Harmonic scalpel for endoscopic treatment of Zenker's diverticulum: a critical review of the literature

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ABSTRACT

Introduction: Endoscopic staple-assisted diverticulostomy (ESD) is generally accepted as the preferred treatment option for patients with Zenker's diverticulum (ZD). However, anatomical factors may preclude the use of ESD in certain patients. In recent years, the harmonic scalpel has been introduced as an alternative device for endoscopic management of ZD, which may be useful in certain cases where diverticulum anatomy prevents the use of ESD. This review aims to assess the efficacy and safety of endoscopic ZD repair using the harmonic scalpel, including comparative analysis of the harmonic and staple-assisted approaches in terms of their surgical outcomes.

Conclusion: Most studies support the use of the harmonic scalpel as a safe and effective treatment option for ZD. Although the harmonic-assisted technique may not replace ESD as the initial treatment of choice for ZD, it may serve as a useful adjunct to treatment in selected cases. However, given the low quality of evidence and concerns regarding treatment complications, large prospective randomised trials comparing the harmonic and staple-assisted techniques are necessary in order to determine whether the harmonic scalpel is truly a viable option for endoscopic ZD management.

INTRODUCTION

Zenker's diverticulum (ZD), also known as a pharyngoesophageal diverticulum or pharyngeal pouch, is a sac-like outpouching of mucosa and submucosa through Killian's dehiscence, a triangular area of muscular weakness situated between the thyropharyngeus and cricopharyngeus muscles (Figure 1).[1-4] ZD is a rare condition with an estimated incidence of 2 per 100,000 people per year in the United Kingdom, and typically affects older individuals during their seventh or eighth decade of life.[3] Furthermore, it is twice as common in males and is the most common type of diverticulum affecting the upper gastrointestinal tract.[5, 6]

Aetiology and pathophysiology of ZD

Although the pathophysiology of ZD is not fully understood, a popular theory is that ZD arises due to impaired relaxation and spasm of the cricopharyngeus muscle, which in turn causes a rise in pressure within the hypopharynx.[2, 7] When a patient swallows, the resultant "pulsion" pressure causes herniation of the hypopharyngeal mucosa through the path of least resistance (Killian's dehiscence) and eventually leads to diverticulum formation.[2, 8] Gastroesophageal reflux disease may be implicated in the pathogenesis of ZD by causing scarring and uncoordinated relaxation of the cricopharyngeus muscle.[7, 9]

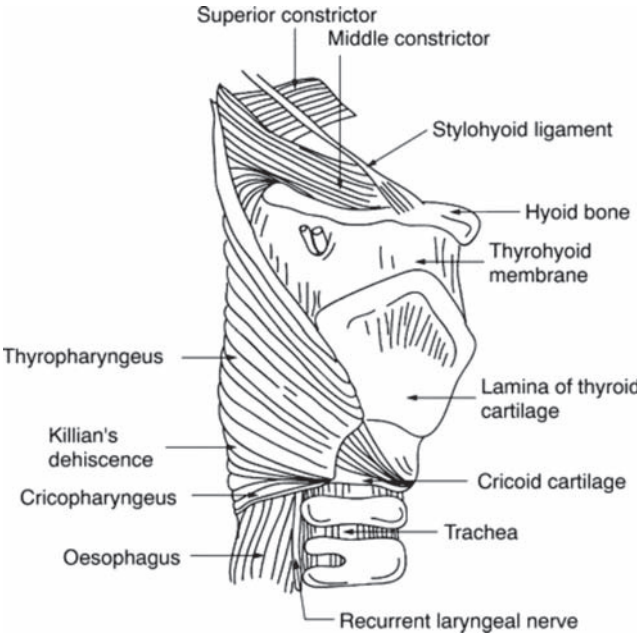

Figure 1: Lateral view of the pharynx illustrating Killian's dehiscence.[3]

Clinical presentation

Despite being relatively uncommon, ZD has the potential to cause significant morbidity in affected individuals due to entrapment of ingested food in the pouch.[2] Symptoms may include progressive oropharyngeal dysphagia, weight loss, malnutrition, halitosis, pulmonary aspiration and food regurgitation.[2, 3] ZD may even give rise to potentially life-threatening aspiration pneumonia or, rarely, squamous cell carcinoma within the diverticulum.[1, 10] In light of these facts, the need for prompt detection and management of symptomatic ZD is crucial.

Diagnosis and treatment

ZD may be diagnosed based on the patient's history, although a barium swallow study is typically performed for confirmation (Figure 2).[2, 7] Following diagnosis, surgery is carried out to eliminate the reservoir that collects food and to release the dysfunctional cricopharyngeus muscle.[7] Surgeons traditionally favoured a transcervical approach for the management of ZD, involving either diverticuloplexy (Figure 3), diverticulectomy (Figure 4), diverticular inversion (all with or without cricopharyngeal myotomy) or myotomy alone.[2, 11] However, less invasive endoscopic procedures have grown in popularity in recent decades due to their benefits of shorter operative time, reduced risk of serious complications, faster resumption of oral intake and shorter stay in hospital.[2, 12] These advantages are particularly important given that ZD predominantly affects elderly individuals who may be poor candidates for open surgery.[13, 14] Consequently, endoscopic repair has become the preferred treatment option for ZD.[15]

