## CLINICAL STUDY

# Management of anastomotic leaks after oesophagectomy and gastric pull-up

Daniel SISKA<sup>1</sup>, Miroslav JANIK<sup>1</sup>, Patrik LAUCEK<sup>1</sup>, Martin LUCENIC<sup>1</sup>, Katarina TARABOVA<sup>2</sup>, Peter JUHOS<sup>1</sup>, Robert BALAZ<sup>1</sup>, Miroslava TURCINOVA<sup>1</sup>, Zuzana GALLIKOVA<sup>1</sup>, Roman BENEJ<sup>1</sup>

Department of Thoracic Surgery, University Hospital Bratislava, Bratislava, Slovakia. pirmin87@gmail.com

#### ABSTRACT

OBJECTIVE: To evaluate the effectiveness of endoscopic and surgical intervention in treating anastomotic leaks after oesophagectomy.

BACKGROUND: Anastomotic leak after oesophagectomy is a severe complication associated with significant morbidity and mortality. This study aimed to analyse our experience with the management of anastomotic leak after oesophagectomy.

METHODS: A retrospective study evaluated the treatment outcome and duration of treatment in patients with anastomotic dehiscence or conduit necrosis after oesophagectomy from November 2008 to November 2021. RESULTS: The group consists of forty-seven patients. Twenty-one (44.7 %) patients had dehiscence of the neck anastomosis, twenty patients (42.6 %) had dehiscence of the chest anastomosis, and six (12.8 %) patients had conduit necrosis. Nineteen patients with dehiscence were primarily treated by endoscopic insertion of a self-expanding metal stent with perianastomotic drainage; the other patients were primarily treated surgically. Mortality associated with anastomosis dehiscence was 27.7 % (thirteen patients). Stent use in treatment was a statistically significant parameter regarding the length of hospital stay and mortality. CONCLUSION: Self-expanding metal stents can reduce leak-related morbidity and mortality after oesophagectomy and may be considered a cost-effective treatment alternative (*Tab. 2, Fig. 2, Ref. 21*). Text in PDF www.elis.sk

KEY WORDS: anastomotic dehiscence, oesophagectomy, stent.

## Introduction

Oesophagectomy is indicated for benign oesophageal diseases with failed endoscopic and drug treatment. This surgical procedure is considered the mainstay of treatment for the management of early stage and locoregionally advanced oesophageal cancer (1-2). However, oesophagectomy carries a significant risk of morbidity and mortality since it is commonly performed on patients with poor nutritional status, serious comorbidities, or other factors resulting in postoperative complications (3). There are factors affecting complications rate such as technical expertise, and standards of perioperative care. Oesophagogastric dehiscence is one of the most severe complications (4).

Anastomotic leak (AL) leads to significant morbidity, prolonged hospital stay, increased mortality risk, and considerable use of healthcare resources. In the long term, AL is associated with poorer quality of life, increased cancer recurrence rates, and subsequently worsened long-term survival (2).

Post-oesophagectomy AL is a common complication, with reported incidence ranging between 10–25 % for cervical anastomoses and 3–25 % for intrathoracic anastomoses (3). Intrathoracic anastomoses have a lower incidence of leaks and strictures than cervical anastomoses, but they tend to carry higher morbidity and usually require more extensive treatment. In addition, AL is associated with stricture formation and postoperative dysphagia (5). Reported mortality rates among patients who develop anastomotic leaks range between 30–60 %, and approximately 40 % of postoperative mortality following oesophagectomy is directly related to anastomotic leaks (6).

Despite the increasing research efforts, the leakage pathophysiology and causal factors remain unclear. Even though AL has a multifactorial aetiology, the tissue perfusion plays a pivotal role in leakage development. Moreover, clinical symptoms for AL often only become manifest in a later stage or are nonspecific, while many diagnostic and treatment options are available yet without a clear consensus on standardised procedures (2).

