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The Effect of Albumin Level and Neutrophil Lymphocyte Ratio on Mortality and Recovery in Fournier's Gangrene

Fournier Gangreninde Albumin Düzeyi ve Nötrofil Lenfosit Oranının Mortalite ve İyileşme Üzerine Etkisi

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Abstract

Background: Fournier's gangrene (FG) is a polymicrobial bacterial infection with a high mortality and morbidity rate, and early diagnosis and treatment in FG is crucial. The mainstay of treatment for FG comprises antibiotics and surgical debridement. Our study aimed to predict mortality more accurately in patients with Fournier's gangrene.

Materials and Methods: The medical records of 60 patients who underwent surgical intervention for FG at our clinic between 2016 and 2021 were retrospectively reviewed.

Results: Of the patients, 15% were urogenital, 61.7% colorectal and 23.3% idiopathic origins. Albumin level was lower for people who died (27.35±4.66) compared to those who recovered (34.53±7.75) (p=0.001). Both the number of surgical debridement and duration of hospitalization were observed to be lower in patients who survived (p<0.05). Being above the age of 59.50 and albumin levels below 31.25 were found to be risk factors for FG mortality. Neutrophil- lymphocyte ratio had no significant effect on mortality (p=0.733 **Conclusion:** Serum albumin level was found to be a predictive value for mortality and recovery in patients with Fournier's gangrene. No significant effect of neutrophil-lymphocyte ratio on mortality and recovery in patient with Fournier's gangrene was found.

Keywords: Fournier's gangrene, albumin level, neutrophil-lymphocyte ratio.

ÖZ

Amaç: Fournier gangreni, mortalite ve morbidite oranı yüksek olan polimikrobiyal bakteriyel enfeksiyondur ve erken tanı ve tedavi önemlidir. Tedavisinin temeli antibiyotikler ve cerrahi debridmandır. Çalışmamızda Fournier gangreninde mortaliteyi daha doğru tahmin etmeyi amaçladık..

Gereç ve Yöntem: 2016 ile 2021 arasında kliniğimizde Fournier gangreni nedeniyle opere edilen 60 hastanın tıbbi kayıtları geriye dönük olarak incelendi.

Bulgular: Hastaların %15'i ürogenital, % 61.7'si kolorektal ve %23.3'ü idiopatik kaynaklıydı. Albümin değeri excitus bireylerde (27.35±4.66), iyileşenlerdeki albümin değerine kıyasla (34.53±7.75) daha düşüktü (p=0,001). Debridman sayısı ve hastanede yatış süresi yaşayan hastalarda düşük gözlendi (p<0,05). Yaşın 59,50 düzeyinin üzerinde olması mortalite de risk teşkil ettiği görüldü. Albumin değerinin 31,25 değerinin altında olmasının mortaliteye risk teşkil ettiği tespit edildi. Nötrofil lenfosit oranının mortalite üzerinde anlamlı etkisinin olmadığı görüldü (p=0.733).

Sonuç: Serum albumin düzeyinin Fournier gangreni hastalarında mortalite ve iyileşme üzerinde prediktif bir değer olduğu tespit edildi. Nötrofil lenfosit oranının Fournier gangreninde mortalite ve iyileşme üzerinde anlamlı etkisi tespit edilmemiştir.

Anahtar Kelimeler: fournier gangreni, albümin düzeyi, nötrofil lenfosit oranı

Highlights

- Fournier's gangrene (FG) is a polymicrobial bacterial infection with a high mortality and morbidity rate.
- Albumin is an important factor both in recovery and wound healing in patients who underwent surgery.
- NLR (neutrophil-lymphocyte ratio) is an indicator of inflammatory processes and immune response.
- Serum albumin level was found to be a predictive value for mortality and recovery in patients with FG.

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Introduction

Fournier's gangrene (FG) is a suppurative polymicrobial bacterial infection with high mortality and morbidity rate. It affects anorectal and perineal regions, as well as the genitourinary tract, and is linked to certain systemic disorders. In other words, FG is acute and potentially fatal infection that causes thrombosis of subcutaneous vessels and progresses with necrotizing fasciitis and gangrene of the skin. The etiologic factors of FG include anorectal infections, abscesses and their surgical interventions, colorectal infections and colorectal surgical interventions, urogenital infections and urogenital surgical interventions, and trauma. The most cases of FG originate in the colorectal region (30-50%), followed by urologic system (20-40%) and skin (20%) (1).

