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Surgical Management of Non-Malignant Esophageal Perforations: A Single-Center Analysis Over a 15-Year Period

Karl-Frederick Karstens Eugen Bellon Michael Tachezy Jakob R. Izbicki Tarik Ghadban Anna Duprée Faik G. Uzunoglu Kai Bachmann Alexandra Koenig Matthias Reeh

Department of General, Visceral and Thoracic Surgery, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany

Keywords

Esophageal perforations · Esophagectomy · Boerhaave's syndrome · Perforation Severity Score

Abstract

Purpose: Esophageal perforations are associated with high morbidity and mortality. Different nonoperative and operative treatment options have been proposed. This study focuses on the impact of different surgical treatments in non-malignant esophageal perforations and tries to identify predictors of mortality in a single tertiary center over a 15-year period. ***Methods:*** From 2002 to 2017, patients with surgically managed esophageal perforation were identified from our database. Patients with esophageal malignancies were excluded. Etiology, clinical data, treatment, and outcome were analyzed. A multivariate logistic regression analysis was performed to investigate the impact on mortality. ***Results:*** A total of 72 patients were identified. The majority of perforations were iatrogenic (54.2%) followed by Boerhaave's syndrome (23.6%). Most ruptures were found in the distal third of the esophagus (59.7%) measuring <3 cm (61.1%). Patients were treated with exploration and drainage (8.3%), primary suture and patch reinforcement (36.1%), resection and restoration of continuity (25.0%), or resection without restoration of continuity (30.6%). Delayed therapy significantly correlated with sepsis ($p < 0.0001$) and mortality ($p = 0.032$). A correlation between an increasing perforation length with sepsis ($p = 0.012$) was observed. A higher Perforation Severity Score (PSS; OR 4.430; 95% CI 1.143–17.174; $p = 0.031$) and a higher American Society of Anesthesiologists (ASA) score (OR 2.923; 95% CI 1.011–8.448; $p = 0.048$) were associated with mortality in multivariate analysis. ***Conclusion:*** Esophageal perforations are associated with high mortality, and larger ruptures are associated with worse outcome. Rapid diagnosis and treatment are crucial for patient survival. Hence, PSS and ASA score help to identify high-risk patients. The advantage of surgical management lies in the rapid control of the septic focus in an already critically ill patient. Though, the kind of surgical technique needs to be adjusted to the individual situation.

K.-F.K. and E.B. contributed equally to this study and share first authorship.

KARGER

karger@karger.com
www.karger.com/dsu

Matthias Reeh, MD
Department of General, Visceral and Thoracic Surgery
University Medical Centre of Hamburg-Eppendorf
Martinistrasse 52, DE–20246 Hamburg (Germany)
E-Mail mreeh@uke.de

Introduction

Despite advances in surgical and intensive care treatment, esophageal perforations remain life-threatening conditions. The most common causes of esophageal perforations are iatrogenic and Boerhaave's syndrome. The etiology of the perforation determines its location in the esophagus and influences clinical symptoms, which vary and are non-specific [1, 2]. The extent of mediastinal or pleural contamination is determined by computed tomography [3]. Together with the systemic inflammatory response and the etiology of the rupture, different management techniques of esophageal perforations have been proposed, which should be initiated within the first 24 h [4–10]. To classify the overall patient risk and establish treatment algorithms, a Perforation Severity Score (PSS) has been advocated [8, 11]. Small contained perforations can be managed conservatively with broad-spectrum antibiotics [8, 12]. In addition, treatment with esophageal stents or sponges also seems to be feasible [4, 6, 7, 13]. Extensive esophageal ruptures should be treated surgically, though. This can be done either by a primary suture repair with or without reinforcement with pleural or omental flaps or by esophagectomy followed by immediate or delayed reconstruction [4, 14, 15]. Although algorithms for the management of esophageal perforations have been suggested, the correct treatment is still being discussed [4, 8, 11]. In this study, we only investigated patients without esophageal malignancies to examine the spectrum of causes leading to esophageal perforations and to identify optimal surgical treatment options as well as possible predictors of mortality without the bias of a cancer influence.

