



Clinical profile and treatment outcomes of Boerhaave's syndrome: A 13-year experience from an upper gastrointestinal surgical unit

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ABSTRACT

Objective: Boerhaave's syndrome (BS) is a rare, but potentially fatal condition, characterized by barogenic esophageal rupture and carries a high mortality. We aimed to study our institutional experience of managing patients with BS.

Material and Methods: A retrospective review of patients with BS presenting to a tertiary care centre from 2005 to 2018 was carried out in this study. Clinical presentation, diagnostic evaluations, treatments received, and treatment outcomes were studied. Perforations were classified as early (<24 hours) and delayed (>24 hours), based on the time elapsed. Surgical complications were graded using Clavien-Dindo grade. The Pittsburgh perforation severity score was correlated with short-term treatment outcomes.

Results: Of the 12 patients [male, 75%; mean (range) age, 53 (28-80) years] included, 10 patients had a delayed (>24 hours) presentation. Chest pain was the dominant symptom (58.3%); six patients presented either in shock (n= 1) or with organ failure (n= 3) or both (n= 2). All the perforations were sited in the lower thoracic esophagus, of which three were contained and nine were uncontained. The seal of the perforation was achieved by surgical repair in four patients (primary repair, 2; repair over a T-tube, 2) and endoscopic techniques in four patients (clipping, 1; stenting, 3). Sepsis drainage [surgical, 7 (open-5, minimally-invasive-2); non-surgical, 5] and feeding jejunostomy were performed in all patients. Five (41.7%) patients received a re-intervention. Median (range) hospital stay was 25.5 (12-101) days, 30-day operative morbidity was 50%, and there was one in-hospital death. The Pittsburgh perforation severity score was as follows: 2-5 in two patients and >5 in 10 patients; there were more delayed presentations, increased surgical interventions, post-procedure morbidity, and in-hospital mortality in the latter group, but the differences were statistically not significant. In 11 patients followed-up [median (range):1507 (17-5929) days], there was no disease recurrence, symptomatic reflux or dysphagia.

Conclusion: Favourable treatment outcomes, including reduced mortality and organ preservation can be achieved for Boerhaave's perforations, through a multimodality approach. Minimally invasive, endoluminal or open surgical techniques may be safely utilized in its management. The Pittsburgh severity score can be a useful clinical tool that can be used to select the initial intervention and to predict treatment outcomes.

Keywords: Boerhaave's syndrome, spontaneous esophageal perforation, surgery, therapeutic endoscopy, Pittsburgh perforation severity score

INTRODUCTION

Boerhaave's syndrome (BS) is a rare, but potentially fatal condition, characterized by transmural esophageal rupture, secondary to the sudden rise in intraluminal pressure, as in forceful emesis (1). The perforation leads to contamination of the surrounding space with esophago-gastric contents, leading to local sepsis, organ failure, and a mortality rate of 24-50% in delayed presentations (2-4). BS diagnosis is often delayed because of its rarity, non-specific symptoms, and frequent initial diagnostic errors (5). Prompt diagnosis and timely intervention correlate with favorable treatment outcomes (3).

Due to its rarity, there is lack of standard guidelines for the optimal treatment of BS. Treatment options vary from conservative treatment to surgery as radical as esophagectomy. Surgical options include primary repair, tube esophagostomy, esophageal exclusion/diversion, and esophagectomy, combined with drainage and debridement of pleuro-mediastinal cavities (5-7). In a series of 88 patients with BS by Yan et al., the best operative outcomes including reduced postoperative esophageal leak, and shorter hospital and intensive care stays have been obtained in patients presenting early and receiving a primary repair, compared to buttressed repairs in the delayed group (8). In another series by Sutcliffe et al., immediate surgery was feasible in all eight patients presenting early but it was possible only

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in 6/10 patients presenting late (9). The rates of postoperative leak (78% vs 12.5%; $p < 0.05$) and mortality (40% vs. 0%; $p < 0.05$) were higher in the late referral group, and within the delayed referral subgroup, the worst mortality was seen in those managed conservatively. The authors have reiterated that the operative principles for BS are pleuro-mediastinal decontamination, debridement or resection of devitalized tissues, primary perforation repair (when feasible), gastric decompression, and enteral feeding access. Aggressive surgery including resection is suggested in delayed cases with extensive esophageal tissue loss (1).

With recent advances in minimally invasive surgery and therapeutic endoscopy, there is a paradigm shift towards a more conservative treatment approach for this condition. The safety and effectiveness of minimally invasive surgical approaches have been demonstrated by Haveman et al., Aref et al., Lee et al., Cho et al., and in a recent review by Aiolfi et al (10-14). Minimally invasive surgery can potentially reduce surgical trauma, but the choice of operative access depends on the site of the perforation, the extent of pleuro-mediastinal contamination/necessity for pleural drainage. Similarly, several authors have reported the role of endoscopic therapy for the management of BS, particularly that of esophageal stents which are utilized both as a primary intervention and also as a salvage procedure for persistent leak following surgical repair (6,15,16).

Although a multitude of treatment options are available for BS and controversy exists concerning the best treatment modality, particularly for delayed presentations, optimal treatment outcomes are often achieved through a multimodality approach. Hence, patients should be managed at a centre, with appropriate facilities and the expertise to deal with this challenging condition.

In this study, it was aimed to review our institutional experience of managing patients with BS over a 13-year period, focusing on their clinical presentation, diagnostic evaluations, treatment approaches and their outcomes. We also attempted to retrospectively grade the severity of the perforation using the Pittsburgh perforation severity score (PPSS) which is a valid tool to grade the severity of esophageal perforations (17,18). PPSS has been shown to correlate with the time interval to presentation, choice of initial therapy and treatment outcomes, particularly in patient subgroups with BS (18-20).

MATERIAL and METHODS

A retrospective review of all adult patients treated for BS in the esophagogastric surgery unit of our centre from January 2005 to January 2018 was performed. The relevant data were retrieved from the hospital's electronic medical records and included demographic details, clinical and laboratory characteristics, details of diagnostic evaluations and treatment,

intensive care unit (ICU) stay details, LoHS, 90-day morbidity (including 30-day operative morbidity), 90-day and in-hospital mortality. The study was approved by the institutional review board [Min.No.13062 (retro) dated 24.06.2020].

