ORIGINAL ARTICLE

Prediction of mortality in patients with Fournier's gangrene: Importance of time to surgery

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ABSTRACT

BACKGROUND: Considering the complex structure and severity of Fournier's Gangrene (FG), it is important to identify prognostic factors to develop treatment strategies and predict clinical outcomes. Early diagnosis of FG patients may result in reducing damage to patients' health, increasing treatment success and survival rates. Our study aims to evaluate the clinical and laboratory findings that predict mortality, the role of five scoring systems in mortality prediction, and the importance of the time from admission to emergency department to surgery in FG patients.

METHODS: A total of 354 patients who were diagnosed with FG were divided into survivors (n=293) and non-survivors (n=61). Multivariate logistic regression analysis was applied for variables that were statistically significant in the univariate analysis regarding factors predicting mortality in patients with FG. Fournier Gangrene Severity Index (FGSI) score, Uludağ Fournier Gangrene Severity Index (UFGSI) score, Age-adjusted Charlson Comorbidity Index (ACCI), Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) index, and the Combined Urology and Plastics Index (CUPI) were analyzed with receiver operating characteristic (ROC) curves for predicting the mortality of FG.

RESULTS: The mortality rate due to FG was found to be 17.2%. Advanced age, increased respiratory rate, high serum chloride, low serum bicarbonate, low serum albumin, and the time between hospital admission and surgery are independent predictors of FG mortality in the multivariate analysis. The area under the ROC curve values of FGSI score, UFGSI score, ACCI, LRINEC index, and CUPI were found to be 0.719, 0.751, 0.641, 0.636, and 0.751, respectively. Mortality was 13.3% in patients with a time of up to 12 h until surgery, and 24.2% in patients with a time of more than 12 h until surgery. Furthermore, a time to surgery longer than 12 h was associated with a longer length of hospital stay (p=0.001).

CONCLUSION: Considering the scoring systems, our results showed that UFGSI and CUPI significantly outperformed ACCI and LRINEC, while FGSI, UFGSI, and CUPI did not differ significantly from one another. One of the most important aspects of reducing mortality is complete debridement within 12 h of hospital admission.

Keywords: Emergency; Fournier's gangrene; mortality; scoring systems; time to surgery.

INTRODUCTION

Fournier's Gangrene (FG) is the form of necrotizing fasciitis that affects the superficial and deep tissues of the genital, scrotal, perineal, and perianal regions.[1] In other words, FG is a subgroup of necrotizing soft tissue infection (NSTI). FG causes obliterative endarteritis. Necrosis occurs due to microvascular obstruction and impaired blood circulation. The

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existing hypoxic environment provides the basis for bacterial proliferation.[2] FG is associated with severe tissue damage, necrosis, and potential systemic complications following spread of infection through soft tissues. It usually presents with signs of sepsis. It can progress to multiple organ failure and septic shock.[3]

In the systematic review covering the years 1993–2018, it was emphasized that mortality due to FG was around 40%.[4] However, another review conducted between 2000 and 2021 found that although the mortality rate due to FG was still high at 7.3%, it had decreased compared to previous years thanks to advances in both the recognition and treatment of the disease.[5]

Considering the complex structure and severity of FG, it is important to identify prognostic factors to develop treatment strategies and predict clinical outcomes. Various scoring systems have been developed to predict the morbidity and mortality of FG patients. Fournier Gangrene Severity Index (FGSI)[6] and Uludağ Fournier Gangrene Severity Index (UFGSI)[7] are scoring systems developed to predict the mortality probability of FG patients. Age-adjusted Charlson Comorbidity Index (ACCI) is a scoring system used to evaluate comorbidities and predict mortality.[8] Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) index is used to differentiate necrotizing fasciitis from other soft tissue infections based on laboratory findings.[9] The Combined Urology and Plastics Index (CUPI) is a scoring system used to predict length of hospital stay (LOS) and morbidity in patients with FG.[10]

Early diagnosis of FG patients may result in reducing the damage to patients' health, increasing treatment success and survival rates. Based on this idea, we aimed to evaluate the clinical and laboratory findings that predict mortality, the role of five existing scoring systems in mortality prediction, and the importance of the time from admission to emergency department to surgery in FG patients.

MATERIALS AND METHODS

This study was approved by the Health Sciences University Izmir Tepecik Training and Research Hospital (Date: 05.02.2025, Decision no: 2025/01-33). Written consent was obtained from all patients during hospitalization, and their clinical data could be used in future studies. This study was conducted in accordance with the ethical standards set forth in the 1964 Declaration of Helsinki. Data of patients diagnosed with FG between 2007 and 2023 in one of the tertiary reference centers in our country were retrospectively examined. Diagnosis was made by physical examination, taking into account the presence of erythema, induration, tenderness, blackness, subcutaneous crepitation, necrosis, and repulsive fecaloid odor. Individuals with perianal, periurethral, or scrotal abscesses without necrosis and soft tissue extension were excluded. As a result of the review, a total of 354 patients over the age of 18 who were diagnosed with FG and had no missing data were included in the study.

A total of 354 patients who met the inclusion criteria were divided into survivors (n=293) and non-survivors (n=62). The following data were collected from FG patients admitted to hospital and compared between the two groups: Patient demographics (age, gender, comorbidities), pulse, respiratory rate (RR), body temperature, disease extent, serum laboratory results (hematocrit, leukocyte, lymphocyte, neutrophil lymphocyte ratio (NLR), albumin, international normalized ratio (INR), procalcitonin, c-reactive protein (CRP), scoring system scores (FGSI score, UFGSI score, ACCI, LRINEC index, CUPI), microbial growth in wound culture, wound culture sterilization time, time to surgery, vacuum-assisted closure (VAC) of a wound, VAC duration, definitive wound closure type, number of debridement in the operating room, need for intensive care unit (ICU), LOS, length of stay in the ICU. Time to surgery was defined as the time from the patient's application to the emergency department to surgical intervention.

