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Original Research Article

Application of the laboratory risk indicator for necrotizing fasciitis score for patients with hand infection in Mexican population

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ABSTRACT

Background: Necrotizing fasciitis (NF) is a severe form of soft tissue infection, early diagnosis, and surgical intervention are direct factors in mortality, it may arise from many infectious aetiologies, at our hospital in Mexico city, it is not uncommon that hand infection patients progress to NF, that in many cases its recognition and treatment may also be delayed, resulting in fatal outcomes. Wong et al in 2004 introduced a laboratory risk indicator for necrotizing fasciitis (LRINEC score) that utilizes common laboratory values of patients with clinical infection and stratifies them by their risk of developing NF, so the aim of our study was to validate this tool in Mexican population.
Methods: We reviewed all patients with an initial diagnosis of hand infection admitted at the emergency department of our hospital in Mexico City, from April 2020 to March 2022 and examined the LRINEC score at admission, post-debridement, and at the end of the hospitalization to evaluate its usefulness in our population.
Results: The LRINEC score at cut-off ≥6 reported sensitivity for the diagnosis of NF of 35.71% (95% CI 12.76-64.86%), specificity of 100% (95% CI 78.2-100%), positive predictive value of 100% (95% CI 71-100%), and negative predictive value of 62.5% (95% CI 53.01-71.12%).
Conclusions: The LRINEC score is a useful tool to distinguish NF from other soft tissue infections, but it is not helpful for early recognition of NF alone, LRINEC score could predict worse hospital outcomes in patients with NF and identify the high-risk patients.

Keywords: Fasciitis, Hand surgery, Infection, LRINEC, Necrosis

INTRODUCTION

Necrotizing fasciitis (NF) is an uncommon but severe and rapidly progressive soft-tissue infection which can be difficult to diagnose and treat early on. involves necrosis of the superficial fascia and subcutaneous tissues and can lead to severe systemic toxicity. In the later stages, the skin becomes painful, red, and necrotic as it is deprived of its blood supply. The fascial necrosis is usually wider than the skin involvement that is visible clinically. Early recognition and surgical intervention at the earliest, is the sole factor in preventing the morbidity and mortality in patients with NF.[1-8]

The diagnosis is essentially clinical and can rely on a clinical signs and laboratory variables. Still, surgical exploration remains the gold standard for definitive diagnosis. I.V. antibiotic treatment should be started immediately, together with surgical debridement of affected tissues, or even consider the possibility of amputation of the affected limb.[5-7]

The paucity of specific cutaneous signs to distinguish NF from other soft tissue infections such as cellulitis makes the diagnosis extremely difficult.[2] Imaging modalities such as computed tomography, magnetic resonance imaging and frozen section biopsy have been previously used in the discrimination between NF and other soft tissue infections but these methods have been limited by cost and availability, NF is known to be the most severe form of soft tissue infections, even if its etiopathology its better known, and there are better therapeutic options, NF mortality has not been modified since many years.[3,5,9]

Making an early diagnosis and prompt management becomes difficult for non-expert trainees, So a scoring system that is easy to follow and cost-effective with high positive and negative predictive value is required in the clinical setting.[2] The use of the patients biochemical profile to facilitate the early diagnosis of NF was first suggested by Wall et al in 2004, introduced as a screening tool to aid in rapid diagnosis, and has subsequently been refined by Wong et al, introducing the laboratory risk indicator for necrotizing fasciitis (LRINEC) score which is based around the routinely performed laboratory tests: C-reactive protein (CRP), white cell count, hemoglobin, serum sodium, serum creatinine and glucose levels (Table 1).[10] With A cutoff value of ≥6, they found a positive predictive value for the diagnosis of NF of 92% and a negative predictive value of 96%. Its usefulness was assessed by determining its predictive performance against the gold standard: surgical biopsy, encountering that this scoring system may be useful in deciding which patients with high risk of NF should undergo urgent debridement. The LRINEC scoring system has been controversial, with papers questioning its role as a scoring system for prognostic identification but when used as a Diagnostic scoring, has the potential to prevent marked morbidity and mortality by accurately diagnosing of NF.[4-9,11]

