

# The effect of Fournier gangrene severity index and microbial culture results on hospital length of stay, frequency of debridement, and mortality

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## ABSTRACT

**BACKGROUND:** Fournier gangrene (FG) is a rapidly progressive soft-tissue necrosis that may be life-threatening unless aggressive treatment is applied immediately. FG severity index was described first by Laor et al. to predict mortality rate but there are few studies on the prognostic significance of FG severity index and especially the microbial agents isolated from debridement on patient prognosis. Hence, in the present study, it has been aimed to investigate the significance of FG severity index and infective agents on hospital stay, frequency of debridement, and mortality.

**METHODS:** Thirty-four patients who were operated with the diagnosis of FG between January 2013 and January 2018 were retrospectively analyzed. FG severity index scores in admission were calculated and patient was divided into two groups according to the cutoff value of FG severity index. Patient was categorized according to the microbial agents isolated from debridement cultures. Patient characteristics were compared between the group of survivors and non-survivors. The effect of FG severity index and microbial agent type on hospital stay, frequency of debridement, and mortality was analyzed.

**RESULTS:** It was found that mortality rate was significantly higher in the group of FG severity index score  $>9$  than the other group (100% vs. 6.7%;  $p=0.001$ ) and it was observed that FG severity index had predicted the mortality rate as 100% and survival rate as 93.3% but there were no significant relation between FG severity index with the frequency of debridement and hospital stay. The mortality rate (50% vs. 4.2%;  $p=0.005$ ) and frequency of debridement ( $3.10\pm 0.73$  vs.  $2.00\pm 0.72$ ;  $p=0.001$ ) were significantly higher in the subgroup of patient infected with clostridial and atypical agents.

**CONCLUSION:** FG severity index was found to be insufficient in determining the frequency of debridement and the hospital stay but it accurately predicts the rates of mortality and survival. The patients who were infected with clostridial and atypical agents are more likely to develop mortality and tend to be need more aggressive surgical interventions than the others.

**Keywords:** Fasiitits; gangrene; infections.

## INTRODUCTION

Although it was first described in 1764 by Baurinne as necrotizing fasciitis in the genital area, the disease was started to be known as Fournier by a case report of French dermatologist Jean Alfred Fournier in 1883.<sup>[1]</sup> The surgical procedure of Fournier gangrene (FG) was first described by Meleney in

the 1920s, and the name Meleney gangrene was started to be used for necrotizing fasciitis patients who had the disease in areas other than the genital area.<sup>[2]</sup>

It is defined as necrotizing fasciitis of the genitalia and perianal region and is a disease not only of men but also of women and children of all ages.<sup>[3,4]</sup> It is a mixed type infectious disease

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which is a life-threatening emergency and requires surgical intervention and causes soft-tissue necrosis that spreads rapidly between the facial plans formed in the perineum and the genital area.<sup>[5,6]</sup>

Age and diabetes mellitus are the most important predisposing factor in transforming perianal or genital infections into necrotizing fasciitis.<sup>[7]</sup> Diabetes-induced obliterative endarteritis causes aggressive progression of disease and necrosis with impaired blood supply due to developing microvascular obstruction. Genital infections, trauma, and iatrogenic interventions play an important role in etiology.<sup>[3]</sup> The disease often occurs with the transmission of the flora from the skin, urethra, or rectum. The mortality incidence varies between 0% and 65% depending on comorbidities and disease burden.<sup>[8]</sup> To predict mortality and to assess the prognosis and severity of the disease, Laor et al.<sup>[9]</sup> identified and presented FG Severity Scoring (FGSI).

In the present study, it has been aimed to investigate the relationship between FGSI at the time of admission and microbial culture results with the frequency of debridement, hospital stay, and mortality rate in patients with FG.

