Original Article

Predictors of Postoperative Mortality in Patients with Fournier's Gangrene

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Key Words
Fournier's gangrene;
Fournier's gangrene severity index score

Purpose. To identify the clinical risk factors associated with postoperative mortality in patients with Fournier's gangrene.
Methods. We retrospectively enrolled 36 patients who were treated for Fournier's gangrene during the period January 2006 to December 2012 at the Changhua Christian Hospital. Univariate and multivariate analyses were used to investigate possible risk factors for post-operative mortality in patients with Fournier's gangrene, including renal dysfunction, intensive care unit admission, age, respiratory rate, potassium, creatinine, medical history (diabetes mellitus, DM; hypertension, renal failure, and liver cirrhosis), origin of infection, history of malignancy, the presence of stoma, the number of operations, vital signs, the level of electrolytes, hematocrit, and Fournier's gangrene severity index.
Results. Mean age was 59.97 ± 15.3 years (range, 24-91 years) and most of the patients were men (32 of 36, 89%). The overall mortality rate was 30.5% (11 of 32). The most common predisposing illnesses were diabetes mellitus (52.8%) and hypertension (50%). The average Fournier's gangrene severity index (FGSI) score on admission was 6.5. All patients required radical surgical debridement and the majority (n = 25, 69%) required more than one session (mean, 2.8; range 2-4). Diverting colostomy was performed in 44.4% of patients. Although the univariate analysis showed that age, sex, renal dysfunction, intensive care unit admission, and most of the individual variables that make up the FGSI score were significant predictors of postoperative death, the mulitivariate analysis revealed that only the index score itself was an in independent predictor of postoperative mortality.
Conclusion. The Fournier's gangrene severity index score at admission is predictive of postoperative outcome.
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Fournier's gangrene (FG) was first mentioned by Baurienne in 1764.[1] However, it was until 1883 that Professor Jean-Alfred Fournier first use "fulminant gangrene" of the penis and scrotum to describe the disease,[2] with 3 main criteria: sudden onset on a health young man, rapid progression and idiopathic.[3] It was subject to male patient without known infection source at first. Since then, the definition of FG had been debated for years. In 1998, a compromised definition was proposed by Simth et al as "Necrotizing

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fasciitis of the perineal, genital or perianal regions".[4] Despite disagreement on terminology, early recognition and prompt surgical debridement remain the main principles of treatment.

Fournier's gangrene is an aggressive, life-threatening, polymicrobial soft tissue infection that specifically affects the genital and perineal regions. The disease is difficult to treat and is associated with a high mortality rate (30% to 50%).[5-8] The majority of infections that cause Fournier's gangrene are caused by mixed infections (anaerobic and aerobic bacteria), which can lead to vascular thrombosis, tissue necrosis, and reduced oxygen delivery. Due to low cellular oxygenation levels, anaerobes grow and produce enzymes together with aerobes, which further damages tissues and leads to fast disease progression.[9,10]

Several parameters have been proposed as factors that can identify patients at high risk of mortality such as the Fournier's gangrene severity index (FGSI)[5] (Table 1), body surface area, age, albumin, and diabetes mellitus (DM).[8-11] However, there is no consensus on the factors that are predictive of outcome of patients with Fournier's gangrene. In this study, we investigated the clinical risk factors associated with postoperative mortality in patients with Fournier's gangrene.

Materials and Methods

In this retrospective study, we enrolled 36 patients who were treated for Fournier's gangrene during the period January 2006 to December 2012 at the Changhua Christian Hospital. All clinical and demographic data were collected from medical records. Clinical diagnoses were based on the results of physical examinations and laboratory tests on admission clinical data.

Vital signs, predisposing illness, original site of infection, white blood cell count, creatinine level, blood gas data, and plasma concentrations of electrolytes were recorded at admission. Duration of stay in the intensive care unit (ICU), duration of hospital admission stay, methods of operation and number of operations, diverting colostomy, antibiotic therapy, and microbiologic test results were collected retrospectively.

Fournier's gangrene severity index

The Fournier's gangrene severity index (FGSI) was created by Laor and colleagues in 1995[5] and is composed of nine parameters, namely temperature, heart rate, respiratory rate, serum sodium level, potassium level, creatinine level, bicarbonate level, hematocrit, and leukocyte count. On admission, the nine parameters were scored using a 0-4 scoring system as described in the Table. A greater FGSI score indicated a higher probability of mortality.

