ORIGINAL ARTICLE

Risk factors for mortality in Fournier's gangrene of anorectal origin

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ABSTRACT

BACKGROUND: In the present study, we aimed to determine the risk factors for mortality in Fournier's gangrene (FG), which has a high morbidity and mortality rate and requires urgent surgical intervention.

METHODS: A retrospective analysis was made of 150 patients who were operated on in our clinic due to FG of anorectal origin between 2010 and 2020. The cases were divided into survival and non-survival groups. Demographic, clinical, laboratory, and treatment data, FG Severity Index (FGSI), and simplified FGSI (SFGSI) scores were analyzed.

RESULTS: Thirty-day mortality rate was 15.3%. In the non-survival group, rate of smoking, diabetes mellitus, malignancy and other chronic diseases, and mean age, duration of symptoms at admission, number of debridements, SFGSI, FGSI, white blood cells, and creatinine were significantly higher, while hematocrit, serum potassium, and albumin levels were significantly lower ($p<0.05$). Among these factors, age (OR=1.147, CI=1.019–1.291; p=0.023), smoking (OR=0.09, CI=0.023–0.418; p=0.002), malignancy (OR=0.038, CI=0.008–0.186; p=0.001), and serum potassium level (OR=0.141, CI=0.022–0.910; p=0.04) were identified as risk factors associated with mortality in FG.

CONCLUSION: FG is a fatal fasciitis still associated with high mortality. Advanced age, smoking, malignancy, and hypopotassemia are independent predictive risk factors for mortality in FG.

Keywords: Anorectal emergencies; Fournier's gangrene; mortality; predictive factors.

INTRODUCTION

Fournier's gangrene (FG) is a fulminant and life-threatening polymicrobial infection characterized by necrotizing fasciitis of the perianal and genitourinary regions.[1,2] Obliterative endarteritis of the subcutaneous arteries develops as secondary to inflammation and edema caused by polymicrobial infection, resulting in progressive gangrene of the subcutaneous tissue and skin on decreased blood flow.[3] It mainly affects men and is most common between the third and sixth decades of life.[4] Necrotizing fasciitis often originates from the anorectum (30–50%), urogenital (20–40%), or genital skin (20%).[5] FG is known to have a strong relationship with diabetes mellitus (DM), chronic alcoholism, perianal diseases, hypertension, smoking, malignancies, human immunodeficiency virus, lymphoproliferative diseases, chronic use of steroids, and local trauma.[2,5] The treatment requires immediate aggressive surgical debridement of the necrotic tissues, broad-spectrum antibiotic therapy, and meticulous clinical and hemodynamic follow-up.

The mortality rates reported in the literature vary from 10% to 43%, but there are also studies reporting mortality rates of up to 88%.[6–8] High mortality rates make early diagnosis and early surgical intervention critical. Therefore, several scoring systems, such as Uludag Fournier's Gangrene Severity Index (UFGSI), FG Severity Index (FGSI), Simplified FGSI (SFGSI), and Acute Physiology and Chronic Health Evaluation II scoring system, have been developed to predict mortality.[7,9–11] The factors associated with mortality have been defined, but are not universally accepted. The identification of prognostic factors remains critical to improve outcomes.

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It is ascertained from the literature that many studies examining predictive factors for mortality in FG involve heterogeneous patient groups independent of anatomical etiology.[4,5,12] In the present study, our aim was to analyze the risk factors associated with mortality in cases with FG of anorectal origin.

MATERIALS AND METHODS

Study Design and Patient Population

The study was approved by the Local Ethics Committee (approval no:11.11.20/514.189.4). A retrospective analysis was made of all cases operated on with the diagnosis of FG between January 2010 and June 2020. FG was diagnosed based on clinical history as well as symptoms and findings such as fever, perianal and perineal erythema, edema, fluctuation, crepitation, and necrosis.

