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# PROGNOSTIC SIGNIFICANCE OF NEUTROPHIL/LYMPHOCYTE RATIO AND SOFA SCORE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE FOLLOWED IN INTENSIVE CARE UNIT

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**Abstract**

**Objective:** Chronic Obstructive Pulmonary Disease (COPD) has become one of the leading causes of increasing morbidity and mortality worldwide. Inflammation is known to play an important role in the pathogenesis of COPD. Neutrophil-lymhocyte ratio (NLR) is an inflammatory biomarker which indicates the balance of the immune system and reflecting systemic inflammation. One of the most commonly used scoring models for predicting mortality in intensive care is the Sepsis Organ Failure Assessment (SOFA) scoring.
The aim of our study is to investigate the prognostic significance of NLR and SOFA score in patients admitted to the intensive care unit (ICU) with COPD.

**Methods:** A retrospective, single-center cohort study was conducted between 01.09.2022-01.09.2024. Patients over the age of 18 who were admitted to the intensive care unit of Kırşehir Training and Research Hospital with a diagnosis of COPD. Data of age, gender, comorbidities, SOFA score, NLR, number of invasive and non-invasive mechanical ventilation days, length of hospital stay, length of ICU stay, and 30-day mortality. Logistic regression analysis was used to predict mortality.

**Results:** Data from 259 patients were evaluated. The mean age of the patients was 72 (14). Sixty-seven patients died and 192 patients were discharged. β coefficient for the NLR was 0.014419 ($p$=0.0383). β coefficient for the SOFA score was 0.382920 ($p$<0.001). From the ROC (Receiver Operating Characteristic) curve, it appears that the model has a high AUC (Area Under Curve), which indicates that the model is quite good at distinguishing classes. SOFA score and NLR were found to be higher in deceased patients.

**Conclusion:** In ICU follow-up, SOFA score and NLR can be examined together to early detect critically COPD patients and predict mortality.

**Keywords:** *COPD, SOFA (The Sepsis Organ Failure Assessment) score, neutrophil-lymhocyte ratio (NLR), ICU, mortality.*

## Introduction

Chronic Obstructive Pulmonary Disease (COPD) has become one of the leading causes of increasing morbidity and mortality worldwide.[1] COPD exacerbations, which adversely affect the prognosis of the disease, cause recurrent hospitalizations, increased workload, and economic loss.[1,2]
COPD is a chronic disease and is characterized by dyspnea and/or increased cough and sputum. Increased local and systemic inflammation, usually due to infection or air pollution, causes COPD exacerbations and patients often categorized as mild, moderate, or severe.[3,4]
Inflammation is known to play an important role in the pathogenesis of COPD. Additionally, elevated inflammatory markers have longly been used to determine the acute exacerbations of COPD and prognosis. Neutrophil-lymhocyte ratio (NLR) is an inflammatory biomarker which indicates the balance of the immune system and reflecting systemic inflammation. The response of circulating leukocytes to inflammatory stress causes an increase in the number of neutrophils and a decrease in the number of lymphocytes. The NLR is used as a marker reflecting the acute state of inflamation. Additionally, NLR has been widely studied in diseases with chronic inflammation, such as evaluating inflammation after coronary artery disease (CAD) and determining the severity of malignancies in patients with a previous oncological diagnosis.[4-6]
The mortality rate of COPD patients admitted to intensive care is affected by age, duration of mechanical ventilation, severity of disease, etc. Scoring models have been widely utilised in the intensive care unit (ICU) and provide objective information to help inform decisions related to the treatment and prognosis of COPD. The Sepsis Organ Failure Assessment (SOFA) Score has been evaluated and validated in many centers and is widely used in most ICUs to predict clinical outcomes.[1]
The primary aim of our study is to investigate the prognostic significance of NLR and SOFA score in patients admitted to the ICU with a diagnosis of COPD. Also, to evaluate predictability of morbidity, length of stay ICU and length of stay in hospital.

## Methods

Ethical approval for the study was granted by the Local Ethics Committee of the Health Sciences Scientific Research Ethics Board (Sağlık Bilimleri Bilimsel Araştırmalar Etik Kurulu) on October 22, 2024 (Approval No: 2024-17/147).

