subsequent studies[33,34,40-43] and clinical trends appear to favor Hook Knife as the preferred endoscopic tool for FESD. The inherent advantage of the Hook Knife is that the upward pulling of muscle fibers prior to obliteration minimizes perforation risk at time of intervention.

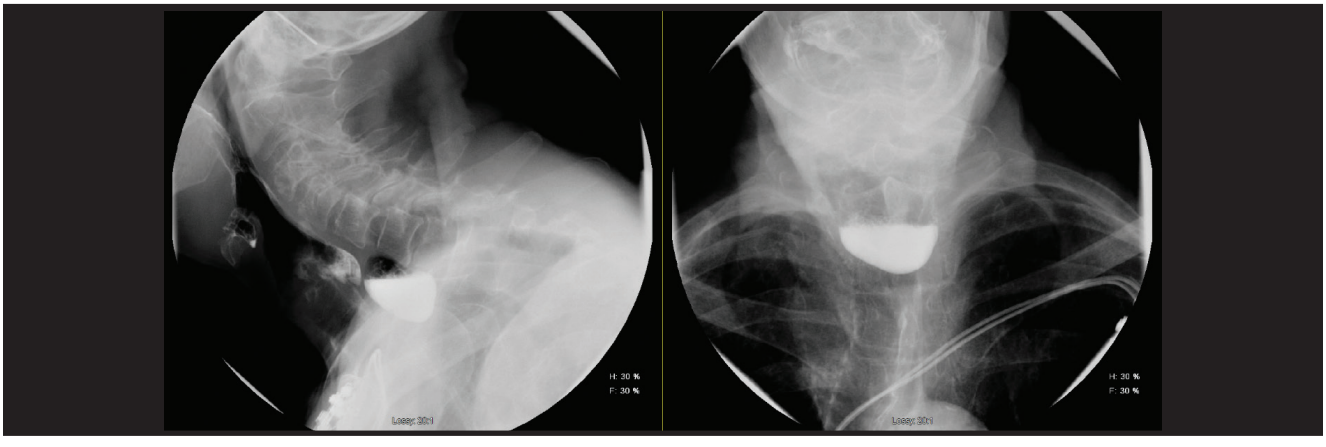


Figure 2. Zenker's Diverticulum Outlined on Barium Esophagram
Lateral (left) and coronal (right) view of barium esophagram highlighting Zenker's Diverticulum.

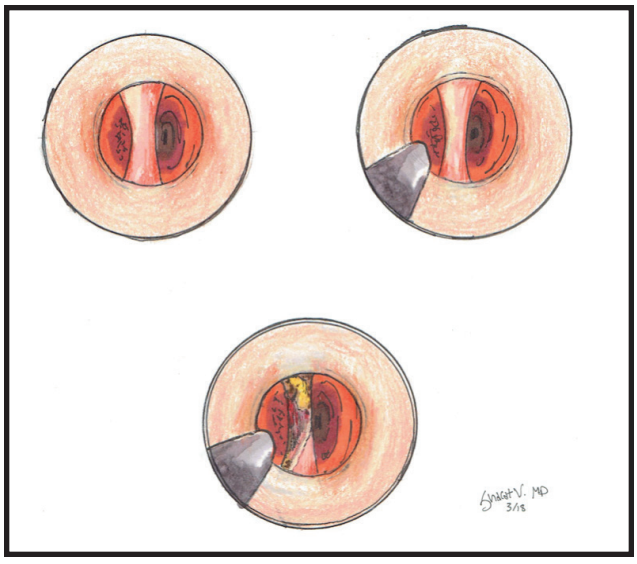


Figure 3. Pictorial depiction of ZD with endoscopic cap (top left). Depiction of instrument through working channel (top right). Illustration of myotomy and exposed cricopharyngeal muscle fibers (bottom). *Image courtesy of Dr. Sharat Vallurupalli.*

