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ORIGINAL ARTICLE

Scoring Systems for the Prediction of Mortality in Patient with Fournier's Gangrene: an Analysis of 60 Patients

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Abstract

The aim of this study was to evaluate demographic and clinical findings in Fournier's gangrene and to assess feasibility of several scoring indexes for predicting morbidity and mortality. Patients who underwent surgery for Fournier's gangrene between 2006 and 2020 were analyzed. Scores of Fournier Gangrene Severity Index, Uludag Fournier Gangrene Severity Index, Age-adjusted Charlson Comorbidity Index, and Sequential Organ Failure System for each patient were calculated. Mortality rate was regarded as the primary outcome. There were 60 patients with a mean age of 61.4 SD 16.0 years. There were 10 deaths with a mortality rate of 16.7%. There were significant differences between non-survivor ($n = 10$) and survivor patients ($n = 50$) with regard to hemoglobin, serum total protein, and serum bicarbonate levels ($p < 0.05$). In all patients who survived, the scores of all indexes were significantly higher than that of the patients who were non-survivors ($p < 0.05$). Although the diagnostic accuracy of Fournier Gangrene Severity Index and Uludag Fournier Gangrene Severity Index for mortality was moderate, diagnostic accuracies of Age-adjusted Charlson Comorbidity Index and Sequential Organ Failure System score for prediction of mortality were regarded as good. Fournier Gangrene Severity Index, Uludag Fournier Gangrene Severity Index, Age-adjusted Charlson Comorbidity Index, and Sequential Organ Failure System score were shown to be associated with mortality in Fournier's gangrene. Diagnostic accuracies of Uludag Fournier Gangrene Severity Index, Age-adjusted Charlson Comorbidity Index, and Sequential Organ Failure System score for prediction of mortality were higher than that of Fournier Gangrene Severity Index.

Keywords Fournier's gangrene · Mortality · Severity · Index

Introduction

Fournier's gangrene (FG) as a necrotizing fasciitis that affects the perineal, genital, and perianal regions is a life-threatening polymicrobial infectious disease [1, 2]. It usually requires prompt surgical intervention. Despite hemodynamic resuscitation, broad-spectrum antibiotic therapy, aggressive surgical debridement, and intensive care facilities, mortality rates

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remain high [2, 3]. Due to this high mortality rates, several scoring systems have been tried to develop to predict the severity of the disease and survival. It has been thought that it is possible to identify the patients requiring more extensive management in consistency with their risks for major complications by using these scoring systems [4, 5].

Among the scoring systems originated for FG, the Fournier Gangrene Severity Index (FGSI) as a modification of the Acute Physiology and Chronic Health Assessment 2 score has been the first system used in patients with FG [6]. The Uludag Fournier Gangrene Severity Index (UFGSI) has been also designed to predict the mortality in FG patients [2]. In addition, several indexes and scoring systems, including the Age-adjusted Charlson Comorbidity Index (ACCI) and the Sequential Organ Failure System (SOFA), have been also used for predicting patient survival in FG [4, 7]. However, no single reliable tool for predicting severity and survival of FG is currently available [8–10]. In addition, there is limited data about the predictive power of the SOFA in FG.

Besides the presence of defined predisposing factors for FG and clinical features affecting mortality, there are still controversial results with regard to the predictive markers for mortality and morbidity [11, 12]. Therefore, efficacies of the instruments to predict morbidity and mortality of FG should be investigated to find the most appropriate scoring index.

In this study, it was aimed to evaluate demographic, clinical, and surgical findings of the patients with FG and assess feasibility of the FGSI, the UFGSI, the ACCI, and the SOFA for predicting morbidity and mortality.

Patients and Methods

This study was a retrospective analysis of the patients who were treated with a diagnosis of FG at the departments of general surgery and urology, a tertiary university hospital in Turkey, between January 2006 and February 2020. Approval was taken from the hospital ethical committee. It was performed in accordance with the Helsinki Declaration on human studies. Written consent could not be taken from the patients due to the retrospective design of the study.

Patients were identified retrospectively from hospital information system by entering the words “Fournier’s” and “gangrene” into a keyword search system function in the information system. All consecutive patients with FG treated surgically for necrotizing soft tissue infections of the perineal and perineal regions were included. Patients with superficial solitary perianal, scrotal, or periurethral abscesses without soft tissue extension and incomplete medical records were excluded in the study.

