


Suitable Diagnosis and Treatment of Esophageal Ruptures in Cases of Non-Boerhaave Syndrome: A Comparison With Boerhaave Syndrome

Journal of Investigative Medicine High
Impact Case Reports
Volume 9: 1–6
© 2021 American Federation for
Medical Research
DOI: 10.1177/23247096211014683
journals.sagepub.com/home/hic


Shunsuke Hayakawa, MD¹, Ryo Ogawa, MD, PhD¹, Sunao Ito, MD¹,
Seiichi Nakaya, MD¹, Tomotaka Okubo, MD, PhD¹, Hiroyuki Sagawa, MD, PhD¹,
Tatsuya Tanaka, MD, PhD¹, Hiroki Takahashi, MD, PhD¹,
Yoichi Matsuo, MD, PhD¹, and Shuji Takiguchi, MD, PhD¹

Abstract

Boerhaave syndrome (BS) is frequently reported in cases of esophageal perforation; however, there are relatively few studies on non-Boerhaave syndrome (nBS). This study clarifies the appropriate diagnosis and treatment for patients with nBS among those with esophageal ruptures. Twelve patients with esophageal ruptures who underwent surgery at our department over 14 years were classified into 2 groups: 4 in the nBS group and 8 in the BS group. Patient characteristics, surgical methods, surgical outcomes, and complications were compared between the groups. The chief complaints varied between the groups. The nBS group had significantly higher preoperative C-reactive protein ($P = .007$) and required 5 days (median) from onset to surgery. Moreover, the perforation diameter was significantly smaller in the nBS group than in the BS group ($P = .013$). Suturing of the perforation site was performed during the initial surgery in 8 BS group patients (100%) and 1 nBS group patient (25%; $P = .018$). Only drainage was performed during the initial surgery for 3 nBS group patients (75%). The complications did not significantly differ between the groups ($P = 1.000$), and no deaths were reported. The chief complaints of patients with nBS are diverse, and esophageal perforation should be cited as a differential diagnosis even in the absence of vomiting or chest pain symptoms. In the initial surgery for patients with nBS, the perforation site does not necessarily need to be closed. It is treatable by second-stage surgery or by natural closing.

Keywords

esophageal perforation, mediastinal abscess, Boerhaave syndrome, diagnosis, drainage

Introduction

Esophageal perforation is associated with a prognostic mortality rate of 20% to 40% and has a relatively poor prognosis.^{1,2} Open surgical closure with suturing by thoracotomy or laparotomy is the gold standard in the treatment of esophageal perforation, although recent reports describe using laparoscopy and thoracoscopy.^{3,4} Esophageal stents and polyglycolic acid sheets in upper gastrointestinal endoscopy are some of the treatments reported to have been attempted for patients with perforations because there are no established treatments.^{5,6} Patients with esophageal perforation frequently experience Boerhaave syndrome (BS), which is an acute-onset condition with vomiting symptoms as the trigger; these patients frequently present with chest pain as the primary complaint.^{7,8} In contrast, esophageal ruptures in patients with non-Boerhaave syndrome (nBS) have a poorly

defined trigger, and a number of patients with chronic onset have nonspecific symptoms, such as fever.^{9,10} Moreover, there are difficult-to-treat patients in whom abscesses are formed in the mediastinum and around the esophagus.¹¹ nBS is heterogeneous; indeed, the course and disease state of chronic-onset nBS is different from that of BS. Therefore, it is necessary for surgeons to be familiar with the

¹Nagoya City University, Nagoya City, Japan

Received February 22, 2021. Revised March 31, 2021.
Accepted April 10, 2021.

Corresponding Author:

Ryo Ogawa, Graduate School of Medical Sciences, Gastroenterological Surgery, Nagoya City University, 1 Banchi Kawasumi, Mizuho-cho, Mizuho-Ku, Nagoya City, Aichi 467-8602, Japan.
Email: r-ogawa@med.nagoya-cu.ac.jp



Table 1. Patient Characteristics.

