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ORIGINAL ARTICLE

Simple scoring system for prediction of mortality in Fournier's gangrene

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Abstract
Purpose To create new scoring system for prediction of hospital mortality for patients with Fournier's gangrene(FG).
Material and method In total, 84 patients with FG were enrolled into this study. The demographic and clinical characteristics of patients were analyzed retrospectively.
Results The mortality rate was 11.9 %. On multivariate analyses, age >60 years, BUN >40 mg/dl, RDW >14.95 %, albumin level <20 mg/dl and presence of sepsis were significant and independent predictors of mortality. The predictive value of our score for mortality was 95.1 %.
Conclusion Our scoring system shows adequate discriminatory function for prediction of mortality in patients with FG. Further larger scale studies can improve the performance of our score.

Keywords Fournier's gangrene · Scoring · Mortality · Prediction

Introduction

Fournier's gangrene (FG) is a rare condition, life threatening—rapidly progressive necrotizing infection of perineal, genital and perianal region. It was firstly described by Alfred John Fournier in 1883 [1]. It is characterized by a polymicrobial infection with an identifiable cause in 95 % of cases, beginning in the genital or perineal regions and frequently spreads to the anterior abdominal wall. Predisposing factors include diabetes mellitus, steroid therapy, older age, perirectal or perineal surgery, HIV infection, anorectal abscess and renal or hepatic disease. Despite advances in treatment, the mortality rates remain high. Early diagnosis and aggressive debridement of necrotic tissue combined with appropriate wide-spectrum antibiotherapy are the corner points of successful treatment [2–5].

There have been efforts to develop a reliable tool to predict severity of the disease. In the past two decades many studies have described the usefulness of different scoring systems in predicting mortality of patients with FG. Fournier's gangrene severity index (FGSI) and Uludag Fournier's gangrene severity index (UFGSI) are used scoring system to evaluate the extent of disease and to predict mortality rates. The FGSI was modified from the Acute Physiology and Chronic Health Evaluation II severity score which was used for outcome evaluation of patients in intensive care unit (ICU) [6, 7]. FGSI can predict mortality with a probability of 75 % and survival with a probability of 78 % for patients with Fournier's gangrene [6]. UFGSI, includes age and extent of disease additionally to FGSI [8].

Aim of this study is to analyze possible factors that may influence the mortality in patients with FG, and create a novel scoring system.

Methods

Ninety-two patients with FG who were admitted to Emergency General Surgery Service at Ankara Numune Training and Research Hospital between 2010 and 2014 included in this study.

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Demographic features of patients, laboratory parameters such as serum total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), urea, creatinine, sodium, potassium, total calcium, lactic dehydrogenase (LDH), fasting blood glucose, total protein, albumin levels, white blood cell, neutrophil, lymphocyte, platelet counts, hemoglobin, hematocrit, red cell distribution width (RDW) levels, length of hospital stay (LOS), types of microorganisms isolated from the wound scrapings, surgical procedure (debridement, grafting and flaps), whether colostomy was opened or not, type of anesthesia (regional or general), co-morbid diseases and presence of sepsis were collected retrospectively from patients chart.

The diagnosis of FG was based on patient history, clinical symptoms and findings such as local tenderness, edema, erythema, rash, swelling, fluctuation, crepitus and necrosis in the perianal, perineal and/or genital areas. Patients with solitary perianal, periurethral and scrotal abscesses were excluded from the analysis if there was no evident soft tissue extension or necrosis. Fever of more than 38 °C (100.4 °F) or less than 36 °C (96.8 °F), heart rate of more than 90 beats per minute, respiratory rate of more than 20 breaths per minute or arterial carbon dioxide tension ($PaCO_2$) of less than 32 mm Hg and abnormal white blood cell count (>12,000 or <4000/μl or >10 % immature (band) forms defined as sepsis criteria.

Before the operation all patients underwent aggressive fluid resuscitation. Third generation cephalosporin and metranidazole intravenous antibiotherapy were administered to all patients as initial treatment. Then the treatment specified according to the wound culture results. Emergency surgical debridement was performed in all patients. Non-viable and infected tissue was excised until healthy tissue was reached. When tissue necrosis persisted in spite of initial intervention, surgical debridement was repeated. Closure of wounds was commenced as soon as healthy, viable tissue allowed reapproximation. When secondary wound closures were not possible, split-thickness skin graft or rotational cutaneous flaps were also used to repair large defects. Colostomy was performed when the source of infection originated from the anorectum and the sphincter was infected. Mortality was defined as disease-related death during hospitalization.