Table 1: Score interpretation.[10]

LRINEC score		
Variable (units)	**Value**	**Score**
C-reactive protein (mg/l)	<150	0
	>150	4
Total white cell count (per mm^3)	<15	0
	15-25	1
	>25	2
Hemoglobin (g/dl)	>13.5	0
	11-13.5	1
	<13.5	2
Sodium (mEq/l)	>135	0
	<135	2
Creatinine (mg/dl)	<1.6	0
	>1.6	2
Glucose (mg/dl)	<180	0
	>180	2

Low (LRINEC score <5), moderate (LRINEC score 6-7), or high (LRINEC score >8) risk categories for NF.

Figure 1: Patients admitted at emergency department and plastic surgery department, with diagnosis of hand infection.

The objective of this study was to evaluate NF arising from hand infections and the usefulness of in our medical institution in Mexico (Figure 1) because even when treated appropriately, hand infections can result in scarring, joint contractures, stiffness, and chronic pain. Although the field of hand surgery has evolved over the past century, infections of the hand, their causes, and treatments remain largely unchanged in parallel with NF.[12] Then again the need for a simple system to help us prevent or promptly treat this disease, such as LRINEC score, but the scoring system was developed and validated in the Far East and doubt has been cast on the applicability in western population due to differing causative organisms.[7]

So, we aimed to validate LRINEC score in our setting, with our patients, as an aid in diagnosis and decision making in a common public health matter.

Pathophysiology and clinical findings

NF progression is often fulminant, it can develop after blunt or penetrating trauma, postoperative complications, injection of intravenous drugs, animal bites, and idiopathic causes. A portal of entry as obvious as a tissue injury or a bite (animal or human) is required for the development of NF. Process begins in the superficial fascia, where bacteria proliferate and produce toxins and enzymes that allow for horizontal spread of the disease along the fascia. There is necrosis of the superficial fascia and microvascular thrombosis, which originates inflammatory mediators producing tissue ischemia, resulting in a vicious cycle of tissular injury. When the fascia is destroyed and there is ischemia of subcutaneous tissue, then infection progress vertically, then affecting deep planes, but also superficial dermis, that's when common local signs appear, Clinically NF usually presents as an erythema of the skin surrounding the affected area, with unregularly marginated edges, warm to the touch, very painful especially in the early stages; within 3 to 5 days from the onset blisters start to emerge, evolving then in skin necrosis. Intense fever is a very

common finding. Gas formation in subcutaneous tissues is frequent mostly in polymicrobial forms, especially in diabetic patients.[3,6,13]

Risk factors

Predisposing factors of NF include advanced age, diabetes mellitus, malnutrition or obesity, drug abuse, corticosteroid use, immunosuppression, AIDS, trauma, and chronic venous or lymph insufficiency. The presence of a foreign body in combination with dead tissue formation, hematomas, angiopathy, are local predisposing factors from all of the above.[1-8] Diabetes mellitus is the most common comorbidity associated with NF, up to 44.5% of patients with this condition are diabetic. Patients with diabetes generally present with polymicrobial disease, and have poorer outcomes, with a higher rate of amputation compared with non-diabetics.[1]

As for hand infections, many result from direct trauma, and other patient comorbidities predispose individuals to a more severe infection such as diabetes mellitus. These patients are at increased risk of idiopathic and postoperative infection and are more likely to require operative intervention for infection. They have a higher rate of severe, necrotizing infection and more frequently require aggressive surgical debridement.[12]

Epidemiology

NF is an uncommon but life-threatening disease. The incidence ranges between 0.4 and 1.3/100,000 according to the country.[6,7] It is known by clinicians and the public as "flesh eating bacteria" and is associated with high morbidity and a mortality of up to 76%. despite advances in modern medical care.[13] Approximately 70 to 90% of such infections are polymicrobial.[5]

Data on the overall epidemiology of hand infections is scarce. domestic animal bites, are more frequently reported. Two-thirds of hand infections occur in men. Individuals of all ages are affected; the mean patient age is 40 years. More than one-third of hand infections are the result of trauma. Postoperative surgical site infections are rare in hand surgery: 1.7 per 1000 procedures. Most infections are effectively treated with oral antibiotics. Morbidity and sequelae infections of the hand can lead to loss of function and disability, even when treated promptly. Infections of the flexor or extensor tendon spaces can lead to tendon necrosis, adhesions, and chronic stiffness or even progress to severe deep space infections and NF resulting in extensive soft tissue damage that sometimes requires flap coverage or amputation.[12]