Procedures

After hospitalization, all patients underwent intravenous fluid resuscitation and empiric broad-spectrum antimicrobial therapy including a third-generation cephalosporin plus metronidazole with dose adjustments according to their renal functions. Antibiotics were modified according to the bacterial culture results.

Surgical debridement of infectious and necrotic tissues was performed following hemodynamic stabilization that was achieved. Tissue samples for microbial cultures were obtained during the surgery. Wound dressings were performed in the operating theater at first and changed daily or if necessary at the wards until secondary skin closure and/or implementation of split-thickness grafting. Povidone-iodine and hydrogen peroxide were used as antiseptic agents during wound dressings. Nitrofurazone gauze rolls moistened with physiological saline solution were used to cover the debrided regions.

Following the initial debridement at every 24 to 48 h, wound exploration and re-debridement was performed in the operating theater if necessary until macroscopic healthy tissues supported by negative bacterial cultures were obtained.

Stoma creation for fecal diversion was performed in selected patients in whom uncontrolled wound contamination with intestinal content was observed. In patients with necrosis at the testis, orchiectomy was performed.

Variables

Demographic data (age, sex), comorbidity, vital signs (body temperature (°C), heart rate (/min), respiratory rate (/min), mean arterial pressure (mmHg)), clinical and laboratory findings, and length of hospital stay (day) were recorded using medical records of the patients. Hemoglobin (g/dL), hematocrit (%), white blood cell count (/mm^3), platelet count (10^3), serum levels of urea (mg/dL), sodium (mmol/L), potassium (mmol/dL), calcium (mg/dL), creatinine (mg/dL), bicarbonate (mg/dL), total protein (g/dL), albumin (g/dL), and C-reactive protein (mg/dL) were measured at the initial diagnosis and recorded.

Etiology of the infection causing FG was searched using medical history and physical examination findings.

Scores of FGSI, UFGSI, ACCI, and SOFA for each patient were calculated and recorded into a prospectively held database using the initial data at the admission.

To calculate the FGSI, nine parameters (body temperature, heart rate, respiratory rate, hematocrit, white blood cell count, sodium, potassium, creatinine, and bicarbonate levels) were measured, and degree of deviation from normal was graded from 0 to 4. Sum of the individual values was defined as the FGSI score [6].

The UFGSI was calculated by adding age and dissemination scores to the FGSI [2]. Age of the patients was stratified

into ≥ 60 years and < 60 years, and "1" point and "0" point were added to the FGSI score, respectively. For dissemination score of the disease, "1" point, "2" points, and "6" points were added to the FGSI score for FG confined to the urogenital and/or anorectal regions, FG confined to the pelvic region, and FG extending beyond the pelvic region, respectively (Suppl. file 1) [2, 6].

To calculate the ACCI score, a sum of 19 medical conditions weighing from 1 to 6 was used as a reference value for Charlson Comorbidity Index [4]. Then, for each one-point increase, another point was added to the reference value for each decade of life over the age of 50. Sum of the individual values was regarded as the ACCI score.

For SOFA score, six different organ systems including include respiratory, circulatory, renal, hematology, hepatic, and central nervous were scored from 1 to 4 according to the degree of dysfunction [7]. The sum of each system score was defined as the SOFA score (Suppl. file 2).

Statistical Analysis

Mortality was defined as disease-related death during the first 30 days after the diagnosis, and the development of mortality (number of dead patients) was regarded as the primary outcome. Distribution of continuous variables was assessed by Shapiro-Wilk's test. Continuous variables are presented as mean and standard deviation (SD) or median (1st-3rd interquartile ranges (IQR)). Categorical variables were presented as number and frequencies. Student's *t* or Mann-Whitney tests were used for comparing the continuous variables based on the distribution. Chi-square test (or Fisher's exact test) was used to compare the categorical variables. The analysis of the receiver operating characteristic (ROC) curve in association with area under curve (AUC) was used to determine the optimal cutoff values of different scoring indices for mortality. Each optimal cutoff value was chosen considering the highest sensitivity and reasonably high specificity, as well as positive and negative predictive values. AUC was interpreted as good if AUC = 0.8–1, moderate if AUC = 0.7–0.8, fair if AUC = 0.6–0.7, and poor if AUC = 0.5–0.6. R software (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analyses.

Results

There were 60 patients with a mean age of 61.4 SD 16.0 years. Female to male ratio was 1 to 3. Demographic and clinical features are given in Table 1.

There were ten non-survivors and 50 survivors. Thus, the mortality rate was 16.7%. In almost half of the patients (51.7%), there was at least one coexisting disease. Among these, cardiovascular disease was the most common comorbidity that was seen in 18 patients (30.0%).

