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What are the Alternatives to the LRINEC Score in Identifying Necrotizing Soft Tissue Infections in the Emergency Department?

Ayça Çalbay[1], Atıf Bayramoğlu[2], Erdem Karadeniz[2]
[1] University of Health Sciences, Gülhane Training and Research Hospital, Department of Emergency Medicine, Ankara, Turkey.
[2] Ataturk University Training and Research Hospital, Department of Emergency Medicine, Erzurum, Turkey.

Abstract

Background: The emergency department (ED) is an dynamically high-risk setting. Our aim is to determine the blood parameters associated with necrotizing soft tissue infections (NSTI) to strengthen the LRINEC score.

Materials and methods: We analyzed 109 patients who were diagnosed with necrotizing soft tissue infection in the Urology, Dermatology, Plastic surgery and General Surgery clinics of Atatürk University between 2013 and 2016. In the same period, we matched 624 patients diagnosed with cellulitis as a control group.

Results: Of four defined clinic's records to Atatürk University Hospital in 2013 to 2016, 109 matched and 624 matched control records were abstracted. Diagnoses associated with the NSTIs were: gangrene (n=47), gas gangrene (n=7), Fournier's gangrene (n=44) and necrotizing fasciitis (n=11). In patients with Necrotizing Soft Tissue Infection, BUN (p=0,00), K (0,011), Neutrofil (p=0,013), Lenfosit (p=0,003), Htc (p=0,00), RDW (p=0,002), Plt (p=0,042), AST (p=0,00), ALT (p=0,00) and INR (p=0,003) values were found to be statistically significant in making the diagnosis.

Conclusion: BUN, K, Neutrofil, Lenfosit, Htc, RDW, Plt, AST, ALT and INR values measured from blood tests of patients diagnosed with NSTI can be used in distinctive diagnosis of Soft Tissue Infection (STI). Increased awareness of these values may improve Emergency Department (ED) decision making and prevent miss diagnose.

Keywords: Cellulitis, gas gangrene, laboratory risk indicator for necrotizing fasciitis, LRINEC, necrotising fasciitis.

Introduction

Necrotizing soft tissue infections (NSTI) are bacterial infections caused by necrotic lesions in any layer of soft tissue.[1] NSTIs; Includes Necrotizing Fasciitis, Fournier's Gangrene, Necrotizing Myositis and other necrotizing infections. Identification is made according to the depth of the necrotized tissue and the anatomically involved area. However, this classification is insufficient to guide the treatment. In the diagnosis of emergency department, the surgical layers cannot be differentiated and microbiological factors cannot be determined. Considering the diagnostic possibilities of the clinics and the limitations of intervention, the diagnosis can be made by evaluating the underlying factors and the findings of the patients.

Etiology includes trauma, chronic skin infections, dental infections, postoperative infections, animal and parasite bites, herpes infections and burns.[1] Infection is most common in the extremities and perineum. The most common complaint of patients is pain with erythema and swelling, which can be seen with many diseases and is uncharacteristic for any disease. Within 24-72 hours, redness and gangrene formation associated with septic shock may occur. It has been shown that mortality is affected when the time from the onset of symptoms to surgical intervention is over 24 hours.[2]

The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score has been developed to make the right decision in differentiating it from other serious soft tissue infections that should be considered in the diagnosis.[3] LRINEC score is calculated by hemoglobin, glucose, c-reactive protein, creatinine, sodium and leukocyte count measured from blood tests taken from patients (Table 1). It has been used since 2004. Using routine laboratory blood values, 89.9% sensitivity and 92% positive predictive value make this score an effective diagnostic tool.[3]

The LRINEC score was defined primarily by studying far eastern communities, and studies were conducted on its adequacy in identifying NSTI patients in different ethnic groups. The microorganisms that each society is exposed to differ due to the living conditions of the social environment, the nutritional habits of the people, the percentage of comorbid diseases, and the presence of substance addiction

Corresponding Author: Ayça ÇALBAY **e-mail:** drycshn@gmail.com
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Table 1: LRINEC Score