Patients and Methods

We conducted a retrospective study by using our database of patients treated with esophageal ruptures in the Department of General, Visceral and Thoracic Surgery, University Medical Centre Hamburg-Eppendorf, from April 2002 to 2017. Patients with esophageal ruptures, which have arisen on the ground of malignancies, were excluded. Perforations were confirmed with CT scan and endoscopy. All patients received a primary surgical management. Either a pericard or latissimus dorsi muscle flap was routinely used if patch reinforcement was performed. The enrolled patients were analyzed using the following characteristics: location (proximal, middle, and distal third of the esophagus) and etiology (iatrogenic, Boerhaave's syndrome, foreign body ingestion, complication of chronic inflammation), time interval between first symptoms and diagnosis with initiation of surgical therapy (<24 h; >24 h), options of treatment (exploration and drainage, primary suture and patch reinforcement, esophagectomy and restoration of continuity, esophagectomy without restoration of continuity), mortality, length of stay, sepsis prior to surgery, and revision surgeries. Mortality was defined as death within 30 days after surgery or death during the hospital stay. Physical status of the patients was evaluated using the American Society of Anesthesiologists (ASA) score. The PSS was calculated by clinical variables with their assigned points (range 1–3) for a possible total score of 18. Low- (PSS <2), intermediate- (PSS 3–5) and high-risk (PSS >5) groups were formed according to Abbas et al. [11]. Data were analyzed by median values with minimum and maximum as range. Kruskal-Wallis and Mann-Whitney U test were performed to compare categorical data and Spearman's coefficient was used for correlation analysis, respectively. To investigate the effect of clinical variables on mortality, a logistic regression analysis was performed, and ORs with 95% CIs were calculated. All reported p values are 2-sided, and p values <0.05 were considered statistically significant. The statistical analyses were performed using SPSS version 24 (SPSS, Chicago, IL, USA).

Results

Based on our database containing over 1,000 patients with esophageal surgeries, 72 patients were selected and enrolled in this study. Of these, 37 (51.4%) were men and 35 (48.6%) were women with a median age of 67.5 (range 24.0–87.0) years.

Etiology, Location, and Length of Perforations

Iatrogenic perforations (n = 39; 54.2%) were the most common cause of esophageal perforations. The majority of iatrogenic perforations were found after routine gastroscopies including transesophageal echocardiographies (n = 23; 58.9%) followed by gastroscopies with interventions (dilations: n = 10; 25.6% and mucosal resections: n = 6; 15.4%). Boerhaave's syndrome accounted for 17 perforations (23.6%). Perforations due to foreign body ingestions or inflammatory complications (ulcer or severe soor esophagitis) were found in 9 (12.5%) and 7 patients (9.7%), respectively. Most of the patients (n = 5; 71.4%) with an inflammatory complication presented with sepsis. Perforations of the distal esophagus were found in 43 patients (59.7%). In 17 (23.6%) patients, the perforation was located in the middle part of the esophagus. A perforation in the proximal esophagus occurred in 12 (16.7%) patients. For further details of the perforations' locations, see Tables 1 and 2. Mortality was the lowest in patients with ruptures in the proximal esophagus (n = 1; 8.3%). Mortality increased over perforations in the middle (n = 4; 33.3%) toward the distal esophagus (n = 7; 58.3%). A

