Laboratory risk indicator for necrotising fasciitis (LRINEC) score for the assessment of early necrotising fasciitis: a systematic review of the literature

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ABSTRACT

INTRODUCTION Early operative debridement of necrotising fasciitis is a major outcome determinant. Identification and diagnosis of such patients can be clinically difficult. The Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) score first published in 2004 is based on routinely performed parameters and offers a method for identifying early cases. No literature review has yet been performed on the application of such a score.

METHODS A systematic review of English-language literature was performed from 2004 to 2014 to identify articles reporting use of LRINEC score and the incidence of necrotising fasciitis. We performed a critical review of PubMed, Medline and Embase in line with the PRISMA statement. A meta-analysis was performed with a random effects model and 95% confidence interval. Suitable correlation coefficient and receiver operating characteristic (ROC) curves were also calculated.

RESULTS After application of inclusion criteria, 16 studies with 846 patients were included. The mean LRINEC score in patients with necrotising fasciitis was 6.06. Two papers reported LRINEC score in patients without necrotising fasciitis with a mean 2.45. All six studies with a reported coefficient of variance were < 1 ; Pearson correlation coefficient was $r = 0.637$ ($P = 0.011$). An ROC curve showed an area under the curve of 0.927.

CONCLUSIONS The LRINEC score is a useful clinical determinant in the diagnosis and surgical treatment of patients with necrotising fasciitis, with a statistically positive correlation between LRINEC score and a true diagnosis of necrotising fasciitis.

KEYWORDS

Necrotising fasciitis – Score – LRINEC – Cellulitis

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Introduction

Necrotising fasciitis is a rare, potentially life-threatening infection involving the fascia and subcutaneous tissues. This can progress to necrosis, leading to a systemic inflammatory response syndrome (SIRS), shock and even death. Features of necrotising fasciitis include purpura, subcutaneous bleeding, bullae, necrosis and gangrene. Mortality from this disease is up to 40%, with around 500 cases per year.^{1,2} Necrotising fasciitis infection is categorised as type 1 (infection from both aerobic and anaerobic bacteria) and type 2 (group A beta-haemolytic *Streptococcus* and *Staphylococcus aureus*).³

The high morbidity and mortality associated with necrotising fasciitis has not changed markedly since its description over 50 years ago.^{4,5} Early clinical differentiation between necrotising fasciitis and cellulitis is important when considering surgical management. Delayed recognition is a key factor when considering the high mortality.⁶ Imaging modalities such as computed tomography, magnetic resonance imaging and frozen section biopsy have been previously

used in the discrimination between necrotising fasciitis and other soft tissue infections but these methods have been limited by cost and availability.^{2,7,8}

The Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) is a clinical tool first described by Wong C *et al.*⁹ The tool is based on six common serum parameters at the time of presentation: C-reactive protein (CRP), total white cell count, haemoglobin, serum sodium, creatinine and glucose (Table 1). An LRINEC of six or greater confers a higher risk of necrotising fasciitis.⁹ The LRINEC scoring system has been controversial, with papers questioning its role as a scoring system for prognostic identification.^{10,11}

Diagnostic scoring has the potential to prevent marked morbidity and mortality in the accurate diagnosis of necrotising fasciitis. There have been no papers to date offering a comprehensive review of the literature to reach consensus regarding the LRINEC score. Our principle objective is to provide the reader with a critical analysis of the literature and LRINEC score for future use.

Table 1 The Laboratory Risk Indicator for Necrotising Fasciitis

Parameter	Range	Score ^a
Hb (g/dl)	>13.5	0
	11–13.5	1
	<11	2
White cells (10 ⁹ /L)	<15	0
	15–25	1
	>25	2
Sodium (mmol/L)	<135	2
Creatinine (μmol/L)	>141	2
Glucose	>10	1
C-reactive protein	>150	4

^aScore ≤5 = <50% risk (low); 6–7 = intermediate risk; ≥8 = >75% risk (high).

Methods

A systematic review of publications in English was conducted of the following electronic databases: EMBASE, MEDLINE and the Cochrane Database of Systematic Reviews. The key words used were (necrotising OR necrotising) AND (fasciitis) AND (score). The inclusion date range was 1 January 2004 to 1 June 2015.