Parameter	Unit	Score
CRP	mg/dL	
<15		0
≥15		4
WBC	Per mm^3	
<15000		0
15000-25000		1
>25000		2
Hemoglobin	g/dL	
>13,5		0
11.0-13.5		1
<11		2
Na	mmol/L	
≥135		0
<135		2
Creatine	mg/dl	
≤1.6		0
>1.6		2
Glucose	mg/dL	
≤180		0
>180		1

<5 low risk(<50% NF probability), 6-7 medium risk (50-75% NF probability), >8 high risk (>75% NF probability)

and immunodeficiency syndromes that have effects on the immune system. Because of these differences, it was shown in a study conducted in England that the sensitivity of the LRINEC score decreased to 43%.[4] The suspicion that the individual differences of the patients may affect the LRINEC score has led to the development of new diagnostic methods.

NSTI is typically caused by toxin-producing bacteria and the inflammatory response to them. This may cause tissue pathology, systemic toxicity, septic shock, and multiple organ failure.[5] The most common agents in the literature are anaerobes, including gram (+) cocci, gram (-) rod and clostridium species.

Diagnosing whether an infection is necrotizing or not is very important for its treatment and patient prognosis. The diagnosis of NSTI should be made early and quickly, and the need for broad-spectrum antibiotics should be determined with recurrent surgical debridements. Hemodynamic support therapy and iv immunoglobulin and hyperbaric oxygen therapy are among the other treatment options that can be evaluated in intensive care units.[6,7]

In our study, we searched an alternative diagnostic method to the LRINEC score in differentiating patients diagnosed with NSTI from other soft tissue infections. We searched for parameters that would increase the sensitivity of the LRINEC score in differential diagnosis. Thus, we wanted to prevent misdiagnosis or missed diagnosis in emergency departments with high patient density and circulation.

Materials and Methods

Study design

We conducted a matched retrospective case-control study of patients older than 18 years who had diagnosed with selulitis or necrotising soft tissue infection like gangrene, gas gangrene, necrotising fasciitis and Fournier gangrene. Study approval was obtained from the coordinating center's Institutional Review Board with waiver of informed consent (Meeting Number: 1 Desicion Number: 24 Date: 04.01.2018).

Settings

Patients were selected from the dermatology, urology, general surgery and plastic surgery clinics between 01.01.2013 and 31.12.2016. The diagnosis of the selected patients was made by residents and specialist doctors who provided patient care in the relevant clinics. The diagnosis of the patients was determined by the examination, lab tests and biopsy materials taken.

Selection of Participants

After marking the ICD codes (L03, N 49.3, A48.0, M72.5, L08.8) suitable for the diagnoses, the cases and control group were reached from the hospital data processing center. Patients with gangrene (n=47), gas gangrene (n=7), necrotizing fasciitis (n=11) and Fournier's gangrene (n=44) constituted our case group with necrotizing soft tissue infections. Patients diagnosed with cellulitis (n=624) constituted the control group, which was chosen to represent soft tissue infection. The blood tests in the electronic file record were examined to see the results of the current status of the cases and the control group on blood values.

We examined standard complete blood count, biochemistry, C-Reactive Protein (CRP) and Sedimentation (ESR) values from laboratory tests applied to case and control groups.

Among the sample, 400 patients were excluded because of missing data (CRP, WBC, Sedim, AST, ALT, INR) and 14 patients were under 18 years of age. As a result, 733 patients were included in the study (Figure 1).

Our sample size was determined by the total number of patients diagnosed with gangrene, gas gangrene, Fournier's gangrene, and Necrotizing fasciitis in the Urology, General surgery, Plastic surgery, and Dermatology clinics and obtained through electronic medical review during a 36-month enrollment period. According to historical data, a total of 733 patients were encountered during this time, with 624 case-control designs.

