# Are neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as effective as Fournier's gangrene severity index for predicting the number of debridements in Fourner's gangrene?

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# ABSTRACT

**BACKGROUND:** Fournier's gangrene (FG) is a rapidly progressive and necrotizing infection of the subcutaneous and fascial tissues with a high mortality rate. In the present study, we aimed to investigate prognostic factors and analyze the outcomes of 68 patients in a tertiary reference hospital.

**METHODS:** Patients admitted to the emergency department were investigated retrospectively between January 2006 and January 2013 and divided into two groups. The patients in Group I (G1) required one debridement, and Group II (G2) patients required more than one. Patient demographic and clinical characteristics were encoded. Fournier's Gangrene Severity Index (FGSI) scores, neutrophillymphocyte ratios (NLR), and platelet-lymphocyte ratios (PLR) were calculated. Prognostic factors were compared between the groups.

**RESULTS:** There were no statistically significant differences between the groups in terms of mean age, female-male ratio, or duration of symptoms on admission; however, there were more infection sources, predisposal factors, and positive culture results in G2. Additionally, hospital stay, total cost, and mortality rate values were high in G2. We found statistically higher NLR and PLR ratios in G2, but there was no significant difference in FGSI scores between the groups.

**CONCLUSION:** The FGSI scoring system was not found to be valuable in determining prognosis. However, NLR and PLR were valuable, and previous use of NLR and PLR for determining Fournier's gangrene prognosis could not be found in the English literature. **Key words:** Fournier's gangrene; neutrophil-lymphocyte ratio; platelet-lymphocyte ratio; prognostic factor.

### **INTRODUCTION**

Fournier's gangrene (FG) is an acute and rapidly progressive polymicrobial inflammatory process. Generally known as necrotizing fasciitis, it affects the subcutaneous and fascial structures on perianal, perineal, and/or genitourinary regions.<sup>[1]</sup> It is named for Jean Alfred Fournier, a Parisian

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Copyright 2014 TJTES dermatologist and venereologist. He presented a young man with perineal gangrene in a lecture in 1883. However, Bourienne in 1764 and Avicenna in 1877 originally described the same disease.<sup>[2]</sup> The main principals of therapy are aggressive debridement, effective antibiotic use, and supportive drugs. Unfortunately, FG still has a high mortality rate despite advances in antimicrobial drugs, surgical techniques, and intensive care facilities. In the largest series, the mortality rate was reported as 16-30%.<sup>[2-5]</sup> The disease predominantly affects adult males but also occurs in females and at every age, even in children with similar patterns.[6-8] There have been many efforts to find valuable prognostic criteria in the literature.<sup>[9-11]</sup> However, we did not find use of the neutrophil-lymphocyte ratio (NLR) and the platelet-lymphocyte ratio (PLR) in the English literature. We aimed to investigate the factors affecting the number of debridements, mortality rate, and cost, as well as the relationship between NLR, PLR, and prognosis.

### MATERIALS AND METHODS

After the approval of the local institution's ethics committee, patients admitted to the emergency department were investigated retrospectively between January 2006 and January 2013. The patients had perineal, genitourinary, or perianal symptoms, such as pain, swelling, and discharge, and were diagnosed with FG and operated on after general surgery consultations. The study hospital, a tertiary referral center, is considered the top site for trauma and emergency surgery in the city. After admission, patients' oral intake was stopped and intravenous fluids, proper broad spectrum antibiotics, and other supportive additives were administered. Serious cases were transferred to the intensive care unit, where medicalsurgical interventions were performed. All of the patients' operations were performed by one of five surgeons who had been working together since 1992 and had been educated with the same surgical notion.

Information was missing from the files of nine patients, so they were excluded from the study. For the 68 patients included in the study, full background information was obtained from the hospital database. Age, gender, origin of the infection, duration between the beginning of the symptoms and admission, and predisposal factors, such as diabetes mellitus, number of debridements, need for protective ostomy, bacteriologic results of wound cultures, routine laboratory test results, NLRs, PLRs, Fournier Gangrene Severity Index (FGSI) scores on admission, mortality rates, and total costs, were encoded. The patients were divided into two groups: Group I (G1) included patients who needed one debridement, and Group II (G2) included patients who needed more than one. Wound and tissue cultures were obtained surgically from each patient.

# **Statistical Analysis**

Data analysis was performed using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, United States). The Shapiro Wilk test was used to test the distributions of continuous variables for normality. Descriptive statistics for continuous data are shown as mean ± standard deviation or median (minimummaximum), as applicable. Categorical data are shown as numbers and percentiles. The differences between groups were compared using Student's t test for means and the Mann-Whitney U-test for medians. Categorical data were analyzed using Pearson's chi-square or Fisher's exact test, as appropriate. Degrees of association among continuous variables were evaluated using Spearman's Correlation analysis. A p value less than 0.05 was considered statistically significant. The cut-off values of parameters for discrimination between the groups were determined using ROC analysis. For each value, the sensitivity and specificity for each outcome under study.