The severity of anastomotic leakage ranges from asymptomatic to full-blown sepsis with multiple organ failure (MOF)- Factors that influence the severity of the anastomotic leakage and have

<sup>&</sup>lt;sup>1</sup>Department of Thoracic Surgery, University Hospital Bratislava, Slovak Medical University, Bratislava, Slovakia, and <sup>2</sup>1<sup>st</sup> Department of Anaesthesiology and Intensive Care Medicine, University Hospital Bratislava, Comenius University, Bratislava, Slovakia

Address for correspondence: Miroslav JANIK, MD, Department of Thoracic Surgery, University Hospital Bratislava, Ruzinovska 6, SK-826 06, Bratislava, Slovakia. Phone: +421248234321

#### Tab. 1. Grading anastomotic leak and conduit necrosis by D. Low et al.

Anastomotic leak			
Type I	Local defect requiring no change in therapy or treated medically or with dietary modification		
Type II	Localized defect requiring interventional but not surgical therapy, for example, interventional radiology drain, stent or bedside opening, and packing of incision		
Type III	Localized defect requiring surgical therapy		
Conduit n	ecrosis		
Type I	Conduit necrosis focal Identified endoscopically Treatment – additional monitoring or non-surgical therapy		
Type II	Identified endoscopically and not associated with free anastomotic or conduit leak Treatment – surgical therapy not involving oesophageal diversion		
Type III	Conduit necrosis extensive Treatment – treated with conduit resection with diversion		

an impact on the appropriate treatment strategy are the location of the anastomosis (intrathoracic or cervical), size of the defect, and extent of contamination (7). Treatment of anastomotic leakage ranges from "conservative" (nil by mouth, antibiotics, gastric drainage, enteral or parenteral feeding, and drainage through percutaneous tubes) to endoscopic treatment with stents or endoscopic vacuum-assisted closure (VAC) devices and surgery (8, 9). However, there is no generally accepted treatment strategy for treating post-oesophagectomy anastomotic leakage. The objective of this study was to analyse our experience in the treatment of patients with anastomotic leaks.

#### **Definition and grading**

A study recently published in Annals of Surgery by Donald Low and Esophagectomy Complications Consensus Group (ECCG) titled "International consensus on standardisation of data collection for complications associated with esophagectomy" represents the first consistent project within a surgical speciality whereby 21 experienced surgeons from 14 countries agreed on a standard definition of complications and quality measures to consider after oesophagectomy. According to these standards, we define anastomotic leakage as a full-thickness GI defect involving the oesophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification and divide it into three types as shown in Table 1, together with dividing the conduit necrosis (10).

#### Materials and methods

The retrospective study analyses 47 patients with anastomotic dehiscence or conduit necrosis who underwent esophagectomy with gastric replacement at the Department of Thoracic Surgery of the University Hospital Bratislava from November 2008 to November 2021. Oesophagectomy with standard en-block oesophagectomy was primarily performed for oesophageal cancer. The anastomosis was constructed either in the thorax or in the neck. All anastomoses were reinforced with mattress sutures or omental wrap. Patients had a nasogastric tube inserted perioperatively below the level of the anastomosis for conduit decompression, and perianastomotic drainage was placed in all cases. Enteral nutrition was provided to each patient via feeding jejunostomy. All patients were postoperatively admitted to the Department of Anaesthesia and Intensive Care

for at least two postoperative days, but mainly until day 7, postoperatively. The anastomotic integrity was tested on day 7 using oral methylene blue and either x-ray or CT oesophagography. The occurrence of the methylene blue dye in the drains or extraluminal leak of the water-soluble contrast media confirmed an anastomotic leak. A methylene blue test was performed before day 7 in the presence of signs which may have been related to anastomosis dehiscence (pathological contents from drains, signs of sepsis or wound infection, inflammatory markers elevation). CT examination with oral water-soluble contrast media or endoscopic examination were indicated in case of a negative result.

The demographic data, comorbidities, anastomotic type, type of anastomotic leak, and conduit necrosis type were evaluated in patients (Tab. 2).

