Retrospective Cohort Study

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Clinical efficacy of different therapeutic strategies in patients with spontaneous rupture of the esophagus: a multicenter retrospective cohort study

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Background: The therapeutic strategy for patients with spontaneous rupture of the esophagus includes surgical repair, endoscopic therapy, supportive care, and others. However, no evidence exists to direct clinical decision-making regarding the choice of operative and nonoperative management. This study aimed to determine the clinical efficacy of different therapeutic strategies in both general and stratified patients.

Methods: This study retrospectively analyzed a consecutive cohort of 101 patients at nine tertiary referral hospital centers in China. Patients were divided into operative and nonoperative groups based on the initial treatment. Short-term outcomes, including 90-day mortality, length of hospital stay, and postoperative leakage, were compared. Subgroup analysis was performed based on treatment timing and Pittsburgh perforation severity score.

Results: Of 101 patients, 60 (58.4%) underwent operative management. A significant difference in 90-day mortality between operative and nonoperative groups was observed (15.0 vs. 34.1%; $P = 0.031$). Operative management tends to yield similar therapeutic benefits in timely [odds ratio (OR), 0.250; 95% confidence interval (CI), 0.05–1.14; $P = 0.073$) and delayed (OR, 0.42; 95% CI, 0.12–1.47; $P = 0.175$) treatment groups. Based on perforation severity score stratification, operative management significantly decreased the risk of 90-day mortality (OR, 0.211; 95% CI, 0.064–0.701; $P = 0.011$) for patients in low-risk and moderate-risk groups but may be detrimental for patients in high-risk group (OR, 1.333; 95% CI, 0.233–7.626; $P = 0.746$).

Conclusions: Operative management might be superior to nonoperative management for low-risk and moderate-risk patients with spontaneous rupture of the esophagus. However, for patients at high risk, operative management might not provide additional benefits compared with nonoperative management. Further research involving larger sample sizes is required for accurate patient stratification and conclusive evidence-based guidelines.

Keywords: 90-day mortality, Boerhaave's syndrome, operative management, patient stratification, spontaneous rupture of the esophagus

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Introduction

Boerhaave's syndrome (BS), also referred to as spontaneous rupture of the esophagus, is a rare but lethal surgical emergency that Hermann Boerhaave first reported in 1724[1,2]. The treatment of BS is a clinical challenge due to the rarity of the disease and unstandardized management strategies[3–5]. Although operative management has been considered the top priority in most cases[6–10], arguments have emerged that primary surgical repair is available only when the interval between onset and initial treatment is less than 24 h[11,12]. Nonoperative methods, such as stent placement via endoscopy, have gradually become useful replacements for surgery, especially for patients identified late or who cannot tolerate operative procedures[13,14]. However, endoscopic stenting might lead to a higher risk of treatment failure and additional surgical interventions[15]. To date, there is no universal consensus about the clinical decision-making regarding the management of BS. The criteria for canceling surgery and using conservative treatment among different practitioners were heterogeneous and ambiguous, including treatment timing, symptoms, signs of sepsis, imaging findings, and drainage efficiency[6,11,12,16]. Determining the applicability of operative and nonoperative management to yield the best therapeutic benefits is still a thorny issue for emergency specialists, surgeons, and healthcare personnel.

The objective of this multicenter retrospective cohort study is to compare the clinical efficacy of different therapeutic strategies in patients with spontaneous rupture of the esophagus. The primary outcome was all-cause 90-day mortality, and the secondary outcomes were the length of hospital stay (LOS) and postoperative leakage. We aim to compare the outcomes between the patients who underwent operative and nonoperative management and determine the optimal therapeutic strategy in risk-stratified patients. We hypothesized that, based on appropriate patient stratification, operative management decreases the risk of unfavorable outcomes on most occasions, while nonoperative management serves as an alternative when surgery is unavailable.

HIGHLIGHTS

- Operative management decreased the risk of 90-day mortality for low-risk/moderate-risk patients with spontaneous rupture of the esophagus.
- Operative management might not provide additional benefits for high-risk patients compared with nonoperative management.
- Delay in treatment might not be an indicator excluding surgery from consideration.