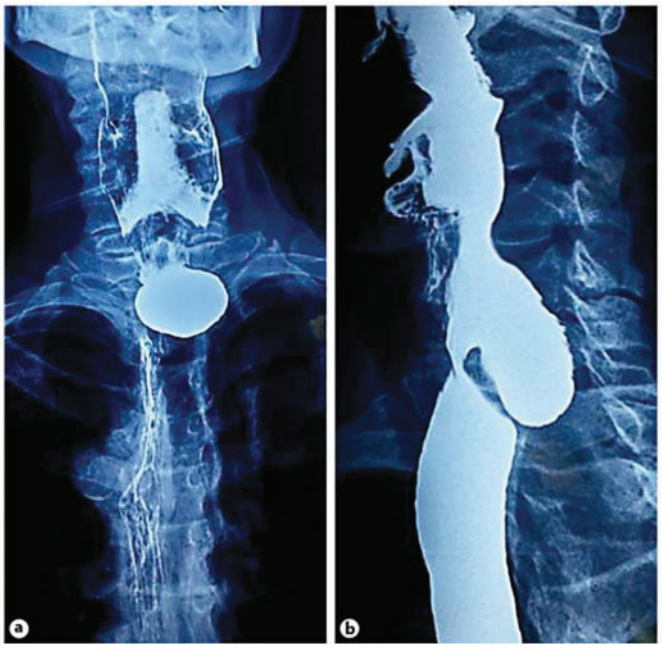

Figure 2: Barium swallow study showing a Zenker's diverticulum
A: anterior-posterior view; B: lateral view[1]

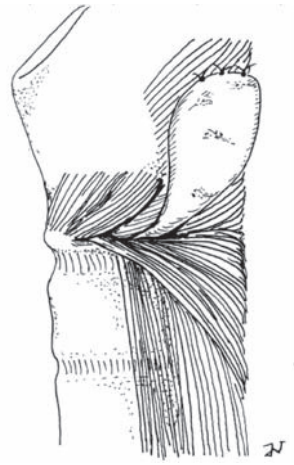

Figure 3:
Diverticuloplexy[16]

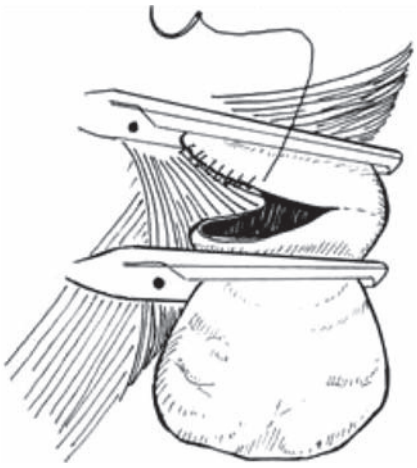

Figure 4:
Diverticulectomy[16]

Transoral endoscopic techniques are used to divide the common wall between the diverticulum sac and the oesophagus, within which the cricopharyngeus muscle is contained, and aim to create an overflow from the diverticulum to the oesophagus, thereby preventing food entrapment and relieving the zone of functional stenosis caused by the cricopharyngeus muscle (Figure 5).[2, 7] Since the first description of endoscopic ZD repair in 1917, numerous modifications have been made to the approach in attempts to improve the technique and minimise patient morbidity and mortality.[2, 14] Notable examples include the use of electrocautery, carbon dioxide (CO2) laser and a stapling device as methods for dividing the common wall between the oesophagus and diverticulum.[17, 22] More recently, flexible endoscopic diverticulotomy has been introduced as a potential alternative to rigid endoscopy for patients who possess kyphotic spines or who cannot tolerate general anaesthesia.[2, 23]