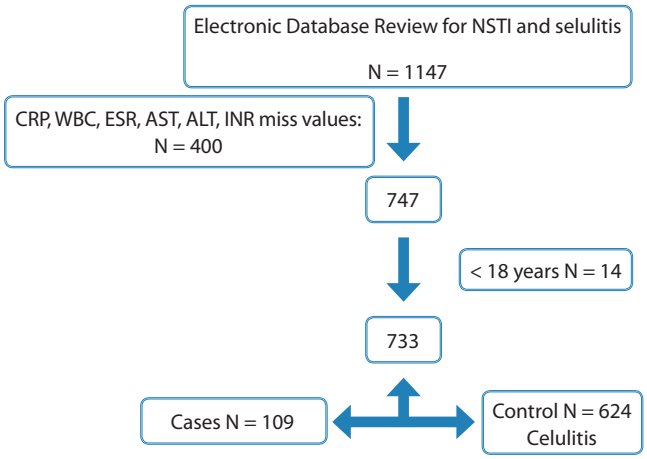

Figure 1: Summary diagram for case-control enrollment.

Methods of Measurement

The LRINEC score is calculated from hemoglobin, glucose, c-reactive protein, creatinine, sodium, and leukocyte counts measured from blood tests from patients. As it is known, it is used to distinguish necrotizing fasciitis from other soft tissue infections.

Fournier's gangrene severity index (FGSI) was first defined in 1995.[8] It is calculated using some clinical and laboratory parameters. These are: body temperature, pulse, respiratory rate, serum sodium-potassium-creatinine levels, hematocrit (%) level, white blood cell count (total/mm3 × 1000) and serum venous bicarbonate level (mmol/l).

In a retrospective study conducted by Ozan Bozkurt et al., the capacity to determine mortality and morbidity was evaluated with three different scoring systems such as FGSI, LRINEC and neutrophile–lym-phocyte ratio (NLR).[9]

Studies have shown that liver and kidney functions are impaired due to multi-organ failure and sepsis in necrotizing soft tissue infections. Accordingly, an increase in coagulopathy values, especially AST, ALT values and serum creatine kinase values was observed.

In the light of all these studies, we compared the blood parameters, kidney function values, liver enzymes and infection markers measured from the complete blood count of the patients in our study. Chronic disease diagnoses, x-ray, ultrasound, computed tomography or magnetic resonance images of the patients could not be accessed due to the loss of data in patients files.

Statistical Analysis

Statistical analysis of the study was performed with SPSS Version 21.0 program (SPSS Inc, Chicago, Illinois, USA). Percentage frequency analysis was performed for demographic characteristics such as gender. For numerical data, CBC parameters, biochemical tests, PT INR, Sedim and LRINEC Score mean ± standard deviation minimum and maximum were calculated (Table 2).

The diagnosis order and number of patients participating in the study were as follows: cellulitis: 624, gangrene: 47, gas gangrene: 7, necrotizing fasciitis: 11, Fournier's gangrene: 44 patients. We collected four diagnoses of necrotizing soft tissue infection in one group. These 109 patients diagnosed with NSTI formed the case group of our study. The control group consists of 624 patients with the diagnosis of cellulitis.

Kolmogorov-Smirnov test was performed to determine the distribution of analyzed blood parameters. Independent t-test (Table 2), which is one of the parametric tests, was used for the analysis of normally distributed parameters, and Mann Whitney U Test was used for those with non-normal distribution (Table 2). p-values less than 0.05 were considered as statistically significant.

Results

During the three-year period determined for the study, 1147 patients diagnosed with cellulite, gangrene, gas gangrene, necrotizing fasciitis and Fournier's gangrene were reached. Of these, 400 were excluded because of missing data (CRP, WBC, Sedim, AST, ALT, INR) and 14 because they were under the age of 18. As a result, 733 patients were included in the study. The diagnosis order and number of patients participating in the study were as follows: cellulitis: 624, gangrene: 47, gas gangrene: 7, necrotizing fasciitis: 11, Fournier's gangrene: 44 patients.

BUN (p=0.00), K (p=0.011), Neutrophil (p=0.013), Lymphocyte (p=0.003), Htc (p=0.00), RDW (p=0.002), Plt (p=0.042), AST (p=0.00), ALT (p=0.00) and INR (p=0.003) values which are not parameters of the LRINEC score were found to be statistically significant in diagnosing (Table 2). Glucose (p=0.013), Na (p=0.00), Creatine (p=0.023), WBC (p=0.001), Hb (p=0.000) and CRP (p=0.012) values, which are among the LRINEC score parameters, were also statistically significant (Table 2).

