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Trends During Initial Consultation Among Amputated and Non-Amputated Patients with NSTI in The Limbs

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1. Abstract

1.1. Background: Necrotizing Soft Tissue Infections (NSTIs) cause rapid necrosis of soft tissue proximal to infected areas and are associated with a mortality rate of up to 35% depending on the type. However, there are no standardized procedures for determining treatment modality (i.e., debridement vs. amputation).

1.2. Methods: In this study, we evaluated outcomes in 18 patients with NSTI in the limbs (type 1: n = 9; type 2: n = 9) to identify potential markers indicating the requirement for amputation upon initial assessment. Sequential Organ Failure Assessment (SOFA), quick (q)SOFA, Acute Disseminated Intravascular Coagulation (DIC), and Laboratory Risk Indicator For Necrotizing Fasciitis (LRINEC) scores and the arterial blood lactate (Lac) value between the amputated and non-amputated groups were compared. Amputation was determined based on preoperative general condition, intraoperative artery occlusion, extensive necrosis of peripheral tissue, or unfavorable functional prognosis.

1.3. Results: Eight patients (type 1: n = 7; type 2: n = 1) undergoing amputation exhibited secondary complications, including diabetes (n = 7), renal failure (n = 4), and arteriosclerosis obliterans (n = 2). There were no significant differences in age, hospitalization duration, or qSOFA, DIC, or LRINEC scores between the groups. However, the average SOFA scores (4.1; range: 0–9; p = 0.04) and Lac values (p = 0.049) were found to be significantly higher in the amputation group than in the non-amputation group.

1.4. Conclusion: These findings suggest that the SOFA scores and Lac values can potentially be used for determining the requirement for amputation in patients with NSTI during initial consultation.

2. Introduction

Necrotizing Soft Tissue Infections (NSTIs) are a spectrum of disease entities characterized by extensive, rapidly progressive soft-tissue necrosis most often affecting the fascia and subcutaneous layers [1]. NSTIs are classified microbiologically into four types. Type 1 is common and polymicrobial (caused by mixed anaerobes and aerobes), type 2 is monomicrobial (usually caused by group A ß-hemolytic Streptococcus), type 3 and type 4 are rare, with type 3 caused by gram-negative bacteria (Vibrio spp.), and type 4 by fungi (Candida spp.) [2] and associated with trauma. The number of NSTI cases has been reported to be 0.3–15 per 100,000 individuals [3,4]; however, conditions rapidly deteriorate and become severe in most cases. The fatality rate is 21% for type 1,5 14%–35% for type 2,6-8 30%–40% for type 3, and over 50% for type 4.2 Early-stage diagnosis and treatment is crucial to avoid mortality. Furthermore, prognosis is particularly affected by early-stage surgical interventions [9-11]. Numerous studies have reported that 10%–50% of patients with NSTIs in the limbs require

amputation [5,9,12,13]; however, no standard treatment policy for conducting either debridement or amputation is in place. We hypothesized that unnecessary debridement can be avoided if the need for amputation can be determined at an early stage. Therefore, in this study, we investigated whether there were differences in various parameters at initial consultation between amputated and non-amputated patients with NSTI in the limbs.

2. Materials and Methods

This study was approved by the institutional review board and ethics committee of Tottori University (approval no. 20A121), and conformed to the ethical guidelines of the Declaration of Helsinki for research involving human subjects. All subjects provided written informed consent. This study involved 18 patients diagnosed with NSTI in the limbs (9 with type 1 NSTI and 9 with type 2 NSTI) who underwent treatment at the Tottori University Hospital between April 2009 and March 2019. Thirteen patients were male and five were female, with the average age of the patients being 61.8 years (range, 43–79 years). Eight patients ultimately underwent amputation. One of the patients who had experienced cardiopulmonary arrest at the time of admission was excluded from the study. Treatment of patients was coordinated with an emergency doctor, infectious disease experts, and an orthopedic surgeon. First, the patient's condition was managed according to SSCG. Concurrently, we used physical findings, laboratory data, and imaging to determine the option that was better for the patient—with or without operation.

