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ORIGINAL ARTICLE

Fournier's gangrene: an analysis of 80 patients and a novel scoring system

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Abstract
Background To create a better scoring system for outcome prediction for patients with Fournier's gangrene in order to design more appropriate and feasible management strategies.
Methods Using logistic regression, the medical records of 80 patients who underwent surgery for Fournier's gangrene in the last 10 years were reviewed using a prospectively maintained database, and a novel scoring system was adopted combining this data with the Fournier's gangrene severity index (FGSI). The new system consists of a physiological score, an age score, and an extent of gangrene score.
Results The mortality rate of the 80 patients was 21%. Using the new scoring system (UFGSI), at a threshold value of 9, there was a 94% probability of death with a score greater than 9 and an 81% probability of survival with a score of 9 or less ($P < 0.001$). The receiver operating characteristics (ROC) analysis concluded that the new scoring system was more powerful than the FGSI ($P = 0.002$).
Conclusions The power of the novel scoring system introduced in this study proves that in patients with Fournier's gangrene, the extent of the gangrene as well as the patient's age and physiological status have a significant effect on the outcome.

Keywords Fournier's gangrene · Mortality · Dissemination · Severity index

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Introduction

Fournier's gangrene is a potentially fatal disease characterized by necrotizing fasciitis of the perineal and genital region resulting from synergistic polymicrobic infection [1–5]. It is a surgical emergency and requires prompt surgical intervention [6–10]. Mortality rates in Fournier's gangrene range from 0 to 67% [1–25], which indicates that the outcome of patients with the disease is multifactorial.

Factors that affect the outcome of patients with Fournier's gangrene can be classified into 3 groups; disease-related factors, host-related factors, and physician-related factors. Prompt and aggressive surgical debridements with appropriate antibiotics are physician-related factors. The physiological status of the patient, which can be monitored by the Acute Physiology and Chronic Health Evaluation (APACHE) II [8, 17] or Fournier's Gangrene Severity Index (FGSI) score [1, 10–13] and age are host-related factors. Dissemination of the disease describes the aggressiveness of the infectious agents that cause Fournier's gangrene or reflects immunodepression of the host. Nevertheless, dissemination of the disease was proven to affect outcomes in previous reports [6, 7, 10, 15].

The FGSI can predict mortality with a probability of 75% and survival with a probability of 78% for patients with Fournier's gangrene [8]. Many authors have found it useful [1, 10–13]; however, we believe that it underscores

the prognosis and may be improved. Therefore, we investigated the effect of the above-mentioned 3 groups of factors on outcome and constructed a novel scoring system by modifying the FGSI. The scoring system takes the acute physiological status of the patient and patient's age and combines these with the extent of the disease, and can easily be applied in routine clinical practice.

Materials and methods

The prospectively maintained medical records of patients presenting with Fournier's gangrene to the Departments of General Surgery and Urology between January 1996 and December 2006 were retrospectively reviewed after obtaining approval from the Institutional Ethical Committee (2007-22/19). The patients who met the inclusion criteria were those undergoing surgery for necrotizing soft tissue infections of the anorectal or urogenital regions with extension to neighboring areas. Patients with solitary abscesses of these regions that were not in the form of necrotizing soft tissue infections were not included in the study.

Management

APACHE II and FGSI scores were calculated using patient admission data. Upon admission, each patient was initially treated with empiric broad-spectrum parenteral antibiotics, most frequently third-generation cephalosporins with aminoglycosides and metronidazole. Within the first 12 h after admission, initial surgical debridement was performed. Microbial cultures obtained in the operating room during each debridement sequence directed later antibiotic management. Wound dressings were routinely changed daily or more often as deemed necessary on the ward. After the initial debridement, patients were taken to the operating room every 48 h for wound exploration. If infection persisted, additional debridement was performed. The term "debridement" was used when any amount of necrotic tissue was removed during wound exploration. Surgical management was continued until fully healthy tissue was obtained macroscopically, or negative tissue cultures were obtained. When secondary wound closures were not possible, skin grafting was used.

Fecal or urinary diversions were performed in select cases. Patients with severe disease or in poor condition were treated in the intensive care unit. Malnourished patients received nutritional support. Hyperbaric oxygen therapy was not used.