The study included patients who were over 18 years of age, with anorectal origin and operated on with the diagnosis of FG for the first time. Patients under 18 years of age, with urogenital or genital-skin origin, scrotal abscess, and a history of FG were excluded from the study. All surgeries were performed by the general surgery team.

Outcome Measures and Data Collection

Clinical data such as age, gender, comorbidities, smoking, duration of symptoms at admission, length of stay in hospital and intensive care unit (ICU), number of debridements, stoma creation, orchiectomy, hyperbaric oxygen therapy, vacuum assisted closure (VAC) therapy, and mortality rate were examined for a total of 150 patients who met the inclusion criteria. The results for hematocrit (Hct), white blood cells (WBC), serum potassium (K), creatinine (Cr), and albumin (Alb) from laboratory parameters obtained at initial admission to emergency service were examined. The FGSI score was calculated by grading the degree of deviation from normal levels from 0 to 4 for 9 parameters, as described by Laor et al.[7] The cutoff value for FGSI was 9. The scores were interpreted as 75% probability of death with a score of >9 and 78% probability of survival with a score of ≤9.[7] The SFGSI score was determined using Hct, K, and Cr. In this scoring system, values from 0 to 4 are attributed to each variable and the SFGSI is calculated by adding the points of each parameter. The cutoff value for SFGSI to predict mortality was accepted as 2, with a sensitivity of 87% and specificity of 77%.[10]

All patients were preoperatively administered fluid resuscitation and parenteral broad-spectrum antibiotic therapy (3rd-generation cephalosporin and metronidazole combination). Adequate enteral or parenteral nutritional support was provided to all patients after the first surgical intervention. Wound cleaning and surgical debridements were performed under general anesthesia in the operating room on patients, for whom this was considered necessary, not later than 48 h after the first debridement. Dressing or wound cleaning at the bedside and under local anesthesia was not included in the number of debridements. A diversion colostomy was performed in case of fasciitis that substantially affected the anal sphincter, causing sphincter deficiency, and fecal incontinence. Mortality was defined as disease-related deaths within the first 30 days after surgery.

Statistical Analysis

The analysis was carried out with the Statistical Package for the Social Sciences (SPSS version 22). Quantitative variables following a normal distribution with Kolmogorov–Smirnov test were defined by mean, standard deviation (SD), and range. Qualitative variables were defined by number of cases and percentage. Quantitative and qualitative variables were compared with independent t-test, or Mann–Whitney U-test when quantitative variables did not follow normal distribution. Univariate analysis was performed using the Chi-square test or the Fisher exact test, when appropriate. Variables that correlated with mortality in the univariate analysis were included in the multivariate analysis that performed using logistic regression. A confidence interval of 95% was adopted and $p<0.05$ was considered as statistically significant.

RESULTS

One hundred and fifty patients were included in the study, 82% of which were men (n=123). The average age was 57.95±13.24 years. Twenty-three of the patients were died and 127 were survived. Thirty-day mortality rate was 15.3%. DM was the most common comorbidity (55.3%) followed by smoking (42.7%) and malignancy (15.3%), respectively. Other chronic diseases such as hypertension, coronary artery disease, chronic renal failure, and cerebrovascular disease were identified in 62 patients (41.3%), (Table 1).

Mean duration of the symptoms up to initial admission was 5.4±2.5 days (range 2–17 days). The mean time of hospitalization was 13.9±7.0 days (range 4–65 days). Thirty-five patients (23.3%) were monitored in the ICU for part of their hospital stay and the average duration of ICU was 8.9±6.0 days (range 1–24 days). The average number of surgical debridement was 1.5±0.7 (range 1–4). In addition to surgical debridement, colostomy was required in 42 patients (28%), orchiectomy in three patients (2.44%). VAC therapy was used in 46 patients and hyperbaric oxygen therapy was used in nine patients. The average SFGSI score was 1.3±1.2 and the average FGSI score was 5.2±1.8. In 16% of patients, the SFGSI score was >2 and in 10% of patients, FGSI score was >9, (Table 1).

