

Original article

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Series of 41 cases of necrotizing fasciitis in a tertiary level hospital. Is as deadly as we think? LRINEC scale is useful today?

*Serie de 41 casos de fascitis necrotizante en un hospital de tercer nivel.
¿Es tan mortal como pensamos? ¿Es útil hoy en día la escala LRINEC?*

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ABSTRACT. Introduction: necrotizing fasciitis (NF) is a rare soft tissue infection that leads to sepsis and death without an early surgical treatment. LRINEC (laboratory risk indicator for necrotizing fasciitis) scale is one of the most accepted tests for diagnosis. This study presents a retrospective evaluation of the usefulness of the LRINEC scale in the diagnosis and prognosis of NF. **Material and methods:** retrospective study of 41 cases of NF in extremities between 2010 and 2019. Based on the score obtained on the LRINEC scale the cases were assigned to: LRINEC lower than 5 in Group 1 with 12 cases, score 6 or 7 in Group 2 also 12 cases, and finally score of 8 or above in Group 3, 17 cases. **Results:** the mean LRINEC score was 7.04 (range: 1-13). 30 patients (73%) had scores above 6, the threshold for suspicion of NF. The mean mortality rate was 26.8%, and was highest in group 3 (5 deaths). The mean amputation rate was 17% (seven patients). **Conclusions:** the LRINEC may facilitate early diagnosis, but as we see in our study its main strength is its ability to assess the severity of the septic process and therefore to provide a prognosis.

Keywords: laboratory risk indicator for necrotizing fasciitis, sepsis, necrotizing fasciitis, surgical debridement, necrosis.

RESUMEN. Introducción: la fascitis necrotizante (NF) es una rara infección de tejidos blandos que conduce a sepsis y muerte sin un tratamiento quirúrgico temprano. La escala LRINEC (*laboratory risk indicator for necrotizing fasciitis*) es una de las pruebas más aceptadas para el diagnóstico. Este estudio presenta una evaluación retrospectiva de la utilidad de la escala LRINEC en el diagnóstico y pronóstico de la NF. **Material y métodos:** estudio retrospectivo de 41 casos de NF en extremidades entre 2010 y 2019. Según la puntuación obtenida en la escala LRINEC los casos fueron asignados a: LRINEC inferior a 5 en el grupo 1 con 12 casos, puntuación 6 o 7 en el grupo 2 también 12 casos, y finalmente puntuación de ocho o más en el grupo 3, 17 casos. **Resultados:** la puntuación media de LRINEC fue de 7.04 (rango: 1-13). Treinta pacientes (73%) tenían puntuaciones superiores a 6, umbral de sospecha de NF. La tasa de mortalidad promedio fue de 26.8%, y fue más alta en el grupo 3 (cinco muertes). La tasa media de amputaciones fue de 17% (siete pacientes). **Conclusiones:** el LRINEC puede facilitar el diagnóstico precoz, pero como vemos en nuestro estudio su principal fortaleza es su capacidad para evaluar la gravedad del proceso séptico y, por tanto, proporcionar un pronóstico.

Palabras clave: indicador de riesgo de laboratorio para fascitis necrotizante, septicemia, fascitis necrotizante, desbridamiento quirúrgico, necrosis.

Level of evidence: III

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Introduction

Necrotizing fasciitis (NF) is a potentially deadly soft tissue infection characterized by necrosis of subcutaneous tissue which progresses rapidly to the skin and muscles and eventually leads to sepsis and death.¹

The condition was first described in 1883 by Fournier, and was initially limited to a specific body area. Meleney later described it as a systemic entity, in 1924, and in 1952 Wilson defined the pathology as necrotizing fasciitis.^{2,3}

The most important prognostic factor of this disease is early diagnosis and surgical treatment, which not only reduces mortality, but also speeds recovery and is associated with the lowest risk of sequelae.⁴ However, in the early stages it is difficult to distinguish NF from cellulitis (*Figure 1*), and so strategies and tests have been designed for early diagnosis of the disease. One of the most widely accepted is the LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis).⁵ This scale indicates the risk of a soft tissue infection being an NF, based on the following biochemical parameters: hemoglobin, glucose, C-reactive protein (CRP), creatinine, serum sodium, and leukocytes.⁶

The method used for the research was a retrospective case series study of the usefulness of the LRINEC scale in the diagnosis and prognosis of NF.

Material and methods

This is a retrospective study of 41 cases of NF in extremities treated in Barcelona (Spain) at our third level



Figure 1: 46-years-old female patient. Pain in leg with erythema and swelling of 12 hours evolution. LRINEC 6. In the early stages it is difficult to distinguish necrotizing fasciitis from cellulitis. LRINEC = laboratory risk indicator for necrotizing fasciitis.

institution between 2010 and 2019. As an observational study, we follow the STROBE guidelines, and the WMA Declaration of Helsinki. Due to the retrospective nature of the study no ethics committee approval was needed, every patient signs a consentment for use of his personal data.