## MATERIALS AND METHODS

### Patient Selection and Data Collection

The thirty-four patients operated with the diagnosis of FG in General Surgery Clinic of Afyonkocatepe University of Health Sciences between January 2013 and January 2018 were evaluated retrospectively and were included in the study. In the physical examination, the patients who were diagnosed with necrosis by the signs such as erythema, induration, swelling, tenderness, cyanosis, and subcutaneous crepitation were accepted as FG. Patients whose information, follow-up, and culture results could not be obtained, FGSI score could not be calculated and necrotizing infection other than perianal, genital, and gluteal regions were excluded from the study. Patient characteristics were compared between the subgroups of survivors and non-survivors.

FGSIs at the time of admission and the wound culture results obtained under sterile conditions during the first debridement of patients were compared with the frequency of debridement, hospital stay, and mortality. Patients were divided into subgroups according to the microbial culture results as no agent/skin flora/non-clostridial agents and clostridial or atypic agents. Patients were divided into two groups according to the FGSI as  $FGSI > 9$  ve  $FGSI \leq 9$  because of the cutoff value of FGSI was determined as nine by Laor et al.<sup>[9]</sup> The pre-operative performance status of patients was determined according to the Eastern Cooperative Oncology Group classification.<sup>[10]</sup>

This study was approved by the Afyonkocatepe University Faculty of Medicine Ethics Committee.

## Surgical Procedure

After stabilizing the vital signs, all the patients underwent surgical intervention and the infected necrotic tissues were debrided until healthy tissue was seen and then sent to microbial culture. The debridements were repeated until getting healthy tissue in patients with infection and tissue necrosis after initial debridement (Fig. 1). After debridement, irrigation with hydrogen peroxide and then dressing were performed in operating room conditions until the infective status regressed. When the wound infection regressed, dressings were continued at the bedside every 2 days. The sigmoid loop colostomy was performed in five patients who were thought to have fecal contamination.

Before the culture results were taken, first ceftriaxone and intravenous metronidazole were started empirically or other antimicrobial agents were applied with taking the opinion of infectious disease specialists according to the general condition of the patient. These regimens were changed based on antimicrobial sensitivity test results.

## Measurement of FG Severity Score

FGSI was developed first in 1995 by Laor et al.<sup>[9]</sup> to predict the severity of FG with a numerical score. In FGSI, nine parameters are measured and rated from 0 to 4. These parameters are heart rate, respiratory rate, body temperature, serum creatinine, sodium, potassium and bicarbonate levels, and hematocrit and leukocyte count in admission (Table 1). FGSI values between 0 and 36 were calculated by summing the scores obtained from the parameters for all patients.

## Statistical Analysis

All numerical variables are given as mean  $\pm$  standard deviation or percentiles. Normal distribution of numerical variables was



**Figure 1.** Condition of an open wound of a patient during washing in the operating room the day after the first debridement.

analyzed using histogram graphics and Kolmogorov–Smirnov test. In comparison of patient characteristics between the groups and in comparison of hospital stay, frequency of debridement, and mortality with culture results and FGSI score, X2 test or Fisher Exact test was used for categorical variables and Student-t-test or Mann–Whitney U Test was used for numerical variables. All p values below 0.05 were considered statistically significant. All statistical analyses were applied in IBM Statistics version 23.0.

## RESULTS

Comparison of patients’ characteristics between the groups of survivors and non-survivors is summarized in Table 2. The mean age was 56.8±15.4 (range 37–82) and 15 (44.1%) of the patients were male. The most common admission symptoms of patients were erythema (94.1%), swelling/induration (82.3%), fever (35.2%), pain (41.1%), and purulent discharge (47%). While 24 of patients were survived, six of those died and the overall mortality rate was 17.6%. The majority of patients were observed to be ASA II and III (totally 94%). The most common comorbid diseases were cardiovascular diseases (67.6%) and diabetes mellitus (44.1%). It was observed that the group of patients who developed mortality was significantly older and had high ASA score, high comorbid disease, and low performance status (p=0.024; p=0.038; p=0.001; and p=0.012, respectively). The two groups were homogenous in terms of gender, smoking, duration of symptoms, and lesion localization. The average length of hospital stay was 17.59±4.93 days and there was no difference between the two groups with and without mortality.

