

Original Research Article

Necrotizing fasciitis: diagnostic and prognostic value of laboratory risk indicator for necrotizing fasciitis score

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ABSTRACT

Background: Necrotizing fasciitis (NF) is a potentially life threatening disease. Delayed recognition and surgical intervention is directly linked to increased mortality. Laboratory risk indicator for necrotizing fasciitis (LRINEC) score, a laboratory oriented tool has potential to prevent morbidity and mortality but there exhibits a controversy regarding its utility which needs re-evaluation to prove it's utility.

Methods: A tertiary care hospital based observational study aims to evaluate diagnostic and prognostic value of LRINEC score. Patient above 18 years clinically diagnosed as SSTI and confirmed as NF histopathologically without co-morbidities were enrolled as subjects. Clinical evaluation and laboratory oriented LRINEC score were the study factors. Outcome factors were morbidity and mortality and histopathological confirmation of NF. Patients were analyzed as cellulitis and NF with identification of factors associated with NF; Univariate analysis with Kaplan-Meier survival analysis and ROC plotting was done.

Results: Total 166 patients were enrolled with mean age of 47.14 ± 15.76 years and 2:1 is the male : female ratio and. A total of 117 patients were diagnosed as Cellulitis and 49 patients were NF. Clinically Discharge, fever and cuticular necrosis was statistically associated with NF ($p < 0.01$). Mortality in NF was 22.4% and no mortality in Cellulitis. Mean LRINEC score in cellulitis and NF was 1.95 ± 0.972 and 7.57 ± 1.51 ($p < 0.01$). Survival analysis graph and ROC showed LRINEC score of 6 as diagnostic and score ≥ 9 as poor prognostic indicator.

Conclusions: LRINEC score is a useful diagnostic and prognostic tool in patients of NF.

Keywords: Skin and soft tissue infection, Cellulitis, Necrotizing fasciitis, LRINEC score, Prognosis

INTRODUCTION

Skin and soft tissue infections (SSTI) were first described in the Hippocratic era and they have variable etiology, clinical presentations and severity. Cellulitis is an uncomplicated form of SSTI and NF is a complicated form. NF is also called as "flesh eating disease". It is an infection of deep fascia and subcutaneous tissue involving any part of the body. It may be due to the portal of entry during a trivial trauma or a surgical wound. But, the exact etiology cannot be found in up to 20-50% cases.

The worldwide incidence of Necrotizing Fasciitis (NF) is 1 per 100,000 per year, documented incidence in the UK is low with 0.4 cases per 100,000, but in the Indian Scenario it is not clear owing to paucity of literature. A patient's co-morbidities can easily transform a mild infection into rapidly advancing threat to life. Hence, it is very important to diagnose the early change.¹

Wong et al described the "Laboratory Risk Indicator for Necrotizing Fasciitis" (LRINEC) score, based on the performed routine laboratory tests.² The treatment of choice for NF is early diagnosis and aggressive surgical

debridement with supportive broad-spectrum antibiotics. The LRINEC score can be a useful tool in the diagnosis of NF from other SSTIs.

This study evaluated all SSTIs and tried to find out the clinical features and laboratory parameters associated with NF specially evaluating the LRINEC score as a diagnostic and prognostic tool.

METHODS

This present study was a hospital based observational study conducted at NKP Salve Institute of Medical Sciences and Lata Mangeshkar Hospital, Nagpur from October 2016 to October 2018, with an aim to study the demographic, clinical and LRINEC score differences between Cellulitis and Necrotizing Fasciitis and to re-evaluate the cut-off score of 6 in LRINEC scoring system valid for local population and to find out cut-off score as predictor of poor prognosis.

All the patients attending Surgery OPD or the Emergency Department and getting admitted in Surgery wards with clinical features of SSTI, above 18 years of age, of either gender presenting with pain and swelling in any part of body associated with fever and signs of toxemia, local signs of acute inflammation with or without fluctuation, with or without cuticular necrosis, with or without foul smelling discharge were enrolled in this study.

