

Original Article

Factors affecting mortality in esophageal perforation

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ABSTRACT

Background: Esophageal perforation have high mortality. Due to its relative rarity and lack of clinical experience, there are no established guidelines for its treatment. Abbas and colleagues developed a perforation severity score (PSS) in 2009, using the patient's clinical parameters at the time of diagnosis for predicting prognosis of the patient. We aimed to identify the prognostic factors affecting mortality for patients with esophageal perforation including PSS.

Materials and Methods: The records of 21 patients with esophageal perforation between 2010 and 2023 were examined retrospectively. The age, gender, Charlson Comorbidity Index, etiology, time to diagnosis, extent of perforation (contained/non-contained), localization, operation and PSS of the patients were recorded and their relationship with mortality was analyzed.

Results: Nine (42.9%) patients were female and the median age was 56 (19-73 years). Cervical perforations were seen in 13 (61.9%) patients and 8 (38.1%) patients had thoracic perforations. Median time to diagnosis was 2 days (1-30 days). Median PSS for non-operative patients was 2 and it was 6 for operative patients ($p = 0.086$). Mortality rate was 19% (4 patients). Patients are grouped according to mortality. Age, sex distribution, comorbidity index, etiology, perforation localization, time to diagnosis, management strategy and PSS between groups were compared. Only localization has statistically significant difference between groups ($p = 0.01$).

Conclusions: Optimum therapy should be chosen according to patients' comorbidities, etiology, perforation localization, extent of perforation, time to diagnosis and medical status of the patient. Patients with low-risk score and who have a contained leak could be treated with non-operative therapies

Keywords: esophageal perforation, perforation severity score, surgery, prognosis, mortality

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Introduction

Esophageal perforation is still a condition with high mortality despite advances in medicine and mortality rate rise up to 40% in past series [1]. The passage of gastric contents and oral intakes into the mediastinum and the mediastinitis it causes, followed by sepsis, is the main mechanism of death [2]. Today, iatrogenic perforations are in the first place among etiologies due to increasing number of diagnostic and therapeutic endoscopic procedures [3]. Diagnosis and treatment of esophageal perforation poses various difficulties for the clinician. Due to its relative rarity and lack of clinical experience, there are no established guidelines for its treatment. Treatment strategy mostly depends on the experience and judgement of the clinician. There are different therapeutic options including surgical and non-surgical interventions and also conservative approaches but yet there is no consensus on which treatment should be given to which patient. Abbas and colleagues developed a perforation severity score (PSS) in 2009, using the patient's clinical parameters at the time of diagnosis for this purpose [4]. There are some publications stating that this scoring system might be helpful for choosing ideal treatment and predicting patient outcomes [3,5,6].

In this study we aimed to identify the factors affecting mortality by examining the characteristics of the patients treated for esophageal perforation in our clinic and used the PSS as a prognostic factor.

Materials and Methods

The records of 21 patients treated in our clinic due to esophageal perforation between 2010 and 2023 were examined retrospectively. This study was approved by the Ankara University Institutional Review Board. Patients with tracheoesophageal fistula, leakage after esophageal surgery were excluded from the study. Diagnosis was made by endoscopy, computed tomography (CT) or esophagography with orally administered contrast media. The intervention decision and method were determined according to the surgeon's preferences. Three patients were treated with non-operative management (no oral intake, iv antibiotics and parenteral nutrition) and others had surgical intervention. Surgical interventions included drainage only, primary repair and

esophagectomy via cervical exploration, thoracotomy or laparotomy. Primary repair was tried if the perforation site was clear or with little contamination and with limited necrosis regardless of the time to diagnosis and reinforced with muscle flaps (strap muscles, sternocleidomastoid muscle, intercostal muscles) whenever possible. Esophagectomy was performed for three patients one with underlying esophageal carcinoma and the others with wide perforations and necrosis. Exploration and drainage was performed for patients unsuitable for primary repair. The age, gender, Charlson Comorbidity Index (CCI), etiology, time to diagnosis, extent of perforation (contained/non-contained), localization, operation and perforation severity scores (PSS) of the patients were recorded and their relationship with mortality was analyzed. Perforation severity score was calculated by scoring the patients' age, tachycardia, leukocytosis, pleural effusion status, fever, extent of perforation, respiratory distress, time until diagnosis, presence of cancer and hypotension separately and getting final score by adding them up (Table 1). Extent of perforation was evaluated with contrast enhanced esophagogram or CT scan with oral contrast and classified as non-contained or contained perforation. Non-contained perforation refers to free extravasation of contrast media to mediastinum, pleura or peritoneum and contained perforation was defined as minimal extravasation of contrast at the perforation site without pleural or peritoneal spillage. Mortality was defined as patients who died within 90 days after hospital admission or died in hospital.

Table 1. Perforation severity score (PSS) variable table.