The severity of the comorbidities was classified using Charlson's comorbidity index (CCI) (21). Based on the time elapsed from the symptom onset to diagnosis, perforations were classified as early (<24 hours) and delayed (>24 hours). Shock was defined as systolic blood pressure <90 mmHg. Diagnosis was confirmed using contrast-esophagography and/or thoracic computed tomography (CT) and an occasional endoscopy. Perforation was classified as uncontained if there was a large amount of contrast extravasation into the pleural space or a large area of mediastinal air-fluid collections regardless of the pleural involvement; contained if there was no contrast extravasation or minimal contrast extravasation with the limited mediastinal air-fluid collection, not breaching the pleural space. Primary intervention was defined as the index procedure(s) aimed at sealing the perforation and/or drainage of sepsis and a re-intervention was defined as any subsequent procedure(s) performed to achieve similar goals. Post-procedure morbidity was recorded at the 90-day mark. Thirty-day postoperative complications were classified using Clavien-Dindo grade (CDG) and a major complication was defined as $CDG \geq 3$ (22).

The severity of the perforation at admission was retrospectively calculated using PPSS. PPSS was calculated by assigning points to each clinical variable to a total score of 18 and three patient risk categories were identified (PPSS: <2, low risk; 2-5 intermediate risk; >5, high risk) (17,18). PPSS category was correlated with time to diagnosis, choice of primary intervention (operative vs. non-operative), the requirement for ICU stay, LoHS, and in-hospital mortality. Follow-up data were obtained from medical records and were strengthened by telephonic conversation.

Categorical variables were expressed as frequencies with percentages, and continuous variables were expressed as mean with standard deviation or median with range. To find associations between two categorical variables, Fisher's exact test or proportion test was used. The differences were considered significant if $p < 0.05$.

RESULTS

Baseline demography, clinical profile and details of radiological evaluations are summarized in Table 1.

Demography and Clinical Presentation

Twelve patients [male:female, 10:2; mean (range) age, 53.75 ± 14.96 (28-80) years] were included. Ten (83.3%) patients had delayed diagnosis. Five patients were referred to our centre following an initial intervention elsewhere (Table 2). Five patients were erroneously diagnosed with pulmonary

Table 1. Demography, clinical profile and details of initial diagnostic evaluations

Variable	n= 12
Year of presentation	
2005-2010	3 (25.0%)
2011-2015	7 (58.3%)
2015-2018	2 (16.7%)
Age; years	53.75 ± 14.96 (28-80)
Sex	
Male	10 (83.3%)
Female	2 (16.7%)
CCI	
CCI < 2	7 (58.3%)
CCI ≥ 2	5 (31.7%)
Time interval ^a	
Early (<24 hours)	2 (16.7%)
Delayed (>24 hours)	10 (83.3%)
Dominant symptom	
Chest pain	7 (58.4%)
Abdomen pain	4 (33.3%)
Dyspnoea	1 (8.3%)
Precipitating factor	
Alcohol + retching/vomiting	6 (50.0%)
No alcohol but retching/vomiting	2 (16.7%)
No precipitating factor reported	4 (33.3%)
Initial admitting department	
Surgical unit	7 (58.3%)
Medical specialities ^b	5 (41.7%)
Presence of shock/organ failure at admission	
Shock alone	1 (8.3%)
Organ failure ^c alone	3 (25.0%)
Shock and organ failure ^c	2 (16.7%)
Laboratory evaluations	
Hemoglobin (g/dL)	13.01 ± 3.17
Albumin (g/dL)	3.1 ± 0.95
Creatinine (mg/dL)	1.08 ± 0.47
Total leukocyte count (cells/cu mm).	12,400 (4,400-19,600)
Diagnostic modality	
Chest radiograph	12
Normal	1
Pleural effusion	11
(Left, right, bilateral)	(7, 3, 1)
Diagnostic endoscopy	3
Contrast-esophagography	2
Thoracic CT scan	12
Location of perforation	
Lower thoracic esophagus	12
Perforation contained? ^d	
Yes	3 (25.0%)
No	9 (75.0%)
CCI: Charlson comorbidity index, CT: Computed tomography. Values expressed in n, n (%), mean ± SD or median (range) as appropriate. ^a : Time interval, from the onset of symptoms to diagnosis/initiation of treatment, ^b : Admitted initially under medical specialities with an alternate diagnosis, ^c : Acute respiratory failure with hypoxia in four patients; acute renal failure in one patient, ^d : As determined by the radiological evaluations.	

conditions and were initially admitted under medical specialities. The dominant presenting symptom was chest pain (58.4%), and Mackler's triad (chest pain, vomiting, subcutaneous emphysema) was present in two (16.7%) patients. A total of six patients presented either in shock (n= 1) or with organ failure (n= 3) or both (n= 2).

Laboratory and Radiological Evaluations

Median total leukocyte count was 12,400 cells/cu mm. The commonest finding in chest radiography was pleural effusion (11 patients; left, 7; right, 3; bilateral 1). Contrast-esophagography was performed in two patients, and contrast extravasation was seen in both. Thoracic CT was performed in all patients; all the perforations were localized to the lower thoracic esophagus and nine (75.0%) perforations were uncontained.

Treatment Details and Outcomes

Individual patient profile and treatments received are detailed in Table 2.

Sealing of the Perforation

Ten patients belonged to the delayed diagnosis group (perforation type: contained, 2; uncontained, 8) and two patients belonged to the early diagnosis group (perforation type: contained, 1; uncontained, 1). Two patients (SL No. 2 and 11) in the delayed but uncontained group, received surgical drainage, debridement and a feeding jejunostomy (FJ) alone. The initial sealing of the perforation was performed in the remaining six patients of the delayed but uncontained group, either using covered stents (n= 3) or surgery (n= 3). Two patients in the delayed but contained group received no esophageal intervention and were managed with a tube thoracostomy and FJ. In the early diagnosis group (n= 2), endo-clipping (n= 1) and surgery (n= 1) were utilized to seal the perforation.

