Predictive factors for mortality in intensive care patients with Fournier's gangrene: five years' experience from a single center in Turkey

F.T. BOZKURT[1], H.F. ÖNCEL[2], R. SALAR[2]

[1]Department of Intensive Care, Şanlıurfa Mehmet Akif Inan Training and Research Hospital, Şanlıurfa, Turkey
[2]Department of Urology, Şanlıurfa Mehmet Akif Inan Training and Research Hospital, Şanlıurfa, Turkey

Abstract. – **OBJECTIVE:** The aim of this study was to analyze mortality-related factors and scoring systems in order to better manage the treatment process of patients monitored in the intensive care unit (ICU) due to Fournier's gangrene (FG).

PATIENTS AND METHODS: The study included 28 male patients who were monitored in the surgical ICU with the diagnosis of FG between December 2018 and August 2022. The patients' comorbidities, acute physiological and chronic health evaluation scoring system II (APACHE II), Fournier gangrene severity index (FGSI), sequential organ failure assessment (SOFA) scores, and laboratory data were evaluated retrospectively.

RESULTS: Of the patients, 67.9% (n=19) had diabetes mellitus, 78.6% (n=22) had hypertension, and 71.4% (n=20) had coronary artery disease. The mortality rate was 42% (n=11). There was no statistically significant difference between the patients who died and those who survived in terms of the SOFA score, comorbidities, and albumin, glucose, and procalcitonin values ($p > 0.05$), but age, APACHE II and FGSI scores, and the C-reactive protein (CRP) value were significantly higher in the non-survivor group. There was a positive correlation between the FGSI, APACHE II, and SOFA scores.

CONCLUSIONS: Older age, high CRP levels at the time of admission, and the presence of comorbidity are still determining factors in the prediction of mortality in patients with FG. We also determined that in predicting mortality in patients monitored in the ICU with the diagnosis of FG, in addition to the routinely used FGSI, the APACHE II score was also useful, but the SOFA score did not have significant predictive value.

Key Words:
 Fournier's gangrene, Fournier's gangrene severity index, Critical care.

Introduction

Fournier's gangrene (FG), first clinically described by Jean Alfred Fournier in 1883, is a rapidly progressive disease affecting the deep and superficial tissues of the perineal, anal, scrotal, and genital regions. FG usually originates from the genitourinary system and can have a fulminant progression, leading to multiple organ failure, septic shock, and death[1]. Although FG is very rare, it has a high mortality rate, ranging from 20% to 80%[2,3]. Predisposing factors include diabetes mellitus (DM), alcoholism, atherosclerosis, peripheral arterial disease, Raynaud's phenomenon, malnutrition, immunosuppression (e.g., chemotherapy, steroids, and malignancy), human immunodeficiency virus infection, leukemia, and liver diseases[4]. Since this condition can progress from early non-specific local skin manifestations to clinical sepsis, urgent treatment with effective surgical debridement, appropriate antibiotic therapy, and hemodynamic support is critical[5]. The Fournier gangrene severity index (FGSI) was developed to classify risky cases and predict mortality in these patients[6-8].

In this study, we aimed to evaluate prognostic indices, including FGSI, acute physiological and chronic health evaluation scoring system II (APACHE II), and sequential organ failure assessment (SOFA) scoring systems, and laboratory parameters at the time of admission in patients who were monitored in the intensive care unit (ICU) due to FG and compare the results according to the patients' mortality status.

Patients and Methods

Patients with FG who were monitored and treated in a third-level surgical ICU between De-

Corresponding Author: Firdevs Tugba Bozkurt, MD; e-mail: drtugbaicu@gmail.com

cember 2018 and August 2022 were included in this study. Approval for the study was obtained from the ethics committee of Harran University Faculty of Medicine (date-number: 12/12/2022-22.24.03). The research was conducted in accordance with the principles of the Declaration of Helsinki. The patients' demographic characteristics, comorbidities, laboratory values, sites of involvement, length of ICU stay, length of hospital stay, and APACHE II, SOFA, and FGSI scores were recorded and analyzed retrospectively.

Statistical Analysis

Descriptive statistical data, including mean, standard deviation, standard error, variance, and median values were calculated and recorded. Following the graphical and statistical determination of the suitability of the data for a normal distribution, the data were statistically analyzed using the Spearman rank correlation analysis, paired-samples *t*-test, or Chi-square test, as appropriate. The Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA) statistical program was used for the statistical analysis of the data. Statistical significance was evaluated at a *p*-value of < 0.01.

Results

A total of 28 male patients were included in this study. The mean age of the patients was 62 years. Six patients were intubated. The mean ± standard deviation value of the APACHE II score was calculated to be 20.7 ± 5.8. The mean length of hospital stay was 20 days, and the mean length of ICU stay was 7.7 days. The mean C-reactive protein (CRP) value at admission was 359 ± 83.6 mg/L. The mean FGSI and SOFA scores were calculated as 7.9 ± 2 and 4.3 ± 1.2, respectively. The mean albumin value was 24 ± 3.2 g/L, and the mean glucose value was 251.1 ± 117.7. The mean procalcitonin values of only nine patients whose data were available were determined as 17.5 ± 32.2 (Table I).