Statistical analyses were performed using multivariable logistic regression to compare the following study criteria between the amputated and non-amputated groups: age, duration from the onset to hospitalization, Quick Sequential Organ Failure Assessment (qSOFA) Score, Glasgow Coma Scale (GCS), Respiratory Rate (RR), Maximum Blood Pressure (SBP), Sequential Organ Failure Assessment (SOFA) score, PaO2/FiO2, (P/F ratio), platelets (Plt), total bilirubin (T. bil), Mean Arterial Pressure (MAP), creatinine (Cr), acute disseminated intravascular coagulation (DIC) score, Systemic Inflammatory Response Syndrome (SIRS), prothrombin time international normalized ratio (PT-INR), D-dimer, Laboratory Risk Indicator For Necrotizing Fasciitis (LRINEC) score, white blood cell count (WBC), C-Reactive Protein (CRP), hemoglobin (Hb) value, blood sodium (Na) value, glucose (Glu) value, arterial blood lactose (Lac) value, shock index (SI), heart rate (HR), and creatine kinase level (CK). Variables with $p < 0.05$ were eligible for inclusion in the multivariable logistic regression. Statistical analysis was performed with EZR (Easy R) software [14].

3. Results

All suspected cases of NSTI underwent surgical intervention based on physical findings, imaging results, or wound infection. The requirement for amputation was determined based on preoperative general conditions, intraoperative artery occlusion, extensive necrosis of the peripheral tissue, or unfavorable functional prognosis in the absence of limb amputation. Seven patients were diagnosed with type 1 NSTI and one patient with type 2 NSTI. Amputation was performed during the first surgery in four patients, as a result of peripheral blood flow disorders in three patients, and due to poor general conditions in one patient. All four patients who underwent amputation during an additional surgery were amputated during the second surgery, which was conducted within 14 days after the first surgery. Need for additional surgery was attributed to impaired blood flow in two patients and poor infection control in the other two. Out of the eight patients who underwent amputation, 7 had a medical history of diabetes, 4 were undergoing dialysis, and 2 had Arteriosclerosis Obliterans (ASO).

No significant differences in age were observed between the amputated and non-amputated groups ($p = 0.480$). The average duration from the onset of NSTI to the start of treatment was 5.6 (1–19) days; however, there was no significant difference between the groups ($p = 0.674$). Furthermore, no significant differences were observed between the groups in the following criteria: qSOFA score, average: 0.7 (0–2, $p = 0.249$); DIC score, average: 2.6 (0–7, $p = 0.155$); D-dimer, average: 13.4 (1.2–59.8, $p = 0.218$); and LRINEC score, average: 8.9 (8–11, $p = 0.060$). Furthermore, individual components of qSOFA, including GCS ($p = 0.078$), RR ($p = 0.238$), and SBP ($p = 0.427$), did not show significant differences. The LRINEC scores, including CRP ($p = 0.319$), WBC ($p = 0.150$), Hb ($p = 0.447$), Na ($p = 0.920$), Cr ($p = 0.082$), and Glu ($p = 0.222$), were also not significantly different between the groups. However, the SOFA score was significantly higher in the amputated group, with an average of 4.1 (0–9) ($p = 0.040$), compared with that in the non-amputated group, but the following components of the SOFA score did not show any significant difference: P/F ratio ($p = 0.486$), Plt ($p = 0.239$), T. bil ($p = 0.467$), MAP ($p = 0.923$), GCS ($p = 0.078$), and Cr ($p = 0.082$). Additionally, acute-phase DIC scores of SIRS ($p = 0.381$), Plt ($p = 0.239$), PT-INR ($p = 0.413$), and D-dimer ($p = 0.218$) did not show significant differences between the groups. CK ($p = 0.424$) and SI index ($p = 0.246$) did not show any significant differences, but the Lac value ($p = 0.049$) showed significant differences between the amputated and non-amputated groups (Table 1). Although there was a significant difference in the results of the binary logistic regression analysis of SOFA scores and Lac values between the groups, no significant differences were observed in the multivariate logistic regression analysis ($p = 0.071$, 0.330) (Table 2).