All surgical repairs were performed through an open trans-hiatal approach. A reinforced primary repair was performed in a patient who presented early but with a contained perforation. Among the three patients in the delayed presentation group receiving esophageal surgery, a buttressed primary repair was performed in one patient and a T-tube repair was performed in two patients.

Drainage of Sepsis

In the uncontained perforation group (n= 9), thoracic drainage was achieved using either thoracoscopy/thoracotomy (n= 7) or a tube thoracostomy (n= 2). In the delayed but contained perforation group (n= 2), a tube thoracostomy alone was used to drain the reactive effusion. In a patient belonging to the early but contained perforation group receiving surgical repair of the perforation, there was no concomitant pleural drainage indicated initially. However, the patient developed a left-sided, serous effusion later, which was drained using a tube thoracostomy.

Table 2. Individual patient profile and treatment details

Year	Case No.	Age/ Sex	Type of intervention before referral	Time of presentation (Early vs. Delayed)	Location of perforation ^a	Perforation size	Contained perforation (Yes/No)	Site of pleural collection	PPSS	Details of primary intervention(s)	Re-intervention
2005	1	67/M	Non-referral	Early	Lower thoracic, 2 cm above GEJ	3 cm	Yes	None ^b	4	Laparotomy, trans-hiatal primary repair, omentoplasty and FJ	Tube thoracostomy for left-sided pleural effusion ^b
2008	2	80/F	Right-sided, tube thoracostomy	Delayed	Lower thoracic	N/I	No	Right	10	Right thoracotomy, drainage, decortication and FJ	None
	3	62/M	Left-sided, tube thoracostomy	Delayed	Lower thoracic	N/A	Yes	Left	3	Left-sided, tube thoracostomy, gastrostomy and FJ	None
2010	4	28/M	Non-referral	Delayed	Lower thoracic	N/A	Yes	Left	9	Left-sided, tube thoracostomy, FJ	None
2011	5	47/M	Right thoracotomy, pleural drainage alone	Delayed	Lower thoracic	N/M	No	Right	9	Right thoracotomy, drainage, decortication, esophageal stenting (FCSEMS) and FJ	Stent migration → endoscopic repositioning
	6	41/M	Left-sided, tube thoracostomy	Delayed	Lower thoracic, 2 cm above GEJ	3 cm	No	Left	10	Laparotomy, trans-hiatal repair over a T-tube, left thoracotomy, drainage, decortication, gastrostomy and FJ	None
2012	7	61/M	Non-referral	Delayed	Lower thoracic, 37-39 cm	2 cm	No	Left	6	Left-sided, tube thoracostomy, esophageal stenting (FCSEMS), FJ	None
2013	8	50/M	Non-referral	Delayed	Lower thoracic	3 cm	No	Left	11	Laparotomy, trans-hiatal repair over a T-tube, left thoracotomy, drainage, decortication, gastrostomy and FJ	None
	9	47/M	Non-referral	Delayed	Lower thoracic, 2 cm above the GEJ	3 cm	No	Bilateral	12	Laparotomy, trans-hiatal primary repair, omentoplasty, bilateral thoracoscopic drainage, gastrostomy and FJ	None

Table 2. (continue) Individual patient profile and treatment details

Year	Case No.	Age/ Sex	Type of intervention before referral	Time of presentation (Early vs. Delayed)	Location of perforation ^a	Perforation size	Contained perforation (Yes/No)	Site of pleural collection	PPSS	Details of primary intervention(s)	Re-intervention
2014	10	55/M	Right thoracotomy, pleural drainage	Delayed	Lower thoracic, 34-36 cm	2 cm	No	Left	6	Left-side, tube thoracotomy, esophageal stenting (FCSEMS) and FJ	Left-sided residual pleural collection → image-guided drainage
2016	11	70/M	Non-referral	Delayed	Lower thoracic, just above the GEJ	1 cm	No	Left	12	On-table endoscopy, left-thoracoscopic drainage, decortication and FJ ^c	Post-op contrast study showed a leak → stented (FCSEMS) → stent migration → endoscopic repositioning
2018	12	37/F	Non-referral	Early	Lower thoracic, 31-33 cm	2 cm	No	Right	8	On-table endoscopy, clipping of the perforation, right-thoracoscopic drainage and FJ	Persistent leak → stented (FCSEMS) → stent migration → endoscopic repositioning

PPSS: Pittsburgh perforation severity score, M: Male, F: Female, GEJ: Gastro-esophageal junction, FJ: Feeding jejunostomy, FCSEMS: Fully covered self-expanding metal stent, N/I: Not identified (The perforation is not identified intra-op), N/A: Not applicable (No endoscopy or esophageal surgery attempted; hence size of the perforation cannot be commented on), N/M: Not mentioned (Although perforation identified either in endoscopy or intra-op, its size was not mentioned).

^a: The location of the perforation was identified using either radiological or endoscopic or intra-op assessment or their combination

^b: Pleural effusion developed following the primary intervention, but there was no evidence of a postoperative esophageal leak in the re-imaging

^c: On-table endoscopy showed an erosion in the lower thoracic esophagus, but the CT showed no obvious contrast leak and the perforation was not identified intra-op; hence stenting was not considered during the index operation.

Feeding Procedure and Gastrostomy

An FJ was performed in all patients, and a surgical venting gastrostomy was created in four patients.

Re-Interventions

A total of five patients required re-intervention; one patient developed migration of the covered esophageal stent, managed by endoscopic stent repositioning, and two patients required stenting following the primary esophageal intervention (failure of clipping, 1; postoperatively evident leak, 1). The patient who received stenting following the failed clipping developed distal migration of the stent and required endoscopic repositioning. In the patient who was stented for an esophageal leak (revealed postoperatively), there were three instances of stent migration, necessitating endoscopic repositioning. Two patients developed residual pleural collection following the primary intervention and required additional drainage procedures (tube thoracostomy, 1; image-guided drainage, 1).