Fournier's gangrene, which first described by Jean Alfred Fournier, a French venerologist-dermatologist, in 1883, is a necrotizing fasciitis involving the scrotum and penis in men and vulva and perineum in women, and may progress to the abdominal wall in advanced stages. It can be fatal if left untreated. FG occurs ten times more frequently among males than females (2,3). Some systemic diseases may be predisposing factors for Fournier's Gangrene by weakening the immune system.

Predisposing factors for this condition include diabetes mellitus, alcoholism, immunosuppression, hepatic and renal failure, obesity, heart failure, hypertension, SLE, leukemia, steroid therapy, local trauma, extravasation of urine into the periurethral area, perirectal or perianal infection, and certain surgical procedures (circumcision, herniorrhaphy, hemorrhoidectomy) (3,4). Today, FG may occur in all age groups but more common among patients older than 50 years (5,6).

Due to the potentially fatal nature of FG, early diagnosis and prompt initiation of treatment are crucial. Consideration should be given to concurrent examination findings in genitourinary tract infections and interventions, perianal infections and interventions, and perineal and scrotal region. Even nonspecific conditions should not be overlooked. Erythema, crepitation and bullae may develop before necrosis, and thus require special medical attention. (3,4,7,8). Treatment should be initiated with emergency surgery. Necrotized and devitalized areas should be extensively and completely debrided until viable tissue is reached. Namely, the mainstay of treatment are broad-spectrum antibiotics and aggressive surgical debridement (4,9). Additionally, intravenous fluid support is required. Routine blood tests are important in follow-up. Concomitant diabetes and renal failure or conditions that may weaken the immune system, if any, should be followed up with the necessary blood tests. There are many factors affecting mortality and morbidity in patients with Fournier gangrene. The common denominator of all comorbid risk factors is impaired immune resistance due to decreased cellular immunity in the organism (2).

In the literature review, Engin et al. investigated the factors affecting mortality in patients with Fournier's gangrene including age, prevalence of infection, presence of comorbidities and duration of intensive care unit (ICU) stay (10). In our study, we aimed to understand the effect of albumin level and neutrophil- lymphocyte ratio on mortality and recovery.

Material and Methods

The medical records of patients who underwent surgical intervention for Fournier's gangrene in our clinic between 2016 and 2021 were retrospectively reviewed. Patients were physically examined at the time of admittance and FG was diagnosed with genital and perineal skin necrosis, cyanosis, gangrene; and subcutaneous crepitation findings. The infected and necrotic tissues were debrided with broad-spectrum antibiotic therapy. The tissues were cleaned with hydrogen peroxide and povidone iodine during and after debridement. In complicated cases with extensive and deep necrosis, VAC was performed with second debridement. In recovered patients, the defect was closed by primary suture or graft. Patients with perianal abscess or simple skin infection without Fournier gangrene were not included in the study.

Statistical Analysis

The fitness of the data to normal distribution was tested using Shapiro Wilk test, Student t test was used to compare the normally distributed characteristics in 2 independent groups, and Mann Whitney u test was used to compare the non-normally distributed characteristics in 2 independent groups. The analysis of the relationship between categorical variables observed in two independent groups was analyzed by Pearson Chi-square test. ROC curve was plotted based on the cutoff values for predicting mortality rate using the variables age, albumin level, the number of debridement and duration of the hospitalization. As descriptive statistics, mean ± standard deviation values were given for numerical variables and number and % values were given for categorical variables. SPSS Windows version 23.0 package program was used for statistical analysis and $P<0.05$ was

considered statistically significant.

Results

Of the 60 patients studied, 16 (24.4%) were female and 44 (75.6%) were male. The mean age of the entire group was 56±14.08 (years). The mean duration of hospitalization was 16.93±19.57 days. The mean number of debridement performed was 2.08±2.19. 15 (25%) patients were over 65 years of age and 35 (58.3%) patients had DM. 10 (16.7%) of our patients died due to FG. The mean time of admission to hospital was 9.23±6.94 days **(Table 1)**. An assessment of underlying etiologic factors in patients revealed that urogenital and colorectal causes were the etiologic factors in 9 (15%) and 37 (61.7%) patients, respectively. The etiologic factor of 14 (23.3%) patients could not be determined **(Figure 1).**

Considering the duration of hospitalization, it was observed that patients with colorectal causes and patients with high albumin values had a shorter hospital stay **(Table 3)**.

