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Original Article

Accurate and quick predictor of necrotizing soft tissue infection: Usefulness of the LRINEC score and NSTI assessment score☆

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ABSTRACT

Objective: The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score is a diagnostic tool for necrotizing soft tissue infection (NSTI), which is validated and is considered to have high diagnostic value. However, some experts criticize LRINEC score for consisting of laboratory test results only.
Methods: In this single-center retrospective study, we created a new scoring system (NSTI assessment score; NAS), which also incorporated vital signs as another diagnostic tool for NSTI using cases from our hospital and also evaluated diagnostic accuracy of LRINEC score. We identified NSTI predictors by comparing 24 NSTI patients and 80 non NSTI patients using uni- and multivariate logistic regression analysis, and created NAS based on odds ratio of variables which are statistically significant in the multivariate model.
Results: We identified mean arterial pressure, C-reactive protein, hemoglobin, serum creatinine, and glucose as a predictor for NSTI. The maximum value of NAS was 11 points with the cut-off value of 6. Sensitivity, specificity, positive predictive value, and negative predictive value of the NAS for diagnosis of NSTI were 87.5%, 91.3%, 75.0%, and 96.1%, respectively. Area under the receiver operating characteristic curve was 0.926 (0.851−1.00) for the NAS and 0.903 (0.833−0.973) for the LRINEC score, and they were not statistically different ($p = 0.167$).
Conclusion: The NAS has high diagnostic accuracy in predicting NSTI, and is comparable with the LRINEC score. The NAS needs to be validated in other cohorts in the future.

1. Introduction

Necrotizing soft tissue infection (NSTI) includes necrotizing fasciitis (NF) forms of cellulitis, myositis, and fasciitis. The characteristics of NSTI are fulminant tissue destruction, systemic signs of toxicity, and high mortality. To treat NSTI, accurate diagnosis and prompt and appropriate interventions including debridement and empirical antibiotic therapy are essential [1].

However, it is often difficult to distinguish NSTI from other soft tissue infections [1]. In the early phase of NSTI, physical findings are similar to other soft tissue infections. Sometimes we can notice the difference after exacerbation of its condition. Modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and frozen section biopsy have been considered to be useful in the early recognition of NSTI, but these modalities has been limited by cost, availability, and accuracy [2,3]. The Laboratory Risk Indicator for Necrotizing fasciitis (LRINEC) score is developed as a convenient tool to support diagnosis of NF [3]. However, there are various opinions on the usefulness of LRINEC among the experts, especially considering that LRINEC is comprised of only laboratory data (Supplementary Table) [2]. It might be possible to develop more useful diagnostic tools.

The purpose of this study was to develop a new scoring system to distinguish NSTI from other soft tissue infections and to compare accuracy of the new scoring system with that of the LRINEC score.

☆ All authors meet the ICMJE authorship criteria.

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2. Patients and methods

A single-center retrospective study was performed at the Japan Red Cross Maebashi Hospital. The study was approved by the Human Research Ethics Committee of Gunma University, and was conducted according to the principles of the declaration of Helsinki. Informed consent was waived by the committee because this study only used data gained from routine clinical practice. 425 hospitalized patients who developed cellulitis, subcutaneous abscesses, necrotizing myositis, Fournier gangrene and necrotizing fasciitis between April 2004 and March 2012 were analyzed for inclusion of this study. Following inclusion criteria were applied; 1) hospitalized patients with diagnosis which fulfilled criteria described in the IDSA guideline 2014 for skin and soft tissue infection [4]. We used permanent histopathologic tissue examination and fresh frozen tissue examination to confirm diagnoses when available. Patients were excluded if 1) those for whom evaluation of the LRINEC score was not possible due to missing data, 2) multiple hospitalization during the study period (only the first hospitalization was included), 3) children under fifteen years of age. We divided the study patients into two groups; those who were diagnosed as necrotizing myositis, Fournier gangrene, or necrotizing fasciitis to the NSTI group; those who were diagnosed as cellulitis or subcutaneous abscesses to the non-NSTI group.

