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ORIGINAL PAPER

Evaluating prognostic indicators for in-Hospital mortality in Fournier's gangrene: A 7-year study in a tertiary Hospital

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Summary ***Background: Fournier's Gangrene Scoring Index (FGSI), Simplified FGSI (SFGSI), Uludag FGSI (UFGSI), Laboratory Risk Indicator for Necrotizing (LRINEC), Neutrophil-Lymphocyte ratio (NLR), and Platelet-lymphocyte ratio (PLR) have been devised to assess the risk of mortality in Fournier's Gangrene (FG) patients. However, the effectiveness of these indicators in predicting mortality at the time of admission remains uncertain. The aim of this study is to assess the prognostic efficacy of FG's various indicators on in-hospital mortality.***

Methods: This study analyzed 123 patients from Dr. Soetomo General Hospital's emergency department in Indonesia from 2014 to 2020. Data included demographics, wound cultures, and parameters like FGSI, UFGSI, SFGSI, NLR, PLR, and LRINEC. In-hospital mortality status was also recorded. The data was subjected to comparative, sensitivity, specificity and regression analyses.

Results: In our study of 123 patients, the median age was 52, with a mortality rate of 17.9%. The majority of patients were male (91.1%) and the most common location was scrotal (54.5%). Non-survivors had a shorter median stay (6.5 days) compared to survivors (14 days). Diabetes was the most prevalent comorbidity (61.8%). The highest sensitivity and specificity were found in FGSI and UFGSI indicators. Multivariate logistic regression identified LoS and FGSI as independent predictors of mortality.

Conclusions: FGSI and UFGSI, upon admission, demonstrated the highest sensitivity and specificity, with hospital stay duration and FGSI as key mortality determinants.

KEY WORDS: Fournier's gangrene; Indicator; Neutrophil/lymphocyte ratio (NLR); Platelet to lymphocit ratio.

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INTRODUCTION

Despite significant strides in technological advancement, *Fournier's Gangrene* (FG) continues to pose a formidable challenge with mortality rates oscillating between 5% and 65% (1). An array of prognostic indicators, encompassing *Fournier's Gangrene Severity Index* (FGSI), *Uludag Fournier's Gangrene Severity Index* (UFGSI), *Simplified Fournier's Gangrene Severity Index* (SFGSI), *Laboratory Risk Indicator for Necrotizing Fasciitis* (LRINEC), *Neutrophil-to-lymphocyte Ratio* (NLR), and *Platelet-to-lymphocyte Ratio* (PLR), have been formulated to estimate the mortality risk in FG patients (2-6). These predictive instruments are invaluable for healthcare professionals, especially urologists and surgeons, as they enable the initiation of more aggressive interventions at an early stage. Some of these indicators, engineered for ease of use and practicality, rely solely on laboratory data (SFGSI, LRINEC, NLR, and PLR), while others are more sophisticated, amalgamating both laboratory and clinical data (FGSI and UFGSI). In the quest for an indicator that harmonizes precision and simplicity, a comparative evaluation of these indicators is indispensable. However, the sensitivity and specificity of these scoring systems remain undetermined. This study seeks to assess the efficacy of FGSI, UFGSI, SFGSI, LRINEC, NLR, and PLR at the point of admission in forecasting mortality outcomes in FG patients.

MATERIALS AND METHODS

A retrospective cross-sectional study from January 2014 to December 2020 was conducted following approval from the *Hospital Review Board* (No. 0528/LOE/301.4.2/VII/2021). The study included all patients with FG admitted to *Dr. Soetomo Hospital*. Patient data was retrieved from the hospital's electronic medical records system. All participants provided written informed consent for the use of their clinical information for research purposes. The study included patients diagnosed with FG by a urologist, excluding those with incomplete data.

Scoring was done at admission, reflecting the emergency assessment when the patient arrived at the hospital. If a patient had test results from another healthcare institution, these tests were repeated.