Characteristics	BS group	nBS group	P
Patients (n)	8	4	—
Age (years)	66 (range = 38.0-86.0)	47.5 (range = 36.0-72.0)	.174
Sex (male/female)	6/2	3/1	1.000
BMI (kg/m ²)	22.2 (range = 17.4-25.8)	22.6 (range = 17.0-30.9)	.865
Abscess forming case (n)	0 (0%)	4 (100%)	.002
Within a day from onset to surgery (n)	8 (100%)	0 (0%)	.002
BT at first consultation (°C)	37.4 (range = 35.4-38.9)	38.4 (range = 36.8-40.9)	.253
HR at first consultation (/min)	93 (range = 60-140)	114 (range = 98-133)	.230
Average BP at first consultation (mmHg)	91 (range = 70-119)	94 (range = 80-94)	.865
Vomiting symptom (n)	8 (100%)	0 (0%)	.002
Chest pain symptom (n)	4 (50%)	1 (25%)	.576
Preoperative WBC (/mm ³)	9150 (range = 3700-20 000)	14 350 (range = 8100-177 00)	.395
Preoperative CRP (mg/dl)	0.38 (range = 0.03-18.19)	25.4 6 (range = 19.7-35.5)	.007
Rupture into chest cavity (n)	5 (62.5%)	2 (50.0%)	1.000

Abbreviations: BS, Boerhaave syndrome; nBS, non-Boerhaave syndrome; BMI, body mass index; BT, body temperature; HR, heart rate; WBC, white blood cell; CRP, C-reactive protein.

characteristics of the disease to provide better diagnosis and treatment for nBS.

In this study, the 2 groups of patients with nBS and BS at our institution were compared with investigate the most appropriate diagnostic and therapeutic methods for nBS.

Cases Description

Classification of Groups

Twelve patients who underwent surgery for esophageal perforation between January 2006 and March 2020 were included. In all patients, the presence of a perforation in the esophagus was confirmed by computed tomography, upper gastrointestinal series contrast radiography, endoscopy, or intraoperative findings (including patients in whom the diagnosis was obtained postoperatively). Patients with perforation due to esophageal cancer and perforation of the esophagogastric junction were excluded. Eight patients with BS who had characteristic triggers, such as severe emesis and acute onset were included in the BS group, whereas 4 patients with nonspecific symptoms were included in the nBS group. Retrospective comparisons were made between the groups' patient characteristics, surgical outcomes, and complications.

This study is in accordance with the Declaration of Helsinki. This study was approved by the ethics review committee of Nagoya City University (No. 60-19-0081). Verbal informed consent was obtained from a legally authorized representatives for anonymized patient information to be published in this article.

Statistical Analysis

The statistical software EZR (a package of the R statistical software) was used to test for significant differences between the 2 groups.¹² The proportion (frequency) test

was determined to be significant using Fisher's exact test, and continuous variables were subjected to Mann-Whitney *U* tests. *P* value <.05 was considered significant.

Patient Characteristics

Twelve patients were included in this study. Their background characteristics are summarized in Table 1.

Eight (100%) patients in the BS group and none (0%) in the nBS group underwent surgery within a day of onset (*P* = .002). The nBS group had a median of 5 days (range = 4-12) from onset to surgery. Vomiting symptoms were observed in 8 patients (100%) in the BS group and none in the nBS group (*P* = .002). There were no significant differences in chest pain symptoms between the 2 groups (*P* = .576). White blood cells and C-reactive protein levels (*P* = .395, *P* = .007, respectively) were high in the nBS group but only C-reactive protein showed a significant difference. Thoracic perforations were observed at a constant rate in both groups, and there was no significant difference between the groups (*P* = 1.000). The perforation sites were the left lateral wall of the lower esophagus in 6 patients, right lateral wall of the lower esophagus in 2 patients in the BS group, cervical esophagus in 2 patients, and middle intrathoracic esophagus in 2 patients in the nBS group (Figure 1).

Patients in nBS Group

Patients in the nBS group are outlined in Table 2.

