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Necrotizing Soft-Tissue Infections: A Retrospective Review of Predictive Factors for Limb Loss

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Background: Emergent diagnosis and treatment are important for the survival of patients with necrotizing soft-tissue infections (NSTIs). Death is the most catastrophic outcome, but limb loss is also one of the most important complications that can have a significant impact on the rest of the patient's life. The purpose of this study was to identify predictive factors for limb loss caused by NSTIs.

Methods: The data of patients at our center who were diagnosed with NSTIs from May 2003 to January 2019 were analyzed retrospectively. The inclusion criteria were patients with a definite diagnosis of NSTI involving the upper or lower limb. A total of 49 patient records were analyzed in terms of demography, laboratory data, microbiological causes, treatment, and final outcome. Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) scores at initial admission were also collected as laboratory data. Final outcomes were classified into survival with limb salvage and survival with limb loss.

Results: The limb loss rate was 20.4% (10/49) in our study. On comparison between the limb salvage group and the limb loss group, independent risk factors of limb loss were as follows: 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; $p = 0.041$). Various microbiological organisms were isolated; the most prevalent specimen was streptococci (32.6%), followed by staphylococci (26.5%). Poor outcomes including limb loss and mortality had no correlation with microbiological organisms.

Conclusions: For patients with NSTIs, 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.

Keywords: *Necrotizing fasciitis, Necrotizing soft tissue infection, Amputation*

The global incidence of necrotizing soft-tissue infections (NSTIs) is reported as 0.4/100,000 per year.[1] 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.[2] 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.[3] 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.[4] Affected patients mostly show comorbidities including immunodeficiency and diabetes mellitus.[1] Type II is a monomicrobial form with group A streptococcus, but of-

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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 $30{,}000 \times 10^3/\mu L$, 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

Table 1. Demographic Data and Outcomes

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)

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 (%).

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.[12] 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.[12] 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 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 anginosus,* 4	Staphylococci 13 (26.5)
	Staphylococci	*Streptococcus agalactiae,* 1	
	Bacillus	*Streptococcus gordonii,* 1	Enterococci 10 (20.4)
		Streptococcus sanguis, 1	
		Streptococcus constellatus, 2	Erysipelothrix 1 (2.0)
		Streptococcus equisimilis, 1	
		Streptococcus pluranimalium, 1	
		Staphylococcus aureus (MSSA), 4	
		S. aureus (MRSA), 1	
		Staphylococcus epidermidis (MSSE), 2	
		Staphylococcus epid ermidis (MRSE), 4	
		Staphylococcus haemolyticus, 1	
		Staphylococcus capitis, 1	
		Enterococcus avium, 1	
		Enterococcus faecalis, 4	
		Enterococcus faecium, 5	
		Erysipelothrix rhusiopathiae, 1	

Table 2. Continued

Family	Different types of bacteria isolated in NSTI	Isolated bacteria in our patients	No. of patients (%)
Gram-negative aerobic	*Escherichia coli*	*Ecsherichia coli*, 4	Escherichia 4 (8.2)
	Pseudomonas aeruginosa	*Acinetobacter baumanni*, 8	Pseudomonas 4 (8.2)
	Enterobacter cloacae	*Pseudomonas aeruginosa*, 4	Klebsiella 4 (8.2)
	Klebsiella	*Klebsiella oxycota*, 1	Proteus 3 (6.1)
	Proteus	*Klebsiella pneumoniae*, 3	Serratia 1 (2.0)
	Serratia	*Proteus hauseri*, 1	Acinetobacter 8 (16.3)
	Acinetobacter calcoaceticus	*Proteus mirabillis*, 2	Aeromonas 2 (4.1)
		Serratia marcescens, 1	Citrobacter 3 (6.1)
	Citrobacter freundii	*Aeromonas veronii biovar sorbia*, 1	Pantoea 1 (2.0)
	Pasteurella multicida	*Aeromonas hydrophila*, 1	
		Citrobacter freundii, 2	
		Citrobacter koseri, 1	
		Pantoea agglomerans, 1	
Anaerobic	*Bacteroides*	*Peptostreptococcus anaerobius*, 3	Peptostreptococcus 3 (6.1)
	Clostridium	*Shewannella algae*, 1	Shewannella 1 (2.0)
	Peptostreptococci	*Actinomyces*, 1	Actinomyces 1 (2.0)
		Plesiomonas shigelloides, 1	Plesiomonas 1 (2.0)
		Prevotella bivia, 1	Prevotella 8 (16.3)
		Prevotella melaninogenica, 2	
		Prevotella buccae, 2	
		Prevotella intermedia, 1	
		Prevotella disiens, 1	
		Prevotella oris, 1	
Marine	*Vibrio spp.*	*Vibrio vulnificus*, 4	Vibrio 5 (10.2)
	Vibrio vulnificus	*Vibrio parahemolyticus*, 1	
	Vibrio parahemolyticus		
	Vibrio damsel		
	Vibrio alginolyticus		
Fungi	*Candida*	-	-
	Aspergillus		
	Rhizopus		

NSTI: necrotizing soft-tissue infections.

