TURKISH JOURNAL OF UROLOGY Turk J Urol 2016; 42(3): 190-6 • DOI: 10.5152/tud.2016.14194

GENERAL UROLOGY

Original Article

Overview of different scoring systems in Fournier's Gangrene and assessment of prognostic factors

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ABSTRACT

Objective: In this study we aimed to evaluate prognostic factors for the survival of patients with Fournier's gangrene (FG), and overview different validated scoring systems for outcome prediction.

Material and methods: We retrospectively analyzed the data of 39 patients treated for FG in our clinic. Data were collected on medical history, symptoms, physical examination findings, vital signs, laboratory parameters at admission and at the end of treatment, timing and extent of surgical debridement, and the antibiotic treatment used. The Fournier's Gangrene Severity Index (FGSI) and Charlson Comorbidity Index (CCI) were used to predict outcome. The data were analyzed in relation with the survival of the patients. Mann-Whitney U test, *chi* -square test, Wilcoxon signed rank test, and Cox regression analysis were used for the statistical analysis.

Results: Of 39 patients analyzed, 8 (20.5%) died and 31 (79.5%) survived. The median FGSI score on admission was 2 (0-9) for the survivors and 6 (2-14) for the non-survivors (p=0.004). The median CCI scores of the survivors and non-survivors were 2 (0-10) and 6.5 (5-11), respectively (p=0.001). Except for urea, albumin and hematocrit levels, no significant differences were found between survivors and non-survivors for other laboratory parameters on admission. Lower albumin levels and advanced age were found to be associated with mortality.

Conclusion: High blood urea, low albumin, and low hematocrit levels were associated with poor prognosis. High CCI and FGSI scores could be associated with a poor prognosis in patients with FG.

Keywords: Fournier's gangrene; genitalia; mortality; prognosis; risk factors.

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Submitted: 23.12.2015

Accepted: 29.02.2016

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Available online at www.turkishjournalofurology.com

Introduction

Fournier's gangrene (FG) is a fulminant and life-threatening condition characterized by necrotizing fasciitis of perianal and genitourinary regions. It was first described by Jean Alfred Fournier in 1883.[1] A number of factors including perianal diseases, urethral strictures, local trauma, diabetes mellitus (DM) and malignancies have been accused for the development of the disease. Despite modern intensive care unit facilities and advances in medical therapy, current mortality of FG has been reported as 30-50%.[2-6] In 1995, Laor et al.[2] developed Fournier's Gangrene Severity Index (FGSI) to predict the prognosis of the patients. The authors stated that, when 9 points was taken as the cut-off score, patients with a FGSI score >9 died with a likelihood of 75%, and they survived with a likelihood of 78% when the score was ≤9.[2] Although some studies in the literature supported these findings, some others claimed that FGSI scores were not different between survivors and non-survivors.[7-11]

Charlson Comorbidity Index (CCI) has been also used in addition to FGSI to predict the prognosis in FG.[12] However, their reliabilities are not yet clear.

In this study, we analyzed the prognostic factors and different prognostic scoring systems in our series of 39 FG patients, and discussed our results in the light of the current literature.

Material and methods

After obtaining the approval of local ethics committee of Ankara Training and Research Hospital and written informed consent of all patients, we retrospectively analysed the data of 39 patients treated in our clinic with the diagnosis of FG between April 2005 and May 2014. The age and gender of the patients, symptoms on admission, time to admission (the duration between the onset of the symptoms and admission to the hospital), physical examination findings, the site of the disease onset, the extent of the disease, presence of comorbid diseases, fever, respiratory rate, operative time, and mortality rate were recorded from the patients' files. The diagnosis of FG was based on presence of fever of >38^{0}C, scrotal or perianal erythema and swelling, purulent - malodorous discharge, and fluctuation or crepitation at the wound. Limited scrotal, periurethral and perianal abscesses without any extension to fascia or soft tissues were not considered as FG. In addition, serum urea, creatinine, sodium, potassium, calcium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, albumin, alkaline phosphatase (ALP) and bicarbonate levels, and hematocrit and white blood cell (WBC) counts were obtained immediately before surgery. The final biochemical parameters were obtained one week after the surgery. The patients were divided into two groups, as survivors and non-survivors. Mortality was defined as all-cause mortality, and FG-related death during initial hospitalization. The extension of FG was determined using modified body surface area nomogram developed for determining the extension of burn injuries. Penile, scrotal and perineal involvements were calculated as 1% for each, and involvement of ischiorectal fossa was calculated as 2.5%.[2]