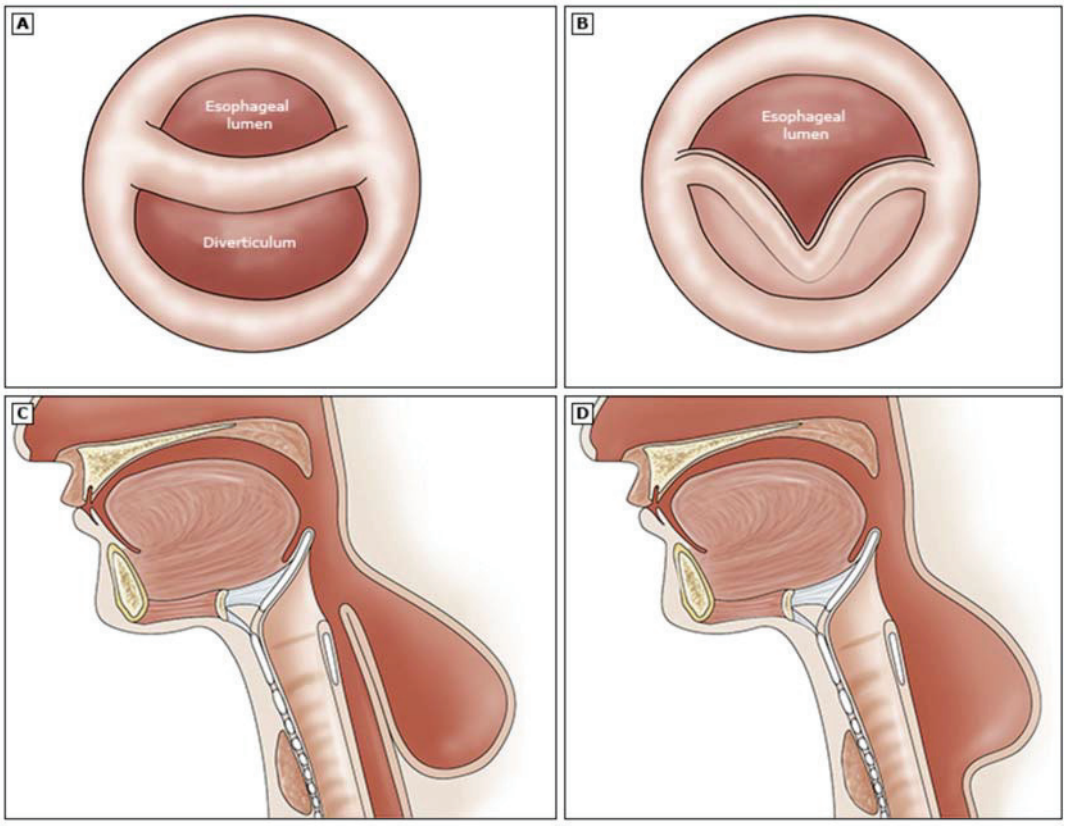

Figure 5:
Illustration of the endoscopic approach to Zenker's diverticulum therapy

A: Proximal luminal view of Zenker's diverticulum, with the common wall separating the diverticulum from the oesophagus;

B: Post-treatment, the common wall has been divided, creating a common cavity between the diverticulum and oesophagus;

C: Lateral view of the neck prior to treatment;

D: Lateral view of the neck after treatment[24]

Despite a lack of evidence from high-quality randomised trials demonstrating the superiority of one technique over another, endoscopic staple-assisted diverticulostomy (ESD) is generally considered to be the treatment of choice for ZD, with numerous studies demonstrating its safety and efficacy relative to other surgical techniques and 83% of UK surgeons regarding it as first choice treatment of ZD.[25-29] The key advantage of the stapling device is that it seals the edges of the cricopharyngeal myotomy with staples, thereby reducing the risk of pharyngeal leakage and subsequent mediastinitis.[30]

As with many surgical interventions however, ESD is not without limitations. Obtaining adequate exposure of the diverticulum can be a significant issue in patients with unfavourable anatomy, such as those with retrognathia or rigid cervical kyphosis, and is a notable cause of treatment failure.[28, 29] Moreover, smaller diverticula (<2cm) may not be amenable to ESD because the stapling device cannot cut the small common wall at its distil tip (Figure 6), resulting in incomplete cricopharyngeal myotomy and a residual pouch being left behind.[2, 14, 30] This may lead to persistent symptoms or an increased risk of diverticulum recurrence[7, 31]. Alternative approaches for dividing the common wall of small diverticula include the CO2 laser and electrocautery. However, these devices risk thermal damage to surrounding tissue and do not seal the mucosal edges following myotomy, thus increasing the risk of complications and post-operative pain.[7, 30, 31]

Figure 6: A: Harmonic scalpel; B: stapling device (the white bracket highlights the distil portion of the stapling devise which does not cut)[14]

More recently, the harmonic scalpel has been introduced as an alternative device for performing endoscopic diverticulostomies.[7] This instrument uses ultrasonic mechanical energy to simultaneously cut and coagulate tissues with minimal spread of thermal energy to adjacent tissues.[2] By causing protein denaturation, blood vessels are sealed and tamponaded, thereby providing effective haemostasis.[2, 31] The harmonic scalpel was traditionally used in laparoscopic surgery, but is increasingly being utilised by surgeons in other disciplines and has shown to be effective in neck dissections, thyroidectomies, parotidectomies, and now Zenker's diverticulostomies.[7, 32] Evidence suggests that the harmonic scalpel can effectively treat small diverticula (<2cm) due to its smaller diameter and its ability to cut at the distil tip (Figure 6).[2, 14] Although a number of studies[7, 14, 31, 32] have evaluated the efficacy of "endoscopic harmonic diverticulostomy" (EHD), there does not yet appear to be a critical review of the overall literature.

Aims

This study aims to assess the efficacy and safety of EHD by means of a structured review of the relevant literature, including comparative analysis of the harmonic- and staple-assisted approaches for treatment of ZD. Subsequently, the practical implications of these findings on ZD management will be explored.

METHODOLOGY

Articles relevant to this review were systematically identified from PubMed, Scopus and Web of Science. Further details regarding the search strategy and study selection are provided in Appendix 1.

RESULTS

A total of 195 records were initially identified from the literature search (Appendix 1, Table 1), 167 of which were retained for analysis following the removal of duplicates. All titles and abstracts were subsequently reviewed and a total of 12 studies were found to be potentially relevant based on the inclusion and exclusion criteria (Appendix 1 Table 2). Finally, upon reading the full text of these remaining articles, 5 studies met the inclusion criteria and hence were included in this review.[7, 14, 31-33]

All 5 studies analysed the use of the harmonic scalpel for endoscopic treatment of ZD in symptomatic patients, with two studies specifically comparing the surgical outcomes of EHD and ESD.[31, 32] A total of 150 patients were treated across all studies, 81 of which were treated with EHD, and all endoscopic procedures were carried out under general anaesthesia. In 4 studies, EHD was performed with rigid endoscopy using a Weerda bivalve diverticuloscope.[7, 14, 31, 32] Conversely, one study performed EHD using flexible endoscopy and a soft diverticuloscope.[33] Fourteen complications were found to be associated with EHD across all papers (Table 1). Moreover, numerous outcome measures were not reported by the majority of studies (Appendices 2 and 3). Further information from each paper is summarised below and in Appendices 2 and 3.