### Study Design and Setting
A retrospective, single-center cohort study was conducted between 01.09.2022-01.09.2024. Patients over the age of 18 who were admitted to the intensive care unit of Kırşehir Training and Research Hospital with a diagnosis of COPD.

### Data Collection
Data of age, gender, comorbidities, SOFA score, NLR, number of invasive and non-invasive mechanical ventilation days, length of hospital stay, length of ICU stay, and 30-day mortality. The scores of SOFA and NLR were calculated for each patient were retrieved from the electronical patient data. SOFA score is based on six different scores. There are cardiovascular, respiratory, coagulation, hepatic, renal, and neurological systems each scored from 0 to 4 with an increasing score reflecting worsening organ dysfunction. Six criteria reflecting the function of these organ system and allocates a score of 0–4. Total score changes 0 and 24.[7]

### Inclusion Criteria
The patients included were those aged >18 years who followed in intensive care with the diagnosis of COPD.

### Exclusion Criteria
Patients with concomitant acute renal failure and/or decompensated heart failure during intensive care admission were excluded from the study. Patients with inflammatory diseases (etc. rheumatic diseases) affecting the NLR ratio and those diagnosed with interstitial lung disease were excluded from the study.

### Data Analysis
Data was analyzed using IBM SPSS Statistics, version 29.0.0 (IBM Corp, Armonk, NY, USA). Descriptive statistics are presented with frequency (n), percentage (%), mean, standard deviation, 95% Confidence Interval (CI), median. The chi-Square ($\chi 2$) test was used to compare qualitative data. The normality distribution of the data was evaluated by the Shapiro-Wilk test. Student's t-test or Mann-Whitney U Test was used for comparisons between the groups. ROC (Receiver Operating Characteristic) analysis was applied to determine whether NLR and SOFA score could be used as tests to predict mortality. Logistic regression analysis was used to predict mortality and Forward method was used in parameter selection. Statistically, $p<0.05$ was considered significant.

## Results

Data from 259 patients were evaluated (Figure 1). Of the patients included in the study, 97 were female and 162 were male. The mean age of the patients was 72 (14) and the age ranged from 21 to 103 years. 67 patients died and 192 patients were discharged. The mean day of invasive mechanical ventilation was 2 (5) and the day ranged from 0 to 40 days. The mean day of non-invasive mechanical ventilation was 5 (6) and the day ranged from 0 to 44 days. The mean length of ICU stay was 7 (7) and the day ranged from 1 to 44 days. The mean length of hospital stay was 11 (11) and the day ranged from 1 to 56 days (Table1).

**Table 1.** Demographic data of patients.

| Parameters | | n | % Mean±SD | Median (Min-Max) |
|---|---|---|---|---|
| **Gender** | **Female** | 97 | 37.5% | |
| | **Male** | 162 | 62.5% | |
| **DM** | | 55 | 21.2% | |
| **HT** | | 76 | 29.3% | |
| **CAD** | | 65 | 25.1% | |
| **CRD** | | 32 | 12.4% | |
| **CVD** | | 38 | 14.7% | |
| **Discharge** | | 192 | 74.1% | |
| **Ex** | | 67 | 25.9% | |
| **Age** | | | 72±14 | 74(21-103) |
| **Invasive MV day** | | | 2±5 | 0(0-40) |
| **Noninvasive MV day** | | | 5±6 | 3(0-44) |
| **ICU LOS** | | | 7±7 | 4(1-44) |
| **Hospital LOS** | | | 11±11 | 7(1-56) |

DM: Diabetes Mellitus, HT: Hypertension, CAD: Coronary Artery Disease, CRD: Chronic Renal Disease, CVD: Cerebrovascular Disease, Invasive MV day: Invasive mechanical ventilation day, Non-invasive MV day: Non-invasive mechanical ventilation day, ICU LOS: ICU length of stay, Hospital LOS: Hospital length of stay, SD: Standard Deviation

When the comorbidities of the patients were examined, 76 patients had hypertension, 55 patients had diabetes mellitus, 65 patients had coronary artery disease,32 patients had chronic renal disease, 38 patients had cerebrovascular disease (Table 1).

The median SOFA score was 2 (0-12). The median NLR was 8.75 (0.08-213.15) (Table 2).

