The global incidence of necrotizing soft-tissue infections (NSTIs) is reported as 0.4/100,000 per year. Despite being a rare condition, NSTIs are an extremely lethal disease requiring immediate and aggressive intervention for resuscitation and limb salvaging. NSTIs, first introduced by Hippocrates in 500 BC, mainly affect the torso, anogenital region, and the extremities. NSTIs are a recently introduced term that explains the disease process more comprehensively than necrotizing fasciitis because necrotizing infections of all soft tissue show similar clinical presentations and require similar approaches and treatments regardless of the depth or anatomical location of the infection. The new, more specific term facilitates the understanding of the disease.

Depending on the isolated microorganism, NSTIs are classified into 4 types. Type I is the most prevalent form and characterized by polymicrobial infection. Affected patients mostly show comorbidities including immunodeficiency and diabetes mellitus. Type II is a monomicrobial form with group A streptococcus, but...
ten occurs with *Staphylococcus aureus*. It is not linked to certain comorbidities and progression can be aggressive with systemic toxicity, septic shock, and multiorgan failure.\(^1,5\) Type III is caused by vibrio species. This type shows fulminant course of disease with multiorgan failure within 24 hours if not treated.\(^6\) Type IV is caused by fungal infection, most commonly Candida species or zygomycete.\(^1\)

The mortality rate of NSTIs has not changed in the past 30 years and is estimated at 6% to 35%, despite the improvements in our understanding and medical care.\(^7\) The depth of the primary site of infection and time to intervention are directly associated with the mortality rate.\(^4,8\) Factors such as advanced age, female sex, multiple comorbidities, and sepsis upon presentation have previously been linked to increased mortality rates.\(^9\)

Several studies have reported that specific characteristics show up on initial examination that predict a higher risk of poor outcomes, including mortality and limb loss. Anaya et al.\(^7\) suggested white blood cell count greater than 30,000 × 10^3/μL, creatinine level greater than 2 mg/dL, and heart disease at hospital admission as independent predictors of mortality and heart disease and shock at hospital admission as independent predictors of limb loss. Other authors suggested numerous risk factors of limb loss and mortality including demographic and laboratory data.\(^10,11\) However, due to the paucity of conciseness caused by the overwhelming number of risk factors for bad outcomes including limb loss and mortality, it is difficult for clinicians to apply those factors in real clinical situations. On the other hand, Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) is a clinical tool described by Wong et al.\(^12\) The tool is based on 6 common parameters including total white cell count, hemoglobin (Hb), creatinine, glucose, serum sodium, and C-reactive protein (CRP). An LRINEC score of 6 or greater confers high risk of NSTI with 92% positive predictive value and 96% negative predictive value and is a useful clinical determinant in the diagnosis of patients with NSTIs. However, although the LRINEC score is a useful tool for the diagnosis of an NSTI, its validity for predicting the prognosis has not been proven.\(^13\) Furthermore, its use is limited when competing inflammation is present, because such a condition might cause similar laboratory derangements. As the LRINEC score alone does not accurately represent the patient’s comprehensive clinical condition, we decided to include some factors including time from diagnosis to surgery, comorbidities, microbiological features, and the patient’s hemodynamic status at the time of visiting the emergency room in the analysis of patients with NSTIs.

NSTIs have been rarely studied in South Korea. We retrospectively reviewed the cases of patients with NSTIs at our tertiary hospital. Limb loss is one of the important complications that can have a significant impact on the rest of the patient’s life. The purpose of this study was to investigate predictive factors of limb loss in NSTI patients. The hypothesis of this study was that specific factors including the LRINEC score may be associated with poor outcomes of NSTIs.

**METHODS**

This study received approval from the Institutional Research Ethics Committee at Dankook University Hospital (2019-11-011). Before the research, informed consent was obtained from patients or immediate family members of the patients. A total of 49 patients at our center who were diagnosed with NSTI from May 2003 to January 2019 were included.