Post-Treatment Outcomes and Follow-Up

Post-treatment outcome and follow-up are elaborated in Table 3. There was one re-operation for intraperitoneal bleeding, three ventilator-associated pneumonia requiring tracheostomy, one

central-line associated infection, and paroxysmal supraventricular tachycardia. Thirty-day postoperative complication was 50.0%, and all were CDG \geq 3 complications. All patients but two required ICU stay, and median (range) LoHS was 25.5 (12-101) days. Among patients who completed 90-day follow-up (n= 9), there was no 90-day mortality. One patient, who required multiple stent re-positioning, succumbed to multi-organ failure on the 101st postoperative day.

All esophageal stents were retrieved in the outpatient clinic, and no patient had a residual leak in the follow-up contrast-esophagography. Among the survivors (n= 11), the median (range) follow-up was 1507 (17-5929) days; one patient died of community-acquired pneumonia at nine months following discharge, and the remaining patients were alive with no recurrence, dysphagia or symptomatic reflux.

The Clinical Significance of PPSS

PPSS was 2-5 in two patients and >5 in 10 patients. When PPSS >5 and 2-5 patient groups were compared, there were more delayed presentation (90.0% vs. 50.0%; p= 0.165), more surgical interventions (70.0% vs. 0.0%), increased rate of overall post-procedure morbidity (70.0% vs. 50.0%; p= 0.583) and in-hospital mortality (10.0% vs. 0.0%) in the former group (Table 4). Eight

Table 3. Post-treatment outcomes and follow-up

Patient SL. No. ^a	Post-procedure additional morbidity ^b	CDG	PPSS	PPSS risk category (Intermediate; 2-5 vs. high; >5)	ICU (Yes/No)	LoHS (Days) (Days)	Mortality (90-day, in-hospital)	Follow-up (Days)	Recurrence (Yes/No)
1	Tracheostomy	3a	4	Intermediate	Yes	31	No, No	5929	No
2	CLABSI, VAP, multi-organ failure	4b	10	High	Yes	68	No, No	1507	No
3	None	N/A	3	Intermediate	Yes	18	No, No	272	No
4	None	N/A	9	High	No	17	No, No	49	No
5	None	N/A	9	High	Yes	20	No, No	3467	No
6	VAP, tracheostomy	3b	10	High	Yes	38	No, No	17	No
7	None	N/A	6	High	Yes	19	No, No	65	No
8	Bleeding from a hiatal vessel needing laparoscopic ligation	3b	11	High	Yes	40	No, No	3007	No
9	PSVT treated medically	3a	12	High	Yes	12	No, No	2956	No
10	None	N/A	6	High	No	32	No, No	2630	No
11	VAP, tracheostomy	5	12	High	Yes	101	No, Yes	N/A	N/A
12	None	N/A	8	High	Yes	17	No, No	1142	No

CDG: Clavien-Dindo grading, ICU: Intensive care unit, LoHS: Length of hospital stay, CLABSI: Central-line associated bloodstream infection, VAP: Ventilator-associated pneumonia, PSVT: Paroxysmal supraventricular tachycardia, N/A: Not applicable.

^a: Patient serial number in the same order as in Table 2.

^b: Additional post-procedure morbidity (excluding any form of esophago-pleural re-interventions).

Table 4. PPSS and its correlation with treatment selection and post-treatment outcomes

Variable	PPSS (n= 12)		p
	Intermediate risk (2-5) (2, 16.7%)	High risk (>5) (10, 83.3%)	
Time of presentation			0.165
<24 hours	1 (50%)	1 (10%)	
>24 hours	1 (50%)	9 (90%)	
Primary intervention(s)			-
Surgery ± other interventions	0 (0%)	7 (70%)	
Endoscopic alone	0 (0%)	0 (0%)	
Radiological alone	2 (100%)	0 (0%)	
Endoscopic & Radiological	0 (0%)	3 (30%)	
Re-intervention requirement ^a			-
Yes	1 (50%)	4 (40%)	
No	1 (50%)	6 (60%)	
Post-procedure morbidity ^b			0.583
Yes	1 (50%)	7 (70%)	
No	1 (50%)	3 (30%)	
Need for ICU stay			0.488
Yes	2 (100%)	8 (80%)	
No	0 (0%)	2 (20%)	
Median LoHS, days	24.5	26	-
Mortality			-
90-day	0% (0%)	0 (0%)	
In-hospital	0% (0%)	1 (10%)	

PPSS: Pittsburgh severity score, ICU: Intensive care unit, LoHS: Length of hospital stay.

^a: Includes the patient in whom a re-intervention was warranted (stenting for persistent esophago-pleural fistula) but refused.

^b: Post-procedure morbidity includes re-interventions also.

PPSS was calculated by assigning points to each clinical variable to a total score of 18 and three patient risk categories were identified (low risk <2, intermediate risk 2-5, high risk >5): 1= age >75 years, heart rate >100 beats per minute, white cell count >10 × 10⁹/mL, pleural effusion; 2= fever (>38.5 °C), uncontained leak (radiological studies), respiratory compromise (respiratory rate >30 per minute, need for increasing oxygen or mechanical ventilation), time of diagnosis >24 h; 3= oesophageal cancer, hypotension (17,18).

