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Can we predict poor prognosis in Fournier gangrene?

Fournier gangreninde kötü prognozu ön görebilirmiyiz?

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Abstract

Aim: Fournier's gangrene (FG) is a rapidly progressing and highly mortal necrotizing fasciitis that develops due to polymicrobial infection of the genital, perineal and perianal regions. Advanced age, comorbidities, width of the infected area, leukocyte-lymphocyte ratio, number of debridement performed, and Fournier's gangrene severity index (FGSI) score are reported as prognostic factors for FG. In our study, we aimed to present the clinical and laboratory findings that can be used to predict poor prognosis in Fournier gangrene.

Methods: In this retrospective cohort study, the files of 83 patients treated for FG were retrospectively analyzed. Demographic data, laboratory findings, treatments, age adjusted Charlson comorbidity index (ACCI), FGSI score, LRINEC score, complications and mortality were noted. Risk factors affecting mortality were determined.

Results: Male/female ratio was 7.3. The mean age of the patients were 55.4 years. The mortality rate was 21.7%. The mean ACCI scores (Mortality group: 6.00 (2.72), survivors' group: 2.66 (2.39)) and FGSI scores (Mortality group; 11.22 (3.2), survivors' group; 3.25 (2.08)) of non-surviving patients were higher than those of survivors (P<0.001, P<0.001, respectively). Also, the mean neutrophil-lymphocyte ratio (Mortality group: 21.05 (15.67), survivors' group: 11.62 (10.50), (P=0.013), and the mean LRINEC score (Mortality group: 7.17 (2.03), survivors' group: 3.18 (2.59)) (P=0.001) were higher among non-survivors. Cut off values for FGSI score, LRINEC, ACCI, and neutrophil / lymphocyte ratio were 7.5 (94.4% sensitivity and 95.4% specificity), 4.5 (94.4% sensitivity and 67.7% specificity), 3.5 (77.8% sensitivity and 73.8% specificity), and 8.70 (72.2% sensitivity and 52.3% specificity), respectively, in predicting mortality. Mortality was higher in female patients compared to males (P=0.02), and among the diabetics (P=0.05).

Conclusion: We think that risk factors such as advanced age, diabetes, female gender, high ACCI score, high FGSI scores, high LRINEC scores and high neutrophil lymphocyte ratio are predictive of poor prognosis in FG.

Keywords: Fournier's gangrene, Mortality, Risk factors

Öz

Amaç: Fournier gangreni (FG), genital, perineal ve perianal bölgelerin polimikrobiyal enfeksiyonuna bağlı olarak gelişen, hızla ilerleyen ve oldukça ölümcül bir nekrotizan fasiittir. İleri yaş, komorbiditeler, enfekte bölgenin genişliği, lökosit-lenfosit oranı, debridman sayısı, Fournier'in kangren şiddet indeksi (FGSI) skoru FG için prognostik faktörler olarak gösterilmiştir. Çalışmamızda fournier gangreninde kötü prognozu tahmin etmede kullanılabilecek klinik ve laboratuvar bulgularını sunmayı amaçladık.

Yöntemler: Bu retrospektif kohort çalışmada FG tedavisi gören 83 hastanın dosyası incelendi. Demografik veriler, laboratuvar bulguları, tedaviler, yaşa göre düzenlenmiş Charlson komorbidite indeksi (ACCI), FGSI skoru, LRINEC skoru, komplikasyonlar ve mortalite dosyalardan kaydedildi. Mortaliteyi etkileyen risk faktörleri belirlendi.