The inclusion criteria were patients with a definite diagnosis of NSTI involving the upper or lower limb. The initial diagnosis of NSTI was based on clinical and intraoperative findings (presence of pus with dish water appearance, facial necrosis, or loss of fascial integrity) and microbiological results. The final diagnosis was confirmed by pathologic specimen reports after surgery. Once these criteria were met, no further exclusion criteria were used.

Plain radiographs were taken in all patients for finding subcutaneous emphysema. Computed tomography scans were additionally conducted for detection of deeper fascial gas or fascial edema and abscess formation in clinically suspicious patients whose plain radiographs showed no evidence of NSTI. All patients underwent more than 1 operation and microbiological data were acquired by analyzing collected samples.

Patient records were analyzed in terms of demographic background and comorbidities. The time interval between the diagnosis of NSTI and the first operation was classified into < 12 hours and ≥ 12 hours. The LRINEC score at initial admission was also collected.\(^12\) The isolated microorganisms and treatment methods were analyzed and the courses of infection, including final outcomes, were reviewed. The included patients were divided into a limb loss group and a limb salvage group and compared for the identification of risk factors.

**Surgical Procedures**

The initial surgery was performed as a radical debridement to remove all suspicious infected tissues, and amputation was not performed initially. The excision was extended at least to the rim of cellulitis in cases where skin...
problems were evident. Serial debridement was needed in all patients because the infection was rarely resolved after a single procedure. Amputation procedures were conducted when the infection rapidly spread toward the pelvis area or included a joint. Amputation was also conducted if the infection spread to most muscle groups, resulting in a useless extremity.

**Statistical Analysis**

To determine the normal distribution of the continuous data, the Kolmogorov–Smirnov test was performed. The continuous variables were analyzed using an independent t-test, and the noncontinuous variables were analyzed using the Pearson chi-square test and Fisher's exact test. Univariate analysis was done for possible risk factors, and significant factors were entered into a multivariate logistic regression model. However, no statistical correlations between factors in multivariate logistic regression test were identified. F-test was performed to identify if the regression model was significant. All statistical analyses were performed using the IBM SPSS ver. 21.0 (IBM Corp., Armonk, NY, USA), and the level of significance was set at $p < 0.05$.

**RESULTS**

**Demographic Data and Comorbidities**

Between May 2003 and January 2019 (17 years), 49 patients were treated for NSTIs in our center. The mean age of the patients was 56.4 years (standard deviation [SD], 14.5). There were 38 male patients (77.6%) and 11 female patients (22.4%). Time taken from diagnosis to initial surgery was < 12 hours in 39 patients (79.5%) and ≥ 12 hours in 10 patients (20.5%). Twenty-nine patients (59.2%) had diabetes mellitus and 13 patients (26.5%) had hypertension. Eight patients (16.3%) were diagnosed with kidney impairment (chronic kidney disease), 5 patients (10.2%) presented with heart disease (chronic heart failure and coronary vessel disease), and 5 patients (10.2%) presented with an immunosuppressed status (high-dose corticosteroid therapy due to ulcerative colitis and rheumatic disorder). Four patients (8.2%) were diagnosed with liver cirrhosis (Child-Pugh class B)$^{14}$ and 3 patients (6.1%) with cerebral vessel disease (cerebrovascular disease) (Table 1).

**Microbiology**

In all patients, microbiologic cultures were assayed for every surgical procedure and antibiotics were changed according to the sensitivity of the identified pathogens. All patients involved in this study were treated with proper

