

# THE PROGNOSTIC ROLE OF NEUTROPHIL-LYMPHOCYTE RATIO IN FOURNIER GANGRENE PATIENTS

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## ABSTRACT

Fournier gangrene is a rare type of necrotizing fasciitis which affects the perineal, genital, or anorectal region. It is considered as a urological emergency as it has a high mortality rate, at 20 to 50% in most reported series. Our aim was to evaluate the role of neutrophil-lymphocyte ratio as a prognostic marker for Fournier gangrene patients. There is an increasing interest in suggesting the correlation between inflammatory status and disease prognosis, one of the most commonly used parameter is the neutrophil-lymphocyte ratio (NLR). This is an analytical study with a retrospective approach evaluating the medical record data of patients diagnosed with Fournier gangrene admitted to Dr. Soetomo General Academic Hospital from January 2012 to November 2020. A total of 109 patients aged approximately 50.31 years old were included in this study. The average NLR of the patients was 15.86, indicating a high NLR compared to the ratio found in healthy people. The area under curve value was 0.65 (95% CI; 0,524-0,754;  $p < 0,05$ ). The Kaplan-Meier curve in figure 2 showed that the NLR cut-off value of 10.9 has a significant impact on the patient's mortality rate (95% CI ; 29,7-19,7;  $p < 0,05$ ). This study revealed that NLR can be used as an indicator of poor prognosis in FG patients with a cut-off point value of 10.9.

**Keywords:** Fournier gangrene, neutrophil-lymphocyte ratio, NLR, prognostic factor

## 1. INTRODUCTION

Fournier gangrene is a rare type of necrotizing fasciitis which affects the perineal, genital, or anorectal region. It is characterized by a widespread soft tissue necrosis and systemic toxicity of the superficial fascia and subcutaneous tissues <sup>[1]</sup>. Even though it is quite uncommon, constituting only 0.02% of all hospital admissions, it is considered as a urological emergency as it has a high mortality rate, at 20 to 50% in most reported series <sup>[2,3]</sup>. In the recent years, the incidence of Fournier gangrene is increasing with the increase of diabetes prevalence and the number of immunocompromised patients due to various causes <sup>[4]</sup>. Previous studies have determined possible risk factors for predicting the prognosis of Fournier gangrene patients <sup>[5-7]</sup>. Parameters to determine the severity and prognosis of the disease have been suggested, one of which is the Fournier Gangrene Severity Index (FGSI), commonly used to assess the severity of the disease by evaluating clinical and laboratory parameters, such as temperature, heart rate, respiratory rate, serum sodium, serum potassium, serum creatinine, serum bicarbonate, hematocrit and white blood cell count <sup>[8]</sup>. Since its introduction by Laor et al, the score has been validated by many studies, however, its accuracy remains questionable <sup>[9,10]</sup>. Nevertheless, it is the only well-known tool to assess severity <sup>[10]</sup>. Recent findings have suggested simple and promising parameters by utilizing normal laboratory findings. There is an increasing interest in predicting the prognosis patients with simple blood test since studies began suggesting the correlation between inflammatory status and disease prognosis. One of the most commonly used parameter is the neutrophil-lymphocyte ratio (NLR) <sup>[11]</sup>. Findings regarding its potential use in predicting the prognosis of Fournier gangrene patients have been reported, however more investigations are still needed to determine its value as a biomarker <sup>[12-14]</sup>. Therefore, we aimed to evaluate the role of neutrophil-lymphocyte ratio as a prognostic marker for Fournier gangrene patients.

## 2. MATERIAL AND METHODS

This is an analytical study with a retrospective approach evaluating the medical record data of patients diagnosed with Fournier gangrene admitted to Dr. Soetomo General Academic Hospital from January 2012 to November 2020. All adult patients aged 18 and above with Fournier gangrene and complete laboratory examination data including neutrophile and lymphocyte count were included for an analysis. Patients with a history of malignancy or chemoradiation were excluded. Patients with incomplete or unclear data in the medical records were also excluded. The data collected and presented included patient age, diagnosis, lesion location, comorbidities, FGSI, bacterial culture results, surgical intervention, and survival status. The collected data were grouped and displayed descriptively in the form of tables and narratives. The association between the binary marker of NLR and the risk of mortality is evaluated using a survival curve. The separation between the curves among patients with a high NLR and a low NLR indicated the prognostic ability of the marker represented by a receiver operating characteristic (ROC) curve <sup>[15]</sup>. The performance of the marker was evaluated by area under the curve (AUC), which is a measure of the ability of a tool to discriminate whether a condition

is present or not. An AUC value of 0.5 indicates that the test has no discriminating ability, whereas an AUC of 1.0 indicates perfect discrimination [16]. The ethical committee of the research and development center of Dr. Soetomo General Academic Hospital approved this study.