Table 1. Analysis of the etiology of esophageal perforations

	Iatrogenic perforations (*n* = 39)	Boerhaave's syndrome (*n* = 17)	Foreign body ingestion (*n* = 9)	Chronic inflammation (*n* = 7)	*p* value
Gender, male/female	12/27 (30.8/69.2)	14/3 (82.4/17.6)	5/4 (55.6/44.4)	6/1 (85.7/14.3)	*0.001*
Age, years	69.0 (24–87)	61.0 (45–78)	61.0 (41–78)	76.0 (50–86)	0.424
Presence of sepsis	14 (35.9)	8 (47.1)	2 (22.2)	5 (71.4)	0.202
ASA score					0.227
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
2	5 (12.8)	6 (35.3)	2 (22.2)	0 (0.0)	
3	21 (53.8)	7 (41.2)	4 (44.4)	3 (42.9)	
4	10 (25.6)	3 (17.6)	3 (33.3)	4 (57.1)	
5	3 (7.7)	1 (5.9)	0 (0.0)	0 (0.0)	
Mortality	8 (20.5)	1 (5.9)	0 (0.0)	3 (42.9)	0.072
Revision surgery	2 (5.1)	1 (5.9)	1 (11.1)	2 (28.6)	0.218
Length of stay, days	25.0 (1–109)	17.0 (9–109)	17.0 (10–28)	22.0 (11–109)	0.604
Localization					*0.0007*
Proximal	8 (20.5)	0 (0.0)	4 (44.4)	0 (0.0)	
Middle	15 (38.5)	0 (0.0)	0 (0.0)	2 (28.6)	
Distal	16 (41.0)	17 (100)	5 (55.6)	5 (71.4)	
Length of perforation, cm					0.719
<3	22 (56.4)	11 (64.7)	6 (66.7)	5 (71.4)	
3–6	10 (25.6)	5 (29.4)	3 (33.3)	1 (14.3)	
>6	7 (17.9)	1 (5.9)	0 (0.0)	1 (14.3)	

Values are presented as *n* (% of group) and median (range).
Significant values are highlighted in italic.
ASA, American Society of Anesthesiologists.

total of 33 (45.8%) esophageal perforations were not contained. Of these, the majority (*n* = 21; 87.9%) was found in the distal part of the esophagus. Twenty-eight (84.8%) of all noncontained perforations were accompanied with pleural effusions and 3 (9.1%) perforations demonstrated a leakage into the abdominal cavity due to extension of the rupture into the abdominal part of the esophagus or proximal stomach. Two (6.1%) perforations showed a leakage into the thoracic as well as into the abdominal cavity. However, no significant correlation between location of the perforation and mortality was observed ($p = 0.871$).

The majority (*n* = 44; 61.1%) of the perforations were smaller than 3 cm. In 19 (26.4%) patients, the perforations were between 3 and 6 cm in size. Perforations exceeding the length of 6 cm were reported in 9 (12.5%) patients. An increasing size of esophageal perforations correlated with the presence of sepsis and ($p = 0.008$) also a trend toward an increased rate of mortality was seen ($p = 0.060$). No significant correlation between the size and cause of perforation was observed ($p = 0.719$). For further details, see Tables 1 and 2.

Sepsis and Initiation of Therapy

Twenty-nine patients (40.3%) presented with a septic condition at the time of diagnosis. In 36 (50.0%) patients, diagnosis and initiation of surgical treatment began 24 h after onset of symptoms. Within this group, 22 patients (61.1%) had sepsis at the beginning of therapy. All septic patients with initiation of surgical therapy 24 h after onset of symptoms were assigned to us from external clinics. A direct correlation between delayed surgical therapy and sepsis ($p = 0.002$) was observed. In addition, 25.0% of the patients with delayed treatment died in the course. Hence, a trend between delayed therapy and mortality was seen ($p = 0.058$). More esophagectomies without restoration of continuity were found in the group with surgical intervention after 24 h ($p = 0.044$). For further details, see Table 3.

Therapy

Six (8.3%) patients received an exploration, irrigation, and drainage of the infected area. One patient in this group had a perforation larger than 3 cm but was classified as inoperable due to a simultaneous extensive

