

Minimally invasive surgery for motility disorders of the oesophagus

Ph.D. Thesis

LÁSZLÓ ANDRÁSI M.D.

Supervisor: György Lázár M.D., Ph.D., D.Sc.



**Department of Surgery Faculty of Medicine
University of Szeged**

Szeged

2021

This doctoral thesis is based on the following publications:

- I. Andrási, László ; Ábrahám, Szabolcs ; Simonka, Zsolt ; Paszt, Attila ; Rovó, László ; Lázár, György A Zenker-diverticulumok transcervicalis és transoralis sebészi kezelésének összehasonlító vizsgálata, rövid és hosszú távú eredmények ORVOSI HETILAP 160 : 16 pp. 629-635. , 7 p. (2019) DOI: 10.1556/650.2019.31360 IF: 0.497
- II. Andrási, László ; Paszt, Attila ; Simonka, Zsolt ; Ábrahám, Szabolcs ; Rosztóczy, András ; Lázár, György Laparoscopic Surgery for Epiphrenic Esophageal Diverticulum JSLS-JOURNAL OF THE SOCIETY OF LAPAROENDOSCOPIC SURGEONS 22 : 2 Paper: 2017.00093 , 8 p. (2018) DOI: 10.4293/JSLS.2017.00093 IF: 1.654
- III. Andrási, László ; Paszt, Attila ; Simonka, Zsolt ; Ábrahám, Szabolcs ; Erdős, Márton ; Rosztóczy, András ; Ollé, Georgina ; Lázár, György Surgical Treatment of Esophageal Achalasia in the Era of Minimally Invasive Surgery JSLS-JOURNAL OF THE SOCIETY OF LAPAROENDOSCOPIC SURGEONS 25 : 1 Paper: e2020.00099 , 12 p. (2021) DOI: 10.4293/JSLS.2020.00099 IF: 2.172

Total impact factor of original papers directly related to the thesis: 4.323

List of abstracts related to the subject of the thesis:

- I. Andrási László, Paszt Attila, Simonka Zsolt, Ábrahám Szabolcs, Rosztóczy András1, Lázár György Laparoscopic surgery for esophageal diverticulum: short-term and long-term results 68th Congress of the Association of Polish Surgeons 2017. kiadványa 1401. sz. abstract, p. 491.
- II. Andrási László, Paszt Attila, Simonka Zsolt, Ábrahám Szabolcs, Rovó László, Lázár György A comparative study of short and long-term outcomes for transcervical versus transoral surgery for Zenker's diverticulum 27th International Congress of the European Association for Endoscopic Surgery Sevilla, 2019. június 12-15.
- III. Andrási László, Paszt Attila, Simonka Zsolt, Ábrahám Szabolcs, Rosztóczy András, Rovó László, Lázár György: Zenker's diverticulumok transcervicalis és transoralis sebészi kezelése: összehasonlító, rövid és hosszú távú eredmények A Magyar Sebész Társaság 64. Kongresszusa Debrecen, 2018. május 24-26.
- IV. Andrási László, Paszt Attila, Simonka Zsolt, Ábrahám Szabolcs, Rosztóczy András1 , Rovó László11, Lázár György: Transoral and transcervical surgery for Zenker's diverticulum : short-term and long-term results 26th International Congress of the European Association for Endoscopic Surgery, London, 2018. május 30-június 1.
- V. Andrási László: Az epiphrenalis nyelőcső diverticulumok minimálisan invazív sebészete: rövid és hosszú távú eredmények MST Sebészeti Endoszkópos Szekció XVII. Kongresszusa, Kecskemét, 2017. október 12-14.
- VI. Andrási László, Paszt Attila, Simonka Zsolt, Ábrahám Szabolcs, Rosztóczy András1, Lázár György Laparoscopic surgery for esophageal diverticulum: short-term and long-term results XXI Annual Meeting of the European Society of Surgery, 2nd European Meeting of Residents and PhD Students in Surgery, Krakkó, Lengyelország, 2017. szeptember 27- 30.

Publications not directly related to the thesis:

1. Ábrahám, Szabolcs; Németh, Tibor ; Benkő, Ria ; Matuz, Mária ; Váczi, Dániel ; Tóth, Illés ; Ottlakán, Aurél ; Andrási, László ; Tajti., János ; Kovács, Viktor et al. Evaluation of the conversion rate as it relates to preoperative risk factors and surgeon experience: a retrospective study of 4013 patients undergoing elective laparoscopic cholecystectomy BMC SURGERY 21 : 1 Paper: 151 , 7 p. (2021) DOI: 10.1186/s12893-021-01152-z IF: 2.102
2. Andrási, László ; Szepes, Zoltán ; Tizslavicz, László ; Lázár, György ; Paszt, Attila Complete laparoscopic-transhiatal removal of duplex benign oesophageal tumour: case report and review of literature BMC GASTROENTEROLOGY 21 : 1 Paper: 47 , 7 p. (2021) DOI: 10.1186/s12876-021-01625-8 IF: 3.067
3. Lorenzon, Laura ; Evrard, Serge ; Beets, Geerard ; Gonzalez-Moreno, Santiago ; Kovacs, Tibor ; D'Ugo, Domenico ; Polom, Karol ; CORSiCA, Study - EYSAC.1 Study Group (Kollaborációs szervezet) ; Andrási, László (Kollaborációs közreműködő) ; Lázár, György (Kollaborációs közreműködő) et al. Global variation in the long-term outcomes of ypT0 rectal cancers EUROPEAN JOURNAL OF SURGICAL ONCOLOGY 46 : 3 pp. 420-428. , 9 p. (2020) DOI: 10.1016/j.ejso.2019.10.010 IF: -
4. Tibor, Novák; László, András ; Zsolt, Szabó ; Gábor, Németh Succesfully treated case of a patient with giant benign ovarian tumor and suicide attempt MAGYAR NŐORVOSOK LAPJA 80 : 5 pp. 231-233. , 3 p. (2017) IF: -
5. Andrasi, L ; Abraham, S ; Lazar, G A minilaparoscopos cholecystectomy mint innovatív eljárás a minimalisan invazív hasi sebeszetben [Mini-laparoscopic cholecystectomy as an innovative method in minimally invasive abdominal surgery] MAGYAR SEBÉSZET 67 : 6 pp. 334-339. , 6 p. (2014) DOI: 10.1556/MaSeb.67.2014.6.3 IF: -
6. Petri, A; Hohn, J ; Balogh, A ; Kovach, K ; Andrasi, L ; Lazar, G Colorectalis rák májáttéteinek sebészi kezelése szinkron májreszekcióval [Surgical Treatment of Liver Metastasis in Colorectal Cancer With Simultaneous Liver Resection] MAGYAR ONKOLÓGIA 54 : 2 pp. 125-128. , 4 p. (2010) DOI: 10.1556/MOnkol.54.2010.2.6 IF: -