Perianal or perirectal and genitourinary infections were seen in 32 (53.3%) and 19 patients (31.7%), respectively.

There were significant differences between non-survivor and survivor patients regarding hemoglobin, serum total protein, and serum bicarbonate levels ($p < 0.05$ for all) (Table 1). However, the presence of cardiovascular disease and diabetes mellitus showed no significant impact on mortality ($p > 0.05$ for both). Median length of hospital days was significantly lower in the non-survivor patients (9.5 days vs. 19.5 days, $p < 0.001$).

The scores of the FGSI, the UFGSI, the ACCI, and the SOFA are given in Table 2. In all patients who survived, the scores of all indexes were significantly higher than that of the patients who were non-survivors ($p < 0.05$ for all) (Fig. 1).

ROC analysis using the sensitivities and specificities based on the mortality revealed that the optimal cutoff values for the FGSI, the UFGSI, the ACCI, and the SOFA were 4, 10, 5, and 4, respectively. Their corresponding sensitivity and specificities based on the optimal cutoff values are given in Table 3. The cutoff SOFA score of ≥ 4 has had the highest sensitivity (0.90) with reasonably high specificity (0.88), positive predictive value (0.60), and negative predictive value (0.98) considering the other scoring systems. Although the diagnostic accuracy of the FGSI and UFGSI for mortality was moderate, the diagnostic accuracies of the ACCI and the SOFA for prediction of mortality were regarded as good. The SOFA has had the highest AUC value (0.914) among the all scores. Figure 2 also represents the schematic view of the AUC values for each scoring system.

Discussion

In this study, we showed that mortality in FG was significantly associated with the FGSI, the UFGSI, the ACCI, and the SOFA. In addition, laboratory investigations, i.e., hemoglobin, serum total protein, and serum bicarbonate levels seemed to be negative prognostic factors. We also showed the significant association of the SOFA with mortality in FG.

In previous studies, various etiological risk factors have been proposed including advanced age, sex, comorbid conditions, extent and severity of the disease [13, 14]. In a systematic review [1], it has been reported that mortality in FG is directly related with DM, heart diseases, renal failure, and kidney disease. In the present study, we showed that presence of malignancy and respiratory systems disorders, hemoglobin, serum total protein, and serum bicarbonate levels was significantly associated with mortality. In our study population, there was no patient with renal failure or kidney disease. Due to this reality, we could not perform such analysis. In addition, several laboratory parameters have been proposed

Table 1 Demographic and clinical features of the patients

		All patients ($n = 60$)	Non-survivor ($n = 10$)	Survivor ($n = 50$)	p value
Age (year)[a]		61.4 SD 16.0	68.5SD 14.1	59.9 SD 16.1	0.124
Sex[b]	Female	15 (25)	1 (10)	14 (28)	0.424
	Male	45 (75)	9 (90)	36 (72)	
Comorbidities[b]		31 (51.7)	7 (70)	24 (48)	0.355
	Cardiovascular	18 (30)	3 (30)	15 (30)	1.0
	DM	11 (18.3)	2 (20)	9 (18)	1.0
	Malignancy	8 (13.3)	4 (40)	4 (8)	NA
	Respiratory	7 (11.7)	4 (40)	3 (6)	NA
	Hematological	5 (8.3)	2 (20)	3 (6)	NA
	Central nervous	2 (3.3)	1 (10)	1 (2)	NA
Laboratory	Hemoglobin (g/dL)[a]	10.9 SD 1.7	9.8 SD 2.0	11.2 SD 1.5	0.014
	WBC (total/mm^3)[c]	12.8 (11.0–15.0)	12.15 (7–34)	13 (0.8–39)	0.409
	Platelet (10^3)[c]	199 (155–242)	225 (168.5–341)	196 (155–230)	0.218
	Urea (mg/dL)[c]	19.5 (14.0–25.3)	23.5 (14.3–57.5)	18.5 (14.0–25.0)	0.330
	Sodium (mmol/L)[a]	133.3 SD 5.5	135.4 SD 3.9	132.8 SD 5.7	0.179
	Potassium (mmol/dL)[c]	4 (3.6–4.7)	4.35 (3.2–5)	4 (3.5–4.6)	0.715
	Calcium (mg/dL)[a]	8.0 SD 1.0	7.91 SD 1.0	8.1 SD 1.0	0.661
	Creatinine (mg/dL)[c]	0.9 (0.7–1.3)	1.0 (0.8–1.7)	0.9 (0.7–1.2)	0.377
	Bicarbonate(mg/dL)[a]	23.9 SD 4.3	19.5 SD 6.0	24.7 SD 3.3	< 0.001
	Total protein (g/dL)[c]	6.7 (6.0–7.1)	5.65 (5.3–6.4)	6.9 (6.2–7.2)	0.005
	Albumine[a]	2.9 SD 0.7	2.7 SD 0.9	2.95 SD 0.6	0.233
	CRP[c]	7 (3.8–13)	12 (6.3–16.7)	7 (3–12.5)	0.055
Colostomy[b]		13 (21.7)	2 (20)	11 (22)	0.888
Orchiectomy[b]		2 (3.3)	0 (0)	2 (4)	1