| Characteristic                  | Value (n = 49) |
|--------------------------------|----------------|
| Age (yr)                       | 56.4 ± 14.5    |
| Hospitalization day            | 64.5 ± 38.4    |
| Number of surgery              | 7.6 ± 7.7      |
| Time to first operation        |                |
| < 12 hr                        | 39 (79.5)      |
| ≥ 12 hr                        | 10 (20.5)      |
| Sex                            |                |
| Male                           | 38 (77.6)      |
| Female                         | 11 (22.4)      |
| Affected limb                  |                |
| Upper limb                     | 13 (27.1)      |
| Lower limb                     | 36 (72.9)      |
| Etiology                       |                |
| Trauma                         | 18 (36.7)      |
| Nontraumatic skin lesion       | 6 (12.2)       |
| Injection                      | 1 (2.0)        |
| Acupuncture                    | 4 (8.2)        |
| Marine                         | 2 (4.1)        |
| Insect bite                    | 1 (2.0)        |
| Burn                           | 2 (4.1)        |
| Unknown                        | 15 (30.6)      |
| Type of necrotizing soft-tissue infections |          |
| 1                              | 43 (87.7)      |
| 2                              | 2 (4.1)        |
| 3                              | 4 (8.2)        |
| Social background              |                |
| Alcoholism                     | 9 (18.4)       |
| Comorbidity                    |                |
| Diabetes mellitus              | 29 (59.2)      |
| Immunosuppression              | 5 (10.2)       |
| Hypertension                   | 13 (26.5)      |
| Heart disease                  | 5 (10.2)       |
| Kidney impairment              | 8 (16.3)       |
| Liver cirrhosis                | 4 (8.2)        |
| Cerebrovascular disease        | 3 (6.1)        |
antibiotics according to their microbiological culture results. Forty-three patients (87.7%) were classified as type I NSTI, 2 (4.1%) as type II NSTI, and 4 (8.2%) as type III NSTI. Type IV NSTI was not found in our patients. The most prevalent species was streptococci (32.6%), followed by staphylococci (26.5%).

The patients were classified into antibiotic-resistant and nonresistant groups, and we compared the prognosis of the two groups. There were no significant prognostic differences between the groups. The LRINEC score was calculated in all patients. Eighteen patients (36.7%) were classified as high risk (LRINEC score ≥ 8), 15 patients (30.6%) as intermediate risk (LRINEC score, 7–8), and 16 patients (32.6%) as low risk (LRINEC score ≤ 5) according to Wong et al. The mean LRINEC score was 6.49 (SD, 3.19) (Table 2).

### Treatment and Outcome

The limb loss rate in our study was 20.4% (10/49). The initial surgery was performed as a radical debridement, which removed all suspicious infected tissues, and amputation was not performed initially. In 39 patients (79.6%), the affected limb could be salvaged. In 27 patients (55.1%), the wounds were managed by secondary suture. Nine

| Table 1. Continued |
|-------------------|
| Characteristic    | Value (n = 49) |
| **Survival outcome** |                     |
| Survived          | 46 (93.9)       |
| Non-survived      | 3 (6.1)         |
| **Limb-salvage outcome** |                   |
| Extremity salvage | 39 (79.6)       |
| Amputation        | 10 (20.4)       |

Values are presented as mean ± standard deviation or number (%).

| Table 2. Lists of Different Types of Bacteria Isolated in NSTI and Isolated Bacteria in Our Patients |
|--------------------------------------------------------------------------------------------------|
| **Family**                                      | **Different types of bacteria isolated in NSTI** | **Isolated bacteria in our patients** | **No. of patients (%)** |
| Gram-positive aerobic                            | Streptococci group                               | Streptococcus viridans, 3              | Streptococci 16 (32.6)  |
|                                                | Streptococci group B                             | Streptococcus pyogenes, 2              |                           |
|                                                | Enterococci                                      | Streptococcus agalactiae, 1            |                           |
|                                                | Staphylococci                                    | Streptococcus gordonii, 1              | Enterococci 10 (20.4)   |
|                                                | Bacillus                                         |                                    |                           |
|                                                | Streptococcus sanguis, 1                         |                                    |                           |
|                                                | *Streptococcus constellatus*, 2                  |                                    | Erysipelothrix 1 (2.0)  |
|                                                | *Streptococcus equisimilis*, 1                   |                                    |                           |
|                                                | *Streptococcus pluransimalium*, 1               |                                    |                           |
|                                                | *Staphylococcus aureus (MSSA)*, 4               |                                    |                           |
|                                                | *S. aureus (MRSA)*, 1                            |                                    |                           |
|                                                | *Staphylococcus epidermidis (MSSE)*, 2          |                                    |                           |
|                                                | *Staphylococcus epidermidis (MRSE)*, 4          |                                    |                           |
|                                                | *Staphylococcus haemolyticus*, 1                |                                    |                           |
|                                                | *Staphylococcus capitis*, 1                      |                                    |                           |
|                                                | Enterococcus avium, 1                            |                                    |                           |
|                                                | Enterococcus faecalis, 4                         |                                    |                           |
|                                                | Enterococcus faecium, 5                          |                                    |                           |
|                                                | *Erysipelothrix rhusiopathiae*, 1               |                                    |                           |
patients (18.4%) required skin graft procedures, 1 patient (2%) required local flap, and 2 patients (4.1%) required free flap for wound healing. Of the 10 patients in the limb loss group, 3 patients (6.1%) underwent above-knee amputation, 3 patients (6.1%) had below-knee amputation, 2 patients (4.1%) had foot amputation, and 2 patients (4.1%)
had forearm amputation.

