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Original Article

Accuracy of Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) Score System as An Early Diagnostic Predictor of Necrotizing Fasciitis in A Tertiary Referral Hospital in Bandung, Indonesia

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Abstract

Background: Necrotizing fasciitis (NF) is a serious infection that can rapidly kill tissue and potentially lead to multiple organ failure. Early diagnosis and treatment are essential for survival. The laboratory risk indicator for necrotizing fasciitis (LRINEC) score may aid in early detection of NF. Although initially promising, studies on the effectiveness of LRINEC have shown mixed results. This study aimed to investigate the accuracy of LRINEC in predicting NF.

Methods: This was an observational prospective cohort study, including patients with NF as well as skin and soft tissue infection (SSTI) who were treated at a tertiary referral hospital in Bandung, Indonesia in 2022. The LRINEC scores was calculated to measure sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The accuracy of LRINEC scores was specified in the area under the curve (AUC) of the receiver operating characteristic (ROC) curve.

Results: Of the total 70 patients, 33 were diagnosed with NF and 37 with SSTI. The LRINEC score with ≥6 points cut-off showed a sensitivity of 90.9% (95%CI; 75.67–98.08%), specificity of 75.60% (95%CI; 58.80–88.23%), PPV of 76.9% (95%CI; 60.67–88.87%), and NPV 90.30% (95%CI; 74.25–97.96%). The area under the ROC (AUROC) curve for the accuracy of the LRINEC scores was 0.895 (95%CI; 0.821–0.969).

Conclusions: The laboratory risk indicator for necrotizing fasciitis (LRINEC) score is an accurate predictor and feasible early diagnostic indicator in NF. However, clinical judgment remains a crucial factor in diagnosing NF..

Keywords: Laboratory risk indicator for necrotizing fasciitis (LRINEC) score, necrotizing fasciitis, skin and soft tissue infection

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Introduction

Necrotizing fasciitis (NF) is a severe, life-threatening infection of the skin and soft tissue with extensive tissue necrosis.[1,2] Necrotizing fasciitis is associated with bacterial invasion of the fascia, which has the ability to spread rapidly to the muscles, subcutaneous fat, and skin. Necrotizing fasciitis often causes multi-organ failure leading to death.[3]

Despite advances in modern modalities, the global mortality rate remains high, ranging between 19–30% in all body parts, including the neck, trunk, perineum, and extremities.[4] Necrotizing fasciitis occurs in 0.4 in every 100,000 people per year in the United States and 1 in every 100,000 in South Asia.[5–7] In Indonesia, there is still no data on the incidence and mortality of necrotizing fasciitis.

The diagnosis of necrotizing fasciitis relies primarily on clinical suspicion. However, early clinical recognition of necrotizing fasciitis is difficult because the disease is often difficult to distinguish from cellulitis or the initial signs of an abscess.[3] Several diagnostic tools that might support diagnosis include ultrasonography (USG),[8] computed tomography (CT),[9] magnetic resonance imaging (MRI),[10,11] laboratory tests, and scoring systems. Three scoring systems are commonly used to assess NF severity, Fournier's gangrene severity index (FGSI), laboratory risk indicator for necrotizing

fasciitis (LRINEC) and neutrophile–lymphocyte ratio (NLR). Among three of them, LRINEC has become the most reliable and frequently used.[3,12–14] Plain radiography has poor sensitivity for excluding necrotizing fasciitis. CT and MRI may recognize early signs of necrotizing fasciitis but may delay definitive surgical intervention.[6] Prompt recognition and aggressive debridement of all necrotic tissue are major prognostic determinants. Moreover, delay in surgical debridement had been found to increase mortality.[3] In the initial clinical condition of necrotizing fasciitis, which is difficult to distinguish from other tissue infections and the limitations of the supporting facilities, it is necessary to choose the diagnostic procedure that can be carried out to help identify early necrotizing fasciitis and not to delay definitive surgical therapy.