An emergent aggressive debridement was performed in all patients. All necrotic tissues were removed until healthy, bleeding tissues were seen. Cystostomy catheters were used in all patients to prevent contact of the urethra with urine. All patients had dual antibiotic treatment (1 g ceftriaxone 3 x 1 IV, and 0.5% 100 mL metranidazole 2 x 1 IV) until the culture results were obtained. When needed, the patients were returned into the operating room at 24 to 48 hours for repeat wound exploration and debridement under epidural anesthesia. Epidural anesthesia was given through the epidural catheter inserted before. At follow up, postoperative dressings were changed three times a day, using sterile gauzes soaked in a mixture of povidone iodine, 0.2% nitrofurazone ointment, and rifampicine 250 mg ampoule. Colostomy was performed in case of perirectal and anal region involvement. The patient was transferred to Plastic and Reconstructive Surgery Clinic when his/her general condition improved and his/her wound was clean.

In our study we used FGSI, developed by Laor et al.[2] in 1995, to predict the severity of the disease, as well as another comorbidity index, CCI.[12] In FGSI, 9 parameters are measured. They are fever, heart rate, serum sodium, potassium, creatinine, bicarbonate levels, hematocrit and leucocyte counts. The degree of deviation from normal is graded between 0 and 4, as described by Laor et al.[2] (Table 1).

Statistical analysis

Data analysis was performed with Statistical Package for the Social Sciences for Windows, version 20 (IBM SPSS Statistics; New York, USA). Mann-Whitney U test was used for intergroup comparisons. Chi-square test was used for comparison of categorical variables. The admission and final parameters in each group were compared with Wilcoxon signed rank test. The significant variables from univariate analysis were then assessed by stepwise methods in Cox regression analysis which isolated the effects of other variables to determine the independent prognostic factors. $P<0.05$ was regarded as statistically significant.

Results

Of 39 patients analyzed, 8 (20.5%) died, and 31 (79.5%) survived. Age of the non-survivors differed significantly from that of the survivors (65 (43-83) vs. 52 (30-90) years, respectively) (p=0.047). There were 29 (93.5%) males among the survivors, and 7 (87.5%) males among the non-survivors (p=0.56). Median admission times of the survived and non-survived patients were 4 (1-30) and 3 (1-6) days, respectively (p=0.037). The median surface area involved was 2.5% (1-7) in survivors and 2.5% (2-8) in non-survivors (p=0.435). The difference between survivors and non-survivors was not significant in terms of the surface area involved.

The area in which the symptoms first began was scrotum in 6 (75%) patients, and perineum in 2 (25%) patients in the non-survived group. In the survived group, the symptoms first started in scrotum (n=18; 58.1%), perineum (n=11; 35.5%), and in both scrotum and perineum (n=2; 6.5%).

All patients underwent radical debridement within 24 hours of hospital admission. Necrotizing tissues were completely removed until viable tissues were identified. Two of the survived and one of the non-survived patients underwent a diverting colostomy.