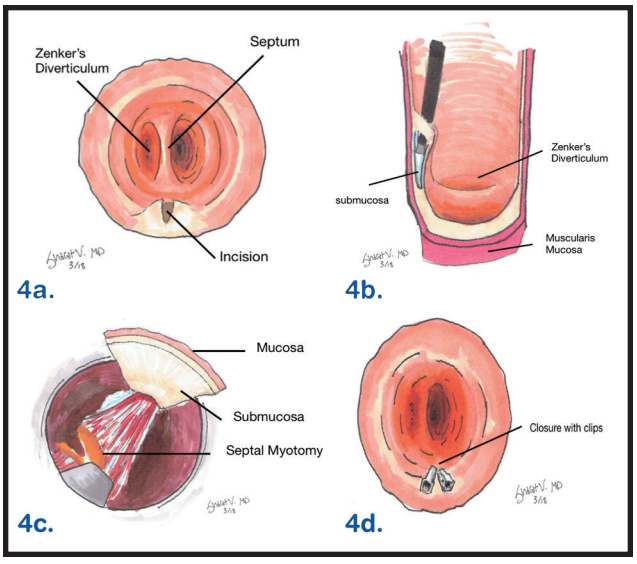


Figure 4. 4a. Mucosal incision following submucosal bleb. 4b.Lateral depiction of submucosal tunneling. 4c. Septal myotomy. 4d. Mucosal closure using through the scope clips. *Image courtesy of Dr. Sharat Vallurupalli.*

Thermal Therapy

Mulder et al. first reported on a pilot study in which Argon Plasma Coagulation (APC) was used to perform FESD with symptom improvement and no AE;[26] similar results are reported with varying reports of perforation which is the concern with the modality.[26, 44-46]

Submucosal Tunneling Endoscopic Septum Division

Submucosal tunneling endoscopic septic division (STESD/Z-POEM) (Figure 4) is a novel endoscopic technique in the management of ZD first reported by Li et al.[47] Z-POEM was created utilizing techniques from peroral endoscopic myotomy (POEM) to decrease the risk of perforation encountered during FESD, which is reported in as high as 6.5% of patients.[27] The approach to Z-POEM consists of the following four steps: mucosal incision (consisting of submucosal injection 3cm proximal to diverticular septum and 1-2cm longitudinal mucosal incision to create tunnel entry), submucosal tunneling (either to the end of the diverticulum or 1-2cm distal), septum division (septal myotomy) and mucosal closure (through the scope clips). Reports from small case series reveal that Z-POEM shows good success with return to normal anatomy, lack of perforation and symptom resolution on follow-up.[47-49] The limited data and the expertise required to perform POEM limit Z-POEM as a widespread therapeutic modality.

Novel Modalities

FESD with the Clutch Cutter (Fujifilm, Tokyo, Japan) has shown promise when used with or without a clear cap; to our knowledge there are only two case reports,[50,51] both reporting success. The device, originally intended for endoscopic submucosal dissection (ESD), and is not approved by the FDA.

The Stag beetle knife (SB-knife; Sumitomo Bakelite, Tokyo, Japan) was first reported in the use of diverticuloplasty in 2013.[52] Initially intended for ESD, SB-knife has shown good outcomes in a small series and case reports.[53-56] with the concomitant use of an overtube. Myotomy was performed in midline fashion except for Battaglia and Golder who provided a novel approach by creating two lateral dissections and using a monopolar snare to complete myotomy. Despite current reported success, further prospective trials are needed to determine long-term efficacy and recurrence rates.