The microorganisms found in qualitative cultures from debrided tissues, the majority was classified as polymicrobial (%88). The most commonly seen microorganisms were as follows: Gram-negative bacteria (*Escherichia coli, Klebsiella sp, Proteus mirabilis, Pseudomonas*), Gram-positive bacteria (*Staphylococci, Clostiridium, Enterococcus*).

Table 1. Main demographic, clinical and laboratory data (n=150)

Variables	Results
Age (years)	57.95±13.24
Gender, n (%)	
Female	27 (18)
Male	123 (82)
Length of hospital stay (days)	13.9±7.0
Number of patients followed in ICU, n (%)	35 (23.3)
Length of ICU stay (days)	8.9±5.9
Diabetes mellitus, n (%)	83 (55.3)
Smoking, n (%)	64 (42.7)
Malignancy, n (%)	23 (15.3)
Other chronic diseases*, n (%)	62 (41.3)
Duration of symptoms at admission (days)	5.4±2.5
Colostomy, n (%)	42 (28%)
Number of debridements	1.5±0.68
Orchiectomy (in male patients), n (%)	3 (2.44)
Hyperbaric oxygen therapy, n (%)	9 (6)
VAC therapy, n (%)	46 (30.7)
SFGSI	1.3±1.2
SFGSI >2, n (%)	24 (16)
FGSI	5.2±1.8
FGSI >9, n (%)	15 (10)
Death (mortality), n (%)	23 (15.3)
Hematocrit (%)	33.7±5.1
WBC (103/mm3)	14.8±6.1
Serum Potassium level (mmol/L)	3.8±0.6
Creatinine level (mg/dL)	0.9± 0.4
Albumin level (g/dL)	3.0±0.5

*Hypertension, coronary artery disease, chronic renal failure, cerebrovascular disease, etc. ICU: Intensive care unit; VAC: Vacuum assisted closure; SFGSI: Simplified Fournier's Gangrene Severity Index; FGSI: Fournier's Gangrene Severity Index; WBC: White blood cell.

Mean age of non-survivor patients (68.5±10.4) were higher than that of survivors (56.0±12.8) (p<0.001). Number of the patients followed in ICU was higher among non-survivors (100% versus 9.4%; p<0.001) and length of ICU stay was longer among non-survivors (11.7±4.4 versus 3.6±1.8; p<0.001). The mortality rates were higher in smokers, patients with DM, patients with malignancy, and patients with other chronic diseases (p<0.05) (Table 2). The duration of symptoms at first admission was significantly higher in non-survivors (8.8±3.3 days vs. 4.7±1.8 days; p<0.001). The number of debridements performed on patients was higher in non-survivors (p<0.001).

SFGSI and FGSI scores were higher among non-survivors (p<0.001). The area under the curve SFGSI score to predict mortality at a cutoff of two was 0.959 (95% CI 0.915–1.000). In 16% of patients (n=24), the SFGSI result was >2. The mortality of patients with SFGSI >2 was of 79.2% versus 3.2% of patients with SFGSI <2 (p<0.001). The area under the curve FGSI score to predict mortality at a cutoff of nine was 0.902 (95% CI 0.818–0.986). In 10% of patients (n=15), the FGSI score was >9. The mortality of patients with FGSI >9 was of 93.3% versus 6.7% of patients with FGSI ≤9 (p<0.001). Comparison of preoperative laboratory parameters showed among the non-survivors that there was lower mean of Hct, serum potassium, and higher WBC and creatinine (p<0.05, Table 2).

Logistic regression was applied to evaluate risk factors for death and variables that correlated with mortality in the univariate analysis were included in the study. Age (OR=1.147, CI=1.019–1.291; p=0.023), smoking (OR=0.09, CI=0.023-0.418; p=0.002), malignancy (OR=0.038, CI=0.008–0.186; p=0.001), and serum potassium level (OR=0.141, CI=0.022–0.910; p=0.04) were correlated independently with mortality (Table 3). Other variables (length of ICU stay, DM, other chronic diseases, duration of symptoms at admission, number of debridements, SFGSI >2, FGSI >9, Hct, WBC, creatinine, and albumin) showed no correlation with mortality in logistic regression.

