

Factors affecting mortality in Fournier's gangrene: experience with fifty-two patients

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INTRODUCTION Fournier's gangrene (FG) is a life-threatening infection of the perineal and genital areas. We examined the comorbid diseases, treatments and factors affecting mortality in FG.

METHODS This retrospective clinical study involved 52 patients who were treated for FG. The demographics, aetiologies, comorbid diseases, laboratory and bacteriology findings, treatment methods and length of hospital stay were compared between patients who died and those who survived the infection.

RESULTS Out of the 52 patients, 12 died and 40 survived. Patients who died and those who survived were similar in terms of their mean age at first presentation (62 vs. 55 years), the mean number of debridements (3.6 vs. 2.9), the mean length of hospital stay (25 vs. 34 days) and gender ($p > 0.05$ for each). However, the mean leukocyte count was higher in patients who died than in surviving patients (33.6 ± 7.2 vs. 14.3 ± 4.9 cells/mm³; $p < 0.05$). The most common aetiology in both groups was perianal abscess. Deviating colostomy was performed in 13 patients. Of the patients who died, nine had haemodialysis-dependent chronic renal failure and type II diabetes mellitus (DM), while one had type II DM and hypertension.

CONCLUSION Haemodialysis-dependent chronic renal failure and a high leukocyte count at first presentation were found to be the factors affecting mortality in FG patients.

Keywords: Fournier's gangrene, mortality, necrotising fasciitis, renal failure
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INTRODUCTION

In 1883, Dr Jean Alfred Fournier defined an infection of unknown origin that led to rapid necrosis of the scrotal skin in young healthy males.⁽¹⁾ This infection is now called Fournier's gangrene (FG), although other names and definitions have been proposed, such as necrotising fasciitis, as suggested by Wilson in 1952.⁽²⁾ The term FG is now more broadly applied to genital, perianal, perirectal and abdominal wall infections. Although the first definition involved no known aetiology, trauma and infection of the perianal and genital regions appear to play an important role.⁽³⁾ FG is now recognised in a wide spectrum of age groups, ranging from newborns to the elderly, and affects both genders equally.⁽⁴⁾ It is most frequently seen in men in their third and sixth decades of life, with the mean age of patients above 50 years.^(4,5) Diabetes mellitus (DM), hypertension, immunosuppression, alcoholism, chronic renal failure (CRF), obesity, cortisone use, malignancy, pulmonary diseases and systemic disorders are known to be the predisposing factors for FG.⁽⁵⁾ The present study analysed patients with FG in order to identify the comorbid diseases, treatment outcomes and factors influencing mortality.

METHODS

This retrospective study examined the data of 52 patients (36 males, 16 females, mean age 55 [range 37-78] years) treated

for FG in the general surgery clinics of Istanbul Training and Research Hospital and Okmeydani Training and Research Hospital, Istanbul, Turkey between January 2005 and July 2008. Patient data was obtained from the hospital archives. Of the 52 patients, 12 died (Group 1) and 40 survived (Group 2), and the two groups were evaluated separately. Patient gender, age, aetiologies, predisposing factors, surgical interventions, the presence of a deviating colostomy, isolated bacterial agents and treatments were evaluated and compared between the two groups. Statistical analysis was performed using the NCSS 2007 (LLC, Kaysville, UT, USA) software package. In addition to descriptive statistical methods (i.e. mean and standard deviation), Mann-Whitney U-test was used to compare paired groups, and Chi-square and Fisher's exact tests were used for comparing qualitative data. A p -value < 0.05 was considered to indicate a significant difference. The research was approved by the ethical committees of the two hospitals.

RESULTS

Data on patient age, gender, leukocyte count at first presentation and length of hospital stay are presented in Table I. Group 1 and 2 patients were found to be similar with regard to age, gender and length of hospital stay ($p > 0.05$). The leukocyte count at first presentation was higher in Group 1 than Group 2 patients (33.6 ± 7.2 vs. 14.3 ± 4.9 cells/mm³, $p < 0.0001$).

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Table I. Patient demographics, mean leukocyte count at first presentation, mean length of hospital stay and comorbid diseases.

Parameter	No. (%)		p-value
	Group 1 (n = 12)	Group 2 (n = 40)	
Age* (yrs)	62.22 ± 8.9	55.64 ± 8.3	0.265
Gender			
Male	8 (66)	28 (70)	0.327
Female	4 (33)	12 (30)	0.450
Leukocyte count at first presentation* (mml)	33.6 ± 7.2	14.3 ± 4.9	0.0001 [†]
Length of hospital stay* (days)	34.2 ± 35.5	25.4 ± 25.3	0.780
Comorbid disease			
Diabetes mellitus	9 (75)	25 (62)	0.618
Hypertension	8 (66)	19 (48)	0.877
Chronic renal failure	9 (75)	0	0.003 [†]
Malignancy	0	2 (5)	0.598
Ulcerative colitis	0	2 (5)	0.598

Group 1: non-survivors; Group 2: survivors

*Data is presented as mean ± standard deviation, [†]Significant at p < 0.05

Table II. Treatments administered.