Patients and methods

Ethics and registration statement

This study was approved by the institutional review board of all the participating institutions, which also waived the need for written informed consent. This study was retrospectively registered in the Chinese clinical trial registry, where the protocol could be found.

Study design and patient population

This is a retrospective, multicenter cohort study. The clinical data were retrieved from the electronic medical record system of nine tertiary referral hospital centers (Supplementary file, Supplemental Digital Content 2, http://links.lww.com/JS9/D5). The work has been reported in line with the STROCSS criteria, Supplemental Digital Content 1 (http://links.lww.com/JS9/D4)[17].

This study included consecutive patients 18 years or older who had esophageal rupture confirmed by contrast esophagogram, computed tomography scan, endoscopy, or surgery between April 16, 2006 and April 5, 2020. Patients with iatrogenic, traumatic, caustic, foreign-body-induced, or malignancy-induced esophageal perforation were excluded from the study. Because of the retrospective design, patients were only involved in the follow-up stage of the study.

Patients were divided into two groups based on the treatment strategy: operative management group and nonoperative management group. Because of a lack of standardized management guidelines, the choice of therapeutic strategy in this multicenter cohort depended on practitioners' experience, hospital volume, and patients' intent. Thoracic/mediastinum debridement with or without primary repair, intraoperative chest/mediastinum drainage tube placement, and esophagectomy combined with gastric reconstruction were defined as 'operative management.' Endoscopic approaches, chest tube insertion, and supportive care without any surgical procedure were defined as 'nonoperative management.' Supportive care included avoidance of oral feeding, broad-spectrum antibiotics, nutritional support, and other symptomatic treatments, which were administered to almost all the included patients.

Outcomes

The primary outcome of this study was all-cause 90-day mortality, including in-hospital death, death after discharge, and death after transfer to other institutions, which were collected by retrieving medical records or telephone interviewing. The secondary outcomes were LOS and postoperative leakage; the former was measured in all the patients, and the latter was measured in patients undergoing primary surgical repair. Postoperative leakage was confirmed by contrast esophagography or the presence of oral agent in the drainage tube.

Data collection and definition

Before medical intervention, history collection, physical examination, and hematological tests were performed. Patients with suspected esophageal perforation underwent computed tomography scan, contrast esophagogram, or endoscopy. Age, sex, rupture size, rupture site (thoracic upper, middle, lower esophagus, and abdominal esophagus), involvement of adjacent structures, and conditions on admissions (respiratory failure, temperature, tachycardia, leukocytosis, pleural effusion, noncontained leak, hypotension, interval between onset and treatment, and sepsis) were collected. Rupture size was defined as the maximum diameter of the rupture estimated by digital radiography, endoscopy, or intraoperative measurement. The involvement of adjacent structures was defined as any structural damage, air collection, fluid contamination, or inflammatory response in the mediastinum or pleural cavities, such as massive or encapsulated pleural effusion, pyopneumothorax, hemopneumothorax, and mediastinal abscess. A noncontained leak was

defined as free extravasation of contrast medium in the mediastinum and pleural cavities. Sepsis was confirmed by SIRS criteria combined with clinical suspicion or microbiological evidence of infection. The interval between onset and treatment of less than 24 h was defined as timely treatment, whereas the rest of the cases were defined as delayed treatment.

Patient stratification

Two types of patient stratification, respectively, based on treatment timing and the Pittsburgh perforation severity score (PSS), were performed for subgroup analysis. PSS was a scoring system used for evaluating the seriousness of esophageal perforation and predicting short-term mortality[18,19]. Based on the PSS score, patients were categorized into three risk groups, and those with higher scores were considered to be at higher risk of mortality and morbidity.

Sample size

The power for the primary endpoint was calculated based on Fisher's exact test with a significance level of 5%. With a sample size of 60 subjects treated with operative management and 41 subjects treated with nonoperative management, the study will have 78% power to detect a difference between the operative and nonoperative groups in the proportion of 90-day mortality, given that the probabilities were approximately 12% for operative management and 35% for nonoperative management, based on previous literature and preliminary analysis of our cohort[10,11,20,21].