Two researchers (JB and GF) independently selected papers from the databases. Papers were selected through two levels of screening. The first level entailed the review of abstracts satisfying the inclusion and exclusion criteria. The second level of screening involved the review of the articles in full, with the same application of inclusion and exclusion criteria. Only studies which passed both the first and second levels of screening were included in our analysis. Articles were included if a subgroup of patients fulfilling the

inclusion and exclusion criteria could be extracted. Our procedure for assessing data within papers was in keeping with the Preferred Reporting Items for Systematic Reviews and Meta-analysis criteria.¹² Articles (not letters or case reports) were included if they met the criteria (Table 2).

Assessment of methodological quality was made according to the Consolidated Standards of Reporting Trials.¹³ The methodological quality of non-randomised studies was assessed using the Methodological Index for Non-Randomised Studies (MINORS) tool.¹⁴

Extracted data (Table 2) were recorded in a Microsoft Excel® spreadsheet. A Kappa statistic was used to measure the agreement between reviewers for included articles. We performed multiple statistical analyses to pooled proportions. All statistical models were produced and presented using Stats Direct (StatsDirect Ltd, Cheshire, UK). Comparisons between groups was made using confidence intervals. Further values were compared using means, standard deviations, Pearson Correlation coefficient (*r*), two-tailed student T test, two-tailed single-sample T test and receiver operator curve (ROC) plots. The threshold for significance was *P* < 0.05.

Results

The literature search identified 77 articles. After the application of inclusion and exclusion criteria at the first and second level of screening, 16 articles were included in the final analysis (Kappa 0.72; Fig 1).^{9,16–19,21–31} The mean MINORS score for comparative studies was 8.6 and 7.0 for non-comparative studies.

A total of 846 patients was included from the selected papers (range 7–209). The continents of origin were Europe for nine papers, Asia for five papers, North America for one paper and Oceania for one paper. The mean number of years of study was 6.5 years (range 1–15 years). The mean LRINEC score for patients with necrotising fasciitis was 6.06. The mean LRINEC score for patients without necrotising fasciitis was 2.45. The Pearson correlation coefficient

Table 2 Inclusion and exclusion criteria

Criterion	Inclusion	Exclusion
Population	Human	Non-human
	Adults (>18yrs)	Non-tissue infection/NF
	Soft tissue infection	Non-English
	Any country of origin	Review articles
	Full article	Conference proceedings
Intervention	LRINEC score	No LRINEC score
Comparator	LRINEC score to necrotising fasciitis and soft-tissue infections	–
Outcomes	Confirmed necrotising fasciitis	Necrotising fasciitis not confirmed
Study design	Any clinical study ^a	Non-clinical study

^a Comparative or non-comparative, randomised or non-randomised

between LRINEC score and positive diagnosis of necrotising fasciitis was $r = 0.637$ ($P = 0.01$). A two-tailed student T test was used to compare patients with a positive diagnosis of necrotising fasciitis and patients with a negative diagnosis. A two-tailed analysis was chosen to accommodate patients with LRINEC scores at the extremes of the range. This revealed $t = 2.98$ ($P = 0.01$). A two-tailed single-sample T test was used to determine the value at which the LRINEC score was statistically significant in patients with necrotising fasciitis; with an LRINEC score of 6, $t = 0.14$ ($P = 0.44$). An LRINEC score of 7.1 was significant ($t = -1.93$, $P = 0.05$). Figure 2 illustrates an ROC curve for patients with and without necrotising fasciitis with calculated LRINEC scores. The fitted ROC area was 0.927. Figure 3 shows a forest plot of papers for LRINEC means, with score range and confidence intervals where indicated.

Discussion

It has been suggested that the LRINEC score is capable of detecting early cases of necrotising fasciitis among patients with severe soft tissue infections. Wong *et al.* suggest a LRINEC threshold of ≥ 6 for patients with a suspicion of necrotising fasciitis and a score of ≥ 8 for patients with a strong prediction for the disease.⁹ The importance of adopting an

evidence-based approach for the diagnosis of necrotising fasciitis has the potential to lead to early diagnosis, surgical intervention and improved morbidity and mortality. Mortality rates vary widely, from over 50% to as low as 8.6%,¹⁵ with the low mortality figures being attributed to a low comparative patient age (less than 62 years) in some studies. The average LRINEC score reported in our study was 6.06, over the threshold of 6 reported by Wong *et al.*⁹ The score also varied markedly for the part of the body affected with necrotising fasciitis, with limbs scoring 6, groin 6.8 and chest/trunk 7.3.

