Original Article

Risk Factors for Mortality in Fournier's Gangrene: Necrotizing Fasciitis in Perineum and Perianal Region, a Single-hospital Experience

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Key Words
Fournier's gangrene;
Risk factors;
Mortality rate;
Fasciitis

Objective. Fournier's gangrene (FG) is a rapidly progressing necrotizing fasciitis of the perineum, genital, and perianal areas associated with a high mortality rate. This study presented our experience with the risk factors for mortality among patients with FG.
Materials and Methods. This was a retrospective study involving 85 patients treated for FG at a single hospital from January 2009 to December 2019. Several clinical and laboratory variables including the Simplified Fournier Gangrene Severe Index Score (SFGSI) were evaluated and correlated with mortality through univariate analysis and logistic regression.
Results. Of the 85 patients, 70 (82.4%) were men, the mean age was 62.2 ± 15.4 (29-95) years, and the main comorbidities were diabetes mellitus in 48 patients (56.5%) and hypertension in 38 patients (44.7%). Six patients did not survive, and the mortality rate was 7.1%. Variables that presented an independent correlation with mortality were extension of the lesion to the abdominal wall (odds ratio (OR) = 78.0, confidence interval (CI) = 6.15-989.03; $p = 0.044$) and a comorbidity of liver cirrhosis (OR = 20.28, CI = 3.14-131.17; $p = 0.022$).
Conclusion. FG extending to the abdominal wall and a comorbidity of liver cirrhosis are independent risk factors for mortality. The simplified form of the FGSI showed a correlation with mortality but was not an independent risk factor for mortality in this study.
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Fournier's gangrene (FG) is a potentially fatal disease characterized by necrotizing fasciitis of the perineal, genital, or perianal region resulting from a synergistic polymicrobial infection;[1-5] FG was first described by Alfred Jean Fournier in 1883.[6] FG affects mainly males, and the etiology of infection may be idiopathic or secondary to anorectal, urogenital, and cutaneous diseases, trauma or prior surgical procedures.[7] The treatment of FG consists mainly of hemodynamic resuscitation and stabilization, aggressive surgical debridement, and broad-spectrum antibiotics.[7,8]

FG is still a disease with high mortality rate between 20 and 40% in most studies, and some reported ranging from 4 to 88%.[2,7,9] The main predisposing factors for FG are diabetes, alcoholism, hypertension, and heavy smoking, which also predispose patients to

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obliterating endarteritis,[10] as well as immunosuppressive diseases such as malignant neoplasia being treated with under chemotherapy and rheumatic disease being treated with prednisolone.[7,11,12]

The Fournier Gangrene Severe Index Score (FGSI), which includes nine clinical and laboratory parameters, was developed by Laor et al. in 1995 to stratify the risks in FG patients and to predict mortality.[13] Few systematic scoring systems were described later but are difficult to implement in clinical practice. In 2014, Lin et al. developed a reliable scoring system, the simplified FGSI (SFGSI), which contains only 3 variables, has a high sensitivity and specificity, and has been easily accepted.[14] The objective of the present study was to demonstrate the main risk factors for FG and to assess the use of the SFGSI to predict mortality among patients with FG in a single hospital.

Materials and Methods

Eighty-five patients were diagnosed with FG between January 2009 and December 2019 and enrolled in this retrospective study. They were treated and followed up until the end of December 2020. The mean follow-up time was 31 months from diagnosis. The diagnosis was based on history, imaging studies, and symptoms of fever with induration, edema, crepitation, and necrosis in the genital, perineal, and perianal areas. Patients with malignant neoplasia related to FG and those with perianal, scrotal, or ischiorectal abscessation without evidence of necrosis or soft tissue extension were excluded.

