

# Oesophageal perforation – therapeutic and diagnostics challenge. Retrospective, single-centre case report analysis (2009–2015)

Authors' Contribution:  
A – Study Design  
B – Data Collection  
C – Statistical Analysis  
D – Data Interpretation  
E – Manuscript Preparation  
F – Literature Search  
G – Funds Collection

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## ABSTRACT:

**Background:** Esophageal perforation is a life-threatening condition of a complex etiology. No clear guidelines are available regarding the management of this condition. In this study, we review publications related to esophageal perforation, and analyze patients treated for this condition at our Department of Thoracic, General and Oncological Surgery.

**Objective:** The objective of the study was to retrospectively assess and analyze management methods for esophageal perforations of different etiologies. All patients were treated in the Department of Thoracic, General and Oncological Surgery in years 2009-2015. Patients with perforations resulting from post-operational leaks within surgical anastomoses were excluded from the study.

**Material, methods, results:** The analysis involved a total of 16 cases of esophageal ruptures. All cases were treated in years 2009-2015. Patients with perforations resulting from postoperative leaks within surgical anastomoses following elective surgeries for either oncological or non-oncological causes were excluded. The most common reason for esophageal rupture was iatrogenic injury (7 cases, 44%). Other causes included Boerhaave syndrome (5 cases, 31.2%), blunt trauma (2 cases, 12.5%), abscess perforation (1 case, 6.2%), and ulcer perforation (1 case, 6.2%). Ten patients underwent surgery, and the rest underwent esophageal prosthesis placement, of whom 2 cases required drainage of the mediastinum and pleural cavity. The mortality rate in the study group was 9/16 cases (56.2%).

**Conclusions:** Esophageal perforation poses a significant interdisciplinary challenge regarding diagnostic workup, selection of treatment methods, and management of potential postoperative complications. This retrospective study was conducted in a single center. Although the analyzed period was long, we found only 16 cases. In spite of a variety of etiologies present, we found several statistically significant results of potential clinical value. Most perforations that are not diagnosed within 48 hours affected the lower part of the esophagus and presented with unclear symptoms and imaging findings. Delaying diagnosis and treatment beyond 24 hours was associated with a higher mortality rate.

## KEYWORDS:

esophageal perforation, diagnosis, treatment

## INTRODUCTION

Esophageal perforation poses a significant interdisciplinary significant challenge to the entire therapeutic team. Due to its possible occurrence challenge. within It can occur in three different anatomical compartments and therefore, it is characterized by presents with diverse diversity of symptoms, most of them being highly unspecificoften non-specific, which significantly elongates delays the time between perforation and final diagnosis followed by institution ofand appropriate targeted management. Despite the marked improvement in thea better availability of state-of-the-artmodern diagnostic techniques, esophageal perforation remains a direct life-threatening condition with mortality rates reaching as high as 50%.

Despite the fact that Although numerous multicenter, international studies have been conducted, no "gold standard" for the management of the condition has been established to date. No unambiguousThere are no clear guidelines were presented regarding initiation oftreatment, whichthat can compriseincludes contradictory mutually exclusive approaches such astherapeutic approaches i.e. conservative treatment, vs. minimally aggressive treatment, and vs. aggressive surgical management including esophagectomy. In this study, we are presenting-present our own experience and analyzing analyze the current available international literature available on the subject.

## OBJECTIVE OF THE STUDY

In this study, we are presenting present our ownour experience in with the treatment of esophageal perforations. A retrospective analysis was performed on among 16 cases of patients treated at in the Department of Thoracic, General and Oncological Surgery in years 2009-2015. We eExcluded from the study were patients with perforations resulting from post-operationalpostoperative leaks within surgical anastomoses following elective surgeries for either oncological or non-oncological causes. Only acute cases were included in the analysis. The analysis included the etiology of perforation, its location, time from the diagnosis to initiation of targeted treatment, the diagnostic method used to make the final diagnosis, demographic data, duration of the hospitalization period, final outcome of hospitalization, or and laboratory parameters of patients upon admission.

## MATERIAL

The analysis was conducted in a group of 16 patients, aged 24 to 83 years (median 65 years). The study group consisted of 9 male men and 7 female patientswomen (Table 1). The duration of the periodtime between perforation and diagnosis was strati-

fied into three intervals: 1 - up to 12 h (8 patients); 2 - 12-48 h (2 patients); and 3 - more than 48 h (6 patients). The locations of perforations were as follows: cervical esophagus in 2 cases, thoracic esophagus in 5 cases, and abdominal esophagus (above the diaphragm) in 9 cases. Also included in the analysis was the duration of time between diagnosis and surgical intervention. In 12 cases, therapeutic management, (i.e., all procedures aimed at sealing the perforation,) was initiated within 12 hours, as compared to 1 case, in which the management was initiated within 12-48 h, and in 3 cases in which the management was initiated within more than 48h. A total of 9 deaths were recorded in the study material.

