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Original Article

Validation of the laboratory risk indicator for necrotizing fasciitis (LRINEC) score for early diagnosis of necrotizing fasciitis

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ABSTRACT

Objective: Necrotizing fasciitis is a surgical emergency. It has a poor outcome after late operative intervention but the clinical diagnosis is difficult. The laboratory risk indicator for necrotizing fasciitis (LRINEC) score was first introduced in 2004 and several clinicians have suggested it is useful for early recognition of necrotizing fasciitis but its validation still needs to be examined. We collected our hospital data from May 2003 to September 2010 to validate whether the LRINEC score can aid in early recognition of necrotizing fasciitis.

Materials and Methods: This is a validation cohort study. We reviewed all necrotizing fasciitis patients admitted from the emergency department at Buddhist Tzu Chi Dalin General Hospital in Taiwan from May 2003 to September 2010. All patients had pathological diagnoses. We used multiple imputations for missing patient data. We analyzed these data and examined whether the LRINEC score had a higher diagnostic value than the clinical diagnosis before admission. We also examined the LRINEC score in patients with severe cellulitis to determine its usefulness in excluding necrotizing fasciitis.

Results: A total of 233 patients with necrotizing fasciitis and 3155 with severe cellulitis were included in our study. A LRINEC score $\geq$6 had a sensitivity of 59.2% (CI 52.9–65.6%), specificity of 83.8% (CI 81.9–85.7%), likelihood ratio of 3.89, positive predictive ratio of 37.9% (95% CI 32.9–42.9%), and negative predictive ratio of 92.5% (95% CI 91.0–94.0%). The rate of clinical diagnosis of necrotizing fasciitis by emergency physicians before admission was 58.4% (95% CI 52.0–64.8%). Of the 97 patients with necrotizing fasciitis who were not clinically diagnosed before admission, 43.3% (95% CI 36.9–49.7%) had a LRINEC score $<$6.

Conclusion: The LRINEC score is an impressive diagnostic tool to distinguish necrotizing fasciitis from other severe soft tissue infections, but it is not useful for early recognition of necrotizing fasciitis.

1. Introduction

Necrotizing fasciitis (NF) is a rapidly progressive infection primarily involving the fascia and subcutaneous tissue. It is the most severe soft tissue infection and without surgical treatment the mortality rate is approximately 50%. Early recognition and aggressive debridement of all necrotic fascia and subcutaneous tissue are very important. Delay in operative debridement has been shown to increase the mortality rate [1–7]. The laboratory risk indicator for necrotizing fasciitis (LRINEC) score was first introduced by Wong et al in 2004 [8]. Laboratory data including hemoglobin, creatinine, glucose, sodium and C-reactive protein (CRP) levels and the white blood cell count are used for early recognition of NF. Only one study validated the score, however, and with a very small group of 28 NF patients. Most studies validated the score system for *Vibrio* necrotizing soft-tissue infection [9–11]. Two studies discussed its prognostic value with NF [12,13]. We collected hospital data from May 2003 to September 2010 to further validate whether the LRINEC score can be used for early recognition of NF.

2. Materials and methods

This validation cohort study included all patients treated at Buddhist Dalin Tzu Chi General Hospital for NF between May 2003 and September 2010. The data were extracted from a computer-generated search through the Medical Records Department for

Conflict of interest: none.

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Table 1
Laboratory risk indicator for necrotizing fasciitis (LRINEC) score.

Variable	Unit	Score
C-reactive protein	mg/dL	
<15		0
≥15		4
WBC	per mm^3	
<15,000		0
15,000–25,000		1
>25,000		2
Hemoglobin	g/dL	
>13.5		0
11.0–13.5		1
<11.0		2
Na	mmol/L	
≥135		0
<135		2
Creatinine	mg/dl	
≤1.6		0
>1.6		2
Glucose	mg/dL	
≤180		0
>180		1

all patients diagnosed with NF (according to the *International Classification of Diseases–9th Revision* definition). We checked every patient to see whether the diagnosis was correct. The definitive diagnosis was a pathological report confirming NF.

A total of 233 patients were identified and included in this study. In addition, 3155 patients were admitted to our institution with a clinical diagnosis of cellulitis or soft tissue infection during the same period. Control patients were selected from this patient pool with intact laboratory data. Patient charts were reviewed to identify patients with severe soft tissue infection. The criteria for severe soft tissue infections were as follows, based on documentation in the patients' charts:

- use of parenteral antibiotics for more than 48 hours in a patient with a soft tissue infection; and
- abscess requiring surgical debridement.

Patients who met anyone of above criteria were diagnosed with severe cellulitis. Of these, 1394 patients fulfilled our criteria for severe soft tissue infection and were used as controls for this study. The LRINEC scoring system is shown in Table 1.