Tab. 2. The demographic data including associated diseases, anastomotic details, leakage and conduit necrosis classification of 47 patients with postoperative anastomotic leakages and conduit necrosis.

Clinical characteristics	Number	Ratio (%)
Sex		
Male	34	72.3
Female	13	27.7
Age	58,3 (41-83)	
Neoadjuvant treatment	9	19.1
Nicotinism	17	36.2
Alcoholism	10	21.3
Cirrhosis hepatis	7	14.9
Obesity	9	19.1
Malnutrition	10	21.3
Cardiovascular disease	27	57.4
COPD	12	25.5
Diabetes mellitus	6	12.8
Systemic disease	4	8.5
Other malignancies	6	12.8
Anastomotic details		
Site of anastomosis		
Neck	22	48.2
Thorax	25	53.2
Hand-sewn anastomosis	15	31.9
Semi-mechanical anastomosis	13	27.7
Stapler anastomosis	19	40.4
Type of dehiscence		
I	0	0
II	16	34
III	25	53.2
Type of conduit necrosis		
Ι	0	0
II	4	8.5
III	2	4.3

COPD - chronic obstructive pulmonary disease

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The patients were divided into two groups, a group of patients who were treated for dehiscence by primary stent placement with perianastomotic drainage and a group of patients who underwent a second operation. In these groups of patients, length of hospital stay and mortality

were assessed depending on the type of treatment. We evaluated patients with neck dehiscence and chest dehiscence separately.

Numerical data are presented as means and standard deviations. The differences between groups with categorical variables were assessed by the chi-square test or the Fisher's exact test. The Mann-Whitney U test assessed differences when the variables were not distributed normally. Statistically significant differences were set as p < 0.05. Statistical analysis was performed using GraphPad Prism (version 8.0; GraphPad Software, Inc.)

The institutional ethics committee approved the study. Informed consent was not required from study participants.

### Results

In 22 patients, oesophagogastric anastomosis was constructed in the neck. In 25 patients, the anastomosis was created in the thorax. Of the 47 patients, 13 patients were diagnosed with anastomotic leak with CT oesophagography, 8 by purulent content or digestive juice in chest tube, 8 by oral intake of methylene blue, 3 by fluoroscopic oesophagography, and 7 by wound infection on the neck. Two patients had a tracheoesophageal fistula diagnosed by tracheoscopy. Conduit necrosis was identified in six patients by gastroscopy; two patients had dehiscence in addition to conduit necrosis. The mean interval between oesophagectomy and anastomotic dehiscence was  $9.1 \pm 4.8$  days. We detected early dehiscence in five patients within three days of surgery. These patients underwent a repeated suturing of anastomosis with flush drainage of the pleural cavity with an antiseptic solution. Six patients with conduit necrosis underwent redo operation. In 4 cases, partial resection of the neo-oesophagus was performed with a formation of a new anastomosis, while in 2 cases, an oesophageal diversion was necessary.

Ten of twenty-one patients with neck dehiscence were treated with an endoscopically inserted stent and perianastomotic drainage, either with sump drain in 5 patients or external vacuumassisted closure (VAC) in 5 patients. Eleven patients were primarily treated without stent placement. One patient with TEF was treated with tracheal suture and esophagectomy. One patient with a broncho-oesophageal fistula (BEF) was reoperated three times with a bronchial and conduit suture with flap formation. In two patients, a T-drain was used, which was inserted into the oesophagus through a dehiscence in the anastomosis. Three patients were treated only with sump drainage, while in 3 cases, external VAC was applied to a cervical incision. Wound dehiscence was treated by a secondary suture in combination with sump drainage in one patient. Two patients were also reoperated for intestinal ischemia. Five patients died of SIRS (systemic inflammatory response syndrome) with MODS (multiple organ dysfunction syndrome). We detected that in patients with cervical anastomosis, the use of a primary stent in treatment of anastomosis dehiscence leads to a





Fig. 1. Stent use related to hospital stay in patients with leak in the neck.