Cumulative impact factor: 9.492

1. INTRODUCTION

Primary motor disorders of the oesophagus consist of achalasia, diffuse oesophageal spasm, nutcracker oesophagus and non-specific oesophageal motility disorders. Usually, oesophageal diverticula are not stated among primary motor disorders, but, in almost every case, they are associated with a certain type of dysmotility which plays a key role in their pathogenesis.

The pharyngoesophageal or Zenker's diverticula are pseudodiverticula of the oesophagus, containing mucosal and submucosal layers, which are typically located in the posterior wall of the hypopharynx, between the oblique fibres of the constrictor pharyngis inferior muscle and the transverse fibres of the cricopharyngeus muscle, in the so-called Killian–Laimer triangle. The lesions are considered to be pulsion type because the pharyngoesophageal intraluminal pressure increases due to the malfunction of the former muscle apparatus (spasm and insufficient relaxation). Epiphrenic diverticulum of the oesophagus is an outpouching of the mucosal and submucosal layers of the oesophagus which generally affects the distal third segment. Lesions are considered to be pulsion type, as they are accompanied by dysmotility of the oesophagus in 70 to 90% of cases, known as primary oesophageal motility disorder. The most common motility disorders are achalasia and diffuse oesophageal spasm (DES); uncommon disorders are the so-called nutcracker oesophagus and hypertensive lower oesophageal sphincter (LES). First described by Sir Thomas Willis in 1674, achalasia is a chronic motility disorder of the oesophagus characterised by a lack of peristalsis and the inability of the LES to relax. The aetiology of achalasia is still unclear, but, ultimately, it is a selective disorder of the inhibitory neurons in the myenteric (or Auerbach's) plexus of the distal oesophagus and the LES. In gastroenterological diagnostics, functional assessments play a primary role.

Regardless of the localization of the functional oesophageal lesion, its manifestation (Zenker's diverticulum, epiphrenic diverticulum and achalasia cardiae) and the choice of surgical type, all surgical therapeutic efforts are aimed at the disruption of abnormal muscle function (myotomy) with or without secondary developed organic lesion (diverticulum) removal. Diverticula cannot be cured by conservative treatment; they gradually grow over time. In the case of motility disorders, surgical therapy is only justified in cases causing complaints, and it is also a solution for the prevention of imminent, often fatal, short- and long-term complications (familiar aspiration, pneumonia, oesophageal perforation and oesophageal cancer).

The treatment of Zenker's diverticula is surgical, with the traditional operative solution consisting of transcervical pharyngoesophageal myotomy and resection of the diverticulum. The so-called transoral procedure has been known for several decades, the essence of which is to cut the common wall of the diverticulum and oesophagus together with the upper oesophageal sphincter (using a rigid or flexible) endoscope with a tissue-separating device, resulting in a common lumen (oesophageal diverticulostomy). First described by Mosher in 1917, the ostomy was created using a scalpel and later an electric knife and a carbon dioxide (CO₂) laser, causing much fewer complications. The Endostapler method has also long been known in the management of the Zenker's diverticulum, and minimally invasive access to the diverticulum was reported by Martin-Hirsch and Collard in 1993. The main point of the surgery is to insert a distending operating laryngoscope into the hypopharynx, the longer end of which is inserted into the oesophagus and the smaller end into the diverticulum. The septum between the diverticulum and the oesophagus is then cut with a laparoscopic stapler, connecting the lumen of the diverticulum and oesophagus while interrupting the upper oesophageal sphincter. The endoscopic option has spread rapidly around the world, and several working groups have already reported positive experiences with the use of the method. Our group reported the application of this approach for the first time in Hungary, which is recommended primarily for the elimination of Zenker's diverticulum greater than 3 cm in elderly patients. The main advantages of the procedure are shorter surgical time, rare occurrence of complications and absence of surgical scar. Postoperative feeding can be started early, so patients quickly become completely asymptomatic. From an economic point of view, it cannot be neglected that hospital care will also be significantly shortened. Surgical treatment for an epiphrenic diverticulum is indicated only in the case of complaints, which consists of resection of the diverticulum and, usually, cardiomyotomy. The latter should be complemented with antireflux surgery (Dor or Toupet) to reduce postoperative GERD, which occurs in a large number of cases. Standard explorations of the oesophagus (thoracotomy and laparotomy) are accompanied by significant morbidity. Minimally invasive surgery has become widely used in the functional treatment of the oesophagus and in the surgical treatment of an epiphrenic diverticulum to reduce morbidity. Currently, transhiatal diverticulectomy with cardiomyotomy and antireflux surgery are the most commonly used surgical techniques. In addition to the low morbidity of the method, patients become asymptomatic, and the intervention provides effective symptom control in 80 to 90% of cases, although publications are limited with regard to long-term results.

The treatment for achalasia is palliative only, and all therapeutic efforts are aimed at facilitating adequate passage through the cardia and, at the same time, preventing late structural and functional oesophageal complications. The minimally invasive (laparoscopic and thoracoscopic) types of Heller myotomy were introduced into clinical practice in the early 1990s. To reduce the risk of GERD following a cardiomyotomy, which had previously been used alone, the procedure was later completed with partial fundoplication (anterior, or Dor, and posterior, or Toupet). This modified laparoscopic Heller cardiomyotomy completed with semifundoplication has proved to be the most effective procedure, with minimal morbidity, both in the short and long term.