Clinicopathological data including age, sex, underlying diseases, smoking history, length of hospital stay, history of colostomy, frequency of surgery, areas of involvement, isolated microorganisms, and mortality rate were analyzed. Laboratory data that were collected at the emergency department or admission, such as the creatinine (Cr), sodium (Na), and potassium (K) levels, hematocrit (Hct), and plasma glucose levels, were analyzed. According to the Hct, K, and Cr values, the SFGSI was applied and calculated by adding the points for each parameter, which ranged from 0 to 4. The SFGSI cutoff point is two, and a value higher than 2 has a sensitivity of 87% and a specificity of 77% to predict mortality.[14]

Colostomy was performed when there was infection involving the anal sphincter or frequently wound stool contaminate post necrotic tissue debridement. Closure of the stoma was performed in cases of total wound healing and intact anal tone. Antibiotic therapy with ceftriaxone and metronidazole was initiated in the emergency room and maintained during hospitalization. Antibiotic therapy was modified according to the results of the microbiological culture of the abscess or tissue that was removed during the first surgery and under the guidance of the hospital infection commission. Patients underwent sequential debridement procedures until all necrotic tissues had been removed and granulation tissue had formed on the wound. Serial primary repairs and flap or graft reconstruction were performed on residual wounds for complete wound healing.

Numerical variables are presented as the mean ± standard deviation (SD) or median with the interquartile range. The associations between continuous variables and mortality were evaluated with Student's t-test, and those between categorical variables and mortality were evaluated with the chi-square test. Variables that were correlated with mortality in the univariate analysis had their risk adjusted by logistic regression. A significance level of $p < 0.05$ and a confidence interval of 95% were adopted. The statistical analysis was performed using the statistical program Statistical Package for the Social Sciences (SPSS version 25).

Results

The clinical and laboratory data of the 85 included patients are shown in Table 1. Seventy patients (82.4%) were male. The average age was 62.2 (29-95) years, and the average body mass index (BMI) was 26.3. The mean length of hospitalization was 25.5 days, and the mean number of debridement procedures was 1.66. Risk factors for FG were identified and included alcoholism in 14 patients (16.5%), heavy smoking in 22 patients (25.9%), immunosuppression in 11 patients

Table 1. Clinicopathological and laboratory data of 85 patients with Fournier's gangrene

Variable	Number (%)	Mean ± SD (range)
Age		62.2 ± 15.4 (29-95)
BMI		26.3 ± 4.6 (17.9-41.9)
Length of hospital stay (days)		25.5 ± 16.8 (3-89)
Hematocrit (%)		35.3 ± 7.1 (17.8-50.5)
Sodium (mmol/L)		133.2 ± 5.5 (118-144)
Potassium (mmol/L)		3.8 ± 0.6 (2.4-5.3)
Creatinine (mg/dL)		2.1 ± 2.5 (0.37-13)
Glucose (mg/dL)		210.7 ± 140.1 (68.5-718)
Debridement (number of times)		1.7 ± 1.0 (1-4)
SFGSI score		1.98 ± 2.2 (0-8)
Male	70 (82.4%)	
Diabetes mellitus	48 (56.5%)	
Hypertension	38 (44.7%)	
CKD	15 (17.6%)	
Liver cirrhosis	11 (12.9%)	
Immunosuppression	11 (12.9%)	
Alcoholism	14 (16.5%)	
Smoking	22 (25.9%)	
Extension to		
Abdominal wall	4 (4.7%)	
Thigh	8 (9.4%)	
Genital	36 (42.4%)	
Perineal	64 (75.3%)	
Perianal	67 (78.8%)	
Perirectal	27 (31.8%)	
Inguinal	27 (31.8%)	
Buttock	45 (52.9%)	
Colostomy	29 (34.1%)	
Closure of stoma	15 (17.6%)	
Wound repair	23 (27.1%)	
Reconstruction	10 (11.8%)	
SFGSI score > 2	29 (34.1%)	
Mortality	6 (7.1%)	
GNB		
E.coli	37 (43.5%)	
Bacteroides sp	34 (40.0%)	
Kleb.pneumoniae	22 (25.9%)	
Prevotella sp	8 (9.4%)	
GPB		
Streptococcus	28 (32.9%)	
Enterococcus	21 (24.7%)	
Staphylococcus	19 (22.4%)	