Multivariate logistic regression analysis was applied for variables that were statistically significant in the univariate analysis regarding factors predicting mortality in patients with FG. Patients who had a time to surgery of more than 12 h and less were compared in terms of mortality, need for ICU, number of debridements performed in the operating room, LOS, and length of stay in the ICU. FGSI score, UFGSI score, ACCI, LRINEC index and CUPI were analyzed with receiver operating characteristic (ROC) curve for the predicting the severity of FG.

After the vital signs of all patients were stabilized, the patient was evaluated by the infectious diseases clinic and empirical antibiotics were started in the emergency room. Antibiotic treatment was changed if deemed necessary by the infectious diseases department based on the patient's wound culture results, clinical and laboratory findings. Surgical intervention was performed by debridement of infected and necrotic tissues until healthy tissues were reached. Depending on the progression of the infection, debridement was repeated in the operating room when the surgeon deemed it necessary. All patients who did not receive VAC treatment were followed up with conventional wound dressing. In patients receiving VAC treatment, the dressing was changed every 72 h. Conventional wound dressing was changed daily with appropriate saline-soaked gauze by the surgeon and nurse.

The FGSI score is a numerical value created by combining clinical and laboratory values. It is created based on body temperature, pulse, RR, serum sodium, potassium, creatinine, hematocrit, leukocyte, and bicarbonate values. A score between 0 and 4 is given for each parameter. The overall score is calculated by summing the points given to each parameter. It has been reported that it is strongly associated with mortality rates.[6] The UFGSI score is another scoring system cre-

ated by adding disease extent and patient age to the FGSI score.[7] ACCI is one of the widely used comorbidity scoring systems. It has 20 parameters. It is used to evaluate the mortality risk based on the severity and number of diseases that the patient has.[8] The LRINEC index is a laboratory-based scoring system that can be used to detect early clinical cases of necrotizing fasciitis. It was created based on serum CRP, leukocyte, hemoglobin, sodium, creatinine, and glucose values. A maximum of 13 points can be obtained by giving points to each parameter.[9] CUPI is a scoring system used for LOS of FG patients. In addition to age, serum hematocrit, calcium, alkaline phosphatase (ALP), albumin, INR, bicarbonate, total bilirubin, and blood urea nitrogen values are taken into account. A total score of up to 15 is obtained from the parameters.[10]

Statistical Analysis

One-sample Kolmogorov–Smirnov test was used to control whether the data showed a normal distribution for numerical variables. Mean ± standard deviation was found in the data with a normal distribution, and median interquartile range values were recorded in the data without a normal distribution. Numerical variables were compared with Student's t test when parametric test criteria were found. In the absence of these criteria, the Mann–Whitney U test was used. In addition, the Mann-Whitney U test was used to compare ordinal categorical variables. Pearson Chi-Square Test was used to determine whether there was a difference between the percentages of categorical variables. Candidate predictors of mortality were first screened using univariable logistic regression; variables with $p<0.05$ were entered into a multivariable logistic regression model using the enter method. Multicollinearity among the final predictors was assessed using the variance inflation factor (VIF), with VIF <5 considered acceptable. Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test, and model discrimination was quantified using the C-statistic (area under the ROC curve), with 95% confidence intervals (CIs) calculated by the DeLong method.

The 12-h interval from presentation to surgical debridement was defined a priori, based on time intervals commonly used in the surgical-delay literature for necrotizing soft tissue infections, and was not derived post hoc from the study outcome data.

The optimal cut-off value for each scoring system was determined using the Youden index (J=sensitivity+specificity−1), identifying the threshold that maximized combined sensitivity and specificity for predicting mortality. At each optimal cut-off, sensitivity, specificity, positive and negative predictive values (PPV, NPV), and positive likelihood ratio (LR+) and negative likelihood ratios were calculated. Ninety-five percent CIs for sensitivity, specificity, PPV, and NPV were estimated using the Wilson score method; the 95% CI for each area under the curve (AUC) was estimated using the DeLong method. Pointwise 95% confidence bands for the ROC curves were obtained by bootstrap resampling (1,000 resamples with replacement, stratified on outcome). Internal validation was performed using bootstrap resampling (1,000 resamples) to estimate optimism-corrected model performance. The apparent C-statistic (0.907) was adjusted for optimism (mean=0.014), yielding an optimism-corrected C-statistic of 0.893.

Pairwise comparisons of the AUC between scoring systems were performed using the DeLong method for correlated ROC curves derived from the same patient cohort. A two-sided $p<0.05$ was considered statistically significant. For all tests, the probability of first-type error was $\alpha=0.05$. Statistical analysis of the study was performed using the IBM Statistical Package for the Social Sciences 22.0 package program.

RESULTS

Considering the inclusion and exclusion criteria, a total of 354 patients followed up due to FG were included in the study. Of these, 293 patients were defined as survivors and 61 patients as non-survivors. Demographic, clinical, and laboratory findings of both groups are compared in Table 1. The mortality rate due to FG was found to be 17.2%. The mean age was 55.3 in survivors and 65.6 in non-survivors, and a statistically significant difference was found ($p<0.001$). While the mean RR was 19.5 in survivors, it was 22.5 in non-survivors, and a statistically significant difference was observed ($p<0.001$). Female gender, comorbidities, increased pulse rate, and advanced disease extent were more common in deceased patients. When laboratory findings were evaluated, serum NLR ($p=0.046$), chloride ($p=0.025$), INR ($p=0.001$), and procalcitonin ($p<0.001$) were found to be, while hematocrit ($p=0.004$), bicarbonate ($p<0.001$), albumin ($p<0.001$), and calcium ($p=0.003$) were found to be low-high in non-survivors. No significant difference was found between the two groups in terms of serum leukocyte ($p=0.951$), sodium ($p=0.934$), potassium ($p=0.544$), CRP ($p=0.309$), and ALP ($p=0.505$) values.