METHODS

This was a validation cohort study. We reviewed all patients with initial diagnosis of hand infection admitted at our emergency department at Hospital General Dr. Ruben Leñero, at Mexico City, from April 2020 to March 2022. We obtained a sample size of 29 patients, given that hand infection represents 0.08% of the total of diagnosis made at emergency department yearly. Everyone that were clinically diagnosed first by emergency department attendees, then received a secondary evaluation made by junior, senior and attendees form our plastic surgery department, along obtaining initial laboratory studies for the LRINEC score, and proceeded with surgical debridement when there where hard signs of hand infection such as purulent discharge, important edema and erythema, pain, and systemic signs of infection with a positive clinical history.

Inclusion criteria

Inclusion criteria for our study were: age between 18 and 80 years, any gender, and presence of clinical signs of infection. Non-inclusion criteria were: need for urgent amputation or rejection of treatment by patient.

Exclusion criteria

Exclusion criteria were: any patient with another source of infection apart than soft tissue, associated comorbidities in the need of priority management and incomplete laboratory records available.

We analyzed patients data and examined whether the LRINEC score at admission, post debridement and at the end of the hospitalization, for each of our cases.

Statistical analysis was performed using the SPSS v25 program and a value of $p \leq 0.05$ was interpreted as statistically significant. The sample was tested with a Kolmogorov-Smirnov test indicating that the variables follow a normal distribution. A Pearson correlation coefficient was computed to assess the linear relationship between LRINEC score and the clinical diagnosis of necrotizing fasciitis from patients at their admission. There was a positive correlation between the two variables, $r(27) = 0.472$, $p < 0.05$.

RESULTS

During the time of our study, we gathered 29 patients in total, gender ratio was 4.8 males per 1 female, average age was 41 years.

Mains comorbidities reported in our population where: diabetes mellitus in 34.5% of the patients, followed by smoking in 24%, and at last place was hypertension with 3.4%.

Main etiology reported for our hand infection/NF cases was trauma (most of it was closed trauma) in 79.3%, insect bite 6.8%, then animal bite, foreign body, surgical site infection, human bite, all presented in 3.4% each. Cultures obtained at the time of surgical debridement

reported: *Staphylococcus aureus* with 10.3%, *Escherichia coli* with 20.6%, and the vast majority (51.7%) didn't report any bacteria (Table 2).

Table 2: Comorbidity and culture results.

Demographic data	Total: 19
Age	41±15
Gender	24 males: 5 females (4.8:1)
Comorbidities	Total: 19
Diabetes mellitus	34.5%
Smoking	24%
Hypertension	3.4%
Infection site culture	Total: 29
Staphylococcus aureus	10.3%
Escherichia coli	20.6
Enterobacter cloacae	3.4%
Aeromonas hydrophila	3.4%
Enterococcus faecalis	3.4%
Candida albicans	3.4%
Raoultella ornithinolytica	3.4%
Hafnia alvei	3.4%
Pseudomona aeruginosa	3.4%
Staphylococcus xylosus	3.4%

Average leucocyte count on admission was 13.54/ mm^3, then 9.08/ mm^3 post debridement and final was 8.83/ mm^3. Average hemoglobin on admission was 13.28 gm/dl, average creatinine on admission was 0.83 mg/dl. Average glucose on admission was 181 mg/dl, dropping to 136.5 mg/dl on average on final laboratory. Average sodium levels on admission were 133.75 mEq/l, and average PCR was 13.69 mg/l dropping to 6.4 after 1st debridement (Table 3).

Table 3: Average laboratory values at the time of admission.