Patient 1 experienced esophageal perforation in the mid-thoracic area, which was caused by the fish bone. The patient complained of upper-right abdominal pain, and surgery was performed on day 4 from the onset. Although postoperative pulmonary atelectasis was observed, the course was generally favorable.

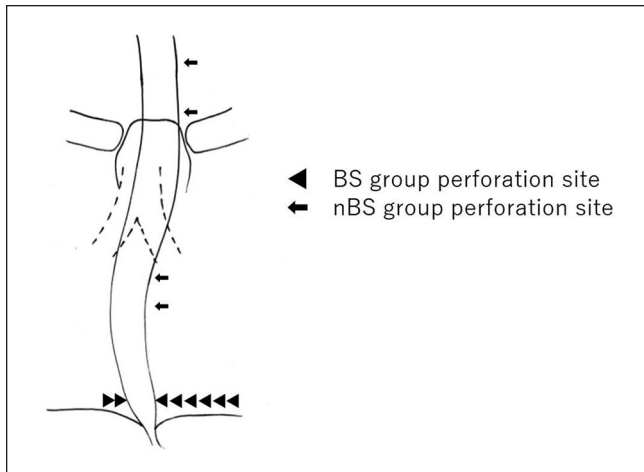


Figure 1. Perforation site. BS, Boerhaave syndrome; nBS, non-BS.

Patient 2 underwent transesophageal echography at another institution, where after febrile symptoms appeared, and on day 2, the patient was in a general condition and catheter ablation treatment could be administered. However, this suddenly changed on day 4, and the patient was transferred to our institution in cardiopulmonary arrest (CPA). Cervical esophageal perforation was diagnosed and surgery was performed through a cervical incision; however, only drainage was performed because the perforation site could not be identified. Although postoperative pneumonia was observed, the postoperative course was favorable without requiring repeat surgery. However, severe cerebral disorder due to hypoxemia at the time of CPA remained.

Patient 3 had a tuberculous esophageal perforation, with the chief complaint being right chest pain, and the perforation site was found in the mid-thoracic area. Although thoracoscopic surgery was performed, the perforation site could not be identified in the initial surgery and only drainage was performed. The perforation site could not be identified, although repeat surgery was performed because of continuation of fever. Therefore, mediastinoscopic esophagectomy was performed at a later date, and the postoperative course was favorable.

Patient 4 visited our institution complaining of hoarseness. Thoracoscopic drainage was performed under the diagnosis of a mediastinal abscess of unknown origin. The patient was subsequently diagnosed with cervical esophageal perforation based on an upper gastrointestinal endoscopy. The drainage was continued for about a month and the patient recovered.

In all 4 patients, the chief complaint and perforation site differed, and it took at least 4 days or more from the onset of symptoms to surgery.

Surgical Results and Complication

The surgical results are described in Table 3. All patients in the BS group underwent open thoracotomy, and thoracoscopy and laparoscopy were not used. In the nBS group,

thoracoscopy was used in 2 patients; one underwent thoracotomy and the other cervical incision. There were no significant differences in the duration of surgery or volume of blood loss between the 2 groups ($P = .089$, $P = .443$, respectively). Identification of the perforation site and suture closure were feasible in all patients in the BS group at the time of the initial surgery, whereas the perforation site was difficult to identify in 3 patients (75%) in the nBS group at the time of the initial surgery ($P = .018$). The perforation diameter was 30 mm (range = 13-40 mm) in the BS group and 3 mm (range = 3-10 mm) in the nBS group. The perforation diameter in the nBS group tended to be smaller ($P = .013$). The perforation site in one case in the BS group was diagnosed by contrast radiography. The diameter of the perforation was unknown because it could not be confirmed by visual inspection (including endoscopy). There were no significant differences in the duration of postoperative hospital stay or the number of days to start of oral intake ($P = .234$, $P = .732$, respectively). In both groups, complications of Clavien–Dindo of ≥ 3 were observed in half of the patients ($P = 1.000$). No in-hospital deaths were reported in either group.