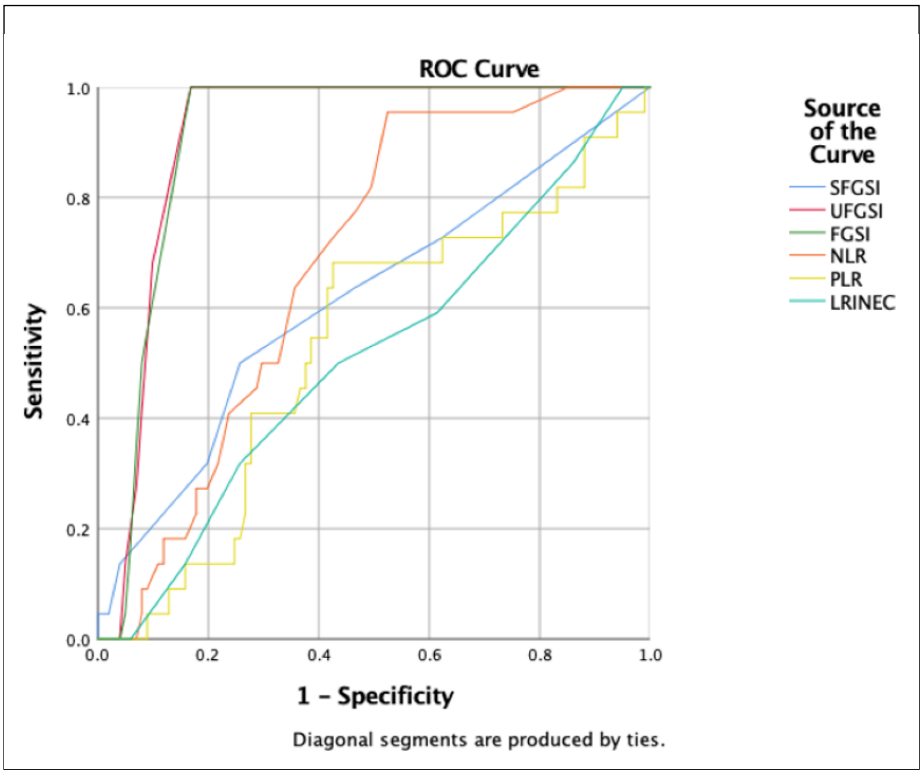
The data examined included demographics (age, sex, etiology, comorbidities, and wound culture results) and parameters (FGSI, UFGSI, SFGSI, LRINEC, PLR, and NLR). Participants were segregated into two categories: those who survived and those who did not. A comparative analysis was conducted between these groups con-

cerning demographic information and scoring. The FGSI, UFGSI, SFGSI, LRINEC, NLR, and PLR were calculated using various parameters (5, 7, 8).

Statistical analysis

Group comparisons were performed using chi-square and Mann Whitney U test as appropriate. The area under the *receiver operating characteristic* (ROC) curve was used to assess sensitivity and specificity, and the Youden index was used to determine the optimal cutoff value. Multivariable logistic regression models were constructed using the stepwise backward LR method. A significance level of $p < 0.05$ was considered statistically significant. Data analyses were performed using IBM SPSS Statistics for Windows version 24.0 (*IBM Corp., Armonk, NY, USA*).

Figure 2.
The ROC curve for FGSI, SFGSI, NLR, PLR, and LRINEC.



Results

Throughout the period under investigation, spanning from January 2014 to December 2020, the emergency department received a total of 135 patients with FG. However, the analysis only incorporated 123 patients (Figure 1). The patients had a median age of 52 (44-61), and the mortality rate was recorded at 17.9%. The study population was predominantly male (91.1%), and the most common location was scrotal (54.5%). Non-survivors had a shorter median duration of stay compared to survivors, with lengths of 6.5 (3-14) days and 14 (7-21) days, respectively (Table 1). Diabetes was identified as the most prevalent comorbidity, present in 61.8% of patients.