NA not applicable, *DM* diabetes mellitus, *WBC*: white blood cell, *CRP* C-reactive protein

[a] Mean and standard deviation (SD)

[b] *n* (%)

[c] Median (IQR)

as prognostic indicators for FG. But most of the studies showed only limited number of such parameters in association with higher mortality [15]. Among these variables, low serum bicarbonate level can be taken into consideration as a marker of decreased renal function although it has been also used for the calculation of both the FGSI and the UFGSI. In accordance with our findings, a significant association between low bicarbonate and higher mortality has been found [10]. Therefore, presence of any decrease in serum bicarbonate levels during treatment of such patients may be an important

Table 2 Association of FGSI, UFGSI, ACCI, and SOFA to mortality

	All patients ($n = 60$)	Non-survivor ($n = 10$)	Survivor ($n = 50$)	p value
FGSI[a]	2 (1–5.25)	7 (4.25–9.25)	2 (1–4)	0.013
UFGSI[a]	5 (3–9.25)	11.5 (7–15.75)	5 (2.25–7.75)	0.001
ACCI[a]	3 (2–4)	5 (4.25–5.75)	3 (2–4)	< 0.001
SOFA[a]	1.5 (1–3.25)	4 (4–4)	1 (1–2)	< 0.001

FGSI the Fournier Gangrene Severity Index, *UFGSI* the Uludag Fournier Gangrene Severity Index, *ACCI* the Age-adjusted Charlson Comorbidity Index, *SOFA* the Sequential Organ Failure System

[a] Median (IQR)