### 3. RESULTS

#### 3.1 Baseline Characteristics

A total of 109 patients aged approximately 50.31 years old were included in this study. The average NLR of the patients was 15.86, indicating a high NLR compared to the ratio found in healthy people [17]. Only 25 patients had an FGSI score of more than nine. A score of more than nine indicates an increased risk of mortality [18]. The scrotal area was the most commonly affected area ( $n = 55$ , 50.46%) compared to other areas. Most patients also suffered from diabetes mellitus ( $n = 40$ , 36.7%) leading to an infection caused mainly by *Pseudomonas aeruginosa* ( $n = 23$ , 21.1%), *Klebsiella pneumonia* ( $n = 21$ , 19.27%), and *Acinetobacter baumannii* ( $n = 20$ , 18.35%). A majority of patients were treated with debridement and necrotomy, followed by incision and drainage of the abscess ( $n = 55$ , 50.46%), after which most patients survived ( $n = 90$ , 82.57%).

#### 3.2. NLR value as a prognostic marker

In this study, the cut-off point of NLR among the patients was 10.9, with a 73.7 % sensitivity and 60 % specificity, as shown in figure 1. The area under curve value was 0.65 (95% CI; 0.524-0.754;  $p < 0.05$ ). The Kaplan-Meier curve in figure 2 showed that the NLR cut-off value of 10.9 has a significant impact on the patient's mortality rate (95% CI ; 29,7-19,7;  $p < 0.05$ ). The univariate analysis indicated that NLR can be used as an independent predictor for mortality in Fournier gangrene patients (HR 5.177 ; 95% CI ; 1,092-8,471;  $p < 0.05$ ).

### 4. DISCUSSION

Fournier gangrene is a rare and serious condition which can be found in immunocompromised patients [19]. Even though FGSI has been validated in numerous studies, its use in clinical settings are often times questionable. There is still a high death rate ranging from 20 to 50% among Fournier gangrene patients due to sepsis [19]. Sepsis is one of the main causes of mortality and extended length of stay in patients with urological infections, including Fournier gangrene [20]. To reduce the severity of the disease, utilization of cheap and simple laboratory parameters, such as white blood cell parameters, erythrocyte sedimentation rate, and C-reactive protein are necessary [21,22]. The use of NLR as a parameter has been suggested by many studies. Kaushik et al recommended its use for a diagnostic and predictor marker in septic patients. Its greatest strengths are its efficiency in time, cost, and application compared to other examinations [23]. Neutrophils are one of the main immune cells against pathogens. It is crucial to produce enzymes during an acute inflammatory phase. Neutrophils are able to lyse infected cells, produce free radicals, and induce the production of pro-inflammatory cytokines [24]. The coordination between the transition from innate to adaptive immunity is handled by the T-lymphocytes. Both innate and adaptive immunity or core components of the body's immune system against a pathogen [25]. The ratio between the two cells indicates a transition between innate and adaptive immunity. The relatively low number of lymphocytes could cause a cytokine storm and severe inflammation, leading to a worse prognosis.

This study showed the potential role of NLR as a prognostic marker for Fournier gangrene patients. Patients with a high NLR had 5.17 times risk of mortality compared to patients with a low NLR. This finding is in line with a study by George et al in 2020 which discovered a significant difference of NLR among septic patients with multiple organ dysfunction syndrome (MODS). They discovered that there most septic patients with MODS had a high NLR. The ratio is deemed superior to a white blood cell count [26]. A study with a large sample size by Li et al in 2016 also showed the predictive capability of NLR in septic patients [27]. However, a study by Ni et al suggested that NLR does not significantly predict septic inpatients with a long hospital stay. The difference of findings may be caused by other factors in their study which could affect the patients' NLR [28]. The increase of NLR in septic patients is difficult to be used as a predictive tool, considering that there are many factors affecting neutrophil and lymphocyte count. However, it can still be used as a mortality predictor in septic patients. The ROC curve, Kaplan-Meier, and hazard ratio findings in this study are in line with the study by Yim et al, which suggested that NLR is a useful independent predictor that is associated with increased mortality in Fournier gangrene patients [10]. This study is limited by its retrospective design and secondary data. Most samples included in this study had a high NLR ratio, indicating that most included patients were classified as severe. The inclusion of more patients with different disease severity should be performed in future studies.

### 5. CONCLUSION

NLR can be used as an indicator of poor prognosis in FG patients with a cut-off point value of 10.9.

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