The analysis of variance and Chi-square tests were used to compare the results of the patients according to their mortality status. There was a significant difference in patient age according to mortality status (73.4 ± 15.2 years in the non-survivor group, 54.5 ± 17.3 years in the survivor group; $p < 0.01$). A statistically significant relationship was found between older age and mortality ($p < 0.01$). Similarly, there were significant differences between the non-survivor and survivor groups in relation to the APACHE II score (25 ± 5.1 and 18 ± 4.4, respectively; $p < 0.01$), the length of hospital stay (10 ± 6.1 and 27.1 ± 8.2 days, respectively; $p < 0.01$), the CRP value (426.6 ± 91.4 and 315.2 ± 37.3, respectively; $p < 0.01$), and the FGSI score (9.3 ± 1.8 and 7 ± 1.6, respectively; $p < 0.01$). However, no statistically significant difference was found in the procalcitonin, glucose, and albumin values according to mortality status (Table I).

Of the patients, 67.9% (n = 19) had DM, 78.6% (n = 22) had hypertension, and 71.4% (n = 20) had coronary artery disease. There was no statistically significant difference in comorbidities ac-

Table I. Comparison of demographic characteristics, laboratory values, and prognostic indices according to mortality status.

	Non-survivors (n = 11) mean ± SD	Survivors (n = 17) mean ± SD	Total (n = 28) mean ± SD	*p**
Age (year)	73.4 ± 15.2	54.5 ± 17.3	62 ± 18.7	0.007
Length of hospital stay (days)	10 ± 6.1	27.1 ± 8.2	20.4 ± 11.2	0.000
Length of ICU stay (days)	7.4 ± 2.1	8 ± 4.4	7.7 ± 3.6	0.708
APACHE II	25 ± 5.1	18 ± 4.4	20.7 ± 5.8	0.001
FGSI	9.3 ± 1.8	7 ± 1.6	7.9 ± 2	0.002
SOFA	4.5 ± 1.2	4.1 ± 1.2	4.3 ± 1.2	0.456
Albumin (mg/L)	24.4 ± 3.8	17.23 ± 8.3	28.24 ± 3.2	0.651
Glucose (mg/dl)	248.9 ± 113.8	252.6 ± 123.6	251.1 ± 117.7	0.936
Procalcitonin (ng/ml)	9.3 ± 10.8	33.8 ± 57.2	17.5 ± 32.2	0.314
CRP (mg/dl)	426.6 ± 91.4	315.2 ± 37.3	359 ± 83.6	0.000

*Analysis of variance and independent-samples *t*-test; statistically significant at *p* < 0.01. ICU: intensive care unit, APACHE II: acute physiologic and chronic health evaluation scoring system II, FGSI: Fournier gangrene severity index, SOFA: sequential organ failure assessment, CRP: C-reactive protein.

Table II. Comorbidities according to mortality status.

	Non-survivors (n = 11)	Survivors (n = 17)	Total (n = 28)	p*
DM	9 (47.4)	10 (52.6)	19 (67.9)	0.203
Hypertension	10 (45.5)	12 (54.5)	22 (78.6)	0.201
CAD	10 (50)	10 (50)	20 (71.4)	0.066
COVID-19	3 (75)	1 (25)	4 (14.3)	0.114
Urogenital involvement	9 (42.9)	12 (57.1)	21 (75)	0.503
Anogenital involvement	11 (45.8)	13 (54.2)	24 (85.7)	0.082
Other	3 (42.9)	4 (57.1)	7 (25)	0.823

DM: diabetes mellitus, CAD: coronary artery disease.

cording to mortality status (Table II). COVID-19 positivity was detected in four patients, of whom three died.

Spearman's rank correlation analysis was used to determine the correlation between the prognostic scoring systems. Accordingly, a statistically significant positive correlation (r = 0.427, *p* < 0.01) was found between the APACHE II and FGSI scores. Similarly, there was a statistically significant positive correlation between the FGSI and SOFA scores (r = 0.546, *p* < 0.01) (Table III).

Discussion

FG remains a disease with high mortality and morbidity rates, despite the improvement in medical treatment options and intensive care conditions[9-11]. Although FG accounts for less than 1% of ICU admissions, approximately half of these patients develop a septic shock at the time of ICU admission, and their mortality rate can reach 80%[12].

In most studies[5,8], DM has been reported to be the most common predisposing factor for mortality[5], while advanced age, late hospital admission, the presence of shock or sepsis findings at admis-

sion, or the presence of any immunosuppressive conditions have been shown to affect mortality[8]. Comorbidities play an important role in determining the course of FG. Comorbid conditions that have been most associated with mortality in FG are DM and cardiovascular diseases[13-15], which both affect the vascular bed in the tissue and organ systems, and tissue ischemia resulting from vascular involvement is known to predispose these patients to FG[16]. In our study, cardiac disease was the most common cause of FG, and DM was the second most common cause.