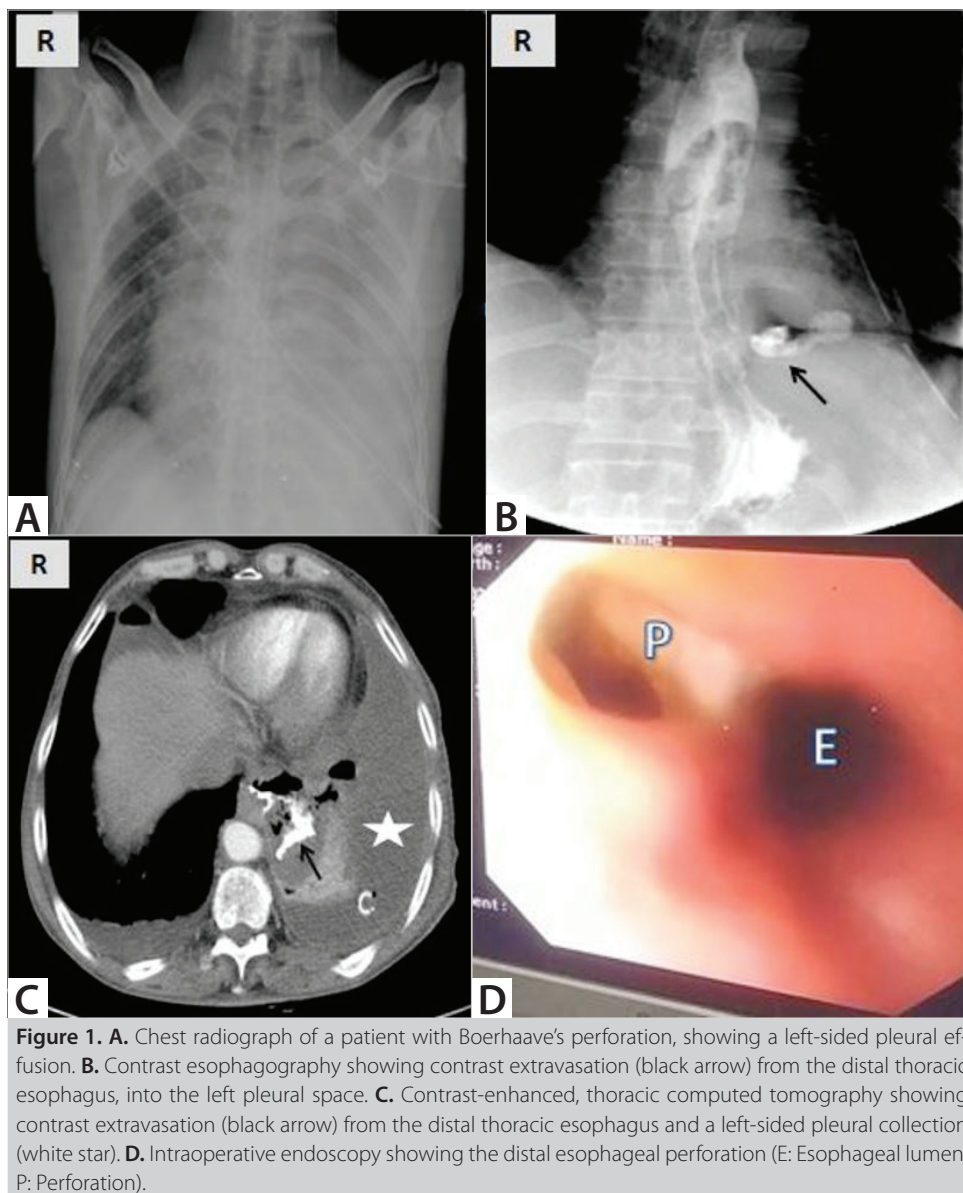
(80%) patients with PPSS > 5 and all patients with PPSS 2-5 required ICU stay (p= 0.488). There was no clinically relevant difference in re-intervention rate (50.0% vs. 50%) or LoHS (24.5 days vs. 26 days) between PPSS patient groups.

DISCUSSION

Early detection and timely management of BS can reduce its morbidity and mortality, but the optimal therapeutic approach remains controversial (18). Traditionally, aggressive surgical approaches including resection were favoured. However, with recent developments in endoluminal therapy and minimally invasive surgery, there is a paradigm shift in the management approach to this condition. This case series reports the treatment outcomes of BS, from an upper gastrointestinal surgical unit, over a period of 13 years. All available treatment options have also evolved over the period of the study.

In our series, majority of the patients were middle-aged males, the diagnosis was often delayed, chest pain was the dominant symptom, and all perforations were sited in the distal thoracic esophagus; a trend concurrent with the reported literature (1,5,20,23). Abnormal chest radiography findings in BS include

pleural effusion (Figure 1A), pneumomediastinum, subcutaneous emphysema, hydropneumothorax, and rarely pneumoperitoneum. In this series, chest radiography showed pleural effusion in all patients. Although contrast-esophagography (Figure 1B) is a useful investigation to confirm diagnosis, false-negative rates can reach 15-25% and its application is often limited by the patient's ability to swallow the contrast; it was possible in two of our patients, confirming the diagnosis in both (5,24). Thoracic CT (Figure 1C) gives valuable information regarding the site of perforation, its contained vs. uncontained nature, and the presence of additional esophageal pathologies and can guide effective sepsis drainage (1,24). In our experience, thoracic CT had excellent sensitivity in detecting perforation, and majority of the perforations (75.0%) were uncontained type. Endoscopy has a sensitivity of 100% and specificity of 80-93% in diagnosis, but can potentially worsen the esophageal tear (1,3,5). Routine diagnostic endoscopy is not performed in our centre but was utilized for intra-operative localization of the perforation in three patients (Figure 1D), where an immediate endoluminal intervention was followed.



Initial management of BS consists of fluid resuscitation, antibiotics and antifungals, acid suppression, analgesia, and cardio-respiratory support. The specific treatment approach depends on the patient's general condition and comorbidities, the location and extent of the perforation, esophageal viability, the extent of pleuro-mediastinal soiling, and the availability of expertise (24). The treatment of BS is primarily aimed at three important steps: 1. sealing the perforation and maintaining the luminal continuity, 2. drainage of sepsis, and 3. nutritional support.

In our series, either surgery or endoscopic interventions were performed to achieve the sealing of the perforation. Although transthoracic approach is considered to be the standard operative approach for BS, trans-hiatal approach was found to

be feasible and safe in our experience, as also reported by others (2,4,9,25). In addition to providing direct access to the perforation, this operative approach allows for the drainage of the mediastinum, placement of an omental patch, performance of a concomitant FJ, and an occasional gastrostomy. During the early part of the series, surgery was often utilized to achieve sealing of the perforation and the technique of repair was either a primary buttressed repair or a T-tube esophagostomy. Primary repair in patients presenting early is reported to have low postoperative leakage, shorter LoHS and ICU stay, and the reinforcement of the repair using vascularized tissues can reduce the postoperative leakage (4,8). A reinforced primary repair was possible in two patients, one each in the early and delayed diagnosis groups, and adequate sealing was achieved

in both. Key steps of primary repair include debridement of non-viable tissues, esophageal myotomy on either end of the perforation to expose healthy mucosal edges and a meticulous closure, preferably in double layers (1,24). Trans-thoracic repair can be reinforced with a pleural, pericardial or intercostal muscle flap or a gastric fundal wrap, whereas an omental or a gastric fundal wrap may be utilized to buttress a trans-hiatal repair (1,12). Although delayed diagnosis does not preclude a primary repair, a high risk of postoperative leak, re-interventions and mortality is reported, particularly when the delay is >48 hours (1,5,8,9,25). In such a scenario, repair over a T-tube is preferred, which creates a controlled esophago-cutaneous fistula; a technique that had successful outcomes in two of our patients presenting late (2,4,7,9). In our opinion, this technique is an attractive alternative in patients with delayed diagnosis, where the feasibility of a primary repair is limited, due to edematous and friable tissues, thereby avoiding or delaying other morbid operative procedures (diversion, exclusion or resection).