Study variables

Age, gender, duration of symptoms, the ratio of direct admission to the referral from other centers, FGSI score, presence of coexisting diseases, origin of infection, extent of gangrene, and method of therapy. The need for the intensive care unit (ICU) or ventilator, the number of days spent in the ICU, and the length of hospital stay were also recorded.

Stratification of extent of the gangrene

Based on the operative data, the extent of Fournier's gangrene was categorized into 3 groups using the Chi-square test. In this way, 3 groups were identified that statistically differed from each other in means of mortality. The first group included cases of Fournier's gangrene localized to the anorectal or urogenital region including the perianal region, perineum, scrotum, and penis or vulva (grade I gangrene). The second group included cases of Fournier's gangrene localized to the previous regions plus the pubic region or thigh–pelvic region (grade II gangrene). This area can best be described as the area covered by underwear. The third group included cases of Fournier's gangrene, which extended beyond the pelvic region (grade III gangrene) (Fig. 1).

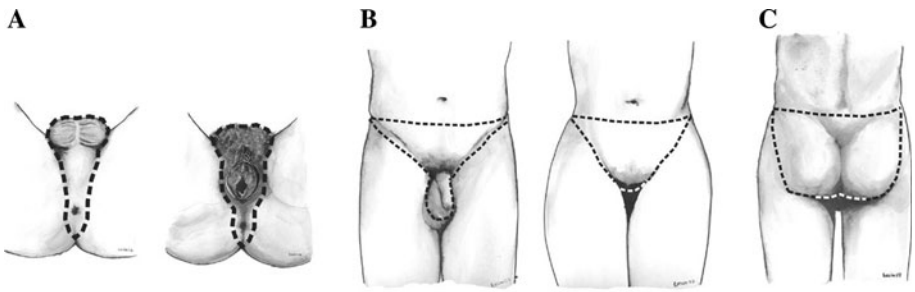

Fig. 1 The anatomic limits used for the grading of dissemination. **a** The surface anatomic limits of grade I dissemination. **b** The surface anatomic limits for grade II dissemination, front view in man and woman, and **c** back view. Extension of the disease to all other parts was considered grade III dissemination. The *dotted lines* in **b** and **c** show the margins of the so-called pelvic region

Statistics

For comparison of the continuous variables, the Wilcoxon test (when there were 2 groups) or the Kruskal–Wallis test (when there were more than 2 groups) was used, and categorical variables were compared using Pearson's chi square or Fischer's exact test. Receiver operating characteristics (ROC) analysis was used to calculate the cutoff values of FGSI scores for mortality. Data are presented as means ± standard error of mean (SEM; parametric) or medians and ranges (nonparametric), as appropriate. The level of statistical significance was set at a value of $P < 0.05$.

A multivariate logistic regression model was obtained using variables that significantly differed between survivors and non-survivors ($P < 0.001$).

The statistical analyses were performed using the Statistical Package for Social Sciences (SPSS®) for Windows Ver.15.0, and MedCalc Ver.7.2.1.0.

Uludag Fournier gangrene's severity index

Significant factors that were determined by the multivariate analysis were added to the FGSI to construct the Uludag Fournier's Gangrene Severity Index (UFGSI) (Table 1). ROC analysis was used to calculate the threshold UFGSI scores for mortality. Effectiveness of the UFGSI was analyzed by Pearson's Chi-square test. Finally, the FGSI and UFGSI were compared using ROC analysis.

Results

There were 80 patients eligible for the study. There were 17 non-survivors and 63 survivors. The mortality rate was 21%. The cause of mortality was sepsis in 8 patients, multi-organ failure in 6 patients, and cardiogenic shock in 3 patients.

Epidemiological results

Table 2 summarizes the baseline characteristics of the patients. There were 57 men and 23 women with a median age of 57 (24–85) years. The survivors were significantly younger than the non-survivors ($P = 0.002$). ROC analysis revealed a threshold value of 60 years for mortality (area under ROC curve: 0.709, 95% CI: 38.5–81.8). Sex was not a factor affecting mortality.

Duration of symptoms was similar between survivors and non-survivors. Fifty-four patients (68%) were referred from other medical centers.

The median FGSI score for the overall group was 4 (0–23). The median FGSI score for survivors and non-survivors was 4 (0–11) and 14 (3–23), respectively ($P < 0.001$). ROC analysis identified a threshold FGSI value of 11 for mortality (area under ROC curve: 0.843; 95% CI: 0.744–0.914; sensitivity: 64.7%; specificity: 100%).