Due to the nature and relative rarity of the oesophageal motility disorders listed, a limited number of studies have been published even in the universal literature. Most often, small case numbers and summaries were obtained without long-term outcomes from which no meaningful conclusion could be drawn. However, the excellent results of specialized centres and multicentre investigations have convinced critical voices over the years, as a result of which a revolution in minimally invasive technology has also taken place in functional oesophageal surgery. Our institute also has a long tradition of oesophageal surgery, the practitioners of which, in addition to the local application of international guidelines, have borne continuous innovation in mind. In Hungary, our working group introduced minimally invasive procedures in oesophageal surgery in the 1990s, which has become a standardly used therapeutic alternative in the wake of encouraging results. The care of previously sporadically appearing functional oesophageal diseases has become more specific at the regional level as a result of complex gastroenterological examination and thorough condition assessment, which has been established by a harmonious surgeon–gastroenterologist collaboration.

For all these reasons, in the surgical manifestations of pharyngoesophageal (Zenker's) diverticulum, epiphrenic diverticulum and achalasia cardiae, we sought to evaluate the factors influencing late quality of life beyond the modern surgical procedure that reflects the current state of science.

2. OBJECTIVES

(1) To compare the perioperative results and the long-term advantages and disadvantages of the two different surgical methods (transcervical diverticulectomy with cricomyotomy [TCD] and transoral stapler diverticulostomy [TSD]) in patients with Zenker's diverticulum (Study I).

(2) To analyse our experience of patients who had undergone laparoscopic-transhiatal diverticulectomy for epiphrenic oesophageal diverticulum focusing on quality of life changes (Study II).

(3) To investigate complex surgical therapy for achalasia concentrating the short- and long-term follow-up results in patients who had undergone laparoscopic Heller–Dor surgery (Study III).

3. PATIENTS AND METHODS

3.1. Patients

Patients who had undergone surgery for Zenker's diverticulum, epiphrenic diverticulum and achalasia between 1 January 2003 and 31 December 2017 were involved in our investigations at the Department of Surgery, University of Szeged.

Study I:

Between 1 January 2006 and 31 December 2016, 29 patients (20 males and 9 females aged 34 to 89 years) were treated for symptomatic Zenker's diverticulum. The mean age of the TCD group was 65.4 years with male dominance (12/1), while the mean age of the TSD group was 68.2 years equally in both genders (8/8). The most common complaints among the patients scheduled for surgery included severe dysphagia and severe regurgitation. Significant weight loss was observed in the TSD group (25%, 4/16). The preoperative work-up showed an average diameter of 47.7 mm of the diverticula, which was almost the same in both groups. The average duration of symptoms was 31.7 months, subdivided into groups: TCD group 46 months, TSD group 18.6 months. In four patients in both groups (TCD: 30%; TSD: 25%), medically treated GERD was diagnosed in addition to diverticulum. One patient had pneumonia in his past history in the TSD group (6.2%).

Study II:

Between 1 January 2003 and 1 March 2016, eight patients (4 men and 4 women; average age: 63 years, 52–76) were treated at our department for symptomatic epiphrenic diverticulum. The

most common complaint was dysphagia, which occurred in 87.5% (7/8) of the patients. The average duration of complaints was 73 months (4–360 months). After we obtained a thorough medical history from the patients, complex gastroenterological check-ups were performed (swallowing X-ray, endoscopy of the upper gastrointestinal tract, pH and manometry of the oesophagus). The average diameter of the diverticulum was 6.5 cm (3–12 cm) before surgery. During the endoscopic examination, diverticula were found an average 34.3 cm (32–38 cm) from the teeth and 5 cm (3–8 cm) from the cardia. They opened mainly in the right, dorsolateral direction (right/left: 5/3). In addition to the diverticulum diagnosis, a small axial-type hiatal hernia was diagnosed in two cases. Manometry of the oesophagus was performed in all cases. Normal LES with prolonged relaxation was detected in two patients (25%), and manometry confirmed achalasia in two cases (25%). The other three findings showed the following: LES with incomplete relaxation and spastic motor disorder (12.5%), incompetent LES (12.5%) and distal oesophageal spasm with involvement of LES (12.5%). One patient had normal manometric findings. pH-metry confirmed abnormal postprandial acid reflux in one case (12.5%), and 50% of the patients had physiological findings.

Study III:

Between 1 January 2008 and 31 December 2017, 54 patients (24 males and 30 females aged 17 to 79 years) with symptomatic oesophageal achalasia were treated at our clinic. The most common complaints among the patients scheduled for surgery included dysphagia, solid food becoming stuck, epigastric pain and, less frequently, weight loss. The mean duration of the symptoms was 57.3 months (3–192). After a detailed history was taken, patients underwent a comprehensive gastroenterological assessment (a swallowing X-ray exam, upper GI endoscopy, and oesophageal pH-metry and manometry). Based on the Chicago classification, the types of achalasia in the laparoscopic group were as follows: TI, TII and TIII achalasia was found in 30, three and nine cases, respectively; diffuse oesophageal spasm (DES) was confirmed in five cases; and jackhammer oesophagus was observed in one patient. Clinical presentation of megaesophagus was diagnosed in four cases. 18.7% (9/48) of the patients in the laparoscopic group and all the patients in the acute and the reconstruction groups (4/4, 100%; 2/2, 100%) were treated with preoperative endoscopic balloon dilation.

3.2. Surgery

3.2.1. Transcervical diverticulectomy and cricomyotomy

In our first study, we analysed patients who had undergone two different surgical techniques for Zenker's diverticulum. In 13 cases, transcervical diverticulectomy was performed with cricomyotomy (TCD), and transoral stapler diverticulostomy (TSD) was carried out in 16 cases. Four patients underwent TCD operation after TSD. Under intratracheal anaesthesia in the supine position, the patient's head was fixed with the right side and back facing backwards. Exploration and resection of the diverticulum and cricopharyngeal myotomy were performed from an oblique incision made along the medial edge of the sternocleidomastoid muscle. During the open method, diverticula were resected using a straight suturing machine (TX60 Linear Stapler, Ethicon Endo-Surgery Inc., Cincinnati, OH, USA) so that no oesophageal stenosis remained after suturing. The myotomy was then performed from the lower edge of the diverticulum to the oesophagus, approximately 3–4 cm long.

