Safety and Efficacy of Nonoperative Treatment in Esophageal Perforation Caused by Foreign Bodies

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INTRODUCTION: Esophageal foreign bodies are often treated by endoscopy, but the treatment of esophageal perforation caused by foreign bodies remains controversial. The purpose of this study was to investigate the safety and efficacy of nonoperative treatment of esophageal perforation caused by foreign bodies.

METHODS: We retrospectively analyzed 270 patients admitted to our hospital for esophageal perforation caused by foreign bodies from January 2012 to December 2020, all of whom received nonoperative treatment.

RESULTS: The mean age of the patients was 56 ± 17 years, and fish bones were the most common type of foreign body. A total of 61.2% of the perforations were in the cervical esophagus. All patients received nonoperative treatment initially, and the foreign body removal rate using endoscopy reached 97%. The perforation healing rate reached 94.8%, whereas 3 patients (1.1%) died during hospitalization. The median (range) duration of hospitalization was 4 days (3–6). Multivariable analysis showed age ≥ 66 years (odds ratio [OR]: 2.196; 95% confidence interval [CI]: 1.232–3.916; P = 0.008), men (OR: 1.934; 95% CI: 1.152–3.246; P = 0.013), and time to treatment (OR: 1.126; 95% CI: 1.027–1.233; P = 0.011) were independent risk factors for infection, whereas the risk of infection was lower when the foreign body type was fish bone (OR: 0.557; 95% CI: 0.330–0.940; P = 0.028).

DISCUSSION: Nonoperative treatment is safe and effective for esophageal perforation caused by foreign bodies. Even if perforation is combined with infection, active nonoperative treatment can still achieve a good effect. Early intervention can effectively reduce the risk of infection and improve patient outcomes.

INTRODUCTION
Esophageal perforation is a rare but life-threatening emergency that presents a great challenge to clinicians (1). Despite the development of medical technology, the mortality rate of esophageal perforation is still high because esophageal perforation is often accompanied by serious complications, such as bleeding, mediastinal abscesses, isolated hemorrhagic pericardial effusion, and sepsis (2–4). The common causes of esophageal perforation include spontaneous, iatrogenic, traumatic, and tumor (5). However, esophageal perforation caused by foreign bodies is not rare in China. At present, the treatment of esophageal perforation is still controversial. With the progress of endoscopic technology, endoscopic therapy has been gradually applied to treat esophageal perforations. Sudarshan et al. (6) believed that surgical treatment is still required for most patients and nonoperative treatment can be successful for carefully selected iatrogenic/traumatic esophageal perforations. Huang et al. (7) retrospectively analyzed the efficacy of surgical treatment for 38 patients with esophageal perforation caused by foreign bodies and concluded that surgical treatment is still the main treatment for esophageal perforation. However, a study involving 25 newborns with esophageal perforation showed that nonoperative treatment with parenteral nutrition and antibiotics was successful (8). Jiang et al. (9) also found that cervical esophageal perforation without signs of abscess formation can be treated conservatively. However, the sample size of these studies was too small, and few studies have examined nonoperative treatment options for foreign body-induced esophageal perforation. Hence, our data here present the safety and efficacy of nonoperative treatment for esophageal perforation caused by foreign bodies.

MATERIALS AND METHODS
Patients and data collection
We retrospectively analyzed the electronic medical record system of the First Affiliated Hospital of Nanchang University from...
January 2012 to December 2020, and 299 patients with esophageal perforation caused by foreign bodies received nonoperative treatment. The exclusion criteria were as follows: (i) no foreign body found by endoscopy or surgery, (ii) foreign body removed in another hospital, (iii) patient discharged automatically without treatment, and (iv) patients with incomplete demographic data. Data collection included sex, age, underlying disease (diabetes, hypertension, cardio-cerebrovascular diseases, and psychosoma), body mass index (BMI), serum albumin, symptoms, time from perforation to treatment, diagnosis method, types of foreign body, location of perforation, complications after perforation (pleural effusion, mediastinal/subcutaneous emphysema, pneumothorax, and pneumonia), therapy method, foreign body removal rate, perforation healing rate, postoperative adverse events (fever, pneumonia, pleural effusion, sepsis, and multisystem organ failure), secondary endoscopic intervention, hospital stay, and death rate. All included cases were recorded in the Human Genetic Resources Center of the First Affiliated Hospital of Nanchang University. This study was approved by the Human Ethics Committee of The First Affiliated Hospital of Nanchang University. All patients provided written informed consent for endoscopic procedure.

