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Laboratory risk indicators for acute necrotizing fasciitis in the emergency setting

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ABSTRACT

Necrotizing fasciitis is a rare bacterial skin condition which forms a major diagnostic challenge and is associated with poor prognosis unless promptly treated. Initial clinical presentation is often misleading with characteristic features developing only late in the course of the disease. In this review, we discuss the applicability and usefulness of laboratory risk indicator for necrotizing fasciitis score in facilitating rapid diagnosis of necrotizing fasciitis in emergency department by differentiating it from other skin infections like cellulitis and abscesses. A high index of suspicion resulting from the laboratory risk indicator for necrotizing fasciitis score can facilitate early diagnosis enabling prompt antibiotic administration and timely referral to surgery for wound debridement, ultimately reducing both the morbidity and mortality.

1. Introduction

Necrotizing fasciitis (NF) is a type of bacterial infection of the soft tissues associated with a high rapid mortality. It is characterized by inflammation and necrosis arising from the fascia involving muscles and subcutaneous fat with resulting necrosis of the overlying skin[1]. This rare disease can be caused by more than one type of bacteria including *Klebsiella*, *Clostridium*, *Escherichia coli*, *Staphylococcus aureus* and *Aeromonas hydrophilia*, but group A streptococcus is considered the most common cause of NF[1].

In the United States, 500 to 1 000 cases of NF are diagnosed each year according to the report by US Center for Disease Control and Prevention[2]. No gender predilection has been observed, however, a clear seasonal fluctuation occurs with more cases being seen in cold months[1].

NF has been classified into two major categories based on microbiology and localization of the infection. Type 1 is polymicrobial involving at least one anaerobe with or without a facultative anaerobe localized mainly on trunk, abdomen and perineum. Type 2 is monomicrobial caused mainly by group A beta hemolytic streptococci and/or other streptococci or staphylococci and occurs mainly on extremities[1,3].

Preexisting medical conditions significantly predispose patients to developing NF. This may be one reason why NF is more common in adults than in children. Diabetes mellitus is the most common risk factor followed by immune suppression, renal failure, liver cirrhosis, pulmonary diseases, malignancy and last injection drug abuse[1,3].

2. Use of laboratory risk indicator for necrotizing fasciitis (LRINEC) tool in emergency department for rapid diagnosis

Diagnosis of NF forms the biggest challenge which has led to further increased morbidity and mortality from the disease[4]. NF can easily be confused with cellulitis or abscesses[5]. According to Lancerotto *et al*., early diagnosis is missed in 85%–100% of cases and forms the single most important cause of fatal outcomes[1].

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At the same time, as the diagnosis forms a challenge, a timely diagnosis, management and surgical referral from emergency department can significantly reduce the resulting morbidity and enable saving not just the life but also the organ. The use of LRINEC has been debated for some time and herein we discuss its usefulness in the setting of an emergency department[6].

The LRINEC score was first proposed by Wong *et al*. utilizing laboratory variables that are routinely measured to assess soft tissue infections[6]. The score, calculated based on the values of C-reactive protein, white blood cell, hemoglobin, Na, serum creatinine and serum glucose measured at the time of admission, enabled categorization of patients into low-, intermediate-, and high risk groups (Table 1). A score of less than or equal to 5 meant a probability of less than 50% for developing NF. A score of 6–7 meant 50%–75% risk of NF whereas any score more than 8 is a high indicator to more than 75% risk being associated with NF with a positive predictive value of as high as 93%[6]. All the parameters needed for the calculation of the score are readily available in emergency department at the 'bedside'[7].

Table 1

Variables included in the laboratory risk indicator for acute NF scoring system.

Variables	Value	LRINEC score point
C-reactive protein (mg/L)	< 150	0
	> 150	4
White blood cell (cells/mm^3)	< 15	0
	15–25	1
	> 25	2
Hemoglobin (g/dL)	> 13.5	0
	11.0–13.5	1
	< 11.0	2
Sodium (mmol/L)	> 135	0
	< 135	2
Creatinine (mg/dL)	< 1.6	0
	> 1.6	2
Glucose (mg/dL)	< 180	0
	> 180	1

Wong *et al*. argued that biochemical and hematologic changes occur early in the course of disease and the LRINEC score can facilitate stratification of patients into high or low risk[6]. NF is associated with severe sepsis in body leading to inflammatory response syndrome. In their experimental cohort of 89 patients with NF, only 13 had a diagnosis or suspicion of NF at the time of admission whereas 80 of these had a LRINEC score of > 6[6].

In another prospective study, Wong and Khin recruited 234 consecutive patients suspected to have soft-tissue infections[8]. Of these, 19 were ultimately labeled to have NF. The application of LRINEC score found a positive predictive value of 40% and negative predictive value of 95%. Thus, the score was seen to have a high specificity but low sensitivity. Although a high false positive rate may be expected, this would still serve the purpose of streamlining the use of additional diagnostic tool to patients with any suspicion of NF based on LRINEC[8].