Independent variables

Age, gender, laboratory parameters, LOS, culture results, surgical intervention, and necessity of colostomy, type of anesthesia, co-morbid diseases and presence of sepsis.

Dependent variable

The primary endpoint (dependent variable) was hospital mortality.

Statistical analysis

Continuous data are presented as the mean values ± standard deviation. Differences in continuous variables were analyzed using the Mann–Whitney *U* test. The Shapiro–Wilk test was used to assess normality. Categorical variables were analyzed using Chi-square tests. Logistic regression was used to identify the factors associated with mortality. Results of the multivariate analysis are shown as odds ratios (OR) with 95 % confidence intervals (CI). Receiver operator characteristic (ROC) curve analyses were used to determine the optimal cutoff values for continuous variables. A clinical score based on the final logistic regression model was constructed in which 1 point was assigned for the presence of each predictive factor. Model discrimination was measured as the area under the ROC curve (AUC). The discrimination of a prognostic model is considered perfect if AUC = 1, good if AUC is >0.8, moderate if AUC is 0.6–0.8, and poor if AUC is <0.6.

Results

Of the 92 patients, 84 patient's data were eligible for study. 53 (63 %) patients were men and 31 (37 %) were women, with a mean age of 55.2 years (range 21–85). Primary anorectal infections and diabetes mellitus were the most common predisposing causes in both the sex. The mean hospitalization time was 27.2 days (range 4–135 days). A total of 10 (11.9 %) patients were dead. The demographic and clinical characteristics of survivor and non-survivor groups are compared in Table 1.

Univariate analyses

In univariate analyses, age, lymphocyte count, hemoglobin, hematocrit rates, RDW rates, urea level, albumin level, total protein level, total calcium level, co-morbid disease and sepsis existence were associated with a greater incidence of mortality.

Multivariate risk prediction model and prediction score

All of the variables that could be assessed before operation were included in the multivariate model. Five variables were significant in this analysis: age >60 years (OR 1.03); urea level >40 mg/dl (OR 1.03); RDW level >14.95 % (OR 1.09); albumin level <20 mg/dl (OR 1.50); and sepsis

Table 1 Demographic and clinical characteristics of patients

Variables	Exitus ($n = 10$) (mean, standard deviation)	Survivor ($n = 74$) (mean, standard deviation)	p value
Gender female/male	2/8	29/45	NS
Age	68 ± 12	54 ± 14	.007
WBC	12.70 ± 7.38	14.76 ± 6.10	NS
Hemoglobin	10.15 ± 1.51	11.88 ± 2.33	.013
Platelet	259.50 ± 150.04	325.89 ± 161.37	NS
RDW	17.24 ± 3.39	14.63 ± 2.45	.004
Fasting blood glucose	135.10 ± 41.49	158.94 ± 98.73	NS
Urea	68.00 ± 33.51	38.43 ± 30.15	.005
Creatinine	1.20 ± .93	.93 ± .60	NS
ALT	23.80 ± 13.35	25.59 ± 16.49	NS
AST	34.20 ± 23.17	28.21 ± 17.21	NS
ALP	120.10 ± 88.60	94.48 ± 42.90	NS
GGT	56.10 ± 68.55	53.75 ± 40.10	NS
LDH	276.10 ± 125.01	229.55 ± 122.01	NS
Total protein	49.96 ± 8.55	59.79 ± 9.99	.007
Albumin	16.89 ± 3.99	27.05 ± 8.92	.000
Total calcium	7.39 ± .61	8.48 ± 1.05	.000
Total bilirubin	.74 ± .45	.89 ± .91	NS
LOS	25 ± 18	27 ± 24	NS
Co-morbid disease (±)	10/0	38/44	.001
Presence of sepsis (±)	10/0	7/75	.000
Culture result (±)	5/5	46/36	NS
Colostomy (±)	1/9	15/67	NS
Surgical procedure			
Debridement	10	72	NS
Debridement + graft	0	1	
Debridement + flap	0	9	

NS Not significant

Table 2 Multivariate logistic regression model for mortality

	Odds ratio	95 % confidence interval	p	Score points
Age >60 years	1.03	0.84–1.09	.040	1
Urea level >40 mg/dl	1.03	0.91–1.02	.043	1
RDW level >14.95 %	1.09	0.60–1.36	.010	1
Albumin level <20 mg/dl	1.50	0.93–2.4	.006	1
Presence of sepsis	1.28	0.87–2.2	.039	1

(OR 1.28) (Table 2). A probability score was calculated by adding the number of points assigned to each variable. Although the regression coefficients ranged from 1.03 to 1.50, for simplicity, one point was assigned to each of these risk factors. The resulting NUMUNE (named after our hospital) Fournier Score (NFS) (age, urea level, RDW level, albumin level, sepsis) ranged from I to V.