Patients with co-morbid conditions like hypertension, diabetes, immune-suppressed conditions, on steroid therapy and cases of lymph edema, filariasis, abscess, carbuncle, furuncle, deep vein thrombosis, patients who underwent surgical debridement for present episode of SSTI were excluded from this study.

The study factors in this present study were the clinical features of SSTI, LRINEC score (HB%, TLC, Sr. Na, Sr. Creatinine, C-reactive protein and Blood glucose level) (Table 1).

Table 1: Laboratory risk indicator for necrotizing fasciitis (LRINEC) scoring system.

Variable	Value	Score
C-reactive protein	150 mg/l	4
	>13.5	0
Hemoglobin (gm/dl)	11-13.5	1
	<11	2
	>15	0
Total leucocyte count (thousand/cumm)	15-25	1
	>25	2
	<135	2
Serum sodium (mmol/L)	<135	2
Serum creatinine (mmol/L)	<1.4	0
	≥1.4	2
Blood glucose level	<100	0
	≥100	1

A score of is considered positive for necrotizing fasciitis.

The outcome factors were the diagnosis of cellulitis and NF confirmed on histopathology and overall prognosis which included survival or death.

The data calculated was fed into an Excel sheet. Basic demographic factors will be described as descriptive statistics for further analysis of data based on histopathological and clinical confirmation. This data was divided into cellulitis and NF and univariate analysis was carried out followed by multivariate analysis of clinical and laboratory factors associated with NF. Mean LRINEC scores of cellulitis and NF for diagnostic purpose was compared on carrying out Survival analysis for both diagnostic and prognostic score. Kaplan-Meier analysis with ROC curve and cut-off scores for diagnosis and prognosis was calculated.

The ethical clearance obtained from institutional ethical committee and informed consent was obtained from patient before enrolling for study.

RESULTS

A total of 166 patients of SSTI were enrolled in this study. Of them 117 were finally diagnosed as Cellulitis and rest 49 as NF. On comparing these two groups, mean age of cellulitis with 46.33 ± 1.54 years as compared to 49.06 ± 13.07 years. The two groups were statistically not significant ($p=0.310$) (NS). The male-female distribution for cellulitis was 79 (67.5%) males and 38 (32.5%) females as compared to 32 (65.3%) males and 17 (34.7%) females in NF. There was no statistically significant gender difference observed ($p=0.782$) (NS). Overweight and obesity i.e. BMI>25 was observed in 56 (47.9%) patients of cellulitis and 27 (55.1%) patients of NF. This was statistically not significant.

The clinical features of swelling and pain in region/location and regional lymphadenopathy were statistically not significant. Only clinical features which were observed in NF and not observed in Cellulitis were discharge from wound ($p=0.000$), fever ($p=0.004$), presence of skin blisters ($p=0.000$) and cuticular necrosis ($p=0.000$) (Table 2).

In order to assess the second outcome i.e. survival or death, there was no death observed in cases of Cellulitis. But mortality rate was 22.4% in NF. This outcome was statistically different in NF when compared to Cellulitis ($p=0.000$) (Table 3).