The mean FGSI score, UFGSI score, ACCI, LRINEC index, and CUPI were 3.5, 5.7, 1.8, 5.5, and 4.3 in survivors and 6.9, 10.5, 2.9, 7.1, and 5.9 in non-survivors, respectively. All of these scores were statistically higher in deceased patients ($p<0.001$ for all). In the comparison of both groups, the median time to surgery was 8 h in surviving patients and 12.5 h in those who died ($p=0.016$). Time to surgery longer than 12 h was associated with increased mortality ($p=0.009$).

The results of multivariate logistic regression analysis of factors predicting mortality in FG patients are shown in Table 2. According to multivariate analysis, advanced age ($p=0.001$), increased RR ($p=0.003$), high serum chloride level ($p=0.027$), low serum bicarbonate level ($p<0.001$), low serum albumin level ($p<0.001$), and prolonged time to surgery ($p=0.005$) were found to be independent factors predicting mortality in FG. All six independent predictors showed VIF values below 1.3, indicating no evidence of multicollinearity. The multivari-

Table 1. Grouping of demographic, clinical, and laboratory data according to mortality

	Survivors (n=293)	Non-survivors (n=61)	p
Age, years, mean±SD	55.3±13.5	65.6±13.5	<0.001[T]
Gender, n (%)			
Female	82 (28)	27 (44.3)	0.012[P]
Male	211 (72)	34 (55.7)	
Presence of risk factors, n (%)	247 (84.3)	56 (91.8)	0.129[P]
Pulse (beats per min), mean±SD	92.3±15.9	100.4±17.5	<0.001[T]
Respiratory rate (breaths per min), mean±SD	19.5±4.9	22.6±5.3	<0.001[T]
Body temperature (°C), median (min–max)	36.6 (36.0–39.6)	37 (36.4–41.0)	<0.001[M]
Comorbidities, n (%)			
No	46 (15.7)	5 (8.2)	0.003[P]
Diabetes mellitus	81 (27.6)	8 (13.1)	
Cancer	21 (7.2)	3 (4.9)	
Immunosuppression	5 (1.7)	3 (4.9)	
Obesity	24 (8.2)	1 (1.6)	
Trauma/Surgery	45 (15.4)	13 (21.3)	
Cardiovascular	60 (20.5)	24 (39.3)	
Chronic kidney disease	11 (3.8)	4 (6.6)	
Disease extend, n (%)			
Urogenital	82 (28)	13 (21.3)	0.005[P]
Anorectal	108 (36.9)	13 (21.3)	
Extending into the pelvis	26 (8.9)	7 (11.5)	
Extending outside the pelvis	48 (16.4)	22 (36.1)	
Anogenital	29 (9.9)	6 (9.8)	
Hematocrit (%), mean±SD	34.2±7.0	31.5±5.3	0.004[T]
Leukocyte (103/µL), mean±SD	16.9±7.9	16.8±8.5	0.951[T]
Lymphocyte (103/µL), median (min–max)	1.3 (0.2–9.8)	1 (0.1–8.3)	0.005[M]
Neutrophil lymphocyte ratio, median (min–max)	12.1 (0.8–119.5)	16.8 (1.3–133)	0.046[M]
Sodium (mmol/L), median (min–max)	134 (115–148)	134 (117–176)	0.934[M]
Potassium (mmol/L), mean±SD	4.3±0.7	4.3±0.9	0.544[T]
Chloride (mmol/L), median (min–max)	99 (79–112)	101 (78–144)	0.025[M]
Bicarbonate (venous) (mmol/L), mean±SD	22.9±2.8	19.1±4.2	<0.001[T]
Calcium (mg/dL), mean±SD	8.6±0.7	8.3±0.7	0.003[T]
Albumin (g/dL), mean±SD	2.9±0.7	2.2±0.7	<0.001[T]
INR, median (min–max)	1.1 (0.1–2.2)	1.2 (0.12–52)	0.001[M]
Procalcitonin (µg/L), median (min–max)	0.4 (0–75)	1.1 (0.03–63)	<0.001[M]
CRP (mg/dL), mean±SD	165.5±136.7	185.0±130.9	0.309[T]
FGSI score, mean±SD	3.5±3.7	6.9±4.8	<0.001[T]
UFGSI score, mean±SD	5.7±4.3	10.5±5.7	<0.001[T]
ACCI, mean±SD	1.8±1.6	2.9±2.3	<0.001[T]
LRINEC index, mean±SD	5.5±3.4	7.1±3.4	<0.001[T]
CUPI, mean±SD	4.3±1.8	5.9±1.7	<0.001[T]
Microbial growth in wound cul-ture, n (%)	163 (60.8)	34 (59.6)	0.869[P]
Wound culture sterilization time (days)	17.6±18.4		
Time to surgery (hours), median (min–max)	8 (0.5–168)	12.5 (1–480)	0.016[T]