Abnormal biochemical test results may be helpful in the diagnosis of necrotizing fasciitis but are not specific. The LRINEC scoring system was a tool to differentiate necrotizing fasciitis from other soft tissue infections. The LRINEC scoring system consists of six laboratory test results, resulting in a total maximum score of 13. A LRINEC score of ≥6 indicates suspicion of necrotizing fasciitis (probability 50–75%), whereas a LRINEC score of ≥8 strongly predicts necrotizing fasciitis (probability >75%).[3]

The LRINEC score has been shown to be robust in detecting even early cases of clinically necrotizing fasciitis in initial retrospective external validation.[3] However, in a recent study, the LRINEC score has reported to have inadequate sensitivity in diagnosing necrotizing fasciitis, ranging from 36 to 83%.[12,15] Moreover, two systemic reviews of the LRINEC score showed conflicting results.[6,15] The LRINEC score is a clinical tool that can be useful in diagnosing necrotizing fasciitis where the sensitivity of the LRINEC score is 68.2% with a LRINEC cut-off score ≥6 and 40.8% with a LRINEC cut-off score ≥8.

Based on the preceding, this study aimed to determine the accuracy of the LRINEC scoring system as a predictor of early diagnosis in necrotizing fasciitis at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia which to the best our knowledge, study on the LRINEC scores has never been carried out in in this city.

Methods

This study was a prospective observational cohort study, including patients with clinically assessed necrotizing fasciitis and patients with early necrotizing soft tissue infection who came to the Emergency Unit of Dr. Hasan Sadikin General Hospital or who were referred from other units in 2022. This study was conducted based on the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines and ethical approval has been attained from the Research Ethics Committee of Dr. Hasan Sadikin General Hospital no. LB.02.01/X.6.5/253/2022.

The inclusion criteria were patients with soft tissue infection, aged ≥18 years old and signed consent for research involvement; and the exlusion criteria were pregnant women, and had a length of hospitalization <48 hours.

Necrotizing fasciitis was defined as an infection that could spread widely and quickly develop into necrosis of the subcutaneous tissue and fascia with thrombosis of the cutaneous microcirculation and is life-threatening; and necrotizing soft tissue infections was defined as infections of the skin, subcutaneous tissue, fascia, and muscles, that covered a wide spectrum of clinical presentations, ranging from cellulitis, abscesses, ulcers and gangrene and no fasciitis was found intraoperatively.

Determination of the sample size was adjusted to the objectives and the type of research data. The design of this tsudy was an unpaired numerical analysis, therefore the number of samples was determined based on the estimated proportion. The proportion of the variables studied was 0.5 to get maximum variability. Then to test the hypothesis, the sample size formula was used between the two populations from the sample size 2.0 program.[16] By setting a 95% confidence level and 90% power test and using Zα and Zβ obtained from the standard normal distribution table, the appropriate value were obtained for Zα=1.96, and for Zβ=1.28, therefore the minimum sample size for each group was 25. A previous study stated that the success rate for LRINEC ranged from 92–95%.[3] Therefore, the number of samples in each group was increased from 30% to 32.5≈33 (minimum number for each group). Thus, the minimum sample size was set at 33 patients per group, totaling 66 patients across both groups, which were patients with NF and patients with skin and soft tissue infection (SSTI).

There were 6 tests needed for LRINEC scoring system consisting of C-reactive protein (CRP), leukocytes, hemoglobin, sodium, blood sugar, and creatinine were collected. A score <5 was designated as low risk (<50% probability); a score of 6–7 indicated intermediate risk (50–75% probability); and a score >8 was high

risk (>75% probability). The cut-off value of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 6 and 8. Receiver operating characteristic (ROC) curves with 95% confidence intervals (CI) were used to evaluate the accuracy of the predictions of LRINEC scores.