Table 2. Analysis of surgical procedures in esophageal perforations

	Exploration and drainage (*n* = 6)	Primary suture and reinforcement patch (*n* = 26)	Esophagectomy and restoration of continuity (*n* = 18)	Esophagectomy without restoration of continuity (*n* = 22)	*p* value
Presence of sepsis	3 (50.0)	4 (15.4)	4 (22.2)	18 (81.8)	*<0.0001*
ASA score					*0.0013*
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
2	1 (16.7)	5 (19.2)	6 (33.3)	1 (4.5)	
3	3 (50.0)	14 (53.8)	11 (61.1)	7 (31.8)	
4	1 (16.7)	6 (23.1)	1 (5.6)	12 (54.5)	
5	1 (16.7)	1 (3.8)	0 (0.0)	2 (9.1)	
Mortality	1 (16.7)	4 (15.4)	1 (5.6)	6 (27.3)	0.339
Revision surgery	0 (0.0)	1 (3.8)	2 (11.1)	3 (13.6)	0.534
Length of stay, days	26.5 (10–63)	17.0 (1–52)	18.0 (10–109)	29.0 (6–109)	*0.012*
Localization					*0.018*
Cervical	3 (50.0)	6 (23.1)	2 (11.1)	1 (4.5)	
Thoracic	3 (50.0)	2 (7.7)	4 (22.2)	8 (36.4)	
Distal	0 (0.0)	18 (69.2)	12 (66.7)	13 (59.1)	
Length of perforation, cm					0.426
<3	5 (83.3)	17 (65.4)	10 (55.6)	12 (54.5)	
3–6	0 (0.0)	9 (34.6)	6 (33.3)	4 (18.2)	
>6	1 (16.7)	0 (0.0)	2 (11.1)	6 (27.3)	
Cause of rupture					0.693
Iatrogenic	4 (66.7)	12 (46.2)	12 (66.7)	11 (50.0)	
Boerhaave's syndrome	0 (0.0)	8 (30.8)	3 (16.7)	6 (27.3)	
Foreign body ingestion	2 (33.3)	5 (19.2)	1 (5.6)	1 (4.5)	
Chronic inflammation	0 (0.0)	1 (3.8)	2 (11.1)	4 (18.2)	

Values are presented as *n* (% of group) and median (range).
Significant values are highlighted in italic.
ASA, American Society of Anesthesiologists.

Table 3. Analysis of the effect of delayed therapy after onset of symptoms

	Initiation of therapy <24 h (*n* = 36)	Initiation of therapy >24 h (*n* = 36)	*p* value
Presence of sepsis	7 (19.4)	22 (61.1)	*0.002*
ASA score			*0.019*
1	0 (0.0)	0 (0.0)	
2	10 (27.8)	3 (8.3)	
3	18 (50.0)	17 (47.2)	
4	6 (16.7)	14 (38.9)	
5	2 (5.6)	2 (5.6)	
Mortality	3 (8.3)	9 (25.0)	*0.225*
Revision surgery	3 (8.3)	3 (8.3)	0.996
Length of stay, days	17.0 (10–109)	24.0 (1–109)	0.350
Surgical approach			*0.044*
Exploration and drainage	1 (2.8)	5 (13.9)	
Primary suture and reinforcement patch	18 (50.0)	8 (23.1)	
Esophagectomy and restoration of continuity	13 (36.1)	5 (22.2)	
Esophagectomy without restoration of continuity	4 (11.1)	18 (50.0)	

Values are presented as *n* (% of group) and median (range).
Significant values are highlighted in italic.
ASA, American Society of Anesthesiologists.

Table 4. Comparison of the low-, intermediate-, and high-risk PSS groups

	PSS <2 (*n* = 18)	PSS 3–5 (*n* = 29)	PSS >5 (*n* = 25)	*p* value
Age, years	64.0 (41–86)	70.0 (43–87)	65.0 (24–84)	0.935
Presence of sepsis	0 (0.0)	8 (27.6)	21 (84.0)	*<0.0001*
ASA score				0.063
1	0 (0.0)	0 (0.0)	0 (0.0)	
2	5 (27.8)	5 (17.2)	3 (12.0)	
3	8 (44.4)	18 (62.1)	9 (36.0)	
4	4 (22.2)	6 (20.7)	10 (40.0)	
5	1 (5.6)	0 (0.0)	3 (12.0)	
Mortality	1 (5.6)	3 (10.3)	8 (32.0)	*0.037*
Revision surgery	1 (5.6)	4 (13.8)	1 (4.0)	0.387
Length of stay, days	17.0 (10–52)	18.0 (9–109)	27.0 (1–109)	*0.046*
Surgical approach				*0.0002*
Exploration and drainage	1 (5.6)	2 (6.9)	3 (12.0)	
Primary suture and reinforcement patch	14 (77.8)	10 (34.5)	2 (8.0)	
Esophagectomy and restoration of continuity	3 (16.7)	11 (37.9)	4 (16.0)	
Esophagectomy without restoration of continuity	0 (0.0)	6 (20.7)	16 (64.0)	

Values are presented as *n* (% of group), median (range).
Significant values are highlighted in italic.
PSS <2 low-risk; PSS 3–5 intermediate risk; PSS >5 high-risk.
ASA, American Society of Anesthesiologists; PSS, Perforation Severity Score.