Figure 1.
Algorithm for the Inclusion and exclusion of patients.

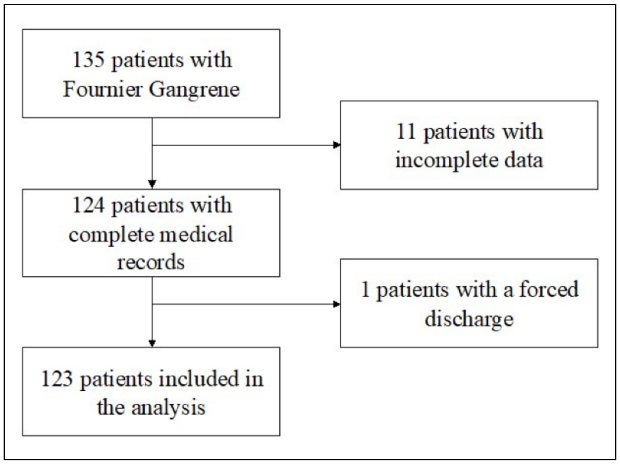


Table 1.
Prognostic correlation with demographic and clinical features.

Variable	Total	Survivor 101 (82.1%)	Non-survivor 22 (17.9%)	p value
Age	52 (44-61)	52 (44-60)	55.5 (44-63)	0.328
Sex				
Male	112 (91.1%)	93 (92.1%)	19 (86.4%)	0.413
Female	11 (8.9%)	8 (7.9%)	3 (13.6%)	
Etiology				
Penoscrotal	18 (14.6%)	16 (15.8%)	2 (9.1%)	0.714
Perineum	38 (30.9%)	31 (30.7%)	7 (31.8%)	
Scrotum	67 (54.5%)	54 (53.5%)	13 (59.1%)	
LoS	12 (5-20)	14 (7-21)	6.5 (3-14)	**0.009**
Comorbidities				
Diabetes mellitus	76 (61.8%)	65 (64.4%)	11 (50.0%)	0.23
Hypertension	31 (25.2%)	29 (28.7%)	2 (9.1%)	0.06
Chronic kidney disease	11 (8.9%)	8 (7.9%)	3 (13.6%)	0.41

**LoS = Length of stay.*

The microorganisms most frequently encountered in our study population were *Pseudomonas spp.*, *Klebsiella pneumonia*, *E. coli*, and *Acinetobacter spp.* (Table 2).

As illustrated in Figure 2, the ROC analysis unveiled cut-off values (sensitivity, specificity) for FGSI, SFGSI, UFGSI, NLR, PLR, and LRINEC predicting mortality as follows: 9 (100%, 83.2%), 2.5 (50%, 74.3%), 10.5 (100%, 83.2%), 7.5 (95.5%, 47.5%), 264.69 (68.2%, 57.4%), and 3.5 (50%, 56.4%), respectively. To identify independent predictors of mortality, a multivariate logistic regression analy-

Table 2.
Findings from the wound culture analysis.

Variable	Total	Survivor	Non-survivor	p value
Acinetobacter	18 (14.6%)	13 (12.9%)	5 (22.7%)	0.31
Candida	6 (4.9%)	3 (3.0%)	3 (13.6%)	0.07
E.coli	18 (14.6%)	15 (14.9%)	3 (13.6%)	1.00
Pseudomonas	23 (18.7%)	19 (18.8%)	4 (18.2%)	1.00
Clostridium	5 (4.1%)	4 (4.0%)	1 (4.5%)	1.00
Streptococcus	4 (3.3%)	4 (4.0%)	0 (0.0%)	1.00
Streptococcus bovis	1 (0.8%)	1 (1.0%)	0 (0.0%)	1.00
Fusobacterium	11 (8.9%)	8 (7.9%)	3 (13.6%)	0.41
Staphylococcus	3 (2.4%)	3 (3.0%)	0 (0.0%)	1.00
Gamella	1 (0.8%)	1 (1.0%)	0 (0.0%)	1.00
Klebsiella p	20 (16.3%)	18 (17.8%)	2 (9.1%)	0.52
Sterile	13 (10.6%)	12 (11.9%)	1 (4.5%)	0.46

Table 3.
Evaluation of the predictive capacity of FGSI, SFGSI, UFGSI, NLR, PLR, and LRINEC through univariate analysis.

