Original Article

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Fournier's Gangrene: A 10-Year Clinical Experience at a Tertiary Academic Medical Center

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Purpose: This retrospective study examined the factors influencing clinical outcomes and mortality in patients with Fournier's Gangrene (FG). The medical history, diagnostic procedures, treatment approaches, complications, and mortality factors associated with FG were analyzed.

Materials and Methods: This study retrospectively analyzed the medical records of 40 patients with FG treated over 10 years. The collected data included the patient demographics, comorbidities, vital signs, laboratory tests, Fournier's Gangrene Severity Index (FGSI) scores, wound swab culture results, treatment approaches, and length of hospitalization.

Results: Among the patients with FG, diabetes mellitus and hypertension were the most common comorbidities. The hemodialysis dependence has been identified as a significant risk factor of mortality. In addition, septic shock and an FGSI >9 were associated with increased mortality. *Escherichia coli* was the most prevalent bacterium in wound swab cultures, and the presence of antibiotic-resistant bacteria was significantly higher in the non-survivors. Treatment involved broad-spectrum antibiotics, emergency surgical debridement, and subsequent adjustments based on culture results.

Conclusions: Early diagnosis and prompt initiation of treatment are essential for improving the outcomes of patients with FG. Hemodialysis dependency, septic shock, FGSI scores, and the presence of antibiotic-resistant bacteria are important factors associated with mortality in patients with FG. Further research will be needed to validate these findings and explore adjunctive therapies to enhance the patient outcomes and improve FG management.

Keywords: Fournier's Gangrene; Septic shock; Antibiotic resistance; Hemodialysis

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INTRODUCTION

Fournier's Gangrene (FG) is a rare but fatal urological emergency defined as necrotizing fasciitis of the perineal, genital, or anorectal regions [1]. Bauriene first reported FG in 1764. The disease was named after French venereologist Jean-Alfred Fournier (1832-1914), who reported cases of 5 men with the disease in 1883 [2].

FG is most common among individuals in their 50s and 60s. Diabetes, high blood pressure, chronic renal failure, cardiovascular disease, alcoholism, and HIV infection have been identified as common comorbidities in FG [3]. The

mortality associated with FG was initially reported to be 80%. The use of potent antibiotics has decreased the mortality rate to less than 40% over the past 15 years [4]. Kuzaka et al. [2] and Topuz et al. [5] reported mortality rates of 0% among patients with FG in 2018 and 2022, respectively.

This study examined 40 cases of FG treated at a hospital over the past 10 years. The underlying medical history, diagnostic process, surgical and medical treatment, complications, and mortality affecting the cause of FG were analyzed. Thus, this study analyzed the demographics of FG patients and evaluated the factors affecting the clinical outcomes and mortality.

MATERIALS AND METHODS

1. Study Design and Participants

This study conducted a retrospective review of the medical records of patients who visited the Pusan National University Hospital for 10 years between January 2012 and June 2022. This study was approved by the Institutional Review Board of Pusan National University Hospital (approval number: 2306-025-128), which waived the requirement for informed consent. FG was diagnosed based on the following: patient's history; clinical symptoms; signs, such as erythema, rash, swelling, crepitus, and necrosis in the perineal, perianal, or genital region; radiological findings, including computed tomography or magnetic resonance imaging.

The patient's age, sex, body mass index (BMI), and presence of comorbidities were examined. At the time of hospitalization, the vital signs (body temperature, pulse rate, respiratory rate, and blood pressure), electrolyte (sodium, potassium) and bicarbonate levels, and other laboratory test results were examined. Based on these findings, this study checked the presence of septic shock and the Fournier's Gangrene Severity Index (FGSI) score for each patient, and the association between patient survival and mortality was verified with FGSI >9 [6]. An intraoperative wound swab culture was performed to determine the pathogenic bacteria and the presence of antibiotic-resistant bacteria (ARB). ARBs are defined as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, extended-spectrum β-lactamase Gram-negative organisms, or carbapenem-resistant *Enterobacteriaceae*.

2. Patient Management

All patients with FG were treated with empirical broad-spectrum antibiotics and underwent emergency surgical debridement. The antibiotics were changed according to the culture results. Enterostomy or additional debridement was performed, depending on the patient's condition. Plastic surgeons performed reconstructive surgery in patients with significant wound defects after infection control, and urologists performed a reconstruction in the remaining cases.

3. Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 27.0 software (IBM Co.). This study compared the baseline characteristics and laboratory test results of the survivors and non-survivors among FG patients using Mann-Whitney U and Fisher's exact tests. Statistical significance was set to $p<0.05$.