# RESULTS

The mean age and standard deviation of the 68 patients were

53.13±15.36 years, and the female-to-male ratio was 5:12. There were 15 (22.06%) patients older than 65 who were categorized in the geriatric patient group. From admission, the mean duration of symptoms was 5.93±4.54 days. Infection sources were identified in 18 (26.47%) cases. There were 10 perianal abscesses and fistulas, one rectal malignancy, four anorectal injuries, two urogenital infections, and one gynecological operation in the patient series (Table 1). Predisposal factors included 22 (32.35%) patients with a diabetes mellitus (DM) history and one patient with an immunosuppressant condition due to chemotherapy. Wound and tissue cultures were positive for only 20 (29.41%) patients. Thirteen Escherichia coli sources, 4 Acinetobacter sources, 2 methicillin resistant Staphylococcus aureus (MRSA) sources, and I Candida source were found (Table 2). One patient required orchiectomy and penectomy, and two patients were treated with vacuum-assisted devices (VAC) in addition to debridement. Debridement of the skin, subcutaneous tissue, and superficial fascia was performed in 33 (48.53%) patients, but 35 (51.47%) cases underwent debridement of deeper tissue. Fifteen (22.06%) patients required colostomy for wound protection from fecal material. The procedure was performed at the time of first debridement for each patient. The mean cost was 8376±9627 Turkish Liras (TL) per patient. Five patients in G2 died; the mortality rate was 7.35%. The mean age of the five patients was  $60.2 \pm 19.07$  years, and the mean age of the surviving patients was 52.57±15.07 years. The difference

 Table I.
 Origins of infection in Fournier's gangrene cases

None	50
Perianal abscesses – fistula	10
Rectal cancer	I
Anorectal injury	4
Urogenital infection	2
Gynecological operation	I
Total	68

Table	2.	Culture	results

lsolated and produced types of microorganisms	Number of cultures	
None	48	
Escherichia coli	13	
Acinetobacter	4	
Methicillin resistant Staphylococcus aureus	2	
(MRSA)		
Candida	L	
Total	68	

Patient characteristics	n	%	Mean±SD
Patients (total number)	68		
Female/male ratio	20/48	42	
Mean age (years)			53.13±15.36
Geriatric patients (older than 65 years)	15	22	
Patients with known sources	18	27	
Patients with diabetes mellitus histories	22	32	
Patients with positive cultures	20	29	
Mean hospital stay (days)			15.37±14.05
Mean cost (Turkish Lira)			8376±9627
Mortality rate	5/68	7	

 Table 4.
 Comparison of parameters between group I (only one debridement) and group II (more than one debridement)

Parameter	Group I	Group II	Þ
Number of patients	27	41	
Female/male ratio	6/21	14/27	0.291
Mean age (years)	51.33±16.05	54.32±14.96	0.437
Patients with known sources	3	15	0.020
Patients with diabetes mellitus histories	4	18	0.012
Mean duration of symptoms (days)	6.33±3.60	5.66±5.10	0.128
Positive cultures	3	17	0.007
Mean hospital stay (days)	6.78±6.71	21.02±14.79	<0.001
Mean cost (Turkish lira)	3502.93±3337.32	585.7 ±  0 9.69	<0.001
Mean Fournier Severity Index Score	2.22±1.58	3.07±2.18	0.121
Neutrophil-lymphocyte ratio	7.69±10.63	14.48±9.30	<0.001
Platelet-lymphocyte ratio	182.45±162.68	304.44±200.82	<0.001

was not statistically significant (p=0.288). Patient characteristics are shown in Table 3.

In G1 and G2, the female-to-male ratios were 2:7 and 14:27, respectively, and there was no statistical difference between the groups (p=0.291). The mean ages were  $51.33\pm16.05$  years and  $54.32\pm14.96$  years, respectively, a difference that was not significant (p=0.437). DM history was detected in 4 of 27 patients in G1 and in 18 of 41 patients in G2, a statistically significant difference (p=0.012). In G2, the source of infection was apparent in a significantly higher number of patients (p=0.020). Positive culture ratios were high in G2 (p=0.007). There was no significant difference between the groups in duration of symptoms on admission (p=0.128). FGSIs were higher in G2 than in G1, but there was no statistically significant difference between the groups (p=0.121). G2 patients

had longer hospital stays and higher health expenditures (p values <0.001; Table 4).