On comparison between the limb salvage group and the limb loss group, significant differences were noted in CRP (191 mg/L [SD, 117.6] vs. 266 mg/L [SD, 146.6], \( p = 0.09 \)), Hb (11.9 g/dL [SD, 2.6] vs. 9.7 g/dL [SD, 2.7], \( p = 0.02 \)), creatinine (1.4 mg/dL [SD, 1.6] vs. 2.9 mg/dL [SD, 1.8], \( p = 0.01 \)), glucose level (183 mg/dL [SD, 81.4] vs. 375.9 mg/dL [SD, 377.5], \( p = 0.01 \)), and LRINEC score (5.9 [SD, 3] vs. 9 [SD, 2.4], \( p = 0.004 \)). The presence of hypotension at admission (odds ratio [OR], 8.2; 95% confidence interval [CI], 1.7–38.3; \( p = 0.008 \)), LRINEC score ≥ 9 (OR, 5.8; 95% CI, 1.3–25.6; \( p = 0.012 \)), and glucose level > 300 mg/dL (OR, 4.5; 95% CI, 0.9–21.9; \( p = 0.041 \)) were independent risk factors of limb loss (Tables 3 and 4).

**DISCUSSION**

The mortality of NSTIs is directly correlated with time-to-operation from hospital admission.\(^{15}\) The amputation rate of 20.4% in our study was similar to the rates in other studies and 39 patients (79.6%) received initial radical debridement within 12 hours. When comparing the limb salvage and limb loss groups, we found a significant difference in their LRINEC scores (limb salvage group: 5.9 [SD, 3] vs. limb loss group: 9 [SD, 2.4], \( p = 0.004 \)). A LRINEC score ≥ 9 indicated 5.8 times greater risk of limb loss in our study. Additionally, the limb loss group showed higher levels of CRP, creatinine, and glucose and lower levels of Hb on their initial blood examinations. Although Cheng et al.\(^{16}\) reported that the presence of diabetes mellitus was associated with a higher risk of limb loss, the risk of limb loss in our study was not associated with the presence of diabetes mellitus, but with a high level of blood glucose at admission; a glucose level over 300 mg/dL indicated 4.5 times greater risk of limb loss. This may indicate NSTI progression is more influenced by the management of diabetes rather than the presence of diabetes itself.

On admission, vital signs were checked in all patients with 81.6% of patients presenting with fever and 24.5% presenting with hypotension. According to Anaya et al.,\(^{17}\) hypotension at hospital admission was an independent predictor of limb loss. In our study, similarly, the presence of hypotension at admission was a significant risk factor of limb loss. The authors believe that hypotension indicates NSTI has already progressed substantially.

Because of its rarity, variable course, and non-specific findings, suspicion of NSTI is most important when physicians encounter suspected patients. Haywood et al.\(^{17}\) reported that 35% of their cases were initially misdiagnosed as non-necrotizing infection or simple cellulitis in a retrospective review. Another study showed only 14% of NSTI patients were diagnosed properly on initial admission.\(^{18}\) In our study, most patients reported trauma as an etiology (36.7%). However, many patients (30.6%) reported unclear etiology. This emphasizes that physicians should not rely on or expect classic etiologies. Four of our patients had a history of receiving acupuncture therapy (traditional Korean medicine), while none of our patients were intravenous drug abusers. This result might be associated with the cultural difference from previous international studies.