In our study, increases in AST and ALT values were observed in a total of 109 patients with necrotizing soft tissue infections. This increase was 64.18±28.64U/L for ALT with the highest mean. It was observed that this ALT value lagged behind the AST measurement with a mean value of 114.98±66.99U/L.

The mean BUN value for the NSTI was 25.28±2.25 mg/dl. In patients with cellulitis, the mean was 20.40±1.49 mg/dl.

In our study, CRP values were >360 mg/dl for both groups, and the mean was 415.80 mg/dl in the Case group (p=0.012).

While the mean value of the LRINEC test used in differential diagnosis was 1.84±0.22 in the control group, it was 3.01±0.27 in the case group.

Table 2: Mean, SD, 95%CI for mean of the labaratory results of patients with NSTI (Necrotising Soft Tissue Infection) and control patients with cellulitis at admission, t-z-p values

Parametre	Normal Values	Unit	Cellulitis		%95 CI			NSTI		%95 CI			
			N	Mean±SD	Lower	Upper	t,Z	N	Mean±SD	Lower	Upper	t, Z	P value
Na	135-145	mmol/L	627	136,9±3,76	-0,87	,75000	-,151	109	136,96±5,13	-1,07000	0,95	-,122	,000
Cr	0,66-1,09	mg/dl	627	0,98±0,08	-,27074	,07000	-1,120	109	1,08±0,09	-,28000	,08000	-1,047	,023
BUN	17-43	mg/dl	624	20,40±1,49	-7,80446	-1,95000	-3,272	109	25,28±2,25	-9,34000	-,40000	-2,161	,000
AST	15-35	U/L	622	29,37±28,01	-140,60199	-30,60000	-3,056	109	114,98±66,99	-218,39532	######	-1,278	,000
Glc	74-110	mg/dl	627	129,07±7,75	-28,77908	1,66000	-1,748	109	142,63±9,21	-31,78000	4,66000	-1,471	,013
ALT	7,0-35	U/L	618	28,30±12,34	-60,11978	-11,64000	-2,906	109	64,18±28,64	-92,66000	######	-1,252	,000
LRINEC	0		627	1,84±0,22	-1,621	-,730	-5,216	109	3,01±0,27	-1,710	-,640	-4,336	,000
WBC	4,4-10,9	10^3cells/uL	627	357,93			-3,234	109	429,29				,010
Hb	11,9-14,6	g/dL	627	386,13			-5,398	109	267,06				,000
CRP	0-5	Mg/L	627	360,28			-2,516	109	415,80				,012
K	3.5-5.5	mmol/L	627	376,84			-2,554	109	320,50				,011
Neu	2,1-8,8	10^3cells/uL	281	151,81			-2,478	30	194,67				0,013
Leu	4,0-11	10^3cells/uL	595	361,05			-2,976	105	297,20				,030
Htc	36,3-44	%	627	385,83			-5,302	109	268,84				,000
RDW	%11.6-%14.6	%	627	358,50			-3,060	109	426,00				,002
Plt	150-400	10^3cells/uL	627	361,86			-2,031	109	406,68				,042
INR	0.8-1.1		331	202,6			-3,001	92	245,82				0,003

(Na, sodium; K, potassium; BUN, Blood Urea Nitrogen; BUN; AST, Aspartat Aminotransferaz; ALT, Alanin aminotransferaz; Cr, creatine; Glc,glucose; WBC, White blood cell; Ne, neutrofile; Leu, Leucosite; Plt, Platelet Count Test; Hb, hemoglobine; Htc, hemotocrite; RDW, red cell distribution width; ESR, eritrosite sedimentation rate; CRP, C-reactive proteine; LRINEC, laboratory risk indicator for necrotising fasciitis; CI, confidence interval)

Discussion

In this case-control study, in which laboratory tests that can be used to differentiate necrotizing soft tissue infections from other soft tissue infections were sought, we determined that Neutrophil, Lymphocyte, Htc, RDW, Plt, BUN, K, AST, ALT and INR values were statistically significant in the diagnosis in addition to the LRINEC score parameters. Our study was repeated with statistics that Na, Creatine, Glucose, WBC, Hb and CRP values were differential in the diagnosis of cases in parallel with the LRINEC score.