Statistical analysis

Continuous and categorical variables were described as median [interquartile range (IQR)] and the number of cases (percentage), respectively. The Mann–Whitney U test was used to compare continuous variables, and χ^2 or Fisher's exact test was used for categorical variables. Logistic regression analysis was applied to estimate the odds ratio (OR) and 95% confidence interval (CI). Statistical analyses were conducted using SPSS, version 26.0. The R package 'forester' was used to create the forest plot. A two-sided P value less than 0.05 was considered to be statistically significant.

Results

Patient characteristics

Clinical characteristics and outcomes of 101 enrolled patients were outlined in Table 1. Of these patients, 95 (94.1%) were men, and six (5.9%) were women. The median age was 53.0 (IQR, 43.0–63.5) years. Seventy-nine (77.5%) patients were between 40 and 69 years of age. Sixty-three (63.4%) patients complained of vomiting as the initial symptom. The median rupture size was 4.0 cm (IQR, 2.0–5.0 cm), with a 0.2–10 cm range. The thoracic lower esophagus had the highest frequency (83.2%) of spontaneous rupture. The rupture usually involves the left pleural cavity (51.5%). The rupture involving bilateral pleural cavities was found in six (5.9%) cases. The median LOS was 23.0 (IQR, 16.0–40.5) days. During the 90 days after the initial treatment, 23 (22.8%) deaths were observed.

Table 1

Clinical characteristics of 101 patients undergoing operative and nonoperative management.

Clinical characteristics	Total, $n=101$	Operative management, $n=60$	Nonoperative management, $n=41$	P
Age, median (IQR), years	53.0 (43.0–63.5)	53.5 (45.0–65.0)	52.0 (40.5–62.5)	0.395
Male, *N* (%)	95 (94.1)	58 (96.7)	37 (90.2)	0.220
Rupture size, median (IQR), cm	4.0 (2.0–5.0)	4.0 (3.0–6.0)	2.0 (1.0–4.0)	< 0.001
Rupture site, *N* (%)				0.726
Thoracic upper esophagus	2 (2.0)	2 (3.3)	0	
Thoracic middle esophagus	12 (11.9)	6 (10.0)	6 (14.6)	
Thoracic lower esophagus	84 (83.2)	50 (83.3)	34 (82.9)	
Abdominal esophagus	3 (3.0)	2 (3.3)	1 (2.4)	
Involvement of adjacent structures, *N* (%)				0.555
None or be confined to mediastinum	11 (10.9)	6 (10.0)	5 (12.2)	
Left pleural cavity	52 (51.5)	33 (55.0)	19 (46.3)	
Right pleural cavity	32 (31.7)	19 (31.7)	13 (31.7)	
Bilateral pleural cavities	6 (5.9)	2 (3.3)	4 (9.8)	
Conditions on admission, *N* (%)				
Respiratory failure	15 (14.9)	9 (15.0)	6 (14.6)	1.000
Temperature > 38.5°C	19 (18.8)	9 (15.0)	10 (24.4)	0.302
Tachycardia	34 (33.7)	20 (33.3)	14 (34.1)	1.000
Leukocytosis	50 (49.5)	31 (51.7)	19 (46.3)	0.687
Pleural effusion	96 (95.0)	56 (93.3)	40 (97.6)	0.646
Noncontained leak	92 (91.1)	55 (91.7)	37 (90.2)	1.000
Hypotension	7 (6.9)	4 (6.7)	3 (7.3)	1.000
Interval between onset and treatment > 24 h	58 (57.4)	30 (50.0)	28 (68.3)	0.101
Sepsis	20 (19.8)	13 (21.7)	7 (17.1)	0.620
Pittsburgh perforation severity score, median (IQR)	3 (2–5)	3 (2–5)	3 (2–4)	0.194
Postoperative leakage, *N* (%)	9 (8.9)	9 (18.0)	NA	NA
Length of hospital stay, median (IQR), days	23.0 (16.0–40.5)	22.0 (16.3–34.5)	25.0 (14.5–52.5)	0.455
90-day mortality, *N* (%)	23 (22.8)	9 (15.0)	14 (34.1)	0.031

IQR, interquartile range.

