Validation of LRINEC (Laboratory Risk Indicators for Diagnosis of Necrotizing Fasciitis) Scoring System for the Diagnosis of Necrotizing Fasciitis

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Abstract

Background: Necrotizing fasciitis (NF) is a rare but potentially fatal infection involving the subcutaneous tissue and fascia. Different classifications and terminology has been used in NF based on affected anatomy, microbial cause and depth of infection.

Clinical scores like the laboratory risk indicators for NF (LRINEC) scores are available to help diagnose NF and differentiate it from other skin and soft tissue infections.

Methods: A total of 100 patients were included in the study between January 2014 to June 2014. This prospective study was done on patients admitted in surgery department of DMCH with symptoms suggestive of soft tissue infections during the study period.

Results: Mean age was found 46.5(±13.8) years in severe cellulitis and 50.9(±9.8) years in necroting fasciitis (p>0.05). Male were predominant (60%). 80% of NF had DM. The validation test for LRINEC score ≤6 vs necrotizing fasciitis had sensitivity of 66%, specificity 84%, accuracy 75%, positive and negative predictive values were 80.49% and 71.19% respectively. Mortality of NF was 6%.

Conclusion: The LRINEC score is an impressive diagnostic tool to distinguish necrotizing fasciitis from other severe soft tissue infections, but it is not useful for early recognition of necrotizing fasciitis.

Keywords: Necrotizing fasciitis; LRINEC score; Cellulitis; Severe cellulitis

Introduction

Necrotizing fasciitis (NF) is a rare but potentially fatal infection involving the subcutaneous tissue and fascia. It is commonly known as flesh-eating disease. Different terms and classifications have been used to describe necrotizing fasciitis of skin and subcutaneous tissue.

These include necrotizing fasciitis, synergistic necrotizing cellulites, streptococcal myonecrosis, and gas gangrene. This variety of classifications and terminology has been based on affected anatomy, microbial cause and depth of infection.

Hippocrates in the fifth century BC gave the first description of this dreaded disease. The first report of this disease in the United States was by a Confederate Army surgeon, Joseph Jones in 1871 and he named the entity “hospital gangrene”. Meleney in 1924 reported an outbreak of hospital gangrene in Beijing and coined the term hemolytic streptococcal gangrene. The term NF was first introduced by Wilson in 1952 and is the preferred term today.
Historically, necrotizing infections were classified according to anatomical sites. Fournier’s gangrene (involving the perineum) and Meleney’s gangrene (involving abdominal wall) are examples. NF can be divided into two categories depending on the causative agents. Type-I disease is polymicrobial, caused by a mixture of aerobic, facultative anaerobic bacteria (Klebsiella sp., Vibrio sp., Aeromonas, Staphylococcus, Clostridia). Type-II disease is usually monomicrobial, caused by Group A streptococci. In general, Group-II NF is a rapid and progressive disease with a poorer prognosis than the type-I.

Immunocompromised, advanced age, peripheral vascular disease and obesity are some predisposing factors. In a Singapore study, 70.3% of patients with NF had diabetes mellitus. Patients with NF may present in later stages with septic shock, toxic shock syndrome and multi-organ failure. These patients may carry a high rate of mortality. Diagnosis of NF is essentially clinical. The gold standard is surgical exploration and tissue biopsy.

To help decide which patients required surgical exploration, particularly in those with equivocal clinical signs, laboratory and radiological tests might sometimes be useful. Clinical scores like the laboratory risk indicators for NF (LRINEC) scores are available to help diagnose NF and differentiate it from other skin and soft tissue infections. The LRINEC score is based around the routinely performed laboratory tests: C-reactive protein (CRP), white cell count, hemoglobin, serum sodium, serum creatinine and glucose levels. In Wong’s retrospective study, the scoring system was applied to 89 consecutive patients admitted with biopsy-proven necrotizing fasciitis. Control patients were randomly selected patients admitted with severe cellulitis during the same period. A cut-off value of e“6 was then reapplied to the patient cohort. They found a positive predictive value for the diagnosis of necrotizing fasciitis of 92% and a negative predictive value of 96%. When this scoring system was applied to a cohort of patients in a different hospital (56 patients with necrotizing fasciitis), 92.9% had a LRINEC score of ≥6. These findings suggest that this scoring system may be useful in deciding which patients with severe soft tissue infections should undergo a frozen section biopsy with a view to urgent debridement.

This study was conceived to determine if the LRINEC scoring system was useful and practical tool in the diagnosis of necrotizing skin infections in the local patient population. The LRINEC score was applied in our hospital and its usefulness was assessed by determining its predictive performance against the gold standard surgical biopsy.