Predisposing factors were evaluated in this cohort. DM was found in 24 patients (61.5%) (19 survivors, and 5 non-survivors, p=0.95). Moreover, chronic renal failure was present in 4 (12.9%)

Turk J Urol 2016; 42(3): 190-6
DOI:10.5152/tud.2016.14194

Table 1. The Fournier's Gangrene Severity Index

	High abnormal values				Normal	Low abnormal values			
Variable	**+4**	**+3**	**+2**	**+1**	**0**	**+1**	**+2**	**+3**	**+4**
Temperature (°C)	>41	39-40.9	-	38.5-35.9	36-38.4	34-35.9	32-33.9	30-31.9	<29.9
Heart rate (beats/minute)	>180	140-179	110-139	-	70-109	-	55-69	40-54	<39
Respiration rate (breaths/minute)	>50	35-49	-	25-34	12-24	10-11	6-9	-	<5
Serum Na (mmol/L)	>180	160-179	155-159	150-154	130-149	-	120-129	111-119	<110
Serum K^{++} (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, x2 for acute renal failure)	>3.5	2-3.4	1.5-1.9	-	0.6-1.4	-	<0.6	-	-
Hematocrit (%)	>60	-	50-59.9	46-49.4	30-45.9	-	20-29.9	-	<20
White blood cell count (total/ mm^3 x1000)	>40	-	20-39.9	15-19.9	3-14.9	-	1-2.9	-	<1
Serum bicarbonate (venous, mmol/L)	>52	41-51.9	-	32-40.9	22-31.9	-	18-21.9	15-17.9	<15

patients (1 patient in survivors, and 3 patients in non-survivors). In the survived group, the patients had previously undergone surgeries for lung cancer (n=1), colon cancer (n=1), and bilateral orchiectomy for prostate cancer (n=1), and radical cystectomy (n=1). In the non-survivor group, patients had history of surgery due to colon cancer (n=1), and transurethral resection for the bladder tumor (n=1). Two patients in the survivor and two patients in non-survivor groups had both hypertension (HT) and coronary artery disease (CAH). One of the survivors had had surgery for pilonidal sinus, and another one had had hemorrhoidectomy.

The most frequent bacterial organisms cultured from wounds were *Escherichia coli* (53.8%, 21 of 39), *Staphylococcus* spp. (20.5%, 8 of 39), *Enterococcus feacalis* (7.6%, 3 of 39), *Pseudomonas aeruginosa* (7.6%, 3 of 39), *Klebsiella pneumoniae* (5.1%, 2 of 39), *Klebsiella ozaenae* (2.5%, 1 of 39), and *Prevotella bivia* (2.5%, 1 of 39). The wound cultures were negative in 8 patients (20.5%).

Etiologic factors for mortality in the non-survivors were sepsis and septic shock (n=4), chronic renal failure (n=1), congestive heart failure (n=2) and pulmonary embolism (n=1).

The median FGSI scores on admission for survivors and non-survivors were 2 (0-9) and 6 (2-14), respectively (p=0.004). All survived patients had a FGSI score <9. Among non-survivors, FGSI was <9 in 6 (75%), and >9 in 2 (25%) patients. The median CCI scores of the survivors and non-survivors were 2 (0-10) and 6.5 (5-11), respectively (p=0.001).

The comparisons of the laboratory parameters on admission and at the end of treatment in the survivors and the non-survivors are shown in Table 2. The parameters included urea, creatinine, sodium, potassium, calcium, AST, ALT, ALP, total protein, albumin levels, WBC count, and hematocrit levels. Except for urea, albumin and hematocrit levels, no significant differences were found between survivors and non-survivors as for other laboratory variables on admission. At the end of the treatment, serum urea, creatinine, AST, ALT, and WBC levels decreased significantly (p=0.003, p=0.006, p=0.044, p=0.007, and p=0.0001, respectively), while sodium levels increased significantly (p=0.022). However, only ALT levels decreased in the non-survivor group (p=0.018).

When Cox regression analysis was performed in order to find the independent factors affecting mortality among the ones which were found significant in univariate analysis between survivor and non-survivor groups, the advanced age and final low albumin level were determined as independent prognostic factors affecting mortality (Table 3, p=0.016 and p=0.004, respectively).

