

Evaluation of LRINEC Scoring System for Diagnosis of Necrotizing Fasciitis in Patients Presenting with Soft Tissue Infections

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ABSTRACT

BACKGROUND

Necrotising fasciitis is an aggressive form of soft tissue infection which, even with modern medical care, has a high mortality rate. Early diagnosis and aggressive treatment are the cornerstones of therapy and any tests that can reliably decrease the interval between presentation and definitive therapy is likely to improve patient outcomes. Paucity of specific cutaneous signs to distinguish necrotizing fasciitis from other soft tissue infections such as cellulitis makes the diagnosis extremely difficult. So, a scoring system which 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 2005 which claims to have a positive predictive value of 92.0% and negative predictive value of 96.0%. Hence we would like to evaluate this scoring system in our patients and if found to have similar comparable predictive values, it would prove to be a boon to developing countries like India where the mortality of the disease ranges from 7 to 76% and also where there resource constraint.

METHODS

All patients visiting the Department of Surgery, RRMCH Bangalore with soft tissue infection from Nov 2017 to April 2019 were included in this prospective study. Upon admission, blood tests (Hb%, Total WBC, RBS, CRP, Sr. Creatinine & Sr. Sodium) included in the LRINEC scoring system were done. Preoperative score is given and correlated with histopathological examination results. Using 2 X 2 table specificity, sensitivity, positive predictive value & negative predictive value were determined.

RESULTS

In our study, LRINEC scoring system had a sensitivity of 90.90%, specificity of 87.5%. It has a positive predictive value of 95.23% & negative predictive value of 77.78%. LRINEC score in diagnosing necrotizing fasciitis is statistically significant ($p < 0.001$).

CONCLUSIONS

LRINEC scoring can be used as a diagnostic tool in patients presenting with soft tissue infection to diagnose & treat necrotising fasciitis at the earliest as it is often mistaken for milder forms of soft tissue infections such as Cellulitis or Lymphangitis, particularly in a developing country like India where resources are limited.

KEYWORDS

Necrotizing Fasciitis, Soft Tissue Infection, LRINEC Score, Histopathology

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BACKGROUND

Necrotizing fasciitis is an uncommon life-threatening soft-tissue infection characterized by rapidly progressing inflammation and necrosis of subcutaneous fascial tissues with relative sparing of overlying skin and underlying muscle. NF represents a subset of all necrotizing soft - tissue infections (NSTIs). Most often it is associated with severe systemic toxicity and has a fulminant course infection and hence considered as a true infectious disease emergency. It is usually rapidly fatal unless promptly recognized and aggressively treated with appropriate antimicrobials and surgical debridement at the earliest. Necrotizing soft tissue infection represents a diverse process; the term itself encompasses a continuum ranging from pyoderma to life threatening infections (clostridial gas gangrene with myonecrosis, anaerobic cellulitis, and severe, necrotizing vibrio infections).

The common pyoderma does not extend beyond the skin (epidermis and dermis) and include erysipelas, impetigo, folliculitis, erythema, furunculosis and carbunculosis. Cellulitis is a deeper skin infection than erysipelas. Necrotizing fasciitis involves the subcutaneous tissue, superficial fascia and deep fascia. These can occur in any anatomical areas, but the common site is the extremities. Necrotizing fasciitis is often underestimated because of the lack of specific clinical findings in the initial stages of the disease. The paucity of specific cutaneous signs to distinguish necrotizing fasciitis from other soft tissue infections such as cellulitis makes the diagnosis extremely difficult. The first and most important consideration for an accurate, prompt diagnosis is to have a high index of suspicion. It has been shown by numerous studies in the past that early recognition and surgical intervention at the earliest is the sole factor in preventing the morbidity and mortality in patients with necrotising fasciitis [1].