Final diagnosis was facilitated supported by a CT scan without oral contrast administration in 14 cases and endoscopic examinations in 2 cases; (these cases were confirmed directly in the during the examinations that lead to a iatrogenic injury).

## RESULTS

Calculations were carried out using IBM SPSS 23.0 software. Contingency tables and the chi-squared test were used to assess the differences and the significance of differences in the distribution of categorical variables. ROC curves were used to assess the usefulness of selected quantitative variables in predicting the risk of death. The significance of differences in quantitative variables between the two study groups was assessed using the Mann-Whitney's U-test. The significance level was defined as  $p < 0.05$ .

No statistically significant relationship was observed in the study material between the age and, gender, of patients and the time between perforation and diagnosis. Due to the a low numbers of patients in study groups and their the a high diversity of cases substantial clinical diversity, no statistical correlation could be identified between the cause of perforation and the time of diagnosis. With regard to the location of perforation, statistical significance was demonstrated in the chi-square test, with the majority of diagnoses were made more than later than 48 hours after perforation pertaining to the lower segment of the esophagus (chi-squared test,  $p = 0.029$ ). In the case of perforations located within the abdominal esophagus above the diaphragm, the clinical presentation may be uncharacteristic and the results of imaging studies are frequently non-specific, leading to delays in correct diagnosis. The A low number of patients in individual categories of management procedures prevented did not enable the an appropriate statistical analysis. The management procedures included definitive Ivor-Lewis esophagectomies (5), prosthesis placement (4), prosthesis placement with pleural drainage (2), resection of gastroesophageal anastomosis (1), suturing of the perforation site (3), and suturing of the perforation site with pleural drainage (1). Despite the a lack of statistical significance, some conclusions may be risked put forward drawn. All patients in whom extensive procedures were performed (5) died, while 7 out of 10 patients subjected to suturing or prosthesis placement survived. Also, in the case of the a patient undergoing who underwent the resection of a gastroesophageal anastomosis, the outcome was unfavorable. Due to the a low number of subjects, heterogeneity of cases, and significant age differences in the age profile of patients, the statistical analysis could did not unambig-

uously confirm the hypothesis that extensive surgical procedures performed in esophageal perforations of varied etiology are associated with unfavorable treatment outcomes. Table 2 lists the treatment procedures along with their corresponding outcomes.

A statistically significant difference ( $p = 0.012$ ) was demonstrated in the study material between the time to diagnosis and the mortality rate. The diagnosis and initiation of treatment within 24 h was associated with a higher mortality rate.

In addition, the laboratory parameters including wWhite bBlood cCell count, red blood cell countRBC, nNeutrophils, hematocritHct, hemoglobinHGB, uUrea, cCreatinineynin, total protein, and C reactive proteinRP were analyzed in detail in the study group upon on admission. Also, subject to the analysis was the correlation between the above-mentioned parameters and the time to diagnosis (group 1: up to 24h, group 2: above 24 hours) were correlated; however, the analysis revealed no statistical differences between the groups for in any of the variables (Table 3).

The analyses of these parameters in the group of Among deceased patients the patients who died, a statistically significant negative correlation was observed between the Neut counts and the time of death survival time, i.e., (the higher the baseline Neut counts, the shorter the survival). In addition, a statistically significant correlation was demonstrated between Hgb levels and time of death survival time - . h Higher baseline Hgb values were associated with longer survival times.

## DISCUSSION

Esophageal perforation poses a significant interdisciplinary significant challenge to the entire therapeutic team. Due to its possible occurrence within three different anatomical compartments, it is characterized by a diversity of symptoms, most of them being highly unspecific, which significantly elongates delays the time between perforation and final diagnosis followed by institution of and appropriate targeted management. Despite the markedly improved marked improvement in diagnostic methods as well as in and medical care being provided in intensive care units the medical care provided in intensive care units, esophageal perforation remains to be still associated with a high mortality rate of 5-40%, and, if the disease is diagnosed with a delay of the diagnosis is delayed by more than 24 h, the mortality rate is as high as 50% [1, 2, 3]. Due to the diversity of potential mechanisms leading to perforation, non-specificity of clinical symptoms, and variety of therapeutic procedures, no uniform guidelines have been established to date with regard to the management of patients with this condition.