**Esophageal perforation management**

All patients with suspected perforation were told to stop oral intake on admission and subsequently undergo neck/chest computed tomography (Figure 1). Patients received nonoperative treatment initially after the diagnosis of esophageal perforation, and the nonoperative treatment included the endoscopic removal of ingested foreign bodies (Figure 2), antibiotic therapy, proton pump inhibitors (PPIs), and nasogastric tube placement for gastric decompression. The expert team composed of gastroenterology, otolaryngology, thoracic surgery, emergency, and anesthesia departments of our hospital monitored the patient’s condition changes, and timely operation was performed to ensure the patient’s safety when the condition was difficult to treat by nonoperative treatment. All the doctors in the team were attending physicians or above, and all the doctors involved in endoscopic intervention had more than 3 years of foreign body removal experience. For patients with a large pneumothorax or pleural effusion diagnosed on computed tomography (CT), closed thoracic drainage was performed. Failure to remove foreign bodies initially using endoscopy was eventually attempted again by an endoscopic physician in the operating room. When the foreign body cannot be removed through the endoscopy, surgery is performed immediately to remove the foreign body. All patients underwent endoscopy or esophagogram (using water-soluble contrast medium) within 1 month after discharge.

**Definitions**

Esophageal perforation was defined as a foreign body penetrating the outer wall of the esophagus, extraluminal air or fluid surrounding the esophagus or within the mediastinum, or pleural effusions, as seen by CT. Closed thoracic drainage was performed. Failure to remove foreign bodies initially using endoscopy was eventually attempted again by an endoscopic physician in the operating room. When the foreign body cannot be removed through the endoscopy, surgery is performed immediately to remove the foreign body. All patients underwent endoscopy or esophagogram (using water-soluble contrast medium) within 1 month after discharge.
bodies. Time to treatment refers to the time between the ingestion of the foreign body and the treatment of perforation. Patients with pyogenic esophagitis, pneumonia, mediastinitis, and empyema were classified into the infection group. Measures used to assess the nutritional status include BMI and albumin, and we used BMI <18.5 kg/m² and/or albumin <3.5 g/L as the general cutoff for underweight (10,11). The total removal rate refers to the success rate of foreign body removal by endoscopy, whereas the initial removal rate refers specifically to the success rate of foreign body removal by initial endoscopy. Through our nonoperative treatment (including endoscopy, antibiotics, and PPIs), esophageal mucosal healed confirmed by endoscopy and perforation healed by esophagogram were regarded as perforation healing, and patients with mucosal healing achieved by additional surgery after initial nonoperative treatment were not included. Patients who failed to have their foreign bodies removed initially under endoscopy received a secondary endoscopic intervention. The death rate refers to the probability of death because of esophageal perforation caused by foreign bodies and directly related complications during hospitalization or within 1 month after discharge.

Statistical analysis
Data are presented as the mean ± SD, median (interquartile range), or ratio. The χ² test or Fisher exact test was used to analyze categorical variables. The Student t test or the Mann-Whitney U test was performed to analyze quantitative data. Bonferroni correction was applied to the comparison of the 3 groups. The optimal cutoff values of quantitative data were determined by receiver operating characteristic curve analysis. Univariable analysis was performed to assess the risk factors associated with infection, and the results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). Variables with P < 0.20 were incorporated into the multivariable analysis. P < 0.05 was considered statistically significant. Cumulative risk for the infection was calculated by using the Kaplan-Meier method. SPSS software version 25.0 (IBM, Chicago, IL) and R statistical software 4.1.1 (www.r-project.org) were used for statistical analysis.