(12.9%), diabetes mellitus in 48 patients (56.5%), and hypertension in 38 patients (44.7%). The genital area was involved in 36 patients (42.4%), the perianal area was involved in 67 patients (78.8%), and the perineal region was affected in 64 patients (75.3%). FG involved other body regions including the inguinal area in 27 patients (31.8%), abdominal wall in 4 patients (4.7%), buttock in 45 patients (52.9%), and thigh in 8 patients (9.4%). Colostomy was required in 29 patients (34.1%), and closure of the colostomy was not performed in 14 patients (48.3%) due to severe anal sphincter injury related to FG. Plastic reconstruction

was performed in 10 patients (11.8%), and primary repair was performed in 23 patients (27.1%) with a good wound base and granulation tissue. Regarding the culture results for microorganisms in the debrided tissues, the following types of microorganisms were identified: Gram-negative bacteria (Escherichia coli in 37 cases (43.5%), Bacteroides spp. in 34 cases (40.0%), Klebsiella spp. in 22 cases (25.9%), and Prevotella spp. in 8 cases (9.4%)), Gram-positive bacteria (Staphylococcus spp. in 28 cases (32.9%), Enterococcus in 21 cases (24.7%), and Peptostreptococcus spp. in 19 cases (22.5%)), and less commonly yeast.

The overall mortality was 7.1% with 6 cases in this study. The variables related to mortality were analyzed (Table 2). Patients with hypertension had a higher mortality than patients without hypertension (83.3% versus 41.8%; $p = 0.048$). Patients with liver cirrhosis had a higher mortality than patients without cirrhosis (66.7% versus 8.9%; $p = 0.002$). The involvement of the abdominal wall was more frequent among nonsurvivors than among survivors (50.0% versus 1.2%; $p = 0.001$), and involvement of the genital area was also more frequent among nonsurvivors than among survivors (83.3% versus 39.2%; $p = 0.035$). When laboratory values including Hct, K, and Cr were summed to calculate SFGSI score, 29 (34.1%) patients had a result > 2. Nonsurvivors had a higher mean SFGSI score than survivors (4.17 versus 1.8; $p = 0.01$), and patients with an SFGSI score > 2 had a higher mortality rate than those with an SFGSI score < 2 (83.3% versus 30.3%; $p = 0.008$). The remaining variables were not significantly associated with mor-

Table 2. Univariate analysis for mortality of Fournier's gangrene

Variable	Percentage or mean ± SD of patients for each variable		
	Survivor (n = 79)	Nonsurvivors (n = 6)	*p* value
Age	62.3 ± 15.4 (29-95)	66.2 ± 10.3 (53-78)	0.52
BMI	26.3 ± 4.4 (18.5-41.9)	26.1 ± 7.4 (17.9-34.1)	0.95
Length of hospital stay (days)	25.5 ± 17.3 (3-89)	26.7 ± 7.9 (19-38)	0.87
Hematocrit (%)	35.4 ± 6.9 (19.4-50.5)	33.5 ± 9.9 (17.8-46.0)	0.53
Sodium (mmol/L)	133.2 ± 5.5 (118-144)	133.7 ± 6.4 (123-142)	0.85
Potassium (mmol/L)	3.8 ± 0.57 (2.4-5.25)	4.1 ± 0.9 (2.9-5.3)	0.44
Creatinine (mg/dL)	2.0 ± 2.46 (0.37-13.0)	3.3 ± 2.9 (0.54-8.7)	0.22
Glucose (mg/dL)	215.3 ± 143.7 (68.5-718)	149.5 ± 51.5 (100-240)	0.27
Debridement (number of times)	1.61 ± 0.9 (1-4)	2.3 ± 1.5 (1-4)	0.073
SFGSI score	1.8 ± 2.1 (0-8)	4.17 ± 2.0 (2-8)	0.01*
Male	65 (82.3%)	5 (83.3%)	0.95
Diabetes mellitus	46 (58.2%)	2 (33.3%)	0.24
Hypertension	33 (41.8%)	5 (83.3%)	0.048*
CKD	13 (16.5%)	2 (33.3%)	0.30
Liver cirrhosis	7 (8.9%)	4 (66.7%)	0.002*
Immunosuppression	10 (12.7%)	1 (16.7%)	0.78
Alcoholism	12 (15.2%)	2 (33.3%)	0.25
Smoking	20 (25.3%)	2 (33.3%)	0.67
Extension to			
Abdominal wall	1 (1.2%)	3 (50.0%)	0.001*
Thigh	7 (8.9%)	1 (16.7%)	0.53
Genital	31 (39.2%)	5 (83.3%)	0.035*
Perineal	58 (73.4%)	6 (100%)	0.15
Perianal	62 (78.4%)	5 (83.3%)	0.78
Perirectal	24 (30.4%)	3 (50.0%)	0.32
Inguinal	23 (29.1%)	4 (66.7%)	0.057
Buttock	42 (53.2%)	3 (50.0%)	0.88
Colostomy	25 (31.6%)	4 (66.7%)	0.08
SFGSI score > 2	24 (30.3%)	5 (83.3%)	0.008*