Surgery after 24 h, n (%)	50 (17.1)	15 (24.6)	0.167[P]
Surgery after 12 h, n (%)	97 (33.1)	31 (50.8)	0.009[P]
Surgery after 6 h, n (%)	176 (60.1)	40 (65.6)	0.422[P]
Surgery after 3 h, n (%)	241 (82.3)	52 (85.2)	0.573[P]
Surgery after 1 h, n (%)	274 (93.5)	58 (95.1)	0.645[P]
VAC of a wound, n (%)	83 (28.3)	16 (26.2)	0.740 [P]
VAC duration, median (min–max)	15 (3–60)	13.5 (1–85)	0.875[M]
Definitive wound closure type, n (%)			
Primary	121 (41.3)	2 (3.3)	<0.001[P]
Secondary	111 (37.9)	2 (3.3)	
Graft-Flap	61 (20.8)	-	
Exitus	-	57 (93.4)	
Number of debridements in the operating room, median (min–max)	1 (1–13)	1 (1–20)	0.966M
Need for ICU, n (%)	109 (37.2)	56 (91.8)	<0.001[P]
Length of hospital stay, days, median (min–max)	15 (1–93)	14 (1–120)	0.374[M]
Length of stay in the ICU, days, median (min–max)	3 (1–35)	6 (1–90)	0.001[M]

SD: Standard deviation; n: Number; min: Minute; INR: International normalized ratio; CRP: C-reactive protein; FGSI: Fournier Gangrene Severity Index; UFGSI: Uludağ Fournier Gangrene Severity Index; ACCI: Age-adjusted Charlson Comorbidity Index; LRINEC: Laboratory risk indicator for necrotizing fasciitis; CUPI: The Combined Urology and Plastics Index; VAC: Vacuum-assisted closure; ICU: Intensive care unit; TStudent T test; MMann-Whitney U test; PPearson's Chi-square test.

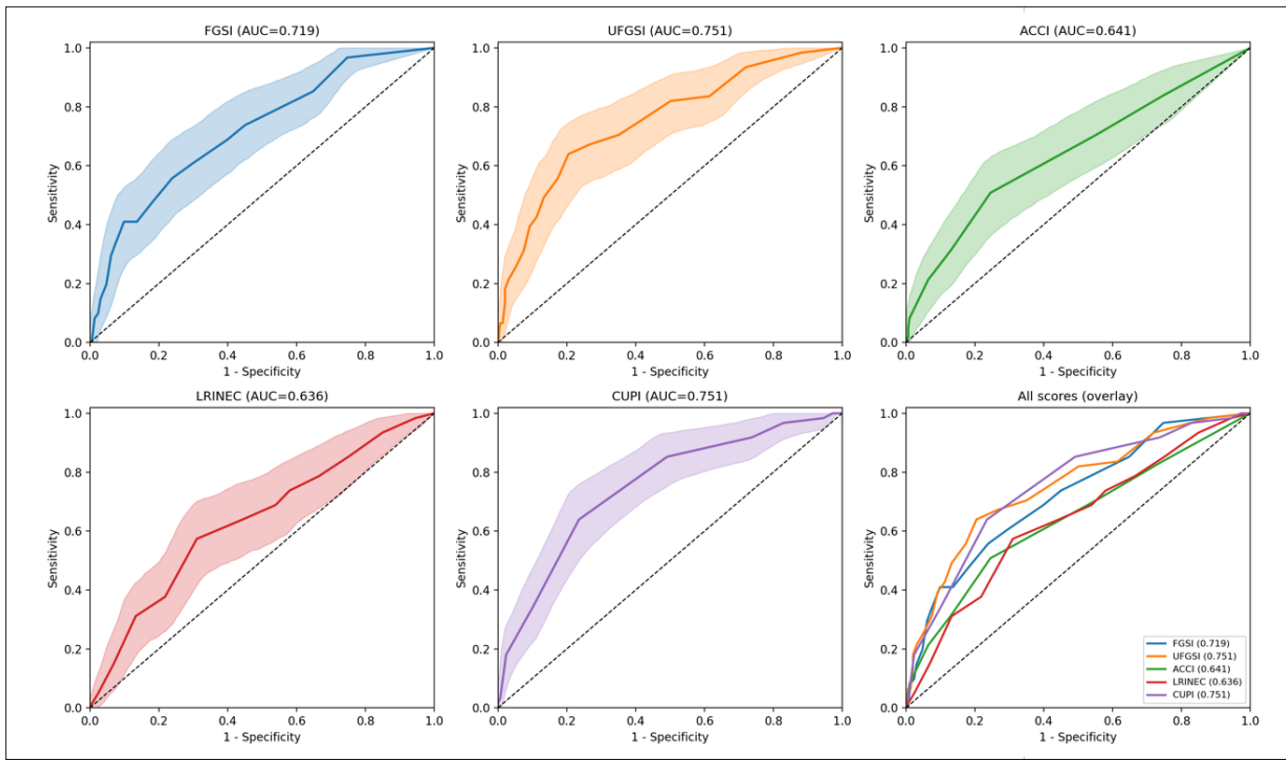

Figure 1. ROC curves for FGSI, UFGSI, ACCI, LRINEC, and CUPI predicting mortality, with 95% bootstrap confidence bands (shaded area); bottom-right panel shows all curves overlaid for comparison. ROC: Receiver operating characteristic; FGSI: Fournier Gangrene Severity Index; UFGSI: Uludağ Fournier Gangrene Severity Index; ACCI: Age-adjusted Charlson Comorbidity Index; LRINEC: Laboratory risk indicator for necrotizing fasciitis; CUPI: The Combined Urology and Plastics Index.