3.2.2. Transoral stapler diverticulostomy

During surgery under intratracheal anaesthesia, the head of the supine patient was fixed in a backward, hyperextended position. The hypopharynx was examined using a rigid, distending operating laryngoscope (Weerda, Karl Storz, Tuttlingen, Germany). Direct visual control was provided with a 5 mm endoscopic camera. The orifices of the oesophagus and diverticulum were explored. The Endostapler (Endo-GIA™ USSC, Norwalk, CT, USA, blue cartridge [45 and 60 mm, respectively]) is inserted into the hypopharynx so that the common wall of the oesophagus and diverticulum is between the stems of the stapler device. By firing the stapler, a V-shaped ostium was formed between the oesophagus and the diverticulum, and its edges were closed with a triple suture row. After the surgeries, swallowing X-rays were performed with a water-soluble contrast agent (Gastrografin® [diatrizoate meglumine]).

Eighty-seven per cent (24/29) of patients registered for surgical follow-up one month after surgery. During the follow-up examinations, we analysed the change in the complaints compared to the preoperative ones, as well as the radiomorphological difference, if necessary. If patients have complaints later, an extraordinary examination and, if necessary, treatment were performed. In our long-term study (mean 86.1 months, 45–128 months), we wanted to assess the effectiveness of the procedure in terms of symptoms.

3.2.3. Laparoscopic transhiatal epiphrenic diverticulum resection

Laparoscopic transhiatal epiphrenic diverticulectomy, Heller cardiomyotomy and Dor anterior partial fundoplication were performed on seven patients. One patient only underwent diverticulectomy, where no motility disorder was present. All the surgeries involved an endoscopic check as well.

Patients were placed in a 30° reverse Trendelenburg position while under general anaesthesia. The surgeon stood between the patients' legs. Three ports were inserted in the abdominal cavity along the left costal arch 15 cm from each other, with one port placed in the epigastrium on the right side and another 10 to 12 mm in diameter, inserted directly above the umbilicus (camera port). Intraoperative endoscopy was used to assess the level of and clear the contents of the diverticulum. The abdominal and lower mediastinal segments of the oesophagus were mobilized with a LigaSure device (Valleylab, Boulder, CO, USA). Then the diverticula were dissected and removed with Endo GIA (USSC, Norwalk, CT, USA) blue cartridge (45 and 60 mm). After the diverticulectomy, a Heller oesophagocardiomyotomy was performed on the opposite side of the proximal edge of the neck of the diverticulum in a segment 2 cm in length along the fundus, and then a Dor partial anterior fundoplication was performed.

The patients participated in a gastroenterological check-up an average of three months after surgery (swallowing examination, oesophagus manometry, pH-metry and oesophagogastrosopy). Follow-up examinations were performed on six patients, whereas two patients were not present at the scheduled follow-up visits after the initial phase of the follow-up period (two and six months after the intervention) – although both patients were asymptomatic. Changes in quality of life with regard to symptoms related to oesophageal function were evaluated in our long-term studies (mean, 60 months; 10–138 months) (six patients). A special questionnaire was prepared based on a scoring system published by Eckardt et al. and modified by Zaninotto et al.. The score was determined before and after surgery. We asked questions about the severity of regurgitation, dysphagia and epigastric/chest pain since the symptoms had started.

3.2.4. Laparoscopic Heller–Dor operation

In our third study, we measured the effects of different surgical procedures adapted to the diverse clinical appearance of achalasia cardia. Forty-eight patients underwent a laparoscopic Heller cardiomyotomy and Dor's anterior partial fundoplication. Oesophageal mucosa integrity was checked with intraoperative endoscopy in each case. A Heller oesophago-cardiomyotomy was performed over a length of 8 cm on the anterior wall of the oesophagus, and over at least 2 cm on the gastric fundus, completed with Dor's partial anterior fundoplication.

3.2.5. Elective oesophageal resection

Gastric replacement involved an upper midline laparotomy, widening the oesophageal hiatus and then mobilizing the oesophagus through the hiatus. After mobilizing the stomach and ligating the left gastric artery, a gastric conduit was created as per Akiyama using linear staplers along the lesser curvature, and then a jejunal feeding catheter was implanted. After drainage, the abdominal section was closed, the patient was turned to a left lateral decubitus position, and the oesophagus was subtotally resected through a right anterolateral thoracotomy with selective intubation. The gastric conduit was pulled from the abdominal cavity through the enlarged hiatus into the thorax, where an anastomosis was performed with a circular stapler between the oesophagus and the stomach.

In a patient who had previously undergone a Heller–Toupet operation and then developed recurrent symptoms and megaesophagus, the previous fundoplication was eliminated, the lower third of the oesophagus and the cardia were resected, and they were replaced with an isoperistaltic jejunal segment positioned under the azygos vein (Merendino procedure).

3.2.6. Emergency surgical interventions

Four patients underwent emergency surgery for an iatrogenic oesophageal perforation due to EBD. In two cases, primary suture repair and Heller–Dor surgery were performed with traditional open surgery, using intraoperative endoscopic control, in non-septic patients with early-stage achalasia (within eight hours). In another two emergency cases, iatrogenic perforation of megaesophagus was confirmed. More than 24 hours had passed between the injury and the surgical treatment, and the patients were in a severe septic condition at the time of surgery. In one of the patients, the perforation was caused by diagnostic oesophagoscopy performed at another institution, while the other patient developed a rupture after EBD, which was followed by two unsuccessful attempts at endoscopic clipping. Both patients underwent an

oesophagectomy as per Torek, a gastrotube was used for decompression purposes, and a jejunal feeding catheter was implanted.

3.2.7. Reconstructive surgery

Ninety-nine and 122 days after Torek's oesophageal resection, successful substernal reconstruction was performed using the right colon and the stomach, respectively.

Follow-up

Patients treated with a laparoscopic myotomy were given gastroenterological check-ups (a swallowing X-ray, oesophageal manometry, pH-metry and oesophago-gastroscopy) an average of three months after the surgery – these assessments were carried out in 37 patients. Regular follow-up occurred with a total of 27 patients, while ten patients did not return for the periodic follow-up visits after the initial period (months 2 and 6 post-surgery), although nine of them were complaint-free.

3.3. Statistics

All data were collected in Excel tables. All statistical analyses were performed with SigmaPlot for Windows (ver. 12.5, 2011 Systat Software, Inc., San Jose, Ca, USA). Values of $P < 0.05$ were considered to be statistically significant. The data were collected on an Excel spreadsheet (Microsoft, Redmond, WA, USA). Quantitative data are provided as means (\pm SD). The paired t test was used to compare pre- and postoperative cumulative mean symptom scores.