There were 24 patients who did not have coexisting diseases. Among the remaining 56 patients, the most common coexisting disease was type II diabetes mellitus

Table 1 The Uludag Fournier's gangrene severity index

Variables	+4	+3	+2	+1	0	+1	+2	+3	+4
a. Physiological parameters									
Temperature (°C)	>41	39–40.9	–	38.5–38.9	36–38.4	34–35.9	32–33.9	30–31.9	<29.9
Heart rate	>180	140–179	110–139	–	70–109	–	55–69	40–54	<39
Respiratory rate	>50	35–49	–	25–34	12–24	10–11	6–9	–	<5
Serum potassium (mmol/L)	>7	6–6.9	–	5.5–5.9	3.5–5.4	3–3.4	2.5–2.9	–	<2.5
Serum sodium (mmol/L)	>180	160–179	155–159	150–154	130–149	–	120–129	110–119	<110
Serum creatinine (mg/100 ml) (×2 for acute renal failure)	>3.5	2–3.4	1.5–1.9	–	0.6–1.4	–	<0.6	–	–
Hematocrit (%)	>60	–	50–59	46–49	30–45	–	20–29	–	<20
White blood count (×1000/mm^3)	>40	–	20–39.9	15–19.9	3–14.9	–	1–2.9	–	<1
Serum bicarbonate, (venous) (mmol/L)	>52	41–51	–	32–40	22–31	–	18–21	15–17	<15
b. Dissemination score									
Fournier's gangrene confined to the urogenital and/or anorectal region, add "1"									
Fournier's gangrene confined to the pelvic region, add "2"									
Fournier's gangrene extending beyond the pelvic region, add "6"									
c. Age score									
Age ≥60 years, add "1"									
Age <60 years, add "0"									

UFGSI = A+B+C

Table 2 Comparison of the baseline characteristics describing survivors and non-survivors

Factors	Survivors (63)	Non-survivors (17)	*P*
Age (median)	55 (24–85)	62 (47–77)	0.002*
Gender (female/male)	15/48	8/9	0.084
Duration of symptoms (day; median)	7 (1–15)	7 (4–25)	0.426
Percent of referred patients	77.4	82.4	0.430
FGSI score (median)	4 (0–23)	14 (3–23)	<0.001*
Presence of DM	57%	58%	0.971
Etiology (anorectal/urogenital)	25/38	9/8	0.240
Extent of the disease (grade I, II, III)	34, 18, 11	0, 6, 11	<0.001[b]
Fecal diversion (total number)	12	6	0.212
Urinary diversion (total number)	3	1	0.352
Need for ICU	8	13	<0.001*
Need for ventilator	3	10	<0.001*
Length of the ICU stay (days; median)[a]	8 (1–12)	7 (1–22)	0.638
Length of hospital stay (days; median)	14 (3–57)	7 (2–32)	0.002*

FGSI Fournier's gangrene severity index, *DM* Diabetes Mellitus, *ICU* Intensive care unit

[a] For the patients who stayed in the ICU. *Wilcoxon test

[b] Kruskal–Wallis test

(DM). There were 46 patients (58%) with DM. The incidence of DM was similar among survivors and non-survivors. There were no immunocompromised patients.

Urogenital diseases were the cause of Fournier's gangrene in 45 patients, anorectal diseases were the cause in 32 patients, and in 3 women, Fournier's gangrene originated from skin lesions (2 furuncles and 1 wound in a diabetic person). There was no significant difference between mortality rates of the patients with Fournier's gangrene originating from anorectal or urogenital regions.

There were 34 patients with grade I disseminated disease none of whom died. Twenty-four patients had grade II disseminated disease, and 6 of these patients died. Grade III disseminated disease was present in 22 patients, and there were 11 deaths. There was a significant difference between mortality rates in groups I and II ($P = 0.024$), groups II and III ($P = 0.009$), and groups I and III ($P < 0.001$).

Fecal diversion was obtained with temporary colostomies in 18 patients, and 4 patients needed cystostomy for urinary diversion. Orchiectomy was required in 8 patients, and one of these patients also had to undergo penectomy.

Microbial cultures of 36 patients were not recorded properly. Of the remaining 44 patients, 6 had negative cultures. Among the 38 patients with a positive culture, infections were polymicrobic in 24 and monomicrobic in 14. The most common infectious agent was *Escherichia coli*, followed by *enterococci, streptococci, staphylococci, Klebsiella,* and *Proteus. Candida albicans* was found in one patient who died. Anaerobic culturing was not possible.