Table 2
Necrotizing fasciitis and severe cellulitis patients comparison.

	Necrotizing fasciitis	Severe cellulitis	*p* value
Total	***233 patients***	***1394 patients***	
Age average	61.2	60.8	0.71
Gender ratio	M:F 2.02	M:F 1.36	<0.05
WBC average	15,951	11,688	<0.05
25,000 > WBC > 15,000	38.2%	18.9%	
WBC >25,000	12.9%	2.7%	
Hgb average	12.26	12.57	0.072
13.5 > Hgb > 11.0	35.2%	40.0%	
Hgb < 11.0	27.5%	22.6%	
Cr average	1.52	1.22	<0.05
Cr >1.6	29.6%	12.8%	
Glucose average	206	165	<0.05
Glucose >180	40.3%	24.9%	
Na average	131.6	134.6	<0.05
Na <135	64.4%	45.4%	
CRP	40.3% without CRP	46.7%without CRP	

Key: Cr – creatine; CRP – C-reactive protein; Hgb – hemoglobin; M:F – male to female ratio; Na – sodium; WBC – white blood cells.

Table 3
Comorbidity and culture results of necrotizing fasciitis patients.

Immunocompromised	Total 128
DM	82.0%
Liver cirrhosis	21.9%
Cancer	5.5%
Others[a]	7.8%
Blood culture	Total 51
Methicillin-resistant *Staphylococcus aureus*	19.6%
Methicillin-sensitive *Staphylococcus aureus*	19.6%
Group A *Streptococcus*	15.7%
Klebsiella pneumoniae	9.9%
Vibrio vulnificus	7.8%
Aeromonas hydrophila	3.9%
Wound culture	Total 199
Methicillin-sensitive *Staphylococcus aureus*	19.1%
Methicillin-resistant *Staphylococcus aureus*	16.6%
Group A streptococcus	10.6%
Klebsiella pneumoniae	7.0%
Vibrio vulnificus	5.0%
Escherichia coli	4.0%
Aeromonas hydrophila	2.0%
Mixed flora or rare-isolated bacteria[b]	21.1%

[a] End-stage renal disease on hemodialysis, autoimmune disease, chronic steroid use, intravenous drug user.
[b] Rare-isolated bacteria were not listed in this table.

3. Results

Baseline and clinical data from our patients and controls were collected and are shown in Table 2. Underlying diseases and culture data are presented in Table 3. Validation was carried out for the patients with NF and severe cellulitis.

We calculated the LRINEC score for all patients and the cut-off level was a score ≥6 according to a previous study [8]. We examined the diagnostic value of the LRINEC score compared with the clinical diagnoses of our emergency physicians. As in the LRINEC score developmental cohort study, the multiple imputation method was used to handle missing CRP data in 94 NF and 651 severe cellulitis patients, similar to the Wong et al study [8]. The five different multiple imputation methods used showed a similar result (Table 4).

We selected the highest sensitivity method for further evaluation. In all patients with NF and severe cellulitis, a LRINEC score ≥6 had a sensitivity of 59.2% (95% confidence interval [CI] 52.9–65.6%) specificity of 83.8% (95% CI 81.9–85.7%), positive predictive value of 37.9% (95% CI 32.9– 42.9%), and negative predictive value of 92.5% (95% CI 91.0–94.0%), as shown in Table 5.

The rate of clinical diagnosis of NF in patients by emergency physicians before admission was 58.4% (95% CI 52.0–64.8%). This showed that the sensitivity of the clinical diagnosis was similar to that of a LRINEC score ≥6 ($p < 0.05$). We also examined whether a LRINEC score can help when the clinical diagnosis did not suggest NF. Ninety-seven of the 233 patients with NF did not have the correct diagnosis before admission. Fifty-five of these 97 (56.7%) patients had a LRINEC score ≥6, and therefore 42 of 97 (43.3%) had LRINEC score <6 (Table 6). We built receiver operating characteristic (ROC) curves for the LRINEC score to determine its utility in the early diagnosis of NF (Fig. 1). We did a sub-group analysis of gram

Table 4
Sensitivity and specificity of five different multiple imputation methods.

	1	2	3	4	5
Sensitivity	59.2%	56.2%	54.9%	55.8%	55.8%
Specificity	84.8%	82.6%	83.8%	82.1%	83.3%

Table 5
LRINEC score of necrotizing fasciitis and severe cellulitis.

	Necrotizing fasciitis	Severe cellulitis
LRINEC≥6	59.2%	16.2%
LRINEC<6	40.8%	83.8%
Total	*233*	*1394*

Sensitivity: 59.2% (95% CI 52.9–65.6%).
Specificity: 83.8% (95% CI 81.9–85.7%).
Positive predictive value: 37.9% (95% CI 32.9–42.9%).
Negative predictive value: 92.5% (95% CI 91.0–94.0%).
Positive likelihood ratio: 3.65.
Negative likelihood ratio: 0.487.

positive coccus infection and gram-negative *Bacillus* infection in NF. A LRINEC score ≥6 had a sensitivity of 61.2% with gram-positive coccus infection and 47.2% with gram-negative *Bacillus* infection in NF (proved by either wound culture or blood culture).