DISCUSSION

The advancement of endoscopic tools, with similar efficacy and decreased risk of AE as compared to prior accepted modalities of surgery and rigid endoscopy, are increasingly making endoscopic therapy the "first line" approach to ZD management. The introduction of the diverticuloscope has allowed for better outcomes in European case series,[38] owing to greater stabilization of the endoscopic field and improved visualization during septum division. In the United States, a transparent cap serves a similar purpose. Emerging tools such as the SB-knife and Clutch Cutter are likely to yield improved outcomes as they allow for grasping and thermal therapy, limiting perforation risk. New endoscopic approaches such Z-POEM appear promising but are limited by endoscopic skill required and lack of data. It is clear that there needs to be highly scrutinized prospective data comparing flexible endoscopy and its wide armament of tools against rigid endoscopic approaches. ■

References

1. Ludlow, A., A case of obstructed deglutition from a preternatural dilatation of and bag formed in the pharynx. Med Observ Inq, 1769. 3: p. 85-101.
2. Haubrich, W.S., von Zenker of Zenker's diverticulum. Gastroenterology, 2004. 126(5): p. 1269.
3. Law, R., D.A. Katzka, and T.H. Baron, Zenker's Diverticulum. Clin Gastroenterol Hepatol, 2014. 12(11): p. 1773-82; quiz e111-2.
4. Watemberg, S., O. Landau, and R. Avrahami, Zenker's diverticulum: reappraisal. Am J Gastroenterol, 1996. 91(8): p. 1494-8.
5. Cook, I.J., et al., Pharyngeal (Zenker's) diverticulum is a disorder of upper esophageal sphincter opening. Gastroenterology, 1992. 103(4): p. 1229-35.
6. Cook, I.J., et al., Structural abnormalities of the cricopharyngeus muscle in patients with pharyngeal (Zenker's) diverticulum. J Gastroenterol Hepatol, 1992. 7(6): p. 556-62.
7. Hillel, A.T. and P.W. Flint, Evolution of endoscopic surgical therapy for Zenker's diverticulum. Laryngoscope, 2009. 119(1): p. 39-44.
8. Sasaki, C.T., D.A. Ross, and J. Hundal, Association between Zenker diverticulum and gastroesophageal reflux disease: development of a working hypothesis. Am J Med, 2003. 115 Suppl 3A: p. 169s-171s.
9. Boucher, S., R. Breheret, and L. Laccourreye, Importance of malnutrition and associated diseases in the management of Zenker's diverticulum. Eur Ann Otorhinolaryngol Head Neck Dis, 2015. 132(3): p. 125-8.
10. Knapp, A.B. and L. Ladetsky, Endoscopic retrieval of a small bowel enteroscopy capsule lodged in a Zenker's diverticulum. Clin Gastroenterol Hepatol, 2005. 3(5): p. xxxiv.