The number of studies that reported an LRINEC score in patients without necrotising fasciitis were comparatively few, with only Chao *et al.*¹⁶ and Holland *et al.*¹⁷ reporting scores of 1.1 and 3.8, respectively. Chao *et al.* reported the use of the LRINEC score uniquely in patients with necrotising fasciitis and soft tissue infection with the atypical micro-organism *Vibrio vulnificus*. The retrospective study examined 125 consecutive patients with this microorganism over 8 years. The LRINEC score in soft tissue infections (necrotising fasciitis negative) may have been biased owing to the atypical nature of this organism. The paper by Holland *et al.*¹⁷ retrospectively examined 28 patients with the

possibility of a necrotising fasciitis diagnosis on admission. Of these, 17 were found to have severe soft tissue infections with a low LRINEC of 3.8. The small numbers of both of these patient groups for a negative necrotising fasciitis LRINEC score lends to a perceived low sensitivity. Of the 16 studies included in this review, only four detailed a coefficient of variance ranging from 0.2 described by Citak *et al.*¹⁸ to 0.7 by Chao *et al.*¹⁶ This suggests a small range of LRINEC scores for a given patient with necrotising fasciitis. Only two papers demonstrated a range of LRINEC scores with confidence intervals (Fig 3).

Swain *et al.*¹⁹ retrospectively studied patients with necrotising fasciitis over a five-year period, recruiting 15 patients with the disease between 2006 and 2011. Of these patients, the mean LRINEC score varied for patients who survived and those who died. The LRINEC score was comparatively higher for patients who died (LRINEC 9) versus those who survived (LRINEC 6.5) with necrotising fasciitis. The paper also examined the comorbidities associated with necrotising fasciitis. The authors found the highest associated comorbidities were diabetes, hypertension, obesity and hypercholesterolaemia.¹⁹

Table 3 Modified Laboratory Risk Indicator for Necrotising Fasciitis score.

Parameters	Range	Score ^a
<i>Laboratory</i>		
C-reactive protein	>150 mg/dl	4
Total white cell count	<15 × 10 ⁶ /mm ³	0
Total white cell count	15–25 × 10 ⁶ /mm ³	1
Total white cell count	>25 × 10 ⁶ /mm ³	2
Erythrocyte count	<4 × 10 ⁶ /μl	1
Haemoglobin	>13.5 g/dl	0
Haemoglobin	11–13.5 g/dl	1
Haemoglobin	<11 g/dl	2
Creatinine	<135 mmol/L	2
Fibrinogen levels	>750 mg/dl	2
<i>Clinical</i>		
Pain	Mild/none	0
	Intermediate	1
	Strong	2
Fever	≤37.5°C	0
	37.6–37.9°C	1
	≥ 38°C	2
Tachycardia	>100 beats/minute	1
Signs of acute renal injury	No	0
	Yes	1

^a ≥8 = strong suspicion for necrotising fasciitis 6–7 = suspicion; ≤no suspicion

The LRINEC score examines six laboratory-based parameters but makes no consideration for patient age, comorbidities, clinical observations and other blood parameters (e.g. lactate) as do other scoring systems such as APACHE II and GLASGOW scoring in pancreatitis. Other perceived criticisms of the LRINEC score are the relatively small cohort used to devise the score, an over-reliance on non-specific CRP (given a maximal score of 4 compared with other parameters). Borschitz *et al.*²⁰ conducted an observational study which recruited 29 patients with necrotising fasciitis and 59 matched comparators. Of the additional parameters, patients with necrotising fasciitis compared with control have statistically increased pain. Patients with renal failure and chronic venous insufficiency also showed a higher risk of diagnosis for necrotising fasciitis. The authors suggested an addition of several parameters (Table 3). Further studies need to be performed to validate the additional parameters suggested by Borschitz *et al.*²⁰ This may take the form of a prospective comparative study, with all patients with suspected cellulitis, abscess and necrotising fasciitis being enrolled with timed follow-up to resolution. This

would elucidate the scores apparent better sensitivity and specificity as compared with the standard LRINEC score.

Conclusion

The LRINEC score is a useful adjunct in the clinical diagnosis of necrotising fasciitis with a statistically positive correlation. The score, however, is amenable to further development, with the possible addition of clinical parameters such as pain, pyrexia and comorbidities.

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