We evaluated the following parameters: age, sex, mean blood pressure, heart rate, temperature, hemoglobin, total white cell count, platelet count, serum sodium, serum creatinine, serum glucose, APACHE II score, SOFA score at the time of hospitalization, surgical intervention, and mortality. We compared these parameters of the NSTI group with the non-NSTI group. We defined all the parameters found to be significantly different with p value < 0.05 between the two groups as potential NSTI predictors.

To develop new diagnostic scoring system, we converted potential NSTI predictors to categorical variables. We determined the cutoff points for each parameter based on the previous reports, data of the present study, and clinical experiences [2,3]. Next, we compared each variable for NSTI group and those for non NSTI group with univariate regression analysis to select variables with statistical significance with p value < 0.05. Then, we entered all such variables into multivariate logistic regression analysis, using stepwise backward selection method. We convert each variable into a simple score based on the adjusted odds ratio. We defined the sum of the component scores as the NSTI assessment score (NAS) [5].

Table 2
The result of univariate and multivariate logistic regression analysis.

	Univariate Analysis			Multivariate Logistic Regression Analysis		
	OR	95% CI	*p*-value	Adjusted OR	95% CI	*p*-value
MAP, mmHg						
≥75,	1	–	–	1	–	–
<75	5.31	1.91–14.8	0.001	14.1	2.25–89.1	0.005
HR, beats/min						
≤100	1	–	–			
>100	1.86	0.733–4.73	0.19	(excluded)		
CRP, mg/L						
<150	1	–	–	1	–	–
≥150	14.5	3.97–53.2	<0.001	22.9	3.31–158	0.002
TW, per mm^3						
<15.0	1	–	–			
≥15.0	3.67	1.42–9.50	0.007	(excluded)		
Hb, g/dL						
≥11.0	1	–	–	1	–	–
<11.0	5.31	1.91–14.8	0.001	6.11	1.13–33.0	0.035
Na, mmol/L						
≥135	1	–	–			
<135	6.42	2.38–17.3	<0.001	(excluded)		
Cre, μmol/L						
≤141	1	–	–	1	–	–
>141	10.7	3.18–36.1	<0.001	6.26	1.02–38.3	0.047
Glucose, mmol/L						
≤10.0	1	–	–	1	–	–
>10.0	7.86	2.87–21.5	<0.001	17.9	3.43–93.7	<0.001

OR, odds ratio; CI, confidence interval; MAP, mean arterial pressure; HR, heart rate; CRP, C-reactive protein; TW, total white blood cell count; Hb, hemoglobin; Na, serum sodium; Cre, serum creatinine. To convert the values of glucose to mg/dL, multiply by 18.015.
To convert the values of creatinine to mg/dL, multiply by 0.01131. Significant factors ($p < 0.05$) in univariate analysis were entered into a multi-variate model and analyzed with a multiple logistic regression approach by means of a backward stepwise selection procedure.

We evaluated the accuracy of the LRINEC score and the NAS for prediction of NSTI and compared the accuracy of these two scores. The accuracy of the LRINEC score and the NAS were expressed as area under the receiver operating characteristic curve, sensitivity, specificity, positive predictive value, and negative predictive value. In evaluation of the LRINEC score, we used two cutoff point, ≥6 and ≥ 8 [3].

Table 1
Baseline characteristics of NSTI patients and non-NSTI patients.

	NSTI (n = 24)	non-NSTI (n = 80)	*p*-value
Age, mean (SD), year[a]	62 (14)	62 (19)	0.91
Male, n (%)[b]	14 (58)	49 (61)	0.99
Mean arterial pressure, mean (SD), mmHg[a]	79.0 (17.7)	92.8 (18.1)	0.002
Heart rate, mean (SD), beats/minute[a]	101.5 (20.1)	91.8 (17.3)	0.038
Body temperature, mean (SD), celsius[a]	37.3 (1.3)	37.8 (1.1)	0.079
LRINEC score, mean (SD)[a]	8.4 (2.7)	3.1 (2.8)	<0.001
C-reactive protein, mean (SD), mg/L[a]	275 (103)	118 (94)	<0.001
Total white cell count, mean (SD), per mm^3[a]	17.8 (10.1)	12.9 (6.3)	0.031
Hemoglobin, mean (SD), g/dL[a]	11.3 (2.1)	13.2 (2.3)	<0.001
Sodium, mean (SD), mmol/L[a]	134 (5.1)	137 (4.8)	0.004
Creatinine, mean (SD), μmol/L[a]	158 (148)	75 (45)	0.012
Glucose, mean (SD), mmol/L[a]	12.8 (6.6)	8.9 (7.2)	0.015
Platelet count, mean (SD), per mm^3[a]	270 (144)	223 (88)	0.14
APACHE II score, mean (SD)[a]	14.5 (7.6)	8.0 (4.9)	<0.001
SOFA score, mean (SD)[a]	5.2 (5.2)	1.7 (2.2)	0.004
Surgical intervention, n (%)[b]	23 (96)	5 (6)	<0.001
Mortality, n (%)[b]	4 (17)	2 (3)	0.035