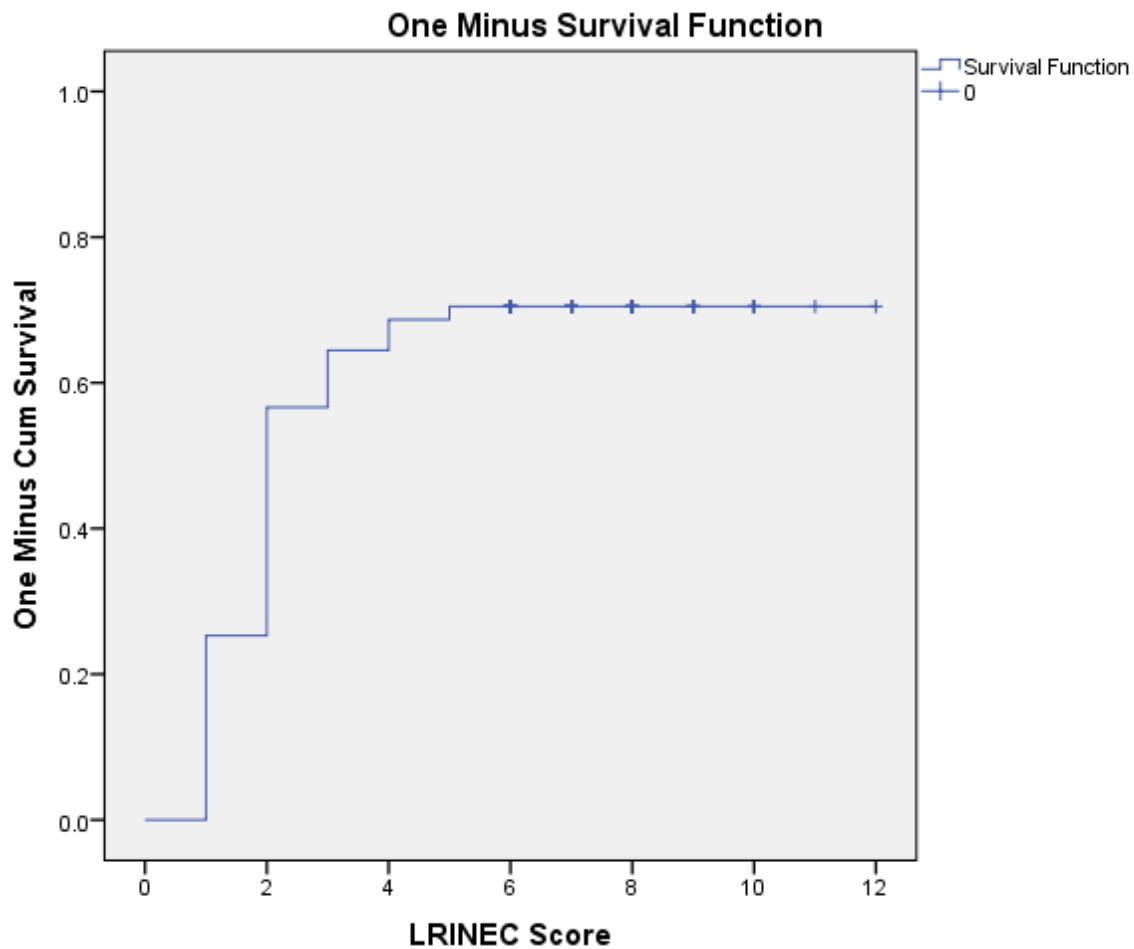
Analyzing results of LRINEC scoring system, Survival analysis using Kaplan –Meier estimator, it was found that mean score in Cellulitis patients was 1.95 ± 0.972 as against 7.57 ± 1.514 in NF. This was statistically significant. On plotting ROC graph, the cut-off point for differentiating between Cellulitis and NF was score of 6 i.e. score probability of having NF is almost 100% in the scores over 6 and more (Figure 1).

Table 2: Distribution of clinical presentations of SSTI.

Clinical presentation		Clinical diagnosis		Total	P value
		Cellulitis	NF		
		N (%)	N (%)	N (%)	
Discharge	No	57 (48.7)	0 (0.0)	57 (34.3)	0.000 (HS)
	Yes	60 (51.3)	49 (100.0)	109 (65.7)	
Fever	No	18 (15.4)	0 (0.0)	18 (10.8)	0.004 (HS)
	Yes	99 (84.6)	49 (100)	148 (89.2)	
Skin blisters	No	116 (99.1)	9 (18.4)	125 (75.3)	0.000 (HS)
	Yes	1 (0.9)	40 (81.6)	41 (24.7)	
Cuticular necrosis	No	116 (99.1)	1 (2.0)	117 (70.5)	0.000 (HS)
	Yes	1 (0.9)	48 (98.0)	49 (29.5)	

Table 3: The distribution of death among the cases of spreading soft tissue infections.

