

Diagnostic Differentiation of Necrotising Fasciitis from Severe Cellulitis and Erysipelas: A Prospective Study of Clinical, Laboratory and Intraoperative Predictors

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ABSTRACT

Background: Necrotising fasciitis (NF) is a rapidly progressive and potentially fatal soft-tissue infection in which early diagnosis remains challenging because its initial clinical appearance may resemble severe cellulitis or erysipelas. Delay in surgical intervention is associated with increased morbidity and mortality. Clinical examination, inflammatory biomarkers and scoring systems such as the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) may assist diagnosis, although none should replace clinical judgement and urgent surgical assessment. **Methods:** This prospective observational study included 50 consecutive adult patients presenting with severe soft-tissue infection and clinical suspicion of either NF, severe cellulitis or erysipelas. Patients were evaluated clinically and underwent complete blood count, C-reactive protein (CRP), serum sodium, creatinine, glucose and other routine biochemical investigations. LRINEC scores were calculated at admission. Patients with suspected NF underwent urgent surgical exploration, with intraoperative findings considered the reference standard. Patients were categorized into a necrotising infection group and a non-necrotising group. Clinical, laboratory and operative variables were compared using chi-square/Fisher's exact test and independent-samples t-test. A p value <0.05 was considered statistically significant. **Results:** Of 50 patients, 21 (42.0%) had surgically confirmed NF and 29 (58.0%) had non-necrotising infection, including severe cellulitis and erysipelas. Severe pain disproportionate to the visible skin findings, edema extending beyond erythema, bullae/skin discoloration, hypotension and altered sensorium were significantly more frequent in NF. Mean CRP, total leukocyte count, serum creatinine and LRINEC score were significantly higher, while serum sodium was significantly lower, in the NF group. A LRINEC score ≥ 6 was present in 16 (76.2%) patients with NF compared with 5 (17.2%) non-NF patients ($p < 0.001$). Intraoperative fascial edema, grayish necrotic fascia, thin brownish fluid and easy blunt dissection were strongly associated with NF. Early surgical exploration within 12 hours was associated with lower postoperative complication rates. **Conclusion:** NF should be suspected in patients with severe pain out of proportion, rapidly progressive edema, systemic toxicity, bullous or necrotic skin changes and characteristic laboratory abnormalities. LRINEC may support clinical assessment but should not be used alone to exclude NF. In patients with significant clinical suspicion, prompt surgical exploration remains the most reliable method of confirming the diagnosis. The practical approach should therefore combine high clinical suspicion, appropriate laboratory assessment and immediate surgical evaluation. When NF is clinically suspected, definitive surgical exploration should not be delayed for laboratory scoring or imaging.

Keywords: *necrotising fasciitis; cellulitis; erysipelas; LRINEC; C-reactive protein; surgical exploration; soft-tissue infection.*

INTRODUCTION

Rapidly increasing inflammation and necrosis affecting the subcutaneous tissues and fascial planes are the hallmarks of necrotizing fasciitis, a severe soft tissue infection [1]. One of the most dangerous types of skin and soft-tissue infections, it can quickly lead to sepsis, multiple organ failure, limb loss, and even death. In emergency and surgical treatment, early clinical symptoms might be confusingly similar to cellulitis or erysipelas, making diagnosis extremely difficult.

Due to the significant differences in therapy, the distinction between necrotizing and non-necrotizing soft-tissue infections is clinically significant. While necrotizing infections necessitate prompt surgical source management in addition to broad-spectrum antibiotic therapy and resuscitation, severe cellulitis and erysipelas are often treated with antimicrobial therapy, supportive care, and drainage as necessary [2]. According to current standards, diagnostic tests should not postpone operative therapy and that a suspected necrotizing infection necessitates immediate surgical consultation [3].

Erythema, warmth, swelling, and tenderness all of which are indicative of cellulitis and erysipelas may be present in the early clinical presentation of NF. However, suspicion of deeper tissue involvement is raised by intense pain that is out of proportion to the apparent cutaneous symptoms, discomfort that extends beyond the erythematous area, quickly increasing swelling, bullae, ecchymosis, skin anesthesia, crepitus, and systemic toxicity [4].