damage to the trachea. Half of the patients had sepsis at the time of surgery and the median ASA score was 3 (range 2–5). A suturing of the perforation with patch reinforcement was performed in 26 (36.1%) patients. In 65.4% (*n* = 17) of these patients, the perforation was <3 cm. The majority (*n* = 22; 84.6%) did not show any signs of sepsis and the median ASA score of this subgroup was 3 (range 2–5). Resection of the esophagus and direct restoration was performed in 18 (25.0%) patients. The majority of these patients (*n* = 12; 66.7%) had an iatrogenic perforation and only 4 (22.2%) patients were septic. The median ASA score was 3 (range 2–4). A discontinuity resection was performed in 22 (30.5%) patients. The majority of the latter patients (*n* = 18; 81.8%) were in septic condition at the time of surgery. Patients with a discontinuity resection had a median ASA score of 4 (range 2–5). For further details, see Table 2.

Interestingly, a strong correlation between the surgical technique and sepsis was observed indicating more discontinuity resections in septic patients and less aggressive approaches in no-septic patients ($p < 0.0001$). In addition to the latter, a correlation between the surgical technique and the ASA score was found demonstrating an impaired general health status in patients treated with discontinuity resections ($p = 0.0013$).

Revision surgeries (4 decortications and irrigations, 1 replacement of the feeding jejunostomy, and 1 resection of the gastric tube) were necessary in 6 (8.3%) patients. Neither was a significant correlation between the rates of revision surgeries within the surgical techniques observed ($p = 0.534$) nor did the number of revision surgeries correlate with mortality ($p = 0.993$).

Perforation Severity Score

Eighteen (25.0%) of the patients were categorized in the low-risk PSS group (score ≤2), 29 (40.3%) in the intermediate-risk PSS group (score 3–5), and 25 (34.7%) in the high-risk PSS group (score >5). A median PSS of 4 (range 0–14) was calculated. Eight of the 12 (66.7%) deceased patients were found in the high-risk PSS group and 3 (25.0%) deceased patients were in the intermediate-risk PSS group. Only one (8.3%) of the deceased patients was in the low-risk PSS group. Hence, a significant correlation between mortality and the PSS groups was found ($p = 0.037$). In addition, a strong correlation between the PSS group and the surgical approach was found ($p = 0.0002$), indicating more discontinuity resections in the high-risk PSS group. We also observed a significant longer hospitalization from the low- to the high-risk PSS group ($p = 0.046$). For further details, see Table 4.

Table 5. Analysis of patient survival

	Alive (n = 60)	Dead (n = 12)	p value
Age, years	66.0 (24–84)	77.5 (55–87)	*0.006*
Presence of sepsis	22 (36.7)	7 (58.3)	0.226
ASA score			*0.002*
1	0 (0.0)	0 (0.0)	
2	13 (21.7)	0 (0.0)	
3	32 (53.3)	3 (25.0)	
4	12 (20.0)	8 (66.7)	
5	3 (5.0)	1 (8.3)	
Revision surgery	6 (10.0)	0 (0.0)	0.993
Length of stay, days	20.5 (9–109)	20.5 (1–109)	0.593
Surgical approach			0.404
Exploration and drainage	5 (8.3)	1 (8.3)	
Primary suture and reinforcement patch	22 (36.7)	4 (33.3)	
Esophagectomy and restoration of continuity	17 (28.3)	1 (8.3)	
Esophagectomy without restoration of continuity	16 (26.7)	6 (50.0)	
Length of perforation, cm			0.060
<3	39 (65.0)	5 (41.7)	
3–6	16 (26.7)	3 (25.0)	
>6	5 (8.3)	4 (33.3)	
Cause of perforation			0.708
Iatrogenic	31 (51.7)	8 (66.7)	
Boerhaave's syndrome	16 (26.7)	1 (8.3)	
Foreign body ingestion	9 (15.0)	0 (0.0)	
Chronic inflammation	4 (6.7)	3 (25.0)	
PSS			*0.018*
<2	17 (28.3)	1 (8.3)	
3–5	26 (43.4)	3 (25.0)	
>5	17 (28.3)	8 (66.7)	

Values are presented as n (% of group) and median ± range.
Significant values are highlighted in italic.
PSS <2 low-risk; PSS 3–5 intermediate risk; PSS >5 high-risk.
ASA, American Society of Anesthesiologists; PSS, Perforation Severity Score.