Four groups of patients were defined based on the NUMUNE Fournier score. The first group, with a score of I, comprised about 64 % of the patients whose risk of mortality was 0 %. The second group included patients with a score of II, who had a 20 % risk of mortality; this group comprised of approximately 15 % of the cohort. The third group, which comprised approximately 6 % of the patients, included those with a NFS of III; whose risk of mortality was 50 %. The fourth group included patients with a score of IV, who had a 100 % risk of mortality (Table 3).

The specificity, sensitivity, positive predictive value, negative predictive value, negative likelihood ratio, and positive likelihood ratio for NFS exceeding II were 70,

96, 70, 96 %, 17.27, and 0.31, respectively. The AUC was 0.957 (95 % CI 0.908–1.0, $p < 0.000$) for the NFS (Fig. 1).

Discussion

FG is a life threatening disease. Although FG diagnosis is based on clinical observation, initial evaluation of the prognostic markers also guides the clinicians to estimate the disease severity and mortality for managing the appropriate therapy. Several studies have evaluated several physiological and laboratory parameters for risk stratification and prediction of mortality, including heart rate, temperature, blood pressure, respiratory rate, extent of disease, age, hematocrit, white blood cell count, serum urea, serum creatinine, serum bicarbonate, serum lactate, serum calcium, serum sodium, serum potassium, serum magnesium and serum albumin, that have been linked to mortality of FG [6, 8–15]. Fournier's gangrene severity index (FGSI), laboratory risk indicator for necrotizing fasciitis (LRINEC) and Uludag's Fournier's severity index, surgical Apgar Score (sAPGAR) are widely accepted and validated scoring systems which have been found to be successful to predict the mortality [6, 8, 16, 17]. However, the variables that influence the outcome of patients with FG, in large part, remain controversial. Rare presentation with heterogeneous clinical findings and the lack of identification of reliable criteria's and statistical analyses are described as the main restrictions to demonstrate similar outcomes with identical prognostic markers [18].

Table 3 Risk of mortality according to the NUMUNE Fournier score

Numune Fournier score		Survivors (%)	Non-survivors (%)
Score	Points		
I	0–2	59 (100)	0
II	3	12 (80)	3 (20)
III	4	3 (50)	3 (50)
IV	5	0	4 (100)

The FG mortality rate varies from 0 to 88 % [10, 13, 15, 18–22]. In our study, we have reviewed 84 cases during four-year period with a mortality rate of 11.9 %. In most published series mortality was presented within the range of 40.9–61.7 years [13, 15]. In present study, the mean age of the present survivors (54 years) was significantly lower ($p = 0.007$) than the non-survivors (68 years). Additionally, in our regression model, patients older than 60 years also have 1.03-fold increased risk of mortality (OR 1.03, 95 % CI 0.84–1.09, $p < 0.05$). Laor et al. found similar findings to our study that patients who survived were significantly younger than those who died [6]. Besides the fact that increasing age was described as an independent predictor of mortality [13], some studies suggested there was no increase in the mortality in elderly patients [23, 24].

FG progressive clinical course usually leads to multiorgan failure. Therefore, higher survival rate depends on the early diagnosis and accurate aggressive surgical and medical treatment. However, rapid and progressive clinical course of the disease results in deteriorated health status that confirmed with several diagnostic tools. Czymek