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.,[7] 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	Ceftraixone	Tazocin	Salvage	Survive
			Serratia marcescens		Clindamycin			
					Doxycycline			
2	Male	49	*Vibrio vulnificus*	11	Clindamycin	Ceftriaxone	Salvage	Survive
					Ceftriaxone			
					Amikacin			
3	Male	55	*Proteus mirabilis*	9	Unasyn	Cefotaxime	Salvage	Survive
			Streptococcus angionosus		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

Table 3. Continued

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
14	Male	71	*S. epidermidis* (MRSE)	3	Ceftriaxone	Vancomycin	Salvage	Survive
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		Maleeropenem	Maleeropenem		
			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		
					Clindamycin	Clindamycin		
26	Male	57	*Streptococcus constellatus*	6	Ceftriaxone	Nafcillin	Salvage	Survive
			S. viridans			Clindamycin		
			Prevotella buccae					
			Prevotella intermedia					
27	Female	35	*E. faecalis*	7	Ceftriaxone	Ceftriaxone	Salvage	Survive
					Metronidazole	Ampicillin + sulbactam metronidazole		
28	Male	53	*S. aureus* (MSSA)	3	Cefbuperazone	Cefepime	Salvage	Survive
			Streptococcus agalactiae					
29	Female	68	*K. pneumoniae*	6	Ceftriaxone	Tazocin	Salvage	Survive
			P. melaninogenica		Isepamicin	Clindamycin		
			P. buccae					
30	Male	51	*Aeromonas veronii biovar sobria*	8	Tazocin	Ceftriaxone	Salvage	Survive
			Plesiomonas shigelloides		Teicoplanin	Ciprofloxacin		
31	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		Isepamicin	Clindamycin		
			P. buccae					
33	Male	69	*S. constellatus*	6	Ceftriaxone	Maleeropenem	Salvage	Survive
			P. melaninogenica		Clindamycin	Tigecycline		
			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		Clindamycin	Clindamycin		
						Ceftriaxone		
36	Male	24	*S. epidermidis* (MRSE)	5	Ceftriaxone	Unasyn (ampicillin + sulbactam)	Salvage	Survive
			Peptostreptococcus anerobius		Clindamycin			
			Peptostreptococcus asaccharolyticus					
			Actinomyces					
37	Male	81	*E. coli*	8	Maleeropenem	Maleeropenem	Salvage	Survive
			Peptococcus anaerobius		Vancomycin			
38	Female	70	*Streptococcus viridans*	2	Cephazedone	Tazocin	Salvage	Survive
					Gentamicin			
39	Female	77	*Vibrio parahaemolyticus*	6	Maleeropenem	Tazocin	Salvage	Survive
			Shewanella algae		Vancomycin			
40	Male	51	*E. faecium*	6	Cephazedone	Vancomycin	Amputation	Survive
41	Male	42	*Enterococcus avium*	11	Tazocin	Tazocin	Amputation	Survive
			Streptococcus sanguis		Teicoplanin	Teicoplanin		

Table 3. Continued

Patients no.	Sex	Age (yr)	Cultured organism	LRINEC	Initial antibiotic	After culture antibiotics	Limb salvage	Mortality
42	Male	84	*Staphylococcus epidermidis* (MSSE)	10	Vancomycin	Ciprofloxacin	Amputation	Survive
					Maleeropenem	Cefepime		
43	Male	48	*E. faecium*	7	Vancomycin	Linezolid	Amputation	Survive
			A. baumannii		Maleeropenem	Maleeropenem		
44	Male	55	*Erysipelothrix rhusiopathiae*	9	Cephazedone	Vancomycin	Amputation	Survive
			Peptostreptococcus spp.			Maleeropenem		
45	Male	68	*S. epidermidis* (MRSE)	10	Maleeropenem	Maleeropenem	Amputation	Survive
			A. baumannii		Vancomycin	Vancomycin		
			Aeromonas hydrophila					
46	Male	44	*S. anginosus*	7	Vancomycin	Tigecycline	Amputation	Survive
			Prevotella bivia		Tazocin			
47	Male	24	*A. baumannii*	6	Ceftriaxone	Vancomycin	Amputation	Death
			P. aeruginosa			Tazocin		
48	Female	67	*K. pneumoniae*	11	Ceftriaxone	Ciprofloxacin	Amputation	Death
			S. viridans		Gentamicin	Clindamycin		
49	Male	66	*C. freundii*	13	Maleeropenem	Colistin	Amputation	Death
			Streptococcus gordonii		Vancomycin	Levofloxacin		

LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis.

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.

the possibility.

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.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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