So, a scoring system which 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 [2] in 2005 which claims to have a positive predictive value of 92.0% and negative predictive value of 96.0%. Hence in this study we have reviewed literature with regard to historical aspects, the epidemiology, aetiology, clinical presentation, diagnosis and treatment. We also have tried to evaluate LRINEC scoring system in patients presenting with symptoms and signs suggestive of necrotizing fasciitis to Rajarajeswari Medical College & hospital over the 18 months (November 2017 to April 2019). If found to have similar comparable predictive values, this would help us diagnose and treat necrotizing fasciitis early and accurately in India where the mortality rates due Necrotizing fasciitis is as high as 76%.

History of Necrotizing Fasciitis

Necrotizing fasciitis was first described by Hippocrates in the 5th century BC.[3] He discussed it as a fulminant, fatal complication of "erysipelas". Throughout the 18th and 19th centuries, several European physicians described cases of

rapidly progressing NSTIs by a variety of names, including 'phagedena ("eating away") gangrenosa', 'necrotising/gangrenous erysipelas', 'non - clostridial gas gangrene', 'synergistic necrotizing cellulitis', 'haemolytic streptococcal gangrene' and 'bacterial synergistic gangrene', putrid ulcer.

The first detailed descriptions in English were provided by a British naval surgeon, Leonard Gillespie, and two British naval physicians, Sir Gilbert Blane and Thomas Trotter, in the late 18th century.[4] In England, from the 1780s through the 1850s, the disease was known as one of the most dreaded to befall those serving in the army and navy.[4] Hospital gangrene was rare in civilian hospitals despite the fact that surgical wound infections, puerperal fever, and erysipelas were quite common in the pre - antiseptic era.[4] In 1883, Fournier described necrotizing infection involving the perineum and genitalia as a Fournier's gangrene. The first description of necrotizing fasciitis in the United States was in 1871 by Joseph Jones,[5] a Confederate Army surgeon, who coined the term "hospital gangrene". By the beginning of the 20th century, it was thought that hospital gangrene was a disease of the past. As stated by Park in 1908, "Hospital gangrene so - called... is now practically never seen." [3] In 1924, Meleney reported an outbreak of hospital gangrene in Beijing characterized by lethal and rapidly progressing soft - tissue infection caused by a microaerophilic streptococcus involving the abdominal wall and termed it as Meleney's gangrene ("haemolytic streptococcal gangrene").[6] He also coined the term "synergistic gangrene," which is characterized by a symbiosis of anaerobic streptococci and Staphylococci.[3]

The term currently in use, "Necrotizing Fasciitis", was first coined by Wilson in 1952 and accurately describes the most consistent feature of the this infection, being fascial necrosis.[7] Recent outbreaks, which have been publicized by the lay press variously as the "Killer Bug," "Flesh - eating Bacteria," and "Galloping Gangrene," have once again piqued people's interest in this uncommon but often fatal disease.[8] The resurgence of interest was fuelled by a 1989 report by Stevens and colleagues [9], of 20 patients with Group A streptococcal toxic shock syndrome, 11 of whom had necrotizing fasciitis. While the understanding of the pathophysiology of necrotizing fasciitis continues to improve, the mortality of this disease remains alarmingly high with reported mortality rates ranging from 6 to 76%.[9]

Anatomy

Certain anatomical considerations are important to understand the pathophysiology of NSTI. Most bacteria and fungi can multiply within viable tissue, but fibrous attachments or "boundaries" between subcutaneous tissues and fascia (e.g., scalp, hands) can help limit the spread of infection. The natural lack of fibrous attachments in the larger areas of the body (e.g., trunk, extremities) facilitates widespread infection. From the surface down and forming concentric circles, we find the skin (epidermis and dermis), superficial fascia or subcutaneous tissue (hypodermis), the deep fascia, and muscles.

The deep fascia continues with the epimysium (connective tissue surrounding muscles), and sends prolongations (intermuscular septa) that divide the different muscle compartments. Since the fascia is a continuum from the surface to the endomysium muscles, it is the route by which a surface process spreads to muscles or bones and vice versa.