We also analyzed methicillin-resistant *Staphylococcus aureus* (MRSA) infection in NF because of its special treatment and the high percentage of cases in this study. A LRINEC score ≥6 had a sensitivity of 47.2% with MRSA infection in NF (proved by wound culture or blood culture).

4. Discussion

The developmental study by Wong et al reported that a LRINEC score ≥6 had a sensitivity of 89.9%, specificity of 96.9%, positive predictive value of 92.0% and negative predictive value of 96.0% [8]. In 2009, Holland studied a group of 28 patients who had received surgery because of suspected NF. Ten patients were diagnosed with NF postoperatively. The results showed a sensitivity of 80%, specificity of 67%, positive predictive value of 57% and negative predictive value of 86% [9]. Our results showed that the LRINEC score had impressive ability to discriminate NF from severe soft tissue infection, but was not a good diagnostic tool for NF. When clinical data did not indicate a diagnosis of NF, 43.3% (95% CI 36.9–49.7%) of patients still had a LRINEC score <6, so a LRINEC score cannot help to decrease the misdiagnosis of patients with NF. Our ROC curve examining the diagnostic ability of a LRINEC score showed moderate value.

Blood and wound culture data showed that MRSA was the most important pathogen causing NF in this study. Our empirical antibiotic regimen does not include routine use of vancomycin. Routine use of this antibiotic for suspected NF should be considered because of the high prevalence of MRSA. However, we must pay attention to the patient's renal function. A LRINEC score≥6 had a sensitivity of 47.2% with MRSA infection in NF. It seems that this score cannot help in the early detection of NF caused by MRSA because of its low sensitivity.

Our study limitations were as follows:

- this is a retrospective study;
- multiple imputations were used for missing CRP data;
- the study group did not include NF patients with an unstable hemodynamic status or other contraindications to surgical intervention; and
- we did not differentiate parts of the body involved, such as finger involvement alone, which may have influenced laboratory data. The definition of severe soft tissue infection was that in Wong et al's developmental study, but this definition is not accepted by all clinicians.

Table 6
Relationship between LRINEC score and clinical diagnosis with necrotizing fasciitis.

	Clinical diagnosis (+)	Clinical diagnosis (-)	Total
LRINEC≥6	61.0%	56.7%	138
LRINEC<6	39.0%	43.3%	95
Total	*136*	*97*	

Clinical diagnosis sensitivity: 58.4% (95% CI 52.0–64.8%).
Clinical miss diagnosis with LRINEC score <6: 43.3% (95% CI 36.9–49.7%).

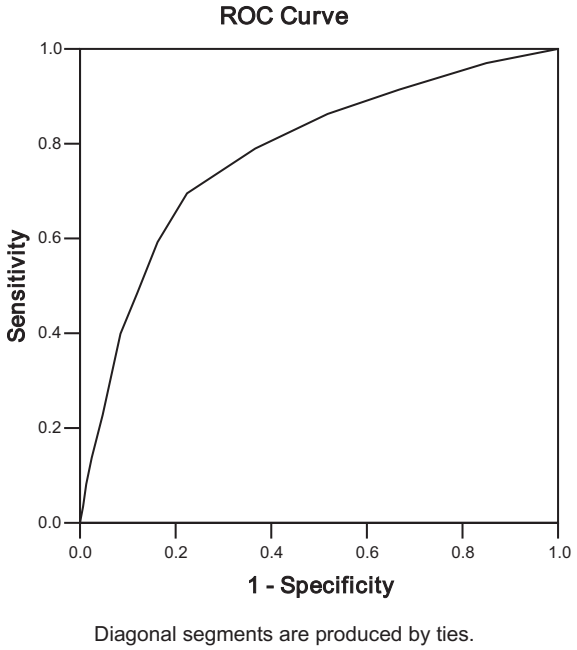

Fig. 1. Receiver operating characteristic curve of the LRINEC score for necrotizing fasciitis (area under the curve = 0.779).

5. Conclusions

In patients where there is a clinical suspicion of severe soft tissue infections, the LRINEC score is an impressive diagnostic tool to distinguish NF from such infections. According to this study, the LRINEC score had an impressive 92% positive predictive value and 96% negative predictive value, which were validated in other hospitals with the same findings. LRINEC score alone, however, is not useful for the early recognition of NF. It is suggested that vancomycin may be routinely used in patients with suspected NF if renal function is not compromised.

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