In this study, a logistic regression analysis was performed aiming to model the effect of mortality with two independent variables, NLR and SOFA score. The analysis results presented the coefficients measuring the effect of each independent variable on mortality and the statistical significance of these coefficients (Table 3).

**Table 2.** Descriptive statistics of SOFA and NLR.

| Variable | Median (Min-Max) | Mean±SD | *p* |
|---|---|---|---|
| **NLR** | 8.75(0.08-213.15) | 14.24±21.73 | 0.0383 |
| **SOFA score** | 2(0-12) | 2.56±2.07 | <0.001 |

SOFA score: The Sepsis Organ Failure Assessment (SOFA) Score, NLR: Neutrophil-lymhocyte ratio, SD: Standard Deviation

The general formula of the model is determined as follows:

$$\text{Mortality (Ex)} = \beta 0 + \beta 1 \ \text{NLR} + \beta 2 \times \text{SOFA} + \varepsilon$$

β coefficient for the NLR was 0.014419. Statistically, $p$=0.0383 was considered significant. Each unit increase in the NLR increases the probability of mortality by 1.45%. β coefficient for the SOFA score was 0.382920. Statistically, $p$<0.001 was considered highly significant. Each unit increase in SOFA score increases the probability of mortality by 46.6% (Table 3).

Deviance values, which evaluate the fit of the model, show that the established model provides a better fit (residual deviance=261.58) and the model is significant, when compared to the deviance in the null model (296.13). From the ROC curve, it appears that the model has a high AUC (Area Under Curve), which indicates that the model is quite good at distinguishing classes (Figure 2). That is, according to ROC curve analysis, evaluating the NLR and SOFA score together is successful in predicting mortality.

**Table 3.** Logistic Regression Analysis Results.

| Predictor | β | Standart error | OR | *p* |
|---|---|---|---|---|
| **Intercept** | -2.3663 | 0.3022 | NA | $4.89\times10^{-15}$ |
| **NLR** | 0.0144 | 0.00696 | 1.0145 | 0.0383 |
| **SOFA score** | 0.3829 | 0.0766 | 1.466 | $5.68\times10^{-7}$ |

SOFA score: The Sepsis Organ Failure Assessment Score, NLR: Neutrophil-lymhocyte ratio, OR: Odds ratio