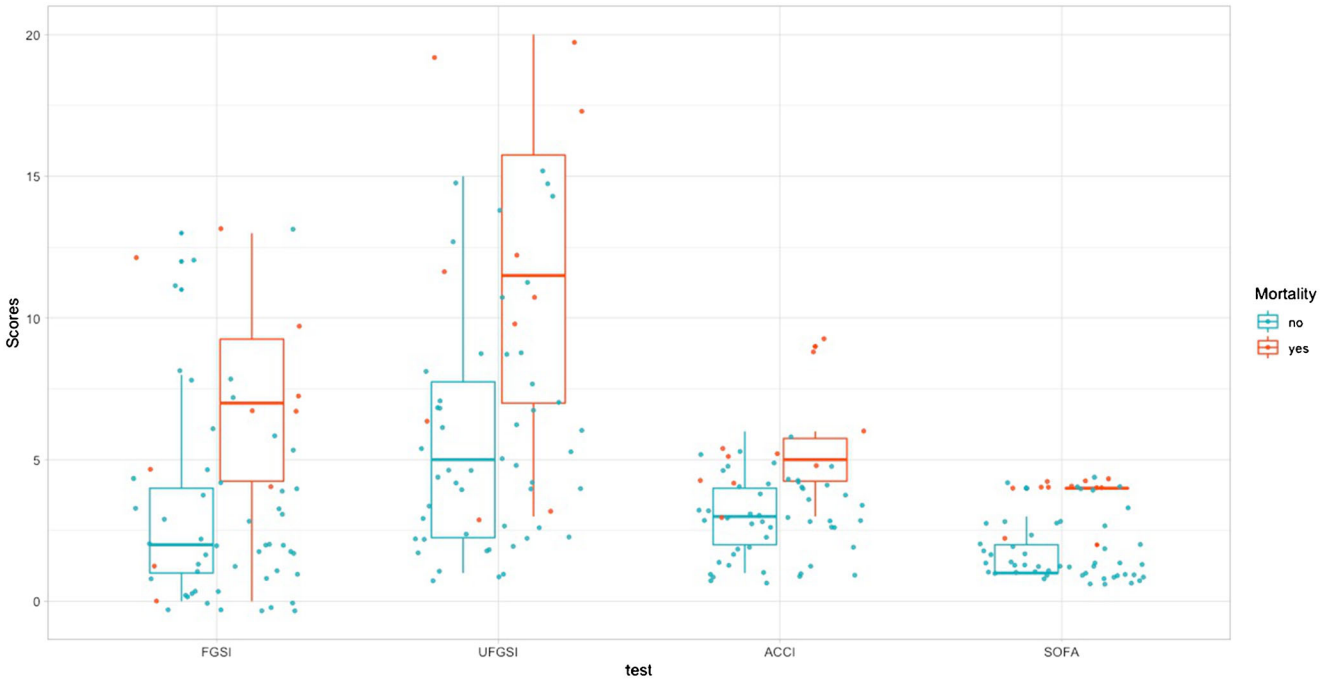

Fig. 1 Dot plot with mean and standard deviations across 4 scoring systems in patients with Fournier's gangrene. FGSI the Fournier Gangrene Severity Index, UFGSI the Uludag Fournier Gangrene Severity Index, ACCI the Age-adjusted Charlson Comorbidity Index, SOFA the Sequential Organ Failure System

measure to be kept in mind for the development of morbidity and mortality. However, heterogeneity in study populations and unstandardized variables may prevent generalizability of the results.

It has been thought that the mortality rates of FG has been also lowered to 10% or less with the advancement of early diagnosis and improved treatment modalities within the last decades [5, 14, 16]. However, mortality rates have been found between 35 and 67% [17]. Majority of the current published studies in relation to FG have reported mortality rates in a range of 11.9 to 42% [3, 4, 8–13, 18–20]. In the present study, the mortality rate was 16.6%. Although lower mortality rates can be attributed to the quality of healthcare systems, characteristics of study populations including advanced age, poor health status, and aggressive nature of the infection may have greater impact on mortality [8, 10]. In previous studies, some researchers showed that advanced age was a significant poor prognostic factor for FG [3, 4, 13, 14, 18]. But such association could not be detected in the present study in accordance with others [9, 15]. So, we believe that a single factor cannot be accused or regarded for the prediction of mortality in FG.

In most of the previously published studies, the presence of DM in patients with FG has been shown as one of the major prognostic factors for morbidity and mortality [1, 16, 20–22]. Nevertheless, some researchers did not report significant associations between DM and FG [2, 3, 19]. In the present study, DM was the second common comorbid disease, and we could not show the effect of DM on mortality for FG. This difference may be originated from the variations in the characteristics of the patients.

In relation to the prediction of mortality in FG by using scoring systems or indexes, there have been controversial results. It has been reported that there was a 75% probability of death in patients with a score of FGSI greater than 9 [6]. The

Table 3 Cutoff values of the applied indexes or scores

Index/score	Cutoff value	AUC (95%)	Sensitivity	Specificity	PPV	NPV	Accuracy
FGSI	≥4	0.747 (0.55–0.94)	0.70	0.78	0.39	0.93	0.77 (0.64–0.88)
UFGSI	≥10	0.767 (0.58–0.95)	0.60	0.84	0.43	0.91	0.80 (0.68–0.89)
ACCI	≥5	0.865 (0.75–0.98)	0.30	0.98	0.75	0.88	0.86 (0.75–0.94)
SOFA	≥4	0.914 (0.84–0.98)	0.90	0.88	0.60	0.98	0.88 (0.77–0.95)

AUC area under curve, *SE* standard error, *PPV* positive predictive value, *NPV* negative predictive value, *FGSI* the Fournier Gangrene Severity Index, *UFGSI* the Uludag Fournier Gangrene Severity Index, *ACCI* the Age-adjusted Charlson Comorbidity Index, *SOFA* the Sequential Organ Failure System