Outcome	Clinical diagnosis		Total
	Cellulitis	NF	
	N (%)	N (%)	N (%)
Death	0 (0.0)	11 (22.4)	11 (6.6)
Survival	117 (100.0)	38 (77.6)	155 (93.4)
Total	117 (100.0)	49 (100.0)	166 (100.0)


Figure 1: ROC of survival analysis of LRINEC score showing diagnostic cut off.

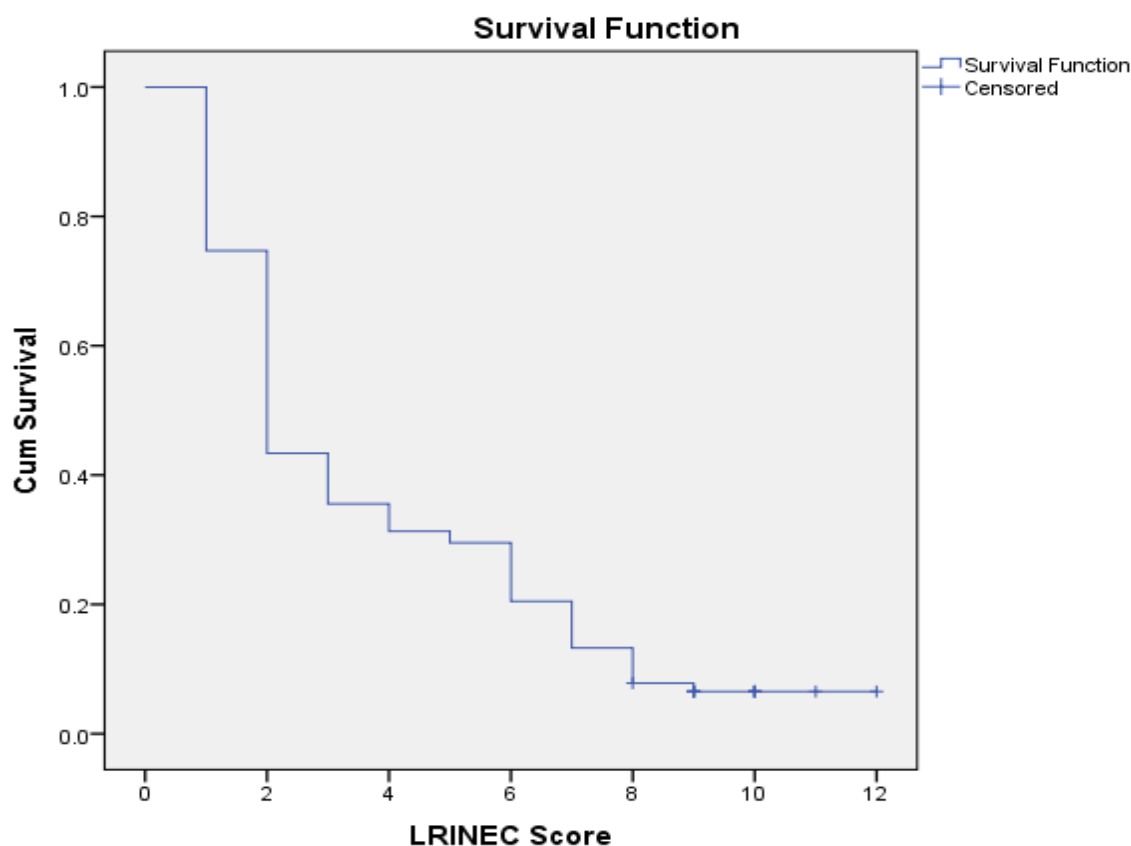


Figure 2: ROC of survival analysis of LRINEC score showing prognostic cut off.

Use of LRINEC score for predicting the outcome was again carried out by plotting ROC curve where the cut-off score was found to be 9. Meaning chances of survival are nil if score is >9 (Figure 2).