In the literature, some scoring systems have been developed to determine the severity of FG and to predict the associated morbidity and mortality. In 1995, Laor et al[17] developed FGSI by modifying the APACHE II scoring system that was originally designed for the evaluation of ICU patients. In the literature, the FGSI score has been found to be higher in non-survivor groups. In a study conducted by Lin et al[18] with 84 patients, the mean FGSI value was found to be 5.5 ± 2.7 in the survivor group and 10.2 ± 4.6 in the non-survivor group, indicating a statistically significant difference. Similarly, in another study conducted by Corcoran et al[19] with 68 patients, the mean FG-

Table III. Correlation analysis between the prognostic indices.

		APACHE II	FGSI	SOFA
APACHE II	r	1	.427*	0.222
	p		0.024	0.257
FGSI	r	.427*	1	.546**
	p	0.024		0.003
SOFA	r	0.222	.546**	1
	p	0.257	0.003	

**Correlation significant at the 0.01 level (two-tailed). *Correlation significant at the 0.05 level (two-tailed). APACHE II: acute physiologic and chronic health evaluation scoring system II, FGSI: Fournier gangrene severity index, SOFA: sequential organ failure assessment.

SI scores of the survivor and non-survivor groups were 5.4 ± 3.5 and 10.9 ± 4.7, respectively, which was statistically significant ($p = 0.006$). In a study from Turkey in which 18 patients were evaluated, Erol et al[20] reported that the FGSI score was 5 ± 2.91 in the survivor group and 13.5 ± 2.62 in the non-survivor group. In the current study, consistent with the literature, the FGSI score was statistically significantly higher in the non-survivor group than in the survived group ($p < 0.01$).

In studies[12] conducted with patients with FG, the most common risk factor for mortality has been shown to be disease severity as reflected by the APACHE II score, and the probability of death has been reported to increase by 16-18% per unit increase in this score. In our study, the APACHE II score of the patients who were monitored in the ICU was higher in the non-survivors compared to the survivors, which is consistent with the literature[21]. Satoh et al[22] demonstrated a weak correlation between the SOFA and APACHE II scores in FGSI. However, a study conducted by Utariani et al[23] revealed a statistically significant positive correlation between the FGSI and SOFA scores. We also found a positive correlation between the two scoring systems in our study.

To date, very few studies[24,25] have examined the SOFA score in patients with FG. In a retrospective study evaluating 60 patients with FG, Usta et al[24] found that the SOFA score was significantly higher in the non-survivor group than in the survivors. In addition, in a larger series study[25] evaluating the data of 168 patients with FG, Lauerman et al[25] demonstrated a significant relationship between primary wound closure and a low SOFA score. In our study, no significant difference was found between the survivors and non-survivors in relation to the SOFA score. The mean SOFA score was 4.5 in the non-survivor group and 4.1 in the survivor group. We consider that this statistical similarity in the SOFA scores of our patients was due to all requiring intensive care. The small number of patients may be another factor that can explain the absence of a significant difference in the SOFA score.

FG can be seen in all age groups, but advanced age is a primary risk factor. Sorensen et al[26] reported that the incidence of FG increased in elderly patients and peaked at the age of 50 years. Similarly, many studies[4,27,28] have shown a statistically significant relationship between advanced age and mortality. In our study, the mean age was significantly higher in the non-survivor group compared to the survivor group.

In the literature, some laboratory parameters have been reported to be prognostic indicators of FG[29]. In our study, we also compared the albumin, procalcitonin, glucose, and CRP values measured at admission to the ICU according to mortality status, and found significantly higher CRP values in the non-survivor group ($p < 0.01$).

COVID-19 is a highly contagious disease responsible for the 2019 coronavirus pandemic that has affected the global population. As of early October 2022, there were more than 619 million cases officially reported by the World Health Organization[30] and more than 6.5 million deaths were attributed to the complications related to the disease. The virus causing this disease may also have unpredictable and potentially devastating consequences when combined with FG[31,32]. In our study, four patients with FG were simultaneously infected with COVID-19, and three of these patients did not survive. This may be due to the COVID-19 infection disrupting tissue circulation with its prothrombotic and inflammatory effects[33].

The limitations of this study include the single-center and retrospective design, and the limited number of patients.

Conclusions

FG is a fulminant, life-threatening disease with high mortality and morbidity rates. Although there is currently no consensus on the use of individual patient admission characteristics or laboratory parameters as prognostic indicators of FG, we determined that a high CRP level and older age were associated with mortality in these patients. We also found that the disease-specific FGSI and APACHE II scores were more significant than SOFA in predicting mortality.

Informed Consent
Informed consent was obtained from all patients included in the study.

ORCID ID

FTB: 0000-0002-1461-5933; RS: 0000-0002-5078-9367; HFO: 0000-0003-4043-5597.

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