Cases were diagnosed clinically and also by suggestive intraoperative findings such as easy dissection or devascularization of the subcutaneous cell tissue, secretion described as «dishwater pus» (*Figure 2*).⁷ All the cases were finally confirmed by pathology study of an intraoperative biopsy. The histologic diagnosis criteria was superficial fascial necrosis with blood vessels occluded by thrombi. A dense infiltration of neutrophils may be observed in deeper parts of the subcutaneous tissue and fascia. Subcutaneous fat necrosis and vasculitis are also evident. Eccrine glands and ducts may be necrotic.

Exclusion criteria were any other soft tissue infection, Fournier gangrene, suspected NF without a biopsy confirmation, and NF in locations other than the limbs (trunk, abdomen, etcetera).

A total of 70 cases were included, and based on the exclusion criteria, finally 41 cases were accepted, and the following data were compiled: demographic data (age, gender), comorbidities, attendance at the emergency service for the associated primary symptoms and likely entry point. Analytical tests were performed on admission to the emergency service, placing special emphasis on the parameters used in the LRINEC scale (hemoglobin, glucose, CRP, creatinine, serum sodium, and leukocytes). Other parameters recorded were the affected limb, length of time (in hours) from emergency service admission until first surgical debridement, type of initial empirical antibiotic used, number of surgical procedures performed, etiological agent (determined by intraoperative cultures), need for limb amputation, mean length of hospital stay and mortality.

Statistical analysis was performed using SPSS version 23.0 (IBM. New York, USA). The following variables were analyzed: age, associated meniscal injury, gender and time from injury to surgery. χ^2 test and Pearson correlation test were performed for this analysis. The alpha level of statistical significance was established at $p < 0.05$.

Based on the score obtained on the LRINEC scale on admission to emergency service, each case was assigned to one of three groups, based on the original description of Wong et al:⁵

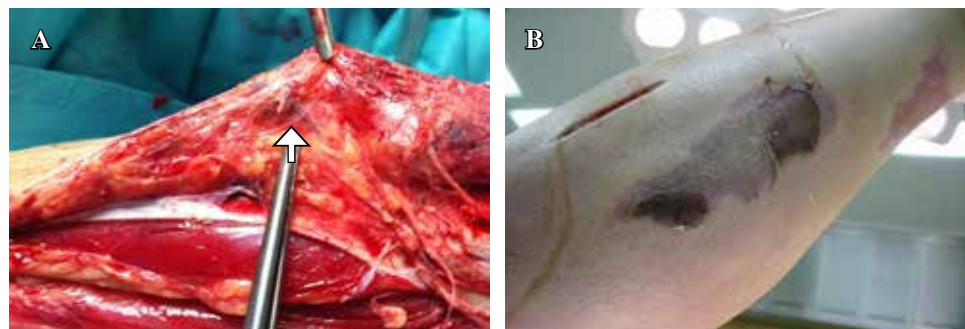


Figure 2:

Intraoperative findings suggestive of necrotizing fasciitis: **A)** Easy dissection, devascularization of the subcutaneous cell tissue, and microthrombosis as see in the image (marked with arrow). **B)** Secretion described as «dishwater pus», with hematic blisters and necrosis.

- Group 1 (low risk) LRINEC score 5 or below.
 Group 2 (medium risk) LRINEC score 6 or 7.
 Group 3 (high risk) LRINEC score 8 or above.

Once diagnosis is suspected empirical antibiotic treatment is started on emergency service. In our series the trend was to start treatment with betalactams or linezolid with aminoglycosides, except in penicillin allergies where clindamycin was used.

Results

Forty-one patients (14 male, 27 female, mean age 53.6 years) were included in the study. The most common initial clinical manifestation was pain and increased limb volume in 29 cases (70.73%). An upper limb was affected in seven cases (17.1%), and a lower limb in 34 (82.9%).

Twenty-nine cases (70%) had comorbidities or associated risk factors, with a mean of two per patient: the most frequent were diabetes mellitus (13 cases), hepatitis C (11 cases), parenteral drug addiction (six cases), and HIV (four cases) (*Table 1*).

Debridement and extensive surgical cleaning were performed in all patients, with the exception of one who died beforehand (40/41). Surgery was performed within 18 hours of admission in 30 cases (73.17%). Patients underwent a mean of three surgical procedures (range: 0-9).