Variable	Total	Survivor	Non-survivor	p value
FGSI	6 (4-10)	5 (4-8)	10.5 (10-11)	0.0001
SFGSI	1 (0-3)	1 (0-3)	2.5 (0-4)	0.085
UFGSI	8 (5-11)	7 (5-9)	12 (11-13)	0.0001
NLR	10 (4-16)	8 (4-15)	13 (10-19)	0.008
PLR	252.53 (164.62-358.97)	243.53 (164.62-359.85)	289.035 (165.07-358.65)	0.611
LRINEC	3 (2-5)	3 (2-5)	3.5 (2-5)	0.859

Table 4.
Outcomes of the multivariate logistic regression analysis.

Variable	β	SE	OR (95% CI)	p value
LoS	-0.105	0.039	0.9 (0.83-0.97)	0.008
FGSI	0.618	0.127	1.856 (1.45-2.38)	0.0001

sis was conducted, including variables that were significantly associated with mortality in the univariate analysis ($p < 0.05$) (Table 3). Among these variables, only length of stay (LoS) and FGSI remained significant predictors of mortality in the multivariate analysis (Table 4).

Discussion

During the study interval, it was observed that the majority of patients were male, with the scrotum being the most frequent site of origin. The length of hospital stay, prevalence of diabetes, and incidence of Pseudomonas spp. were also noteworthy among patients. An analysis of sensitivity, specificity, and independent risk factors for mortality revealed that both FGSI and UFGSI demonstrated the highest sensitivity and specificity.

Furthermore, the length of hospital stay and FGSI were identified as independent prognostic value.

Despite significant advancements, the mortality associated with FG remains alarmingly high (9-11). Our study, conducted at a tertiary hospital in Indonesia's second-largest city, yielded a mortality rate of 17.9%, which could be attributed to the availability of advanced medical facilities and expertise. Notably, the demographics between groups were comparable, with the exception of LoS, which was significantly lower among non-survivors.

In this study, we investigated established indicators employed at admission to predict FG mortality, including FGSI, SFGSI, NLR, PLR, and LRINEC. FGSI, recognized as the earliest and most frequently utilized indicator, is designed to assess the likelihood of mortality in FG patients (12). Our findings indicated that individuals who did not survive exhibited elevated FGSI values compared to those who did. The optimal cut-off for FGSI, along with its sensitivity and specificity, was identified as 9, 100%, and 83.2%, respectively. These results outperformed those of previous studies, which reported sensitivity range of 69% to 100% and specificity range of 57% to 97% (4, 7, 13). The established cut-off of 9 at admission aligns with the accepted threshold for mortality prediction. Therefore, FGSI with this recognized cut-off can be effectively utilized for early assessment and aggressive intervention.

An analysis of the SFGSI, a simplified version of the FGSI that utilizes only three variables, revealed no differences between groups. The optimal cut-off, sensitivity, and specificity for SFGSI were determined to be 2.5, 50%, and 74.3%, respectively. The cut-off was similar to the consensus, which considered values above 2 as indicating a high risk of mortality (4). However, the reliability of SFGSI on admission to predict mortality in FG patients could not be confirmed.

The UFGSI, a version of FGSI that includes age and disease extent, was studied. UFGSI values were found to be

Supplementary Table 1.
Measured parameters and cut-off score of each scoring system from the literature.