Fig. 2. Stent use related to mortality in patients with intrathoracic leak.

shorter hospital stay (42.75  $\pm$  25.08 vs78.75  $\pm$  42.48 days; p = 0.046) (Fig. 1).

Nine of twenty patients with intrathoracic anastomosis dehiscence were treated with an endoscopically inserted stent, and placement of chest tubes for continuous irrigation of the pleural cavity with an antiseptic solution. Eleven patients were primarily treated without stent placement. One patient with BEF was reoperated three times. Oesophageal diversion with pneumonectomy was performed for poor healing of the suture. Ten patients were treated with suture of dehiscence and continuous irrigation of the pleural cavity. Seven patients who underwent suture of dehiscence required further reoperation or stent placement. Seven patients died of sepsis. In this series of patients, we detected that the use of a stent primarily in the treatment of intrathoracic dehiscence significantly reduced mortality (p = 0.0125) (Fig. 2).

### Discussion

Anastomotic leakage is the most critical surgical complication after oesophagectomy. It requires further surgical or endoscopic therapy and leads to high perioperative mortality and morbidity (11). A lack of standardised definitions for postoperative complications has led to a wide variation in reporting incidence and outcomes from anastomotic leaks (12). The recent UK National Audit and many other series have reported anastomotic leak rates without defining whether this includes conduit necroses and stapler-line leaks (13). The ECCG recently proposed definitions for all post-oesophagectomy complications. Anastomotic leaks incorporate all full-thickness gastrointestinal defects and are divided into three subgroups based on the management required. Strict adherence to these definitions should ensure that future series and audits become more comparable. Many efforts have been made to identify etiological factors and improve the oesophagogastric anastomosis technique (14). Yet, anastomotic leakage remains a disastrous complication that is responsible for approximately 30 % to 40 % of postoperative deaths (15). In our cohort of patients with dehiscence, mortality associated with anastomosis dehiscence was 27.7 % (thirteen patients).

CT with oral radiographic contrast is a feasible and sensitive way to diagnose an anastomotic leak (16). In our study, nearly onethird of patients were diagnosed by CT with oral water-soluble contrast. CT scan allows evaluation of the magnitude and location of the leak, which is helpful in placing the chest tubes directly into the infected collections and pleural effusions. An early diagnosis reduces the severity of contamination and sepsis, which are important determinants of surgical intervention (17). Non-operative management should not be considered as a conservative treatment. An aggressive treatment with antimicrobials including antifungals and radiological insertion of drains, with or without critical care admission, are important components of patient care. Enteral nutrition is essential for patient recovery. The placement of a feeding jejunostomy at the time of oesophagectomy allows routine postoperative feeding, but more importantly, it also allows extended feeding in the event of an anastomotic leak (18).

Routine stenting in the management of anastomotic leaks has been reported to achieve good radiological and clinical outcomes, with overall mortality rates of 13 % (19). In our cohort of patients with intrathoracic dehiscence, who were primarily treated with stent placement, there was a statistically significant decrease in mortality compared to patients treated with aggressive surgical treatment (p = 0.0125).

Stents can also cause severe complications. Migration, tracheobronchial fistulation, erosion, haemorrhage and perforation at the time of stent removal have all been described along with stent-related mortality. In one series of 17 patients, three died from stent erosion into the thoracic aorta. (20). In our cohort of patients, we noted complications in terms of stent migration and retrograde leakage. This problem can be solved by exchanging the stent for a larger one or by modifying the stent with its suture fixation in the mouth area. We did not notice any fatal complications. Although SEMS treatment provides a good seal after upper gastrointestinal leakage surgery, the use of SEMS does not appear to shorten hospitalisation time as compared to other conservative procedures such as drainage placement and enteral nutrition by feeding jejunostomy (12). This statement is confirmed by the literature review of Dasari et al (21). In our group of patients with neck anastomosis dehiscence who were primarily treated with stent insertion and perianastomotic drainage, we demonstrated a significant reduction in hospitalisation time (p = 0.046) in contrast to patients treated without stents, but this was not confirmed in cases with stent used in treatment of intrathoracic dehiscence.