In our study, most patients were classified as type I NSTI (87.7%) and none of our patients showed clostridial infection. Clostridial infections, known as gas gangrene, were one of the representative historical diseases of type I NSTI. However, improvement of personal hygiene might have contributed to lower clostridial infection rates.\(^{4}\) Only 2 patients (4.1%) were classified into type II NSTI; they were 27- and 63-year-old each and neither had any comorbidities. Both patients survived with limb salvage, without toxic shock syndrome.

Type III NSTIs are an infection caused by Vibrio vulnificus and commonly acquired in coastal communities. Multisystem organ failure and cardiovascular collapse can occur without the evidence of infection.\(^{19}\) The biggest risk factor for type 3 NSTIs is moderate to severe liver disease and this type of NSTIs shows a fulminant course that might be fatal if not treated properly and promptly.\(^{4}\) In our study, 4 patients (8.2%) were classified into type III NSTIs and only 1 of them presented with a history of marine-associated trauma and the remaining 3 patients had unknown etiologies. In 2 patients with type III NSTIs, liver cirrhosis of Child-Pugh class B was present. Fortunately, all 4 patients showed clinical infection signs before the cardiovascular collapse and multisystem organ failure. They were given immediate operations within 12 hours and consequently survived with limb salvage. Hence, most of our patients were classified as type I NSTIs (87.7%) and all the eventual limb loss and non-survival cases were in this group. Of note, the relatively small number of type II cases might have affected the results.

In all patients, microbiologic cultures were assayed for every surgical procedure and antibiotics were changed according to the sensitivity of the identified pathogens. We used proper empiric antibiotics in 9 of 49 patients, which is sensitive to microbiologic cultures. All 9 patients survived although 2 of them lost the limb. Although it is difficult to conclude that the initial use of proper antibiotics contributed to the lower mortality rate due to the small number of cases, the clinical results of our study suggest...
### Table 3. Microbiologic Results, Used Antibiotics, and Treatment Outcomes in Our Patients