All variables between the necrotizing fasciitis and early necrotizing soft tissue infections (cellulitis, abscess) groups were compared and analyzed using the SPSS statistical software (IBM SPSS 26, Armonk, NY: IBM Corp). Univariate analysis was utilized to identify risk factors for necrotizing fasciitis. Numerical variables were first tested for normality using the Shapiro-Wilk test. The data was normally distributed if the p-value> 0.05. An independent T-test was performed if the data was normally distributed; if the data was not, the test was continued with the Mann-Whitney U test. The Pearson Chi-Square test was used to analyze 2x2 or nx2 categorical data. If there was an expected count <5 as much as >25%, then the test was continued using Fischer's exact test. The value of p<0.05 was considered significant. The ROC curve with 95% CI was used for the accuracy of LRINEC score prediction. The risk score prediction accuracy was expressed as the area under the ROC curve (AUROC).

Results

IIn this study, 70 patients were included, of which 33 patients with necrotizing fasciitis and 37 patients with other soft tissue infections. Necrotizing fasciitis was diagnosed in 58.3% among men and 35.3% among women, and there was no difference in the proportion between gender (p=0.054). Female were more prevalent in SSTI (64.7%). The region that experienced the most fasciitis was the lower extremity region (69.7%), and the second most were the thoracic and abdominal regions (Table 1).

The most comorbid factors in necrotizing fasciitis patients were congestive heart failure (CHF), followed by diabetes mellitus (DM), and hypertension (HT). There was a significant difference in the prevalence of comorbid factors between patients with necrotizing fasciitis and those with other infections (p=0.039). Three patients died in necrotizing fasciitis, and none in the other infection groups.

Table 1 Characteristic of Patients with Necrotizing Fasciitis and Patients With Skin and Soft Tissue Infection (SSTI)

Characteristics	Diagnosis		P-value
	Necrotizing Fasciitis n (%)	SSTI n (%)	
Gender			
Male	21 (58.3)	15 (41.7)	0.054[a]
Female	12 (35.3)	22 (64.7)	
Age			
<60 years old	20 (50.0)	20 (50.0)	0.580[a]
≥60 years old	13 (43.3)	17 (56.7)	
Region			
Superior extremity	1 (50.0)	1 (50.0)	0.352[a]
Inferior extremity	23 (45.1)	28 (5.9)	
Thorax abdomen	6 (75.0)	2 (25.0)	
Perineum sacrum	3 (33.3)	6 (66.7)	
Comorbid factors			
Congestive heart failure	2 (100.0)	0 (0.0)	0.039[a]
Diabetes mellitus	21 (61.8)	13 (38.2)	
Hypertension	1 (20.0)	4 (80.0)	
Chronic kidney gisease	0 (0.0)	1(100.0)	
No comorbid	9 (32.1)	19 (67.9)	
Mortality			
Alive	30 (44.8)	37 (55.2)	0.100[b]
Dead	3 (100.0)	0 (0.0)	

Note: [a] Pearson Chi-square, [b] Fisher's exact test, SSTI= Skin and soft tissue infection

Table 2 Laboratory Parameters Between Patients with Necrotizing Fasciitis and Other Soft Tissue Infection

Variable	Diagnosis		P-value
	Necrotizing Fasciitis	SSTI	
CRP			
Mean ± SD	267.38 ± 93.72	136.20 ± 102.48	0.000
Median	257.00	102.30	
Range (min-max)	406.90 (144.70-551.60)	428.00 (12.90–440.90)	
Leukocyte			
Mean ± SD	25006.03 ± 11655.07	19481.35 ± 12310.98	0.059
Median	23320.00	14890.00	
Range (min-max)	63180.00 (11010.00–74190.00)	61870.00 (6940.00–68810.00)	
Haemoglobin			
Mean ± SD	10.95 ± 2.79	10.35 ± 2.82	0.378
Median	11.10	10.40	
Range (min-max)	12,60 (5.50-18.10)	11.4 (4.30-15.70)	
Natrium			
Mean ± SD	128.93 ± 6.87	135.00 ± 9.79	0.004
Median	130.00	135.00	
Range (min-max)	29.00 (115.00–144.00)	50.00(112.00–62.00)	
Creatinine			
Mean ± SD	1.98 ± 1.30	2.07 ± 3.36	0.883
Median	1.74	1.07	
Range (min-max)	5.79 (0.53–6.32)	16.16 (0.37–16.53)	
Random blood glucose			
Mean ± SD	242.69 ± 201.67	175.97 ± 107.66	0.084
Median	163	133	
Range (min-max)	832.00 (26.00–858.00)	399 (73.00–472.00)	
LRINEC score			
Mean ± SD	9.72 ± 2.09	5.02 ± 2.84	0.000
Median	10.00	4.00	
Range (min-max)	10.00 (3.00–13.00)	10.00 (1.00–11.00)	