Fama et al. (2009)

Fama et al.[7] published the first series to assess the use of EHD for ZD repair in symptomatic patients. This involved a retrospective analysis of 25 patients who were treated between March 2007 and August 2008. The harmonic scalpel was used to divide the common diverticular wall down to the inferior aspect of the pharyngeal pouch. Five individuals were initially treated with ESD, but because of a residual common wall between the diverticulum and oesophagus, surgery was completed using the harmonic scalpel.

Complication	Number of patients	Percentage
Chest pain	4	4.9
Pharyngeal leak	3	3.7
Recurrence	3	3.7
Subcutaneous emphysema	2	2.5
Aspiration pneumonia	1	1.2
NSTEMI	1	1.2
Overall morbidity	14	17.3
Mortality	0	0

Table 1: Complications associated with endoscopic harmonic diverticulostomy NSTEMI = non-ST elevation myocardial infarction

Although all patients were reportedly treated successfully and safely with EHD, five individuals (20%) developed complications postoperatively and one patient (4%) developed a recurrent diverticulum at follow up which had to be treated with open surgery (Appendix 2). Most of the complications were attributed to the comorbidities of the elderly participants, rather than the surgical procedure itself, and no patients died or suffered from haemorrhage, infection or mediastinitis. Furthermore, figures relating to the duration of surgery and time to resumption of oral intake were not explicitly reported (Appendix 2), although the authors did comment that "duration of surgery with the harmonic scalpel is similar to that of other endoscopic techniques" and that 80% of patients were tolerating a liquid diet the day after surgery.

Sharp et al. (2009)

Sharp et al.[31] performed a non-randomised retrospective study comparing EHD and ESD for treatment of ZD. Overall, 20 patients were treated with EHD, 28 patients with ESD, and 2 patients were treated using both techniques. The decision to use a stapling device or harmonic scalpel was made by the senior author at the time of surgery and was based upon device availability and diverticulum size. Diverticula which were not amenable to ESD were treated using the harmonic scalpel.

Across all groups, 88% of patients reported complete resolution of their symptoms postoperatively. However, the authors made no explicit comments concerning the recovery rate within each treatment group (Appendix 3). In terms of complication rates, the difference between groups was not found to be statistically significant ($P<0.38$), although the authors did suggest that this difference may have become significant had their study sample size been doubled, with fewer complications being seen in the EHD group. Diverticulum size was a potential confounding factor in their study, with the average diverticulum size being significantly smaller in the EHD group versus the ESD group ($P<0.0017$) and no complications being associated with diverticula ≤2cm. Consequently, diverticulum size may have accounted for the lower complication rate in the EHD group, rather than the harmonic scalpel itself (Appendix 3).

May et al. (2011)

More recently, May et al.[14] carried out a retrospective series which described the use of EHD for ZD repair in 7 patients who could not undergo ESD for anatomical reasons. After surgery, patients were followed up for an average of 4 months and all reported complete resolution of their symptoms at the last follow-up. Each patient was tolerating a regular oral diet without any complications. The authors concluded that EHD was a safe and effective treatment option for ZD based on the favourable results demonstrated by this technique (Appendix 2).

Hondo et al. (2011)

Hondo et al.[33]conducted a prospective case series to assess the feasibility and efficacy of EHD in 5 patients with ZD. All EHD procedures were performed by a single endoscopist using flexible endoscopy and a soft diverticuloscope (Figures 7 and 8). Furthermore, a blinded research assistant assessed patients' symptoms before and after EHD by means of a dysphagia scoring system (Table 2).

EHD using a soft diverticuloscope was concluded to be a feasible and effective approach given that all patients demonstrated improvement in their dysphagia scores following treatment, without any major complications. However, one patient (20%) with recurrent symptoms required a second treatment session to complete dissection of the diverticular common wall (Appendix 2). The authors also commented that a technically challenging aspect of the endoscopic procedure related to the positioning of the soft diverticuloscope.

Severity of dysphagia	Score
No dysphagia	0
Dysphagia for solids	I
Dysphagia for semisolids	II
Dysphagia for liquids	III
Dysphagia with inability to swallow saliva	IV

Table 2: Dysphagia scoring system used by Hondo et al.[33]

Figure 7: Soft diverticuloscope[33]

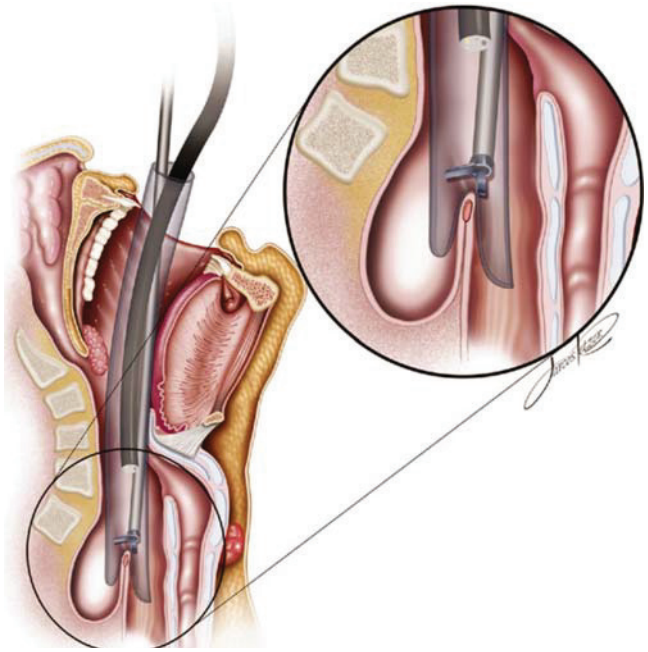

Figure 8: Endoscopic harmonic diverticulostomy using a flexible endoscope and soft diverticuloscope[33]

Whited et al. (2012)

Most recently, Whited et al.[32] performed a non-randomised retrospective study comparing the surgical outcomes of EHD and ESD in a cohort of 65 patients with ZD. Of all participants, 24 were allocated to the EHD group in a "consecutive chronological" fashion rather than being based on characteristics such as diverticulum size or symptoms. This was the only study to report the use of sutures for retraction of the diverticular common wall prior to surgical incision (Figure 9).