Table 3 Significant factors affecting mortality in logistic regression analysis

Factors	Coefficient (β)	SE	Wald λ^2	*P*	Exp (β)
Age ≤60 years	2.240	0.763	8.619	0.003	9.393
FGSI	0.361	0.133	7.390	0.007	1.435
Grade I gangrene	–	–	11.821	0.003	–
Grade II gangrene	2.688	1.196	5.050	0.025	15.699
Grade III gangrene	4.088	1.210	11.412	0.001	59.599

Model $\lambda^2 = 29.190$; $P \leq 0.001$

SE Standard error, *FGSI* Fournier's gangrene severity index

Of the 80 patients, 21 required intensive care. The median length of ICU stay was 8 (1–22) days. Twelve of the 80 patients were in septic shock on admission. They all required mechanical respiratory support and only 2 survived.

The overall length of hospital stay for the 80 patients was 10 (2–57) days. Survivors stayed in the hospital for a significantly longer period of time than non-survivors.

Logistic regression analysis results

Age, FGSI score, extent of the gangrene, and the need for treatment in the ICU were the factors that differed between survivors and non-survivors. Among these factors, multivariate analysis determined that FGSI, age, and extent of the disease were independent risk factors affecting mortality of patients with Fournier's gangrene (Table 3). Using the logistic regression results, the contribution of age and extent of gangrene to the FGSI was calculated, which gave

rise to a novel scoring system for outcome prediction in patients with Fournier's gangrene.

The odds ratios of the significant factors (age and the grade of extent of the gangrene) were taken into consideration to calculate how these factors contributed to the scoring system. To simplify the contributive points, the odds ratio values were divided by 10 and rounded up to integers. For example, the odds ratio of age was 9.393. When divided by 10, this becomes 0.9393, and when rounded to an integer, becomes equal to one, the contributive point to the scoring system. If age was greater than 60, one point was added to the FGSI score. Grade I extended gangrene was used as the point of reference to calculate the power of the extent of the gangrene in the logistic regression model. However, the presence of the disease cannot be excluded, so one point was recorded for grade I gangrene. If the lesions were confined to the perineum, or the urogenital or perianal regions (grade I gangrene), an extra point was added to the patient's previous score. The odds ratio for disease confined to the pelvic region (grade II gangrene) was 15.699. When divided by ten and rounded up, it was equal to 2. The odds ratio for diseases extending beyond the pelvis (grade III gangrene) was 59.599. When divided by 10 and rounded up, this became 6. Later, by adding the age and extent of the gangrene scores to the FGSI score, the UFGSI score was calculated (Table 1).

The median UFGSI was 8 (range 1–30) for the overall group, 7 (range 1–15) for survivors, and 18 (range 9–30) for non-survivors ($P < 0.001$). ROC analysis revealed a threshold UFGSI value of 9 for mortality (area under the ROC curve: 0.947; 95% CI: 0.873–0.994). Using a UFGSI threshold value of 9, there was a 94% probability of death with a score greater than 9, and a score of 9 or less was associated with an 81% probability of survival (Pearson's Chi-square test, $P < 0.001$). None of the patients who had higher scores than 18 survived.

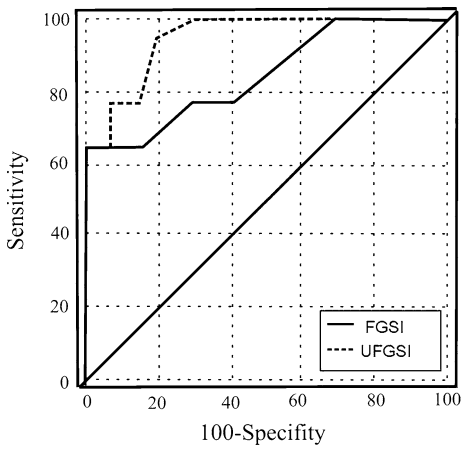

Fig. 2 The comparison of Fournier's gangrene severity index and Uludag Fournier's gangrene severity index ROC curves

Table 4 The comparison of ROC curves of FGSI and UFGSI

Scoring system	Area under ROC curve	SE	95% CI
FGSI	0.843	0.0625	0.744–0.914
UFGSI	0.947	0.0386	0.873–0.994

Difference between areas: 0.105

Standard error: 0.0339

95% Confidence interval: 0.0381 to 0.171

Significance level: $P = 0.002$

ROC Receiver operator characteristics, *SE* Standard error, *CI* Confidence interval

FGSI Fournier's gangrene severity index, *UFGSI* Uludag Fournier's gangrene severity index

The ROC analysis result of the comparison of the 2 scoring systems is shown in Fig. 2. The difference between areas under ROC curves of UFGSI and FGSI is 0.105, with a significance level of 0.002 (Table 4).