Considering the factors affecting mortality, female gender, advanced age and patients with FG due to causes other than colorectal and urogenital causes were found to have a higher mortality rate **(Table 4)**.

Albumin level was statistically significantly lower for the mortality group (27.35±4.66) compared to that of recovered group (34.53±7.75) (p=0.001). According to the ROC curve analysis on age, albumin, number of debridement and duration of hospitalization, which showed statistically significant differences on mortality; it was shown that age over 59.50 was effective in mortality (sensitivity 90%, specificity 72%), similarly, albumin level below 31.25 (sensitivity 66%, specificity 90%) similarly increased mortality.

Table 1. Patient Characteristics

Parameters	N	%	Mean ± SD
Patients (total number)	60		
Female/Male ratio	16/44	26.7/73.3	
Mean age (years)			56.00 ± 14.08
Geriatric patients (over 65 years of age)	15	25	
Patients with a known source	46	76.7	
Patients with a history of diabetes mellitus	35	58.3	
Mean duration of hospitalization (days)			16.93 ± 19.57
Mean number of debridements			2.08 ± 2.19
Mortality rate	10	16.7	
Time for admission to hospital			9.23 ± 6.94

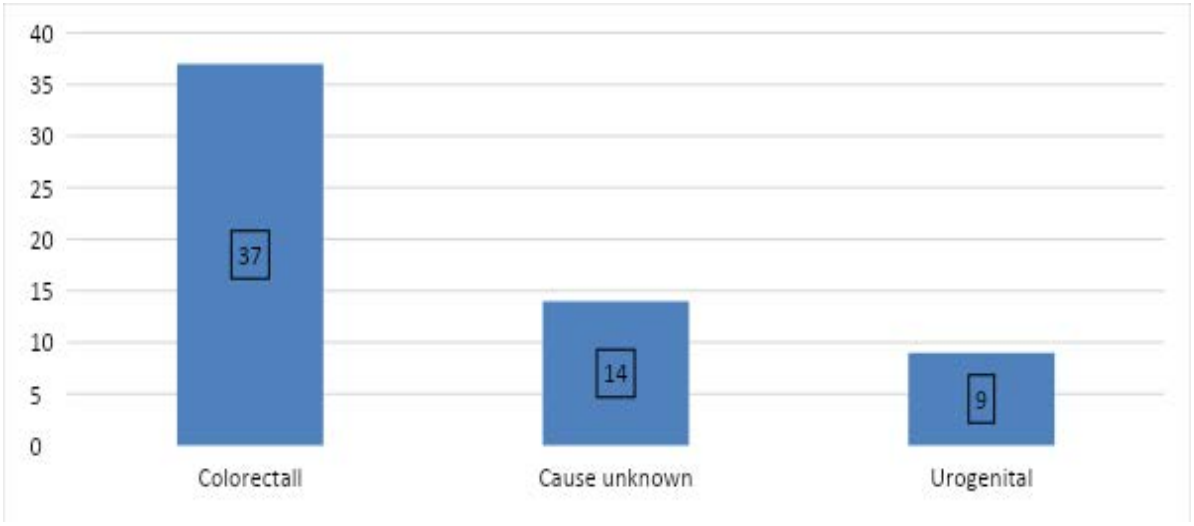

Figure 1. Origin of infection in cases of Fournier's gangrene

Table 3. Factors affecting the duration of hospitalization

Parameters	≤14 day	>14 day	p
Number of patients n (%)	41 (63.8)	19 (31.7)	
Female/male ratio n (%)	10(24.4)/31(75.6)	6(31.6)/13(68.4)	0.558
Age (years) (mean±SD)	53.90 ± 14.75	60.53 ± 11.62	0.090
Urogenital n (%)	4 (9.8)	5 (26.3)	0.095
Cause unknown n (%)	8 (19.5)	6 (31.6)	0.304
Colorectal n (%)	29 (70.7)	8 (42.1)	**0.034**
Patients with a history of diabetes mellitus n (%)	22 (53.7)	13 (68.4)	0.281
Time (days) of admission to hospital (mean±SD)	7.73 ± 5.43	12.47 ± 8.73	0.063
Neutrophil-to-lymphocyte ratio (mean±SD)	11.80 ± 12.65	27.48 ± 75.37	0.733
Platelet-to-lymphocyte ratio (mean±SD)	250.33 ± 325.04	237.28 ± 135.52	0.201
Albumin level (mean±SD)	35.31 ± 7.87	29.08 ± 5.72	**0.004**