Discussion

Fournier's Gangrene is a fulminant and life-threatening disorder characterized by necrotizing fasciitis of the perineal and genitourinary area resulting from a polymicrobial infection. This rapidly progressive disorder is the result of impaired host resistance due to reduced cellular immunity which leads to a suppurative bacterial infection. Thrombosis occurs in small subcutaneous vessels, and the combination of these two disease processes causes gangrene of the overlying skin.

Table 2. Serum admission and final parameters in survivors and non-survivors

Variable	Survivors median (Min-Max)	Non-survivors median (Min-Max)	p
Age (year)	52 (30-90)	65 (43-83)	0.047
Admission time (day)	4 (1-30)	3 (1-6)	0.037
Affected area (%)	2.5 (1-7)	2.5 (2-8)	0.435
Urea (mg/dL)			
Admission	41 (19-185)	141 (32-211)	0.011
Final	33 (11-79)	80 (23-180)	0.005
Creatinine (mg/dL)			
Admission	1.2 (0.7-11.5)	1.8 (0.6-9.7)	0.105
Final	0.9 (0.6-9.2)	1.6 (0.6-8.5)	0.076
Sodium (mmol/L)			
Admission	134.5±5.5	136.8±7.66	0.441
Final	137±4.0	135.2±6.3	0.585
Potassium (mmol/L)			
Admission	4.2±0.59	4.2±1.30	0.807
Final	4.2±0.47	3.9±0.47	0.176
Calcium (mg/dL)			
Admission	8.4±1.0	7.8±0.85	0.091
Final	8.7±0.67	8.0±0.88	0.090
AST (Units/Litre)			
Admission	23.5 (11-102)	31.5 (18-83)	0.282
Final	20.5 (9-99)	21 (9-68)	0.721
ALT (Units/Litre)			
Admission	21 (9-145)	29 (1-975)	0.390
Final	14 (4-106)	11 (2-162)	0.376
ALP (Units/Litre)			
Admission	96.5 (59-738)	108 (76-314)	0.298
Final	79 (55-328)	120 (50-258)	0.148
Total protein (gram/dL)			
Admission	5.8 (3.1-7.9)	4.6 (4.2-6.5)	0.192
Final	6.5 (4.0-7.7)	4.8 (4.6-5.3)	0.052
Albumin (gram/dL)			
Admission	2.9±0.72	2.12±0.37	0.004
Final	3.0±0.40	2.23±0.47	0.0001
WBC (gram/dL)			
Admission	13.2 (7-34.4)	18.2 (8.2-21.5)	0.410
Final	9.1 (5.4-15.7)	10.6 (5.2-48.6)	0.632
Hematocrit (gram/dL)			
Admission	39.7 (23-45)	31.7 (24-43)	0.041
Final	35.8 (28-51)	26 (23-38)	0.010
Operative time (min)	75 (45-180)	85 (60-120)	0.238
FGSI Score	2 (0-9)	6 (2-14)	0.004
CCI Score	2 (0-10)	6.5 (5-11)	0.001

AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; WBC: white blood cell; FGSI: Fournier's Gangrene Severity Index; CCI: Charlson Comorbidity Index

Table 3. Cox regression analysis for age and final albumin values

Variables in the equation

	B	SE	Wald	df	p	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Age	0.089	0.037	5.801	1	0.016	1.093	1.017	1.176
final albumin	-5.826	2.041	8.149	1	0.004	0.003	0.000	0.161

SE: standard error; df: difference; CI: confidence interval; exp: exponent

Male-to-female ratio is approximately 10:1 in large series. The reason for low prevalence of FG in females may be better drainage of the perineal region by vaginal secretions in women. Currently, FG is seen at an advanced age. It is most frequently seen between the ages of 40-60 years.[2,3,10,13] Some previous studies showed a younger age in survivors, although some others did not find any difference at the age of disease onset between survivors and non-survivors.[2,4,10,11,14] In our study group, there were 36 (92.3%) males, and the survivor group consisted of significantly younger patients (p=0.047). Cox regression analysis found advanced age as an independent prognostic risk factor in our study (p=0.016, 95% CI 1.017-1.176).