Short-term outcomes of patients undergoing operative and nonoperative management

Of the 101 patients, 60 (58.4%) patients underwent operative management, including three who crossed over from nonoperative management. In the operative group, 50 patients underwent primary surgical repair, five patients underwent surgical debridement without primary repair, two patients underwent surgical debridement plus endoscopic stent placement, and three patients underwent esophagectomy combined with gastric reconstruction. In the nonoperative group ($n=41$), 11 patients underwent endoscopic stent placement, one patient underwent endoscopic clip therapy, one patient underwent endoscopic clip therapy plus flap transplantation, 21 patients underwent chest tube insertion, and seven patients underwent supportive care without any other intervention. The 90-day mortality of each therapeutic approach is listed in Table 2.

The baseline characteristics, including demographic features, clinical conditions on admission, and PSS scores, were comparable between operative and nonoperative groups except for the rupture size (Table 1). Patients who underwent nonoperative management had worse 90-day mortality than patients who underwent surgery (34.1 vs. 15.0%; $P=0.031$), even if the rupture size in the operative group was significantly larger than the nonoperative group (4.0 vs. 2.0, $P<0.001$). When we put three cross-over cases back into the nonoperative group, the 90-day mortality of patients who underwent nonoperative management was still higher than that of the patients who underwent surgery (34.1 vs. 14.0%; $P=0.030$). Logistic regression analyses showed that operative management decreased the risk of 90-day mortality (OR, 0.34; 95% CI, 0.131–0.888; $P=0.028$). Although delayed treatment increased the risk of 90-day mortality (OR, 1.202; 95% CI, 0.465–3.106), the P value (0.704) was not statistically significant. This negative finding negated the decisive role of treatment timing in clinical decision-making.

Regarding the secondary outcomes, the median LOS was 22.0 (IQR, 16.3–34.5) days and 25.0 (IQR, 14.5–52.5) days in the operative and nonoperative groups, respectively. The P value (0.455) suggested that there was no clinically meaningful difference. Postoperative leakage was observed in nine patients, accounting for 18% of the patients undergoing primary surgical repair. This event may slightly increase the LOS (27.89 vs. 23.76; $P=0.901$) but was not significantly associated with a high risk of 90-day mortality (OR, 2.057; 95% CI, 0.330–12.809; $P=0.439$).

Table 2

Therapeutic approaches and corresponding 90-day mortalities.

Therapeutic approaches	Cases (%)	90-day mortality (%)
Operative management ($n=60$)		
Primary surgical repair	50 (83.3)	7 (14)
Surgical debridement without primary repair	5 (8.3)	0
Surgical debridement plus endoscopic stent placement	2 (3.3)	0
Esophagectomy combined with gastric reconstruction	3 (5.0)	2 (66.7)
Nonoperative management ($n=41$)		
Endoscopic stent placement	11 (26.8)	4 (36.4)
Endoscopic clip therapy	1 (2.4)	0
Endoscopic clip therapy plus flap transplantation	1 (2.4)	0
Chest tube insertion	21 (51.2)	7 (33.3)
Supportive care without any other intervention	7 (17.1)	3 (42.9)

Subgroup analysis based on treatment timing and perforation severity score risk stratification

Given that operative management decreased the risk of 90-day mortality in the entire BS cohort, we then performed subgroup analysis to evaluate whether operative management could yield therapeutic benefits among specific subpopulations. Firstly, patients were divided into two subgroups by treatment timing. There were 30 operative cases, and 13 nonoperative cases underwent timely treatment (< 24 h), while 30 operative cases and 28 nonoperative cases underwent delayed treatment (≥ 24 h). The results showed that the OR values of 90-day mortality were similar between timely (OR, 0.250; 95% CI, 0.05–1.14; $P=0.073$) and delayed (OR, 0.42; 95% CI, 0.12–1.47; $P=0.175$) treatment groups (Fig. 1). Moreover, among the operative cases, the 90-day mortality of patients who received timely treatment was not superior to those who received delayed treatment (13.3 vs. 16.7%, $P>0.999$), and the postoperative leakage rates were also similar (16.7 vs. 13.3%, $P>0.999$).