If sepsis and MODS develop in necrotizing soft tissue infections, liver and kidney functions will be affected. The expected increase in laboratory values from these markers was observed in our study in parallel with other studies. In some studies, ALT value increased more than AST value, while in our study, the increase in AST values was higher. While the mean BUN value was >18 mg/dl in other studies[10], it was above 19 mg/dl in our cases. In the studies scanned in the literature to date, no data has been found that BUN value measurements can be diagnostic for NSTI. Our study is the first study to contribute to the literature in this context.

An increase in WBC value in all groups as an indicator of infection was an expected result. The increase in Neutrophile and Leucosite values with Wbc may be due to the effect of multifactorial agents.

One of the important results of our study is that Htc, RDW, Plt, Neutrophile, Leucosite values obtained from complete blood count can be used to differentiate NSTI cases from the control group. In our study, it has been shown that the Htc value is valuable in diagnosing, as in the study of FGSI and Ozan Bozkurt et al. Although there is no study about the prognostic Plt value when the literature is scanned, there are data showing that high Plt values are associated with mortality.[11]

CRP value, one of the evaluated parameters, can give an idea about the follow-up and progression of NSTIs. In a retrospective study by Moore et al. on 134 patients, CRP levels were shown to be highly correlated with mortality.[12] In a study by Kincius et al., it was shown that the basal CRP level of 41 patients with Fournier's gangrene was higher in those who did not survive.[13] In some studies, it has been stated that increased serum creatinine, sodium and lactate levels are proportional to the increase in mortality, but the same relationship cannot be said for CRP.[14,15] In our study, the mean CRP value was measured as 415.80 Mg/L in the case group. This study does not contribute to the effect of CRP value, which is expected to increase proportionally with infection, on prognosis.

When the studies carried out to date are examined, no data has been found that AST, ALT, RDW, Plt and INR values can be used to differentiate NSTI and cellulitis cases. Our study is the first with its contribution to this evaluation.

Other methods that can be used for early diagnosis of NSTI are radiological imaging methods. It is important to observe gas in the tissue on direct radiographs, and the presence of bullae and crepitation on examination. Computed tomography (CT), which is available in many emergency departments and is easily accessible, is more useful than plain radiographs. On CT, an increase in adipose tissue and thinning of the fascia can be seen in the affected area. It shows edema in soft tissue better than direct radiographs. The sensitivity of magnetic resonance (MR) imaging is high in terms of necrotizing fasciitis (93-100%).[16] Tissue necrosis and inflammatory edema cause abnormal signal increase on T2-weighted images. On T1-weighted images, edema and necrosis create variable signal intensity throughout the weakened deep fascia tissue.[17] The gold standard diagnosis is made with amputated tissue in surgery.

As a conclusion the most important step in the diagnosis of NSTI patients is awareness. Patients' histories, predisposing factors, clinical symptoms and diagnostic parameters are red flags that guide treatment. In clinics where patient density and circulation are fast, it is necessary to minimize the risk of missing these diagnoses, which have a serious impact on prognosis and mortality. Effective diagnostic methods should be used in emergency department in order to speed up the diagnosis process of patients and shorten the access time to treatment. BUN, K, Neutrophil, Lymphocyte, Htc, RDW, Plt, AST, ALT and INR values were observed to be statistically significant in line with the data we obtained in our study. It should be remembered that these parameters can be used in addition to the LRINEC score parameters. In this patient group, where delayed treatment and intervention increase mortality, evaluations with high diagnostic value should be kept in mind.