| Patients no. | Sex   | Age (yr) | Cultured organism                  | LRINEC | Initial antibiotic | After culture antibiotics | Limb salvage | Mortality |
|-------------|-------|----------|-----------------------------------|--------|--------------------|---------------------------|--------------|-----------|
| 1           | Male  | 40       | *Proteus hauseri*                 | 7      | Ceftriaxone         | Tazocin                   | Salvage      | Survive   |
|             |       |          | *Serratia marcescens*             |        |                    | Clindamycin               |              |           |
|             |       |          |                                   |        |                    | Doxycycline               |              |           |
| 2           | Male  | 49       | *Vibrio vulnificus*               | 11     | Clindamycin         | Ceftriaxone               | Salvage      | Survive   |
|             |       |          |                                   |        |                    | Amikacin                  |              |           |
| 3           | Male  | 55       | *Proteus mirabilis*               | 9      | Unasyn             | Cefotaxime                | Salvage      | Survive   |
|             |       |          | *Streptococcus anginosus*         |        |                    | Ceftriaxone               | Maleetronidazole|           |
| 4           | Male  | 53       | *P. mirabilis*                    | 6      | Vancomycin          | Tazocin                   | Salvage      | Survive   |
|             |       |          | *Enterococcus faecalis*           |        |                    | Tazocin                   | Tigecycline  |           |
|             |       |          | *Enterococcus faecium*            |        |                    |                           |              |           |
|             |       |          | *Acinetobacter baumannii*         |        |                    |                           |              |           |
| 5           | Male  | 57       | *Pseudomonas aeruginosa*          | 3      | Tigecycline         | Vancomycin                | Salvage      | Survive   |
|             |       |          | *A. baumannii*                    |        |                    |                           | Imipenem     |           |
|             |       |          | *E. faecium*                      |        |                    |                           |              |           |
|             |       |          | *E. faecalis*                     |        |                    |                           |              |           |
| 6           | Male  | 54       | *Staphylococcus aureus* (MSSA)    | 13     | Cephazedone         | Nafcillin                 | Salvage      | Survive   |
| 7           | Female| 73       | *S. aureus* (MSSA)                | 7      | Ceftriaxone         | Nafcillin                 | Salvage      | Survive   |
| 8           | Male  | 64       | *S. aureus* (MRSA)                | 4      | Clindamycin         | Vancomycin                | Salvage      | Survive   |
|             |       |          |                                   |        |                    | Ceftriaxone               |              |           |
| 9           | Male  | 42       | *Pantoea agglomerans*             | 2      | Cefazolin           | Cefazolin                 | Salvage      | Survive   |
|             |       |          | *S. aureus* (MSSA)                |        |                    | Ceftriaxone               | Augmentin    |           |
|             |       |          | *E. faecalis*                     |        |                    | Clindamycin               |              |           |
| 10          | Female| 27       | *Streprococcus pyogenes*          | 6      | Cefazolin           | Cefazolin                 | Salvage      | Survive   |
| Patients no. | Sex  | Age (yr) | Cultured organism            | LRINEC | Initial antibiotic | After culture antibiotics | Limb salvage | Mortality |
|------------|------|----------|-----------------------------|-------|-------------------|---------------------------|--------------|-----------|
| 11         | Male | 61       | S. aureus (MSSA)            | 9     | Cephazedone       | Nafcillin                 | Salvage      | Survive   |
|            |      |          |                             |       |                   | Isepamicin                |              |           |
| 12         | Male | 71       | S. epidermidis (MRSE)       | 0     | Ceftriaxone       | Vancomycin                | Salvage      | Survive   |
|            |      |          |                             |       |                   | Isepamicin                |              |           |
| 13         | Male | 61       | Citrobacter koseri          | 6     | Ciprofloxacin     | Imipenem                  | Salvage      | Survive   |
|            |      |          |                             |       |                   | Isepamicin                |              |           |
| 14         | Male | 71       | S. epidermidis (MRSE)       | 3     | Ceftriaxone       | Vancomycin                | Salvage      | Survive   |
|            |      |          |                             |       |                   | Isepamicin                |              |           |
| 15         | Female | 51   | Klebsiella pneumoniae        | 9     | Ceftriaxone       | Clindamycin               | Salvage      | Survive   |
|            |      |          | E. faecium                  |       | Doxycycline       |                           |              |           |
|            |      |          | Citrobacter freundii        |       |                   | Vancomycin                |              |           |
| 16         | Male | 63       | S. pyogenes                 | 4     | Ceftriaxone       | Cefotaxime                | Salvage      | Survive   |
|            |      |          |                             |       |                   | Isepamicin                |              |           |
| 17         | Male | 29       | S. anginosus                 | 7     | Cephazedone       | Vancomycin                | Salvage      | Survive   |
|            |      |          | Escherichia coli            |       |                   | Tazocin                   |              |           |
|            |      |          | P. aeruginosa               |       |                   |                           |              |           |
| 18         | Male | 55       | S. pluranimalium            | 10    | Cephazedone       | Tigecycline               | Salvage      | Survive   |
|            |      |          | Prevotella disiens          |       |                   | Maleetronidazole          |              |           |
|            |      |          | Prevotella oris             |       |                   | Isepamicin                |              |           |
|            |      |          | A. baumannii                |       |                   |                           |              |           |
| 19         | Male | 63       | E. coli                     | 5     | Tazocin           | Ceftriaxone               | Salvage      | Survive   |
|            |      |          |                             |       |                   | Vancomycin                |              |           |
| 20         | Female | 75 | S. epidermidis               | 1     | Cephazedone       | Ceftriaxone               | Salvage      | Survive   |
|            |      |          | P. aeruginosa               |       |                   | Clindamycin               |              |           |
|            |      |          | E. coli                     |       |                   | Ciprofloxacin             |              |           |
| 21         | Male | 54       | V. vulnificus               | 9     | Cefotaxime        | Imipenem                  | Salvage      | Survive   |