11. Simmons, D.T. and T.H. Baron, Endoscopic retrieval of a capsule endoscope from a Zenker's diverticulum. Dis Esophagus, 2005. 18(5): p. 338-9.
12. Ziachehabi, A., et al., Capsule retention in a Zenker's diverticulum. Endoscopy, 2011. 43 Suppl 2 UCTN: p. E387.
13. Bullock, W.K. and E.N. Snyder, Jr., Carcinoma in situ occurring in a pharyngeal diverticulum. Cancer, 1952. 5(4): p. 737-9.
14. Donald, P.J. and D.I. Huffman, Carcinoma in a Zenker's diverticulum. Head Neck Surg, 1979. 2(1): p. 71-5.
15. Rojas, F.A., R.T. Szymanowski, and S. Fujita, Zenker's diverticulum- carcinoma of the esophagus? J Otolaryngol, 1979. 8(3): p. 266-70.
16. Zitsch, R.P., C.J. O'Brien, and W.A. Maddox, Pharyngoesophageal diverticulum complicated by squamous cell carcinoma. Head Neck Surg, 1987. 9(5): p. 290-4.
17. Kerner, M.M., et al., Carcinoma-in-situ occurring in a Zenker's diverticulum. Am J Otolaryngol, 1994. 15(3): p. 223-6.
18. Marini, T., et al., Imaging of the oesophagus: beyond cancer. Insights Imaging, 2017. 8(3): p. 365-376.
19. Komatsu, M., T. Komatsu, and K. Inove, Ultrasonography of Zenker's diverticulum: special reference to differential diagnosis from thyroid nodules. Eur J Ultrasound, 2000. 11(2): p. 123-5.
20. DeFriend, D.E. and P.A. Dubbins, Sonographic demonstration of a pharyngoesophageal diverticulum. J Clin Ultrasound, 2000. 28(9): p. 485-7.
21. Kumar, A., S. Aggarwal, and D.H. Pham, Pharyngoesophageal (Zenker's) diverticulum mimicking thyroid nodule on ultrasonography: report of two cases. J Ultrasound Med, 1994. 13(4): p. 319-22.
22. Biggi, E., et al., Sonographic findings of Zenker's diverticulum. J Clin Ultrasound, 1982. 10(8): p. 395-6.
23. Colpaert, C., et al., Changes in Swallowing-related Quality of Life After Endoscopic Treatment For Zenker's Diverticulum Using SWAL-QOL Questionnaire. Dysphagia, 2017. 32(3): p. 339-344.
24. Dakkak, M. and J.R. Bennett, A new dysphagia score with objective validation. J Clin Gastroenterol, 1992. 14(2): p. 99-100.
25. Ishaq, S., et al., New and emerging techniques for endoscopic treatment of zenker's diverticulum - A state-of-the-art review. Dig Endosc, 2018.
26. Mulder, C.J., et al., Flexible endoscopic treatment of Zenker's diverticulum: a new approach. Endoscopy, 1995. 27(6): p. 438-42.
27. Ishaq, S., et al., Flexible endoscopic treatment for Zenker's diverticulum: a systematic review and meta-analysis. Gastrointest Endosc, 2016. 83(6): p. 1076-1089.e5.
28. Sawyer, R., C. Phillips, and N. Vakil, Short- and long-term outcome of esophageal perforation. Gastrointest Endosc, 1995. 41(2): p. 130-4.
29. Costamagna, G., et al., Flexible endoscopic Zenker's