Table 4. Factors affecting mortality

Parameters	Death	Recovery	p
Number of patients n(%)	10 (16.7)	50 (83.3)	
Female/male ratio n(%)	6(60)/4(40)	10(20)/40(80)	**0.009**
Age (years) (mean±SD)	69.0 ± 15.10	53.40 ± 12.47	**0.001**
Urogenital n(%)	1 (10.0)	8 (16.0)	0.628
Cause unknown n(%)	5 (50.0)	9 (18.0)	**0.029**
Colorectal n(%)	4 (40.0)	33 (66.0)	0.123
Patients with a history of diabetes mellitus n(%)	8 (80.0)	27 (54.0)	0.128
Time (days) of admission to hospital (mean±SD))	16.90 ± 8.48	7.70 ± 5.51	0.063
Neutrophil-lymphocyte ratio (mean±SD)	21.72 ± 17.71	15.77 ± 47.10	0.733
Platelet-lymphocyte ratio (mean±SD)	456.97 ± 577.14	204.04 ± 144.84	0.201
Albumin level (mean±SD)	27.35 ± 4.66	34.53 ± 7.75	**0.001**
Number of debridement (mean±SD)	2.60 ± 2.37	1.98 ± 2.16	**<0.001**
Duration of Hospitalization (days) (mean±SD)	20.70 ± 18.51	16.18 ± 19.87	**<0.001**

Table 5. Roc analysis for mortality

Parameters	Cut-off	AUC	p	Sensitivity	Specificity
Age	>59,50	0,822	0,001	0,90	0,72
Albumin level (first hospitalization)	<31,25	0,771	0,007	0,66	0,90
Number of debridements under anesthesia	>1,5	0,626	0,211	0,70	0,52
Total duration of hospitalization	>6,5	0,654	0,127	0,99	0,44

Abbreviations: AUC: Area Under Curve

Discussion

FG is a rapidly progressive clinical condition characterized by severe necrosis that may affect the fascia and subcutaneous tissues in the perianal, perineal and genitourinary regions. The disease can affect both sexes at any age but predominantly affects adult males. The disease is a polymicrobial infection, both aerobic and anaerobic. The disease is characterized by polymicrobial and synergistic infection. The pathophysiology is probably triggered by endarteritis obliterans and microthrombosis of the small vessels in subcutaneous tissues (11,12). As is known, its pathophysiology is characterized by the heparinase and collagenase produced by the anaerobes and platelet aggregation and complement fixation induced by the aerobes and lead to microvascular thrombosis and dermal necrosis. Due to its rapid and aggressive progression, it remains a highly lethal in course. Depending on the degree of progression, the skin may appear normal, red or shiny or may show signs of ecchymosis and crepitation (13). An urgent and multidisciplinary approach is required in treatment.

In our study, the mean duration of admission of patients who died was 16.9+-8.48 days and the mean duration of admission of patients who recovered was 7.7+-5.51 days, which was not statistically significant (p=0.063).

A study found that patients who had died were admitted to the hospital at least 5 days after the onset of the symptoms (14). Our study found that the duration of admission was not significant factor for the death of patients, but a study showed that laboratory findings deteriorated rapidly if there was a delay in Necrotizing Fasciitis (14).

FG generally requires surgery and broad-spectrum antibiotic therapy, maintenance fluid therapy and additional surgical treatments such as cystostomy and colostomy if necessary. Testicular involvement is rare in FG because of the separate blood supply to the testes. The testes are usually spared as their blood supply originates intra-abdominally through spermatic cord. The involvement of the testis suggests retroperitoneal origin or spread of infection (7,8). However, orchiectomy and penectomy may occur rarely. In our study, additional surgeries such as cystostomy, colostomy and orchiectomy were not required.

Surgical debridement should be performed carefully until viable tissue is reached. It should be supported with broad-spectrum antibiotics and maintenance fluid therapy. It may be required to perform repeated debridement as necrotic tissues manifest. The number of debridement was significantly lower for patients who survived in our series. This could be due to the fact that the necrosis was not severe, rendering debridement unnecessary.

The mortality rate for FG remains high (43-53%) notwithstanding the progress made in intensive care and medical treatment, owing to its fulminating nature (15,16). Our study observed a significantly lower mortality rate (16.7%) in comparison to the literature.