4. RESULTS

4.1. Comparative study of the transoral and transcervical surgical treatment of Zenker's diverticulum: short- and long-term outcomes (Study I)

With minor blood loss (50–100 ml), the mean surgical time was 70 min (TCD group: 98 ± 62 min, TSD group: 42.5 ± 27.5 min, $p < 0.001$). No intraoperative complication occurred in either group. In the TSD group, two patients underwent conventional surgery (15%) due to a cause of visualization problem. One patient in the TSD group (1/16, 6%) underwent reoperation due to bleeding, while another in the TCD group was confirmed as having pneumonia (1/13, 7%) (Table 1).

	TSD	TCD
Gender (F/M)	8/8	1/12
Age (years)	68.2 (47–89)	65.4 (34–86)
Mean diverticulum size (mm)	46.6 (30–140)	49 (30–120)
Operative time	42.5 (15–70)	98 (36–160)
Visualization difficulty (n,%)	n=2 (15 %)	
Staple line leak (n)	0	0
Complication requiring reoperation (n)	1 (bleeding)	
Mortality	0	0
Onset of oral feeding (day)	2.9 (1–7)	4.6 (3–7)
Hospital stay	7.3 (5–10)	9.7 (7–12)

No suture line insufficiency (0/29, 0%) and no perioperative mortality occurred. After late follow-up, patients' quality of life improved significantly, and their severe preoperative symptoms, mainly dysphagia and regurgitation, were reduced to a minimum or completely eliminated. In the TSD group, we found a recurrent complaint in half of the patients (6/12, 50%), and transcervical surgery was performed later in four (4/12, 33%) cases. The main complaints of patients who received re-intervention were severe regurgitation (2/4), severe dysphagia (1/4) and, in one case, a combination of the two complaints (1/4). Of these, three

patients complained half a year after the primary surgery, while four of them reported complaints four years after the primary surgery.

4.2. Laparoscopic surgery for epiphrenic oesophageal diverticulum: short- and long-term outcomes (Study II)

The duration of the surgery was an average of 165 (130–195) minutes with minimal blood loss (50–150 mL), and conversion was not necessary. One patient developed bleeding in the early postoperative period, the bleeding myotomy site was successfully managed using sealing device during re-laparoscopy. A swallowing test performed with the administration of a water-soluble contrast agent (diatrizoate meglumine) on postoperative day 4 confirmed leakage along the sutures in one case (1/8, 12.5%). There was no mortality. After a negative swallowing test, oral nutrition for patients was phased in gradually, and patients were discharged without any complaints. Average duration of care was 14 days (8–41 days). After the surgeries, functional tests were performed on three patients (gastroscopy, manometry and pH-metry), which showed normal function.

Six patients (6/8, 75%) completed the questionnaires on long-term symptoms. The oesophagus-related mean cumulative score before the intervention was 6.3 (3–9), and it dropped to 1.6 (0–5) after the intervention, which is an average of 74% ($p < 0.001$) subjective improvement (Table 6). Proton pump inhibitor (PPI) therapy was started in four patients who had GERD develop after a six-month (2–12 months) complaint-free period in the case of four patients. In three cases, complaints were resolved with drug therapy. In one patient, laparoscopic antireflux surgery (Nissen) was performed because conservative therapy had been ineffective, and the patient became completely asymptomatic by the first six-month follow-up visit.

Symptoms	Preoperative severity mean score (points)	Postoperative severity mean score (points)	Symptom relief (%)	Statistics
Dysphagia	2.5 (0–3)	0.17 (0–1)	93.3	
Epigastric pain	1.83 (0–3)	0.83 (0–3)	55.5	
Regurgitation	2 (0–3)	0.66 (0–2)	66.6	
Mean (SD) cumulative score/patient	6.33 (\pm 2.06)	1.66 (\pm 1.86)	74	p<0.001

4.3. Complex surgical treatment of oesophageal achalasia in the era of minimally invasive surgery (Study III)

The average duration of the laparoscopic procedures was 72 minutes (62–90 minutes) with minimal blood loss (50 to 100 mL). No intraoperative complications were observed, and conversion was required in one case (1/48, 2%) for adhesions. The swallowing test conducted with a water-soluble contrast agent (Gastrografin®) on postoperative day 4 (on average) revealed a leak from the site of the sutures in one case (1/48, 2%), which was treated with emergency reoperation and suture placement. The average length of stay was 7.3 days (5–28 days) in the elective, laparoscopic group.

There was one case of hydrothorax formation requiring a puncture and one case of atrial fibrillation in the emergency surgery group. There were no mortalities. Patients with primary suture repair were discharged after 16.5 days (13–20 days), following a swallowing X-ray with normal results, while those who had undergone Torek's operation were discharged after 15.5 days (14–17 days). Later, reconstructive surgeries performed with a colon or gastric pull-up after Torek's operation were accompanied by neither intraoperative nor postoperative complications, and patients were discharged on day 14.5 after a swallowing X-ray with normal results and gradually introduced oral feeding.

Long-term follow-up

At the 1–6-month follow-up visit, all the patients, except for one, reported unrestricted swallowing, which was also confirmed by the functional assessments. Those returning for later gastroenterological check-ups were evaluated based on follow-up intervals and their swallowing function.

At the 6–12-month follow-up visit, non-severe recurrent dysphagia was reported in eight patients. In two cases, dietary changes and medical treatment resulted in notable improvement, while persistent complaints were recorded despite therapy in two others. EBD was indicated in an additional four cases (8.3%), with one of these patients requiring oesophageal resection for recurrent complaints despite the EBD, considering the patient's young age and the significantly dilated oesophagus. At the 12–24-month visit, the number of patients being followed up for dysphagia (8) had not changed, but there were three new cases. Medical therapy was successful in one, and a successful EBD was performed in another; however, one patient had persistent complaints. During the follow-up visits after 24 months, a total of seven patients were followed up for dysphagia, one of them being a new patient, who became complaint-free after conservative therapy. Those with complaints despite surgery mostly suffered from spastic motility disorders (TIII and DES).

