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

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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 esophagus11 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
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 to 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. 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.

### 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/m²)             | 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 (/mm³) | 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.
In the nBS group, the BS group underwent open thoracotomy, and thoracoscopic drainage 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 ($P = .91$); 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.\(^1\)\(^2\)\(^3\) 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.\(^3\)\(^4\) 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...
esophagectomy, and 13% (3/23) with esophageal perforations (benign). 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%).

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 | Drainage | 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.

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.

| Characteristics | 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.
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. 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. However, 25% of the patients with stents have been reported to require surgical conversion. 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.

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**Ethics Approval**

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**Informed Consent**

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

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