During the later phase of the study, endoscopic stenting with covered self-expanding metal stents (Figure 2) was more commonly used. Stenting is an effective, minimally invasive, primary modality for sealing the perforation in BS. Initial successful stenting can avoid radical surgeries, facilitates early oral alimentation, and can shorten the LoHS, ICU stay, and ventilator days (15,16,26). It can also be a salvage option in patients with persistent postoperative leak (6,7). In three of our patients with delayed diagnosis, the initial sealing of the perforation could be achieved by stenting. Additionally, one patient received stenting for a perforation that was not localized during the index operation but revealed later (Patient SL No. 11). Endoscopic clips, particularly over the scope clips are recommended for early perforations, measuring up to 30 mm

(1,3,24). Although we utilized this technique in one patient who presented early, a persistent leak warranted stent implantation later. This patient had an uncontained perforation which perhaps increased the likelihood of a re-leak, despite initial thoracic drainage.

The selection of primary esophageal intervention should be individualized based on patient and perforation characteristics. In a recent meta-analysis, surgery has been found to be the most favoured therapeutic approach, being utilized in 76% of the patients with BS, particularly when the diagnosis is made early; endoluminal techniques and non-operative management (NOM) are utilized predominantly in case of a delayed diagnosis (27). We prefer surgical repair over stenting for patients presenting early. However, in the early phase of this study, surgery was also performed in patients with a delayed diagnosis if the perforations were localized near the gastro-esophageal junction (GEJ) and patients could tolerate esophageal surgery, a practice similarly reported by others (8,9,25). Stenting, as the primary treatment modality for BS, has been demonstrated to have favourable clinical success, irrespective of the time to diagnosis (6,15,16,26). However, when the diagnosis is delayed, stenting may be associated with increased re-interventions, morbidity and mortality (16,26). In our recent experience, stenting was often utilized in delayed presentations, particularly if the perforations were localized away from the GEJ or the local esophageal condition and if the patient's poor general condition did not permit an immediate esophageal surgery. However, we ensured adequate pleuro-mediastinal drainage \pm debridement in all patients receiving stenting, which perhaps contributed to the absence of persistent leakage in this subgroup. Distal migration can frequently be seen in patients with BS receiving stenting (20-33%) and a high risk of persistent dysphagia is expected following a failed endoluminal

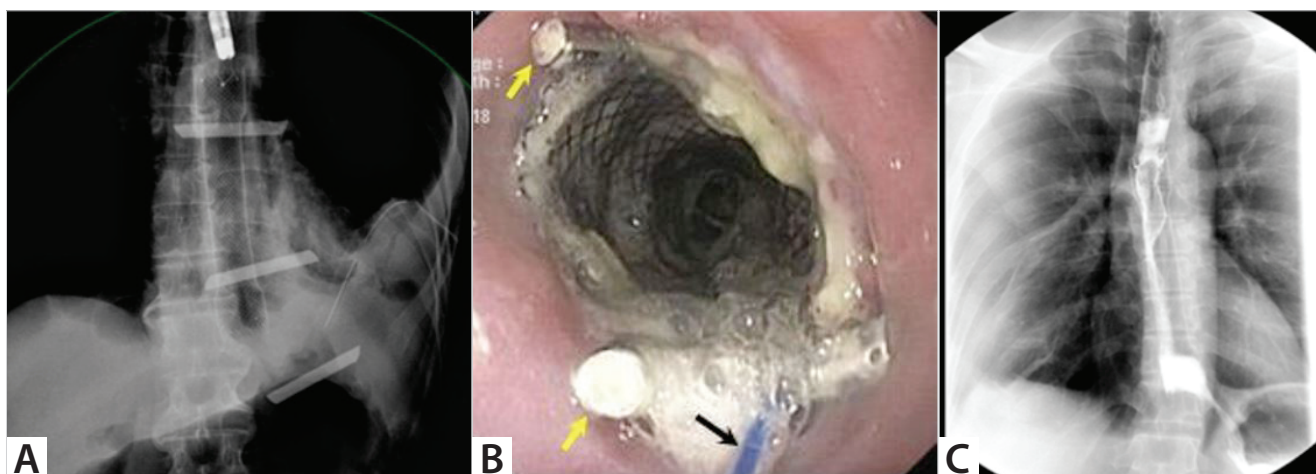


Figure 2. A. Endoluminal stenting for a Boerhaave's perforation, as seen in an image-intensifier. B. Endoscopic view of a fully deployed esophageal stent, anchored utilizing endoclips (yellow arrows) and a prolene thread (black arrow). C. Contrast esophagogram, showing an esophageal stent, providing adequate sealing of the distal thoracic esophageal perforation.

stenting (3,6,15,16,26). Although stent migration developed in three of our patients, these were successfully re-positioned endoscopically, and immediate additional interventions were not indicated in any patient, except one. There were no instances of esophageal stenosis and symptomatic reflux in the stented group. In our opinion, appropriate patient and stent type selection, the availability of expertise, and adequate sepsis drainage are paramount to minimise stent failure and its complications.

Adequate pleuro-mediastinal sepsis control is the key component in the treatment of BS and is a mandatory step to improve the success of any esophageal interventions. Tube thoracostomy or image-guided drainage is an accepted initial modality for drainage of localized contaminations, as utilized in five of our patients. However, since perforation in BS is barogenic, thoracic cavity is frequently contaminated with alimentary contents, warranting surgical debridement and drainage at some time point. In our series, majority of the patients with an uncontained perforation received surgical drainage and debridement, particularly when the diagnosis was delayed or when the pleural collections were loculated.