Table 1: Demographic and clinical parameters and their association with amputation in patients with necrotizing soft tissue infections

Parameter[a]	Amputated (n = 8)	Non-amputated (n = 10)	Odds ratio	Lower limit	Upper limit	p-value[b]
Age (years)	63.88 ± 8.13	60.20 ± 13.33	0.97	0.89	1.06	0.48
Length of hospitalization (days)	59.75 ± 33.86	100.70 ± 47.20	1	1	1	0.424
Duration from onset to hospitalization (days)	6.13 ± 5.46	5.10 ± 5.32	0.96	0.8	1.15	0.674
qSOFA	1.00 ± 0.93	0.40 ± 0.52	0.44	0.11	1.79	0.249
sBP (mmHg)	114.83 ± 9.04	120.80 ± 20.82	1.03	0.96	1.1	0.427
Respiratory rate (times/min)	113.50 ± 37.55	99.90 ± 14.50	0.87	0.685	1.1	0.238
GCS	14.38 ± 0.52	14.80 ± 0.42	6.67	0.81	55	0.078
SOFA	5.63 ± 1.60	2.40 ± 2.01	0.36	0.13	0.96	0.04
P/F ratio	329.13 ± 157.15	375.44 ± 97.66	1	0.95	1.01	0.486
Plt ($\times 10^3/\mu L$)	193.88 ± 118.32	195.20 ± 99.82	1	0.99	1	0.239
T.bil (mg/dL)	1.58 ± 1.71	1.08 ± 1.20	0.77	0.37	1.57	0.467
MAP (mmHg)	84.95 ± 9.89	85.4 ± 10.44	1	0.91	1.11	0.923
Cr (mg/dL)	4.19 ± 2.87	1.82 ± 1.36	0.54	0.27	1.08	0.082
DIC score	3.25 ± 1.16	2.00 ± 2.00	0.61	0.31	1.2	0.155
SIRS	2.25 ± 0.70	2.50 ± 0.53	2.09	0.4	10.8	0.381
PT-INR	1.71 ± 1.10	1.38 ± 0.30	0.49	0.009	2.68	0.413
D-dimer (μg/mL)	24.09 ± 24.47	4.78 ± 4.48	0.89	0.73	1.07	0.218
LRENIC score	84.95 ± 9.89	85.4 ± 10.44	**0.42**	0.17	1.04	**0.06**
WBC ($\times 10^3/\mu L$)	275.63 ± 189.56	173.00 ± 71.54	1	1	1	0.15
CRP (mg/dL)	34.96 ± 12.08	30.19 ± 8.29	0.95	0.86	1.05	0.319
Hb (g/dL)	10.96 ± 2.85	11.91 ± 2.60	1.16	0.8	1.68	0.447
Na (mEq/L)	132.13 ± 4.19	132.4 ± 7.26	1.01	0.86	1.18	0.92
Glu (mg/dL)	255.63 ± 250.11	139.10 ± 58.82	1	0.99	1	0.222
Lac (mg/dL)	3.04 ± 0.75	1.81 ± 1.19	**0.34**	0.12	1	**0.049**
SI	0.99 ± 0.33	0.85 ± 0.18	0.07	0.001	5.45	0.246
HR (times/min)	113.50 ± 37.55	99.90 ± 14.50	0.98	0.94	1.02	0.304
CK (IU/L)	490.88 ± 924.13	1,036.20 ± 1,715.52	1	1	1	0.424

Abbreviations: CK, creatine kinase; Cr, creatinine; CRP, C-reactive protein; DIC, disseminated intravascular coagulation; GCS, Glasgow coma scale; Glu, glucose; Hb, hemoglobin; HR, heart rate; Lac, arterial blood lactose; LRINEC, score laboratory risk indicator for necrotizing fasciitis score; MAP, mean arterial pressure; Plt, platelet count; P/F ratio, PaO2/FiO2 ratio; PT-INR, prothrombin time international normalized ratio; qSOFA, quick SOFA; sBP, systolic blood pressure; SI, shock index; SIRS, systemic inflammatory response syndrome; SOFA, sequential organ failure assessment; T.bil, Total bilirubin; WBC, white blood cell count.

a All values are represented as mean ± standard deviation of the mean.

b Statistical significance was assessed by binary logistic regression analysis.

Table 2. Elements involved in amputation for NSTI (multivariate logistic regression analysis)

	Amputated (n = 8)	Non-amputated (n = 10)	Odds ratio	Range	p-value
SOFA	5.63 ± 1.60	2.40 ± 2.01	0.47	0.10–2.17	0.33
Lac (mg/dL)	3.04 ± 0.75	1.81 ± 1.19	0.36	0.12–1.09	0.071

Patient characteristics associated with amputation in patients with necrotizing soft tissue infections (multivariate logistic regression analysis)

The p-values were calculated using EZR ver. 3.4.1.