Incidence

The number of cases reported for necrotizing fasciitis in adults is 0.40 cases per 100,000 people/year while the incidence in children is higher at 0.08 cases per 100,000 people/year^[10]. Necrotizing Fasciitis is considered a rare condition; however, the mortality rate remains high. Evidence has estimated the mortality rate to be at 20 - 40%.^[11] According to the Center for Disease Control there is an estimated 9,000 - 11,500 cases of necrotizing fasciitis occur each year in the United States, with a resultant 1,000 - 1,800 death annually

Pathophysiology

Understanding the pathophysiology of necrotizing fasciitis is important in distinguishing the clinical presentation of necrotizing fasciitis. Most cases commence with trauma to the skin surface with seeding of the bacteria.

The primary site of pathology is in the superficial fascia. Bacteria proliferate within the superficial fascia and elaborate enzymes such as hyaluronidase, haemolysins, DNAase, protease and collagenase which degrades the fascia which enables the organisms to spread through the fascia. Lack of fibrous attachments in the trunk and limbs, however, can lead to widespread infection and tissue destruction. Infection also spreads to venous and lymphatic channels, leading to oedema. The end result of this uncontrolled proliferation of bacteria is angiothrombotic microbial invasion, liquefactive necrosis of the superficial fascia and agonizing pain, which is out of proportion to any external signs and is the earliest clinical feature that is common to all types of necrotizing fasciitis. As nerves supplying the necrotizing area of skin die, the central areas become anaesthetic,^[12] while laterally the tissues overlying the deep spreading fascial infection remain tender.

Finally, the infection in the deep layer ascends, producing oedema of the epidermal and dermal layer (peau d orange) and a woody firmness of tissues. Initially a horizontal phase predominates with rapid spread through the fascia with extensive undermining of the apparently normal looking skin. As the disease progresses, there is occlusion of perforating nutrient vessels to the skin causes progressive skin ischemia necrosis of the skin with gangrene of the subcutaneous fat, dermis and epidermis, manifesting progressively as bullae formation, ulceration and skin necrosis. Soft tissue gas almost exclusively occurs in anaerobic infections. The notable exception to this necrotizing fasciitis is in diabetic patients. In diabetic's small vessel disease, altered leukocyte function and elevated tissue glucose level predispose to an environment low in oxygen tension and substrate for bacterial growth.

The tissue damage and systemic toxicity of necrotizing fasciitis are believed to be due to the release of bacterial toxins and endogenous cytotoxins.^[13,14] Exotoxins A and B have been implicated in the invasive Group A Streptococcal infection.^[15] Exotoxin A has been demonstrated in case of invasive streptococcal infection whereas absent in non - invasive streptococcal infection. In addition, Talkington. Et al^[16] found that the strains of streptococcal associated with necrotizing fasciitis secrete abnormally high levels of cysteinease, a protease that break down protein.

Histology

Stamenkovic and Lew described histological criteria for diagnosis necrotizing fasciitis, and it was reliably even to identify early cases of necrotizing fasciitis^[17].

Histological Criteria for Diagnosis

- Necrosis of the superficial fascia.
- Polymorphonuclear infiltration of the dermis and fascia.
- Fibrinous thrombi of arteries and veins coursing through the fascia.
- Angiitis with fibrinoid necrosis of arterial and venous walls.
- Presence of microorganisms within the destroyed fascia and dermis.
- Absence of muscle involvement.

Histology is important particularly in cases where the operative findings are equivocal for early necrotizing fasciitis, as it determines the need for an early, second look and repeat debridement.

METHODS

This was a prospective study done on 30 patients presenting with symptoms suggestive of soft tissue infections to O.P.D. of surgery department in Rajarajeswari Medical College between November 2017 to April 2019. Patients below 15 yrs. or above 75 yrs. of age were excluded from the study. Patients who have received antibiotic treatment in the last 48 hours or a minimum of 3 doses of antibiotic prior to presentation and Patient who has undergone surgical debridement for present episode of soft tissue infection were also excluded from the study. Patients with boils or furuncles with no evidence of cellulitis were excluded from the current study. All the patients underwent clinical examinations and and routine investigations including haemoglobin, total white cell counts, random blood sugar, serum creatinine, serum sodium, serum C - reactive protein.