Further diagnostic information can be obtained during laboratory examinations. C-reactive protein, total leukocyte count, hemoglobin, sodium, creatinine, and glucose were used to create the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score [5]. A score of ≥ 6 was linked to significant diagnostic value in the initial trial. A low LRINEC score, however, may not be a reliable way to rule out necrotizing soft-tissue infection, according to systematic review data and additional investigations that have revealed varying sensitivity.

When the diagnosis is still unclear, imaging may be helpful. While MRI can detect deep fascial abnormalities, CT can show fascial thickness, fluid collections, gas, and inflammatory alterations along fascial planes. However, when clinical suspicion is high, imaging should not postpone a definitive surgical evaluation [6-7].

Because necrotic tissue, thin fluid, bloated, grayish fascia, and easy separation of tissue planes are direct indicators of necrotizing infection, intraoperative inspection is still crucial [8].

MATERIALS AND METHODS

Study Design

This was a prospective observational study conducted in the Department of General Surgery at a tertiary-care hospital over a defined study period. Fifty adult patients presenting with severe soft-tissue infection and clinical suspicion of either necrotising or non-necrotising infection were enrolled.

Study population

Patients aged ≥ 18 years presenting with erythema, swelling, pain, fever, skin discoloration or other manifestations of severe soft-tissue infection were considered for inclusion.

Inclusion criteria

Patients were included if they had:

- Acute severe soft-tissue infection involving skin or subcutaneous tissues.
- Clinical suspicion of NF, severe cellulitis or erysipelas.
- Age ≥ 18 years.
- Availability of admission laboratory investigations.
- Written informed consent for participation.

Exclusion criteria

- Patients with postoperative wound infection, chronic ulcers without acute infection, isolated abscess without surrounding severe cellulitis, previously established malignancy involving the affected region, or incomplete clinical/laboratory records were excluded.

Clinical assessment

At admission, detailed history and examination were performed. Variables recorded included duration of symptoms, site of infection, fever, tachycardia, hypotension, severe pain, pain disproportionate to visible findings, edema extending beyond erythema, bullae, ecchymosis, skin necrosis, crepitus and sensory changes.

Laboratory investigations

Baseline investigations included complete blood count, hemoglobin, total leukocyte count, platelet count, serum CRP, sodium, creatinine, glucose and other routine biochemical parameters.

Surgical Assessment

Patients with substantial clinical suspicion of NF were taken for urgent surgical exploration. Intraoperative findings were documented, including fascial edema, grayish discoloration of fascia, necrotic fascia, thin brownish fluid, lack of normal tissue resistance and easy

blunt separation of tissue planes. Deep tissue samples were obtained for microbiological examination where appropriate.

Statistical Analysis

Data were analyzed using standard statistical software. Continuous variables were expressed as mean $\pm$ standard

deviation and categorical variables as frequency and percentage. Continuous variables were compared using the independent-samples t-test, while categorical variables were compared using chi-square test or Fisher's exact test as appropriate. A p value <0.05 was considered statistically significant.

RESULTS

Fifty patients were included in the analysis. Based on clinical evaluation and definitive operative assessment, 21 (42.0%) patients had necrotising fasciitis and 29 (58.0%) had non-necrotising infection. Among the non-NF group, 22 patients had severe cellulitis and 7 had erysipelas.

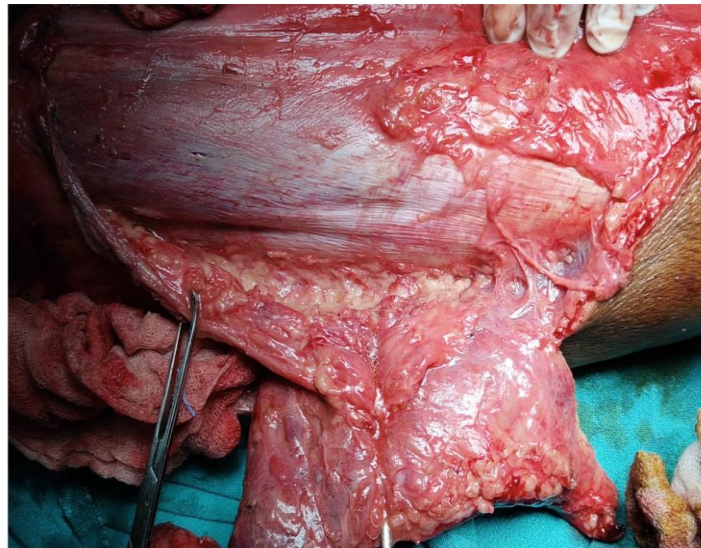
The mean age of patients with NF was 56.8 ± 13.7 years compared with 51.2 ± 15.1 years among patients with non-necrotising infection. Diabetes mellitus was more frequent in the NF group (61.9% vs 37.9%), although the difference was not statistically significant. Lower-limb involvement was the most frequent anatomical presentation in both groups.