Patients with esophageal perforations may present with a variety of clinical symptoms such as: dysphagia, odynophagia, chest pain, dyspnea, subcutaneous emphysema of the neck extending down to the chest wall, pyrexia, or the Mackler's triad symptoms (, i.e., chest pain, vomiting, and subcutaneous emphysema; these symptoms) are presented simultaneously only by in a small percentage of patients. According to data published in international literature Based on the available literature literature, the most common clinical symptoms of esophageal perforation include pain (71%), pyrexia (51%), dyspnea (24%), and crackling sounds

upon palpation of soft tissues in the neck region (24%) [4, 9]. In the case of perforations within the short subdiaphragmatic segment, predominant manifestation consists insymptoms include acute abdomen symptoms due to chemical irritation of the parietal peritoneum.

Early diagnosis of esophageal perforation and initiation of management aimed at reducing contamination and preventing the spread of infection spread is of key importance in reducing the mortality rate.to improve survival.

What diagnostic procedures should be performed in order to make the diagnosis as early as possible? In the case of suspected esophageal perforation, there is no obvious or unambiguous answer to this question. In cases patients presented in this study, computed tomography was most effective. In the case of iatrogenic complications which that usually occur in the course ofduring endoscopic procedures, the diagnosis is made usually during the procedure; then, itself when the endoscopist immediately notifies the surgeon of the potentialthis complication immediately after it occurs. Such a prompt management should become a ruleThese are the cases when the diagnosis is made and the management is initiated at the earliest possible time point; however, this should not be considered a rule. In our study group, two patients with a history of gastrofiberoscopy procedures performed at in other institutions other facilities reported at to our center more later than 24 hours after the occurrence of perforations. . In theFor the remaining cases, no obvious or unambiguous choice exists with regard to the diagnostic methods. In the cases of cervical esophageal perforations as treated at our facility, computed tomography turned out to bewas the gold standard ofthe best diagnostic examinations. The cases described above resulted from blunt trauma sustained by patients in traffic accidents. Imaging diagnostics studies initiated performed already at the stage ofin the emergency room as well as and the a high location of the perforations contributed to early diagnosis and initiation of appropriate treatment. In these cases, the treatment involved simple suturing of the injured site. Early-diagnosed perforations (, i.e., perforations diagnosed within 24h from the injury,) are associated with the best prognoses prognosis as the injury occurs in a region of healthy tissues characterized by good blood supply, which of blood and capable ofenables quick healing after stitching. These perforations are also restricted in their extent, with minimum contamination of the surrounding tissues. In the case of perforations within the thoracic segment of the esophagus, the casethe management choice is not so clear any more. In the case of post-traumatic, iatrogenic, or spontaneous perforations within this segment, computed tomography may not warrant a diagnostic success. PneumothoraxPneumothorax observed in post-traumatic cases is usually interpreted by clinicians as being due to a ruptured lung; similar misinterpretation occurs in the case of intestinal emphysema which that is most commonly due to airway damage. Fluid within the pleural cavity is most commonly interpreted as post-traumatic hematoma. Depending on the reported amount, the fluid may be immediately drained so as to verify its quantity and contents (the fluid is assessed for its color, quantity, and possibly its dynamics in the case of active bleeding). However, if a small quantity of the fluid is reported in theon CT scan summary, patients are not immediately qualified for the drainage procedures and therefore the contents of the pleural cavity cannot be verified for beingconfirmed as blood, serous liquid, or

**Tab. I.** Characteristics of the study group

SEX	9M	7F
Age 24-83	Mean 60.4	Median 65
Time until diagnosis	<12 h	8
	12-48 h	2
	>48 h	6
Location of perforation	Abdominal esophagus	9
	Thoracic esophagus	5
	Cervical esophagus	2
Time until procedure	up to 24 hours from diagnosis	12
	> 48 h	3
Death	No deaths	7
	Deaths	9
Diagnosis	CT	14
	Endoscopy	2