To predict debridement numbers, the NLRs and PLRs were calculated; the ratios were statistically higher in G2 compared to G1 (p<0.001). Cut-off values were calculated using ROC curve analysis for NLR and PLR, and were 8.595 and 198.1, respectively. Sensitivity, specificity, positive predictive value, and negative predictive value for NLR were 70.73%, 70.37%, 78.38%, and 61.29%, respectively. The same values for PLR were 75.61%, 74.07%, 81.85%, and 66.67%, respectively. Higher NLR and PLR values were significantly associated with higher fecal ostomy rate (p=0.002 and p=0.038, respectively). Culture positive patients had significantly higher NLR and PLR levels than culture negative cases on admission (p=0.001 and p=0.022, respectively). FGSI scores

and the need for preventive ostomy were not statistically correlated (p=0.234).

# DISCUSSION

Fournier's gangrene is an aggressive clinical condition that affects subcutaneous and fascial tissues on perianal, perineal, and/or genitourinary areas and causes severe necrosis. Fournier's gangrene has been known since the 18th century. The disease may affect all ages and both genders but predominantly strikes adult males.<sup>[1-3]</sup> In our series, there were 68 patients with a median age of 53 years, 58% of whom were male and 22% of whom were older than 65 years. Old age itself is not a predisposing factor, but those with poor self-care and poor nutritional status are more susceptible to the disease and have a poor prognosis.<sup>[12]</sup> In the present study, no difference in prognosis was observed in the older patient group. Five patients died during the study. The mean age of these patients was higher than of the survived patients, but the difference was not statistically significant because the number who died was small (p=0.288).

The characteristic feature of the disease is polymicrobial and synergistic infection. Pathophysiology is probably triggered with endarteritis obliterans and microthrombosis of small vessels in the subcutaneous tissues.<sup>[13,14]</sup> Collagenase and heparinase produced by anaerobes, combined with platelet aggregation and complement fixation induced by aerobes, causes microvascular thrombosis with subsequent dermal necrosis. Hyaluronidase, streptokinase, and streptodornase produced by *Streptococcus* and *Staphylococcus* contribute to tissue damage.<sup>[6]</sup> Our study was limited by the lower rate of culture positive patients. Surgery under emergency conditions and the necessity of beginning broad spectrum antibiotics early without first being able to obtain a culture were the probable reasons. Microorganisms were produced in 20 (29.41%) cases, the majority of which were *E. coli*.

The clinical presentation of Fournier's gangrene changes from obscure onset and slow progression to rapid onset and fulminant course. Tissue necrosis can progress as fast as 2 cm per hour.<sup>[13,15,16]</sup> Thus, early intervention is very important and life-saving. Our mortality rate (7%) was lower than the literature average of 16-30%.<sup>[2-5]</sup> Our hospital is an accepted trauma and urgent surgery tertiary care center. Patients who apply under urgent conditions and are found to have indications for urgent operation immediately undergo surgery.

Depending upon the degree of progression, the skin may be normal, red, or shiny in appearance or may show evidence of ecchymosis, crepitus, or gangrene.<sup>[17]</sup> The spread of infection is along the fascial planes and is usually limited by the attachment of the Colles' fascia in the perineum. Deeper infection that extends below the fascial layers causing myonecrosis is not generally thought of as classical Fournier's gangrene, although it has been described. When performing debridement, care must be taken not to accidentally open deeper fascial planes that were not initially involved.<sup>[2,4]</sup> In our series, debridement was performed at the skin, subcutaneous tissue, and superficial fascia level in 33 (48.53%) patients but deeper in 35 (51.47%) cases.

Testicular involvement is rare in FG. Testicles are usually spared as their blood supplies originate intra-abdominally. Testicular involvement indicates retroperitoneal origin or spread of infection.<sup>[2,4]</sup> We had only one case that required orchiectomy and penectomy. Usually scrotal skin and subcutaneous tissues over the testes are excised during the debridement procedure, and testes are placed into the inguinal subcutaneous areas after healing.<sup>[14]</sup>

Initially, FG was defined as an idiopathic entity, but the sources of infection are known in the vast majority of cases today. In most series, they are categorized into four groups to determine origin: anorectal, genitourinary, dermatologic, and idiopathic.<sup>[2,4,15]</sup> In our series, there were 15 anorectal and 3 genitourinary origins. Many predisposal factors have been documented in the literature. DM is the most mentioned factor, affecting up to 70% of patients in a series. Alcohol abuse, smoking, and immunocompromised status have also been reported.<sup>[6,18]</sup> Hyperglycemia has been found to affect adherence, chemotaxis, and bactericidal activities of phagocytes. It has also been shown to have detrimental effects on cellular immunity.<sup>[14,18]</sup> In the present series, there were 22 (32.35%) diabetic patients and one immunosuppressed patient, due to chemotherapy.

Fecal and/or urinary diversion procedures should be undertaken for prevention against additional contamination of debridement areas. In a study of 37 patients with FG of the anorectal region, a preventive colostomy was found necessary for 19 patients.<sup>[18]</sup> Special silicone catheters, such as the Flexi-seal<sup>®</sup> Fecal Management System (FMS, ConvaTec, USA), can be used for this purpose.<sup>[4]</sup> Fifteen (22.06%) of our patients required colostomy, and the procedure was performed during the first debridement.