RESULTS
Patient characteristics
A total of 270 patients with esophageal perforation caused by foreign bodies were included (Figure 3). All patients received initial nonoperative treatment in our hospital. The baseline characteristics of the patients are presented in Table 1. The mean age of these patients was 56 ± 17 years, and 144 of these patients (53.3%) were female. These patients had an average BMI of 21.6 ± 4.0 kg/m² and an average albumin of 4.3 ± 0.5 g/L. Ten (3.7%) had diabetes, 52 (19.2%) had hypertension, 8 (2.9%) had cardio-cerebrovascular diseases, and 6 (2.2%) had psychosoma. Chest
Table 2. Characteristics of perforated lesions

| Variable                     | N = 270 |
|------------------------------|---------|
| Types of foreign body, n (%) |         |
| Fish bones                   | 160 (59.2) |
| Jujube pit                   | 26 (9.6) |
| Animal bones                 | 64 (23.7) |
| False tooth                  | 3 (1.1) |
| Others                       | 17 (6.4) |
| Endoscopy, n (%)             |         |
| Esophagoscopy                | 120 (44.4) |
| Gastroscopy                  | 150 (55.6) |
| Time to treatment, n (%)     |         |
| ≤24 hr                       | 104 (38.5) |
| >24 hr                       | 166 (61.5) |
| Location of perforation, n (%) |       |
| Cervical                     | 166 (61.5) |
| Thoracic                     | 92 (34.1) |
| Abdominal                    | 12 (4.4) |
| Complications after perforation, n (%) | |
| Pyogenic esophagitis         | 88 (32.5) |
| Pleural effusion             | 33 (12.2) |
| Mediastinal/subcutaneous emphysema | 51 (18.9) |
| Pneumonia                    | 43 (15.9) |
| Pneumothorax                 | 11 (4.0) |
| Mediastinitis/empyema        | 3 (1.1) |

Characteristics of perforated lesions

In our study, the most common foreign body that caused esophageal perforation was fish bones, which accounted for 59.6% of the foreign bodies, followed by animal bones (23.7%) and jujube pits (9.6%). Most of the perforations were in the cervical esophageal region (61.5%), whereas 92 (34.1%) were in the thoracic esophageal region and 12 (4.4%) were in the abdominal esophageal region. Foreign bodies were removed under gastroscopy in 150 patients and esophagoscopy in 120 patients. Of 166 patients who received treatment for perforation after 24 hours, only 38.5% (104/270) received treatment within 24 hours. Thus, 88 patients developed pyogenic esophagitis, 33 had pleural effusion, 51 had mediastinal/subcutaneous emphysema, and 43 had pneumonia (Table 2).

Outcome of nonoperative treatment

All patients were followed up 1 month after discharge. The success rate of foreign body removal by initial endoscopy was 94.4%, whereas the total removal rate was 97%. Perforations healed in 94.8% of the patients, and 3 patients (1.1%) died of multisystem organ failure during hospitalization. Seven patients (2.6%) successfully removed the foreign body during the second endoscopic treatment. All patients initially received endoscopic therapy, PPIs, and antibiotics. A total of 220 patients (81.5%) underwent nasogastric tube placement after foreign body removal, and the median (range) period of nasogastric tube placement was 5 days (3–7). The median (range) duration of hospitalization was 4 days (3–6) (Table 3).

Comparison between infection and noninfection groups

There were no significant differences between the infection and noninfection groups for diabetes, hypertension, cardiovascular diseases, psychosomnemima, BMI, albumin, or the location of perforation (Table 4). The mean age of the infection group was 60 ± 17 years, which was significantly higher than that of the noninfection group (P = 0.001). A total of 54.3% of the infection group were men, whereas most of the noninfection group were women (P = 0.017). Most of the patients in the infection group received treatment for perforation after 24 hours, compared with 46.9% in the noninfection group (P < 0.001). However, there were no significant differences in the foreign body removal rate, secondary intervention rate, postoperative adverse events, or mortality between the infection and noninfection groups. The perforation healing rate of the noninfection group was 97.2%, which was slightly higher than that of the infection group (92.1%). There was no significant difference between the groups. The median duration of hospitalization was longer in patients with infection (5 days; range 3–7 days) than in those without infection (4 days; range 3–6 days; P = 0.005).