tality in the univariate analysis.

Logistic regression was applied to identify risk factors for mortality (Table 3). Variables that were independently correlated with mortality were extension of the lesion to the abdominal wall (odds ratio (OR) = 78.0, confidence interval (CI) = 6.15-989.03; p = 0.044), and a comorbidity of liver cirrhosis (OR = 20.28, CI = 3.14-131.17; p = 0.022). The remaining variables including the SFGSI score showed no correlation with mortality in the logistic regression analysis.

Table 3. Multivariate analysis for mortality of Fournier's gangrene

Variable	OR (odds ratio)	CI (confidence interval)	p value
Hypertension	6.97	0.78-62.47	0.990
Liver cirrhosis	20.28	3.14-131.17	0.022*
Extension to			
Abdominal wall	78.0	6.15-989.03	0.044*
Genital	7.74	0.863-69.45	0.674
SFGSI score > 2	11.45	1.27-103.4	0.964

Discussion

FG is a life-threatening disease with a high mortality rate; the most frequent causes of death are sepsis and multiple organ failure. Significantly increased mortality rates have been detected in patients with diabetes, heart disease, renal failure, and kidney disease. However, there is no association between mortality rates and comorbid hypertension, lung disease, liver disease, or malignancy.[15,16] In the multivariate analysis of this study, the main parameters associated with mortality were lesion extension to the abdominal wall and comorbid liver cirrhosis. Other parameters including the SFGSI score were not statistically significant predictors of mortality. Diabetes mellitus and chronic kidney disease were not statistically significant in the univariate analysis to predict mortality associated with FG.

Liver cirrhosis was an independent risk factor for mortality associated with FG (p = 0.022) in this study, and Kuo, C. et al. found a similar association in patients in northern Taiwan.[11] Liver cirrhosis is related to a high mortality rate in major surgery, and the Child-Pughscore is independently correlated with high perioperative mortality in emergent operations.[17,18] Eleven patients with liver cirrhosis were included in this study, and four of these patients were nonsurvivors group (66.7%), including two patients with a cirrhosis Child-Pughscore of C (50.0%). Patients with underlying disease including liver cirrhosis who undergo emergent FG debridement or fasciectomy might have a high mortality rate.

Whether hypertension is a risk factor for mortality associated with FG remains unknown. Some studies did not identify hypertension as a risk factor for mortality associated with FG;[15,16] however, other studies found that hypertension could be risk factor[5] for mortality. Sorensen found that four specific comorbidities were associated with increased mortality risk, including hypertension, congestive heart failure, renal failure, and coagulopathy.[2,19] In this study, more nonsurvivors had a comorbidity of hypertension than survivors (83.3% vs. 41.8%, p = 0.048). In the logistic regression analysis, however, hypertension was not identified an independent risk factor for mortality. Among nonsurvivors, two patients had a history of ischemic heart disease and heart function impairment within 2 years, and heart failure occurred in one patient. Among survivors, no comorbidities of hypertension or histories of ischemic heart disease or heart failure were recorded. Patients with ischemic heart disease and impaired heart function before surgery for FG might related have an increased mortality rate.