Table 3. Continued
| Patients no. | Sex | Age (yr) | Cultured organism              | LRINEC | Initial antibiotic | After culture antibiotics | Limb salvage | Mortality |
|-------------|-----|----------|--------------------------------|--------|-------------------|---------------------------|--------------|-----------|
| 22          | Male| 76       | A. baumannii                   | 5      | Vancomycin        | Vancomycin                | Salvage      | Survive   |
|             |     |          | Staphylococcus haemolyticus    |        |                   |                           |              |           |
|             |     |          | Staphylococcus capitis         |        |                   |                           |              |           |
| 23          | Male| 54       | S. equisimilis                 | 8      | Cefazolin         | Cefazolin                 | Salvage      | Survive   |
| 24          | Female| 70     | S. aureus (MSSA)              | 2      | Ciprofloxacin     | Nafcillin                 | Salvage      | Survive   |
| 25          | Male| 66       | V. vulnificus                  | 1      | Vancomycin        | Vancomycin                | Salvage      | Survive   |
|             |     |          |                                |        | Ceftazidime       | Ceftazidime               |              |           |
|             |     |          |                                |        |                   |                           |              |           |
| 26          | Male| 57       | Streptococcus constellatus     | 6      | Ceftriaxone       | Nafcillin                 | Salvage      | Survive   |
|             |     |          | S. viridans                    |        |                   |                           |              |           |
|             |     |          | Prevotella buccae              |        |                   |                           |              |           |
|             |     |          | Prevotella intermedia          |        |                   |                           |              |           |
|             | Male| 53       | S. aureus (MSSA)              | 3      | Cefbuperazone     | Cefepime                  | Salvage      | Survive   |
|             |     |          | Streptococcus agalactiae      |        |                   |                           |              |           |
|             | Female| 68     | K. pneumoniae                  | 6      | Ceftriaxone       | Tazocin                   | Salvage      | Survive   |
|             |     |          | P. melaninogenica             |        |                   |                           |              |           |
|             |     |          | P. buccae                     |        |                   |                           |              |           |
|             | Male| 51       | Aeromonas veronii biovar sobria | 8     | Tazocin           | Ceftriaxone               | Salvage      | Survive   |
|             |     |          | Plesiomonas shigelloides      |        |                   |                           |              |           |
|             | Female| 56     | Klebsiella oxytoca            | 1      | Tazocin           | Ciprofloxacin             | Salvage      | Survive   |