Treatment	No. (%)		p-value
	Group 1 (n = 12)	Group 2 (n = 40)	
No. of debridements [†]	3.6 ± 1.5	2.9 ± 1.4	0.912
Colostomy	5 (41)	8 (20)	0.699
Honey dressing	8 (66)	19 (48)	0.384
HBO	3 (25)	12 (30)	0.872
VAC	1 (8)	5 (13)	0.381
HBO + honey dressing	2 (16)	10 (25)	0.498
Honey dressing + HBO + VAC	0	5 (13)	0.262

Group 1: non-survivors; Group 2: survivors [†]Data is presented as mean ± standard deviation.

HBO: hyperbaric oxygen; VAC: vacuum-assisted closure

In Group 1 (n = 12), the underlying aetiologies were perianal abscess in eight patients and necrosis of the scrotal skin in two patients, while the aetiology could not be identified in the remaining patients. For Group 2 (n = 40), the aetiologies were perianal abscess in 22 patients, necrosis of the scrotal skin in seven patients, rectosigmoid tumour perforation in two patients and haemorrhoidectomy in one patient, while the aetiology could not be identified in eight patients. The two groups were similar with regard to the underlying aetiology (p > 0.05). The most frequently isolated organisms in both groups were *Escherichia coli* and *Bacteroides (B.) fragilis*. Other detected bacteria included *Enterococci*, *Pseudomonas aeruginosa* and *Proteus mirabilis*. The bacteria types were also similar in both groups.

The patients' comorbid diseases are listed in Table I. Haemodialysis-dependent CRF was found to be more common in Group 1 than Group 2 patients (p < 0.003). Following diagnosis, all patients were administered broad-spectrum antibiotics (Flagyl[®], Eczacbası Co, Istanbul, Turkey and Cefaday[®], Biofarma Co, Istanbul, Turkey) and underwent large surgical debridement. The debridement procedure was repeated in some patients depending on the lesion status. Data regarding the mean number of debridements, presence of a colostomy, treatment with honey dressing, hyperbaric oxygen (HBO) and vacuum-assisted closure

(VAC) are presented in Table II. Both groups were found to have received similar treatment (p > 0.05).

DISCUSSION

FG is a severe and progressive infection that can involve the genital region, perineum and lower abdominal wall, separately or together. Patients tend to be aged 25–75 years, and the mortality rate is 3%–67%, although age has not been reported to be a significant prognostic factor for mortality.^(3–6) While FG is mostly known to be a disease of the male gender, as scrotal involvement used to be an essential component of the original FG definition, the definition has since been broadened, as women are also diagnosed with this disease now, albeit at a lower rate.⁽⁷⁾ The mean age of the patients in the present study was 55 years and the mortality rate was 23.8%. The female-male ratio for Group 1 patients was 1:2. Our findings indicate that age and gender were not significant factors influencing mortality (Table I). Similarly, Yanar et al reported that although the mortality rate in female FG patients was high despite a lower number of female patients, female gender was not a prognostic factor for mortality.⁽⁵⁾

Previously, FG was generally known as a urological disease but is now primarily a concern of general surgeons, since the most common aetiology is infections of the colorectal origin. In FG of colorectal origin, infection usually progresses first to the Colles' fascia. It may then extend to the dartos fascia of the scrotum, Buck's fascia of the penis, and sometimes the Scarpa's fascia of the lower abdomen. As a result, FG causes thrombosis in the arterioles of the subcutaneous tissue and leads to necrosis of the skin, subcutaneous tissue and fascia.⁽⁸⁾ Stephens et al found a higher mortality in patients with FG of colorectal origin compared to other aetiologies.⁽⁹⁾ In the present study, although an aetiology of perianal abscess was detected in eight (66.6%) of the patients who died and in 22 (55%) of the surviving patients, it was not found to affect mortality.

Various comorbid diseases are generally present in a majority of FG patients. In the present study, DM was found to be the leading comorbid disease, followed by hypertension, CRF and

ulcerative colitis. No comorbid disease was detected in three patients. Although DM was the leading predisposing factor for FG, it was not found to affect mortality. In contrast, while CRF was only the third most frequent comorbid disease, it was detected in nine out of the 12 patients who died (75%) and found to be a prognostic factor for mortality ($p < 0.003$). Consistent with the present findings, other studies have also reported DM as the main predisposing factor for FG, while alcoholism, obesity, CRF, hypertension, cardiac disease, malignancy and immunosuppressive drug use were found to be associated with FG.⁽¹⁰⁻¹²⁾ Although alcoholism had been identified as the main predisposing factor for FG in some series,^(13,14) it was not identified as a factor in the present study, probably due to the social and religious mores influencing this study population. Jeong et al likewise found that DM did not affect mortality in FG patients, even though it was the major predisposing factor; instead, the main prognostic factor influencing mortality was found to be haemodialysis-dependent CRF, with a death rate of 50%.⁽¹²⁾