Following which information regarding the demographics & covariates of soft tissue infections was collected using a pretested semi - structured proforma cum observational checklist. LRINEC scoring system was applied to each of the study subjects. The confirmatory diagnosis for necrotising fasciitis was done vide histopathology for all patients, irrespective of the result of the LRINEC scoring system.

Statistical Methods

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min - Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made -

1. Dependent variables should be normally distributed,
2. Samples drawn from the population should be random,
3. Cases of the samples should be independent.

Chi - square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Diagnostic statistics viz. Sensitivity, Specificity, PPV, NPV and Accuracy have been computed to find the correlation of LRINEC with HPE findings.

Diagnostic Statistics.^[18 - 22]

Disease					
Test	Present	N	Absent	n	Total
Positive	True Positive	a	False Positive	c	a + c
Negative	False Negative	b	True Negative	d	b + d
Total	a + b		c + d		

Table 1. 2 X 2 Table

The following statistics can be defined

- Sensitivity: probability that a test result will be positive when the disease is present (true positive rate, expressed as a percentage). = $a / (a + b)$
- Specificity: probability that a test result will be negative when the disease is not present (true negative rate, expressed as a percentage). = $d / (c + d)$
- Positive predictive value: probability that the disease is present when the test is positive (expressed as a percentage). = $a / (a + c)$
- Negative predictive value: probability that the disease is not present when the test is negative (expressed as a percentage). = $d / (b + d)$
- Accuracy is the sum of true positive and true negative divided by number of cases.

RESULTS

Most common age group affected with necrotizing fasciitis was between 41 - 50 years and 61 - 70 years. Second group being between 51 - 60 years. Mean age group was 55.50 ± 12.24 years (Mean \pm SD). Males were commonly affected by necrotizing fasciitis accounting to 73% in our study. 56.7% of the total patients had haemoglobin levels less than 11 g/dL whereas 33.3% had haemoglobin levels in the range of 11 to 13.5 g/dL. 56.7% of the patients had total WBC counts in the range of 15000 to 25000 cc/m³ whereas 43.3% had < 15000 cc/m³ and none of the patients had total WBC counts > 25000 cc/m³. 30 % had a random blood sugar >180 mg/dL. 60% of the patients had serum creatinine >1.4. 90% presented with hyponatremia. Out of the 30 patients in the

study, 6 patients (20%) had CRP >150 whereas 24 patients (80 %) had CRP < 150.

LRINEC	Total	Percentage
<6	9	30%
≥ 6	21	70%
Total	30	100%

Table 2. LRINEC Scoring System for Necrotizing Fasciitis 70% of the Patients had a LRINEC Score >6.

Histopathology	Total	Percentage
Necrotizing Fasciitis	22	73.3%
No Necrotizing Fasciitis	8	26.7%
Total	30	100%

Table 3. Histopathology was Positive in 73.3% of the Patients

Clinical variables	Histopathology		P Value
	Negative (n=8)	Positive (n=22)	
Age in years			
<50 years	4 (13.3%)	8 (26.67%)	0.400
>50 years	4 (13.3%)	14 (46.67%)	
Gender			
Male	7 (23.33%)	15 (50%)	0.391
Female	1 (3.33%)	7 (23.33%)	
Haemoglobin			
<11.0	3 (10%)	14 (46.67%)	0.403
11.0 - 13.5	4 (13.3%)	6 (20%)	
>13.5	1 (3.33%)	2 (6.67%)	
Total count			
<15000	2 (6.67%)	11 (36.67%)	0.407
15000 - 25000	6 (20%)	11 (36.67%)	
>25000	0 (0%)	0 (0%)	
RBS			
≤ 180	8 (26.67%)	13 (43.33%)	0.067+
>180	0 (0%)	9 (30%)	
Serum Creatinine			
≤ 1.4	6 (20%)	6 (20%)	0.034*
>1.4	2 (6.67%)	16 (53.33%)	
Sodium			
<135	6 (20%)	21 (70%)	0.166
135 - 146	2 (6.67%)	1 (3.33%)	
>146	0 (0%)	0 (0%)	
CRP			
<150	8 (26.67%)	17 (56.67%)	0.287
>150	0 (0%)	5 (16.67%)	