Patients were then categorized into low-risk (score ≤2, $n=27$), moderate-risk (3 < score <5, $n=52$), and high-risk (score ≥6, $n=22$) groups based on PSS stratification (Table 3). As the risk level rose, the 90-day mortality was higher, and the LOS was longer. There were 19 (70.4%), 31 (59.6%), and 10 (45.5%) operative cases in the low-risk, moderate-risk, and high-risk groups, indicating that operative management was more likely to be selected for the patients with lower PSS. Importantly, operative management decreased the risk of 90-day mortality in the low-risk group (OR, 0.009; 95% CI, 0.01–1.09; $P=0.059$) and moderate-risk group (OR, 0.30; 95% CI, 0.07–1.19; $P=0.086$), and the upper bond of the 95% CI was less than 1 when the two groups were combined for analysis (OR, 0.211; 95% CI, 0.064–0.701; $P=0.011$). After adjusted by potential confounding factors, the result (Supplementary file, Supplemental Digital Content 2, http://links.lww.com/JS9/D5) still showed that operative management significantly decreased the risk of fatal outcome compared with nonoperative management (OR, 0.094; 95% CI, 0.016–0.550; $P=0.009$). However, for patients in the high-risk group, operative management might not provide any significant therapeutic benefit (OR, 1.33; 95% CI, 0.23–7.63; $P=0.746$) (Fig. 1).

Discussion

Spontaneous rupture of the esophagus is distinguished from traumatic or iatrogenic esophageal rupture and perforation. Most cases directly break into the pleural cavity and form a hydropneumothorax, while others may first be confine within the mediastinum, and then involve the chest cavity several hours or days later[21]. The stomach and esophageal contents quickly enter the nearby mediastinum and pleural cavities promoted by vomiting-induced high pressure, leading to a cascade of events, including mediastinal and pleural contamination, toxin absorption, and robust inflammatory response[22]. Without timely diagnosis and effective treatment, the general condition can

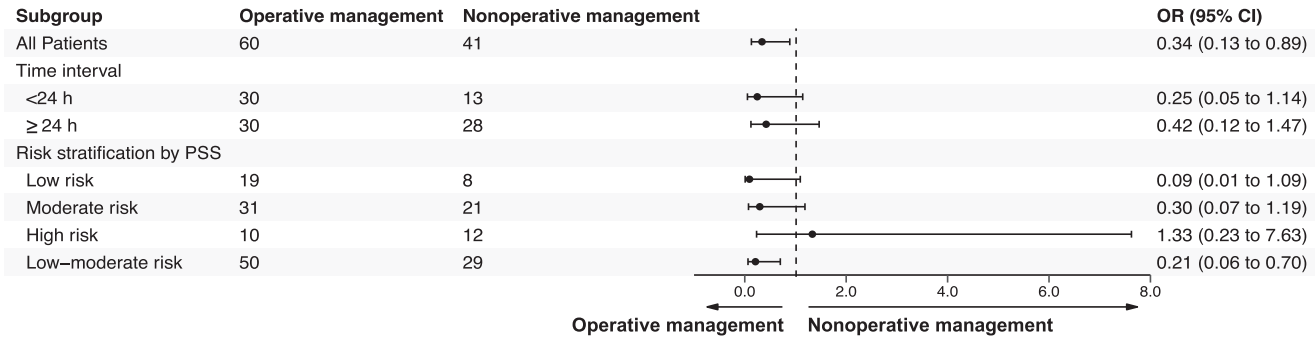

Figure 1. Subgroup analysis of operative management in 90-day mortality stratified by treatment timing and Pittsburgh perforation severity score.

deteriorate quickly, and patients eventually die from septic shock, acidosis, severe infection, and respiratory failure. Operative management is currently the most effective method for wound closure and debridement[10], while conservative or endoscopic treatment is recommended for patients who are not suitable for surgery. We hypothesized that, based on appropriate patient stratification, operative management decreases the risk of unfavorable outcomes on most occasions, while nonoperative management serves as an alternative when surgery is unavailable.