Baseline comparison of treatment groups revealed no significant difference between them in terms of average participant age (P=0.09) or diverticulum size (P=0.44). However, postoperative complication rates were found to be significantly higher in the EHD group compared to the ESD group (P=0.044). None of these complications were associated with diverticula <2cm and there were no complications of haemorrhage, mediastinitis or death (Appendices 2 and 3).

DISCUSSION

This literature review has highlighted that there are a growing number of studies describing the use of the harmonic scalpel for endoscopic ZD repair. However, there are significant methodological differences between papers and inconsistent reporting of results across all studies (Appendix 2), making comparative analysis challenging.

Safety and efficacy of EHD

Initial reports appear to support the use of EHD as a potential treatment option for ZD (either via Weerda or soft diverticuloscope) based on the favourable results demonstrated by this technique, including high recovery rates (80-100%), low recurrence rates (0-20%) and no mortalities (Appendix 2). Furthermore, 3 studies[7, 14, 31] demonstrated that EHD could be successfully performed in situations where ESD had failed, such as in patients with small diverticula or unfavourable anatomy. In terms of complication rates however, the overall evidence is less promising. Although 3 papers[14, 31, 33] reported minimal complications with EHD, the evidence from larger studies[7, 32] suggests that EHD complication rates are closer to 20%, which is comparatively higher than the complication rates reported by studies using other endoscopic approaches in the wider literature.[23] Nevertheless, no major complications of haemorrhage, infection or mediastinitis were identified across the 5 studies (Table 1) and no complications were associated with diverticula <2cm. Moreover, the low recurrence rates reported by 4 studies[7, 14, 32, 33] may just reflect a lack of long-term follow-up of patients, with the longest reported follow-up duration only being 10.3 months on average (Appendix 2). As such, this highlights the need for more long-term follow-up studies.

It is difficult to make reliable conclusions regarding the duration of surgery, length of hospitalisation (LOH) and time to resumption of oral intake for patients treated with EHD as these outcome measures were not consistently reported within the literature, if at all, and all studies used different protocols dictating intraoperative and postoperative management of patients. However, the limited available evidence suggests that "duration of surgery with the harmonic scalpel is similar to that of

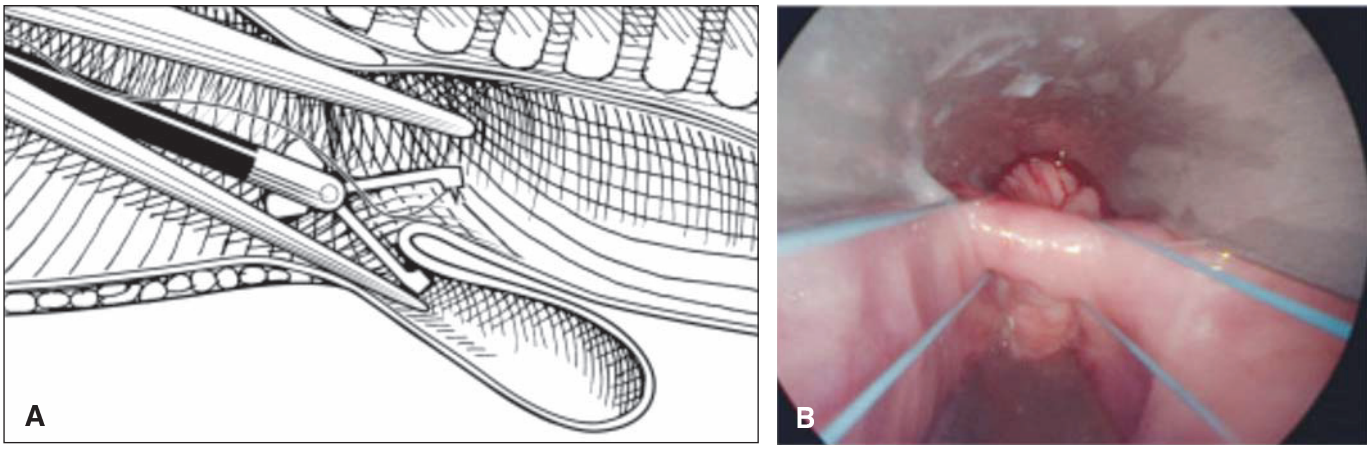

Figure 9: A: placement of retraction sutures in the proximal common diverticulum wall; B: endoscopic photograph of sutures in place[34]

other endoscopic techniques",[7] with the longest reported operative time being 35.1 minutes on average (Appendix 2). Furthermore, patients are likely to remain hospitalised for a short duration postoperatively, with the longest reported duration being 1.9 days on average (Appendix 2). In terms of the time taken for patients to resume an oral diet following EHD, the only study to provide explicit figures found that patients were nil by mouth for an average of 7.6 days.[14] However, this result was likely influenced by the protocol used in the study, which specified that patients must be kept on nasogastric feeding postoperatively until their first follow-up appointment. This limits the external validity of the finding as other studies did not adopt similar protocols. In light of the limited evidence, future studies should clearly report all outcome measures pertaining to EHD treatment, and attempts should be made to standardise intraoperative and postoperative care to allow for more effective comparative analysis between studies, although the latter suggestion may be impractical given that there is currently no universally accepted standard for ZD management.[11]

EHD versus ESD

Of the two studies[31, 32] which directly compared EHD and ESD, a considerable amount of information concerning the treatment outcomes was not provided, as previously mentioned (Appendix 3). Consequently, EHD and ESD could only be adequately compared in terms of their complication rates, recurrence rates and LOH.