Table 2. Multivariate logistic regression analysis of factors predicting mortality in patients with Fournier gangrene

Binary logistic regression (n=354)

	Univariate model			Multivariate model		
	OR	95% CI	p	OR	95% CI	p
Age	1.065	1.039–1.092	<0.001	1.055	1.022–1.090	0.001
Gender (refer-ence: Female)	0.489	0.278–0.862	0.013			
Presence of risk factors	2.086	0.793–5.488	0.136			
Pulse	1.029	1.012–1.046	0.001			
Respiratory rate	1.113	1.055–1.173	<0.001	1.107	1.035–1.185	0.003
Body tempera-ture (°C)	2.235	1.569–3.185	<0.001			
Disease extent (reference: Urogenital)	1.302	1.063–1.594	0.011			
Hematocrit	0.945	0.907–0.984	0.006			
Leukocyte	0.999	0.965–1.034	0.951			
Lymphocyte	0.905	0.681–1.204	0.494			
Neutrophil lymphocyte ra-tio	1.023	1.006–1.040	0.008			
Sodium	1.016	0.970–1.063	0.509			
Potassium	1.123	0.772–1.634	0.543			
Chloride	1.060	1.012–1.110	0.014	1.075	1.008–1.146	0.027
Bicarbonate	0.731	0.668–0.801	<0.001	0.776	0.700–0.860	<0.001
Calcium	0.557	0.378–0.821	0.003			
Albumin	0.186	0.109–0.317	<0.001	0.245	0.125–0.478	<0.001
INR	6.274	1.184–20.888	0.003			
Procalcitonin	1.027	1.000–1.055	0.047			
CRP	1.001	0.999–1.003	0.308			
FGSI score	1.193	1.119–1.271	<0.001			
UFGSI score	1.201	1.135–1.271	<0.001			
ACCI	1.331	1.156–1.531	<0.001			
LRINEC Index	1.151	1.056–1.255	0.001			
CUPI	1.775	1.460–2.158	<0.001			
Time to surgery (hours)	1.012	1.006–1.019	<0.001	1.014	1.004–1.024	0.005
Δ-hours >12	2.088	1.195–3.647	0.010			
Number of deb-ridements	1.069	0.980–1.167	0.131			
VAC	0.900	0.482–1.680	0.740			
VAC duration	1.026	0.995–1.058	0.097			

n: Number; INR: International normalized ratio; CRP: C-reactive protein; OR: Odds ratio; FGSI: Fournier Gangrene Severity Index; UFGSI: Uludağ Fournier Gangrene Severity Index; ACCI: Age-adjusted Charlson Comorbidity Index; LRINEC: Laboratory risk indicator for necrotizing fasciitis; CUPI: The Combined Urology and Plastics Index; VAC: Vacuum assisted closure; ICU: Intensive care unit.

able model demonstrated good calibration (Hosmer–Lemeshow χ^2=7.95, degrees of freedom=8, p=0.438) and excellent discrimination (C-statistic=0.907, 95% CI 0.863–0.950).

When the survivors and the deceased were compared in Table 1, it was determined that the time to surgery exceeding 12 h was a statistically significant difference between the two groups. For this reason, patients whose time to surgery exceeded 12 h and those who did not exceed 12 h were evaluated separately in Table 3. In Table 3, patients with a time to surgery of up to 12 h (n=226) and patients with a time to surgery of more than 12 h (n=128) were compared with each other. Accordingly, mortality was 13.3% in patients with a time of up to 12 h until surgery, and 24.2% in patients with a time of more than 12 h until surgery (p=0.009). Furthermore, a time to surgery longer than 12 h was associated with longer LOS (p=0.001) and longer length of stay in the

Table 3. Effect of time to surgery longer than 12 h on mortality and length of hospital stay

	Δ-hours <12 (n=226)	Δ-hours >12 (n=128)	p
Mortality, n (%)	30 (13.3)	31 (24.2)	0.009[P]
Need for ICU, n (%)	102 (45.1)	63 (49.2)	0.459[P]
Number of deb-ridements in the operating room, medi-an (min–max)	1 (1–20)	1 (1–18)	0.774[M]
Length of hospital stay, days, median (min–max)	14 (1–103)	19 (1–120)	0.001[M]
Length of stay in the ICU, days, me-dian (min–max)	3 (1–64)	6 (1–90)	0.044[M]

n: Number; ICU: Intensive care unit; [M]Mann–Whitney U test; [P]Pearson's Chi-square test.

Table 4. Pairwise DeLong comparisons

Comparison	AUC 1	AUC 2	Difference	SE	Z	95% CI (diff)/p-value
FGSI versus UFGSI	0.719	0.751	−0.032	0.018	−1.804	(−0.067, 0.003); p=0.071
FGSI versus ACCI	0.719	0.641	0.078	0.044	1.775	(−0.008, 0.163); p=0.076
FGSI versus LRINEC	0.719	0.636	0.083	0.033	2.522	(0.019, 0.148); p=0.012
FGSI versus CUPI	0.719	0.751	−0.032	0.035	−0.924	(−0.099, 0.036); p=0.356
UFGSI versus ACCI	0.751	0.641	0.110	0.046	2.394	(0.020, 0.200); p=0.017
UFGSI versus LRINEC	0.751	0.636	0.116	0.035	3.283	(0.047, 0.185); p=0.001
UFGSI versus CUPI	0.751	0.751	0.000	0.035	0.010	(−0.068, 0.069); p=0.992
ACCI versus LRINEC	0.641	0.636	0.006	0.048	0.123	(−0.087, 0.099); p=0.902
ACCI versus CUPI	0.641	0.751	−0.109	0.041	−2.675	(−0.190, -0.029); p=0.008
LRINEC ver-sus CUPI	0.636	0.751	−0.115	0.043	−2.661	(−0.200, -0.030); p=0.008

Bold p-values indicate statistically significant differences (p<0.05). CI: Confidence interval; SE: Standard error of the AUC difference; Z: DeLong test statistic; FGSI: Fournier Gangrene Severity Index; UFGSI: Uludağ Fournier Gangrene Severity Index; ACCI: Age-adjusted Charlson Comorbidity Index; LRINEC: Laboratory risk indicator for necrotizing fasciitis; CUPI: The Combined Urology and Plastics Index; AUC: Area under the curve.