Limitations

Our study has limitations. First of all, as in every retrospective study, the deficiencies in the data scanned backwards decreased the number of cases in our study. Second, Incomplete blood tests from the cases prevented some cases from being included in the study. Third, the fact that the groups were evaluated with blood values and biopsy results caused the patients to be taken from clinics other than the emergency department. For the same reason, necrotizing soft tissue infection patients and cellulitis patients diagnosed in the emergency department were not included in the study. Fourth, the absence of vital signs in the electronic files of the case and control groups prevented us from interpreting according to FGSI. Fifth, since the discharge status and short-term (1 week) follow-up of the patients included in the study could not be performed, so that no comment could be made regarding the contribution of the evaluation to the prognosis.

References

1. Çalbay A. (2019). Ortopedik Aciller pp 341-349, Ankara: Akademisyen Kitapevi ISBN: 978-605-258-394-4.
2. Liu Y-M, Chi C-Y, Ho M-W et al. Microbiology and factors affecting mortality in necrotizing fasciitis. J Microbiol Immunol Infect. 2005 Dec;38(6):430–5.
3. Wong C-H, Khin L-W, Heng K-S, Tan K-C, Low C-O. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med. 2004 Jul;32(7):1535–41.
4. Al-Hindawi A1, McGhee J2, Lockey J1, Vizcaychipi M1.Validation of the laboratory risk indicator for necrotising fasciitis scoring system (LRINEC) in a Northern European population. J Plast Reconstr Aesthet Surg. 2017 Jan;70(1):141-143.
5. Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. J Hosp Infect. 2010 Aug;75(4):249–57.
6. Hakkarainen TW, Kopari NM, Pham TN, Evans HL. Necrotizing soft tissue infections: review and current concepts in treatment, systems of care, and outcomes. Curr Probl Surg. 2014 Aug;51(8):344–62.
7. Hussein QA, Anaya DA. Necrotizing soft tissue infections. Crit Care Clin. 2013 Oct;29(4):795–806.
8. Laor E, Palmer LS, Tolia BM, Reid RE, Winter HI (1995) Outcome prediction in patients with Fournier's gangrene. J Urol 154(1):89–92.
9. Bozkurt O, Sen V, Demir O, Esen A.Evaluation of the utility of different scoring systems (FGSI, LRINEC and NLR) in the management of Fournier's gangrene. Int Urol Nephrol. 2015 Feb;47(2):243-8.
10. Taro Shimizu 1, Yasuharu Tokuda. Necrotizing fasciitis. Intern Med. 2010;49(12):1051-7.
11. Sung Jin Park, Dong Heon Kim , Chang In Choi , Sung Pil Yun , Jae Hun Kim , Hyung Il Seo. Necrotizing soft tissue infection: analysis of the factors related to mortality in 30 cases of a single institution for 5 years. Ann Surg Treat Res. 2016 Jul;91(1):45-50.
12. Moore SA, Levy BH, Prematilake C, Dissanaike S. The Prediction Predicament: Rethinking Necrotizing Soft Tissue Infections Mortality. Surg Infect (Larchmt). 2015 Aug 10;10.1089/sur.2015.002 [Epub ahead of print].
13. Kincius M, Telksnys T, Trumbeckas D, Jievaltas M, Milonas D. Evaluation of LRINEC Scale Feasibility for Predicting Outcomes of Fournier Gangrene. Surg Infect (Larchmt). 2016 Mar 29.
14. Krieg A, Dizdar L, Verde PE, Knoefel WT. Predictors of mortality for necrotizing soft-tissue infections: a retrospective analysis of 64 cases. Langenbecks Arch Surg.2014 Mar;399(3):333–41.
15. Keeley J, Kaji A, Kim D, et al. Predictors of mortality in necrotizing soft tissue infection.Am Surg. 2014 Oct;80(10):989–93.
16. Young MH, Aronoff DM, Engleberg NC. Necrotizing fasciitis: pathogenesis and treatment. Expert Rev Anti Infect Ther. 2005 Apr;3(2):279–94.
17. Fugitt JB, Puckett ML, Quigley MM, Kerr SM. Necrotizing fasiitis, Radiographics 2004; 24: 1472-1476.