Bulgular: Erkek / kadın oranı 7,3 idi. Ortalama yaş 55,4 idi. Ölüm oranı % 21,7 olarak saptandı. Mortalitesi olan hastaların ortalama ACCI skorları (mortalite grubu; 6,00 (2,72) - sağ kalanlar grubu; 2,66 (2,39)) ve FGSI skorları (mortalite grubu; 11,22 (3,2) - sağ kalanlar grubu; 3,25 (2.08)), sağ kalanlardan daha yüksekti (sırasıyla, P<0,001, P<0,001). Ayrıca ortalama nötrofil-lenfosit oranı (mortalite grubu; 21,05 (15,67) - hayatta kalanlar grubu; 11,62 (10,50)) (P=0,013) ve ortalama LRINEC skoru (mortalite grubu; 7,17 (2,03) - hayatta kalanlar grubu; 3,18 (2,59)). FGSI skoru için kesme değeri 7,5 (%94,4 duyarlılık ve %95,4 özgüllük), LRINEC için 4,5 (%94,4 duyarlılık ve %67,7 özgüllük), ACCI 3,5 için (%77,8 duyarlılık ve %73,8 özgüllük), nötrofil / lenfosit oranı için mortaliteyi öngörmede 8,70 (%72,2 duyarlılık ve %52,3 özgüllük) olarak saptandı. Kadın hastalarda mortalite erkeklere göre daha yüksekti (P=0,02) ve diyabetli hastalarda mortalite daha yüksekti (P=0,05).

Sonuç: İleri yaş, diyabet, kadın cinsiyet, yüksek ACCI skoru, yüksek FGSI skoru, yüksek LRINEC skoru ve yüksek nötrofil lenfosit oranı gibi risk faktörlerinin FG'de kötü prognozu öngörmede kullanılabileceğini düşünmekteyiz.

Anahtar kelimeler: Fournier gangreni, Mortalite, Risk faktörleri

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Introduction

Fournier's gangrene (FG) is an idiopathic polymicrobial necrotizing fasciitis observed in the scrotal, perineal and perianal areas. FG can be observed in both genders and at all ages [1]. Local trauma, anorectal and scrotal infections are important factors in etiology [2]. Emergency debridement and antibiotherapy are used in the treatment [3]. Repeated debridement can be performed in the follow-up of patients. After the complete regression of the infection, the exposed area is closed with skin flaps.

It is still a disease with a high mortality (16-40%) despite emergency debridement and adequate antibiotherapy [4,5]. In the literature, the factors affecting mortality are reported as age, coexisting comorbidities, the width of the infection area, intensive care requirement, the number of debridement performed, the leukocyte-lymphocyte ratio, and the lymphocyte-platelet ratio [6-8]. Laor et al. published the Fournier Gangrene Severity Index (FGSI) score for predicting mortality [7], which includes temperature, heart rate, respiratory rate, white blood cell count, hematocrit, serum creatinine, sodium, bicarbonate, and potassium. After FGSI, alternative scoring systems were determined for predicting mortality in FG [9-12], including simplified Fournier gangrene severity index (SFGSI), Uludag FGSI (UFGSI), sAPGAR, Age-Adjusted Charlson Comorbidity Index (ACCI), Laboratory Risk Indicator for Necrotizing Fasciitis score (LRINEC), and APACHE II. LRINEC score is calculated by measuring leukocyte count, hemoglobin, serum creatinine sodium, C-reactive protein, and glucose levels. In our study, we aimed to reveal the treatment outcomes of the patients who were followed up and treated for FG and investigate the factors that may affect the prognosis.

Materials and methods

Study population

Patients who underwent surgery with the diagnosis of Fournier's gangrene in the urology departments of our tertiary hospital, where approximately 80000 patients were admitted annually, were included in this study. Informed consent forms were obtained from all patients for surgical intervention.

Subject selection

In this retrospective cohort study, the data of 83 patients who were treated for Fournier's gangrene in our hospital between 2015 and 2019 were analyzed. Patients who underwent surgical intervention in the urology department were included in the study. Per-operative consultation was requested from the department of general surgery when needed. The postoperative follow-up of the patients was performed by the urology department (except when intensive care was required).