Fig 1:



Fig 2:



Fig 3:**Table 1: Demographic and clinical characteristics of study participants**

Variable	NF (n=21)	Severe cellulitis/erysipelas (n=29)	p value
Age, years, mean $\pm$ SD	56.8 $\pm$ 13.7	51.2 $\pm$ 15.1	0.19
Male sex, n (%)	14 (66.7)	18 (62.1)	0.74
Diabetes mellitus, n (%)	13 (61.9)	11 (37.9)	0.09
Hypertension, n (%)	9 (42.9)	8 (27.6)	0.27
Lower-limb involvement, n (%)	15 (71.4)	19 (65.5)	0.65
Severe pain out of proportion, n (%)	16 (76.2)	7 (24.1)	<0.001
Edema beyond erythema, n (%)	15 (71.4)	8 (27.6)	0.002
Bullae/ecchymosis, n (%)	11 (52.4)	4 (13.8)	0.003
Crepitus, n (%)	6 (28.6)	1 (3.4)	0.011
Hypotension, n (%)	7 (33.3)	2 (6.9)	0.015
Altered sensorium, n (%)	5 (23.8)	1 (3.4)	0.041

Severe pain disproportionate to the visible skin findings was the strongest clinical discriminator, occurring in 76.2% of NF patients compared with 24.1% of non-NF patients ($p < 0.001$). Edema extending beyond the area of erythema was also significantly more frequent in NF (71.4% vs 27.6%; $p = 0.002$). Bullae/ecchymosis, crepitus, hypotension and altered sensorium were also significantly associated with NF.

These findings are consistent with established clinical descriptions of NF, in which disproportionate pain, rapidly extending edema, systemic toxicity, bullae and skin necrosis are important warning signs.

Table 2: Comparison of laboratory parameters and LRINEC score

Laboratory parameter	NF (n=21)	Non-NF (n=29)	p value
WBC count (μ L), mean $\pm$ SD	18,240 $\pm$ 5,160	12,480 $\pm$ 4,210	<0.001
CRP (mg/L), mean $\pm$ SD	238.5 $\pm$ 92.4	108.6 $\pm$ 67.3	<0.001
Hemoglobin (g/dL), mean $\pm$ SD	11.4 $\pm$ 1.8	12.6 $\pm$ 1.7	0.019
Sodium (mmol/L), mean $\pm$ SD	132.1 $\pm$ 4.9	136.2 $\pm$ 3.8	0.002
Creatinine (mg/dL), mean $\pm$ SD	1.74 $\pm$ 0.82	1.19 $\pm$ 0.51	0.006
Glucose (mg/dL), mean $\pm$ SD	188.6 $\pm$ 68.4	153.7 $\pm$ 54.1	0.052
LRINEC score, mean $\pm$ SD	7.05 $\pm$ 2.21	3.62 $\pm$ 1.72	<0.001
LRINEC ≥ 6 , n (%)	16 (76.2)	5 (17.2)	<0.001

Patients with NF had significantly higher WBC counts and CRP concentrations than patients with severe cellulitis or erysipelas. Serum sodium was significantly lower, while creatinine was significantly higher in NF. The mean LRINEC score was substantially higher in the NF group.

A LRINEC score ≥ 6 was observed in 76.2% of NF patients compared with only 17.2% of non-NF patients ($p < 0.001$). Thus, in this study, a high LRINEC score was strongly associated with operative confirmation of NF.

However, the results should not be interpreted as demonstrating that LRINEC can safely exclude NF. Contemporary evidence indicates that LRINEC has limited sensitivity and should be regarded as an adjunct rather than a replacement for clinical assessment and surgical consultation.