RESULTS

1. Baseline Characteristics

Of the 40 patients, 8 (20.0%) died, and 32 (80.0%) were discharged after treatment. Only 1 patient was female and a non-survivor. The age difference between survivors and non-survivors was insignificant (63.66±11.02 vs. 58.75±14.26; p=0.42). No significant difference in mean BMI was observed between the 2 groups (24.03±4.16 vs. 24.09±10.66; p=0.73). The most common comorbidity was hypertension, followed by diabetes mellitus (DM) (n=21, 52.5%; n=18, 45.0%, respectively). These trends were consistent when analyzed separately for survivors and non-survivors. Patients with chronic kidney disease (CKD) had a higher proportion of non-survivors, but this was not statistically significant (n=3, 9.4% vs. n=2, 25.0%; p=0.26). On the other hand, 2 of the patients who were on hemodialysis were in the non-survivor group ($p<0.05$) (Table 1).

2. Disease Presentations

No significant differences in the vital signs and laboratory tests, other than heart rate (HR), were observed between the survivors and non-survivors. On the other hand, the proportion of patients with septic shock was higher in the non-survivor group (n=7, 21.9% vs. n=5, 62.5%; $p<0.05$). The FGSI scores were examined based on the laboratory

Table 1. Comparison of the baseline characteristics between survivors and non-survivors

Variable	Survivor	Non-survivor	Total	p-value
N (%)	32 (80.0)	8 (20.0)	40 (100)	
Age (y)	63.66±11.02	58.75±14.26	62.68±11.71	0.42
Sex				0.20
Male	32 (100.0)	7 (87.5)	39 (97.5)	
Female	0 (0.0)	1 (12.5)	1 (2.5)	
BMI	24.03±4.16	24.09±10.66		0.73
Comorbidity (%)	1.72±1.09	2.13±1.73	1.80±1.22	0.67
Presence	30 (93.8)	7 (87.5)	37 (92.5)	0.50
DM	15 (46.9)	3 (37.5)	18 (45.0)	0.71
HT	17 (53.1)	4 (50.0)	21 (52.5)	1.00
CVD	3 (9.4)	1 (12.5)	4 (10.0)	1.00
CKD	3 (9.4)	2 (25.0)	5 (12.5)	0.26
Hemodialysis	0 (0.0)	2 (25.0)	2 (5.0)	<0.05
COPD	1 (3.1)	0 (0.0)	1 (2.5)	1.00
Liver cirrhosis	3 (9.4)	1 (12.5)	4 (10.0)	1.00
Multiple comorbidities	15 (46.9)	4 (50.0)	19 (47.5)	1.00

Values are presented as number (%) or mean±standard deviation.
BMI: body mass index, DM: diabetes mellitus, HT: hypertension, CVD: cardiovascular disease, CKD: chronic kidney disease, COPD: chronic obstructive pulmonary disease.

Table 2. Comparison of disease presentation between the survivors and non-survivors

Variable	Survivor (n=32)	Non-survivor (n=8)	p-value
Temperature (^{o}C)	37.12±0.81	36.89±0.72	0.54
HR	101.72±16.39	85.38±21.20	<0.05
RR	17.72±3.21	16.75±2.12	0.43
WBC ($\times10^{3}/\mu l$)	17.82±7.62	19.79±7.78	0.61
Hct (%)	34.89±7.72	28.74±7.84	0.07
Neutrophils ($\times10^{3}/\mu l$)	15.50±6.97	17.90±7.75	0.42
Serum sodium (mmol/L)	132.00±4.71	134.93±5.65	0.22
Serum potassium (mmol/L)	4.28±0.84	4.05±0.40	0.61
Bicarbonate (mmol/L)	20.56±14.70	18.35±3.67	0.83
BUN (mg/dl)	34.03±21.22	44.06±24.45	0.20
Serum creatinine (mg/dl)	1.73±1.07	2.29±1.76	0.61
Creatinine >2	9 (28.1)	3 (37.5)	0.68
AST (U/L)	38.88±33.70	164.5±375.66	0.70
ALT (U/L)	28.47±22.87	64.88±123.35	0.86
Septic shock	7 (21.9)	5 (62.5)	<0.05
FGSI score	5.91±2.57	6.88±3.40	0.23
FGSI >9	3 (9.4)	3 (37.5)	<0.05

Values are presented as mean±standard deviation or number (%).
HR: heart rate, RR: respiratory rate, WBC: white blood cell, Hct: hematocrit, BUN: blood urine nitrogen, AST: aspartate transapinase, ALT: alanine aminotransferase, FGSI: Fournier's Gangrene Severity Index.

findings; the mean scores were similar in the 2 groups. There was a significant number and proportion of patients with an FGSI >9 in the non-survivor group than in the survivor group (n=3, 9.4% vs. n=3, 37.5%; p<0.05) (Table 2).