The length of hospitalization and the number of debridements were significantly higher in patients with colostomy compared to patients without a colostomy (p=0.001 and p=0.023, respectively) (Table 4). There were no statistically significant difference between the length of stay in the ICU and mortality rates of patients with and without colostomy (p=0.625 and p=0.467, respectively).

DISCUSSION

Despite significant advances in treatment, FG is still an aggressive fasciitis with an unpredictable high mortality rate. Identification of patients with a high risk of mortality at the time of diagnosis can provide a faster and aggressive treatment plan, and survival benefit. For this purpose, in this study, we wanted to analyze the risk factors for mortality in FG. The mortality rate in this series of 150 patients was 15.3%. Our study data revealed that age, smoking, DM, malignancy, other chronic diseases, duration of symptoms at admission, number of debridements, SFGSI, FGSI, WBC, and Cr were significantly higher, while Hct, serum potassium, and Alb were significantly lower in the non-survival group. Among these factors, age, smoking, malignancy, and serum potassium were identified as independent risk factors for mortality in FG.

There are studies reporting an unclear relationship between age and FG mortality.[13,14] Similar to our study, Vyas et al.[12] reported that increased age was a significant predictive factor for mortality. There are limited studies examining the relationship between smoking and FG. Nisbet et al. reported that smoking was associated with FG, but did not ex-

Table 2. Comparison of demographic, clinical and laboratory data of survivors and non-survivors

	Survivors n=127 (%)	Non-survivors n=23 (%)	p-value
Age (years)	56.0±12.8	68.5±10.4	<0.001
Male	107 (84.3)	16 (69.6)	0.14
Length of hospital stay (days)	13.4±6.5	16.5±8.9	0.168
Number of patients followed in ICU	12 (9.4)	23 (100)	<0.001
Length of ICU stay (days)	3.6±1.79	11.6±4.4	<0.001
Smoking	46 (36.2)	18 (78.3)	<0.001
Diabetes mellitus	65 (51.2)	18 (78.5)	0.016
Malignancy	10 (7.87)	13 (56.5)	<0.001
Other chronic diseases*	47 (37)	15 (65)	0.011
Duration of symptoms at admission (days)	4.7±1.8	8.8±3.3	<0.001
Colostomy	37 (29.1)	5 (21.74)	0.46
Number of debridements	1.4±0.6	2.3±0.8	<0.001
Orchiectomy (in male patients)	1 (0.8)	2 (8.7)	0.048
Hyperbaric oxygen therapy	8 (6.3)	1 (4.3)	1
VAC therapy	37 (29.1)	9 (39.1)	0.33
SFGSI	0.9±0.8	3.4±1.1	<0.001
SFGSI >2	5 (3.9)	19(82.6)	<0.001
FGSI	4.7±1.3	7.7±1.8	<0.001
FGSI>9	1 (0.79)	14 (60.9)	<0.001
Hematocrit (%)	34.7±4.6	27.8±3.9	0.01
WBC (103/mm3)	14±5.9	19.3±5.0	0.002
Serum Potassium level (mmol/L)	3.89±0.5	3.3±0.6	<0.001
Creatinine level (mg/dL)	0.91±0.3	1,3±0.7	0.015
Albumin level (g/dL)	3.1±0.5	2.7±0.5	0.005

*Hypertension, coronary artery disease, chronic renal failure, cerebrovascular disease, etc. ICU: Intensive care unit; VAC: Vacuum assisted closure; SFGSI: Simplified Fournier's Gangrene Severity Index; FGSI: Fournier's Gangrene Severity Index; WBC: White blood cell.