Univariate and multivariate analysis of risk factors for infection

The risk factors for infection after esophageal perforation caused by foreign bodies are provided in Table 5. Univariate analysis showed that having an age of 66 years or older, being male, and time to treatment were risk factors for infection after esophageal perforation caused by foreign bodies, and the fish bone type of foreign body had a lower risk of infection (Figure 4). According to
In the multivariable analysis, age 66 years or older (OR: 2.196; 95% CI: 1.232–3.916; \( P = 0.008 \)), male (OR: 1.934; 95% CI: 1.152–3.246; \( P = 0.013 \)), and time to treatment (OR: 1.126; 95% CI: 1.027–1.233; \( P = 0.011 \)) were independent risk factors for infection, whereas the risk of infection was lower when the foreign body type was fish bone (OR: 0.557; 95% CI: 0.330–0.940; \( P = 0.028 \)) (Figure 5). Figure 6 shows the increased risk of infection with the extension of intervention time.

### Outcome comparison of different location of perforation

In our study, the perforation healing rate of thoracic esophageal perforation was 97.8%, which was higher than that of the cervical group (94.0%) and abdominal group (83.3%), but not statistically significant. The endoscopic foreign body removal rate of the thoracic group was as high as 100%, which was significantly higher than that of the abdominal group (\( P = 0.047 \)). There were no significant differences between the cervical group and thoracic group or between the cervical group and abdominal group. In addition, there were no significant differences in the secondary intervention rate, postoperative adverse events, duration of hospitalization, or death rate among the different perforation sites (Table 6).

### DISCUSSION

Foreign body ingestion is common worldwide, and most foreign bodies can spontaneously pass through the gastrointestinal tract (12,13). However, some foreign bodies may stay in the gastrointestinal tract and cause serious complications, complicating treatment (14,15). Esophageal perforation caused by foreign bodies is still an urgent problem to be solved. At present, the treatment of esophageal perforation is becoming diversified (16), but the efficacy of endoscopic therapy has not been fully explored. As a large tertiary hospital, our hospital has set up a multidisciplinary expert team for the treatment of esophageal perforation caused by foreign bodies. Therefore, we designed this research to...

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**Table 4. Comparison between infection and noninfection groups**

| Variable                              | Infection group (n = 127) | Noninfection group (n = 143) | \( P \) |
|---------------------------------------|---------------------------|-------------------------------|--------|
| Age, yr, mean ± SD                    | 60 ± 17                   | 53 ± 16                       | 0.001  |
| Sex, n (%)                            |                           |                               | 0.017  |
| Female                                | 58 (45.7)                 | 86 (60.1)                     |        |
| Male                                  | 69 (54.3)                 | 57 (39.9)                     |        |
| Underlying diseases, n (%)            |                           |                               |        |
| Diabetes                              | 7 (5.5)                   | 3 (2.1)                       | 0.246  |
| Hypertension                          | 21 (16.5)                 | 31 (21.7)                     | 0.285  |
| Cardio-cerebrovascular diseases       | 5 (3.9)                   | 3 (2.1)                       | 0.996  |
| Psychoneurosis                        | 2 (1.6)                   | 4 (2.8)                       | 0.790  |
| BMI <18.5 kg/m², n (%)                | 29 (22.8)                 | 20 (14.0)                     | 0.060  |
| Albumin <3.5 g/L, n (%)               | 11 (8.7)                  | 6 (4.2)                       | 0.132  |
| Types of foreign body, n (%)          |                           |                               | 0.011  |
| Fish bones                            | 65 (51.2)                 | 95 (66.4)                     |        |
| Others                                | 62 (48.8)                 | 48 (33.6)                     |        |
| Location of perforation, n (%)        |                           |                               | 0.871  |
| Cervical                              | 76 (59.9)                 | 90 (62.9)                     |        |
| Thoracic                              | 45 (35.4)                 | 47 (32.9)                     |        |
| Abdominal                             | 6 (4.7)                   | 6 (4.2)                       |        |
| Time to treatment, n (%)              |                           |                               | <0.001 |
| \( \leq \) 24 hr                     | 28 (22.0)                 | 76 (53.1)                     |        |
| >24 hr                                | 99 (78.0)                 | 67 (46.9)                     |        |
| WBC, 10⁹/L, mean ± SD                 | 11.42 ± 4.22              | 8.59 ± 2.21                   | <0.001 |
| Foreign body removal, n (%)           | 123 (96.9)                | 139 (97.2)                    | 0.865  |
| Secondary endoscopic intervention, n (%) | 3 (2.4)                  | 4 (2.8)                       | 0.822  |
| Perforation healing, n (%)            | 117 (92.1)                | 139 (97.2)                    | 0.060  |
| Postoperative adverse events, n (%)   | 28 (22.0)                 | 19 (13.3)                     | 0.058  |
| Hospitalization, d, median (IQR)      | 5 (3–7)                   | 4 (3–6)                       | 0.005  |
| Death rate, n (%)                     | 3 (2.4)                   | 0 (0)                         | 0.205  |