Table 3. Continued
| Patients no. | Sex  | Age (yr) | Cultured organism          | LRINEC | Initial antibiotic | After culture antibiotics | Limb salvage | Mortality |
|------------|------|----------|-----------------------------|--------|--------------------|---------------------------|--------------|----------|
| 32         | Male | 51       | *S. anginosus*              | 10     | Ceftriaxone        | Ceftriaxone               | Salvage      | Survive  |
|            |      |          | *P. melaninogenica*         |        |                    |                           |              |          |
|            |      |          | *P. buccae*                 |        |                    |                           |              |          |
| 33         | Male | 69       | *S. constellatus*           | 6      | Ceftriaxone        | Maleeropenem              | Salvage      | Survive  |
|            |      |          | *P. melaninogenica*         |        |                    |                           |              |          |
|            |      |          | *A. baumannii*              |        |                    |                           |              |          |
| 34         | Male | 46       | *V. vulnificus*             | 5      | Ceftriaxone        | Ceftaxidime               | Salvage      | Survive  |
|            |      |          | *Doxycycline*               |        |                    |                           |              |          |
| 35         | Male | 41       | *S. anginosus*              | 8      | Ceftriaxone        | Penicillin G              | Salvage      | Survive  |
|            |      |          | *E. coli*                   |        |                    |                           |              |          |
| 36         | Male | 24       | *S. epidermidis* (MRSE)     | 5      | Ceftriaxone        | Unasyn (ampicillin + sulbactam) | Salvage      | Survive  |
|            |      |          | *Peptostreptococcus anerobius* |      |                    |                           |              |          |
|            |      |          | *Peptostreptococcus asaccharolyticus* |      |                    |                           |              |          |
|            |      |          | *Actinomyces*                |        |                    |                           |              |          |
| 37         | Male | 81       | *E. coli*                   | 8      | Maleeropenem       | Maleeropenem              | Salvage      | Survive  |
|            |      |          | *Peptococcus anaerobius*     |        |                    |                           |              |          |
| 38         | Female | 70     | *Streptococcus viridans*    | 2      | Cephazedone        | Tazocin                   | Salvage      | Survive  |
|            |      |          | *Gentamicin*                 |        |                    |                           |              |          |
| 39         | Female | 77     | *Vibrio parahaemolyticus*   | 6      | Maleeropenem       | Tazocin                   | Salvage      | Survive  |
|            |      |          | *Shewanella algae*          |        |                    |                           |              |          |
| 40         | Male | 51       | *E. faecium*                | 6      | Cephazedone        | Vancomycin                | Amputation    | Survive  |
| 41         | Male | 42       | *Enterococcus avium*        | 11     | Tazocin            | Tazocin                   | Amputation    | Survive  |
|            |      |          | *Streptococcus sanguis*     |        |                    |                           |              |          |
| Patients no. | Sex | Age (yr) | Cultured organism | LRINEC | Initial antibiotic | Culture antibiotics | After culture antibiotics | Limb salvage | Mortality |
|-------------|-----|----------|-------------------|--------|---------------------|---------------------|--------------------------|--------------|-----------|
| 42          | Male| 84       | *S. epidermidis* (MSSE) | 10     | Vancomycin          | Ciprofloxacin       | Maleeropenem              | Amputation   | Survive   |
| 43          | Male| 48       | *E. faecium*        | 7      | Vancomycin          |            | Linezolid                | Maleeropenem  | Survive   |
| 44          | Male| 55       | *A. baumannii*      | 9      | Cefepime            | Ciprofloxacin       | Maleeropenem              | Vancomycin   | Survive   |
| 45          | Male| 68       | *E. faecium*        | 7      | Vancomycin          | Ciprofloxacin       | Maleeropenem              | Amputation    | Survive   |
| 46          | Male| 44       | *S. anginosus*      | 7      | Vancomycin          | Ciprofloxacin       | Maleeropenem              | Amputation    | Survive   |
| 47          | Male| 24       | *P. aeruginosa*     | 6      | Ceftriazone         | Tazocin            | Maleeropenem              | Vancomycin   | Death     |
| 48          | Female| 67    | *K. pneumoniae*     | 11     | Ceftriazone         | Tazocin            | Clindamycin              | Gentamicin   | Death     |
| 49          | Male| 66       | *S. viridans*       | 13     | Maleeropenem        | Tazocin            | Clindamycin              | Vancomycin   | Death     |

LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis.
This study has several limitations. First, this study was a retrospective study, and the number of patients was relatively small. Due to the retrospective nature of the study, we could not establish the time factor precisely. It would have been better to collect data from the onset of clinical symptoms to the operation than from diagnosis to surgery. A small sample size often leads to a type II error, but the adequacy of the present study was proven on the basis of the post hoc analysis results with a power of 80.7%. Second, the period of the study was 17 years, which was relatively longer than that in other studies. However, the same protocol of treatment from diagnosis was applied, per the policy of our center, during the entire period.

The presence of hypotension at admission, a high glucose level (> 300 mg/dL), and a high LRINEC score (> 9) were independent risk factors for limb loss in the NSTI patients. To prevent limb loss, prompt intervention and greater attention are necessary when these risk factors are present.

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### Table 4. Independent Predictors of Limb Loss in Patients with NSTI

| Variable                  | Odds ratio (95% CI) | p-value |
|---------------------------|--------------------|---------|
| LRINEC score ≥ 9          | 5.8 (1.3–25.6)     | 0.012   |
| Glucose level > 300 mg/dL | 4.5 (0.9–21.9)     | 0.041   |
| Hypotension at admission  | 8.2 (1.7–38.3)     | 0.008   |

NSTI: necrotizing soft-tissue infection, CI: confidence interval, LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis.
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