A study carried out by Su *et al*. recruited a large series of patients retrospectively and divided the patients into two groups based on whether the LRINEC score was greater/equal to 6 or less than 6[9]. It was seen that patients with LRINEC score greater/equal to 6 developed more complications and had a higher mortality and amputation rate[9,10].

The score is not only valid for type 1 and type 2 NF but also has been applied successfully to identify NF caused by atypical organisms like *Vibrio vulnificus* (*V. vulnificus*). With a specificity and PPV both greater than 80%, a score of 2 or greater was regarded to be a strong indicator of NF in patients with *V. vulnificus*-related skin and soft tissue infections. In contrast to other studies where the LRINEC cutoff score was taken to be 6, a lower cutoff was justified for *V. vulnificus* based on the rapid progression of the disease owing to the higher virulence and pathogenicity of the organism[3].

There are case reports in which the diagnosis was enabled by a high LRINEC score. In a case report of a 6-year-old girl who presented with pyrexia, abdominal tenderness and right lower limb pain and erythema, an immediate explorative fasciotomy was considered based on a LRINEC score of 8 which saved both the life and the limb owing to timely discovery[11]. LRINEC can also be a useful tool in predicting the chances of complications occurring in soft tissue infection as reported by Corbin *et al*., who saw a higher rate of complication in patients with LRINEC score greater than 6[12]. But a few reported cases also stated that the patients had a low LRINEC score but NF was found through other modalities like ultrasound[13].

The utility of the scoring system is also attested by another case report from India of an elderly diabetic and immunocompromised patient. On the day of admission his score was found to be 7 which rose to 11 by the 5th day of admission. Although the score prompted early surgical intervention and antibiotic treatment, the patient could not be saved. This was mainly due to the immunocompromised state of the patient and the polymicrobial nature of the infection[14].

Borschitz *et al*. further stressed in their study that the LRINEC score is helpful to discern patients at risk of NF from cellulitis[15–17]. However, they suggested a modification of the score and validated it from the findings of their study. He compared 29 NF patients with 59 patients with severe erysipelas and found that although the overall score was significantly higher in NF patients, their modified scoring system led to a clear improvement. The levels of C-reactive protein remained prominent importance, but the serum sodium and glucose levels were found to be of less significance in the scoring system. They, instead, considered the erythrocyte count[18], and fibrinogen levels in their modified scoring system and strongly suggested combination of the score with clinical findings of strong pain. With this modification, the positive predictive value of the score was increased to 93% for suspicious or strongly suspicious cases of NF. Serum lactate level was suggested by the study to be considered in further research[15,19].

A major limitation to serial LRINEC exists that once the patient is in the hospital, management with intravenous saline, insulin infusions and blood transfusions may interfere with the accuracy of the score. Also in patients with multiple comorbidities, the laboratory findings may be bunted[6].

With immunocompromised patients, it may not be readily possible to stratify cases of NF based on the LRINEC score owing to their inability to catalyze an appropriate inflammatory response. A retrospective study was conducted in Singapore on patients with hematological malignancies developing NF. It was seen that 75% of the patients in this cohort had a LRINEC score of < 6. This could be attributed to leukopenia and thrombocytopenia owing to the hematological condition of these patients but points out that LRINEC score may not be a sensitive score in such patients[20].

Literature has cited a few cases where the use of LRINEC has completely failed to prompt a diagnosis of NF. A case of a 37-year-old man was confirmed to have NF at surgery despite a LRINEC score of zero. Although he had been complaining of symptoms for 3 days, the zero score could be attributable to his young age and multiple previous surgeries which allowed a more rapidly progressing aggressive infection[21,22].

In a five-year retrospective study of 15 patients diagnosed with NF reported at a tertiary care referral unit in the United Kingdom, the LRINEC was calculated and found to classify 12 of the cases as having a high or intermediate likelihood of NF, and the three remaining cases would have been classified as having low likelihood on the basis of the score. The patients in this study showed scores from 1 to 12 with a median of 6.5. Six of the patients were in the intermediate risk category and the remaining 6 were in the high risk category[23].

Other means of diagnosing NF include frozen section biopsy or magnetic resonance imaging of affected part. Another option is finger test which is performed under local anesthesia[6]. However, these cannot be applied to all patients with soft tissue infection or suspicion of NF owing mainly to the cost of the procedure, time delay from admission to procedure and also the invasive nature of procedures like biopsy and finger test. Hence, there is a need for a tool that can be employed by the bed side and enable stratification of patients for further work-up.

3. Conclusions

Clinical acumen based on clinical presentations is of paramount significance in identifying a case of NF, but the calculation of LRINEC score may form a very powerful tool in aiding the diagnosis of NF in a patient with soft tissue infection presented to emergency department. This high score can then prompt further more expensive and invasive diagnostic modalities or referral to surgery. More prospective studies are needed to further validate the usefulness of LRINEC score in emergency setting.

NF remains a significant life-threatening event. The need for heightened index of clinical suspicion cannot be over-emphasized, especially in the acute and front line setting such as the emergency department.

Conflict of interest statement

The authors report no conflict of interest.

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