In this study, short-term outcomes were compared between patients undergoing operative and nonoperative management based on a multicenter retrospective BS cohort. Our results suggested that operative management yielded better short-term outcomes and decreased the risk of 90-day mortality compared with nonoperative management, which was in line with several previous literature. Wang *et al*.[21] reported a significant difference between patients who underwent surgical and conservative interventions (2/12, 16.7% vs. 3/3, 100%; $P = 0.022$). A retrospective study comparing primary operative management with endoscopic stent insertion found that the odds for fatal outcomes were 3.3 times higher in the endoscopic group compared with the operative group (OR, 3.32; 95% CI, 0.15–213.98)[15]. They also concluded that endoscopic stent placement offered no advantage regarding comorbidity, intensive care unit, or hospital stay but frequently led to treatment failure requiring surgical intervention. However, these results cannot be simply interpreted as operative management is superior to nonoperative management since the optimal choice for each patient largely depends on the status of the disease at presentation. Therefore, patient stratification is of critical significance for treatment selection. Our results suggested that operative management was more appropriate than nonoperative management for patients in low-risk and moderate-risk groups (OR, 0.21; 95% CI, 0.06–0.70), which accounted for 78.2% of the cohort. Conversely, operative management tended to result in unfavorable outcomes for patients in a high-risk group (OR, 1.33; 95% CI, 0.23–7.63); thus, it should be carefully considered to avoid excessive medical intervention.

Given that the OR values for timely treatment (OR, 0.250; 95% CI, 0.05–1.14) and delayed treatment (OR, 0.42; 95% CI, 0.12–1.47) subgroups were similar and that operative management tended to decrease the risk of 90-day mortality in both subgroups, delay in treatment was not an indicator excluding surgery from consideration. This standpoint has been supported by increasing evidence. By retrospectively studying 25 patients who were operated on by surgery, Jougon *et al*.[20] found that there was no significant difference in in-hospital mortality between the early group and the late group (44 vs. 13%), indicating that surgical primary repair could be performed whatever the interval was. Similar findings were published by Lawrence *et al*.[9], who reported acceptable mortality (17.6%, $n = 17$) of patients underwent operative management, even though most patients received treatment more than 24 hours. In another cohort of 10 BS patients operated on by surgery, including five patients who experienced delayed treatment, no operative mortality was observed, and all postoperative complications were controllable[23].

Based on our results, we suggested a PSS-based clinical algorithm for the management of BS (Fig. 2). History collection, hematological test, and imaging examination should be performed on admission for early diagnosis and rapid decision-

Table 3

Treatments and outcomes of patients stratified by Pittsburgh perforation severity score.

	Low-risk group (score ≤2), *n* = 27	Moderate-risk group (score 3–5), *n* = 52	High-risk group (score ≥6), *n* = 22	*P*
Treatment				0.216
Operative management, *N* (%)	19 (70.4)	31 (59.6)	10 (45.5)	
Nonoperative management, *N* (%)	8 (29.6)	21 (40.4)	12 (54.5)	
Outcome				
Length of hospital stay, median (IQR), days	21.0 (14.0–44.0)	23.5 (14.3–38.5)	26.0 (19.8–48.8)	0.375
Postoperative leakage, *N* (%)	2 (10.5)	6 (19.4)	1 (10.0)	1.000
90-day mortality, *N* (%)	4 (14.8)	11 (21.2)	8 (36.4)	0.207

IQR, interquartile range.

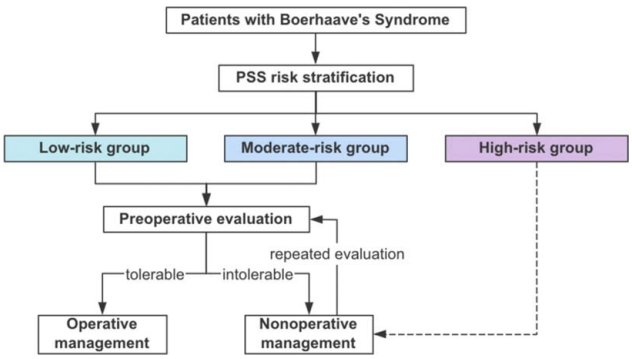

Figure 2. Clinical algorithm for Boerhaave's syndrome management based on Pittsburgh perforation severity score.

making. Among patients at low and moderate risk (PSS ≤ 5), prompt operative management is recommended for those who can tolerate surgical procedures, while the others should receive conservative nonoperative management and undergo repeated evaluation until the operative management becomes available. For patients at high risk (PSS ≥ 6), nonoperative management is recommended since aggressive surgery may increase the risk of fatal outcomes.