BMI, body mass index; IQR, interquartile range; WBC, white blood cell.
share our experience in the nonoperative treatment of esophageal perforation caused by foreign bodies.

In our study, the cervical esophagus was the most common site for perforation, which may be related to the special anatomical and physiological structure of the cervical esophagus, thus leading to foreign body incarceration and perforation (14). A total of 59.6% of the patients presented with chest pain as the first symptom. Unlike previous studies (17,18), fish bones were the most common cause of perforations, we think it may be the people’s preference for fish in China that accounts for the discrepancy with the data from western medical centers. Besides, jujube pits were also common cause of perforations. In China, red jujube is considered a nutrient and is consumed by many people. However, the core of red jujube (jujube pits) is often sharp at both sides and easily can cause esophageal perforation. Moreover, most of the perforations caused by foreign bodies were small; many patients do not take the ingestion of foreign bodies seriously, so more than 60% of the patients do not arrive at the hospital until 24 hours after perforation.

Delayed diagnosis and treatment of esophageal perforation is often accompanied by infection, which affects the patient’s prognosis (19–21). In our study, up to 47% of the patients had secondary infections when they were diagnosed. To further analyze the efficacy of nonoperative treatment, we compared patients with esophageal perforation complicated with infection with those without infection. We found that although 3 patients died in the infection group, there was no significant difference compared with the noninfection group. This shows that even patients with infection can achieve a good outcome through aggressive nonoperative treatment.

To analyze the risk factors for perforation combined with infection by

| Variable                        | Univariate OR (95% CI)       | P         | Multivariate OR (95% CI) | P         |
|---------------------------------|------------------------------|-----------|--------------------------|-----------|
| Age ≥66 yr                      | 2.566 (1.514–4.349)         | <0.001    | 2.196 (1.232–3.916)      | 0.008     |
| Sex (male)                      | 1.795 (1.107–2.911)         | 0.018     | 1.934 (1.152–3.246)      | 0.013     |
| Underlying diseases             |                              |           |                          |           |
| Diabetes                        | 2.722 (0.689–10.759)        | 0.153     | 2.240 (0.528–9.506)      | 0.274     |
| Hypertension                    | 0.716 (0.387–1.323)         | 0.286     | —                        | —         |
| Cardio-cerebrovascular diseases | 1.913 (0.448–8.168)         | 0.381     | —                        | —         |
| Psychosoma                      | 0.556 (0.100–3.088)         | 0.502     | —                        | —         |
| BMI <18.5 kg/m²                 | 1.820 (0.971–3.412)         | 0.062     | 1.321 (0.656–2.660)      | 0.435     |
| Albumin <3.5 g/L                | 2.165 (0.777–6.035)         | 0.140     | 1.248 (0.403–3.868)      | 0.701     |
| Types of foreign body (fishbones) | 0.530 (0.324–0.866)     | 0.011     | 0.557 (0.330–0.940)      | 0.028     |
| Location of perforation         |                              |           |                          |           |
| Cervical                        | —                            | —         | —                        | —         |
| Thoracic                        | 1.134 (0.681–1.889)         | 0.629     | —                        | —         |
| Abdominal                       | 1.184 (0.367–3.823)         | 0.777     | —                        | —         |
| Time to treatment, per 1 day    | 1.143 (1.039–1.258)         | 0.006     | 1.126 (1.027–1.233)      | 0.011     |

BMI, body mass index; CI, confidence interval; OR, odds ratio.
logistic regression. Univariate and multivariate analyses showed that age $\geq 66$ years, male, and time to treatment were independent risk factors for infection. Elderly patients who are prone to infection after perforation may have had an underlying immunodeficiency. Delayed treatment is considered a risk factor for adverse outcomes (22,23), and our study also found that with the extension of foreign body retention time, the risk of coinfection increased. Therefore, early diagnosis and treatment of esophageal perforation is very important to improve the prognosis of patients. Although we also found that the risk of infection was lower when the foreign body type was fish bone, it may be related to the smaller perforation caused by ingestible fish bone than others.