### Conclusions

Leaks after oesophagectomy manifest in different ways and have a high variety of clinical impacts, ranging from local wound infections to life-threatening sepsis. The appropriate therapy must be chosen with regard to the status of the neo-oesophagus and patient's general condition. Surgical treatment of dehiscence is often replaced by stent placement with a treatment success rate of over 80%. One of the advantages of this endoscopic treatment is the early oral alimentation of the patient. However, in the case of conduit necrosis, immediate and decisive surgery is required. These cases are still associated with high morbidity and mortality.

The treatment in high-volume centres and application of novel methods that rely on effective, less invasive interventions improve the outcome of patients with anastomotic leaks after oesophagectomy.

#### References

**1. Mormando J, Barbetta A, Molena D.** Esophagectomy for benign disease. J Thorac Dis 2018; 10 (3): 2026–2033. DOI: 10.21037/jtd.2018.01.165.

**2. Fabbi M, Hagens ERC, van Berge Henegouwen MI, Gisbertz SS.** Anastomotic leakage after esophagectomy for esophageal cancer: definitions, diagnostics, and treatment. Dis Esophagus 2021; 34 (1): doaa039. DOI: 10.1093/dote/doaa039.

**3. Manghelli JL, Ceppa DP, Greenberg JW, Blitzer D, Hicks A, Rieger KM, Birdas TJ.** Management of anastomotic leaks following esophagectomy: when to intervene? J Thorac Dis 2019; 11 (1): 131–137. DOI: 10.21037/jtd.2018.12.13.

4. Grimminger PP, Goense L, Gockel I, Bergeat D, Bertheuil N, Chandramohan SM, Chen KN, Chon SH, Denis C, Goh KL, Gronnier C, Liu JF, Meunier B, Nafteux P, Pirchi ED, Schiesser M, Thieme R, Wu A, Wu PC, Buttar N, Chang AC. Diagnosis, assessment, and management of surgical complications following esophagectomy. Ann N Y Acad Sci 2018; 1434 (1): 254–273. DOI: 10.1111/nyas.13920.

5. Yeung JC. Management of Complications After Esophagectomy. Thorac Surg Clin 2020; 30 (3): 359–366. DOI: 10.1016/j.thorsurg.2020.04.002.

**6.** Tverskov V, Wiesel O, Solomon D, Orgad R, Kashtan H. The impact of cervical anastomotic leak after esophagectomy on long-term survival of patients with esophageal cancer. Surgery 2021: S0039–6060 (21)00969–7. DOI: 10.1016/j.surg.2021.10.011.

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7. Verstegen MHP, Bouwense SAW, van Workum F, Ten Broek R, Siersema PD, Rovers M, Rosman C. Management of intrathoracic and cervical anastomotic leakage after esophagectomy for esophageal cancer: a systematic review. World J Emerg Surg 2019; 14: 17. DOI: 10.1186/s13017-019-0235-4.

8. Zeng Q, Liu L, Zhang F, Zhao C, Wu Z, Lin X, Zheng C, Xiang Y, Tu S, Zhang X, He Z. Efficacy and analysis of modified "three-tube method" in the treatment of intrathoracic anastomotic leakage after esophagectomy. Ann Palliat Med 2021; 10 (10): 10821–10829. DOI: 10.21037/ apm-21-2583.

**9.** Yin Q, Zhou S, Song Y, Xun X, Liu N, Liu L. Treatment of intrathoracic anastomotic leak after esophagectomy with the sump drainage tube. J Cardiothorac Surg 2021; 16 (1): 46. DOI: 10.1186/s13019-021-01429-7.