4. Discussion

Early-stage surgical intervention is considered to improve the survival rate of patients with NSTIs. Patients who had undergone surgery within 24 h of hospitalization have been reported to show significant differences in the survival rate compared with those who had undergone surgery after 24 h, and the mortality rates were significantly improved when the surgery is performed within 6 h.9-11 None of the patients died during this study. One patient experienced cardiopulmonary arrest at the time of hospitalization and was excluded. Four patients had no problematic outcomes, but underwent several rounds of debridement, and ultimately amputation. It was hypothesized that the burden on patients could be reduced if the requirement of amputation could be determined based on findings from the initial consultation.

Su et al [15] reported significant differences between groups with an LRINEC score of six or higher for amputation, and those with a score below six. The results for the patients in our study did not show significant differences in the LRINEC scores between the amputated and non-amputated groups (p = 0.06). However, the number of patients was higher than that in the study of Su et al, with all patients in our study having a score of six or higher, and all amputated patients except one having a score of 10 or higher. Su

et al15 reported that surgical interventions and amputations were performed in 96% and 26% of patients, respectively. The LRINEC score of patients without amputation was lower than that of patients with amputations as their study included patients without NSTI; therefore, further examinations in patients with NSTI are warranted.

Anaya et al [16] reported that surgical interventions were conducted in 98% of patients, among whom 26% of patients underwent limb amputations. Reportedly, SBP below 90 mmHg contributed to amputation. However, no patient had an SBP below 90 mmHg at the time of the initial visit in our study. Furthermore, no significant difference was observed in the SBP between the groups. Nevertheless, two-thirds of the patients experienced shock and required a pressor agent post-hospitalization or surgery. Therefore, it is important that the blood pressure of patients is assessed after admission as their condition can rapidly change for the worse.

Madsen et al [17] reported amputations conducted in 22% of the patients with NSTI, where there was a correlation between the increase in Lac value and amputation (hazard ratio of 1.07, 95% CI of 1.01–1.13, p = 0.0194). Similarly, our findings showed a significant difference in Lac values between the amputated and non-amputated groups. The fact that the circulation indicators SI, MAP, and SBP did not show any significant difference between the groups, but the Lac value did, indicated the possibility of using this criterion as an early-stage indicator for peripheral circulation in the limbs.

Anaya et al [16] reported that the presence or absence of a history of heart disease contributed to amputation, although the reasons for this were unknown. In our study, we reported one patient with a history of atrial fibrillation in the amputated group and one patient with a history of myocardial infarction in the non-amputated group. There were no trends that indicated higher frequencies of heart disease. In a total of eight amputated patients, seven had NSTI type 1. Diabetes with some type of peripheral circulatory insufficiency (seven patients), chronic renal failure (four patients), and ASO (two patients) were also reported in these seven patients. We therefore hypothesized that these conditions may be considered a risk factor for amputation.

Significant differences in the SOFA score were observed between the amputated and non-amputated groups. Furthermore, no significant differences were observed in the individual components of SOFA. However, as the p values of GCS and Cr were 0.078 and 0.082, respectively, this suggested a possibility that GCS was low, whereas the Cr level was high in the amputated group. In this study, a patient had undergone amputation during the first round of surgery due to poor general conditions and a high SOFA score. Hence, a high SOFA score could be considered a factor indicating amputation requirement.

Anaya et al [16] also reported that Clostridium infection showed significant correlation with amputation with respect to the causative organism. In this study, Streptococcus pyogenes infection was observed in six patients, followed by S. aureus infection in five. There were a few patients with Bacteroides infection, which we attribute to the fact that nine patients had been administered antibacterial drugs up until hospitalization, which may have decreased bacterial detection (Table 3).

However, our study also had a few limitations. First, it involved a small number of cases. Second, the amputation decision was based on general conditions and intraoperative findings. Third, 13 patients were treated with antibacterial drugs before the study began, with one patient having undergone debridement.

Table 3. Detected bacterial species in patients with necrotizing soft tissue infections at admission.