Currently, VAC devices are widely used in FG cases. VAC devices support the reduction of edema and can increase fibroblast migration and cell proliferation, improving clinical outcome.<sup>[2,4,17]</sup> In the current study, this technique was used in two cases. In addition, topical wound care agents, such as honey and hyperbaric oxygen therapy, are among more recent alternatives.<sup>[17]</sup> We have had no experience with honey or hyperbaric oxygen.

The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) is a robust laboratory measurement score capable of determining even clinically early cases of necrotizing fasciitis.<sup>[9]</sup> FGSI scores were determined according to the Acute Physiology and Chronic Health Evaluation score (APACHE II) developed by Laor and colleagues in 1995.<sup>[10]</sup> They reported that a severity index above 9 indicates a 75% mortality probability, while a score under 9 indicates a 78% survival probability. This scoring system is widely used in the literature, and there are many studies supporting these results.<sup>[13-15,19]</sup> However, a study by Sallami et al. reported the opposite results.<sup>[20]</sup> Yilmazlar et al.<sup>[11]</sup> modified this scoring system and added two parameters: dissemination degree and age scores. In a study of 36 cases, the factors affecting the number of debridements in FG were investigated. The study found no significant differences between the clinical data of patients who required single and multiple debridement sessions; however, FGSI was found to be useful in deciding on repeated procedures.<sup>[16]</sup> In the present study, original FGSI scores were used. Patients were divided into two groups, and the multiple debridement group was determined to have higher FGSI scores than the single debridement group. Similar correlations between FGSI scores and hospital stay durations, and between FGSI scores and total expenditures were also found. The five patients who died had higher FGSI scores than those who survived.

NLR and PLR were used to predict the prognoses of patients with different inflammatory and ischemic events in the literature.<sup>[21-23]</sup> However, we did not find use of these parameters for determining prognosis in cases of FG in the English literature. In our study, we identified strong correlations between these parameters and the prognosis of the disease. High NLR and PLR values were associated with statistically significant increases in the number of debridements, hospital stay duration, cost, and mortality rate.

#### Conclusion

FG is still a disease with a high rate of mortality. Early and effective treatment is as essential as early diagnosis. Estimation of poor prognosis is possible with calculated FGSI scores and NLR and PLR values. If these values are found to be high, it is possible to inform the patient and relatives about clinical course and outcome.

Conflict of interest: None declared.

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#### KLİNİK ÇALIŞMA - ÖZET

# Fournier gangreninde debridman sayısını öngörmede nötrofil lenfosit oranı ve trombosit lenfosit oranı Fournier gangreni şiddet indeksi kadar etkili midir?

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AMAÇ: Fournier gangreni (FG) ciltaltı ve fasial dokuların hızlı seyirli, nekrotizan ve ölümcül enfeksiyöz bir hastalığıdır. Bu çalışmada, tersiyer bir referans hastanesinde 68 hastaya ait prognostik faktörleri ve tedavi sonuçlarını irdelemeyi amaçladık.

GEREÇ VE YÖNTEM: Ocak 2006 ve Ocak 2013 tarihleri arasında acil servise başvuran hastalar iki gruba ayrıldı ve geriye dönük olarak incelendi. Grup I'deki (G1) hastalar bir debridman gereksimi duyanlar ve Grup II'deki (G2) hastalar birden fazla debridman gereksinimi olanlardı. Demografik ve klinik özellikler kaydedildi. Fournier gangreni şiddet indeksi (FGSI) puanları, nötrofil-lenfosit oranları (NLO) ve trombosit-lenfosit oranları (TLO) hesaplandı. Prognostik faktörler gruplar arasında karşılaştırıldı.

BULGULAR: Gruplar arasında yaş ortalaması, kadın-erkek oranı, başvuru anındaki belirti süresi yönünden fark yoktu ama enfeksiyon kaynağı, predispozan faktör, pozitif kültür sonuçları G2'de yüksekti. Hastanede kalış süresi, toplam maliyet ve mortalite oranı da G2'de yüksekti. G2'de NLO ve TLO yönünden istatistiksel olarak anlamlı yükseklik vardı ama FGSI skorları yönünden gruplar arasında fark saptanmadı.

TARTIŞMA: Bulgularımıza göre FGSI puanlama sisteminin prognoz belirlemede değeri yoktu. Buna karşılık daha önce İngilizce literatürde bu amaçla kullanımına rastlayamadığımız NLO ve TLO değerli bulundu.

Anahtar sözcükler: Fournier gangreni; nötrofil lenfosit oranı; platelet lenfosit oranı; prognostik faktör.

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