The surgical complications are described in Table 4. Re-operation was performed in one patient (12.5%) in the BS group and one patient (25%) in the nBS group ($P = 1.000$). There were 2 (50%) patients with refractory fistulas in the nBS group ($P = .091$); one underwent esophagectomy and drainage treatment was continued for the other for around a month, resulting in complete resolution.

Discussion

Esophageal perforation is a condition associated with a high mortality rate and difficult-to-treat patients are common. BS and iatrogenicity account for majority of the esophageal ruptures, and the primary iatrogenic causes include endoscopic penetration.^{13,14} Eight (67%) idiopathic patients and one (8%) iatrogenic patient in our study demonstrated a low rate of iatrogenicity. Among patients experiencing esophageal ruptures, BS is frequently observed, and numerous studies have reported this disease state and its associated treatments.^{8,15} However, nBS is rarely observed and many points require further clarification. Therefore, retrospective comparisons with BS were made to clarify the appropriate diagnoses and treatments for nBS. Although vomiting and chest pain are known triggers and chief complaints for BS, vomiting was not observed in nBS and chest pain was only observed in one patient; therefore, the symptoms differed across patients. Furthermore, nBS presented as mediastinal abscess in all patients; however, there was one patient in whom the diagnosis of esophageal rupture was difficult. Hence, it took place at another department before surgery was performed.

Of the mediastinal abscesses requiring treatment, 52% (12/23) involved the esophagus, including 17% (4/23) with perforations from esophageal cancer, 22% (5/23) after

Table 2. Cases of nBS Group.

Case no.	Age (years)	Sex	Chief complaint	Causes of perforation	Perforation site	Time until surgery (days)	Surgical procedure	Perforation site size (mm)	Postoperative hospital stay (days)	CD classification	Outcome
1	41	Female	Upper right abdominal pain	Fish bone	Mt	4	Right thoracotomy and simple suture	10	30	I	Alive
2	54	Male	CPA	Iatrogenic	Ce	4	Drainage	Unknown	31	II	Alive
3	36	Male	Right chest pain	Tuberculosis	Mt	6	^a	3	64	IIIb	Alive
4	72	Male	Hoarseness	Unclear	Ce	12	Right thoracotomy and drainage	3	44	II	Alive

Abbreviations: CD, Clavien–Dindo; CPA, cardiopulmonary arrest; nBS, non-Boerhaave syndrome.

^aFirst surgery: thoracoscopic right thoracic drainage. Second surgery: transhiatal laparoscopic mediastinal drainage. Third surgery: thoracoscopic esophagectomy.

Table 3. Surgical Results.

Characteristics	BS group (n = 8)	nBS group (n = 4)	P
Operation time (minutes)	181 (range = 96-360)	108.5 (range = 85-148)	.089
Blood loss (median)	70 (range = 14-520)	70 (range = 14-750)	.443
Perforation site unknown at first surgery (n)	0 (0%)	3 (75%)	.018
Perforation size (mm)	30 (range = 13-40)	3 (range = 3-10)	.013
Suture treatment of perforation site (n)	8 (100%)	1 (25%)	.018
Postoperative hospital stay (days)	56.5 (range = 16-134)	37.5 (range = 30-64)	.234
Start of oral intake (days)	38 (range = 4-87)	34 (range = 19-51)	.732
CD classification ≥ 3 (n)	4 (50%)	2 (50%)	1.000
Hospital mortality (n)	0 (0%)	0 (0%)	1.000

Abbreviations: BS, Boerhaave syndrome; nBS, non-Boerhaave syndrome; CD, Clavien–Dindo.

Table 4. Surgical Complications.

	BS group (n = 8)	nBS group (n = 4)	P
Re-operation (n)	1 (12.5%)	1 (25%)	1.000
Leakage (n)	2 (25%)	0 (0%)	0.515
Residual abscess (n)	1 (12.5%)	0 (0%)	1.000
Surgical site infection (n)	2 (25%)	0 (0%)	0.515
Uncontrollable fistula (n)	0 (0%)	2 (50%)	0.091
Others (n)	1 (12.5%)	0 (0%)	1.000

Abbreviations: BS, Boerhaave syndrome; nBS, non-Boerhaave syndrome.

esophagectomy, and 13% (3/23) with esophageal perforations (benign).¹¹ Mediastinal abscesses may be caused by esophageal perforation, but the timing of surgery may be missed without a diagnosis. Therefore, even in the absence of vomiting and chest pain, suspicion of esophageal perforation in cases of mediastinal abscesses is crucial for the diagnosis.