Total patients :29	LRINEC score on admission
WBC average	13.54 (mm^3)
WBC >15000-25000	20.6%
WBC >25000	13.7%
Hgb average	13.28 mg/dl
Hgb >11-13.5	41.37%
Hgb <11	13.7%
Creatinine average	0.83 mEq/l
Cr>1.6	0%
Glucosa average	181 mg/dl
Glucosa >180	13.7%
Sodium average	133.75
Sodium <135	44.8%
CRP average	13.69 mg/l
CRP15	24.13%

Most of our patients had a positive outcome, defined as improvement of LRINEC score during hospital stay and improvement or disappearance of clinical infection. Reporting 24% tertiary closures, 17.25% skin grafts, 17.25% direct closure, 6.8% pedicled flap, 6.8% local flaps, 6.8% free flap.

Negative outcome was defined as worsening of LRINEC score even with treatment, worsening of NF and clinical infection, need for amputation, and death. Reporting 17.25% amputation (3 mayor/ hand amputated, and 2 minor/ fingers amputated) and 3.4% (1) fatality (Figure 2).

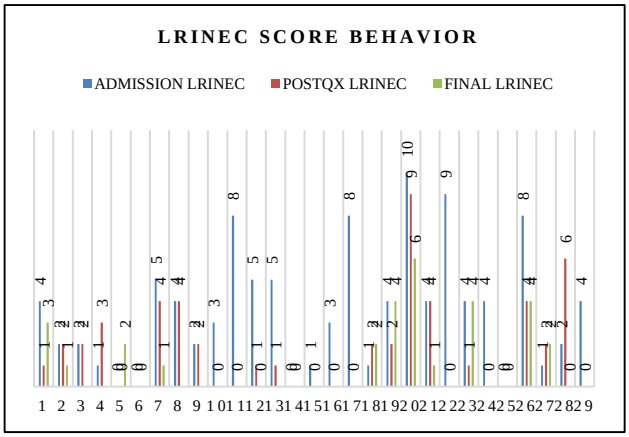

Figure 2: LRINEC score behavior of every patient in the studio, blue bar stands for the score at admission, orange bar is for score post-surgical debridement, and gray bar is for the final score obtained during hospital stay.

When compared the LRINEC score as ≥6 (ROC curve cut-point value). Clinical diagnosis of necrotizing fasciitis it results in a sensitivity of 35.71% [95% confidence interval (CI) 12.76-64.86%], specificity of 100% (95% CI 78.2-100%), positive predictive value of 100% (95% CI 71-100%), and negative predictive value of 62.5% (95% CI 53.01-71.12%).

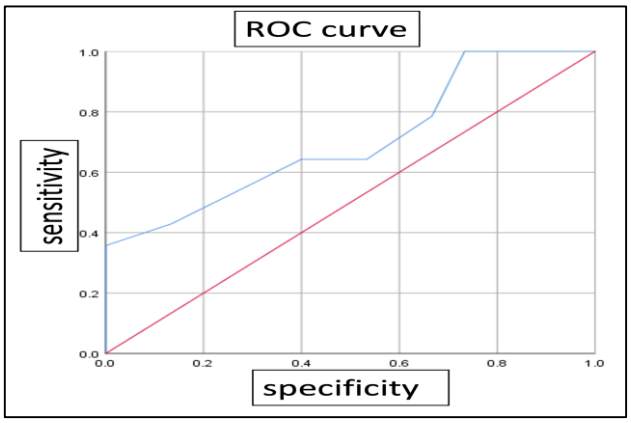

Figure 3: ROC curve for LRINEC score cut-off at 6 points.

The rate of clinical diagnosis of necrotizing fasciitis patients by emergency physicians at admission was

48.28%. This showed that the sensitivity of LRINEC score ≥6 was 13% lower than clinical diagnosis ($p<0.05$). (Figure 3).

DISCUSSION

Despite increased awareness of this condition, it is still associated with a high rate of mortality (between 12.1% and 41.6% of cases) and amputation (between 4.1% and 27.8%). Diabetes mellitus is the most common predisposing factor associated with NF. swelling, tenderness and erythema were the most common presenting signs and symptoms, it's been also reported that fewer than half of the patients had systemic signs at presentation, The heterogeneity of presenting signs renders it difficult to make an early diagnosis in these patients. During the time of our study, we had a 17.25% amputation rate, of which 3 were mayor amputations (whole hand amputated), and 2 were minor amputations, (fingers amputated) and only presented 3.4% (1) fatality rate.