Discussion

This study gave rise to a novel scoring system to predict the outcome of patients with Fournier's gangrene by using data from 80 patients who underwent surgery at our center. This series of patients is one of the largest series reported and had a moderate mortality rate (21%). The extent of disease was classified for the first time in this study, and by combining this factor with FGSI and age, a powerful scoring system was developed that can predict mortality from this disease with a probability of 94%, and survival with a probability of 81%.

The FGSI was first introduced by Laor and colleagues in 1995 [8]. Considering that homeostasis was affected by the severity of the disease, they modified the APACHE II scoring system by using only the first part of it to create the FGSI. The FGSI can predict mortality with a probability of 75% and survival with a probability of 78%. Later, the use of the FGSI was verified by additional reports [1, 10–13]. In a recent report from Turkey, Ersay and co-workers found that the FGSI was an independent risk factor for mortality in 70 patients with Fournier's gangrene [1]. The analysis of our patients also supports these findings. We calculated a threshold FGSI value of 11 for mortality with death probability of 100% and survival probability of 65%. The FGSI was also found to be an independent risk factor in our logistic regression model (OR: 1.435, $P = 0.007$). However, some of our patients with high FGSI scores have survived, and other patients with low FGSI scores did not survive. Therefore, we investigated other possible factors affecting mortality.

When Fournier's gangrene was first described by John Alfred Fournier [14], 3 main properties, "unknown origin, young age, and male gender" were identified. However, today Fournier's gangrene is more frequent among older patients as are other necrotizing soft tissue infections [6, 7]. It is now known that older patients have a lower survival rate [2]. We also calculated a threshold age of 60 years in the ROC analysis (area under ROC curve: 0.709, 95% CI:38.5–81.8). Logistic regression analysis identified age as an independent risk factor for mortality in patients with Fournier's gangrene.

In a previous report, we showed the effect of the extent of necrotizing soft tissue infections on the outcome of patients with these diseases [7]. There have also been some reports that support our opinion [6, 10, 15]. However, lack of grading of the extent of the gangrene has been a major problem. Palmer and colleagues calculated the ratio of the diseased surface area to the body surface area and concluded that patients with gangrene that involved less than five percent of the total body surface had a better survival rate [16]. However, this study was the only one that attempted to calculate the extent of the disease quantitatively. For quantification of Fournier's gangrene, we grouped the operative findings of our patients with the help of statistics. Eventually, we were able to classify the extent of the gangrene into 3 groups. The logistic regression model found that the grade of dissemination was an independent risk factor for mortality.

Combining these logistic regression findings with knowledge gained from the literature, the Uludag Fournier's gangrene severity index (UFGSI) was constructed. The predictive power of UFGSI is much better (94% probability of death with a score $\geq$9 and 81% probability of survival with a score less than 9) than the FGSI (the difference between areas under ROC curves of the UFGSI and FGSI is 0.105 with a significance level of 0.002) and easier to use in day-to-day clinical settings.

UFGSI scores may be used to direct patient management. Patients over 60 years of age, with extensive disease (patients with UFGSI scores higher than 18) are patients with a high probability of death. They should always be considered high risk patients and treated by an experienced team in the ICU. However, patients who have UFGSI scores less than 9 are those with a high probability of survival and they rarely need intensive care. They may be treated in the ward to avoid unnecessary costs or morbidity due to ICU.

The retrospective nature of this study, despite the prospective database, is its main drawback. However, it is one of the largest series reported in the literature. This novel scoring system should be validated through other prospective studies and independent observations.

Despite the well-defined disease management, there are still some issues to be clarified regarding Fournier's gangrene. With its significant results, particularly as regards analysis of the extent of the gangrene, this study adds useful information to the understanding of this devastating disease. The quantification of the extent of the disease may help determine more precise outcome predictions for patients with Fournier's gangrene.

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