Patients underwent at least one, at most, 4 times debridement, and the average debridement frequency was found to be 2.32±0.87. Significantly, more debridement was observed in the group developing mortality (3.00±0.63 vs. 2.18±0.86; p=0.029). The FGSI scores of the patients at the time of ad-

mission were calculated as the lowest three and the highest 11, and the FGSI scores of the patients in the mortality group were significantly higher than the other group (9.50±1.64 vs. 5.00±1.74; p=0.001).

When the patient was divided into two groups according to the cutoff value of FGSI score defined by Laor et al., it was found that mortality rate was significantly higher in the group of FGSI score >9 than the other group (100% vs. 6.7%; p=0.001>). With these results, it was observed that FGSI had predicted the mortality rate as 100% and survival rate as 93.3%. However, the frequency of debridement and hospital stay was not different between the groups (Table 3).

The most frequently isolated agents in culture results were skin flora, Strep.spp, Staf.spp, *Escherichia coli*, Klebsiella spp, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Clostridium spp. In six patients, there was no growth in culture and growth of clostridia or atypical agents was seen in ten patients. When the patient was divided into two groups according to the culture results as no agent/flora agents/ non-clostridial and clostridial or atypical agents, it was found that the mortality rate (50% vs. 4.2%; p=0.005) and frequency of debridement (3.10±0.73 vs. 2.00±0.72; p=0.001) were significantly higher in the subgroup of clostridial or atypical agents. However, there was no difference between the subgroups according to the hospital stay (Table 4).

## DISCUSSION

Mortality rates in FG can be observed at the high rates which can reach up to 65%.<sup>[8]</sup> When the mortality rate was around 80% in the first series published, it decreased to below 40% with the introduction of strong antibiotics in the past 15 years.<sup>[11]</sup> Although it has been suggested that concomitant diseases do not affect mortality by Francis et al.<sup>[12]</sup> Faucher et al.,<sup>[13]</sup> reported that mortality was 50% in patients with three

**Table 1.** Fournier gangrene Severity Score (FGSI) calculating table

Physiologic variables	High abnormal values				Normal	Low abnormal values			
	+4	+3	+2	+1		+1	+2	+3	+4
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 (bpm)	“/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) (x <sup>2</sup> 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 (91000/mm <sup>3</sup> )	“/40	–	20–39.9	15–19.9	3–14.9	–	1–2.9	–	<1
Serumbicarbonate, (venous) (mmol/L)	“/52	41–51	–	32–40	22–31	–	18–21	15–17	<15

**Table 2.** Comparison of patient characteristics between the subgroups of survivors and non-survivors

Variables	Total (n=34)	Survivors (n=28)	Non-Survivors (n=6)	p-value
Age	56.8±15.4	52.62±13.76	60.06±17.28	0.024
Gender (male)	15(44.1)	12(42.8)	3(50)	0.352
BMI (kg/m <sup>2</sup> )	22.45±8.23	20.36±6.27	25.24±7.25	0.046
ASA score				
I	2 (6)	2 (7.1)	0 (0)	0.038
II	18 (52.9)	17 (60.7)	1 (16.6)	
III	14 (41.1)	9 (32.1)	5 (83.3)	
Comorbid diseases				
DM	15 (44.1)	11 (39.2)	4 (66.6)	0.001
Cardiovascular disease	23 (67.6)	18 (64.2)	5 (83.3)	
Pulmonary disease	6 (17.6)	4 (14.2)	2 (33.3)	
Chronic renal failure	8 (23.5)	5 (17.8)	3 (50)	
ECOG <sup>a</sup>				
I	27 (79.4)	24 (85.7)	3 (50)	0.012
II	4 (11.7)	2 (7.1)	2 (33.3)	
III	3 (8.8)	2 (7.1)	1 (16.6)	
Smoking	11 (32.3)	9 (32.1)	2 (33.3)	0.684
Signs and symptoms				
Erythema	32 (94.1)	26 (92.8)	6 (100)	0.086
Swelling/Induration	28 (82.3)	22 (78.5)	6 (100)	
Fever	12 (35.2)	9 (32.1)	3 (50)	
Pain	14 (41.1)	12 (42.8)	2 (33.3)	
Purulent discharge	16 (47)	12 (42.8)	4 (66.6)	
Duration of symptoms (day)	3.64±2.47	3.68±2.25	3.58±2.92	0.516
Lesion location				
Perianal	15 (44.1)	12 (42.8)	3 (50)	
Genital	11 (32.3)	9 (32.1)	2 (33.3)	
Gluteal	8 (23.5)	7 (25)	1 (16.6)	0.258
Number of debridement	2.32±0.87	2.18±0.86	3.00±0.63	0.029
Hospital stay (day)	17.59±4.93	17.75±4.87	16.83±5.63	0.803
FGSI score <sup>**</sup>	5.79±2.43	5.00±1.74	9.50±1.64	0.001>