Variable	Score
Age: > 75 years	1
Tachycardia: >100 bpm	1
Leukocytosis: >10 000 WBC/ml	1
Pleural effusion: present	1
Fever: >38.5oC	2
Extent of perforation: non-contained	2
Respiratory compromise: respiratory rate >30/min, increasing oxygen requirement, need mechanical ventilation	2
Time to diagnosis: >24 hours	2
Cancer: present	3
Hypotension: present	3

Abbrev.: Bpm: beat per minute, WBC/ml: White blood cell / milliliter. PSS adds up the scores of variables suitable for patient clinic at admission.

Statistical Analyses

The data obtained in the study was evaluated with the SPSS (Statistical Package for the Social Sciences) program version 23 for Windows. Descriptive data were presented in mean \pm standard deviation (SD), median (min-max) or number and frequency where applicable. Mann Whitney U test or Student t-test was used to compare numerical variables of two independent groups. Chi-Square and Fisher Exact tests were used in the analysis of categorical variables. P value lower than 0.05 was accepted as statistically significant.

Results

Among 21 patients, 9 (42.9%) of them were female and the median age was 56 (19-73 years). Median CCI was 2 and only three patients had ≥ 4 score. Non-operative patients median CCI was 3 and for operative patients it was 1.5 ($p = 0.12$). While 9 patients had iatrogenic perforation (endoscopy, cervical spine surgery, esophageal intubation), 6 patients had perforation due to foreign body ingestion (chicken bone, meat bone, packaged medicine), 2 patients had spontaneous (one after vomiting [Boerhaave syndrome], one with chemoradiotherapy for laryngeal carcinoma), 1 patient had traumatic (gun-shot wound) perforation and the cause of perforation could not be determined in 3 patients. Cervical perforations were seen in 13 (61.9%) patients and 8 (38.1%) patients had thoracic perforations. Median time to diagnosis was 2 days (1-30 days). Median PSS for non-operative patients was 2 and it was 6 for operative patients ($p = 0.086$). Non-operative management was preferred for 3 patients and all of them had cervical esophageal perforations. These patients comorbidity scores were 3, two of them had PSS 2 and only one patient's PSS was 6 due to laryngeal cancer. All three patients had contained perforations and were medically stable. They had no oral intake for at least ten days, iv antibiotics were administered and waited for spontaneous healing. Ten patients with cervical perforations had operative management (77%) and 6 (46%) of them had primary repair. Only 2 of these patients underwent thoracotomy all the others had cervical exploration. All 8 patients with thoracic esophageal perforation had operative management. Three patients had emergency esophagectomy

and 2 of them died in the early postoperative period. Three patients had left thoracotomy and primary esophageal repair. One of these patients needed esophageal stent at the same time with the operation because of the wide perforation area. One patient had right thoracotomy and drainage, one patient had drainage via laparotomy because of the severe emphysematous lungs. Patients had no oral intake at least 7 days and they had total parenteral nutrition. If the healing period exceeds over one week gastrostomy or jejunostomy routes were used for feeding. Six patients (28.5%) had never oral intake (4 patients died in the postoperative period, one patient died 3 months after the surgery and one patient had gastric perforation after the surgery and still followed with jejunostomy). Median time for oral intake resume was 14 days (7-365 days) (Table 2).

Mortality rate was 19% (4 patients). Patients are grouped according to mortality and age, sex distribution, comorbidity index, etiology, perforation localization, time to diagnosis, management strategy and PSS between groups were compared. Only localization has statistically significant difference between groups ($p = 0.01$) (Table 3).

Discussion

Iatrogenic perforations are leading etiology for esophageal perforation nowadays and also in our study 42.8% of patients had iatrogenic perforations due to endoscopy, cervical spine surgery or esophageal intubation [1-4]. In the study of Eroğlu et al 36 esophageal perforations occurred between 1989 and 2002 was reviewed. Although it represents an earlier timeline, again most of the patients had iatrogenic perforations (63.9%) [7].

Studies from America, Europe, Norway and Germany gives rates of late time to diagnosis (>24 hours) between 24.6% and 50% [1,5,6,8,9]. Our late time to diagnosis rate is 38% and comparable with worldwide. In a meta-analysis published by Vermeulen et al [10] including 25 studies and 960 patients with esophageal perforation, early diagnosis (≤ 24 hours) was associated with only a 6% decrease in overall mortality. Also in our study there was no difference in mortality rates between early and late diagnosis. This may be interpreted as time to diagnosis is not strong enough to determine the patient prognosis.

Table 2. Patient list with important clinical characteristics.