According to the origin of onset, FG has been classified into four categories in studies: colorectal, genitourinary, dermatologic, and idiopathic (4,6,17). In these series, it was reported that 56% of cases were genitourinary, 22% were colorectal, 17% were dermatologic, and 5% were idiopathic origins. In our series, 15% of cases were urogenital, 61.7% were colorectal, and 23.3% were idiopathic origins.

There are several risk factors for FG. These include poor nutritional status, diabetes mellitus, immunosuppressive therapy, malignancy, alcoholism, and certain systemic diseases that have detrimental effects on blood circulation. Hyperglycemia has been found to affect the adhesion, chemotaxis, and bactericidal activity of phagocytes. It has also been demonstrated to have detrimental effects on cellular immunity (12,18). Hyperglycemia has been shown to be a risk factor for FG and to negatively affect the recovery process. In our series, DM was detected among 58.3% of the patients and was found to be a risk factor. However, no negative effect on hospitalization duration and mortality was observed.

Studies have shown the predictive value of BUN/albumin ratio in sepsis and hospital-acquired pneumonia (19,20). Another research found that BUN/albumin ratio was associated with a severe course in acute pancreatitis (21). The risk of mortality, the need for intensive care unit admission and the duration of hospitalization are expected to increase as BUN/albumin ratio raises. Ferzad Allameh et al. studied the BUN/albumin ratio in terms of FG mortality and prognosis and showed that the BUN/albumin ratio significantly affected mortality (22).

A study made to determine hospital mortality in critically ill intensive care patients found that the BUN level and BUN/albumin ratio of non-survivors were higher, and the albumin level of non-survivors was lower. Albumin <3.2 g/dL, BUN ≥32 mg/dL, and BUN/albumin ratio ≥10 found to be statistically significant on mortality. This study also showed that hypoalbuminemia alone is a more powerful predictor of in-hospital mortality than BUN or BUN/albumin ratio in those patients (23). In another study albumin is also found to be a valuable parameter predicting no-reflow rates in patients with ST elevated myocardial infarction (24)

In our study, the albumin level was significantly lower for patients who died (27.35±4.66) compared to the albumin level observed in recovered patients (34.53±7.75) (p=0.001). The number of debridement and duration of hospitalization were also significantly lower for patients who survived (p<0.05).

Our study also showed that albumin level was effective in prognosis, duration of hospitalization and intensive care unit admission. ROC analysis revealed that age over 59.50 was associated with a higher a risk for mortality (sensitivity 90%, Specificity 72%) and similarly, as did albumin level less than 31.25 (sensitivity 66%, Specificity 90%). Similarly, a study of 34 patients revealed a mean age of 58.4 years (14).

A research discovered that high NLR (neutrophil-lymphocyte ratio) and PLR (platelet-lymphocyte ratio) levels were associated with statistically significant increases in the number of surgical debridement, duration of hospitalization, cost and mortality rate.(25) Although NLR and PLR have been used in the literature to predict the prognosis of patients with different inflammatory and ischemic events, Şahin Kahramanca et al. found strong correlations between these parameters and the prognosis of the disease in their study and high NLR and PLR levels were associated with statistically significant increases in the number of surgical debridement, duration of hospitalization, cost and mortality rate (26,27). However, in our study found that NLR had no significant effect on mortality rate (p=0.733).

To date, the following indices have been used in predicting the prognosis of Fournier's gangrene prognosis: Fournier Gangrene Severity Index (FGSI), Uludag Fournier Gangrene Severity Index (UFGSI), Age-Adjusted Charlson Comorbidity Index (ACCI), Laboratory Risk Indicator for Necrotizing Fasciitis (LINEC) score, Combined Urology and Plastic Index (CUPI), as well as neutrophil-to-lymphocyte ratio (NLR) and surgical APGAR (sAPGAR) parameters were included (22).

Study Limitations

In this study, although the limited number of patients and the retrospective design are limitations, the evaluation of neutrophil and lymphocyte levels along with albumin levels in relation to patient recovery makes our research stand out.

Conclusion

FG is still an illness with a high mortality rate. Early and effective treatment is as critical as early diagnosis. Decreased albumin and increased NLR levels can predict poor prognosis. If albumin is determined to be high and NLR is determined to be low, it may be of particular importance for FG patients to receive more aggressive treatments and close follow-up. More studies with large sample sizes are needed to better determine whether these parameters are effective or not.

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