Table 5. Diagnostic performance at the optimal (Youden-Index) cut-off

Score	Cut-off (≥)	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+/LR−	Youden index (J)
FGSI	≥6	0.719 (0.649–0.790)	55.7 (43.3–67.5)	76.1 (70.9–80.6)	32.7 (24.4–42.2)	89.2 (84.7–92.5)	2.33/0.58	0.318
UFGSI	≥9	0.751 (0.681–0.821)	63.9 (51.4–74.8)	79.5 (74.5–83.7)	39.4 (30.3–49.2)	91.4 (87.3–94.2)	3.12/0.45	0.435
ACCI	≥3	0.641 (0.561–0.722)	50.8 (38.6–62.9)	75.4 (70.2–80.0)	30.1 (22.1–39.5)	88.0 (83.5–91.5)	2.07/0.65	0.262
LRINEC	≥8	0.636 (0.557–0.714)	57.4 (44.9–69.0)	68.9 (63.4–74.0)	27.8 (20.7–36.2)	88.6 (83.8–92.1)	1.85/0.62	0.263
CUPI	≥6	0.751 (0.684–0.818)	63.9 (51.4–74.8)	76.5 (71.3–80.9)	36.1 (27.7–45.5)	91.1 (86.8–94.0)	2.71/0.47	0.404

AUC: Area under the curve; CI: Confidence interval; PPV: Positive and predictive values; NPV: Negative predictive values; LR+: Positive likelihood ratios; LR−: Negative likelihood ratios; FGSI: Fournier Gangrene Severity Index; UFGSI: Uludağ Fournier Gangrene Severity Index; ACCI: Age-adjusted Charlson Comorbidity Index; LRINEC: Laboratory risk indicator for necrotizing fasciitis; CUPI: The Combined Urology and Plastics Index.

ICU (p=0.044). No significant difference was found in need for ICU (p=0.459) and number of debridement in the operating room (p=0.774).

Details of the ROC analysis of the scoring systems predicting FG mortality were shown in Figure 1. Individual AUC values (DeLong 95% CI) of FGSI score, UFGSI score, ACCI, LRINEC index, CUPI found to be (0.719, 95% CI 0.649–0.790, 0.751, 95% CI 0.681–0.821, AUC = 0.641, 95% CI 0.561–0.722, 0.636, 95% CI 0.557–0.714, 0.751, 95% CI 0.684–0.818)

Pairwise comparison of the AUC values using the DeLong

test for correlated ROC curves demonstrated that UFGSI and CUPI had significantly higher discriminative ability for mortality than ACCI (p=0.017 and p=0.008, respectively) and LRINEC (p=0.001 and p=0.008, respectively). FGSI also showed superior discrimination compared with LRINEC (p=0.012). No statistically significant differences were observed between FGSI and UFGSI (p=0.071), FGSI and ACCI (p=0.076), FGSI and CUPI (p = 0.356), UFGSI and CUPI (p=0.992), or ACCI and LRINEC (p=0.902) (Table 4).

Using Youden-index-derived optimal cut-offs (Table 5), UFGSI (≥9) and CUPI (≥6) showed the best overall diagnostic performance, each with a sensitivity of 63.9% and specificity of 79.5% and 76.5%, respectively, and the highest Youden indices (J=0.435 and 0.404). FGSI (≥6) demonstrated a specificity of 76.1% with a Youden index of 0.318, while ACCI (≥3) and LRINEC (≥8) showed comparatively lower discriminative performance (J=0.262 and 0.263, respectively). NPV were uniformly high across all five scores (88.0–91.4%), reflecting the relatively low overall mortality rate in this cohort (17.2%), whereas PPV remained modest (27.8–39.4%), as expected for a low-prevalence outcome. The LR+ was highest for UFGSI (LR+=3.12), indicating the greatest increase in the post-test probability of mortality among patients scoring above the optimal threshold.

DISCUSSION

FG treatment is mainly based on hemodynamic stabilization, regulation of fluid and electrolyte balance, early extensive debridement of infected and necrotic tissues, and parenteral broad-spectrum antibiotics.[11] In a disease with high mortality rates, such as FG, determining the factors that will affect the course of the disease is one of the most important elements. By determining these factors, it is possible to prevent the morbidity and mortality that accompany FG.[12]

Advancing age causes a decrease in physiological functions and a weakening of the immune system. This can mean both an increased risk of infection and a reduced ability to fight infection. At the same time, comorbidities that may occur due to advanced age can cause a more dramatic course of FG.[13] While age is not included in the FGSI score and LRINEC index, it is one of the parameters in the UFGSI and CUPI scores. Although there are studies claiming the contrary,[14,15] many studies have stated that advanced age is associated with mortality due to FG.[13,16] In the regression analysis of mortality due to FG in the study by Sugihara et al.,[17] advanced age was found to be an independent risk factor, similar to our study.

Although RR is one of the parameters of the two most commonly used scoring systems for FG (FGSI and UFGSI), there are studies showing that RR is higher in the group of patients who deceased,[15,18] as well as studies showing that there is no significant difference between survivors and non-survivors.[19,20] In our study, multivariate regression analysis showed that increased RR was one of the independent factors predicting mortality (p=0.003).

Chloride is an electrolyte that is often overlooked but has important effects on the patient, which can lead to many disorders, including disorders of hemostasis, acid-base balance, and immunomodulation.[21] Increased serum chloride levels may lead to metabolic acidosis, renal failure, and hemodynamic instability.[22] Although the literature indicates that mortality rates increase in patients with hyperchloremia, it is not yet clear whether the effect of chloride levels on mortality is direct or indirect.[23] In our study, high serum chloride level was found to be an independent predictor of FG-related mortality. With this result, our study suggests there may be a link between serum chloride levels and FG-related mortality.