Bacterial species	**Number of patients (n)**
Type 1	
Streptococcus aureus	4
Morganella	2
Corynebacterium	2
S. constellatus	1
S. agalactiae	1
S. dysgalactiae	1
Streptococcus spp.	2
Bacteroides fragilis	2
Type 2	
S. pyogenes	6
CNS	1
Klebsiella	1

Detected bacterial species in patients with necrotizing soft tissue infections at admission.

6. Conclusion

In this study, we observed significant differences in the Lac value and SOFA score between the amputated and non-amputated groups at the initial consultation. That may be one of the factors determining the requirement of amputation.

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9. Declaration of conflicting interests

The Authors declare that there is no conflict of interest.

10. Ethical approval and informed consent

This study was approved by the institutional review board and eth-

ics committee of Tottori University (approval no. 20A121), and conformed to the ethical guidelines of the Declaration of Helsinki for research involving human subjects.

References

1. Nawijn F, Verhiel SHWL, Lunn KN, Eberlin KR, Hietbrink F, Chen NC. Factors associated with mortality and amputation caused by necrotizing soft tissue infections of the upper extremity: a retrospective cohort study. World J Surg. 2020; 44: 730-40.
2. Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. J Hosp Infect. 2010; 75: 249-57.
3. Stevens DL, Bryant AE. Necrotizing soft-tissue infections. N Engl J Med. 2017; 377: 2253-65.
4. Das DK, Baker MG, Venugopal K. Increasing incidence of necrotizing fasciitis in New Zealand: a nationwide study over the period 1990 to 2006. J Infect. 2011; 63: 429-33.
5. Wong CH, Chang HC, Pasupathy S, Khin LW, Tan JL, Low CO. Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. J Bone Joint Surg Am. 2003; 85: 1454-60.
6. Stevens DL, Tanner MH, Winship J, Swarts R, Ries KM, Kaplan E. Severe group A streptococcal infections associated with a toxic shock-like syndrome and scarlet fever toxin A. N Engl J Med. 1989; 321: 1-7.
7. Kaul R, McGeer A, Low DE, Green K, Schwartz B. Population-based surveillance for group A streptococcal necrotizing fasciitis: Clinical features, prognostic indicators, and microbiologic analysis of seventy-seven cases. Ontario group A Streptococcal Study. Am J Med. 1997; 103: 18-24.
8. Darenberg J, Luca-Harari B, Jasir A, Sandgren A, Pettersson H, Pettersson H, et al. Molecular and clinical characteristics of invasive group A streptococcal infection in Sweden. Clin Infect Dis. 2007; 45: 450-8.
9. McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of mortality for necrotizing soft-tissue infections. Ann Surg. 1995; 221: 558-65.
10. Bucca K, Spencer R, Orford N, Cattigan C, Athan E, McDonald A. Early diagnosis and treatment of necrotizing fasciitis can improve survival: an observational intensive care unit cohort study. ANZ J Surg. 2013; 83: 365-70.
11. Hadeed GJ, Smith J, O'Keeffe T, Kulvatunyou N, Wynne JL, Joseph B, et al. Early surgical intervention and its impact on patients presenting with necrotizing soft tissue infections: A single academic center experience. J Emerg Trauma Shock. 2016; 9: 22-27.
12. Mathieu D, Favory R, Cesari JF, et al. Necrotizing soft tissue infections. In: Mathieu D, eds. Handbook on Hyperbaric Medicine. Chapter 2.2.4 Springer. 2006; 263-89.
13. Hua C, Bosc R, Sbidian E, De Prost N, Hughes C, Jabre P, et al. Interventions for necrotizing soft tissue infections in adults. Cochrane Database Syst Rev. 2018; 5: CD011680.
14. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant. 2013; 48: 452-8.
15. Su YS, Chen HW, Hong YC, Chen CT, Hsiao CT, Chen IC. Laboratory risk indicator for necrotizing fasciitis score and the outcomes. ANZ J Surg. 2008; 78: 968-72.
16. Anaya DA, McMahon K, Nathens AB, Sullivan SR, Foy H, Bulger E. Predictors of mortality and limb loss in necrotizing soft tissue infections. Arch Surg. 2005; 140: 151-8.
17. Madsen MB, Skrede S, Perner A, Arnell P, Nekludov M, Bruun T, et al. Patient's characteristics and outcomes in necrotising soft-tissue infections: results from a Scandinavian, multicentre, prospective cohort study. Intensive Care Med. 2019; 45: 1241-51.