Scoring system	Number of parameters	Parameters	Cut-off score
FGSI	9	Temperature, heart rate, respiratory rate, serum sodium, potassium, serum creatinine, hematocrit, leucocyte counts, and serum bicarbonate	> 9 (13)
UFGSI	11	Age and dissemination score in addition to the measured parameters from FGSI	≥ 9 (7)
SFGSI	3	Serum creatinine, hematocrit, and serum potassium	> 2 (4)
NLR	1	The ratio was calculated by dividing the number of neutrophils by the number of lymphocytes.	> 8 (14)
PLR	1	The ratio was calculated by dividing the number of platelets by the number of lymphocytes.	> 140 (14)
LRINEC	6	C-reactive protein, white blood cell counts, hemoglobin, serum sodium, serum creatinine, and blood glucose	≥ 6 (17)

FGSI: Fournier's Gangrene Severity Index; UFGSI: Uludag Fournier's Gangrene Severity Index; SFGSI: Simplified Fournier's Gangrene Severity Index; NLR: Neutrophil-to-lymphocyte Ratio (NLR); PLR: Platelet-to-lymphocyte Ratio (PLR); LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis.

higher in non-survivors. The optimal cut-off, sensitivity, and specificity for UFGSI were identified as 10.5, 100%, and 83.2%, respectively. These values were similar to those of the FGSI. While previous research suggested that UFGSI performs better than FGSI, the difference in our findings could be due to the lack of pelvic and beyond involvement in our study population (3).

NLR and PLR have been used as mortality predictors in FG patients in previous studies (5, 6, 14). High NLR and PLR have been linked with mortality predictors in FG patients (5, 14). One study found NLR and PLR to be better than FGSI (14), while another found NLR to be better than PLR (6). However, our study showed significantly higher NLR levels in non-survivors compared to survivors. Despite this, neither NLR nor PLR predicted in-hospital mortality in our study. NLR and PLR are known markers of inflammation and infection (15). The divergence in results suggests that NLR and PLR may be influenced by the disease phase, whether acute or chronic, a distinction challenging to ascertain in a tertiary hospital setting primarily consisting of referred patients (16).

The LRINEC score, which overlaps with FGSI in some variables, is a laboratory-centric indicator employed to evaluate mortality in patients suffering from FG. While certain studies have identified a significant correlation between elevated LRINEC scores and mortality (5, 17), our research did not discern a notable difference between survivors and non-survivors, nor could it prognosticate in-hospital mortality for FG. These findings may be profoundly influenced by the specific laboratory equipment utilized and the disease's stage at the time of examination. Given the inconsistent results obtained using laboratory-based indicators like SFGSI, LRINEC, NLR, and PLR, employing a scoring system (FGSI and UFGSI) at the time of admission could potentially provide a more accurate prediction of mortality for FG patients.

Despite its strengths, this study has certain limitations. First, it utilized a retrospective design, which restricted to influence the laboratory blood draws. Second, the study analysed data from a single tertiary referral center, potentially leading to a sample population skewed towards more severe cases. Thirdly, each patient may have been in a distinct disease stage upon admission, given our hospital's tertiary status and frequent intake of referred patients. Lastly, despite the confirmation of all FG cases through a thorough review of medical and surgical records, some positive cases might have been missed due to the absence of comprehensive retrospective records. Future prospective studies involving multiple centers are imperative to identify the most sensitive parameters for predicting patient mortality.

Conclusions

In this study, it was observed that FGSI and UFGSI showed the highest sensitivity and specificity among the current indicators upon admission. The duration of hospital stay and FGSI were recognized as independent determinants of mortality. These indicators could potentially offer a more accurate prediction of mortality. However, it is essential to exercise caution when interpreting laboratory-only indicators in a tertiary hospital setting due to possible biases arising from disease stage. To validate these results, a multicenter prospective study is recommended. This would aid in verifying the reliability and applicability of these indicators across various settings and patient demographics.

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