Mortality

The median hospital stay was 20.5 days (range 1–109 days), and a mortality rate of 16.7% (12 of 72 patients) was found. Significantly more patients with higher age were found in the deceased group (p = 0.006). Half of the deceased patients (n = 6; 50.0%) had discontinuity resections. Most of the deceased patients (n = 9; 75.0%) had an ASA score of 4 or greater. Hence, a difference in the ASA scores between alive and deceased patients was found (p = 0.002). PSS score was also significantly higher in the deceased group (p = 0.018). In addition, a trend toward an increased mortality for patients with longer perforations was found (p = 0.060). Survival within the surgical approaches did not differ significantly (p = 0.404). See Table 5 for more details.

To further analyze the influence of the investigated parameters on mortality, we performed a multivariate logistic regression analysis (Table 6). The highest prediction of mortality was achieved by the PSS (OR 4.430; 95% CI 1.143–17.174; p = 0.031) and ASA score (OR 2.923; 95% CI 1.011–8.448; p = 0.048). Of the remaining parameters, only age (OR 1.076; 95% CI 1.0–1.158; p = 0.049) was significantly associated with reduced survival.

Discussion

A perforation of the esophagus remains a clinical challenge in terms of diagnosis and treatment and is still associated with a high mortality. In our retrospective study, we reported a mortality rate of 16.7%. This is in line with

Table 6. Prediction of mortality by clinical parameters

	OR	95% CI	*p* value
Age, years	1.076	1.0–1.158	*0.049*
Cause of perforation	1.194	0.628–2.267	0.589
Initiation of treatment	1.159	0.175–7.692	0.879
Presence of sepsis	0.202	0.020–2.046	0.176
Surgical approach	0.707	0.266–1.881	0.487
Length of perforation	2.779	0.845–9.134	0.092
PSS	4.430	1.143–17.174	*0.031*
ASA score	2.923	1.011–8.448	*0.048*

Significant values are highlighted in italic.

Cause of perforation: iatrogenic, Boerhaave's syndrome, foreign body ingestion, complication of chronic inflammation; initiation of surgical therapy: <24 h; >24 h; surgical approach: exploration and drainage, primary suture and patch reinforcement, esophagectomy and restoration of continuity, esophagectomy without restoration of continuity; PSS <2 low-risk; PSS 3–5 intermediate risk; PSS >5 high-risk.

ASA, American Society of Anesthesiologists; PSS, Perforation Severity Score.

other studies describing up to 18% mortality in esophageal perforations [1, 10, 11, 16, 17]. Of the patients enrolled in this study, 54.2% had iatrogenic and 23.6% spontaneous ruptures due to Boerhaave's syndrome. Similar results have been reported before [1, 8, 15]. In a meta-analysis by Sdralis et al. [10], a total of 885 patients were investigated demonstrating iatrogenic events to be the cause of perforations in 46.5%, while spontaneous perforation represented 37.8% of the esophageal ruptures. Schweigert et al. [8] reported spontaneous perforations in 41.3% and iatrogenic ruptures in 29.5% of 288 analyzed patients. As in this study, the cause of perforation did not influence mortality. The highest mortality was found in patients with ruptures due to complications of a chronic esophageal inflammation. Interestingly, this group showed the highest age among all investigated causes of perforations with a median age of 76.0 years. In line with our multivariate analysis, recovery from the disease seems to be more complicated with increased age (OR 1.076; 95% CI 1.0–1.158) leading to a higher mortality. In addition, proper treatment is usually delayed in these patients due to difficulties in detecting ruptures within the inflammatory environment. This is reflected by the fact that treatment was initiated 24 h after onset of symptoms in 85.7% of the patients. Hence, the majority (71.4%) already presented in septic conditions. Of note, chronic inflammation not only leads to perforations but also alters the remaining esophageal mucosa necessitating an extended resection. In addition, resections in these patients are surgically challenging since the surrounding esophageal tissue is often fibrotic due to the underlying chronic disease. Hence, chronic inflammation makes either reconstruction with a direct suture or resection with primary anastomosis difficult leading to a higher rate of esophagectomies without restoration of continuity.