Surgical treatment procedure

Surgical debridement procedures were performed by a urologist or colorectal specialist in all patients. After the operation, hemodynamically unstable patients and patients with respiratory failure were admit-

Table 1. Fournier's gangrene severity index

Physiological variables	High abnormal values				Normal	Low abnormal values			
Point assignment	4+	3+	2+	1+	0	1+	2+	3+	4+
Body 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	-	56-69	40-54	< 39
Respiratory rate	> 50	35-49	-	25-34	12-24	10-11	6-9	-	< 5
Serum sodium (mmol/L)	> 180	160-179	155-159	150-154	130-149	-	120-129	111-119	< 110
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 creatinine (mg/100 mL)	> 3.5	2-3.4	1.5-1.9	-	0.6-1.4	-	< 0.6	-	-
Hematocrit (%)	> 60	-	50-59.9	46-49.9	30-45.9	-	20-29.9	-	< 20
Leukocytes (total/mm^3 × 1000)	> 40	-	20-39.9	15-19.9	3-14.9	-	1-2.9	-	< 1
Serum bicarbonate	> 52	41-51.9	-	32-40.9	22-31.9	-	18-21.9	15-17.9	< 15

ted to the ICU. Colostomy was reserved for patients with poor wound healing, patients with poor self-care habits, and patients with evidence of incontinence. Empiric antibiotics were given to all patients and were modified as needed based on results of microbiological examinations. Delayed wound closure or local flap was arranged if needed.

Statistical analysis

Data were recorded on a computer database. Possible predictors of postoperative mortality included medical history (diabetes mellitus, DM; hypertension, renal failure, and liver cirrhosis), origin of infection, history of malignancy, the presence of stoma, the number of operations, vital signs, the level of electrolytes, hematocrit, and Fournier's gangrene severity index. We used the chi-square test or Fisher's exact test for categorical comparisons of data and the Mann-Whitney U-test to determine differences in the means of continuous variables. Significant predictors in the univariate analyses were included in a stepwise multivariate logistic regression model to identify the most important risk factors for postoperative mortality. A *p*-value less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed with the statistical package SPSS for Windows (Version 16.0, SPSS Inc; Chicago, IL, USA).

Results

A total of 36 patients were enrolled in this study. Demographic and clinical features of the patients are presented in Table 2. Mean age was 59.97 ± 15.3 years (range, 24-91 years) and most of the patients were men (32 of 36, 89%). The overall mortality rate was 30.5% (11 of 32). The mean age of patients who survived was 56.24 ± 14.67 years (range, 24-79) and that of patients who died was 68.45 ± 13.74 years (range, 48-91). The difference in age between survivors and non-survivors was statistically significant ($p = 0.020$). The majority (28 of 36, 78%) of patients had a history of DM, hypertension, renal failure, and/or liver cirrhosis. One patient had four co-existing disorders (3%), six patients had three co-existing disorders (18%), 10 patients had two co-existing disorders (29%), and 11 patients had one disorder (32%). DM (52.8%) and hypertension (50%) were the most common underlying medical conditions; however, there was no significant difference in those conditions between survivors and non-survivors. The only predisposing illness that had an adverse effect on mortality was renal dysfunction. The most common infection source was the urogenital area (n = 19, 52.8%). All patients required radical surgical debridement and the majority (n = 25, 69%) required more than one session (mean, 2.8; range 2-4). Diverting colostomy was performed in 11 patients (45%) in the survival group and in five patients (45.5%) in the non-survival group. The number of surgical debridement procedures and the need for diverting colostomy did not have an effect on postoperative mortality. There was no significant difference in mean hospital stay between survivors (mean, 25.88 ± 12.60 days; range, 8-55 days) and non-survivors (mean, 24.36 ± 26.02 days; range, 2-74 days) ($p = 0.154$). However, the length of ICU stay was significantly longer for non-survivors (mean, 21.91 ± 23.28 days; range, 2-66 days) than for survivors (mean, 3.48 ± 5.45 days; range, 0-17 days) ($p < 0.001$). Of the FGSI parameters, faster respiratory rates, higher potassium levels, higher creatinine levels, and lower hematocrit levels were significant predictors of postoperative mortality. The mean FGSI score in the non-survival group (9.73 ± 3.9) was significantly higher than that in the survival group (5.12 ± 3.24) ($p = 0.003$). In the non-survival group, six patients (54.5%) had a FGSI score > 9. Only one patient (4.0%) in the survival group had a FGSI score > 9. Univariate analyses revealed that renal failure (odds ratio 20.00, 95% confidence interval 1.954-204.728, $p = 0.012$), ICU stay (odds ratio 1.194, 95% confidence interval 1.037-1.375, $p = 0.014$), age (odds ratio 1.063, 95% confidence interval 1.005-1.125, $p = 0.034$) and FGSI score (odds ratio 28.800, 95% confidence interval 2.813-294.809, $p = 0.005$) were independent predictors of postoperative survival (Table 3). However, the multivariate analysis revealed that FGSI score at admission was the only independent predictor of postoperative mortality.