[a] Welch's *t*-test.
[b] χ^2 test.

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Table 3
Risk indicator for NSTI Assessment Score (NAS).

	OR	approximation	Score
Mean arterial pressure, mmHg			
≥75	1		0
<75	14.1	14.1/6 = 2.35	2
C-reactive protein, mg/L			
<150	1		0
≥150	22.9	22.9/6 = 3.82	4
Hemoglobin, g/dL			
≥11.0	1		0
<11.0	6.11	6.11/6 = 1.02	1
Creatinine, μmol/L			
≤141	1		0
>141	6.26	6.26/6 = 1.04	1
Glucose, mmol/L			
≤10.0	1		0
>10.0	17.9	17.9/6 = 2.98	3

OR, odds ratio from multivariate logistic regression analysis (Table 3).
The maximum score is 11, and cutoff point is 6.

2.1. Statistical analysis

Between the NSTI group and the non NSTI group, we compared categorical variables with the χ^2 test and continuous variables with the Welch's *t*-test, respectively. To interpret area under the receiver operating characteristic (ROC) curve (AUC) as an indicator of the accuracy of the tests, we used these definition: an AUC of more than 0.9 was defined outstanding, 0.8 to 0.9 was excellent, and 0.7 to 0.8 was acceptable [6]. Statistical significance was defined with 2-sided p values of <0.05. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria, version 3.2.3) [7].

3. Results

One-hundred and four patients out of 425 patients were included as the study patients in this analysis. Twenty-four patients were grouped into the NSTI group, and 80 patients were grouped into the non NSTI group (Table 1). In the NSTI group, 96% of patients received surgical treatment, but in the non NSTI group, only 6% of patients received. Age and sex were similar between the groups. Mean arterial pressure, hemoglobin and serum sodium were significantly lower in the NSTI group than the non NSTI group. Heart rate, LRINEC score, C-reactive protein, total white cell count, creatinine, glucose, APACHE II score, SOFA score, and mortality were significantly greater in the NSTI group than the non NSTI group.

Mean arterial pressure, C-reactive protein, hemoglobin, creatinine, and glucose were selected as the variables to compose the NAS (Table 2). The score for each variable was developed based on the adjusted odds ratio in the results of the multivariate logistic regression analysis (Table 3).

AUC, sensitivity, specificity, positive predictive value, and negative predictive value of the NAS for diagnosis of NSTI were 0.926, 87.5%, 91.3%, 75.0%, and 96.1% (with cutoff value of 6), respectively; for the LRINEC score, they were, with cutoff of 6, 0.903, 87.5%, 80.0%, 56.8%, and 95.5%, and with cutoff of 8, 0.903, 70.8%, 90%, 68%, and 91.1%, respectively (Table 4). When comparing the area under the receiver operating characteristic curve, there was no significant difference between the NAS and the LRINEC score (Fig. 1).

4. Discussion

In this single-center study, we tried to develop a new prediction score for NSTI which include not only laboratory data, but also vital signs and compared its usefulness with LRINEC score, which is

Table 4
The Comparison of NAS and LRINEC score.

Cut-off value	NAS	LRINEC score		*p*-value
	≥6	≥6	≥8	
AUC	0.926 (0.851–1.00)	0.903 (0.833–0.973)		0.167
Sensitivity	87.5 (67.6–97.3)	87.5 (67.6–97.3)	70.8 (48.9–87.4)	
Specificity	91.2 (82.8–96.4)	80.0 (69.6–88.1)	90.0 (81.2–95.6)	
Positive predictive value	75.0 (55.1–89.3)	56.8 (39.5–72.9)	68.0 (46.5–85.1)	
Negative predictive value	96.1 (88.9–99.2)	95.5 (87.5–99.1)	91.1 (82.6–96.4)	

AUC, area under the ROC curve; ROC, receiver operating characteristic.