The most frequent type of NF in our series was type II (monomicrobial), with 23 cases. The most frequently identified etiological agent was *Streptococcus pyogenes* (10 cases), followed by *Staphylococcus aureus* and *Escherichia coli* (three cases each). Seventeen patients presented type I (polymicrobial) NF, in which the most frequent combination was a Gram-positive and a Gram-negative agent. In one patient no microbiological agent was identified (*Table 2*).

The mean LRINEC score was 7.04. Thirty patients (72%) had scores above 6, the threshold for suspicion of NF. The sample was classified according to LRINEC score (*Table 2*): group 1 (low risk) with LRINEC scores under 6, included 12 cases (29.26%, mean age 47); group 2 (moderate risk) with LRINEC scores 6 or 7 also included 12 patients (29.26%, mean age 49), and group 3 (high risk) with LRINEC scores of 8 or higher comprised 17 cases (41.46%, mean age 65 years).

The mean mortality rate was 26.82% (11 cases). The mortality rate was highest in group 3 (five deaths, 45.45%), followed by group 2 (four deaths, 33.33%), and finally group 1 (two deaths, 16.66%). Higher LRINEC score is associated with higher mortality, we found a positive correlation (Pearson test) of 0.738.

The mean amputation rate was 17% (seven patients). The highest rate was recorded in group 3, with five cases (29%). Groups 1 and 2 each had one amputation (8.33%). Mean hospital stay was 35.3 days, with means of 28 days in group 1, 55 days in group 2 and 43 days in group 3. Higher LRINEC score is also associated with higher number of amputations, with a positive correlation (Pearson test) of 0.65.

Table 1: Epidemiological characteristics of cases according to laboratory risk indicator for necrotizing fasciitis (LRINEC).

Variable	Group 1	Group 2	Group 3
Number of cases	12	12	17
Mean age (years)	47	49	65
Upper limb (7)	3	2	2
Lower limb (34)	9	10	15
Amputation rate (7)	1	1	5
Deaths, n (%)	2 (16.7)	4 (36.4)	5 (45.4)
Comorbidities, n			
Diabetes mellitus (13)	1	6	6
Arterial hypertension (12)	2	6	4
Chronic renal failure (6)	0	2	4
HIV infection (4)	0	4	0
Liver disease hepatitis C (11)	2	4	5
Malignancy (3)	2	1	0
Rheumatoid arthritis (3)	0	2	1
Anticoagulant treatment (4)	1	2	1
Drug user (6)	2	3	1

HIV = human immunodeficiency virus.

Discussion

The LRINEC scale was designed by Wong CH^{5,8,9} to help to distinguish between NF and other soft tissue infections based on laboratory parameters. A score of 8 on the LRINEC scale is highly suggestive of NF, with a predictive value of 93.4%. Salgado¹⁰ noted that the level of recommendation for the use of the scale is currently IIB (a recommendation with moderate evidence in favor, which is supported by more than one well-designed but non-randomized study).

In this series of 41 patients diagnosed with necrotizing fasciitis (NF) in the limbs, the mean mortality rate was 26%, the mean amputation rate 17% and the mean hospital stay was 35.3 days. Majeski et al, in a classic study¹¹ compared the mortality rate in two groups of patients diagnosed with NF: one group of 20 patients treated between 1965 and 1980, and another group of 10 patients treated between 1980 and 2000. Clinical and epidemiological characteristics were similar, but the mortality rate fell from 50% in the first of these groups to 0% in the second. This improvement in survival was attributed to earlier diagnosis and radical debridement.

In a series of 89 cases of NF between 1997 and 2002, Wong CH⁵ found that the only independent factor associated with higher mortality was a delay of more than 24 hours in performing the surgical debridement.

The mortality rate in our series (26%) is similar to those reported in the literature.^{12,13,14} We attribute this to the fact that in most patients (27 cases, 71%) debridement was performed within 18 hours of emergency admission.

There were no significant differences in amputation rate and mortality related to gender. Deaths and amputations were significantly more frequent in NF in the lower limbs (*Table 1*).

With regard to the LRINEC scale, we observed that 22 cases (53.6%) had scores of 6 or above (high or medium suspicion of NF) and 19 (46.3%) had scores of 5 or below but were indeed NF. A probable explanation for this is that, in developed countries like ours with rapid access to the health system, patients are admitted to the emergency service before the infectious process has developed and so their laboratory parameters do not tend to be greatly altered.