The mortality rate of FG ranges between 7 and 53%, and this variable outcome of the disease indicates that it is multifactorial.[2,3,10,15,16] In general, factors related to disease and host are important prognostic factors. These factors include an anorectal source, advanced age, extensive disease (involving abdominal wall or thighs), shock or sepsis, renal failure, and hepatic dysfunction. Death generally results from the systemic illness such as sepsis, coagulopathy, acute renal failure, diabetic ketoacidosis or multiple organ failure. In the present study, in spite of the developments in treatment options and antibiotic therapy, the mortality rate was 20.5 percent. In our study, severe sepsis and multiple organ failure, chronic renal failure, and pulmonary embolism were major factors for mortality.

Fournier's Gangrene rapidly progresses causing thrombosis and irreversible necrosis. Previous studies showed that delay in the first debridement of the necrotizing tissue worsened outcome.[17,18] Early admission, rapid diagnosis, and effective treatment are essential components for reaching a successful outcome. Yeniyol et al.[10] found significantly shorter times to consult in survivors when compared with non-survivors (1.9±0.7 vs. 4.1±1.4 days respectively, p=0.002). On the contrary, some other studies have not shown any difference between survivors and non-survivors as for the time to admission.[7,11] Furthermore, in their studies McCormack et al.[19] determined that the time be-

Turk J Urol 2016; 42(3): 190–6
DOI:10.5152/tud.2016.14194

tween admission and the surgery was not statistically significant between survivors and non-survivors. Interestingly, we found a higher median time to admission in survivors (p=0.037). Although we cannot explain this finding, we suppose that some extreme values in this group (eg. 30 days) caused it.

Logically, an increased body percent involved would cause sepsis and result in an increased risk for mortality, however two studies proposed that the extent of the disease was not predictive of outcome.[2,4] Three separate studies found significantly higher incidence of the disease in body in the non-survivors.[8,10,11,14] Corcoran et al.[7] found that although total body surface area (TBSA) involved was suggestive of a poor prognosis among all operative characteristics investigated, only lower extremity or abdominal wall involvement was associated with inpatient mortality. In our study, the involved surface area was similar in survivor and non-survivor groups.

A number of predisposing factors have been reported for FG, including DM, chronic renal failure, malignancy, perianal disease, urethral stricture, hemorrhoids, urinary tract infections, testicular and epididymal diseases.[4,15,17] DM was the most common comorbidity associated with FG, and it was present in 50% (24-72%) of the patients at the time of admission.[2,7,8,10,19-22] Tissue ischemia resulting from the involvement of small vessels has been accounted for increased tendency of diabetics to FG. On the other hand, multifactorial immunologic system dysfunction in diabetics might have caused increased mortality. In our study, the major predisposing factor was DM (61.5%, 19 survivors and 5 non-survivors) followed by chronic renal failure, operation history for pilonidal sinus or hemorrhoids, and malignities such as colon cancer. Our results demonstrated that the patients with DM are more susceptible to FG.

Both anaerobic and aerobic organisms isolated from wound cultures have been reported as causative bacteriologic agents.[6,23] Paty and Smith found that *E. coli*, *Bacteroides*, and *Streptococci* were the most commonly isolated organisms.[17] Laor et al.[2] reported *E. coli* and *Streptococcus* species as the most commonly isolated organisms, and stated that *Staphylococcus* and *Enterococcus* were more frequently isolated compared with *Bacteroides*. In the present study, similar bacteriologic agents, namely *E. coli*, *Staphylococcus* and *Enterococcus*, were the most frequently isolated microorganisms from the cultures of our patients.