Regarding complication rates, Sharp et al.[31] reported no significant difference between techniques. However, their study was limited by patient selection bias and the impact of confounding variables, most notably diverticulum size. For this reason, the authors concluded that postoperative complications were more likely due to the size of the diverticulum rather than the surgical equipment used in their study. Whited et al.,[32] on the other hand, found a significantly higher complication rate in the EHD group versus the ESD group. This finding appears to be more reliable given that both treatment groups were comparable in terms of baseline characteristics (diverticulum size and age), thereby reducing the risk of bias due to confounding variables (Appendix 3). However, the results of Whited et al. may have been influenced by other factors such as the expertise of the operating surgeon and the learning curve associated with novel application of EHD.

With regards to LOH and recurrence rates, the short-term results of Whited et al.[32] suggest minimal discrepancies between EHD and ESD (Appendix 3). In light of the overall evidence from their study, large prospective randomised trials are warranted to validate these findings and to determine long-term patient outcomes.

Practical implications for ZD management

Although EHD may not replace ESD as the first choice treatment for ZD, the evidence from this literature review suggests that the harmonic scalpel could be a useful alternative in cases where diverticulum anatomy precludes ESD, such as diverticula <2cm, or serve as an adjunct to treatment in the case of larger diverticula where the stapling device cannot completely incise the diverticular common wall. Thus, combining the techniques of ESD and EHD in selected patients may serve to improve treatment efficacy and safety, with division of the diverticular common wall initially being performed using the stapling device and subsequently completed with the harmonic scalpel.[31] However, in light of recent concerns regarding EHD-associated complications, alternative options may be more feasible for treatment of diverticula <2cm, such as the use of retraction sutures[34] and modifications to the stapling device.[35]

Despite the potential advantages offered by the harmonic scalpel, patients undergoing ZD repair must still be appropriate candidates for transoral rigid endoscopy, with sufficient oral cavity opening and cervical hyperextension.[7] For those who do not meet these criteria, flexible endoscopy or open surgery may serve as suitable alternatives.[7] Ultimately, surgeons should use the approach which they feel most confident with, but this literature review suggests that the harmonic scalpel is a useful option.

Further limitations of the literature

The quality of evidence from this review is limited by the fact that most included studies adopted retrospective study designs with small sample sizes, and no randomised comparative trials were identified. This further emphasises the need for large-scale randomised comparative studies.

Finally, the use of EHD with flexible endoscopy in Hondo et al.'s study[33] appears somewhat counterintuitive given that their endoscopic protocol required patients to be placed under general anaesthesia with neck hyperextension (Figure 8). Consequently, this negates the benefits offered by flexible endoscopy. Given the difficulties encountered by the group with positioning of the soft diverticuloscope and the limited advantages offered by flexible endoscopy in this situation, the use of EHD with rigid endoscopy appears to be the more logical approach for ZD management.

CONCLUSION

Despite methodological discrepancies and inconsistent reporting of information within the literature, most studies support the use of EHD for ZD repair based on the favourable results demonstrated by this technique, including high recovery rates, low recurrence rates and no mortalities. Practically speaking, the harmonic scalpel may be useful for the treatment of diverticula <2cm and may serve as a useful adjunct to endoscopic ZD repair in situations where the stapling device cannot completely incise the diverticular common wall. However, much of the supporting evidence comes from small, retrospective studies with short follow-up periods, and the largest study comparing EHD and ESD found complication rates to be significantly higher in patients treated with EHD. Consequently, large prospective randomised trials comparing EHD and ESD are warranted in order to determine whether the harmonic scalpel is truly a viable option for endoscopic ZD management.