Nutritional access is a key treatment component for BS. We performed tube jejunostomy in all patients to facilitate early enteral nutrition. A nasojejunal tube is also an accepted alternative for feeding. Venting gastrostomy can reduce the incidence of postoperative reflux, particularly in perforations near the GEJ, and was performed in four of our patients. We generally avoid routine feeding or venting gastrostomy for perforations related to B, since it allows gastric preservation, for esophageal reconstruction, if an esophagectomy is indicated.

Surgical repair of esophageal perforation and sepsis drainage could also be achieved with minimally invasive surgery (10,12,13,19,23). Haveman et al. have demonstrated comparable effectiveness and safety of pleural sepsis drainage utilizing video-assisted thoracoscopic surgery (VATS) and open thoracotomy techniques (10). In a recent review, minimally invasive surgery has been found to be feasible and safe for esophageal repair and thoracic debridement/drainage, especially in patients presenting early with stable vitals (14). Recently, VATS is our preferred operative approach for addressing thoracic sepsis, as in three of our patients. Although we preferred laparotomy for the repair of the perforations, the feasibility and safety of laparoscopic, trans-hiatal, and video-assisted trans-thoracic repairs have been shown by other authors, including in patients with delayed diagnosis (12,13,19,23).

In carefully selected patients with BS, successful treatment outcomes are achievable by NOM, provided the following criteria are satisfied: a contained perforation within the mediastinum and drainage flowing back to the esophageal

lumen, minimal symptoms, no overt signs of systemic sepsis, and availability of appropriate radiological studies and thoracic surgery expertise (28). A true NOM consist of nil by mouth, intravenous fluids, anti-acid therapy, broad-spectrum antibiotics and enteral tube feeding, but is rarely possible in BS, due to its frequent delayed presentation. No patient received a true NOM in our series, but two patients with delayed but contained type perforation with no overt signs of sepsis, received conservative treatment approach including tube thoracostomy and nutritional access, without esophageal interventions, and their recovery was uneventful. An initial esophageal intervention is preferably avoided in this sub-group of patients and favourable treatment outcomes could result from drainage and nutritional support alone (1,2).

PPSS is a valuable clinical tool to stratify risk among patients with esophageal perforation, particularly in the context of BS (17-20). Patients who present early with a contained leak and do not have overt signs of sepsis often have a low PPSS and are ideal candidates for initial NOM in specialized esophageal centres (1). An operation in this subset of patients may have a worse treatment outcome (17,23). In our series, none of the patients had PPSS of ≤ 2 and no patient received a true NOM. The severity of complications, LoHS and mortality is shown to correlate with PPSS (17). In this study, there were more delayed presentations, increased surgical interventions, increased post-procedure morbidity, and in-hospital mortality in those patients with a PPSS ≥ 5 , compared to those with PPSS 2-5 but these differences were not statistically significant. Further analysis to evaluate the effect of PPSS on treatment selection and outcomes was not feasible in this study, considering its small study population.

Despite advances in therapeutics for BS, treatment-related morbidity can reach 70.0%, major operative morbidity can reach 36.0%, re-intervention rate can be 40%, mortality can be 8-40%, and prolonged ICU care and LoHS is not uncommon (10,13,19,20,23,27). In this study, overall post-treatment complication was 50% (CDG ≥ 3 , 100%), and majority of the patients had a prolonged LoHS. However, despite these adverse outcomes, there was only one death (8.3%) and the esophagus could be salvaged in all patients. No patients required esophageal re-interventions following discharge; all stents were successfully retrieved and there were no stent-related complications, except the migrations. Further, there were no instances of dysphagia, symptomatic reflux or recurrent perforation.

Owing to the rarity and life-threatening nature of this condition, prospective studies to evaluate the effects of different treatment approaches are difficult to execute, and hence, the current evidence concerning the efficacy and safety of various treatment options are retrospective studies. A treatment