Low serum bicarbonate is an indicator of metabolic acidosis. In metabolic acidosis, interleukin production is stimulated by macrophages and lymphocyte function is suppressed. This leads to increased inflammation and impaired immune response.[24] Studies have generally reported that serum bicarbonate levels were statistically significantly lower in patients who died of FG.[20,25] In our study, low serum bicarbonate level was found to be one of the independent predictors of FG-related mortality (p<0.001).

Serum albumin is known as a negative acute phase reactant. Hypoalbuminemia may be observed in patients with metabolic stress. Serum albumin levels may reflect the patient's nutritional status and immune function.[26] Low serum albumin levels may play a role in the progression of the disease, and advanced disease may cause a decrease in serum albumin levels. Although it was also stated that there were similar results regarding serum albumin levels between patients who survived and died after FG,[18] low serum albumin level was found to be an independent risk factor for mortality related to FG in the multivariate regression analysis in the study of Çomçalı et al.[27] and in the study of Shin et al.,[28] as in our study.

More than 10 scoring systems, both specific and non-specific to FG, have been investigated in the literature to predict mortality in FG.[15] Scoring systems should be easy to calculate, relatively less time-consuming, and have high sensitivity and specificity. There is no clear consensus in the literature on whether scoring systems are useful in FG and, if so, which system should be used first.[29]

The FGSI is the first and most commonly used FG-specific scoring method, but it is time-consuming to calculate. The threshold value for FGSI was found to be 9. It was stated that if it was higher than 9, the mortality rate would be 75%, and if it was lower than 9, the mortality rate would drop to 22%.[6] In the meta-analysis of El-Qushayri et al.,[30] it was stated that comorbidities should also be included in the FGSI scoring. The threshold value for the UFGSI score was accepted as 9, as in the FGSI score. The authors stated that the predictive power was higher and emphasized that if the score was high-

er than 9, the mortality rate would be 94%, while when it was 9 or less, this rate would drop to 18%.[7] The calculation is time-consuming. Although ACCI is not a scoring system specific to FG, it is used to evaluate the mortality risk based on the severity and number of diseases the patient has. It is easy to calculate and has validation for a large number of diseases. In the study by Sugihara et al.,[17] it was stated that increased ACCI was an independent risk factor for FG-related mortality in multivariate regression analysis. LRINEC index is an easy-to-calculate scoring system. It is not specific to FG and was developed for diagnostic purposes. In the LRINEC index, patients are divided into three risk categories for NSTIs: Low (LRINEC index ≤5), intermediate (LRINEC index 6–7), and high (LRINEC index ≥8). A LRINEC index of 6 and above increases suspicion of necrotizing fasciitis, and a score of 8 and above is a strong predictor of this disease.[9] Some studies suggest that the LRINEC index is helpful in the diagnosis of necrotizing fasciitis, but clinical evaluation and radiological methods should also be used in the diagnosis.[31,32] CUPI is specific for FG and is the first scoring system that prioritizes morbidity and LOS in FG patients. The threshold value for CUPI was found to be 5. For values 5 and below, the mean LOS was 25 days, while for values above 5, the mean LOS was 71 days.[10] CUPI is a scoring system that has not been studied much. It is a complement to the existing prognosis prediction model. Identifying high-risk FG patients in CUPI may shorten LOS and improve prognosis.[33]

If we evaluate the studies comparing the scoring systems predicting FG-related mortality, in the meta-analysis conducted by Tufano et al.[34] investigating the predictive values of FGSI and UFGSI scores for mortality in patients with FG, they stated that mortality increased as scores increased in both scoring systems, but the accuracy rate of UFGSI was higher. Among the studies comparing FGSI, UFGSI, and ACCI, Tuncel et al.[35] reported that only UFGSI has predictive value for mortality. In the study by Azmi et al.[15] comparing FGSI, UFGSI, ACCI, and LRINEC scores, all scoring systems were found to be significantly higher in non-survivors, but among these, FGSI was found to be superior to the other 3 scoring systems. In the study by Arıkan et al.,[36] where they compared FGSI, UFGSI, ACCI, and LRINEC, it was found that FGSI and UFGSI scores were superior to others in multivariate analysis, and among these, UFGSI was stated to be the most accurate and LRINEC the least accurate in mortality prediction. In our study, although all 5 scoring systems were found to be statistically higher in the non-survivors ($p<0.001$). To formally compare the discriminative performance of the five scoring systems, we performed pairwise DeLong tests for correlated ROC curves. This analysis showed that UFGSI and CUPI significantly outperformed ACCI and LRINEC (all $p<0.02$), while FGSI, UFGSI, and CUPI did not differ significantly from one another.