DISCUSSION

Necrotizing Fasciitis (NF) is a life-threatening soft tissue infection, which is characterized by progressive necrosis of the fascia, subcutaneous tissue and skin. In 1950, Wilson contemporarily described and defined this disease, in which he observed that fascial necrosis is much more common than skin necrosis.³ Etiologically, urogenital infections, anorectal infection and trauma has a significant role.⁴⁻⁶ But, minor injuries like tissue abrasions and lacerations, insect bites and intramuscular injection may also cause NF. It should always be considered that there may not always be a detectable cause for NF.⁷⁻¹⁰ Even by providing immediate antibiotic therapy and surgery, the mortality rate is 20 – 30%.^{5,6,11}

Diagnosis of NF is usually done through clinical examination, but may be difficult as it is many a times confused with the other skin and soft tissue infections. Hence, a scoring system called LRINEC was developed in 2004 by Wong et al and they showed that it is useful for distinguishing NF from other SSTIs.² In further studies, it was reported that LRINEC scoring can be used

in early diagnosis of NF.¹²⁻¹⁶ For LRINEC score calculation, HB%, TLC, serum sodium, serum creatinine, C-reactive protein and blood glucose values of the patient are measured on admission. Then a certain score value is obtained. Score of ≤ 6 indicated the most likely diagnosis of NF.^{2, 12-16} The more is the LRINEC score (≤ 8), the survival of the patient with NF decreases.

In this study, the mean age of the patients of Spreading soft tissue infections was 47.14 years and this is quite consistent with the literature.¹⁷⁻²⁶ It is quite evident from literature and present study that SSTI's mainly affects in the age group of 45 to 60 years. Male patients were more commonly involved accounting for 2/3rd of the patients while rest 1/3rd were females. This ratio in literature ranges from 8:1 to 1.3:1. But comparing with Indian studies our Male: Female ratio is quite consistent with available literature.^{17,19,21,24,26-30}

Patients with abundance of subcutaneous fats and associated co-morbid conditions like overweight and obesity are more prone to SSTI, hence BMI was calculated in the present study. Almost 1/2 of our patients were either overweight or obese. These results are consistent with the literature.^{27,31,32} Patients more than BMI of 25 are at more risk for NF.

Pain and swelling were the main presenting symptom of NF in the present study and is quite consistent with the literature.^{17,19,27,30} Fever was the next commonest symptom observed in 90% of the patients which has variable incidence (32.8% to 76%) in the studies available from the literature.^{17,19,21,24,30} Blister formation and cuticular necrosis were characteristic of NF which was observed in 29.5% of the patients.^{21,24,27,30}

Early diagnosis and on time appropriate surgical debridement are crucial for the outcome of NF. LRINEC scoring is a useful diagnostic tool to identify and diagnose Necrotizing Fasciitis and can also be a instrument for potential prognostic value. In present study, a cut-off score of 6 was found to be diagnostic of NF. This is quite consistent with the literature which showed the cut-off score of 6 in LRINEC scoring system.^{13,20,24,33,34}

Of the 49 cases of NF diagnosed clinically, by LRINEC score and tissue histopathology, the mortality rate was 22.44%. To prognosticate the survival, LRINEC score was used in the present study. Considering death as a poor outcome utilizing survival analysis and plotting a ROC curve, a cut-off of 9 was an indicator of poor outcome i.e. death. There is no study in literature which has used LRINEC score for predicting death in NF patients. Hence comparison cannot be done with the literature and also Wong et al never developed this scoring system for predicting prognosis.

The drawback of this study is no formal sample size calculation was carried out. The study excluded co-morbid conditions hence the external validity of the study is restricted to patients of NF without co-morbid conditions and there is a need to compare another study with co-morbid patients included for generalization of result.

CONCLUSION

NF predominantly occurs in males of 4th to 6th decade with BMI >25 presenting with swelling, pain, fever, skin blisters cuticular necrosis and discharge which are significantly associated with NF clinically. Laboratory based LRINEC score of 6 is validated to be a true cut-off for Indian population. Using LRINEC score for prognosticizing showed a score of 9 predicting death in patients of NF. However, this fact later needs further evaluation.

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