10. Low DE, Alderson D, Cecconello I, Chang AC, Darling GE, D'Journo XB, Griffin SM, Hölscher AH, Hofstetter WL, Jobe BA, Kitagawa Y, Kucharczuk JC, Law SY, Lerut TE, Maynard N, Pera M, Peters JH, Pramesh CS, Reynolds JV, Smithers BM, van Lanschot JJ. International Consensus on Standardization of Data Collection for Complications Associated with Esophagectomy: Esophagectomy Complications Consensus Group (ECCG). Ann Surg 2015; 262 (2): 286–294. DOI: 10.1097/SLA.00000000001098.

11. Famiglietti A, Lazar JF, Henderson H, Hamm M, Malouf S, Margolis M, Watson TJ, Khaitan PG. Management of anastomotic leaks after esophagectomy and gastric pull-up. J Thorac Dis 2020; 12 (3): 1022–1030. DOI: 10.21037/jtd.2020.01.15.

**12. Dent B, Griffin SM, Jones R, Wahed S, Immanuel A, Hayes N.** Management and outcomes of anastomotic leaks after oesophagectomy. Br J Surg 2016; 103 (8): 1033–1038. DOI: 10.1002/bjs.10175.

**13. Health and Social Care Information Centre.** National Oesophagogastric Cancer Audit – 2013, Annual Report. http://www.hscic.gov.uk/ catalogue/PUB11093 [accessed 24 August 2015].

**14. Smith EA, Daly SC, Smith B, Hinojosa M, Nguyen NT.** The Role of Endoscopic Stent in Management of Postesophagectomy Leaks. Am Surg 2020; 86 (10): 1411–1417. DOI: 10.1177/0003134820964495.

**15. Griffin SM, Lamb PJ, Dresner SM, Richardson DL, Hayes N.** Diagnosis and management of a mediastinal leak following radical oesophagectomy. Br J Surg 2001; 88 (10): 1346–1351. DOI: 10.1046/j.0007-1323.2001.01918.x.

**16. Barbaro A, Eldredge TA, Shenfine J.** Diagnosing anastomotic leak post-esophagectomy: a systematic review. Dis Esophagus 2021; 34 (2): doaa076. DOI: 10.1093/dote/doaa076.

17. Ubels S, Verstegen M, Klarenbeek B, Bouwense S, van Berge Henegouwen M, Daams F, van Det MJ, Griffiths EA, Haveman JW, Heisterkamp J, Koshy R, Nieuwenhuijzen G, Polat F, Siersema PD, Singh P, Wijnhoven B, Hannink G, van Workum F, Rosman C; TEN-TACLE—Esophagus Collaborative Group. Severity of oEsophageal Anastomotic Leak in patients after oesophagectomy: the SEAL score. Br J Surg 2022; 109 (9): 864–871. DOI: 10.1093/bjs/znac226.

**18.** Holmén A, Hayami M, Szabo E, Rouvelas I, Agustsson T, Klevebro F. Nutritional jejunostomy in esophagectomy for cancer, a national register-based cohort study of associations with postoperative outcomes and survival. Langenbecks Arch Surg 2021; 406 (5): 1415–1423. DOI: 10.1007/s00423-020-02037-0.

**19. Bi Y, Wu Z, Yi M, Han X, Ren J.** Three-tube method and covered metallic stent for the treatment of anastomotic leakage after esophagectomy. BMC Gastroenterol 2020; 20 (1): 330. DOI: 10.1186/s12876-020-01480-z.

**20.** Schweigert M, Dubecz A, Stadlhuber RJ, Muschweck H, Stein HJ. Risk of stent-related aortic erosion after endoscopic stent insertion for intrathoracic anastomotic leaks after esophagectomy. Ann Thorac Surg 2011; 92 (2): 513–518. DOI: 10.1016/j.athoracsur.2011.02.083.

**21.** Dasari BV, Neely D, Kennedy A, Spence G, Rice P, Mackle E, Epanomeritakis E. The role of esophageal stents in the management of esophageal anastomotic leaks and benign esophageal perforations. Ann Surg 2014; 259 (5): 852–860. DOI: 10.1097/SLA.00000000000564.

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