Data collection and outcome measures

The study was approved by Pamukkale University Ethics Committee on 10.12.19 with the decision number 21. All information of the patients was obtained from the hospital information management system retrospectively. The patients with skin infection who were found to have necrosis in the genital and perianal areas in clinical examination and underwent debridement with the diagnosis of FG were included in the study. Patients underwent debridement immediately after the diagnosis. Broad-spectrum parenteral antibiotic treatment was initiated. Repeated debridement was performed in patients who had infection findings in the follow-up. In patients with open wound sites, when the infection regressed and granulation tissue formed after antibiotherapy, wound sites were closed with skin flaps. All patients' demographic information, systemic diseases, etiological factors for FG, initial lesion sites, laboratory findings, number of debridement performed, skin flap counts used, duration of hospital stay, whether cystostomy and/or colostomy was performed, and mortality data were determined. Charlson comorbidity index scores, defined by Charlson ME, who revealed the morbidity and mortality risks of cases with systemic diseases, were calculated [13]. The presence of diabetes, cardiovascular, pulmonary, neurological, gastrointestinal, urinary, hematological disease and malignancy were noted, ACCI scores were calculated based on the severity of these comorbidities. Respiratory rate, heart rate, white blood cell count, hematocrit level, serum sodium, potassium, creatinine, and bicarbonate levels were recorded for calculating FGSI score.

Statistical analysis

The tests to compare data were decided in line with the central limit theory. To evaluate the findings obtained in this study, IBM SPSS Statistics 22 for statistical analysis (SPSS IBM, Turkey) program was used. Normal distribution of the data was tested by visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov / Shapiro-Wilks tests). Number, percentage, median and interquartile range values were used for descriptive statistics. The Mann–Whitney U test and Student-t test were used for nonnormally and normally distributed parameters, respectively. Categorical variables were evaluated with the Chi square test or Fisher exact test (when Chi ‑square test assumptions do not hold due to low expected cell counts). Correlation analyses were performed using the Pearson test, and the Spearman correlation test when the Pearson test was not suitable. The cut-off points were chosen based on the ROC (receiver operating characteristics) curve analysis. When a significant cut-off value was observed, the sensitivity and specificity were presented. While evaluating the area under the curve (AUC), a 5% type-1 error level was used to accept the statistically significant predictive value of the test variables. The significance value for the results was set as $P<0.05$.

Results

In our study, 73 (87.9%) of the patients were male and 10 (12.1%) were female (Table 1). The overall mean age of the patients was 55.4 (17.65) years. Gangrene developed in the scrotal region in 55 patients, in the perianal region in 20 patients and in the penile region in 8 patients. FG occurred due to colorectal cancer in 3 patients, due to perianal abscess in 20 patients, due to penile cancer in 1 patient, and after penile prosthesis implantation in 1 patient. Gangrene developed idiopathically in 58 patients. The predisposing factors for the formation of FG were diabetes in 43 patients, malignancy in 5 patients and paraplegia in 7 patients (Table 1). The mean ACCI scores evaluating the coexisting diseases of the patients was 3.06 (2.6). The mean blood leukocyte count and neutrophil-lymphocyte ratio of all patients were 16444 (2200-51000) mcL and 13.66 (12.6), respectively (Table 1).

Table 1: Patients' demographics, comorbidities and mortality

			Total patients (n=83)
Age (years) mean (SD)			55.4 (17.65)
Sex	-	Female n(%)	10 (12.1)
	-	Male n(%)	73 (87.9)
Diabetes n(%)			43 (51.8)
Malignancy n(%)			5 (6.02)
Paraplegia n(%)			7 (8.43)
Mortality n(%)			18 (21.7)
Etiology	-	İdiopathic n(%)	58(69.87)
	-	Perianal abscess n(%)	20(24.09)
	-	Colorectal cancer n(%)	3(3.61)
	-	Penile cancer n(%)	1(1.20)
	-	Penile prosthesis n(%)	1(1.20)
First lesion region	-	Scrotal n(%)	55(66.26)
	-	Perianal n(%)	20(24.09)
	-	Penile n(%)	8(9.63)
Laboratory findings	-	Blood leukocyte count n(%)	16444 (9579)
	-	Neutrophil/lymphocyte ratio n(%)	13.66 (12.6)
Diversion	-	Cystostomy n(%)	4 (3.1)
	-	Colostomy n(%)	15 (11.5)
Number of debridement mean (SD)			1.69 (0.79)
Number of flaps mean (SD)			1.05 (0.76)
Mean hospital stay (days) mean (SD)			24.92 (18.96)

All patients underwent debridement immediately after the diagnosis. Cystostomy was performed in 4 patients (3.1%), and colostomy was required in 15 patients (11.5%) in order to prevent wound site contamination during debridement. Debridement was repated in patients who had infection findings during follow-up. The mean number of debridement performed was 1.69 (0.79). After the wound infection of the patients regressed and granulation tissue formed, the wound sites were closed by turning flaps. In patients with reinfected or opened wound sites, the wound sites were closed by turning flaps again after the treatment. The mean number of flaps used was 1.05 (0.76), and the mean duration of hospitalization was 24.92 (18.96) days (Table 1).