Numerical variables are given as mean±standard deviation or n(%). BMI: Body Mass Index; ASA: American Society of Anesthesiologist; DM: Diabetes Mellitus; ECOG: Eastern Cooperative Oncology Group; FGSI: Fournier Gangrene Severity Index. <sup>a</sup>Preoperative performance status of patient was determined according to the ECOG Classification).<sup>110</sup> <sup>\*\*</sup>FGSI scores were determined according to the study of Laor et al.<sup>19</sup>

or more risk factors such as over 50 years of age, malnutrition, hypertension, diabetes, alcohol, and intravenous drug dependence.

The Uludag FG severity score (UFGSI), which was defined by Yılmazlar in 2010 after FGSI was defined and accepted in 1995, has also been widely used.<sup>[14]</sup> A large series of 120 patients with this scoring was reported and generally accepted.<sup>[15]</sup> The reason for the use of FGSI in our study is that it has been in use for a longer time than UFGSI and there are more studies on its prognostic accuracy.

In the present study, the most common symptom was erythema and swelling/induration in all patients (94.1% and 82.3%, respectively). Pain and fever, which are two of the classic signs of infection, were relatively low compared to other symptoms (41.1% and 35.2%, respectively). The reason for this situation is that the gangrene affects the subcutaneous nerve roots and that the existing pain is usually lost during the admission to the hospital. Lack of pain delays the duration of admission to the health unit in these patients and the discomfort caused by the discharge and necrosis smell often leads to patients suggesting the severity of the condition; thus

**Table 3.** Comparison of hospital stay, frequency of debridement and mortality according to FGSI cutoff value

Variable	FGSI score ≤9 (n=30)	FGSI score >9 (n=4)	p-value
Hospital stay	17.27±5.06	20.00±3.36	0.305
Number of debridement	2.23±0.85	3.00±0.81	0.102
Mortality	2 (6.7%)	4 (100%)	0.001>

Numerical variables are given as mean±standard deviation or n (%). FGSI: Fournier gangrene severity index.

**Table 4.** Comparison of hospital stay, frequency of debridement and mortality according to subgroup of microbial culture results

Variable	No agent/flora/ non-clostridial agents (n=24)	Clostridial or atypical agents (n=10)	p-value
Hospital stay	18.46±4.82	15.50±4.79	0.113
Number of debridement	2.00±0.72	3.10±0.73	0.001
Mortality	1 (4.2%)	5 (50%)	0.005

Numerical variables are given as mean±standard deviation or n (%).

the amount of tissue requiring debridement increases. Fever usually occurs after the disease is disseminated.

In a study consisting of 20 patients, it was found that the most common starting point of the gangrene in the perineum was the scrotum in eight patients.<sup>[16]</sup> In the present study, the most common disease locations were perianal and then genital areas and it has been found that no relationship between disease location and mortality rate. However, it should be kept in mind that more complex and frequent surgical debridement may be required in the lesions of the perianal or genital areas that adhere to the lesions in the gluteal region.