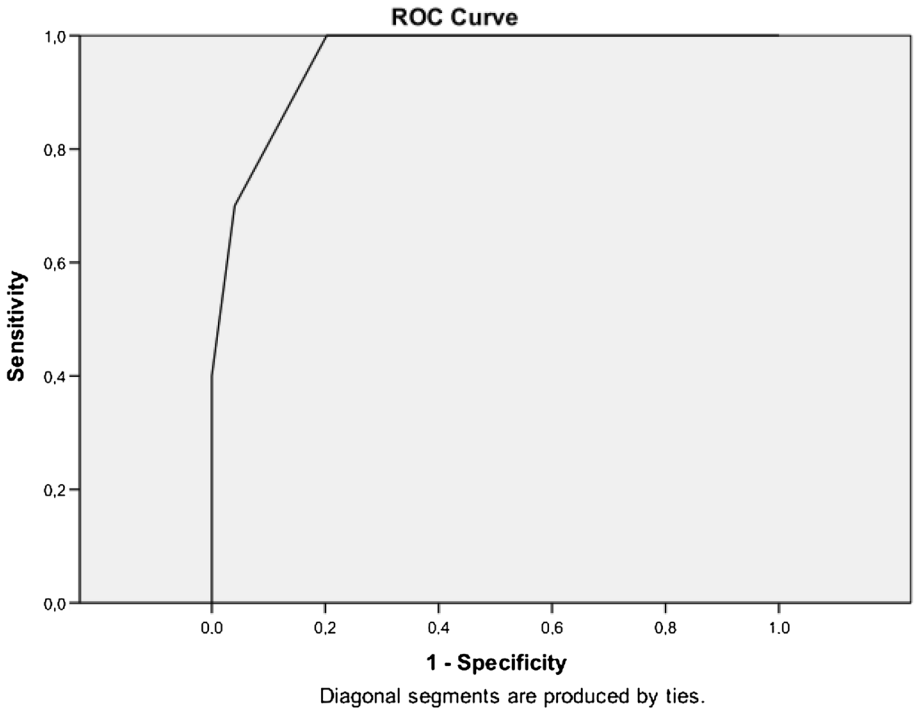

Fig. 1 Receiver operating characteristic curves of NFS for mortality

et al. have evaluated mental and physiological status of FG patients that 50 % were in poor general condition and were unable to perform their daily routine activities when compared to the normal population during hospital stay [25]. Sepsis is an important cause of morbidity and mortality. Yanar et al. reported that presence of sepsis was the only significant independent risk factor for mortality in FG [26]. In our study sepsis on admission, described as clinical symptoms of systemic disease such as mental status changes, fever and low blood pressure, was a predictive factor for mortality in FG (OR 1.28, 95 % CI 0.87–2.2, $p = 0.039$). This result is also supported by other published studies [11, 12, 22, 27].

Decreased albumin level is generally encountered in hospitalized patients and it can be associated with several different diseases, including malnutrition, cirrhosis, nephrotic syndrome and sepsis [28]. Whatever the cause, decreased albumin level has a powerful predictive value on mortality and morbidity. Although, there is a consensus about hypoalbuminemia and mortality, decreased albumin level has been shown to be associated with high mortality rate in many studies [6, 12, 21, 29, 30]. In our model hypoalbuminemia was the most effective and predictive prognostic factor of mortality with the highest odds ratio (OR 1.50, 95 % CI 0.93–2.4, $p = 0.006$) on admission.

High urea levels may reflect dehydration and poor general condition due to disease. Clayton et al. reported that survival of patients with necrotizing fasciitis was significantly associated with a blood urea nitrogen level of less than 50 mg/dl at presentation [31]. In our study the mortality rate was significantly higher in patients with higher urea levels ($p = 0.04$). Several studies have supported our findings, as they reported that elevated urea levels are associated with higher mortality rates [6, 10, 12, 21].

Recent studies reported reduced hemoglobin levels also show the worsening of the general status [21, 29, 30]. Ruiz Tovar et al. report that hemoglobin levels lower than 10 g/dl present a risk 9.6-fold higher risk of mortality [30]. RDW is a quantitative measure of variability in the size of circulating erythrocytes and a part of the complete blood count panel. In response to extended disease, inflammatory markers such as interleukin-6 and TNF which can suppress the maturation of red blood cells and reduce the half-life of red blood cells and result in elevated RDW level [32–34]. In the present study, we observed that mean RDW level of non-survivor group, was significantly higher than survivor group in both univariate and multivariate analyses ($p = 0.004$ and 0.010, respectively). Although no clinical data have been described for the relationship between RDW and FG, recent reports presented the elevated serum RDW level and mortality risk in such clinical manifestations [33–35]. Şenol et al. reported that elevated RDW at admission is an independent risk factor for mortality in acute pancreatitis [36].

Initial evaluation of progressive disease with simple predictive markers and management of appropriate treatment modality to reduce the mortality rates are the essential causes to constitute a novel scoring system

The new scoring system termed as the Numune Fournier score is objective and easy and quick to measure. Additionally, during the assessment of these factors observer error is unlikely. However, Numune Fournier score needs to be validated by new studies, before using into routine clinical practice.

Compliance with ethical standards

Conflict of interest Ahmet Erdoğan, İhsan Aydoğan, Kazım Şenol, Enes Malik Üçkan, Şiyar Ersöz and Mesut Tez declare that they have no conflict of interest.

Compliance with ethical requirements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

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