Table 2. Demographics and clinical data of patients with Fournier's gangrene

	Survivors	Non survivors		Total
	n = 25	*n* = 11	*p*	*N* = 36
Age (y)	56.24 ± 14.67	68.45 ± 13.74	0.020	59.97 ± 15.30
Gender (Male/Female)	21/4	11/0	0.290	32/4
Medical history, n (%)				
Diabetes mellitus	12 (48.0)	7 (63.6)	0.481	19 (52.8)
Hypertension	12 (48.0)	6 (54.5)	1	18 (50.0)
Renal failure	1 (4.0)	5 (45.5)	0.006	6 (16.7)
Cirrhosis	5 (20.0)	3 (27.3)	0.678	8 (22.2)
History of malignancy, n (%)	2 (8.0)	2 (18.2)	0.570	4 (11.1)
Total stoma; n (%)	11 (44.0)	5 (45.5)	1	16 (44.4)
Stoma	6/19	3/8	1	9/27
Delayed stoma formation (Yes/No)	5/20	2/9	1	7/29
Debridement (sessions)			0.109	
1	5 (20.0)	6 (54.5)		11 (30.6)
2	9 (36.0)	4 (36.4)		13 (36.1)
3	6 (24.0)	1 (9.1)		7 (19.4)
4	5 (20.0)	0 (0)		5 (13.9)
Original site			0.481	
Urogenital	12 (48.0)	7 (63.6)		19 (52.8)
Anorectal	13 (52.0)	4 (36.4)		17 (47.2)
Hospital stay (days)	25.88 ± 12.60	24.36 ± 26.02	0.154	25.42 ± 17.40
ICU stay (days)	3.48 ± 5.45	21.91 ± 23.28	< 0.001	9.11 ± 15.79
SBP	122.73 ± 17.23	108 ± 21.39	0.172	114 ± 19.68
DBP	74.56 ± 15.00	63.91 ± 24.56	0.210	71.31 ± 18.75
Body temperature (C)	37.57 ± .99	37.08 ± 1.25	0.197	37.42 ± 1.08
Heart rate	111.64 ± 24.13	107.64 ± 15.62	0.757	110.42 ± 21.74
Respiratory rate	20.52 ± 1.50	22.91 ± 3.42	0.022	21.25 ± 2.48
Sodium (mEq/l)	131.28 ± 6.86	131.91 ± 6.96	0.796	131.47 ± 6.80
K	3.68 ± .62	4.22 ± .61	0.024	3.85 ± .66
Cr	1.27 ± .71	4.52 ± 2.83	< 0.001	2.26 ± 2.22
Hct	35.95 ± 6.72	31.60 ± 6.13	0.046	34.62 ± 6.77
WBC	16.50 ± 6.91	16.05 ± 11.71	0.823	16.36 ± 8.48
Fournier's gangrene severity index	5.12 ± 3.24	9.73 ± 3.90	0.003	6.53 ± 4.03
Fournier's gangrene severity index				
≤ 9	24 (96.0)	5 (45.5)	0.001	29 (80.6)
> 9	1 (4.0)	6 (54.5)		7 (19.4)

n/N: number; ICU: intensive care unit; SBP: systolic blood pressure; DBP: diastolic blood pressure; K: potassium; Cr : creatinine; Hct: hematocrit; WBC: white blood cells.

Discussion

Fournier's gangrene is an aggressive, life-threatening, polymicrobial soft tissue infection that specifically affects the genital and perineal regions. The disease is difficult to treat and is associated with a high mortality rate. It is, therefore, essential to identify predictors of mortality in these patients. Although the univariate analysis conducted in this study showed that age, sex, renal dysfunction, length of intensive care unit stay, and most of the individual variables that make up the FGSI score were significant predictors of

Table 3. Univariate analysis of factors associated with mortality among patients with Fournier's gangrene

Parameters	Odds ratio	95% CI	*p*-value
Renal failure	20.00	1.954-204.728	0.012
ICU stay	1.194	1.037-1.375	0.014
Age	1.063	1.005-1.125	0.034
Respiratory rate	1.543	1.061-2.243	0.023
K	4.067	1.124-14.713	0.032
Cr	4.254	1.563-11.579	0.005
Hct	0.901	0.799-1.015	0.086
Fournier's gangrene severity index	1.430	1.109-1.844	0.006
Fournier's gangrene severity index > 9	28.800	2.813-294.809	0.005

ICU: intensive care unit; K: potassium; Cr: creatinine; Hct: hematocrit.

postoperative death, the mulitivariate analysis revealed that only the index score itself was an independent predictor of postoperative mortality.