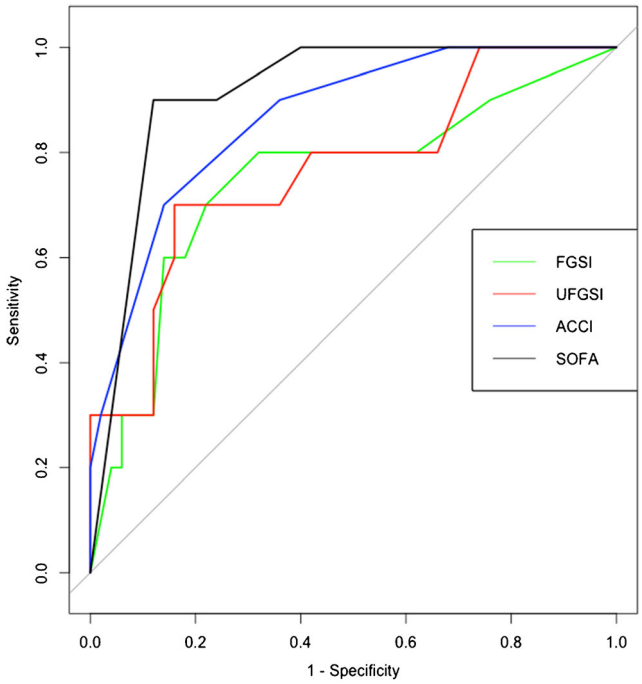

Fig. 2 Area under curve analysis of the scoring systems. FGSI the Fournier Gangrene Severity Index, UFGSI the Uludag Fournier Gangrene Severity Index, ACCI the Age-adjusted Charlson Comorbidity Index, SOFA the Sequential Organ Failure System

benefit of the FGSI has been also shown by other studies [3, 8, 9, 11, 12, 16, 20]. However, some researchers showed that there was no significant association between FGSI and mortality [10, 13]. The UFGSI has been developed to obtain better outcome prediction for FG as 94% of probability in patients with an index score of greater than 9 [2]. Some researchers found similar results [13, 20]. Nevertheless, others speculated that the UFGSI does not seem to be more powerful scoring system than the others [4]. In addition, many researchers have tried to find new scoring systems in relation to FG to overcome the diagnostic accuracy problems of the scoring systems [14, 15, 18]. Therefore, it has been thought that each scoring system may not reflect the disease severity and treatment outcomes in patients with FG [13]. We showed significant associations between mortality of FG and all indexes. So, we believe that each index or scoring system is useful to predict morbidity and mortality in patients with FG.

Use of the cutoff values for both the FGSI and the UFGSI causes additional controversies due to the fact that these values were not been validated in other studies [13, 14]. Although we showed significant associations of the FGSI and the UFGSI on the outcome of FG, the cutoff values of both showed differences at 4.5 and 10, respectively. A threshold value of greater than 9 was calculated for the FGSI [6]. It has been found that the predictive power of the UFGSI for probability of death was much better if it is ≥ 9 [2]. Although our cutoff values showed important variations especially for the FGSI, we have difficulty to explain this difference. Therefore, the use of these systems with their optimal cutoff values should be re-evaluated with larger-scale studies.

Due to the close association of the poor prognosis of FG and the presence of comorbidities, the ACCI has been studied as a general scoring system for such conditions [4, 13]. In previous studies, worse prognosis of FG in patients with higher ACCI score has been reported as in accordance with this study. However, there are still controversial findings in this issue [13].

The SOFA score has been used for identification of sepsis among patients who are critically ill [23]. Up to date, there is only one study in which the SOFA score was studied in FG patients [7]. In this study, the authors reported that lower mean SOFA scores (1.70 SD 2.30 vs. 2.98 SD 3.36) were significantly associated with the probability of primary wound closure. Besides, the SOFA score remained its significance on logistic regression analysis. In the present study, the mean SOFA scores were calculated as 1.8 SD 1.1 and 3.8 SD 0.6 for survivors and non-survivors similar to the above mentioned study [7]. Besides, we showed its predictive power for mortality of FG. Therefore, the SOFA score can also be used for this purpose. Prospective studies with follow-up are needed to clarify its possible use in FG.

Retrospective design of the study and the relative low number of the patients were the major limitations of the study. However, inclusion of the SOFA as a scoring system for FG was the major strength.

In conclusion, Fournier's gangrene seems to be still a potentially lethal disease. Several indexes and scoring systems including the Fournier Gangrene Severity Index, the Uludag Fournier Gangrene Severity Index, the Age-adjusted Charlson Comorbidity Index, and the Sequential Organ Failure System score were shown to be associated with mortality in Fournier's gangrene. The diagnostic accuracies of the Uludag Fournier Gangrene Severity Index, the Age-adjusted Charlson Comorbidity Index, and the Sequential Organ Failure System score for prediction of mortality were higher than that of the Fournier Gangrene Severity Index. We suggest that each one can be used for proper management of Fournier's gangrene in clinical practice.

Compliance with Ethical Standards Approval was taken from the hospital ethical committee. It was performed in accordance with the Helsinki Declaration on human studies. Written consent could not be taken from the patients due to the retrospective design of the study.

Conflict of Interest The authors declare that they have no conflict of interest.

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