REFERENCES

1. Nuno-Guzman CM, Garcia-Carrasco D, Haro M, Arroniz-Jauregui J, Corona JL, Salcido M. Zenker's Diverticulum: diagnostic approach and surgical management. Case Rep Gastroenterol 2014;8(3):346-52.
2. Bizzotto A, Iacopini F, Landi R, Costamagna G. Zenker's diverticulum: exploring treatment options. Acta Otorhinolaryngol Ital 2013;33(4):219-29.
3. Siddiq MA, Sood S, Strachan D. Pharyngeal pouch (Zenker's diverticulum). Postgrad Med J 2001;77(910):506-11.
4. Nehring P, Krasnodebski IW. Zenker's diverticulum: aetiopathogenesis, symptoms and diagnosis. Comparison of operative methods. Przeglad gastroenterologiczny 2013;8(5):284-9.
5. Yuan Y, Zhao YF, Hu Y, Chen LQ. Surgical treatment of Zenker's diverticulum. Dig Surg 2013;30(3):207-18.
6. Ferreira LE, Simmons DT, Baron TH. Zenker's diverticula: pathophysiology, clinical presentation, and flexible endoscopic management. Dis Esophagus 2008;21(1):1-8.
7. Fama AF, Moore EJ, Kasperbauer JL. Harmonic scalpel in the treatment of Zenker's diverticulum. Laryngoscope 2009;119(7):1265-9.
8. Hillel AT, Flint PW. Evolution of endoscopic surgical therapy for Zenker's diverticulum. Laryngoscope 2009;119(1):39-44.
9. Sasaki CT, Ross DA, Hundal J. Association between Zenker diverticulum and gastroesophageal reflux disease: development of a working hypothesis. Am J Med 2003;115 Suppl 3A:169S-71S.
10. Brucher BL, Sarbia M, Oestreicher E, et al. Squamous cell carcinoma and Zenker diverticulum. Dis Esophagus 2007;20(1):75-8.
11. Sen P, Lowe DA, Farnan T. Surgical interventions for pharyngeal pouch. The Cochrane database of systematic reviews. 2005(3):CD004459.
12. Aiolfi A, Scolari F, Saino G, Bonavina L. Current status of minimally invasive endoscopic management for Zenker diverticulum. World Journal of Gastrointestinal Endoscopy 2015;7(2):87-93.
13. Repici A. Endoscopic treatment of zenker diverticulum. Gastroenterol Hepatol 2010;6(10):628-30.
14. May JT, Padhya TA, McCaffrey TV. Endoscopic repair of Zenker's diverticulum by harmonic scalpel. Am J Otolaryngol 2011;32(6):553-6.
15. Dzeletovic I, Ekbom DC, Baron TH. Flexible endoscopic and surgical management of Zenker's diverticulum. Expert Rev of Gastroenterol Hepatol 2012;6(4):449-65; quiz 66.
16. Constantin A, Mates IN, Predescu D, Hoara P, Achim FI, Constantinoiu S. Principles of surgical treatment of Zenker diverticulum. J Med Life 2012;5(1):92-7.
17. Dohlman G, Mattsson O. The endoscopic operation for hypopharyngeal diverticula: a roentgencinematographic study. AMA Arch Otolaryngol. 1960;71:744-52.
18. van Overbeek JJ, Hoeksema PE, Edens ET. Microendoscopic surgery of the hypopharyngeal diverticulum using electrocoagulation or carbon dioxide laser. Ann Otol Rhinol Laryngol 1984;93(1 Pt 1):34-6.
19. Collard JM, Otte JB, Kestens PJ. Endoscopic stapling technique of esophagodiverticulostomy for Zenker's diverticulum. Ann Thorac Sur. 1993;56(3):573-6.
20. Martin-Hirsch DP, Newbegin CJ. Autosuture GIA gun: a new application in the treatment of hypopharyngeal diverticula. J Laryngol Otol 1993;107(8):723-5.
21. Scher RL, Richtsmeier WJ. Endoscopic staple-assisted esophagodiverticulostomy for Zenker's diverticulum. Laryngoscope 1996;106(8):951-6.
22. Scher RL, Richtsmeier WJ. Long-term experience with endoscopic staple-assisted esophagodiverticulostomy for Zenker's diverticulum. Laryngoscope 1998;108(2):200-5.
23. Ishaq S, Hassan C, Antonello A, et al. Flexible endoscopic treatment for Zenker's diverticulum: a systematic review and meta-analysis. Gastrointest Endosc 2016;83(6):1076-89 e5.
24. Law R, Katzka DA, Baron TH. Zenker's diverticulum. Clin Gastroenterol Hepatol 2014;12(11):1773-82; quiz e111-2.
25. Cook RD, Huang PC, Richstmeier WJ, Scher RL. Endoscopic staple-assisted esophagodiverticulostomy: an excellent treatment of choice for Zenker's diverticulum. Laryngoscope 2000;110(12):2020-5.
26. Philippsen LP, Weisberger EC, Whiteman TS, Schmidt JL. Endoscopic stapled diverticulotomy: treatment of choice for Zenker's diverticulum. Laryngoscope 2000;110(8):1283-6.
27. Miller FR, Bartley J, Otto RA. The endoscopic management of Zenker diverticulum: CO2 laser versus endoscopic stapling. Laryngoscope 2006;116(9):1608-11.
28. Leong SC, Wilkie MD, Webb CJ. Endoscopic stapling of Zenker's diverticulum: establishing national baselines for auditing clinical outcomes in the United Kingdom. Eur Arch Otorhinolaryngol 2012;269(8):1877-84.
29. Verdonck J, Morton RP. Systematic review on treatment of Zenker's diverticulum. Eur Arch Otorhinolaryngol 2015;272(11):3095-107.
30. Allen J, Belafsky PC. Endoscopic cricopharyngeal myotomy for Zenker diverticulum using the harmonic scalpel. Ear Nose Throat J 2010;89(5):216-8.
31. Sharp DB, Newman JR, Magnuson JS. Endoscopic management of Zenker's diverticulum: stapler assisted versus Harmonic Ace. Laryngoscope 2009;119(10):1906-12.
32. Whited C, Lee WT, Scher R. Evaluation of endoscopic harmonic diverticulostomy. Laryngoscope 2012;122(6):1297-300.
33. Hondo FY, Maluf-Filho F, Giordano-Nappi JH, Neves CZ, Cecconello I, Sakai P. Endoscopic treatment of Zenker's diverticulum by harmonic scalpel. Gastrointest Endosc 2011;74(3):666-71.