Table 3: Intraoperative findings among patients with confirmed necrotising fasciitis

Intraoperative finding	NF patients (n=21)	p value*
Marked fascial edema	19 (90.5%)	<0.001
Grayish/dusky fascia	18 (85.7%)	<0.001
Easy blunt separation of fascial planes	17 (81.0%)	<0.001
Thin brownish/serosanguineous fluid	16 (76.2%)	<0.001
Fascial necrosis	21 (100%)	<0.001
Subcutaneous tissue necrosis	19 (90.5%)	<0.001
Positive deep tissue culture	15 (71.4%)	0.002
Muscle involvement	5 (23.8%)	0.041

*p values represent comparison with patients without corresponding operative evidence of necrotising infection.

All 21 patients diagnosed with NF demonstrated fascial necrosis during surgical exploration. Marked fascial edema was present in 90.5%, grayish or dusky fascia in 85.7%, easy blunt separation of tissue planes in 81.0% and thin brownish/serosanguineous fluid in 76.2%.

The intraoperative appearance therefore provided the most direct evidence of the depth and nature of infection. This is consistent with guideline recommendations that operative examination of the fascia and subcutaneous tissue remains a key component of definitive diagnosis.

Table 4: Association of diagnostic predictors with postoperative complications in NF patients

Predictor	Complication present n/N (%)	Complication absent n/N (%)	p value
LRINEC ≥ 6	9/16 (56.3)	2/5 (40.0)	0.60
Pain out of proportion	9/16 (56.3)	2/5 (40.0)	0.60
Hypotension at presentation	6/7 (85.7)	5/14 (35.7)	0.036
Surgical delay >12 h	7/8 (87.5)	4/13 (30.8)	0.018
Multiple debridements	8/11 (72.7)	3/10 (30.0)	0.049
Diabetes mellitus	8/13 (61.5)	3/8 (37.5)	0.33

Postoperative complications occurred more frequently among patients who presented with hypotension and among those in whom surgical intervention was delayed beyond 12 hours. Surgical delay >12 hours was significantly associated with postoperative complications (87.5% vs 30.8%; $p = 0.018$).

DISCUSSION

The principal finding of this prospective study was that NF could be differentiated from severe cellulitis and erysipelas by a combination of characteristic clinical findings, inflammatory laboratory abnormalities and intraoperative tissue changes[9]. No single clinical or laboratory variable was sufficiently reliable to establish or exclude the diagnosis in every patient.

The distinction is particularly difficult during the early phase of NF. The initial cutaneous findings may resemble cellulitis, and classic findings such as crepitus,

bullae and necrosis may occur relatively late. Current guidelines emphasize that rapidly progressive infection, severe pain out of proportion, edema extending beyond erythema, systemic toxicity and bullous or necrotic changes should increase clinical suspicion[10].

In our study, pain out of proportion was present in 76.2% of patients with NF compared with 24.1% of non-NF patients. This was the strongest clinical predictor. The biological basis is related to inflammatory destruction and involvement of deep tissue structures, resulting in severe pain before extensive surface changes

become apparent. Nevertheless, absence of disproportionate pain should not be considered sufficient to exclude NF[11]. A large diagnostic meta-analysis found that individual physical examination findings have insufficient sensitivity to reliably rule out necrotising infection.

The LRINEC score was significantly higher among patients with NF. In the original description by Wong et al., six laboratory variables were combined into a score intended to discriminate NF from severe cellulitis and other soft-tissue infections. In the present study, 76.2% of patients with NF had LRINEC ≥ 6 compared with 17.2% of patients with non-necrotising infection[12-13]. However, LRINEC should be interpreted cautiously. Subsequent diagnostic research has demonstrated that its sensitivity is inadequate for excluding NF. Fernando et al., in a systematic review and meta-analysis, reported sensitivity of approximately 68% for LRINEC ≥ 6 and concluded that a low score should not be used to rule out necrotising infection[14]. Therefore, the practical role of LRINEC is best considered supportive: a high score can strengthen suspicion, but a low score should not override concerning clinical findings.