Materials and Methods
The study was conducted in Dhaka Medical College Hospital from January, 2014 to June, 2014. It was a prospective observational cross-sectional study. A total of 100 patients were included in the study (50 were necrotizing fasciitis and 50 were severe cellulitis). Study population was based on all patients admitted in surgery department of DMCH with symptoms suggestive of soft tissue infections and purposive sampling technique was used. Statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

Inclusion criteria:
All patients with symptoms suggestive of soft tissue infections during the study period

Exclusion criteria:
1. Patients who have received antibiotic treatment in the last 48 hours or a minimum of 3 doses of antibiotic prior to presentation.
2. Patients who have undergone surgical debridement for present episode of soft tissue infection.
3. Patients with localized soft tissue infection.

Severe Cellulitis
The criteria for severe soft tissue infections were as follows based on documentation in the patients' charts: use of parenteral antibiotics for more than 48 hours in a patient with a soft tissue infection; and abscess requiring surgical debridement.
The LRINEC (laboratory risk indicator for necrotizing fasciitis) score

| Variable                     | Score |
|------------------------------|-------|
| C-reactive protein (mg/l)    |       |
| <150                         | 0     |
| 150 or more                  | 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     |
| <11                          | 2     |
| Sodium (mmol/l)              |       |
| 135 or more                  | 0     |
| <135                         | 2     |
| Creatinine (umol/l)          |       |
| 141 or less                  | 0     |
| >41                          | 2     |
| Glucose (mmol/l)             |       |
| 10 or less                   | 0     |
| >10                          | 1     |

LRINEC score of 6 or greater is considered positive for necrotizing fasciitis.

Results

Mean age was found 46.5(±13.8) years in severe cellulitis and 50.9(±9.8) years in necrotizing fasciitis ($p>0.05$) (Table 1). Male were predominant, majority (60%) were male and 40% were female. Majority patients had DM in both groups, which was 35(70.0%) in severe cellulitis group and 40(80.0%) in necrotizing fasciitis group as shown in table 2. Among 100 cases 20 patients had no complication in both groups. Rest of 80 complicated cases: septicemia 14(28%) were severe cellulitis and 38(76%) were necrotizing fasciitis, anaemia 08(16%) were severe cellulitis and 05(10%) were necrotizing fasciitis. The validation test for LRINEC score $e^6$ vs necrotizing fasciitis had sensitivity of 66%, specificity 84%, accuracy 75%, positive and negative predictive values were 80.49% and 71.19% respectively (Table 5). 58% of patients cured in severe cellulitis group and 48% in Necrotizing fasciitis group, 06% mortality were found in necrotizing fasciitis group.

Table 1. Distribution of age of the study population

| Age in year | Severe Cellulitis | Necrotizing fasciitis | Total | P value |
|-------------|-------------------|-----------------------|-------|---------|
| 21-30       | 7                 | 2                     | 09    |         |
| 31-40       | 12                | 4                     | 16    |         |
| 41-50       | 14                | 23                    | 37    |         |
| 51-60       | 8                 | 15                    | 23    |         |
| > 60        | 9                 | 6                     | 15    |         |
| Total       | 50                | 50                    | 100   |         |

Mean±(SD) 46.5(±13.8) 50.9(±9.8) 48.7(±12.1) 0.069

P value reached from unpaired t-test

Table 2. Co-morbidities of the study population

| Co-morbidities         | Severe Cellulitis | NF | Total | P value |
|------------------------|-------------------|----|-------|---------|
| DM                     | 35                | 40 | 75    | 0.248   |
| Liver cirrhosis        | 9                 | 7  | 40    | 0.585   |
| Cancer                 | 7                 | 5  | 12    | 0.527   |
| Peripheral vascular disease | 8             | 15 | 23    | 0.096   |
| Others                 | 6                 | 4  | 10    | 0.505   |

P value reached from chi square test
Table 3. Distribution of site involvement of the study population

| Site            | Severe cellulitis | NF  | Total | P value |
|-----------------|-------------------|-----|-------|---------|
| Lower extremities | 37                | 30  | 67    | 0.20    |
| Upper extremities | 07                | 06  | 13    | 0.76    |
| Perineum        | 00                | 12  | 12    | <0.001  |
| Trunk           | 03                | 02  | 05    | 1.0     |
| Head & neck     | 03                | 02  | 05    | 1.0     |

P value reached from chi square test

Table 4. Distribution of complications according to study patients

| Complications          | Severe cellulitis | NF  | Total |
|------------------------|-------------------|-----|-------|
| No complication        | 18 (36%)          | 02 (04%) | 20    |
| Septicemia             | 14 (28%)          | 38 (76%) | 52    |
| Anaemia                | 08 (16%)          | 05 (10%) | 13    |
| Joint stiffness        | 07 (14%)          | 02 (4%) | 09    |
| Chronic osteomyelitis  | 03 (6%)           | 00   | 03    |
| Multiorgan failure     | 00                | 03 (6%) | 03    |