Table 3. Independent risk factors for mortality

Variables	OR	CI	p-value
Age	1.147	1.019–1.291	0.023
Smoking	0.09	0.023-0.418	0.002
Malignancy	0.038	0.008–0.186	0.001
Serum potassium	0.141	0.022–0.910	0.04

OR: Odds ratio; CI: Confidence interval.

amine its effect on mortality.[15] The present study, in turn, determined smoking as a risk factor for FG etiology and mortality. The most known comorbidity associated with FG is DM. However, it is controversial whether it is an independent risk factor for mortality.[4,15,16] It has been proven that individuals with malignancy have a higher tendency to develop FG. In parallel with our study, Ruiz-Tovar et al.[17] reported that malignancy was a predictive factor for mortality in FG.

Table 4. Comparison of patients with and without a colostomy

Variables	Patients with a colostomy	Patients without a colostomy	p-value
Length of hospital stay (days)	16.2±6.8	12.9±6.9	0.001
Length of ICU stay (days)	8.2±7.4	9.3±5.0	0.625
Number of debridements	1.3±0.5	1.6±0.7	0.023
Mortality, n (%)	5 (11.9)	18 (16.6)	0.467

ICU: Intensive care unit.

The time from onset of symptoms to initial admission is in favor of necrosis and the disease may present as extensive tissue damage and sepsis. This has been shown to increase the mortality rate in several studies.[18–20] Therefore, delayed admission is an important problem in FG management. Conversely, there are studies reporting that late admission is not

a major predictive factor for mortality.[21] Delayed admission in FG has been examined in a few studies in the literature and the present study observed that the duration of symptoms at admission was significantly longer in the non-survivors group, but it was not a risk factor for mortality.

One of the most common scoring systems used to predict mortality in FG is FGSI, described by Laor et al.[7] The biggest disadvantage of this scoring system, which includes nine parameters, is that it is difficult to apply at admission due to the large number of parameters. Some authors have reported that the five parameters included in FGSI had no effect on mortality.[22] Janane et al.[18] argued that this index did not predict the severity of the disease and patient survival. Roghmann et al.[23] conducted a study to compare four different scoring systems including the FGSI score and reported that all scores were useful in predicting mortality and that elderly patients who needed mechanical ventilation and blood transfusion had a higher risk of mortality. The authors also recommended the use of the age-adjusted Charlson Comorbidity Index and surgical APGAR scores in the daily routine.[23] The present study established that this index was not a predictive factor for mortality, although the number of patients with an FGSI score >9 was significantly higher among non-survivors.

A SFGSI was developed as a result of the search for scoring systems that would be more useful for trauma surgeons in daily practice.[10] This index consists of three laboratory parameters (Hct, serum Cr, and serum K). Tenorio et al.[4] demonstrated that an SFGSI score of >2 was strongly correlated with mortality. On the other hand, Yasri and Wiwanitkit criticized this study and expressed their concerns. According to the authors, first, the SFGSI score cannot be used quickly at initial admission, because the results of laboratory parameters should be weighted. Second, the three parameters can be affected by several possible concomitant disorders.[24] The present study found that the number of patients with an SFGSI score of >2 was significantly higher in the non-survivors group, but it was not a predictive factor for mortality.

Uludag FGSI, one of the most current scoring systems for FG, proves that in patients with FG, the extent of the gangrene as well as the patient's age and physiological status have a significant effect on the outcome.[9,25] In the present study, we found that prognosis of patients with FG also is affected by their chronic health status (presence of malignancy) and age. In terms of these results, the present study supports UFGSI.

Several abnormal laboratory parameters such as low Hct, serum sodium, magnesium, and albumin; elevated WBC, glucose, creatinine, blood urea nitrogen, and C-reactive protein; and low or high serum potassium and bicarbonate levels have been reported as prognostic factors in FG.[2,12,17] Several studies have demonstrated that renal failure is associated with high mortality.[10,23] Accordingly, early diagnosis of this group of patients and considering alternatives such as dialysis besides surgical debridement may give patients a chance for survival.[2] We found that only serum potassium, among the laboratory parameters evaluated in our study, was a predictive factor for mortality in FG.