As study results, FGSI was found to be insufficient in predicting the frequency of debridement and hospital stay but sufficient in the prediction of mortality or survival. The development of early mortality in patients with the high FGSI score and who may require more debridement can explain the similarity of hospital stay and frequency of debridement compared to those patients with the low FGSI score. While the mortality and survival prediction rates were 75% and 78%, respectively, in the study of Laor et al.,<sup>[9]</sup> in the present study, it was seen that FGSI predicts mortality and survival rate as 100% and 93.3%, respectively.

In FG, as in all septic diseases, the most important factor affecting mortality is the patient's age, comorbidity, and fondness.<sup>[7]</sup> The decrease in age-related tissue replacement capacity with microvascular disease due to diabetes mellitus, cardiovascular diseases, and smoking affects the wound healing duration negatively. In the present study, it was found that the most of the patients died have older age, lower performance status, and more comorbid diseases such as diabetes mellitus. In this group of patients, FGSI scores are higher and the mortality rates increase dramatically because of the combination of later admission to hospital due to depression of symptoms and rapid progression or burden of disease. Patients with the high FGSI scores at the time of application should be taken to surgery immediately as Meleney said years ago ("Surgery should not be delayed an hour after the diagnosis has been made") and fluid replacement, effective antibiotic therapy, and aggressive support treatment should be planned in intensive care conditions during the post-operative period.<sup>[17]</sup>

When the microbial agents isolated from debridement cultures analyzed, it has been found that there was a significant relationship between microbial agent type and mortality and frequency of debridement. The patients who were infected with atypical agents were the patients who needed the most dressing and debridement and the mortality rate was significantly higher than the other patients. FG is often characterized by polymicrobial infections accompanied by urogenital, fecal, and skin flora in which aerobic and anaerobic microorganisms coexist.<sup>[18]</sup> This polymicrobial nature of FG facilitates the spreading of infection among fascia plans by the production of various enzymes and exotoxins, such as collagenase, hyaluronidase, heparinase, streptodornase, and streptokinase, with the contribution of aerobic and anaerobic bacteria. Aerobic bacteria cause platelet aggregation to accelerate coagulation and microthrombin. Collagenase produced by anaerobic bacteria and heparinase promotes clot formation. This thrombus-induced tissue ischemia creates a vicious cycle by causing the gangrene and the medium for bacteria. This cycle can only be broken by the removal of ischemic-necrotic tissues from the area by surgical debridement. Supporting debridement with strong and broad-spectrum antibiotics is an integral part of the treatment. Prophylactic antibiotherapy should be effective against staphylococcus, streptococci, Gram-negative bacteria, pseudomonas, bacteroides species, coli form, and clostridium in FG patients.<sup>[19]</sup> The culture and antibiogram results obtained in the debridement should be regulated depending on the sensitivity of the antibiotics. Therefore, FG culture results are important. In the present study, the most frequently isolated bacterium was the *E. coli* and flora bacterium, which was 52.9% (18 patients) of all cases. In a retrospective cohort study published by Tang et al.,<sup>[20]</sup> it was shown that *E. coli* (46.6%) was the most frequently isolated bacterium after polymicrobial infections (54%). We think that this is due to the fact that the fecal flora is dominant among the flora that causes FG. However, infections developing with

clostridial or atypical agents tend to be more aggressive and more likely to lead to mortality. In the present study, in ten patients with clostridial or atypical agents, the mortality rate was 50% compared with the others with flora bacterium or non-clostridial agents and the frequency of debridement was significantly more than the others due to rapid progression of necrosis caused by these highly toxic agents. For these reasons, microbial cultures should be taken from all patients operated for FG and more aggressive treatments should be planned in patients with clostridial or atypical infectious agent growth.

### Limitations

The main limitations of the study are possible selection bias due to being of a retrospective study and the limited adaptability of the results to the general population due to the relatively low sample size.