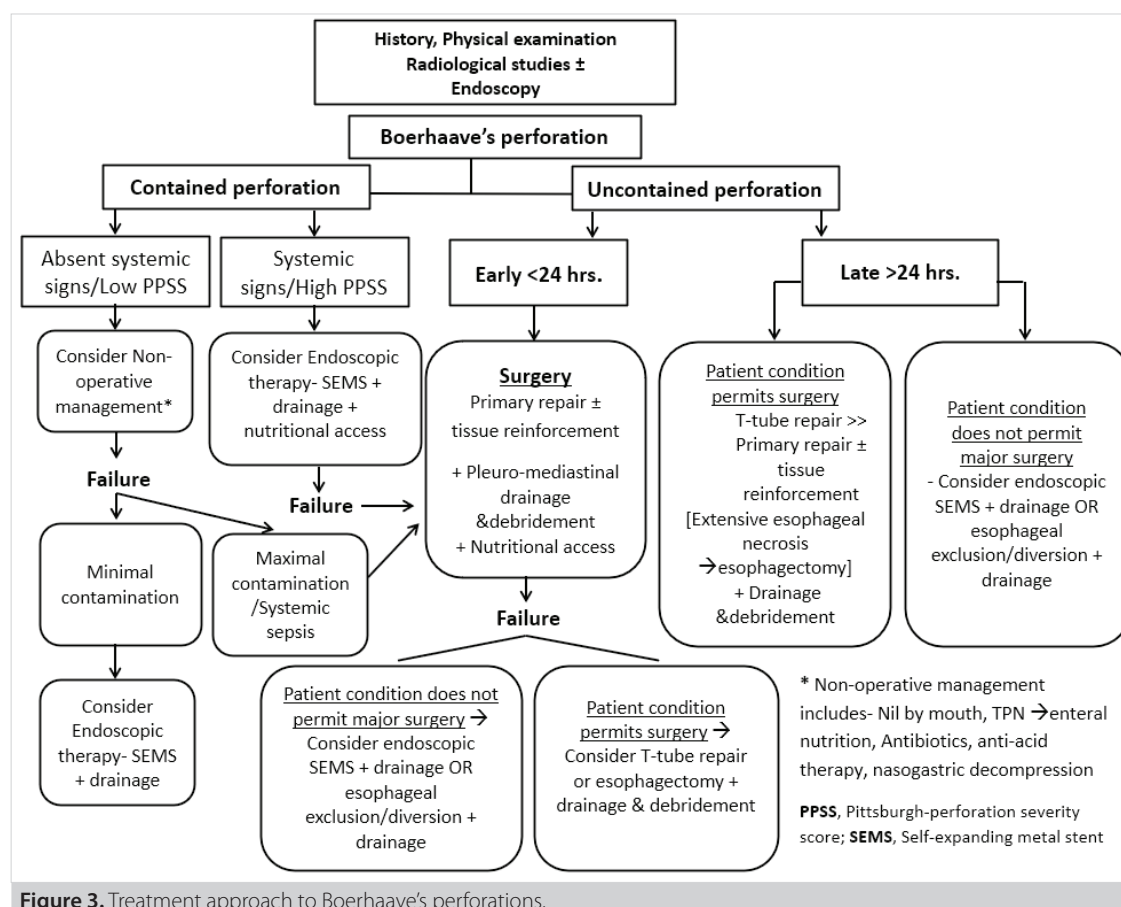


Figure 3. Treatment approach to Boerhaave's perforations.

algorithm based on our experience and the data available in the literature is formed (Figure 3).

This study had a few limitations. Firstly, it was a single institution, retrospective study with a relatively small number of patients, and hence, has its inherent biases. Secondly, a few patients were referred to us following some form of primary intervention at the index hospital. Hence, PPSS at the presentation in our centre is not a true reflection of their actual PPSS. Lastly, various patient and treatment-related factors which can help choose a particular treatment strategy and predict the treatment success could not be established, due to the small study population. Keeping aside the limitations, the current study focused solely on BS-related perforations, from a low-middle-income country, where timely access to a specialized esophageal centre is often limited. Also, the results from this study do support the view that favourable treatment outcomes could be achieved, by utilizing hybrid therapeutic techniques. We feel that future studies should focus on a multidimensional approach to BS, rather than comparing various therapeutic approaches.

CONCLUSION

Boerhaave's syndrome is a rare esophageal emergency and remains a diagnostic and therapeutic challenge. Despite an inc-

reased disease and treatment-related morbidity and prolonged hospital stay, successful treatment outcomes including reduced mortality, organ preservation, and better functional outcomes could be achieved through timely, individualized, multimodality management. Recent advances in minimally invasive, endoluminal and surgical techniques can further improve treatment outcomes. Pittsburgh severity score is a useful tool to select the initial treatment strategy and can possibly predict treatment-related outcomes.

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ORJİNAL ÇALIŞMA-ÖZET

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Boerhaave sendromunun klinik profili ve tedavi sonuçları: Bir üst gastrointestinal cerrahi ünitesinin 13 yıllık deneyimi

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ÖZET

Giriş ve Amaç: Boerhaave sendromu (BS), barojenik özofagus rüptürü ile karakterize, nadir fakat potansiyel olarak ölümcül bir durumdur ve yüksek mortalite taşır. BS'li hastaları yönetme konusundaki kurumsal deneyimimizi incelemeyi amaçladık.

Gereç ve Yöntem: Bu çalışmada 2005'ten 2018'e kadar üçüncü basamak bir bakım merkezine başvuran BS'li hastaların retrospektif bir incelemesi yapılmıştır. Klinik prezentasyon, tanısal değerlendirmeler, alınan tedaviler ve tedavi sonuçları incelendi. Perforasyonlar geçen süreye göre erken (<24 saat) ve gecikmiş (>24 saat) olarak sınıflandırıldı. Cerrahi komplikasyonlar Clavien-Dindo derecesine göre derecelendirildi. Pittsburgh perforasyon şiddeti skoru, kısa vadeli tedavi sonuçları ile korele idi.

Bulgular: Dahil edilmiş 12 hastanın [erkek, %75; ortalama (aralık) yaş, 53 (28-80) yıl] 10'unda gecikmiş (>24 saat) başvuru vardı. Göğüs ağrısı baskın semptomdu (%58.3); altı hasta ya şokta (n= 1) ya da organ yetmezliği (n= 3) ya da her ikisi (n= 2) ile başvurdu. Tüm perforasyonlar alt torasik özofagus yerleştirilmiş olup, bunların üçü kontrollü ve dokuzu kontrolsüz idi. Perforasyonun kapatılması dört hastada cerrahi onarım (primer onarım, 2; T-tüpü üzerinden onarım, 2) ve dört hastada endoskopik teknikler (klipsleme, 1; stentleme, 3) ile sağlandı. Sepsis drenajı [cerrahi, 7 (açık-5, minimal invaziv-2); cerrahi olmayan, 5] ve beslenme jejunostomisi tüm hastalara uygulandı. Beş (%41,7) hasta yeniden girişim aldı. Ortanca (aralık) hastanede kalış süresi 25,5 (12-101) gündü, 30 günlük operatif morbidite %50 idi ve bir hastane içi ölüm meydana geldi. Pittsburgh perforasyon şiddeti skoru iki hastada 2-5 ve 10 hastada >5; ikinci grupta daha fazla gecikmiş başvurular, artmış cerrahi müdahaleler, işlem sonrası morbidite ve hastane içi mortalite vardı ancak farklılıklar istatistiksel olarak anlamlı değildi. Takip edilen 11 hastada [medyan (aralık): 1507 (17-5929) gün] hastalık nüksü, semptomatik reflü veya disfaji görülmüdü.

Sonuç: Boerhaave perforasyonları için çok yönlü bir yaklaşımla, azaltılmış mortalite ve organ koruması da dahil olmak üzere olumlu tedavi sonuçları elde edilebilir. Tedavisinde minimal invaziv, endoluminal veya açık cerrahi teknikler güvenle kullanılabilir. Pittsburgh şiddet skoru, ilk müdahaleyi seçmek ve tedavi sonuçlarını tahmin etmek için kullanılabilir.

Anahtar Kelimeler: Boerhaave sendromu, spontan özofagus perforasyonu, cerrahi, terapötik endoskopi, Pittsburgh perforasyon şiddet skoru

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