The general consensus among surgeons is that the earlier the necrotic tissue is debrided, the better the outcome. However, how early is early enough is not well defined.[37] Studies on this subject mainly cover NSTIs, which are a more general definition. In the meta-analysis by Nawijn et al.,[38] they noted that the time from the onset of NSTI symptoms to hospital admission or surgery did not affect mortality. It was stated that surgical treatment within 12 h of hospital admission is necessary to reduce mortality rate, but surgical treatment within 6 h may further improve outcomes. Patients with severe sepsis may undergo delayed surgery because they require initial stabilization. Conversely, the sickest patients may undergo surgery immediately. It should be kept in mind that such confounding factors can affect time-to-surgery outcomes. In the study by Gelbard et al.,[39] in patients with NSTI, mortality was found to be 14% and 25.8% in patients with a time to surgery of less than and more than 12 h, respectively. In a systematic review evaluating patients with necrotizing fasciitis, it was found that the survival rate decreased from 93.2% to 75.2% when the time from admission to surgery was increased from 24 to 48 h.[40] Lin et al.[41] found that the only significant factor in comparing surviving and deceased patients with FG was time to surgery. It has been stated that the appropriate time for surgical debridement of FG is the first 14 h, and any delay is associated with increased mortality. In our study, in the multivariate regression analysis investigating the factors affecting mortality in patients with FG, the time to surgery was found to be an independent predictor ($p=0.005$). When the time to surgery was compared between survivors and non-survivors, the median time to surgery was 8 h in survivors and 12.5 h in non-survivors ($p=0.016$). In our study, mortality was 13.3% in patients with a time of up to 12 h until surgery, and 24.2% in patients with a time of more than 12 h until surgery ($p=0.009$).

Although our study includes a certain population, it includes a larger number of patients compared to similar studies. One of the limitations of the study is that not all scoring systems were used. In addition, the lack of detailed information on the type of microorganism isolated in the wound culture, the antibiotic therapy administered, and the antibiotic resistance pattern of patients with FG is among the limitations of the study. In addition, data regarding "time from symptom onset to hospital admission" and "time from symptom onset to surgery" were not available in our study. The retrospective, single-center nature is a potential source of bias and another limitation that prevents generalization of the study results. Furthermore, there is no external validation available for our study. A multicenter prospective study with a larger sample size is needed for further confirmation.

CONCLUSION

There are various clinical, laboratory findings, and scoring systems that help us predict the relationship between FG and mortality. According to our study, advanced age, increased RR, high serum chloride, low serum bicarbonate, low serum albumin, and the time between hospital admission and surgery are independent predictors of FG mortality. Consider-

ing the scoring systems, our results showed that UFGSI and CUPI significantly outperformed ACCI and LRINEC, while FGSI, UFGSI, and CUPI did not differ significantly from one another. Prompt, complete debridement is the basis for patient survival. One of the most important aspects of reducing mortality is complete debridement within 12 h of hospital admission.

Ethics Committee Approval: This study was approved by the Health Sciences University Izmir Tepecik Training and Research Hospital (Date: 05.02.2025, Decision No: 2025/01-33).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Fournier gangreni olan hastalarda ölüm oraninin tahmini: Ameliyata kadar geçen sürenin önemi

AMAÇ: Fournier gangreninin (FG) karmaşık yapısı ve ciddiyeti göz önüne alındığında, tedavi stratejileri geliştirmek ve klinik sonuçları tahmin etmek için prognostik faktörleri belirlemek önemlidir. FG hastalarının erken teşhisi, hastaların sağlık durumlarına verilen zararı azaltabilir, tedavi başarısını ve hayatta kalma oranlarını artırabilir. Çalışmamızın amacı, FG hastalarında mortaliteyi öngören klinik ve laboratuvar bulgularını, mortalite tahmininde beş puanlama sisteminin rolünü ve acil servise başvuru anından ameliyat anına kadar geçen sürenin önemini değerlendirmektir.
GEREÇ VE YÖNTEM: FG tanısı konulan toplam 354 hasta, hayatta kalanlar (n=293) ve hayatını kaybedenler (n=61) olmak üzere iki gruba ayrıldı. FG hastalarında mortaliteyi öngören faktörlere ilişkin tek değişkenli analizde istatistiksel anlamlı bulunan değişkenler için çok değişkenli lojistik regresyon analizi uygulandı. Fournier Gangren Şiddet İndeksi (FGSI) skoru, Uludağ Fournier Gangren Şiddet İndeksi (UFGSI) skoru, Yaşa Göre Ayarlanmış Charlson Komorbidite İndeksi (ACCI), Nekrotizan Fasiit için Laboratuvar Risk Göstergesi (LRINEC) İndeksi ve Kombine Üroloji ve Plastik Cerrahi İndeksi (CUPI); FG'nin mortalitesini tahmin etmek için ROC eğrisi ile analiz edildi.
BULGULAR: FG'ye bağlı ölüm oranı %17.2 olarak bulunmuştur. İleri yaş, artmış solunum hızı, yüksek serum klorür, düşük serum bikarbonat, düşük serum albümin ve hastaneye yatış ile ameliyat arasındaki süre, çok değişkenli analizde FG mortalitesinin bağımsız belirleyicileridir. FGSI skoru, UFGSI skoru, ACCI, LRINEC indeksi ve CUPI'nin ROC eğrisi altındaki alan (AUC) değerleri sırasıyla 0.719, 0.751, 0.641, 0.636 ve 0.751 olarak bulunmuştur. Ölüm oranı ameliyata kadar geçen süre 12 saate kadar olan hastalarda %13.3, ameliyata kadar geçen süre 12 saatten fazla olan hastalarda ise %24.2 idi. Ayrıca, ameliyata kadar geçen sürenin 12 saatten uzun olması, hastanede kalış süresinin de uzamasıyla ilişkiliydi (p=0.001).
SONUÇ: Skorlama sistemlerini dikkate aldığımızda, sonuçlarımız UFGSI ve CUPI'nin ACCI ve LRINEC'ten önemli ölçüde daha iyi performans gösterdiğini, FGSI, UFGSI ve CUPI arasında ise anlamlı bir fark olmadığını ortaya koymuştur. Ölüm oranını azaltmanın en önemli yönlerinden biri, hastaneye yatıştan sonraki 12 saat içinde tam debridmanın yapılmasıdır.

Anahtar sözcükler: Acil; ameliyata kadar geçen süre; Fournier gangreni; ölüm oranı; skorlama sistemleri.

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