Table 4. Correlation of Clinical Variables with Histopathology Findings

LRINEC	Histopathology		Total
	Necrotizing Fasciitis	No Necrotizing Fasciitis	
<6	2 (9.1%)	7 (87.5%)	9 (30%)
≥ 6	20 (90.9%)	1 (12.5%)	21 (70%)
Total	22 (100%)	8 (100%)	30 (100%)

Table 5. Correlation of LRINEC with Histopathology Findings

	True Positive	False Positive	False Negative	True Negative	Total	P Value
Observation	20	1	2	7	30	<0.001**
	Sensitivity Specificity PPV NPV Accuracy					
Evaluation (%)	90.90	87.5	95.23	77.78	90	

Table 6. Diagnostic role of LRINEC

+ Suggestive significance (p value: $0.05 < P < 0.10$), * Moderately significant (p value: $0.01 < P < 0.05$), ** Strongly significant (p value: 0.01)

Correlation between histopathological and various laboratory parameters were significant in relation to serum creatinine and random blood sugar where the P values were 0.034 and 0.067 respectively. Out of total patients of 22 histologically proved to have necrotizing fasciitis, 20 patients

i.e. 90.9% had a LRINEC score >6. Correlation of LRINEC with histopathology was significant when LRINEC score >6 i.e. P value <0.0001.

In Our Series

Sensitivity of LRINEC score is 90.90%

Specificity of LRINEC score is 87.5%

Positive predictive value of LRINEC is 95.23%

Negative predictive value of LRINEC is 77.78%

Accuracy of LRINEC in diagnosing necrotizing fasciitis is 90.

LRINEC score in diagnosing necrotizing fasciitis is statistically significant (P<0.001).

DISCUSSION

Total of 30 patients presenting with symptoms and signs of necrotizing fasciitis to hospital (Rajarajeswari Medical College & Hospital) were recruited into the study based on the inclusion and exclusion criteria mentioned earlier. Most common age group was between 41 - 50 years and 61 - 70 years both accounting for 30% of cases each. Second group being between 51 - 60 years. Mean age group was 55.50 ± 12.24 years.

Necrotizing fasciitis is a spreading fascial gangrene that destroys the fascia while sparing skin and muscle. At the end of our observations, we reviewed the literature to compare our results with world statistics. Some of the elegant studies that have been done by Rekha et al, David et al and Faucher L.D. et al and Wong et al were used for comparisons.

A review of literature states that there is no age or gender prediction for necrotizing fasciitis. Most common age group was between 41 - 50 years, and 61 - 70 years both accounting for 30% of cases each. While mean age group was 55.50 ± 12.24 years in the present study, it was 51.5 and 57.8 in David et al and L.D. Faucher et al respectively.

Mean Age Group Years	Present Study	David et.al.	Faucher. L.D et al
	55.50 ± 12.24	51.5	57.8

Table 7. Age Comparison between Different Studies

In our study, 73.3% of the patients were males whereas it was 37%, 51 % and 75% in David et al, L.D. Faucher et al and Rekha et al respectively.

CONCLUSIONS

In patients with severe soft tissue infections, LRINEC scoring based on laboratory parameters is an easy and reliable diagnostic tool to diagnose necrotizing fasciitis accurately. In our study we also found that the correlation between histopathology and laboratory parameters such as serum creatinine and random blood sugar were statistically significant with P values 0.034 and 0.067 respectively.

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