Mortality was observed in 18 patients (21.7%). The mean ACCI score (6.00 (2.72)) of the non-surviving patients was statistically significantly higher compared to those who survived (2.66 (2.39)) (P<0.001). The mean FGSI, LRINEC scores, and neutrophil-lymphocyte ratios of non-survivors (P<0.001, P<0.001, and P=0.013, respectively) were significantly higher compared to patients who were discharged. The mean age of non-survivors (68.28 years) was higher compared to surviving patients (50.02 years) (P<0.001). Mortality was observed significantly more frequently in female patients compared to male patients (P=0.02), and among diabetics (P=0.05). No statistically significant relationship was found between the number of debridement, requiring cystostomy or colostomy and mortality (Table 2). ROC curve analysis showed that FGSI score, LRINEC score, ACCI score and Neutrophil/lymphocyte ratios can be used as markers for predicting mortality in FG. When the cut-off value is 7.5 for FGSI score, it predicts mortality with 94.4% sensitivity and 95.4% specificity [AUC=0.988, P<0.001, 95% CI (0.000-1.000]. A cut-off value of 4.5 for LRINEC score predicts mortality with 94.4% sensitivity and 67.7% specificity [AUC=0.868, P<0.001, 95% CI (0.791-0.944], and a cut-off value of 3.5 for ACCI score predicts mortality with 77.8% sensitivity and 73.8% specificity [AUC=0.832, P<0.001, 95% CI (0.723-0.941]. Values above 8.70 for neutrophil/lymphocyte ratio predict mortality with 72.2% sensitivity and 52.3% specificity [AUC=0.692, P=0.013, 95% CI (0.539-0.846] (Figure 1).

A significant correlation was found between mortality and gender, age, LRINEC score, FGSI score, ACCI score and neutrophil-lymphocyte ratio (Table 3).

Table 2: Factors affecting mortality

	Non-surviving Patients (n=18) mean (SD)	Discharged Patients (n=65) mean (SD)	*P*-value
Age (year)	68.28 (14.58)	50.02 (16.40)	<0.001
Female gender n(%)	5 (27.7)	5 (7.6)	0.002
Diabetes n(%)	13 (72.2)	30 (46.1)	0.005
Cystostomy n(%)	2 (11.1)	2 (3.0)	0,159
Colostomy n(%)	5 (27.7)	13 (20.0)	0,227
Number of debridement	1.50 (0.85)	1.74 (0.77)	0.142
Neutrophile/lymphocyte ratio	21.05 (15.67)	11.62 (10.50)	0.013
Charlson Comorbidity score	6.00 (2.72)	2.66 (2.39)	<0.001
FGSI score	11.22 (3.2)	3.25 (2.08)	<0.001
LRINEC score	7.17 (2.03)	3.18 (2.59)	<0.001

Table 3: Correlation analysis between mortality and gender, age, LRINEC, FGSI, ACCI score and neutrophil-lymphocyte ratio

	Gender	Age	LRINEC score	FGSI score	ACCI score	Neutrophil-lymphocyte ratio
rho	-0.254	0.433	0.529	0.700	0.480	0.275
P-value	0.020	<0.001	<0.001	<0.001	<0.001	0.012