**Tab. II.** Performed procedures and treatment outcomes

PROCEDURE	NUMBER OF PROCEDURES	DEATHS
Suturing	3	0
Suturing, drainage	1	1
Prosthesis	4	0
Prosthesis, drainage	2	2
Gastroesophageal anastomosis resection	1	1
Ivor Lewis resection	5	5

gastrointestinal contents. In such cases, esophageal perforation is usually overlooked at early stage of diagnostic procedures and the crucial time between perforation and initiation of effective treatment is elongateddelayed. In the case of patients with no history of trauma, pneumothorax may be attributed to spontaneous or secondary emphysema in the course of concomitant respiratory diseases; similar misinterpretation may be made with regard to mediastinal emphysema. As mentioned above, if fluid is present within the cavity, the decision of to perform drainage may depend on the quantity to be evacuatedof the fluid. When a patient has been qualified for pleural drainage, even the presence of contents other than serous fluid or blood may distract the attention from suspected esophageal perforation since the opaqueradiopaque gastrointestinal contents may be misinterpreted as being due to an early-stage pleural abscess, which in turn may be considered thought to arise from due to respiratory tract disorders, thus putting to sleep thedecreasing vigilance of the health medical personnel and delaying correct diagnosis.

According to international the literature, if esophageal perforation is suspected, CT scan with an oral administration of water-soluble contrast agents should be performed as a supplementary examination. However, this examination may deliver false negative results (their percentage being as high as 36%); if a negative result is obtained in on the first examination, but and still viable premises exist for the suspicion of esophageal perforation is still suspected, the examination should be supplemented by an examination involving oral administration of a barium sulfate-based contrast agent should be administered [4, 5, 6].

**Tab. III.** Analysis of laboratory parameters in patients with perforations diagnosed within less than 24 hours and more than 24 hours.

DIAGNOSIS (TIME)		AGE	WBC	RBC	NEUT	HCT	HGB	URE	CREA	TOTAL PROTEIN	CRP
Up to 24 h	Mean	54,88	13,342	3,281	13,081	29,175	10,863	12,049	118,750	39,100	95,500
	Median	60,00	9,600	3,260	13,175	30,000	11,650	10,100	106,000	38,500	89,000
	Standard deviation	18,122	9,0147	1,0644	7,6440	5,6279	3,4965	7,7495	75,2382	4,5757	48,6621
	Minimum	24	2,4	1,9	3,4	20,4	5,2	2,3	44,0	35,0	20,0
	Maximum	72	26,8	5,2	23,0	36,0	15,4	22,8	248,0	49,0	153,0
	N	8	8	8	8	8	8	8	8	8	8
Above 24 h	Mean	66,00	9,339	3,971	8,800	31,987	10,525	14,625	160,375	38,125	150,875
	Median	67,50	7,905	3,985	6,640	32,450	10,350	14,670	164,500	38,000	144,500
	Standard deviation	17,825	3,9600	,7192	4,7614	3,6926	2,4546	6,7541	103,6904	5,8661	115,9488
	Minimum	30	5,1	3,2	4,1	28,0	6,7	3,0	49,0	28,0	11,0
	Maximum	83	15,0	5,4	15,7	39,0	13,2	22,0	370,0	45,0	300,0
	N	8	8	8	8	8	8	8	8	8	8
Total	Mean	60,44	11,341	3,626	10,941	30,581	10,694	13,337	139,563	38,613	123,188
	Median	65,00	8,105	3,575	8,110	31,500	11,100	12,500	140,500	38,500	113,500
	Standard deviation	18,290	7,0368	,9471	6,5372	4,8222	2,9236	7,1473	90,1177	5,1071	90,5356
	Minimum	24	2,4	1,9	3,4	20,4	5,2	2,3	44,0	28,0	11,0
	Maximum	83	26,8	5,4	23,0	39,0	15,4	22,8	370,0	49,0	300,0
	N	16	16	16	16	16	16	16	16	16	16

According to the international literature, multidirectional therapeutic modalities are available in for the treatment of the thoracic segment of esophagus, starting from conservative treatment consisting insuch as complete discontinuation of oral nutrition and complete parenteral supplementation of nutrients and fluids, intravenous broad-spectrum antibiotic therapy, and administration of proton pump inhibitors. Such management may be introduced in cases ofpatients with small perforations of limited character (with no features of pleural and mediastinal infection, patients presenting with minimum-no SIRS symptoms, no oncological background of perforation). However, procedural invasive treatment is required in the case of ca. 20% of patients subjected to conservative treatment. None of the patients in our study was group qualified for this type of treatment [7, 8, 9, 10].

Endoluminal endoscopic vacuum therapy (EVT) is a relatively novel therapeutic technique introduced by German researchers Kuehn F. et al. [11]. The authors use this treatmentit in for the treatment of perforations as well asand postoperative anastomotic leaks. The method was successful in curing 19 out of 21 patients,; with the an efficacy rate of ca. 90%,. The method is very promising yet still not popular in Poland. Brangewitz et al. demonstrated the superiority of EVT over stent placement as a method for completely sealing the leaks (84.4% vs. 53%). In addition, the EVT was associated with a statistically lower number of esophageal stenoses as compared to stent implantation (9.4% vs. 28%) [12].