Note: CRP= C-reactive protein; LRINEC= Laboratory risk indicator for necrotizing fasciitis; SD= Standard deviation; SSTI= Skin and soft tissue infection

The average CRP level in patients with necrotizing fasciitis (267.38±93.72) was significantly higher than that in patients with other infections (136.20±102.48) (p=0.000).

There was no significant difference in hemoglobin levels and leukocyte count. Moreover, the average sodium level was significantly lower in necrotizing fasciitis patients (128.93±6.87) compared to those with other infections (135.00±9.79) (p=0.004), whereas no significant difference between the two groups for creatinine and random blood glucose level.

Interestingly, the average LRINEC score of necrotizing fasciitis patients was significantly higher (9.72±2.09) than that of patients with other infections (5.02±2.84) (p=0.000). The receiver operating characteristics (ROC) curve of the LRINEC score was 50%, suggesting a good probability value (Figure 1).

The LRINEC score had the area under curve (AUC) results of 89.5% (p=0.000), which was a good value (range 80–90% for good AUC criteria), indicating that LRNEC score had a glood predicting value for necrotizing fasciitis.

The optimal cut point was between point 8 and point 9. Point 8 had a sensitivity of 90.9% (95% CI; 75.67–98.08%), and a specificity of 75.6% (95%CI; 58.80–88.23%), while point 9 had a sensitivity of 78.8% and a specificity of 81.1%. The point 8 was chosen as the cut-off point, and the LRINEC score was 7.5. Patients with a LRINEC score >7.5 were diagnosed with necrotizing fasciitis (Figure 2).

Patients with an LRINEC score >7.5 had p=0.000 (OR 31.11) compared to patients with an LRINEC score ≤7.5 for necrotic fasciitis, thus, patients with an LRINEC score >7.5 had 31 times higher risk of developing fasciitis (Table 3).

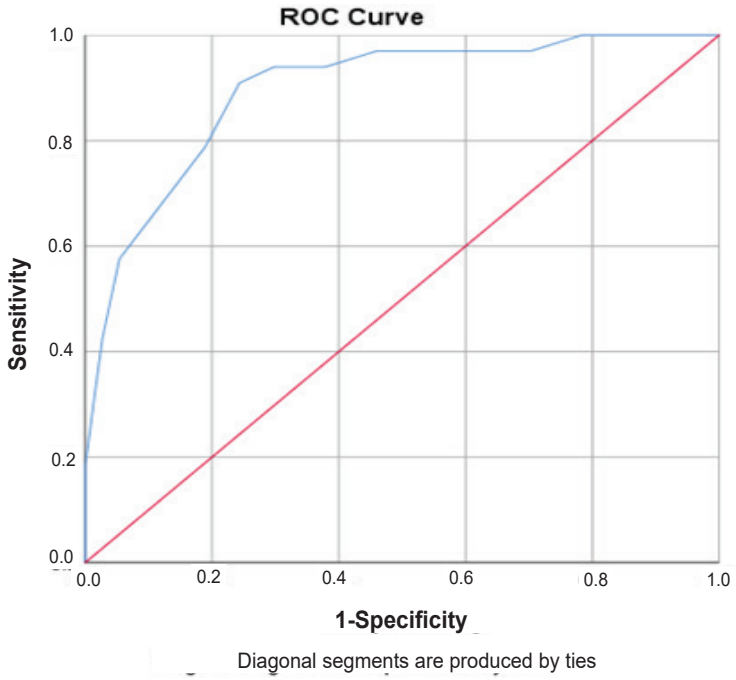

Figure 1 Curve Receiver Operating Characteristics (ROC) LRINEC Score

The sensitivity and specificity scores of LRINEC were 90.91% (95% CI; 75.67–98.08%) and 75.68% (95%CI; 58.80–88.23%), respectively; whereas the postivie and negative predictive value were 76.92% (95%CI; 60.67–88.87%) and 90.32% (95%CI; 74.25–97.96%), respectively.