Leukocyte counts in FG patients generally increase in accordance with the severity of infection. In this study, the mean leukocyte counts at first presentation were 33.6 ± 7.2 cells/mml in patients who died and 14.3 ± 4.9 cells/mml in patients who survived ($p < 0.0001$). Consistent with these findings, Villanueva-Sáenz et al reported that a high mean leukocyte count at first presentation was a prognostic factor for mortality.⁽¹⁰⁾ It is generally accepted that FG is associated with both aerobic and anaerobic bacteria, and a relationship between mortality rates and bacteria types has previously been reported.^(3,5,15,16) We found that although *E. coli* and *B. fragilis* were the most frequently observed bacteria in our study, they did not affect the mortality rates. Similar findings were reported in a study of 44 patients by Kuo et al and in a study of 33 patients by Akgün and Yılmaz.^(17,18)

Early diagnosis, effective debridement and appropriate medical treatment have been reported to increase the likelihood of surviving FG.^(17,19) FG cases should be treated as medical emergencies, and necrotic tissue should be debrided, broad-spectrum antibiotics administered, and fluid and electrolyte balance controlled. Some studies recommend that following wound debridement, a colostomy should be performed if anal insufficiency, rectum perforation, excessive necrosis in the perineum or a fistula is present.^(20,21) In our series, the mean number of debridements was 3.6 ± 1.5 in patients who died and 2.9 ± 1.4 in those who survived, and the corresponding number of patients who underwent a colostomy was five and eight, respectively. The number of debridements and the colostomy ratio were found to be significant factors, but they did not influence mortality (Table II). Large wounds caused by debridement in FG patients generally take a long time to heal and thus require a long hospital stay. Although Ersay et al⁽¹¹⁾ have found that a longer hospital stay was a factor affecting survival, it was not the case in the present study, as the length of hospital stay was not found to be a significant factor for mortality (Table I).

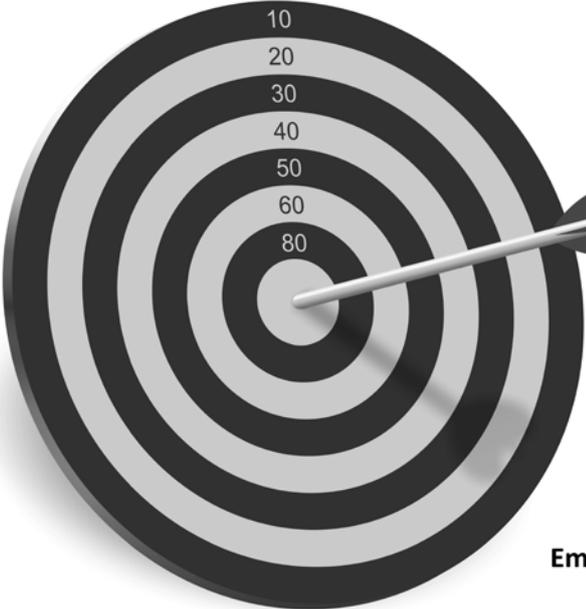
A range of supportive treatments has been used to improve wound healing in FG patients. In the present study, some patients were treated using HBO, honey dressing and VAC (Table II). However, none of these methods were found to affect the mortality rate. In a series consisting of 42 patients, Mindrup et al treated 16 patients with surgical and medical procedures and 26 patients with HBO. The authors found that HBO was associated with more complications, higher costs and a higher mortality rate.⁽²²⁾ In contrast, Hollabaugh et al treated 14 out of 26 patients with HBO and surgical debridement, and found that the group administered HBO had a lower mortality rate compared to the group that did not receive HBO therapy.⁽²³⁾ The differing findings may reflect the patient heterogeneity in each study. There is a long history of using honey dressings for wounds, including FG-associated wounds. Due to its low pH, high osmotic effect and enzymatic content, honey contributes to the breakdown of necrotic tissue and accelerates wound healing by stimulating new epithelia formation.⁽²⁴⁾ While some FG studies have reported the positive effects of honey dressings, there is no evidence that they lower the mortality rate.^(25,26) The VAC system is a recent method developed to induce rapid healing of large wounds. While some studies have found that VAC has a positive effect on FG wounds, there is insufficient evidence to suggest that it reduces mortality rates.^(27,28)

In conclusion, FG continues to have a high mortality rate despite interventions such as multiple debridements, antibiotic treatment and various types of supportive treatments. We have found that CRF and a high leukocyte count at first presentation were factors influencing mortality, whereas age and gender were not, and neither was DM, even though it was the leading predisposing factor for FG.

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