Wound swab cultures identified a single bacterium in 18 patients (45.0%) and 2 or more bacteria in 22 patients (55.0%). There were no significant differences in the presence of multiple bacteria between the survivor and non-survivor groups (n=17, 53.1% vs. n=5, 62.5%; p=0.71).

Escherichia coli (*E. coli*) was the most common organism in the wound swab culture results (n=19, 47.5%), followed by *Streptococcus*, *Klebsiella pneumoniae*, and *Enterococcus* (n=11, 27.5%, respectively). The wound swab culture report showed that the percentage of ARBs was higher in the non-survivor group (n=5, 15.6% vs. n=5, 62.5%; p<0.05) (Table 3).

3. Disease Management

All patients were treated with empirical broad-spectrum antibiotics and emergent surgical debridement. Antibiotics

Table 3. Wound swab culture results

Variable	Survivor (n=32)	Non-survivor (n=8)	Total (n=40)	p-value
Bacteria number				0.71
Single	15 (46.9)	3 (37.5)	18 (45.0)	
Multiple	17 (53.1)	5 (62.5)	22 (55.0)	
Antibiotic category				
Escherichia coli	15 (46.9)	4 (50.0)	19 (47.5)	0.99
Streptococcus	9 (28.1)	2 (25.0)	11 (27.5)	0.99
Klebsiella pneumoniae	9 (28.1)	2 (25.0)	11 (27.5)	0.99
Pseudomonas	1 (3.1)	1 (12.5)	2 (5.0)	0.99
Staphylococcus	5 (15.6)	1 (12.5)	6 (15.0)	0.99
Enterococcus	9 (28.1)	2 (25.0)	11 (27.5)	0.99
Proteus	2 (6.3)	0 (0.0)	2 (5.0)	0.99
Bacteroides	4 (12.5)	0 (0.0)	4 (10.0)	0.57
Acinetobacter baumanni	0 (0.0)	2 (25.0)	2 (5.0)	<0.05
Candida spp.	0 (0.0)	1 (12.5)	1 (2.5)	0.20
Clostridium perfringenes	1 (3.1)	0 (0.0)	1 (2.5)	0.99
Antibiotic-resistant bacteria	5 (15.6)	5 (62.5)	10 (25.0)	<0.05

Values are presented as number (%).
Antibiotic-resistant bacteria are defined as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, extended-spectrum β-lactamase Gram-negative organisms, or carbapenem-resistant *Enterobacteriaceae*.

Table 4. Patients hospitalization and management

Variable	Survivor (n=32)	Non-survivor (n=8)	p-value
Antibiotic duration (d)	53.47±25.70	26.0±23.50	<0.05
Antibiotic treatment			
Penicillin	21 (65.6)	3 (37.5)	0.23
Cephalosporin	26 (81.3)	6 (75.0)	0.65
Aminoglycoside	11 (34.4)	2 (25.0)	0.99
Fluoroquinolone	15 (46.9)	0 (0.0)	<0.05
Carbapenem	21 (65.6)	3 (37.5)	0.23
Doxycycline	1 (3.1)	0 (0.0)	0.98
Clindamycin	9 (28.1)	2 (25.0)	0.99
Vancomycin	11 (34.4)	3 (37.5)	0.99
Metronidazole	23 (71.9)	7 (87.5)	0.65
Surgical management			
Debridement within one day of diagnosis	17 (53.1)	6 (75.0)	0.43
Debridement count	1.72±1.20	1.13±0.99	0.16
Multiple debridement	15 (46.9)	2 (25.0)	0.43
Enterostomy	11 (34.4)	1 (12.5)	0.40

Values are presented as mean±standard deviation or number (%).

were changed during hospitalization based on the wound swab culture results. The duration of antibiotic use was longer in the survivor group than in the non-survivor group (53.47±25.70 vs. 26.0±23.50; p<0.05). The number of debridements did not differ between the 2 groups (1.72±1.20 vs. 1.13±0.99; p=0.16), nor did multiple debridements and whether an enterostomy was performed. Debridement within one day of diagnosis was not a significant factor in survival (n=17, 53.1% vs. n=6, 75.0%; p=0.43) (Table 4).