Postoperative reflux did not occur during the 6–12-month follow-up period, while it developed in three patients in total (3/48, 6.2%) during the 12–24-month and >24-month follow-up; however, it was controlled well medically.

Our study also revealed that at the 12–24-month follow-up visits, symptomatic and symptom-free patients had undergone surgery at approximately the same age (53.5 years vs. 48.1 years), and the duration of symptoms was longer in symptomatic patients (20.3 months vs. 112.8 months). However, there was no difference in preoperative EBD (symptom-free 11% vs. 10%). During the >2-year follow-up, there was still no difference in age (53.1 years vs. 54.8 years), and patients with satisfactory symptom control underwent surgery later than those in the symptomatic group (82.2 months vs. 40.5 months).

5. DISCUSSION

The treatment tactics of oesophageal motility diseases have undergone unbroken development over the years with the patenting of technological advances and the introduction of modern gastroenterological diagnostics that help to establish a correct surgical indication. Minimally invasive surgical procedures on the oesophagus, with adequate proficiency and a stable radiological, internal medicine and intensive care infrastructure, no longer carry an extreme risk, and the surgical burden is significantly lower than in conventional surgeries. Together, these factors result in rapid recovery of patients and a good long-term quality of life. The surgical solution for functional diseases of the oesophagus can actually be considered palliative, as there is no possibility of causal treatment according to the current state of our science. In fact, all operative efforts are aimed at eliminating the already established abnormal muscle function and the resulting secondary pathological manifestations (diverticula and oesophageal dilatation) in order to prevent potential subsequent serious complications (oesophageal perforation and oesophageal cancer). Based on the literature, the benefits of the minimal access approach and less radical surgery of the oesophagus in all cervical, thoracic and abdominal sections are indisputable, their efficacy is outstanding, and the results of late follow-up are convincing.

5.1. Comparative study of the transoral and transcervical surgical treatment of Zenker's diverticulum: short- and long-term outcomes (Study I)

Both surgical procedures performed by our team (TSD and TCD) are operations with the same low morbidity and satisfactory long-term results as the world literature data. In the present study, no deaths occurred; in one case, we observed more significant postoperative morbidity: one reoperation was needed due to bleeding, and pneumonia developed in another case. TSD surgery lasted significantly shorter, and oral feeding was started earlier; however, recurrent/residual complaints occurred during follow-up, which necessitated four transcervical surgeries. There was no reintervention due to recurrent complaints in the TCD group. However, one patient in the TCD group developed persistent hoarseness, presumably due to a recurrent laryngeal nerve lesion associated with cervical dissection. In the case of surgical treatment of Zenker's diverticulum, four basic issues definitely need to be discussed: the size of the diverticulum, the age of the patient, the issue of cricomyotomy and the choice of the best approach.

The treatment strategy for Zenker's diverticulum under 2 cm is determined by cricomyotomy alone; no resection is required. For lesions between 3 and 6 cm transoral therapy are optimal. Septotomy is not sufficient for a small diverticulum, while for larger ones a massive septum must be cut, which poses potential dangers: elevated bleeding complications with high-energy cutters, higher suture failure rates after stapler use and the pocket may cause regurgitation in the long term. Regardless of the different approaches to surgeries, one concept has not changed over time: the development of Zenker's diverticulum is based on dysfunction of the cricopharyngeus muscle, so its myotomy is the key. Previous studies have clearly attributed the reason for the recurrence of diverticula to a previous insufficient myotomy. The open procedure carries a higher risk as regards longer operative time and recovery period. Minimizing the risk of surgical trauma is crucial in patients with Zenker's diverticulum, who are usually in or beyond their seventies and suffering from chronic diseases resulting in a worse general condition. The transoral (rigid or flexible variant) access could thus be an ideal solution for patients with less reserve capacity.

Disadvantages of endoscopic therapy include technical failure and recurrent complaints. The failure of this approach results in incomplete diverticulostomy and insufficient dissection of the muscle, which may be responsible for persistent/recurrent complaints. It is indisputable that the completeness of myotomy, whether open or endoscopic, is an essential part of a standard surgical solution. In our study, visualization difficulties occurred in two patients, because of which surgery was continued transcervically (15%).

In our present clinical investigation, we wanted to introduce oral feeding after a negative leak test. Our team ordered a swallowing X-ray with a water-soluble contrast agent on the fourth postoperative day in the TCD group and on the second postoperative day in the TSD group.

Although the TSD method is a quick and technically feasible intervention, it is not always a perfect choice, as the patient's anatomical features and diverticulum parameters could be sources of failure. Along with open and rigid endoscope procedures, it is essential to note the alternative provided by flexible endoscopy. Flexible endoscopy preserves the principle of rigid endoscopy, namely, by creating a common lumen by cutting the common septum, automatically performing the myotomy and high-risk elderly patients benefit most from it. Studies comparing flexible endoscopy and Endostapler report similar results in terms of hospital stay, symptom improvement and incidence of complications; however, the duration of intervention is longer in the Endostapler group. In terms of clinical efficacy, flexible endoscopy shows a varied picture with a success rate of 56–100%, in which dysphagia improvement reached 84–100%.

Using flexible endoscopy, an approximately 20% recurrence is expected based on current literature data. Predictors of recurrence may be pre-treatment diverticulum size more than 5 cm, post-treatment diverticulum size more than 1 cm and septotomy length less than 2.5 cm. Antonello et al. successfully demonstrated the efficacy of flexible endoscopy in both open and rigid endoscopic recurrences after achieving 84% complete complaint relief in the study group. Complications of the procedure include cervical abscess/mediastinitis (0–27%) and bleeding (0–10%) due to perforation. Nonetheless, it can be seen that both endoscopic and open methods are safe and predominantly alleviate complaints. Previous cervical surgeries, poor general condition and advanced age all call for less surgical time and trauma, thus suggesting a choice of endoscopic therapy. An open mode is recommended for young patients in good health due to proven better long-term outcomes and low probability of corrective surgery. Whatever the mode of intervention, the experience of the surgeon and the preference of the patient are decisive in choosing the optimal procedure.