The death rate in this study was 1.1% (3/270), and all 3 patients died of multisystem organ failure, which was slightly lower than that in a previous study (19). The initial removal rate under endoscopy reached 94.4%, whereas the total removal rate reached 97%, and the perforation healing rate was 94.8%. The results are encouraging. Nevertheless, some patients had additional subsequent surgeries for infections that were hard to control. Previous studies have suggested that neck perforations can be treated nonsurgically, whereas chest perforations usually require surgery (9,24), so we evaluated the efficacy of nonoperative treatment outcomes in different perforation sites. Finally, we found that the endoscopic foreign body removal rate was lower only in abdominal esophageal perforation than in thoracic perforation, with no significant difference in other outcome measures. Therefore, we believe that nonoperative treatment is effective for different perforation sites. Although the removal rate of foreign bodies using endoscopy is high, it is still necessary to guard against damage to peripheral large vessels and nerves during the endoscopic therapy to avoid secondary injury. Patients’ vital signs should be closely monitored after the procedure, and accurate
monitoring of the diagnosis and the appropriate treatment should be given in the face of changes in the patient’s condition. Additional surgical treatment may be needed.

There were several limitations to this study. First, this was a single-center retrospective study. Second, the sample size of this study was not large. Third, owing to the difficulty of foreign body removal using endoscopy, highly qualified and experienced endoscopic healthcare providers are often required to achieve successful endoscopic removal. Fourth, owing to the differences in eating habits between China and Western countries, esophageal perforation caused by foreign bodies may not be common in the west, which may affect the generalization of the findings in other settings. Hence, large-sample, multicenter studies are still needed.

In conclusion, nonoperative treatment is safe and effective for esophageal perforation caused by foreign bodies. Even if perforation is combined with infection, active nonoperative treatment can also achieve a good effect. Early intervention can effectively reduce the risk of infection and improve patient outcomes.

CONFLICTS OF INTEREST
Guarantor of the article: Xu Shu, MD.

Specific author contributions: F.L. collected data, analyzed relevant information, and drafted the manuscript; Z.Z., X.P., B.L., Y.Z., and Y.C. clinically managed the patient. X.S. designed the article, approved the final submission, and clinically managed the patient.

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Study Highlights

WHAT IS KNOWN

- Esophageal perforation is a rare but life-threatening emergency.
- Surgical treatment is considered to be the main treatment for esophageal perforation at present.

WHAT IS NEW HERE

- Nonoperative treatment is safe and effective for esophageal perforation caused by foreign bodies.
- Even if esophageal perforation is combined with infection, active nonoperative treatment can still achieve a good effect.
- While, early intervention can effectively reduce the risk of infection and improve patient outcomes.

Table 6. Outcome comparison of different location of perforation

| Outcome                              | Cervical group (n = 166) | Thoracic group (n = 92) | Abdominal group (n = 12) | P     |
|--------------------------------------|--------------------------|-------------------------|--------------------------|-------|
| Foreign body removal, n (%)         | 159 (95.8)               | 92 (100.0)a             | 11 (91.7)a                | 0.047 |
| Perforation healing, n (%)          | 156 (94.0)               | 90 (97.8)               | 10 (83.3)                | 0.075 |
| Secondary endoscopic intervention, n (%) | 5 (3.0)                   | 2 (2.2)                 | 0 (0)                    | 0.779 |
| Postoperative adverse events, n (%) | 27 (16.3)                | 19 (20.7)               | 1 (8.3)                  | 0.446 |
| Hospitalization, d, median (IQR)    | 5 (3–6)                  | 4 (2–5)                 | 4 (2–7)                  | 0.169 |
| Death rate, n (%)                   | 1 (0.6)                  | 1 (1.1)                 | 1 (8.3)                  | 0.167 |

IQR, interquartile range.

aBonferroni correction found a statistically significant difference between the 2 groups.

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