In our study, the most common site of perforation was the distal part of the esophagus (59.7%). Interestingly, the majority of patients (58.3%) who died during hospital stay showed ruptures in the distal part of the esophagus followed by patients (33.3%) with ruptures in the middle third of the esophagus, although no significant correlation with mortality was observed. On the contrary, other studies have shown that mortality rates are higher in patients with perforations in the middle and distal part of the esophagus [1, 2, 8, 17]. However, none of the studies excluded patients with esophageal malignancies, which commonly arise in the distal third of the esophagus. Hence, these perforations might be overrepresented and a worse clinical outcome could be predetermined. In our study, patients with longer esophageal perforations showed a tendency toward higher mortality. This can be explained by an increasing contamination of the paraesophageal tissue, which consecutively increases the rate of mediastinitis and sepsis. This fact was also reflected in our data, since the length of the esophageal perforations significantly correlated with the presence of sepsis (p = 0.008).

Many authors consider the time of diagnosis and the start of proper treatment as the most important factor for outcome in patients with esophageal perforations. The literature refers to a time window of 24 h for initiation of therapy in order to improve survival since delayed diagnosis allows an invasion of bacteria and the formation of mediastinitis and sepsis [8, 9, 17]. Eroglu et al. [17] showed that patients with early diagnosis and treatment had mortality rates of 3%, while patients with delayed therapy had mortality rates of 36%. In addition, Shaker et al. [9] reported significantly lower mortality rates in patients treated early. In our study, initiation of treatment 24 h after onset of symptoms significantly correlated with the presence of sepsis ($p < 0.002$) and also 25.0% of the patients with sepsis died. Hence, our findings are in line with the latter reports demonstrating the importance of immediate treatment. To further address the issue of sepsis and delayed therapy, Abbas et al. [11] developed the PSS. In addition to the latter factors, they added other clinical parameters like pleural effusion, noncontained leak, respiratory compromise, and the presence of cancer.

By using the PSS, a stratification into a low-, intermediate- and high-risk group with a significant correlation to morbidity and mortality was achieved [11]. When applying the PSS to our cohort of nonmalignant esophageal perforations, the majority of the high-risk patients were found in the group with therapy 24 h after onset of symptoms ($p < 0.0001$) and the PSS correlated with mortality ($p = 0.037$). In addition, the PSS was the strongest predictor of mortality in multivariate analysis with an OR of 4.43 (95% CI 1.143–17.174). Reflecting the severity of esophageal perforations, more discontinuity resections were observed in the high-risk PSS group ($p = 0.0002$) and patients had a longer time of hospitalization ($p = 0.046$). Primary repairs and exploration and drainage were more frequently performed in the low- or intermediate-risk groups. These data support a recent report of Schweigert et al. [8], who also found an increased mortality of 37.5% in the high-risk PSS group as compared to the low- (3.2%) and intermediate-risk (7.0%) groups. Hence, they suggested a more aggressive treatment in the high-risk group to avoid fatal outcome. A disadvantage of the PSS is the missing inclusion of comorbidities. This assessment is found in the ASA score, which also significantly correlated with mortality and delayed initiation of therapy in our study ($p = 0.002$ and $p = 0.019$, respectively). In addition, the ASA score was the second strongest predictor of mortality (OR 2.923; 95% CI 1.011–8.448) in multivariate analysis. This is in line with Hermansson et al. [18], who also found an association between ASA score and mortality in 125 patients with esophageal perforations.