In the present study, swallowing function improved in patients in both groups. Our results investigating the postoperative swallowing function confirm that a large percentage of complaints remain after transoral procedures, which need to be corrected with another, preferably open surgery. In our own study, we demonstrated that the main complaints of our patients were severe and regular dysphagia and regurgitation, which almost completely disappeared after TCD surgery. In the TSD group, due to permanent complaints, four (4/29, 13.7%) cases needed to undergo further surgery. Then the transcervical diverticulum resection and cricomyotomy resulted in complete asymptomatic relief.

5.2. Laparoscopic surgery for epiphrenic oesophageal diverticulum: short- and long-term outcomes (Study II)

Laparoscopic transhiatal epiphrenic diverticulum resection with the Heller–Dor surgical method, which we use, is an intervention with low morbidity and adequate long-term results comparable with international data. Partial insufficiency of mechanical suture was detected in one case (1/8; 12.5%), which was resolved with conservative therapy, and no perioperative mortality occurred. Patient follow-up lasted for an average of 60 months, quality of life improved significantly, and symptoms detected before surgery decreased to a minimum. Although half of the patients exhibited GERD symptoms, the reflux was controlled with drug therapy in three cases. Another surgical intervention (Nissen surgery) was necessary because of persistent symptoms in one case.

With a prevalence of 8 to 23%, staple line insufficiency is one of the most frequent and serious complications after an oesophageal diverticulum resection. Mortality is low (0%–7%).

There are two important questions as regards minimally invasive surgery for epiphrenic diverticulum that should be discussed: the necessity of cardiomyotomy and antireflux surgery. The choice of surgical method is determined not only by the size of the diverticulum, but also by the associated motility disorder; therefore, removal of the diverticulum alone is not sufficient to prevent complications and to provide an asymptomatic condition. Data in the literature confirm that suture insufficiency and the incidence of disease recurrence are more common after surgery performed without myotomy. A study conducted with 21 patients at the Mayo Clinic showed high rates of suture insufficiency and disease recurrence (24 and 19%, respectively) in patients without myotomy after diverticulectomy, whereas these sequelae did not occur in the myotomy group. The required length of the myotomy is still debatable. Long myotomy is well-known, although several publications and our own data confirm the necessity of an intervention of 1.5 to 2.0 cm in length from the upper edge of the diverticulum to the proximal segment of the stomach. If a myotomy is necessary, surgery must be complemented with an antireflux procedure as well. Most surgeons prefer partial fundoplication (Dor or Toupet), as this procedure avoids hypertension in the LES and decreases the incidence of GERD. However, others recommend complete fundoplication, as their results show that this procedure does not increase postoperative dysphagia and provides better reflux control.

We wanted to evaluate the success of our surgical interventions and changes in quality of life in patients with the patient-reported outcome (PRO) measurements used more commonly in clinical and pharmacological studies and healthcare analyses. This score was used by an Italian group for evaluating the outcome of epiphrenic diverticulum. The condition of our patient group was determined with an evaluation scheme similar to a scoring system based on a subjective evaluation of patients known as the “patient symptom score” with data gathered via questionnaires. In a long-term study, Rosati et al. confirmed a permanent asymptomatic condition in 85% of patients undergoing laparoscopic treatment of epiphrenic oesophageal diverticula. Zaninotto et al. considered improvement of more than 50% in the patient symptom score to be successful, and this was the case in 70.8% of the patients.

5.3. Complex surgical treatment of oesophageal achalasia in the era of minimally invasive surgery (Study III)

The treatment strategy for patients with achalasia in centres specialized in oesophageal diseases is determined by close cooperation between gastroenterologists and surgeons. In addition to the ever growing variety of effective medical interventions, patients with persistent symptoms may undergo surgery at different stages and with different timings. The first documented surgery for achalasia was performed by Ernst Heller in 1913; it was an extramucosal myotomy at the level of the cardia, thus reducing the pressure of the LES and facilitating the passage of solid food into the stomach. Originally, Heller recommended a double (anterior and posterior) myotomy; however, a simple myotomy, a procedure still used today, was described by Zaaijer, a Dutch surgeon, in 1923. The traditional open surgeries of the oesophagus (via thoracotomy or laparotomy) have considerable morbidity rates. To reduce them, the minimally invasive surgical technique is currently an excellent alternative in the surgical treatment of functional disorders of the oesophagus, including oesophageal achalasia.

Laparoscopic Heller–Dor surgery

Laparoscopic Heller–Dor surgery was introduced at the end of the last century and since then has become the gold standard in the surgical treatment of oesophageal achalasia. It has excellent mortality and morbidity rates of 0.01% and 6%, respectively, (73,81; Table 9) and it provides a long-term symptom control rate of about 90%, the success of which also depends on the Chicago classification. Mucosal injury may occur during the procedure in 6.9% (0–33%) of cases, and it may remain hidden in most cases or may be treated immediately during surgery.

Based on our own results, it can be established that the success rate beyond 24 months is 85.5%, which can be considered 93.7% with the supplementary conservative medical treatment of symptomatic patients. In the patient group studied, one patient in total (1/48, 2%) developed a surgery-related complication, oesophageal mucosal lesion, which was discovered with the swallowing X-ray performed with a water-soluble contrast agent on postoperative day 1. The injury was supposedly caused by intraoperative thermal damage, which was not seen during the endoscopic follow-up exam after the primary surgery. No complications were observed in the other 47 patients (98%) in the group, and there was no mortality. All in all, the clinical results of this study are clearly consistent with international standards, considering both long-term symptomatic control and the morbidity rate.

As to LHM, there are two issues to be discussed: achieving a symptom-free status post-surgery (eliminating dysphagia) and the course of postoperative reflux. Both factors can basically be traced back to the proper performance of the myotomy. The 2018 ISDE (International Society of Diseases of the Esophagus) guidelines on achalasia state that a laparoscopic Heller myotomy is recommended over a length of at least 6 cm on the oesophagus and 2 to 3 cm on the stomach for effective control of symptoms.

Based on our previous clinical study, it is clear that an inadequate myotomy, either in the aboral or the oral direction, may cause recurrent symptoms, which can be corrected with repeat surgery. Our current study also demonstrates that recurrent symptoms are more common in patients with a spastic-type oesophageal disorder (TIII achalasia and DES) than in those with TI or TII disease. Our results are expressive primarily after twelve months, although symptoms returned earlier among TIII cases (3/9, 33%). The trend continues in the 1–2-year follow-up period, since the rate of symptomatic patients is relatively high in the spastic group (TIII: 33%; DES: 60%), while in the case of the classic form, it does not change much when analysing the time intervals (6–12 months: 14.5%; 12–24 months: 20.8%; >24 months: 18.7%). We may thus conclude that, in certain cases, the increased tone of the oesophagus may extend well above the level of the LES, where conventional and a properly performed myotomy cannot always reach.