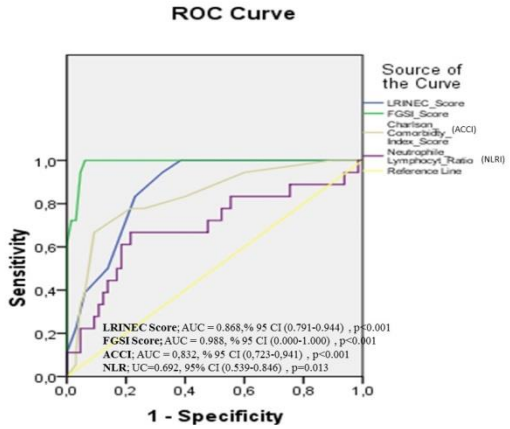

Figure 1: ROC curve analysis for determining mortality

Discussion

FG is a rare serious disease, with an incidence of 1.6 in 100,000 [5]. It is approximately 10 times more common in men [14]. In our study, the male-female ratio was 7.3. It is usually observed between the ages of 50-70 years [15]. The mean age of the patients in our study (55.4 years) was in accordance with the literature.

FG is most common in the genital and perianal regions [16]. We also found it mostly in the scrotal region, then in the perianal region. It begins as a local skin infection, and after abscess formation, necrosis begins on the skin. There are predisposing factors such as diabetes, malignancy, alcoholism, liver and kidney failure that usually facilitate the formation and progression of infection [17]. Diabetes facilitates FG by disrupting the function of phagocytes and cellular immunity [3]. Alcoholism, malignancy, liver and kidney failure also facilitate FG by causing immunosuppression. However, some cases are idiopathic and there are no predisposing factors. In our study, in most of the patients, FG developed due to idiopathic genital or perianal region infections. The most common predisposing factor was diabetes, followed by paraplegia and malignancies.

Although the diagnosis of FG is easily made by physical examination, the prognosis is not always favorable. It is of vital importance to perform emergency debridement immediately after the diagnosis [18]. In our study, emergency debridement was performed after all patients were diagnosed. In the studies

conducted, 16-40% mortality was found despite early interventions [4,5,14,19]. In our study, 21.7% mortality was observed in accordance with the literature. The time between the onset of infection and the admission to the hospital is as important as emergency debridement for the prognosis. Other prognostic factors were the width of the lesion, age, female gender, accompanying malignancy and diabetes [20]. Many studies, regarding factors affecting prognosis, were carried out to predict mortality. Laor et al. [7] revealed a scoring system called Fournier gangrene severity score (FGSS), which included vital signs and laboratory results. This scoring system indicated that 75% mortality was observed in patients with 9 points and higher. Wong et al. described the LRINEC scoring system, like FGSS, to predict the prognosis [9]. Hsiao et al. [21] and Gönüllü et al. [22] have also revealed that the LRINEC score can be used to predict mortality. Based on the above-mentioned research, we used ACCI, FGSI and LRINEC score to predict mortality, and found that the mean ACCI, FGSI and LRINEC scores were significantly higher in non-survivors.

Advanced age has been shown as one of the factors affecting mortality in FG [5,14], which was also a finding of our study. This is associated with an increase in comorbidities and a decrease in immune system function in older age.

In parallel to our study, female gender was reported to increase mortality [23]. This may be because the female genital anatomy makes it easier and faster for the infection to spread to the retroperitoneum.

It is controversial that the number of debridement may be a risk factor for mortality. Laor et al. [7] did not find a relationship between the number of debridement performed and mortality, while Chawla et al. found that the number of debridement was significantly higher among non-survivors [24]. We think that in cases with high number of debridement, the area of infection is larger, and therefore the prognosis is worse. However, in our study, we could not find a significant relationship between debridement number and mortality.

Yim et al. [25] determined that neutrophil-lymphocyte ratio is more effective than FGSI for predicting mortality in FG. We determined that non-surviving patients had higher neutrophil-lymphocyte ratios than survivors.

Furthermore, we found that factors such as FGSI score, ACCI score, advanced age, female gender, presence of diabetes, neutrophil-lymphocyte ratio increased mortality, in accordance with the literature.

Limitations

The fact that our study was a retrospective study conducted with a limited group may have limited the generalizability of the findings. Prospective randomized controlled studies are required for further deductions.

Conclusion

It is of vital importance to perform emergency debridement and initiate antibiotherapy after the diagnosis in FG, which is a disease with high mortality and morbidity. However, mortality is observed in some cases despite all efforts. We found that advanced age, high Charlson score, female gender, high neutrophil-lymphocyte ratio and the presence of diabetes were the factors affecting mortality.

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