Patient no	Etiology	Localization	Time to diagnosis (days)	Management	PSS	Mortality
1	Iatrogenic	Cervical	1	Non-operative	6	0
2	Iatrogenic	Cervical	5	Cervical exploration+drainage	7	0
3	Spontaneous	Thoracic	1	Left thoracotomy+primary repair	11	0
4	Traumatic	Thoracic	1	Esophagectomy	3	1
5	Unknown	Cervical	7	Cervical exploration+drainage	7	0
6	Spontaneous	Cervical	7	Right thoracotomy+drainage	16	0
7	Foreign body	Thoracic	2	Laparotomy+drainage	13	1
8	Iatrogenic	Cervical	4	Cervical exploration+drainage	8	0
9	Iatrogenic	Cervical	1	Cervical exploration+primary repair	2	0
10	Iatrogenic	Cervical	30	Cervical exploration+primary repair	4	0
11	Unknown	Cervical	2	Non-operative	2	0
12	Foreign body	Thoracic	1	Left thoracotomy+primary repair+stent	4	1
13	Foreign body	Thoracic	1	Left thoracotomy+primary repair	3	0
14	Iatrogenic	Cervical	2	Cervical exploration+primary repair	5	0
15	Iatrogenic	Cervical	12	Cervical exploration+primary repair	4	0
16	Foreign body	Cervical	1	Cervical exploration+primary repair	6	0
17	Iatrogenic	Cervical	1	Right thoracotomy+cervical exploration+primary repair	5	0
18	Foreign body	Thoracic	4	Right thoracotomy+drainage	6	0
19	Iatrogenic	Thoracic	2	Esophagectomy	15	1
20	Unknown	Thoracic	7	Esophagectomy	13	0
21	Foreign body	Cervical	4	Non-operative	2	0

Abbrev.; PSS: perforation severity score

Table 3. Analysis between patient characteristics and mortality.

Variables, n (%)	Alive: 17 (81)	Exitus: 4 (19)	p
Age (mean±SD)	52.6±13	58.6±17	0.47
Sex			1
Female	7 (41.2)	2 (50)	
Male	10 (58.8)	2 (50)	
CCI (median)	2	3	0.33
Etiology			0.60
Iatrogenic	8 (47.1)	1 (25)	
Others	9 (52.9)	3 (75)	
Localization			0.01
Cervical	13 (76.5)	0	
Thoracic	4 (23.5)	4 (100)	
Time to diagnosis			0.62
≤24 h	6 (35.3)	2 (50)	
>24 h	11 (64.7)	2 (50)	
Management			1
Non-operative	3 (17.6)	0	
Operative	14 (82.4)	4 (100)	
PSS (median)	6	8.5	0.59

Abbrev.; CCI: Charlson comorbidity index, PSS: perforation severity score

In the published series of esophageal perforation the rate of surgical interventions as first line treatment is given between 47%-77% [1,3-7,10,11]. Surgical therapies include primary repair, drainage only, or esophagectomy

mostly. Nowadays endoscopic stenting and other endoscopic modalities have an increasing trend over surgery. In the study of Gray et al [12] with 2543 esophageal perforations, 48.3% of the patients had stents for treatment

and stenting increased from 7.0% in 2009 to 78.1% in 2019. In our series only one patient had stent at the same time with surgery because of wide perforation area.

Management strategies differs from center to center, patient to patient as there are no clear guidelines. Optimum therapy should be chosen according to patients' comorbidities, etiology, perforation localization, extent of perforation, time to diagnosis and medical status of the patient. Abbas et al [4] proposed a perforation severity score (PSS) to guide selecting patients for operative or non-operative management. $PSS \leq 2$ low-risk, PSS 3-5 intermediate-risk and $PSS > 5$ is estimated to be related with high-risk groups. In our study there was no mortality in low-risk group and median PSS was higher for patients with mortality although statistically not significant (8.5 / 6, $p = 0.59$ respectively). Patients with low-risk score and who have a contained leak could be treated with non-operative therapies. High-risk group should be treated with aggressive management because mortality rates are high. Intermediate risk group can be treated with individualized therapies based on underlying etiology, comorbidities, localization and extent of perforation. No patient with cervical perforation died in our cohort. Our mortality rate is 19% and it is comparable with the literature (13%-23.4%) [1-8].

Cervical perforations have low mortality risk so they can be managed as low-risk group [6]. Comorbidity scores of patients and underlying esophageal pathologies could be included in the PSS because these factors directly influence the operative management strategies. [5].

In conclusion, as this is a retrospective study with limited number of patients and also patients were not treated according to PSS or any other guideline, the results should be interpreted carefully. It can give an idea of treatment strategies for a rare and urgent clinical situation.

Declaration of conflicting interests

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Ethics approval

This study was approved by the Ankara University, Institutional Review Board (2024/279, No: I03-286-24)).

Authors' contribution

GK: conceptualized and designed the study, collected, analyzed and interpreted the data, wrote the paper, YK: collected the data, reviewed the literature, MÖ: revised the final version of the manuscript, and co-wrote the paper, BY: revised the final version of the manuscript. All authors read and approved the final manuscript.

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