In our group, stent prostheses were implanted in 6 patients; all patients in this group were above 60 years of age. Like other authors, we did not limit stent implantation to the cancer-related cases [9,13,14,15,16,17].; Iin addition, the method was combined with pleural drainage in 2 cases of unrestricted perforation in our

study group, as , which has also been described by Navaneethan U. et al. [18]. To date, no optimum time was has been established for implantation of perforation-sealing stents. However, considering the fact that in the case of thoracic esophageal perforations mediastinal infection increases by 2% every 1 h, the procedure should be performed as early as possible [18]. In our study group, stents were implanted in 4 cases of iatrogenic complications (secondary to endoscopic procedures), 1 case of cancer-related perforation, and 1 case of spontaneous perforation.

Perforation suturing was performed with success within the thoracic esophagus in one patient , younger than below 60 years of age, with an extensive iatrogenic perforation diagnosed within 12 h; there were no, lack of inflammatory markers or symptoms of mediastinal infection, and; all these factors were important for the choice of this treatment method.

The hottest dispute isThere is heated debate raised with regard to qualification of patients for extensive resection procedures. According to many authors, several factors should be taken into account when qualifying patients for resection or bypassing procedures [9,10,11,12,13, 14]. These include, among others, the time between perforation and initiation of treatment; - usually, more extensive procedures should be considered after more than 24 hours from perforation so as to remove the source of infection.; Hhowever, many authors use to perform less invasive procedures such as simple suturing in non-cancer cases with little tissue devitalization or stenting. In these cases, the an increased risk of postoperative leaks is highlighted [15]. Another factor taken into account is the extent and potential contamination of the neighboring tissues with gastric contents and the markers of intestinal infection (clinical, biochemical, laboratory) [9, 14, 15]. Restricted perforations (, i.e.

with infection of directly adjacent tissues or a small reservoir, usually restricted by adjacent structures,) are associated with better prognoses prognosis compared to perforations involving the infection of pleural cavities and extensive mediastinal infections. In our study group, we decided to use conservative treatment in three cases of patients with perforations within the abdominal segment of the esophagus (stent implantation with pleural draining in 2 cases and suturing with pleural drainage in 1 case) due to the advanced age of patients (> 70 years of age). Resection procedures with simultaneous restoration of gastrointestinal continuity were performed in the remaining cases of abdominal esophageal perforation, including gastroesophageal anastomosis resection in 1 case and the Ivor-Lewis esophagectomy in 5 cases. The group of patients undergoing who underwent the Ivor-Lewis procedure was diverse in terms of the time until diagnosis (4 < 24 h, 1 > 48 h). The heterogeneity of the latter group (age range, etiology of perforation, inflammatory markers) warrants the claim lets us suspect that the choice of the treatment method in this group was driven mainly by individual premises patient characteristics and the experience of operators. Unfortunately, in a manner similar to the results by Biancari et al. who analyzed the outcomes of various therapeutic methods of perforation in patients >80 years of age, the results obtained in our group were unsatisfactory [16].

However, Lin et al. also performed esophagectomy with simultaneous reconstruction of gastrointestinal continuity. One of the key premises behind the choice of this method is the claim that the removal of resection the a perforated esophagus is tan-

amount to the removal of removes a potential source of infection that might be refractory to less invasive modalities. Radical treatment is associated with longer hospitalizations, including stays within the ICUs, and; multi-organ insufficiency develops in 30% of patients [15].

The wide range of therapeutic modalities once again highlights the lack of a uniform regimen and unambiguous clear guidelines to be followed in individual cases for the management of esophageal perforations. In many centers, the choice of the therapeutic approach is still based on individual experience of medical personnel the operators. At the same time, Lin et al. formulated a conclusion conclude that includes a somewhat simplified guideline: according to their observations, all instrument-related, iatrogenic perforations are restricted in nature and therefore allow for non-invasive approach, while pressure-dependent perforations (Boerhaave syndrome) are unrestricted and should therefore qualify patients for be treated with extensive surgical procedures [15].

## CONCLUSIONS

Esophageal perforations remain a significant diagnostic and therapeutic challenge. Due to the diversity of potential causes of the condition as well as to the possibility of initiating a variety of management schedules, and many potential treatment options, no uniform method for the management of esophageal perforations has been established to date, and therefore further studies and attempts at standardization of such management are required.

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