34. McGinn JD. Endoscopic approach to cricopharyngeal hypertonicity and hypopharyngeal diverticulum. Operative Techniques in Otolaryngology - Head and Neck Surgery 2016;27(2):67-73.
35. Richtsmeier WJ. Myotomy length determinants in endoscopic staple-assisted esophagodiverticulostomy for small Zenker's diverticula. Ann Otol Rhinol Laryngol 2005;114(5):341-6.

APPENDICES

Appendix 1: Methods

Search strategy

The electronic databases, PubMed, Scopus and Web of Science, were systematically searched in February 2017 to identify peer-reviewed articles which assessed the efficacy and safety of EHD for ZD repair in symptomatic patients, including comparative studies. An initial analysis of the literature concerning Zenker's diverticulum and the harmonic scalpel indicated that the chosen search terms (Appendix 1 Table 1) were most relevant and commonly used within articles. Additionally, the reference lists of relevant papers were inspected to ensure comprehensiveness of the literature search.

Data extraction

Upon selection of relevant articles, the following parameters were extracted from each study to allow for comparative analysis: study design, number of participants, average age of participants, average diverticulum size, choice of diverticuloscope, average follow-up time, routine use of perioperative antibiotics, average operative time, average time to resumption of oral intake, recovery rate, complication rate, mortality rate and recurrence rate. A 'recovery' was defined as complete or partial resolution of ZD-associated symptoms following one endoscopic treatment session.

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		Number of results		
Set	**Search Phrase**	**PubMed**	**Scopus**	**Web of Science**
#1	"Zenker's diverticulum" OR "Zenker diverticulum" OR "Zenker's diverticula" OR "Zenker diverticula" OR "Pharyngeal pouch" OR "Pharyngoesophageal diverticulum" OR "Cricopharyngeal diverticulum" OR "Hypopharyngeal diverticulum"	1,765	5,133	1,306
#2	"Harmonic" OR "Ultracision" OR "Ultrasonic" OR "Ultrasonographic"	106,940	1,262,221	346,725
#3	#1 AND #2	15	176	18
#4	Search limited to articles published in English	14	165	16

Appendix 1 Table 1: Results from literature search

		Demographics			Methods			Results						
Reference	**Study design**	**Number of participants**	**Average age of participants**	**Average diverticulum size (cm)**	**Diverticuloscope**	**Average follow-up duration**	**Use of antibiotics**	**Average operative time (min)**	**Average LOH (days)**	**Time to resumption of oral intake (days)**	**Recovery rate (%)**	**Complication rate (%)**	**Mortality rate (%)**	**Recurrence rate (%)**
Fama et al. (2009)	Retrospective case series	25	76	NR	Weerda	10.3 months	NR	NR	1.3	NR	100	20	0	4
Sharp et al. (2009)	Non-randomised retrospective comparative	20	NR	2.1	Weerda	NR (range 1-4 weeks)	Yes	NR	NR [a]	NR [a]	NR	5	0	NR
May et al. (2011)	Retrospective Case series	7	75.6	NR (range 1-5)	Weerda	4 months	NR	35.1	1.9 [a]	7.6 [a]	100	0	0	0
Hondo et al. (2011)	Prospective case series	5	69.6	3.6*	Soft diverticuloscope	NR	Yes	17.33	NR [a]	NR [a]	80	0	0	20
Whited et al. (2012)	Non-randomised retrospective comparative	24	68	3.24	Weerda	NR	No	NR	0.71 [a]	NR [a]	NR	25	0	4.2

Appendix 2: Summary of included studies (only including data for patients treated with endoscopic harmonic diverticulostomy)

*Small diverticula (<2cm) were excluded from the stud, [a] Studies had protocols dictating time to resumption of oral intake and LOH
LOH = length of hospitalisation; NR = not reported; EHD = endoscopic harmonic-assisted diverticulostomy; ESD = endoscopic staple-assisted diverticulostom

		Demographics			Methods			Results						
Reference	**Study design**	**Number of participants**	**Average age of participants**	**Diverticulum size (cm)**	**Diverticuloscope**	**Average follow-up duration**	**Use of antibiotics**	**Average operative time (min)**	**LOH (days)**	**Time to resumption of oral intake (days)**	**Recovery rate (%)**	**Complication rate (%)**	**Mortality rate (%)**	**Recurrence rate (%)**
Sharp et al. (2009)	Non-randomised retrospective comparative	EHD: 20 ESD: 28 EHD+ESD: 2	69.2[§]	EHD: 2.1 ESD: 2.9 **P<0.0017**	Weerda	NR (range 1-4 weeks)	Yes	NR	1.1 [a] (±0.42)	NR[a]	88[§]	EHD: 5 ESD: 17.9 **P<0.38**	0	NR
Whited et al. (2012)	Non-randomised retrospective comparative	EHD: 24 ESD: 41	EHD: 68 ESD: 77 **P=0.09**	EHD: 3.24 ESD: 3.68 **P=0.44**	Weerda	NR	No	NR	EHD: 0.71[a] ESD: 0.69[a]	NR[a]	NR	EHD: 25 ESD: 4.88 **P=0.044**	0	EHD: 4.2 ESD: 2.4

Appendix 3: Summary of comparative studies (including data for patients treated with harmonic- and staple-assisted approaches)

[§] Data not provided for individual treatment groups, [a] Studies had protocols dictating time to resumption of oral intake and LOH
LOH = length of hospitalisation; NR = not reported; EHD = endoscopic harmonic-assisted diverticulostomy; ESD = endoscopic staple-assisted diverticulostomy