diverticulotomy: cap-assisted technique vs. diverticuloscope-assisted technique. Endoscopy, 2007. 39(2): p. 146-52.
30. Ishioka, S., et al., Endoscopic incision of Zenker's diverticula. Endoscopy, 1995. 27(6): p. 433-7.
31. Hashiba, K., et al., Endoscopic treatment of Zenker's diverticulum. Gastrointest Endosc, 1999. 49(1): p. 93-7.
32. Al-Kadi, A.S., et al., Endoscopic treatment of Zenker diverticulum: results of a 7-year experience. J Am Coll Surg, 2010. 211(2): p. 239-43.
33. Halland, M., K.V. Grooteman, and T.H. Baron, Flexible endosopic management of Zenker's diverticulum: characteristics and outcomes of 52 cases at a tertiary referral center. Dis Esophagus, 2016. 29(3): p. 273-7.
34. Pescarus, R., et al., Trans-oral cricomyotomy using a flexible endoscope: technique and clinical outcomes. Surg Endosc, 2016. 30(5): p. 1784-9.
35. Huberty, V., et al., Endoscopic treatment for Zenker's diverticulum: long-term results (with video). Gastrointest Endosc, 2013. 77(5): p. 701-7.
36. Vogelsang, A., et al., Endotherapy of Zenker's diverticulum using the needle-knife technique: long-term follow-up. Endoscopy, 2007. 39(2): p. 131-6.
37. Case, D.J. and T.H. Baron, Flexible endoscopic management of Zenker diverticulum: the Mayo Clinic experience. Mayo Clin Proc, 2010. 85(8): p. 719-22.
38. Costamagna, G., et al., Prognostic variables for the clinical success of flexible endoscopic septotomy of Zenker's diverticulum. Gastrointest Endosc, 2016. 83(4): p. 765-73.
39. Repici, A., et al., Endoscopic flexible treatment of Zenker's diverticulum: a modification of the needle-knife technique. Endoscopy, 2010. 42(7): p. 532-5.
40. Repici, A., et al., Transoral treatment of Zenker diverticulum: flexible endoscopy versus endoscopic stapling. A retrospective comparison of outcomes. Dis Esophagus, 2011. 24(4): p. 235-9.
41. Antonello, A., et al., The role of flexible endotherapy for the treatment of recurrent Zenker's diverticula after surgery and endoscopic stapling. Surg Endosc, 2016. 30(6): p. 2351-7.
42. Brueckner, J., et al., Long-term symptomatic control of Zenker diverticulum by flexible endoscopic mucomyotomy with the hook knife and predisposing factors for clinical recurrence. Scand J Gastroenterol, 2016. 51(6): p. 666-71.
43. Rouquette, O., et al., Usefulness of the Hook knife in flexible endoscopic myotomy for Zenker's diverticulum. World J Gastrointest Endosc, 2017. 9(8): p. 411-416.
44. Rabenstein, T., et al., Argon plasma coagulation for flexible endoscopic Zenker's diverticulotomy. Endoscopy, 2007. 39(2): p. 141-5.
45. Wahab, P.J., et al., Argon plasma coagulation in flexible gastrointestinal endoscopy: pilot experiences. Endoscopy, 1997. 29(3): p. 176-81.
46. Manner, H., et al., Safety and efficacy of a new high power argon plasma coagulation system (hp-APC) in lesions of the upper gastrointestinal tract. Dig Liver Dis, 2006. 38(7): p. 471-8.
47. Li, Q.L., et al., Submucosal Tunneling Endoscopic Septum Division: A Novel Technique for Treating Zenker's Diverticulum. Gastroenterology, 2016. 151(6): p. 1071-1074.
48. Hernandez Mondragon, O.V., M.O. Solorzano Pineda, and J.M. Blancas Valencia, Zenker's diverticulum: Submucosal tunneling endoscopic septum division (Z-POEM). Dig Endosc, 2018. 30(1): p. 124.
49. Brieau, B., et al., Submucosal tunneling endoscopic septum division for Zenker's diverticulum: a reproducible procedure for endoscopists who perform peroral endoscopic myotomy. Endoscopy, 2017. 49(6): p. 613-614.
50. Gonzalez, N., D. Debenedetti, and A. Taullard, Endoscopic retreatment of Zenker's diverticulum using novel endoscopic scissors - The Clutch Cutter device. Rev Esp Enferm Dig, 2017. 109(9): p. 669.
51. Neumann, H., et al., Endoscopic therapy of Zenker's diverticulum using a novel endoscopic scissor - the Clutch Cutter device. Endoscopy, 2015. 47 Suppl 1 UCTN: p. E430-1.
52. Ramchandani, M. and D. Nageshwar Reddy, New endoscopic "scissors" to treat Zenker's diverticulum (with video). Gastrointest Endosc, 2013. 78(4): p. 645-8.
53. Ishaq, S., G. Battaglia, and A. Antonello, Double incision and snare resection in symptomatic Zenker's diverticulum: a modification of the stag-beetle knife technique. Endoscopy, 2018. 50(2): p. 182.
54. Chandran, S., Y. Shimamura, and C. Teshima, Novel endoscopic scissors for the treatment of Zenker's diverticulum. Gastrointest Endosc, 2017. 85(5): p. 1109-1110.
55. Goelder, S.K., J. Brueckner, and H. Messmann, Endoscopic treatment of Zenker's diverticulum with the stag beetle knife (sb knife) - feasibility and follow-up. Scand J Gastroenterol, 2016. 51(10): p. 1155-8.
56. Battaglia, G., et al., Flexible endoscopic treatment for Zenker's diverticulum with the SB Knife. Preliminary results from a single-center experience. Dig Endosc, 2015. 27(7): p. 728-33.