In our experience with the management of BS, primary surgical repair was the preferred treatment of choice, especially for those who were expected to tolerate the surgical procedure. Meticulous intraoperative repair is one of the keys to achieving successful treatment. The rupture in the mucosa is sometimes longer than that in the muscle layer, and surgical suture at both ends of the mucosal rupture should not be omitted. The purposes of surgery were to thoroughly remove the contaminant from pleural cavities to overcome SIRS and persistent bacterial infection, release the lung from the constraint of the fibrous membrane to expand fully, which is essential to accelerate the recovery of respiratory function and wound healing, establish effective drainage and nutritional support pathway, and repair or reinforce the tear.

For patients with late diagnosis, surgical repair can be attempted, but most of the cases may not achieve primary healing[24]. Therefore, closing the ruptured esophagus may not be necessary if the mediastinitis was severe or the interval between onset and treatment exceeds 24 h[11]. However, successful treatment still depended on thorough surgical debridement, effective drainage, and sufficient nutrition support. In addition to a well-placed chest drainage tube, a gastrointestinal decompression tube, and a jejunal fistula or nasoenteral nutrition tube are also essential. Five patients in our cohort underwent surgical debridement without primary repair, and two patients underwent surgical debridement plus stent placement. The average PSS of these patients was 4.57, and most of these cases did not receive timely treatment within 24 h. The results showed that the systematic infection was effectively controlled without significant mediastinal abscess or respiratory failure, which could hinder the process of wound healing. Stent placement appeared to be an alternative treatment choice for postoperative patients without primary repair, although stent displacement occurred in one of the two patients.

Based on the PSS scoring system, Schweigert and colleagues proposed that patients at low risk are candidates for nonoperative management. However, our results indicated that nonoperative management only serves as an alternative strategy for those who cannot tolerate surgery or are not predicted to benefit from surgery, most of which are allocated in the high-risk group. The difference between the two treatment preferences was partly because esophageal perforation is a group of highly heterogeneous acute and chronic diseases that have different etiologies, pathophysiological processes, and outcomes, while BS is a lethal emergency with a progressive nature requiring aggressive surgical intervention. Therefore, the treatment strategy of BS should be clearly distinguished from iatrogenic, foreign-body-induced, and malignant esophageal perforation, which also puts forward higher requirements for early diagnosis. Patients with high risk require further stratification to identify patients who can benefit from surgery.

The main strength of this study is that it contains clinical data from a large-scale multicenter cohort, especially given the fact that BS is an extremely rare disease and the relevant literature is sparse. The data were collected from 2005 to 2020, thus providing contemporary clinical implications and up-to-date evidence in accordance with the rapid development of BS surgical management.

Limitations of this study included: the retrospective nature of the study; the retrospective multicenter design made it difficult to collect sufficient details about diagnostic and therapeutic procedures in each patient, especially the reasons for treatment selection; and although this study is one of the largest focusing on spontaneous rupture of the esophagus, the statistical power was still insufficient to obtain potentially significant results in various aspects, including treatment timing, LOS, and the best treatment for high-risk patients.

Conclusion

Operative management might be superior to nonoperative management for low-risk and moderate-risk patients with spontaneous rupture of the esophagus. However, for patients at high risk, operative management might not provide additional benefits compared with nonoperative management. Further research involving larger sample sizes is required for accurate patient stratification and conclusive evidence-based guidelines.

Ethical approval

This study was approved by the Biomedical Research Ethics Committee of West China Hospital, Sichuan University, which also waived the need for written informed consent (ID, 2020 171; Date, February 25, 2020).

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Author contribution

S.L. and X.X.: conceptualization, data curation, investigation, methodology, writing – original draft, and writing – review and editing. X.Z.: investigation, methodology, and writing – review and editing. J.R., W.L., J.L., X.M., X.Z., R.L., Y.D., M.F., G.S., S.D., Y.W., C.L., Y.W., G.L., and C.Y.: investigation, data curation, and writing – review and editing. J.Z., C.M., and W.H.: investigation and writing – review and editing. L.C.: investigation, data curation, and writing – review and editing. Y.Y. and Y.Y.: conceptualization, investigation, methodology, supervision, writing – review and editing, and funding acquisition.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: Chinese clinical trial registry.
2. Unique identifying number or registration ID: ChiCTR2000033341.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): http://www.chictr.org.cn/showproj.aspx?proj=53800.

Guarantor

Prof. Yong Yuan and Prof. Yushang Yang.

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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