The other myotomy-related complaint is the development of GERD. Based on observations by Campos and other authors, reflux occurs in 41.5% without an antireflux procedure and only in 14.5% with one, thus confirming that if the LES, the main barrier, is damaged, reflux may be expected. By completing the procedure with partial fundoplication, the occurrence of postoperative reflux can be decreased considerably, without increasing the pressure of the LES. Both anterior (Dor, 180°) and posterior (Toupet, 270°) semifundoplication is widely used after a cardiomyotomy. Comparing these two methods, there were no significant differences between the three RCT trials and their meta-analysis with regard to postoperative dysphagia and GERD.

Based on our results, it is clear that the rate of GERD after a Heller–Dor procedure was minimal (6.2%, 3/48) in the medium term (24-month follow-up) and was controlled with conservative therapy.

Megaoesophagus, postendoscopic oesophageal injury

In the case of reconstruction, all three eligible organs were used (stomach, jejunum and colon), neither an anastomotic leak nor pneumonia was observed after the interventions, and there was no mortality. The swallowing function of these patients is now satisfactory, and no anastomotic stricture or other complications were found during the follow-up visits. In our own patient population, a young woman with sigmoid oesophagus underwent LHM after multiple unsuccessful endoscopic dilations, and satisfactory swallowing function was observed for almost six months. However, since dysphagia returned after the complaint-free period, Merendino procedure was performed. At present, after more than a decade of follow-up, the patient is completely symptom-free, her swallowing is unrestricted, and her quality of life is excellent. The mortality rate for oesophageal perforation ranges between 18 and 22% – even despite early recognition and treatment. If the time elapsed between injury and surgery exceeds 24 hours, the mortality rate may even reach 27 to 40%. In the case of oesophageal injury, a personalized treatment strategy is required in each case, and the following factors should be taken into account: aetiology of the injury, existing underlying oesophageal disease, time from injury to diagnosis, septic condition, comorbidities and physical capacity. Post-EBD oesophageal perforations are traditionally treated surgically, but therapeutic methods also include conservative treatment and modern endoscopic techniques (OTSC clip and stent implantation). In our practice, primary suture repair is used in cases that are recognised early, within 24 hours, and it is always completed with the cardiomyotomy and antireflux procedure, which has a beneficial effect on the healing of the lesion and, at the same time, may result in long-term symptom-free status. In the case of perforations beyond 24 hours, patients usually undergo resection without reconstruction (on rare occasion, with immediate reconstruction) because of the septic condition that has developed and the reduced tendency of the oesophageal wall to heal. In the case of megaoesophagus, a worse-than-average condition of the oesophagus supports resection, which is worth including during surgical treatment in all cases.

Every patient in our acute surgery group was admitted to our unit for an oesophagoscopy-associated injury. In the two early cases (recognised within 24 hours), primary suture repair occurred with Heller–Dor surgery, taking the condition of the patients into account, while oesophageal resection without reconstruction was performed in the two other cases with an old perforation complicated by megaoesophagus. There was no mortality or notable morbidity in the emergency group.

1. CONCLUSION

(1) According to our study, both TCD and TSD procedures are safe operations for Zenker's diverticula. The transoral approach has all the advantages offered by a minimally invasive manner, but is optimal primarily in the setting of a mid-sized diverticulum (3–6 cm). We can expect a significant quality of life improvement after the procedures, but recurrent symptoms may be developed in a certain proportion of patients. Our working group was among the first to employ the transoral stapler diverticulostomy as an innovative method in the management of Zenker's diverticulum in a study involving the largest cohort in this topic area in Hungary with both short- and long-term results.

(2) Based on our results, similarly to the literature data, it may be established that laparoscopic-transhiatal epiphrenic diverticulum resection with the Heller–Dor procedure can be considered a safe surgical procedure with low morbidity and satisfying long-term outcomes. Myotomy and antireflux surgery are essential for lasting and reliable clinical success. Our working group was the first to publish short- and long-term results of a new minimally invasive method in Hungary.

(3) As reported in our comprehensive research, laparoscopic Heller–Dor surgery is a safe and effective surgical method for treating oesophageal achalasia. Symptom control in patients who have undergone minimally invasive surgery is adequate even in the long term, and the rate of postoperative reflux is low. However, patients with the spastic type may develop recurrent symptoms at a higher rate. Advanced and emergency conditions are still a major challenge for surgeons, and choosing the proper therapeutic strategy depends on several factors.

7. ACKNOWLEDGEMENTS

I wish to express my deep and sincere gratitude to my supervisor, **Dr. György Lázár**, Professor and Head of the Department of Surgery, University of Szeged, for giving me the opportunity to conduct research and providing invaluable guidance throughout. His immense knowledge, vision, sincerity and motivation have deeply inspired me. It has been a great privilege and honour to work and study under his guidance.

I would like to offer my special thanks to my research colleagues, **Dr. Attila Paszt**, **Dr. Zsolt Simonka** and **Dr. Szabolcs Ábrahám**, for their assistance and encouragement at every stage of the research project, as well as to **Dr. Márton Erdős** for his help with the data analysis.

I wish to extend my thanks to **Dr. András Rosztóczy** and **Dr. Georgina Ollé**, and all the members of the motility group at the 1st Department of Internal Medicine, University of Szeged, for their genuine support and harmonious collaboration throughout this research.

I would also like to acknowledge **Dr. László Rovó**, Professor and Head of the Department of Oto-Rhino-Laryngology and Head-Neck Surgery, University of Szeged, as a co-author of the Zenker's diverticulum study for his very valuable comments.

Thanks go to **Andrea Vida** as well for her kindness and technical support in my studies.

Thank you as well to all the people at the Department of Surgery, University of Szeged, who have directly or indirectly supported me in completing the research .

I am extremely grateful to my parents for their love, caring and sacrifices in educating and preparing me for my future. I am very thankful to my wife and my children for their love, understanding and continuing support as I completed this research.