### Conclusion

FGSI was found to be insufficient in determining the frequency of debridement and the hospital stay but it accurately predicts the rates of mortality and survival. The patients who were infected with clostridial or atypical agents are more likely to develop mortality and tend to be required more aggressive surgical interventions than the others. As a result, considering the higher rate of mortality, the patients with FGSI score >9 and infected with clostridial or atypical agents should be taken to surgery immediately after stabilizing the vital signs and controlled fluid replacement, effective combined antibiotic therapies, and aggressive treatments such as mechanic ventilation or nutritional support should be planned in intensive care conditions during the post-operative period.

**Ethics Committee Approval:** This study was approved by the Afyonkarahisar University of Health Sciences Clinical Research Ethics Committee (Date: 01.11.2019, Decision No: 2011/KAEK-2).

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ORJİNAL ÇALIŞMA - ÖZ

## Fournier gangreni ciddiyet skorlaması ve mikrobiyal kültür sonuçlarının hastanede kalış süresi, debridman sıklığı ve mortalite üzerindeki etkisi

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**AMAÇ:** Fournier gangreni hızlı ilerleyen bir yumuşak doku nekrozu olup agresif cerrahi tedavi uygulanmadığında yaşamı tehdit edebilir. Fournier gagreni ciddiyet skorlaması ilk olarak Laor ve arkadaşları tarafından mortalite oranını tahmin etmek için tanımlanmıştır. Bu skorlamanın prognostik önemi kanıtlanmış olmakla birlikte gangrene neden olan mikrobik ajanlarla bağlantısı ya da hastaların tedavi süreçlerinin uzunluğu ile ilgisini araştıran çok az çalışma vardır. Bu çalışmada, Fournier gangreni ciddiyet skorlaması ve yara yerlerinden izole edilen enfektif ajanların hastanede kalış, debridman sıklığı ve mortalite üzerindeki etkisi araştırıldı.

**GEREÇ VE YÖNTEM:** Ocak 2013–Ocak 2018 tarihleri arasında Fournier gagreni tanısıyla ameliyat edilen 34 hasta geriye dönük olarak incelendi. Başvuru sırasındaki Fournier gagreni ciddiyet skorları hesaplandı ve hastalar eşik değerine göre iki gruba ayrıldı. Ayrıca, debridman kültürlerinden izole edilen mikrobiyal ajanlara göre kategorize edilerek iki ayrı grup oluşturuldu. Fournier gagreni ciddiyet skorlaması ve mikrobiyal ajan tipinin hastanede kalış, debridman sıklığı ve mortaliteye etkisi analiz edildi. Hayatta kalan ve hayatta kalmayanlar grubu arasında hasta özellikleri karşılaştırıldı.

**BULGULAR:** Fournier gagreni ciddiyet skoru >9 olan grupta diğer gruba göre mortalite oranının anlamlı olarak yüksek olduğu (%100'e karşı %6.7;  $p=0.001$ ) ve bu skorlamanın mortalite oranını %100 ve sağkalım oranını ise %93.3 öngördüğü görüldü. Fournier gagreni ciddiyet skoru ile debridman sıklığı ve hastanede kalış sıklığı arasında anlamlı bir ilişki yoktu. Kolostridial ve atipik ajanlarla enfekte hasta alt grubunda mortalite oranı (%50'ye karşı %4.2;  $p=0.005$ ) ve debridman sıklığı ( $3.10\pm 0.73$ 'e karşı  $2.00\pm 0.72$ ;  $p=0.001$ ) anlamlı olarak daha yüksekti.

**TARTIŞMA:** Fournier gagreni ciddiyet skorunun prognozu başarılı bir şekilde öngörebilmesine karşın debridman sıklığını ve hastanede kalış süresini belirlemede yetersiz olduğu görüldü. Ayrıca çalışma kolostridial ve atipik ajanlarla enfekte hastaların daha fazla sayıda debridman gerektireceğini ve mortalite geliştirme olasılığının daha yüksek olduğu öngörmüştür. Bu grubun ilk debridmanda daha agresif cerrahiye ihtiyaç duyma eğiliminde olduğu söylenebilir.

**Anahtar sözcükler:** Fasiit; gangren; enfeksiyon.

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