BS cases are said to occur more frequently as perforations in the left lateral wall of the lower thoracic esophagus; however, esophageal ruptures of nBS cases that present with abscesses can have various causes and perforations can also develop in various locations. In this study, there were 2 nBS

patients with cervical perforations and 2 nBS patients with middle intrathoracic perforations. One patient eventually underwent esophagectomy. Because the treatment is likely to be complicated, treatment of nBS at institutions experienced in esophageal surgery is considered necessary.

Two important points in the treatment of esophageal rupture are “treatment of the perforation” and “drainage of the contaminated mediastinal and thoracic cavity.” In BS patients, the perforation sites can be identified and the suture closed in the initial surgery in all patients. However, in nBS patients, the perforation site was unknown in 3 patients (75%). In the nBS group, the diameter was significantly

smaller than in the BS group (30 mm in the BS group vs 3 mm in the nBS group), thereby making it difficult to identify the perforation site because of the long time from onset to surgery and the contamination of the surgical field. All patients in whom the perforation site was unknown survived as a result of performing only local irrigation and drainage. In particular, Patient 2 (Table 4) was saved despite his CPA status at the time of diagnosis. If identifying the perforation site is difficult in the initial surgery for chronic-onset nBS, it does not appear to be necessary to take time to identify the perforation site. Although the duration of surgery was not significantly different between nBS (108.5 minutes) and BS (181 minutes) patients in this study, the short duration may have resulted in the high life-saving rate.

In addition to surgery, methods of abscess drainage include computed tomography-guided drainage and trans-esophageal abscess puncture.^{16,17} However, in either option, it should be ensured that the general condition of the patient is stable and management of the perforation site is conducted simultaneously. In this study, BS was treated with sutures (or suture plus T-tube insertion) in all patients, whereas suture closure was performed in one nBS patient and spontaneous closure was observed in 2 nBS patients (one patient became refractory and closure took about a month and one patient was refractory). Spontaneous closure was considered possible at a certain rate. In the last case, esophagectomy was performed after their general condition improved. As a result of this review, in chronic nBS, we believe that it is important to complete “treating the perforation site” and “performing abscess drainage,” even if they were at a different time.

For refractory fistulas after esophageal rupture, there are reports of using stent insertion, polyglycolic acid sheets, and fibrin glue as opposed to surgery.^{5,6,18,19} However, 25% of the patients with stents have been reported to require surgical conversion.²⁰ Therefore, the use of stent may need to be carefully considered in view of the risks of surgery.

The major limitation of this study is the small number of cases, because there are only a few cases of nBS. Future, larger-scale studies are therefore warranted. Although the number of cases is small, we should learn from the present study in cases of nBS that the primary symptoms are diverse and may not need repairing of perforation site in first surgery.

Conclusion

The chief complaints of patients with nBS are diverse and esophageal perforation should be cited as a differential diagnosis even in the absence of symptoms of vomiting or chest pain.

In the initial surgery for patients with nBS, the perforation site does not necessarily need to be closed; it might be treatable by second-stage surgery or by natural closing.

Acknowledgments

We would like to thank Enago (www.enago.jp) for the English language review.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

This study is in accordance with the Declaration of Helsinki. This study was approved by the Ethics Review Committee of Nagoya City University (No. 60-19-0081).

Informed Consent

Verbal informed consent was obtained from a legally authorized representatives for anonymized patient information to be published in this article.