Discussion

Diagnosing necrotizing fasciitis poses a major challenge to clinicians. The soft tissue infection starts spreading from the deeper layers, masking signs of infection, and producing confusing nonspecific symptoms.[5,17]

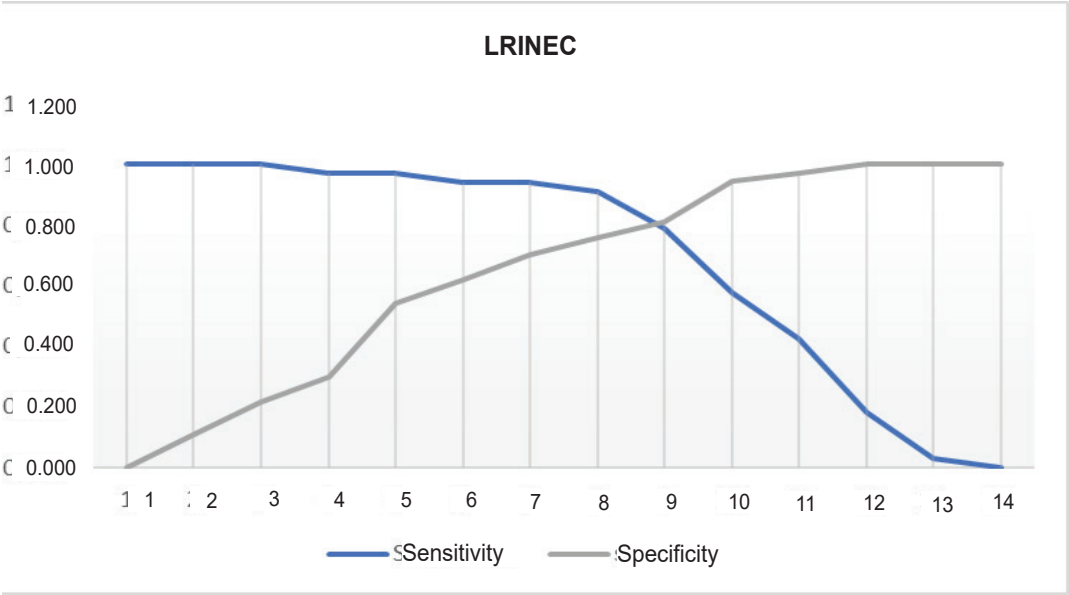

Figure 2 Intersection for Sensitivity and Specificity Value of LRINEC

Table 3 Comparison of the Risk of Necrotizing Fasciitis based on the LRINEC Score

LRINEC Score	n	Diagnosis		OR (95% CI)	P-value
		Necrotizing Fasciitis n (%)	SSTI n (%)		
>7.5	39	30 (76.9)	9 (23.1)	31.11 (7.63-126.72)	0.000
≤7.5	31	3 (9.7)	28 (90.3)	Reff	

Note: CI= Confidence interval; LRINEC= Laboratory risk indicator for necrotizing fasciitis; OR= Odds ratio; SD= Standard deviation; SSTI= Skin and soft tissue infection

Table 4 Sensitivity and Specificity Scores of LRINEC

Statistic	Value (%)	95% CI, %
Sensitivity	90.91%	75.67% to 98.08%
Specificity	75.68%	58.80% to 88.23%
Positive likelihood ratio	3.74	2.10 to 6.67
Negative likelihood ratio	0.12	0.04 to 0.36
Disease prevalence	47.14%	35.09% to 59.45%
Positive predictive value	76.92%	60.67% to 88.87%
Negative predictive value	90.32%	74.25% to 97.96%
Accuracy	82.86%	71.97% to 90.82%

Note: CI= Confidence interval; LRINEC= Laboratory risk indicator for necrotizing fasciitis