Total 50 (100%) 50 (100%) 100

Table 5. LRINEC score of necrotizing fasciitis and severe cellulitis

| LRINEC | Severe Cellulitis | NF | Total | p value |
|--------|-------------------|----|-------|---------|
| < 6    | 42 (84%) (TN)     | 17 (34%) (FN) | 59    | < 0.001 |
| ≥6     | 8 (16%) (FP)      | 33 (66%) (TP) | 41    |         |

Total 50 (100) 50 (100) 100

P value obtained from chi-square test. TP: True positive; FP: False. The test result variable(s): LRINEC score (0.854), necrotizing fasciitis (0.39) has at least one tie between the positive actual state group and the negative actual state group, 95% Confidence Interval of the difference lower -0.77 and upper -0.93.

Figure 1. ROC of LRINEC score of necrotizing fasciitis and severe cellulitis

Figure 2. Outcome of the study population
Discussion
The present study was prospective observational cross sectional study which was done in Department of Surgery of Dhaka Medical College Hospital, Dhaka. Inclusion criteria were the patients with soft tissue infections during the study period those given informed written consent for the research.

In this study mean age was found 46.5 (±13.8) years in severe cellulitis and 50.9 (±9.8) years in necrotizing fasciitis. Male were predominant, majority 60% were male and 40% were female. More common were in males aged 50-60. In different studies\(^8-10\), the average age of patients was 55.6; our study was found to be consistent with the literature. Female patient dominance was observed in the series of Tilkorn and colleagues\(^11\).

Current study showed majority patients had DM in both groups, which was 35 (70.0%) in severe cellulitis group and 40 (80.0%) in necrotizing fasciitis group. Liao et al.\(^12\) found DM in 82.0% of cases, liver cirrhosis in 21.9%, Cancer in 5.5% and others in 7.8% of cases. The most common co-morbid diseases observed in NF are DM, immunosuppression, chronic renal failure, the underlying malignancy, atherosclerosis, chronic obstructive pulmonary disease, and obesity\(^13-15\). In their study, the most common co-morbid disease was DM (52%).

This study shows that sensitivity LRINEC score e\(^6\) 6 against necrotizing fasciitis was 66%, specificity 84%, accuracy 75%, positive and negative predictive values were 80.49% and 71.19% respectively. The probability of having NF in patients with a LRINEC score of 6 or higher was calculated as 92% in the study of Su et al.\(^13\). Wong et al.\(^14\) reported that mortality also significantly increases in patients with LRINEC score of 6 or higher. Corbin\(^15\) also showed in his study that the complication risk is higher in patients with LRINEC score of 6 or higher. Mortality is reported in the range of 20-30% in various series\(^8,9,16,17\).

Clayton et al.\(^18\) presented that mortality is significantly lower in young patients, in patients with BUN of 50 mg/dl or below, and in patients without ongoing sepsis. Faucher et al.\(^19\) proposed that co-morbid diseases do not affect mortality. On the other hand, Francis et al.\(^20\) proposed that mortality is 50% in patients with 3 or more risk factors (being 50 years old or older, diabetes, malnutrition, hypertension, or intravenous drug abuse). As a result of this study, we propose that increased number of debridement due to severity of disease, factor grown in the deep tissue culture (Pseudomonas aeruginosa), and LRINEC scores might be relative to mortality.

The developmental study by Wong et al reported that a LRINEC score of more than 6 had a sensitivity of 89.9%, specificity of 96.9%, positive predictive value of 92.0% and negative predictive value of 96%\(^9\). In 2009, Holland studied a group of 28 patients who had received surgery because of suspected NF. Ten patients were diagnosed with NF postoperatively. The results showed a sensitivity of 80%, specificity of 67%, positive predictive value of 57% and negative predictive value of 86%\(^21\). Liao et al.\(^12\) results showed that the LRINEC score had impressive ability to discriminate NF from severe soft tissue infection, but was not a good diagnostic tool for NF. When clinical data did not indicate a diagnosis of NF, 43.3% (95% CI; 36.9-49.7%) of patients still had a LRINEC score <6, so a LRINEC score cannot help to decrease the misdiagnosis of patients with NF. Our ROC curve examining the diagnostic ability of a LRINEC score showed moderate value.

Conclusion
This study showed that male was predominant; common co-morbidities were DM, liver cirrhosis, cancer and peripheral vascular disease. Lower extremities were major site of involvement. The LRINEC score is an impressive diagnostic tool to distinguish necrotizing fasciitis from other severe soft tissue infections, but it is not useful for early recognition of necrotizing fasciitis.

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