The initial presentation of Fournier's gangrene starts with a period of genital discomfort and pruritus, followed by erythema, edema, pain, induration and necrosis, usually combined with fever. In some patients, it is difficult to differentiate Fournier's gangrene from cellulitis in the initial stage of the disease, leading to a delay in treatment.[8,9] Radiological examinations may help to identify the extent of air and necrotic tissue. However, ultrasonography, computed tomography, and magnetic resonance imaging are more sensitive in detecting deep abscess foci.[13-15]

Most patients with Fournier's gangrene have predisposing medical illnesses.[7] Approximately 50% of the patients in our study had more than one underlying illness, with DM (52.8%) and hypertension (50%) being the most common. The incidence of DM in patients with Fournier's gangrene ranges from 39% to 64%;[16-19] however, the relationship between the two diseases has not been established. In our study, neither DM nor hypertension was associated with adverse outcome. The only predisposing factor was renal dysfunction.

The mainstay of treatment is radical debridement, broad-spectrum antibiotics and adequate supportive care. Early and radical debridement is the most important step in treatment of Fournier's gangrene.[15] In our study, 70% of patients required multiple surgical debridement sessions. However, the number of debridement surgeries did not differ significantly between survivors and non-survivors. Ulug et al. reported a similar finding.[8]

Diverting colostomy is suggested for patients at high risk of fecal contamination; however, there is no consensus as to when a colostomy should be performed. In our study, colostomy was performed in 44% of our patients. Of them, 25% received colostomy during the first debridement and 19% received colostomy 1 to 9 days after the debridement procedure. There was no difference in survival between patients who received colostomy during the first debridement and those who received the procedure 1 to 9 days after debridement. To date, there is no consensus on the reliability of FGSI score as a predictor of outcome in patients with Fournier's gangrene. For example, Yeniyol et al. and Ulug et al. found that an FGSI score of 9 was a strong predictor of mortality,[8,11] and Laor et al. reported that patients with an FGSI score > 9 had a 75% probability of death and that those with an FGSI score ≤ 9 had a 78% probability of survival.[5] Janane et al. and Tuncel et al., however, reported no significant difference in FGSI score between survivors and non-survivors.[10,20] We found that patients with an FGSI score > 9 had an 86% probability of death and that those with an FGSI score ≤ 9 had an 83% probability of survival. Multivariate analysis revealed that FGSI score was the only independent predictor of mortality.

Conclusion

FGSI score at admission is an independent predictor of postoperative mortality among patients with Fournier's gangrene.

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原　著

弗尼爾氏壞疽患者術後死亡率的預後因子

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目的　確認弗尼爾氏壞疽患者術後死亡率的危險因子。

方法　這是一篇回溯性的統計研究，自 2006 年 1 月到 2012 年 12 月期間，共 36 位診斷為弗尼爾氏壞疽的患者。我們使用單變數與多變數邏輯迴歸分析計算出勝算比。

結果　36 位弗尼爾氏壞疽患者中，有 32 位男性 (89%) 及 4 位女性 (11%)。平均年齡為 59.97 ± 15.3 歲 (範圍：24-91 歲)。整體死亡率為 30.5%。最常見的病史為糖尿病 (52.8%) 與高血壓 (50%)。弗尼爾氏壞疽嚴重指數平均落在 6.5 分。所有患者平均清創 2.17 次。44.4% 患者接收分流性大腸造口。根據單變數分析，與術後死亡率有關的預後因子為年齡、腎功能、加護病房住院天數、呼吸速率、血鉀、血清肌酸酐、血容比與弗尼爾氏壞疽嚴重指數。再進一步作多變數分析，弗尼爾氏壞疽嚴重指數是其中唯一獨立的預後因子。

結論　入院時的弗尼爾氏壞疽嚴重指數是唯一獨立的預後因子，可以量化弗尼爾氏壞疽的嚴重度與預後，藉此早期辨識高危險患者並積極治療，以達到降低死亡率的目標。

關鍵詞　弗尼爾氏壞疽、弗尼爾氏壞疽嚴重指數。