There is no consensus regarding whether the extent of FG infection is associated with a poorer prognosis. Previous studies have shown that the mortality rate is statistically increased in patients with a larger impaired area[20] but is not correlated with the mean extent of the involved body surface area.[21] In this study, extension of FG to the abdominal wall was a predictor of mortality with statistical significance (p < 0.044). This finding was also confirmed with reports that extension of gangrene beyond the perineum or to the abdominal wall was an independent predictor of mortality.[16,22-25] FG extending to the abdominal wall and genital soft tissue or fascia is complex and makes it easy for bacteria to spread. Comprehensive debride-

ment of necrotic and infected abdominal wall or genital tissues is more difficult than treatment of other extended body areas. Unclear and delayed debridement may cause high mortality,[26] and early surgical intervention could maximize the survival of high-risk patients with FG.[14] Therefore, aggressive and frequent debridement should be performed in patients with FG extending to the abdominal wall.

The FGSI is a good predictor of FG mortality with a high sensitivity and specificity; it consists of nine clinical and laboratory parameters (temperature, heart rate, respiratory rate, Na, K, Cr, leukocytes, Hct and bicarbonate). In our study, the serum bicarbonate levels were not available in all patients because in our clinical practice, serum bicarbonate was only evaluated in patients who had unstable hemodynamics or electrolyte imbalances. In a recent study, Lin et al. demonstrated that the plasmatic Hct, Cr, and K are the FGSI variables that are the most correlated with mortality. A reliable scoring system called the simplified FGSI (SFGSI), which only includes the above mentioned 3 variables, was developed and easily accepted.[14] The SFGSI was not inferior to the FGSI and showed a sensitivity of 87% and specificity of 77% when the sum of the scores was greater than 2.[4]

The SFGSI contains minimal parameters, it is fast and easy to use at the time of initial diagnosis, and it can facilitate risk stratification of FG and detect patients who are at high risk of mortality. In this study, the SFGSI score was identified as a risk factor for high mortality associated with FG and was statistically significant in the univariate analysis ($p = 0.008$); however, no clinical or laboratory parameters were statistically significant predictors of mortality associated with FG. The SFGSI score was not an independent risk factor for mortality associated with FG in the logistic regression analysis. Subgroup patients with genital involved with FG were separated and analysis, and there was no statistically significant related to mortality. We cannot fully explain this situation according to the present clinical data.

This study has some limitations, which must be highlighted. We recruited patients over a period of 10 years, and potential bias might exist in the data quality and due to different clinical practices. As this was a retrospective study performed in single hospital, we cannot generalize our findings to other populations.

Conclusions

FG extending to the abdominal wall and a comorbidity of liver cirrhosis were identified as independent risk factors for mortality. The SFGSI score was correlated with mortality but was not an independent risk factor for mortality.

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原　著

福尼爾氏壞疽：肛周及會陰部壞死性筋膜炎的死亡風險因子的單一醫院經驗

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目的　福尼爾氏壞疽是會陰部，生殖器和肛周區域迅速發展且死亡率很高的壞死性筋膜炎。這篇研究呈現福尼爾氏壞疽死亡率的危險因素的探討與分析。

方法　這是一項回顧性研究，收集從 2009 年 1 月到 2019 年 12 月在單一醫院治療的 85 名福尼爾氏壞疽患者。通過單變量分析和邏輯回歸，評估了臨床特徵、檢驗數據和簡化的福尼爾氏壞疽嚴重指數評分 (SFGSI) 與死亡率的關聯性。

結果　在 85 位患者中，有 70 名 (82.4%) 為男性，平均年齡為 62.2 ± 15.4 (29-95) 歲，主要合併症是糖尿病 48 位 (56.5%) 和高血壓 38 位 (44.7%)。其中有 6 位患者沒有存活，死亡率為 7.1%。統計結果顯示壞疽病變擴展至腹壁 (OR = 78.0, CI = 6.15-989.03; p = 0.044) 及肝硬化 (OR = 20.28, CI = 3.14-131.17; p = 0.022) 與死亡率有顯著相關。

結論　福尼爾氏壞疽病變擴展至腹壁和肝硬化是導致死亡的獨立危險因子。簡化的福尼爾氏壞疽嚴重指數評分 (SFGSI) 與死亡率有相關性，在本研究中並無顯著意義。

關鍵詞　福尼爾氏壞疽、風險因子、死亡率、筋膜炎。