In patients with severe conditions, it is crucial to identify those at high risk in the early stages and to use objective parameters, alongside clinical judgment, to assess disease severity. To this end, the LRINEC score has been introduced to enable patient risk stratification and differentiation of necrotizing fasciitis from non-necrotizing soft tissue infections and as a robust score that can even detect early cases of necrotizing fasciitis.[3]

In this study, the lower extremity had the highest incidence of necrotizing fasciitis. A study in India found that 75% of necrotizing fasciitis occurred in the lower extremities.[18] Similarly, another study conducted in India in the previous years also found that the most common region affected by necrotizing fasciitis was the lower extremities (68.33%),[19] which was in accordance with the findings of this study.

Regarding comorbid factors, diabetes mellitus was the most common comorbidity in necrotizing fasciitis and it was concluded as part of a high-risk score. Similar finding was obtained in a study conducted in India, showing a significant relationship between necrotizing fasciitis and comorbid diabetes mellitus.[17] Another finding of that study includes mortality rate in necrotizing fasciitis patients, which showed a significant relationship.[18] In contrast to this study, the mortality rate in necrotizing fasciitis was found in 9% of the patients. In this study, death occurred in patients with a high-risk LRINEC score with septic shock and irreversible multi-organ damage.[13] This suggests that an aggressive treatment plan can be implemented promptly. Mortality can be reduced through early recognition of necrotizing fasciitis, with aggressive serial debridement of all necrotic and subcutaneous fascia being the main prognostic determinant,[4] early administration of intravenous antibiotics,[19] and delayed operative intervention has been shown to increase morbidity and mortality.

Of the six variables in the LRINEC score, it was found that CRP level and sodium level had a significant relationship in the LRINEC score, similar to a study in Australia.[15] This association might be attributed to CRP's role as a potent marker of inflammation, while low sodium levels could indicate renal dysfunction resulting from multiorgan impairment due to severe infections or may reflect fluid sequestration in cases of more extensive soft tissue involvement.[15,20] The use LRINEC score may prove to be useful in detecting necrotizing fasciitis in its early stages. A previous study suggested suspicion of necrotizing fasciitis in patients with LRINEC score ≥6 and a strong prediction of necrotizing fasciitis in patients with LRINEC score ≥8 (PPV 92%, NPV 96%).[3] Adopting an evidence-based approach to the diagnosis of necrotizing fasciitis is important and could lead to early diagnosis, surgical intervention, and decreased morbidity and

mortality. Our study showed that there was a significant difference between the average LRINEC score in the group of necrotizing fasciitis patients and patients with other infections. At an LRINEC score >7.5, the PPV was 76.92% (95%CI; 60.67 – 88.87%), NPV was 90.32% (95%CI; 74.25–97.96%), and OR was 31.1%, indicating that the presence or absence of necrotizing fasciitis can be determined with a high degree of confidence based on a score >7.5. Similar results were also found in a study conducted in Australia and in many systematic review and meta-analysis studies.[21–23]

With its significant accuracy, the LRINEC score also has potential as a clinical diagnostic predictor. Given its simplicity in calculation, it can be quickly applied in clinical judgment. However, it must be emphasized that the diagnosis of necrotizing fasciitis remains a clinical decision. While a high LRINEC score raises suspicion in a patient who present with clinical feature of necrotizing fasciitis, a low score does not necessarily rule out the diagnosis.

The limitation in this study is that the diagnosis is relied on surgery for necrotizing fasciitis, while other infections were diagnosed clinically. Imaging and biopsies had not been performed for all cases, and prior antibiotics are not excluded. The small sample size from a single center limits generalizability. Future studies across multiple hospitals with larger samples are needed. Despite these limitations, the LRINEC score shows promise as an early predictor of necrotizing fasciitis, especially in resource-limited settings. Its ease of use and low cost make it a valuable tool for managing soft tissue infections.

In conclusion, the LRINEC score is an accurate predictor and feasible early diagnostic indicator in NF. However, clinical judgment remains an important factor in diagnosing NF

Consent for publication
Written consent for publication has been obtained from the participants.

Underlying data and material
All data are available within the manuscript.

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