Laboratory parameters have been reported as prognostic indicators in the previous studies. These include low hematocrit, and serum albumin levels, high blood urea nitrogen, creatinine and high alkaline phosphatase levels.[2,10,11,14,24] In addition, Corcoran et al.[7] found that specific metabolic parameters such as serum creatinine, bicarbonate, lactate, and calcium were important prognostic factors. Similarly, high blood urea nitrogen, low serum albumin, and hematocrit levels were associated with inpatient mortality in our series. Except for these parameters, no significant differences were observed between survivors and non-survivors in our series. Final low albumin was found as an independent prognostic factor in Cox regression analysis (p=0.004, 95% CI 0.000-0.161). Laor et al.[2] found that WBC count, and blood urea nitrogen level dropped significantly one week after surgery in survivors, however serum potassium, bicarbonate, total protein and albumin levels increased. In our study, we similarly found that serum urea, creatinine, AST, ALT levels, and WBC counts significantly decreased, and sodium levels significantly increased at the end of the treatment. However, only ALT levels decreased in the non-survivors. Increased levels of those parameters indicate that homeostasis of the patients was impaired due to disseminated infection. Decreased levels of these parametres after control of the infection supported this hypothesis. On the other hand, controversies in the literature regarding prognostic significance of biochemical and hematologic parameters in survivors and non-survivors make us think that a single factor cannot be accused for the progression of the disease.

Fournier Gangrene Severity Index was described by Laor et al.[2] to help clinicians for predicting the prognosis of FG patients. This index includes nine metabolic and physiologic parameters. Laor et al.[2] found that a FGSI score greater than 9 indicated a 75% likelihood of mortality while a score of 9 or less was associated with a 78% likelihood of survival. This result was also confirmed by other recent studies.[7,10,25] Corcoran et al.[7] found an inpatient mortality rate of 10%, with a significant difference in FGSI scores between survivors and non-survivors (5.3 in survivors vs. 10.9 in non-survivors, p=0.002). In a recent study, Tarchouli et al,[25] reported that this index was a simple, reliable and valuable method for predicting disease severity and patient survival. However, the study by Tuncel et al.[11] on 20 men with FG found no association between FGSI scores and mortality. This result was also confirmed by the same author's recent study.[14] In the present study, the median FGSI score was 2 (0-9) for survivors and 6 (2-14) for those who died with a significant difference between groups.

In a recent study, Erol et al.[8] found that CCI score was higher, and the life expectancy was 10 years shorter in non-survivors when compared with survivors. Similarly in the present study we have found that the median CCI score was greater in the non-survivors compared with survivors [6.5 (5-11) vs. 2 (0-10) respectively]. A high CCI score could be associated with a poor

outcome, and was probably responsible for mortality. CCI could be useful to evaluate the outcome of patients with FG.

In conclusion, Fournier's gangrene is a fulminant and life-threatening disease characterized by necrotizing fasciitis of the genitalia and perineum, and has high mortality and morbidity rates. High blood urea nitrogen, low serum albumin, and low hematocrit levels were associated with a poor prognosis in our series. While there is no current compromise regarding the use of individual patient admission characteristics or laboratory parameters as prognostic indicators, final low albumin and advanced age were associated with mortality in our series. High CCI and FGSI scores could well be associated with a poor prognosis in patient with FG. Metabolic parameters and predisposing factors should be evaluated together for predicting prognosis.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ankara Training and Research Hospital.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Ö.G.D., C.N.Y.; Design – M.A.K.; Supervision - T.K., C.B.Ö.; Resources – H.S.; Data Collection and/or Processing – M.A.K., H.S.; Analysis and/or Interpretation - M.E., M.F.K.; Literature Search - T.K.; Writing Manuscript – Ö.G.D.; Critical Review – M.E., M.F.K., C.N.Y.; Other – C.B.Ö.

Acknowledgements: We appreciate to Selen Bozkurt because of her helps in our statistical evaluations.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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