In world literature, *Staphylococcus aureus* is the most common organism in NF, while in our setting, *Escherichia coli* is the most common organism involved. Patients with NF require urgent surgical debridement and intravenous antibiotics. Diabetic patients tend to have many co-morbidities and polymicrobial infections, and they may present atypically with less tenderness and hypotension. This may result in higher rates of misdiagnosis and a longer time to surgery leading to longer hospital stays and higher rates of amputation.[1]

NF is a surgical emergency. Early recognition and prompt aggressive surgical debridement of all necrotic tissue are critical for survival. Distinguishing an NF that necessitates surgical debridement from non-necrotizing cellulitis that responds solely to antibiotic therapy however can be difficult. The paucity of cutaneous findings early in the course of disease makes it difficult to diagnose the condition early. So, a scoring system that is easy to follow and cost-effective with high positive and negative predictive value is required. One such scoring system is the LRINEC scoring system devised by Wong, et al in 2004 which claims to have a positive predictive value of 92.0% and a negative predictive value of 96.0%.[2,10]

Biochemical tests can demonstrate some classical changes in severe sepsis. These biochemical and hematological changes are not at all specific for NF and may be seen in all cases of severe sepsis. While the LRINEC scoring system is prone to have a high false positive rate, it is likely to pick up most patients with NF.[4] Few studies have been done correlating LRINEC score with the clinical features of NF and using it in the early surgical management of this entity, Patients with LRINEC score of <6 responded well to expectant management and had shorter hospital stay. Score between 6 to 10 needed aggressive and serial debridement and had longer hospital stay. Score more than 10 was associated with grave outcome, such patients needed limb sacrificing surgeries and in spite of best efforts, mortality remains an issue.[5]

In the study done by Wong et al, using the LRINEC score, he stratified the patients into three groups, low (LRINEC score <5), moderate (LRINEC score 6-7), or high (LRINEC score >8) risk categories for NF. These risk groups corresponded to a probability developing NF of <50%, 50-75%, and >75%, respectively. A LRINEC score of >6 should raise the suspicion of NF, and a score >8 of is strongly predictive of this disease. The LRINEC score can significantly decrease the time to diagnosis by stratifying patients into risk categories for NF warranting immediate further evaluation.[10,13] Hence we needed to validate this scoring system in our patients and if found to have similar comparable predictive values, it would prove to be useful in our medical system.

The validation of LRINEC in our group of patients, at a cut-off of 6 points, had a similar positive predictive value (100%) but a lesser negative predictive value (62.5%), LRINEC score at our hospital and with our resources showed a reduced sensibility of only 35% (12.76% to 64.86% at 95% CI), but a specificity of up to a 100%. With a negative likelihood ratio of 0.64 (estimated change in probability of 15% less chances to have the disease), that basically mean LRINEC score can be used not for diagnosing NF, but a method to discard this severe entity, and proceed les invasively in patients that don't need it.

Limitations of this study were mainly regarding availability of complete laboratory records to calculate LRINEC score in some patients, this mainly due to lack of resources at the laboratory itself at some points of time during the data recollection time, thus having to exclude several patients diagnosed with hand infection, from this study.

CONCLUSION

Even though we have a low-test sensitivity reported, making LRINEC score and inappropriate screening tool, so it can't be applied as a diagnostic tool for NF, but more of a guide for junior residents at the emergency department, who lack of clinical experience to accurately differentiate any other less severe skin and soft tissue infection from NF, using LRINEC score as a guide for decision making when in doubt, not as a diagnostic tool.

LRINEC scoring could predict worse hospital outcomes in patients with NF and simply identify the high-risk patients. However, further prospective studies are needed to support this finding.

The LRINEC score is a useful tool to distinguish necrotizing fasciitis from other severe soft tissue

infections, but it is not useful for early recognition of necrotizing fasciitis.

The development of diagnostic score that includes clinical as well as laboratory variables would be better for recognition of doubtful cases of a severe infection, in the early stages, when there are no clear clinical signs, but biochemical disarrangements are present, to start proper and effective treatment.

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