DISCUSSION

Necrotizing fasciitis is a severe soft tissue infection involving the fascia and subcutaneous tissue, progressing rapidly along the fascia. The disease can be fatal if not detected early and treated appropriately. Fournier's gangrene is a type of necrotizing fasciitis that affects the scrotum, penis, or vulva [7].

DM and age are important predisposing factors for perianal or genital infections that develop into necrotizing fasciitis. DM-induced obliterative endarteritis worsens FG, resulting in poor blood supply and necrosis due to capillary

occlusion [8]. In the present study, DM was the second most common comorbidity, but the presence of DM did not affect mortality significantly. This finding differs from those of other studies. The complications associated with DM mortality are associated with DM duration. The patients with DM in this study were younger than those in other studies and had a large proportion of patients with a relatively short duration of DM, which may explain the lack of difference between the groups [9].

Previous studies only analyzed the presence of CKD. The present study analyzed the presence of hemodialysis in addition to CKD, which was a significant factor in FG mortality. Hemodialysis-dependent patients are more susceptible to infections than other patients because of the dysfunction of the innate and adaptive immune systems caused by end-stage renal disease. In the uremic environment of these patients, the antigen-presenting function of monocytes is reduced, T cells and B lymphocytes are dysfunctional, apoptosis is induced, and the bactericidal ability of neutrophils is reduced [10]. These biological mechanisms are reflected in these findings.

In this study, the non-survivor group had a lower HR than the survivor group. This could be a statistical artifact of a statistically small number of patients. On the other hand, the non-survivors included people with end stage renal disease (ESRD) on hemodialysis, and their HR was particularly low, which likely contributed to the significantly lower overall mean HR in the non-survivor group. This may be related to cardiovascular autonomic dysfunction in ESRD. Cardiovascular autonomic dysfunction due to ESRD can lower the baseline HR and decrease variability [11,12]. The significantly lower HR in ESRD patients is likely to be related to this.

In this study, the septic shock and FGSI >9 rates were higher in the non-survivor group. The FGSI is a parameter used to assess the FG severity, and several studies have shown increased mortality with FGSI >9, similar to these findings. Therefore, patients in the non-survivor group had more severe FG during hospitalization. Other studies reported that the non-survivor group tended to be hospitalized later [13]. Therefore, for a better prognosis, FG should be diagnosed promptly, and treatment should be started immediately.

Several studies have identified *E. coli* as the most common organism in wound swab cultures from patients with FG [14,15]. In this study, *E. coli* was the most common bacterium, which is consistent with the results of other studies. *E. coli* is followed by *Streptococcus*, *Enterococcus*, and *Klebsiella*, which are common alongside *E. coli* [14,16]. Other bacteria were identified in the cultures, but the presence of specific bacteria or the isolation of more than one type of bacteria did not affect the survival rates. On the other hand, the proportion of ARB was significantly higher in the non-survivors. Therefore, it can be interpreted as being associated with mortality. Other studies only analyzed the bacteria grown in the culture without mentioning antibiotic resistance. Hence, this study could be an essential addition to future FG analyses.

Empirical antibiotic treatments should be applied to Gram-positive, Gram-negative, and anaerobic organisms. In general, empirical treatment with FG regimens included carbapenem or piperacillin-tazobactam plus an agent with activity against methicillin-resistant *S. aureus*. Clindamycin should be considered if there is evidence of beta-hemolytic *Streptococcus* and *S. aureus* because of its antitoxic effects [17]. Hence, it is necessary to change the antibiotic regimen of patients according to the organism identified through surgical intervention or biopsy cultures.

As in other cases of necrotizing fasciitis, FG requires immediate surgical treatment. Necrotic tissue must be removed because it hinders wound healing and can encourage bacterial development, which worsens the infection at the location of the gangrene. Repeated debridement is necessary if necrosis persists [15].

This study had several limitations. First, this retrospective study included a relatively small number of patients. Therefore, the findings of this study cannot be generalized to the general population. In addition, there were no analyses of the conservative treatments applicable to FG, such as recently introduced hyperbaric oxygen therapy. Therefore, further analysis of the efficacy of supportive treatment is required.

CONCLUSIONS

FG is a rare but life-threatening disease with a high mortality rate. In addition to DM and other well-known risk factors, the hemodialysis status may be an important predisposing factor for mortality. Various bacteria are responsible for this, and antibiotic-resistant bacteria can significantly predict mortality. Further research is required

to validate the findings of the present study.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

W.S.S., A.R.K., and B.J.K. participated in data collection and wrote the manuscript. B.J.K. and K.H.K. participated in the study design and performed the statistical analysis. H.K.H. participated in the study design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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