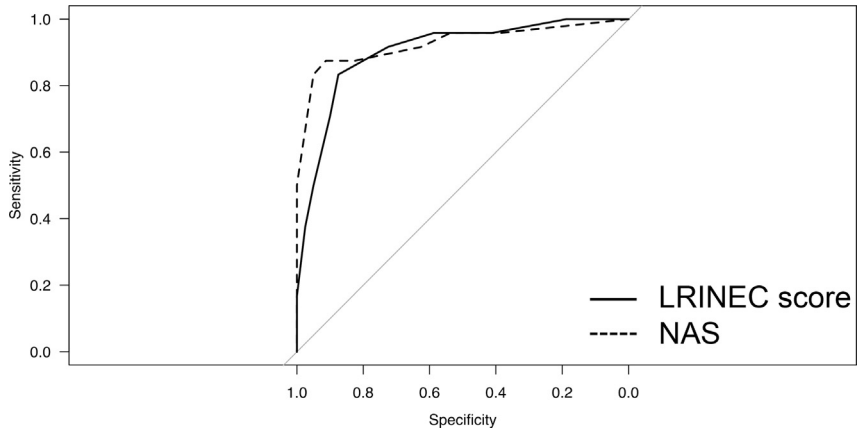

Fig. 1. Receiver Operating Characteristic curves for LRINEC score and NAS score. LRINEC: The Laboratory Risk Indicator for Necrotizing Fasciitis, NAS: necrotizing soft tissue infection assessment score.

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comprised of only laboratory data [8]. In the variables collected, the severity of the NSTI group was higher than that of the non NSTI group, and it appeared that the parameters affected by systemic inflammation were more evidently worse in the NSTI group. A decrease in MAP and an increase in HR were considered to be due to probable systemic inflammatory response syndrome (SIRS), and a decrease of Hb was thought to be a reflection of wasting anemia associated with SIRS [9]. An increase in glucose and an increase in creatinine may also be affected by SIRS, but this may be associated with diabetes mellitus, which is an important comorbidity and a risk factor for NSTI [10]. In this study, we could not fully confirm diagnosis of diabetes mellitus for all cases, because of deficits in data. However, identifying comorbidities for patients with NSTI is important in the medical treatment of NSTI, and it is worth to examine association of diabetes mellitus and other parameters in patients with NSTI in the future.

In this study, sensitivity and positive predictive value of LRINEC score was lower than the previous study [3]. On the other hand, specificity and negative predictive value of LRINEC score was similar between the present study and the previous study. In the previous study, sensitivity, specificity, positive predictive value, and negative predictive value of the LRINEC score were 89.9%, 96.6%, 92.0%, and 96.0% [3]. Although various opinions exist for the usefulness of the LRINEC score, the present study showed that the LRINEC score is highly useful for diagnosis of NSTIs.

One of the issues for the LRINEC score is that it is a score comprised of only laboratory data, and some experts, including surgeons, insist that it should include vital signs as well. Another issue is that the score has two cut-off values, which often confuse clinical judgement of health care professionals treating NSTIs [2].

In contrast to the LRINEC score which only includes laboratory data, the NAS includes both laboratory data and vital signs. The diagnostic accuracy of the NAS is very similar to that of the LRINEC score. It is regrettable that we did not have a cohort for validation of the NAS in the present study.

There are several limitations in this study. First, we could not validate the NAS with other cohorts. The NAS needs to be validated in the future to evaluate its usefulness. Second, because of the retrospective nature of this study, we could not collect data on lactate and coagulation systems, which can be important for the scoring system to distinguish NSTI from other soft tissue infections.

As a conclusion, the NAS, which includes not only laboratory data but also vital signs, was developed as a scoring system for the diagnosis of NSTI, and diagnostic accuracy was very similar to the LRINEC score in this study. Although the NAS needs to be validated in other cohorts, it may be a useful scoring system for diagnosis of NSTI.

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Declaration of Competing Interest

There is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jiac.2019.10.007.

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