The cornerstones of the treatment of this life-threatening condition are immediate resuscitation, broad-spectrum antibiotic therapy, and radical surgical debridement. The average number of debridements recommended for adequate infection control is 3.5.[26] McCormack et al.[27] argued that additional debridement would not be necessary for patients, who are hemodynamically stable, and for whom good visualization can be achieved at the bedside. In the present study, there was no significant difference in the number of debridements between the groups. Diversion colostomy is indicated in cases of anal sphincter deficiency, fecal incontinence, and persistent fecal contamination affecting wound healing. Sarofim et al.[28] reported that the use of diversional stoma in FG is a predictor of poor outcomes. A Flexi-Seal fecal management system was developed as an alternative method to colostomy.[2] The present study, which included only cases with FG of anorectal origin, established no significant difference in mortality between those with and without stoma, and found that stomas significantly reduced the number of debridements.

The limitations of this clinical study are its retrospective and single-center design. However, the most important difference with this study from the many other studies investigating the same issue is the examination of a homogeneous patient group for etiology by excluding cases with urogenital, genital-skin origin.

Conclusion

FG is a fatal infectious fasciitis requiring a multidisciplinary approach, which is still associated with high mortality. According to the data of our study, advanced age, smoking, malignancy, and hypopotassemia are independent risk factors for mortality in FG. DM, other chronic comorbidities, delayed admission, FGSI, SFGSI, leukocyte count, Hct, creatinine, and albumin can be considered as helpful indicators for prognosis.

Ethics Committee Approval: This study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (Date: 11.11.2020, Decision No: 514/189/4).

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Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Anorektal kaynaklı Fournier gangreninde mortaliteye etki eden risk faktörleri

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AMAÇ: Bu çalışmada yüksek morbidite ve mortalite ile seyreden ve acil cerrahi girişim gerektiren Fournier gangreninde mortaliteye etki eden risk faktörlerini belirlemeyi amaçladık.

GEREÇ VE YÖNTEM: 2010–2020 yılları arasında anorektal orijinli Fournier gangreni nedeniyle kliniğimizde ameliyat edilen 150 hasta geriye dönük olarak incelendi. Olgular hayatta kalan ve ölen olarak iki gruba ayrıldı. Demografik, klinik, laboratuvar, tedavi verileri ve Fournier gangreni Severity Index (FGSI), simplified FGSI (SFGSI) skorları analiz edildi.

BULGULAR: Otuz günlük mortalite oranı %15.3 idi. Ölenlerin olduğu grupta; sigara, diyabetes mellitus, malignite ve diğer kronik hastalıkların oranı; ortalama yaş, başvuruya kadar geçen süre, debridman sayısı, SFGSI, FGSI, lökosit ve kreatinin anlamlı ölçüde yüksek; hematokrit, serum potasyum ve albumin düzeyleri ise anlamlı ölçüde düşük bulunmuştur (p<0.05). Bu faktörlerden yaş (OR=1.147, CI=1.019–1.291; p=0.023), sigara (OR=0.09, CI=0.023–0.418; p=0.002), malignite (OR=0.038, CI=0.008–0.186; p=0.001) ve serum potasyum düzeyi (OR=0.141, CI=0.022–0.910; p=0.04) Fournier gangreninde mortalite ile ilişkili risk faktörleri olarak tespit edilmiştir.

TARTIŞMA: Fournier gangreni halen yüksek mortalite ile seyreden fatal bir fasiittir. İleri yaş, sigara, malignite ve hipopotasemi Fournier gangreninde mortalite için bağımsız prediktif risk faktörlerdir.

Anahtar sözcükler: Anorektal aciller; Fournier gangreni; mortalite; prediktif faktörler.

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