Although it is rare, its mortality rate remains high. The etiology is still not fully understood and cannot be identified in many cases. Therefore we insist that the principal diagnosis of this disease should be based on high clinical suspicion, especially in cases of soft tissue infection in which: a) the pain is intense and difficult to control, b) the infectious process progresses rapidly even with antibiotic treatment (Figure 3), c) the patient presents general malaise or even shock, d) the patient presents risk factors such as immunosuppression or oncological disease; these patients may not show classic signs and symptoms of NF and diagnosis may be delayed, resulting in increased morbidity and mortality.^{14,15,16}

However, the LRINEC scale may be useful as a prognostic marker since it assesses parameters of sepsis. Several studies confirm that cases of NF with initial LRINEC scores of 6 or more have higher mortality and amputation rates and longer mean hospital stay,^{17,18,19} these findings are confirmed by Corbin²⁰ in a prospective study. Our results were similar to those reported elsewhere in the literature, with higher mortality and amputation rates and longer hospital stay with LRINEC scores above 6.

The initial empiric antibiotic therapy should be broad spectrum with coverage for Gram +, Gram - and anaerobics (carbapenems, etcetera). It should be started early and associated with clindamycin, especially if there is suspicion

of *S. pyogenes*. When starting treatment with clindamycin in combination, lower mortality rates in NF due to *S. pyogenes* have been reported,²¹ and now the IDSA (Infectious Diseases Society of America) recommends the use of clindamycin in cases associated with this germ.^{22,23}

The IDSA (Infectious Diseases Society of America) guide²² recommends early radical surgical debridement in NF associated with initial empirical treatment with vancomycin + piperacillin/tazobactam, and, in patients allergic to betalactams, clindamycin or metronidazole associated with an aminoglycoside or a fluoroquinolone. In our series the trend was to start treatment with betalactams; no significant differences in clinical outcome were found using other combinations of antibiotics (linezolid, clindamycin).

Hyperbaric oxygen has been proposed as an adjunctive therapy after surgical debridement for NF.²⁴ The fascia is known to be a relatively hypoxic environment owing to



Figure 3: Case of Figure 1 at 18 hours of evolution. Classical aggressive evolution of a necrotizing fasciitis with association of hematic blisters and necrosis.

Table 2: Associated etiological agents.

Type of necrotizing fasciitis (NF)	Number of cases	Mean LRINEC	Cure (n)	Amputation (n)	Deaths (n)
Type 1 (polymicrobial)	17	11			
Mixture (Gram + & Gram -)	13	12	4	2	8
Only					
Gram +	4	10	3	1	0
Gram -	0	—	—	—	—
Type 2 (monomicrobial)	23	6			
<i>E. coli</i>	3	12	2	0	1
<i>S. pyogenes</i>	10	9	6	2	2
<i>S. pneumoniae</i>	2	6	1	1	0
<i>S. aureus</i>	3	6	2	1	0
<i>S. anginosus</i>	2	5	2	0	0
<i>M. morgagnii</i>	1	3	1	0	0
<i>S. agalactiae</i>	1	2	1	0	0
Not identified*	1	4	1	0	0
Total	41	21	23	7	11

LRINEC = laboratory risk indicator for necrotizing fasciitis.
 * Negative microbiology cultures.

its tenuous blood supply when compared to surrounding muscle or skin. By increasing plasma dissolved oxygen concentration, hyperbaric oxygen is believed to potentially enhance oxygen delivery to hypoxic tissues surrounding areas of necrosis, directly killing anaerobic bacteria and improving leukocyte activity.²⁵ These studies are not compelling to recommend hyperbaric therapy.²⁶

The results of this retrospective, single-center study, need to be verified in prospective, multicenter trials in order to establish the usefulness of the LRINEC scale, but thanks to the tenacity and perseverance of research teams worldwide it is conceivable that biochemical markers facilitating early diagnosis will be found in the near future like procalcitonin,²⁷ and that new imaging study tools may be introduced, some studies have suggested the use of ultrasound in soft tissue in the emergency unit, evaluating for subcutaneous thickening, air, and fascial fluid (STAFF protocol).²⁸ These improvements are oriented towards early surgical debridement so as to enable survivors to resume their daily lives with as few sequelae as possible.

Finally, once NF is diagnosed, early radical surgical debridement should be performed combined with empirical broad spectrum antibiotic treatment. The LRINEC scale can be helpful, but clinical suspicion should remain the main criterion, given that several cases of NF in our series had initial values on the LRINEC scale below 6.

Conclusions

Immediately after NF diagnosis, exhaustive debridement should be carried out, in combination with polymicrobial broad spectrum antibiotic treatment. At present, these are the only tools that have been shown to improve survival.

The LRINEC may facilitate early diagnosis, but as we see in our study its main strength is its ability to assess the severity of the septic process and therefore to provide a prognosis, so our study suggest is correlated with mortality and amputation rate, so is a valuable prognostic tool and must be performed for every patient with any suspected NF.

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