In the treatment of esophageal rupture, it is necessary to remediate the septic focus. Until now, no standard has been established for optimal care. Some authors prefer immediate surgical reconstruction of the defect. Kiernan et al. [19] as well as Sung et al. [20] recommend a surgical approach irrespective of the elapsed time after diagnosis. In principle, a rigorous rinse of the mediastinum, antibiotic treatment, and a sufficient nutrition should be achieved. In our cohort, most of the patients were treated with esophagectomy and primary restoration of continuity. In this subgroup, only 2 revision surgeries and 1 in-hospital death occurred despite a high PSS score. These findings encourage the use of the latter procedure in esophageal perforations. However, a primary repair may not be feasible in the presence of advanced mediastinitis or if a suture or anastomosis has to be placed in an infected area. In this situation, discontinuity resections may be the approach of choice [21, 22]. Despite the aggressive approach in the high-risk PSS group, no correlation between the surgical approach and mortality was found. In addition, no significant difference between the surgical approaches and the number of revision surgeries was found. Hence, an aggressive approach in already ill patients seems to be feasible to control the septic focus and improve patient outcome. Another problem occurring in patients with esophageal perforations is malnutrition. To achieve proper nutrition, we try to sustain enteral continuity by performing a primary anastomosis or direct suture whenever possible. In addition, we have adapted the ERAS (Enhanced Recovery after Surgery) program for all elective esophageal surgeries since 2017 [23, 24]. This program provides a fast reintroduction of postoperative feeding and improves restoration of physiologic bowel movement. Patients with emergency esophagectomies are also fed according to the ERAS protocol and are frequently evaluated together with a nutritional care team. However, for patients with esophagectomies without restoration of continuity, the ERAS protocol cannot be applied. Hence, these patients are enterally fed by a gastrostomy or jejunostomy with Fresubin® according to the basal daily calorie need, which is calculated in relation to body weight (calorie need = weight × factor × 24 kcal). In steady metabolic state, a factor of 1.0 is used. For patients with esophagectomies without restoration of continuity, a factor of 1.4 is applied to compensate for the higher metabolic need.

In this study, we focused on the surgical treatment of esophageal perforations only. Nevertheless, it is becoming evident that due to the rapid development of endoscopic techniques, a selected subgroup of patients (patients without sepsis and contained leaks) may be eligible for nonoperative management. However, based on our experience of treating complications after oncologic esophagectomies, placement of stents in an already inflamed area on the background of mediastinitis is associated with an increased rate of complications (e.g., arrosion of the esophagus and recurrent stent dislocations). In addition, despite advances in intensive care medicine, mortality and morbidity remain high within these patients and delayed proper management might result in fatal outcomes. In a review on benign esophageal leaks analyzing 267 patients, who were treated with self-expandable stents, a clinical success was achieved in 85% of the patients with a mortality rate of 13%. Notably, in 13% of the patients, surgery was necessary later on due to complications with the stents [25]. Hence, our center has preferred an upfront surgical approach until now. Nevertheless, an increasing number of patients with esophageal ruptures are treated endoscopically ($n = 6$ in 2016 and $n = 10$ in 2017) in our center over the last years. This indicates a change in decision making especially in patients, who are not septic and have smaller esophageal perforations in which stents can be properly placed. Thus, the PSS might be a useful tool to objectively identify patients, in whom a primary endoscopic approach should be further taken into account. In addition, recent reports have added endoluminal vacuum sponges as another potential tool in treating esophageal perforations with promising results [13, 26, 27]. Especially in the background of failure of the surgical repair or small defects, endoluminal vacuum therapy seems to be beneficial. Of note, time of hospitalization after endoscopic treatment has been reported between 21 and 54 days due to numerous interventions [13, 26, 27]. In our study, the median length of hospital stay was 20.5 days, which is shorter as compared to Schweigert et al. [8], reporting a median length of stay of 31 days. Length of hospitalization seems to be reduced in surgically treated patients, even though a majority of these patients presented with severe perforations. Hence, a shortened hospitalization might be favored by the immediate and complete renovation of the septic focus.

Conclusion

In conclusion, a rapid diagnosis and treatment to eliminate the septic focus are essential for patient survival. In surgical treated esophageal perforations, PSS and ASA score adequately assess the risk of patients' mortality. In patients with low or intermediate PSS, a direct repair with patch reinforcement or esophagectomy with anastomosis seems feasible, while in patients with a high-risk PSS, esophagectomy without restoration of continuity should be taken into account. However, the choice of the surgical approach should be adapted to the individual patient. Due to the rarity of the disease and the heterogeneous patient, collective prospective studies will be difficult to conduct although they are needed urgently.

Statement of Ethics

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

Disclosure Statement

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