The present study has several limitations. First, the sample size was relatively small and derived from a single institution. Second, the study population included patients selected because of clinical suspicion of severe infection, which may limit generalizability. Third, the sample size limited the ability to perform robust multivariable regression[15]. Fourth, imaging was not systematically performed in every patient because management was determined by clinical urgency. Finally, the numerical findings presented here require validation in a larger prospective cohort before being used to establish diagnostic thresholds.

Despite these limitations, the study reinforces an important clinical principle: the diagnosis of NF is fundamentally clinical and surgical. Laboratory scores may help stratify risk, but they should never delay surgical consultation when the clinical presentation is concerning[16].

Strengths of the Study

This study has several important strengths. First, it used a prospective observational design, allowing clinical, laboratory, and operative findings to be assessed systematically during the diagnostic evaluation of suspected necrotising fasciitis. Second, the study directly compared patients with surgically confirmed necrotising fasciitis with those having severe cellulitis or erysipelas, thereby addressing an important diagnostic challenge in acute surgical practice. Third, the study incorporated multiple complementary diagnostic domains, including clinical warning signs, inflammatory and biochemical laboratory parameters, and the LRINEC score. Fourth,

intraoperative assessment of the fascia and tissue planes provided direct operative evidence of necrotising infection and strengthened the diagnostic evaluation. Finally, the study identified clinically relevant predictors such as disproportionate pain, edema extending beyond erythema, bullae/ecchymosis, hypotension, altered sensorium, elevated inflammatory markers, hyponatremia, renal dysfunction, and elevated LRINEC score, providing a practical framework for early clinical suspicion and surgical decision-making.

Future Research / Recommendations

Future studies should involve larger, multicentre prospective cohorts to improve the generalisability and external validity of the findings. Multivariable statistical modelling should be performed in adequately powered populations to determine which clinical and laboratory variables independently predict necrotising fasciitis. Future research should also evaluate the diagnostic performance of individual clinical findings and the LRINEC score using sensitivity, specificity, positive and negative predictive values, and receiver operating characteristic analysis.

Imaging modalities such as computed tomography and magnetic resonance imaging may be systematically evaluated alongside clinical and laboratory findings to determine their incremental diagnostic value when the diagnosis remains uncertain. Longer-term studies should also examine postoperative complications, mortality, limb loss, repeated debridement, intensive-care requirements, and functional outcomes. Standardised diagnostic protocols combining clinical assessment, laboratory markers, scoring systems, imaging when appropriate, and prompt surgical consultation should be developed and prospectively validated.

Most importantly, future research should continue to emphasize that diagnostic scoring systems should support rather than delay urgent surgical assessment when necrotising fasciitis is clinically suspected.

CONCLUSION

Necrotising fasciitis remains difficult to distinguish from severe cellulitis and erysipelas during its early stages. In this study, severe pain disproportionate to skin findings, edema extending beyond erythema, bullae/ecchymosis, hypotension and altered sensorium were significantly associated with NF. Elevated WBC count and CRP, hyponatremia, renal dysfunction and a high LRINEC score provided additional diagnostic support.

A LRINEC score ≥ 6 was strongly associated with NF but should not be used as a stand-alone exclusion test. Intraoperative identification of necrotic fascia, grayish discoloration, fascial edema, thin fluid and easy tissue-plane separation provided the most definitive diagnostic evidence.

DECLARATIONS

Ethics Approval and Consent to Participate

The study was conducted in accordance with the ethical principles governing research involving human participants. Written informed consent was obtained from all participants before enrolment. The study protocol was reviewed and approved by the appropriate Institutional Ethics Committee before commencement of the study.

Consent for Publication

Not applicable. No individually identifiable patient information or identifiable images are presented in this manuscript.

Availability of Data and Materials

The datasets generated and/or analysed during the current study are not publicly available because of participant confidentiality and institutional considerations but may be made available from the corresponding author on reasonable request, subject to appropriate ethical and institutional approval.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

All authors contributed to the conception and design of the study, clinical assessment and/or data collection, interpretation of the findings, and critical revision of the manuscript. Dr. Avneet Singh Setia contributed to study supervision and clinical management. Dr. Rohit Kapoor contributed to clinical assessment, patient management, and critical revision of the manuscript. Dr. Ayushi Gupta contributed to data collection, data analysis, manuscript preparation, and correspondence. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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Clinical Trial Registration

Not applicable. This was a prospective observational study and was not registered as an interventional clinical trial.

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