References

1. Brinster CJ, Singhal S, Lee L, et al. Evolving options in the management of esophageal perforation. *Ann Thorac Surg.* 2004;77:1475-1483.
2. Pezzetta E, Kokudo T, Uldry E, et al. The surgical management of spontaneous esophageal perforation (Boerhaave's syndrome): 20 years of experience. *Biosci Trends.* 2016;10:120-124.
3. Hayakawa S, Mitsui A, Kato Y, et al. Laparoscopic transhiatal suture closure for spontaneous esophageal rupture: a case report. *Surg Case Rep.* 2019;5:149.
4. Cho JS, Kim YD, Kim JW, Seok HI, Kim MS. Thoracoscopic primary esophageal repair in patients with Boerhaave's syndrome. *Ann Thorac Surg.* 2011;91:1552-1555.
5. Wu G, Zhao YS, Fang Y, et al. Treatment of spontaneous esophageal rupture with transnasal thoracic drainage and temporary esophageal stent and jejunal feeding tube placement. *J Trauma Acute Care Surg.* 2017;82:141-149.
6. Ishikawa Y, Tagami T, Hirashima H, Fukuda R, Moroe Y, Unemoto K. Endoscopic treatment of Boerhaave syndrome using polyglycolic acid sheets and fibrin glue: a report of two cases. *J Nippon Med Sch.* 2017;84:241-245.
7. Kincaid K, Ramirez EG. Esophageal rupture: Boerhaave syndrome. *Crit Care Nurs Q.* 2012;35:196-202.
8. Griffin SM, Lamb PJ, Shenfine J, Richardson DL, Karat D, Hayes N. Spontaneous rupture of the oesophagus. *Br J Surg.* 2008;95:1115-1120.
9. Kupeli M, Dogan A. Successful treatment of a late diagnosed esophageal perforation with mediastinitis and pericardial abscess. *J Coll Phys Surg Pak.* 2018;28:972-973.
10. Shibuya H, Ikehara H, Andoh K, et al. Endoscopic ultrasound-guided drainage of a mediastinal abscess caused by an ingested fish bone. *Intern Med.* 2019;58:2173-2177.

11. Arellano RS, Gervais DA, Mueller PR. Computed tomography-guided drainage of mediastinal abscesses: clinical experience with 23 patients. *J Vasc Interv Radiol.* 2011;22:673-677.
12. Kanda Y. Investigation of the freely available easy-to-use software "EZR" for medical statistics. *Bone Marrow Transplant.* 2013;48:452-458.
13. Lindenmann J, Matzi V, Neuboek N, et al. Management of esophageal perforation in 120 consecutive patients: clinical impact of a structured treatment algorithm. *J Gastrointest Surg.* 2013;17:1036-1043.
14. Schweigert M, Sousa HS, Solymosi N, et al. Spotlight on esophageal perforation: a multinational study using the Pittsburgh esophageal perforation severity scoring system. *J Thorac Cardiovasc Surg.* 2016;151:1002-1009.
15. Han D, Huang Z, Xiang J, Li H, Hang J. The role of operation in the treatment of Boerhaave's syndrome. *Biomed Res Int.* 2018;2018:8483401.
16. Wehrmann T, Stergiou N, Vogel B, Riphaut A, Köckerling F, Frenz MB. Endoscopic debridement of paraesophageal, mediastinal abscesses: a prospective case series. *Gastrointest Endosc.* 2005;62:344-349.
17. Latif A, Selim M, Kapoor V, Ali M, Mirza MM, Stavas JM. Successful percutaneous computed tomography guided drainage of mediastinal abscess in esophageal perforation. *Intractable Rare Dis Res.* 2019;8:221-223.
18. Kimura T, Takemoto T, Fujiwara Y, Yane K, Shiono H. Esophageal perforation caused by a fish bone treated with surgically indwelling drainage and fibrin glue injection for fistula formation. *Ann Thorac Cardiovasc Surg.* 2013;19:289-292.
19. Ong GKB, Freeman RK, Ascoti AJ, et al. Patient outcomes after stent failure for the treatment of acute esophageal perforation. *Ann Thorac Surg.* 2018;106:830-835.
20. Glatz T, Marjanovic G, Kulemann B, et al. Management and outcome of esophageal stenting for spontaneous esophageal perforations. *Dis Esophagus.* 2017;30:1-6.