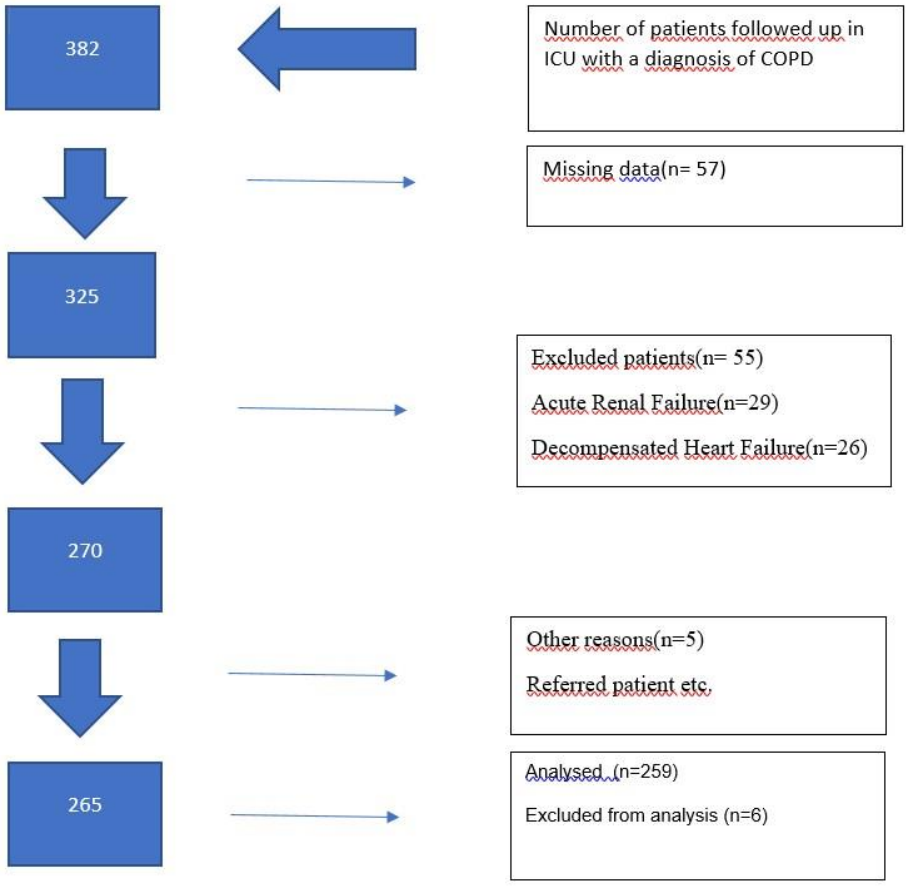


**Figure 1.** Flow diagram.

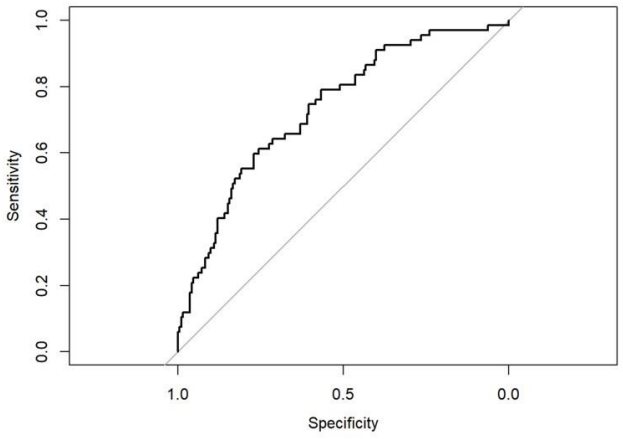


**Figure 2.** The ROC curves of SOFA score and NLR for predicting the mortality (AUC=0.734).

## Discussion

In this study, we mainly examined the predictability of SOFA score and NLR predicting mortality in COPD patients in intensive care unit. In conclusion, both NLR and SOFA score are significant predictors of mortality probability, but the sensitivity of SOFA score is more pronounced and stronger.

Many studies have been conducted to predict mortality by evaluating SOFA score and NLR with other variables. Rodríguez et al. showed that patients with COPD, non-survivors had significantly higher SOFA scores than survivors at ICU admission and up to day 7.[8] In a study, Cırık et al., the predictive power of SOFA score was found to be significantly higher than that of the c-reactive protein/albumin ratio (CAR).[9] Akhter et al. reported that when compared with CURB-65 (Confusion; Urea; Respiratory Rate; Blood Pressure) and APACHE II (Acute Physiology and Chronic HealthEvaluation), the SOFA score was not as effective in predicting mortality.[2] Xiao et al. showed that the sensitivity and AUC of the SOFA score were significantly higher than the other scoring models, but the specificity of the SOFA score was lower than the APACHE II score. The combined prognostic value for patients of the two scoring models (SOFA and APACHE II) did not improve significantly.[1] In a study, Xie et al., the predictive value of LAR (lactate-albumin ratio) for 28-day mortality in patients with COPD was the same as that of SOFA score.[10] Similarly, in our study, SOFA score is significant predictors of mortality.

Tanrıverdi et al. reported that procalcitonin (PCT) was a better marker for predicting bacterial infection compared with C-reactive protein (CRP) and the NLR ratio especially patients with COPD in ICU. But, both sensitivity and specificity of PCT were <70% for predicting bacterial etiology. So, it may not be an ideal marker. CRP and the NLR showed inferior but similar results for predicting bacterial infection and the fact that they are cheaper and more easily accessible.[11] In a systematic review and meta-analysis, Paliogiannis et al., NLR values are significantly higher in patients with acute COPD exacerbation than in those with stable COPD. These findings suggest a potential clinical use of NLR in COPD.[12]

In a systematic review, Pascual-Gonzalez et al., NLR is higher in patients with exacerbations compared to patients with stable COPD. NLR is a good marker for evaluating acute exacerbation in COPD patients. There is also a significant correlation between NLR and clinical/functional parameters. In conclusion, NLR can be used to predict the risk of in-hospital and late mortality in COPD patients.[13] In a retrospective study, Cai et al., in acute exacerbations of COPD, increased inflammation markers such as NLR, PLR (Platelet-Lymphocyte Ratio) and MLR (Monocyte-Lymphocyte Ratio) were significantly increased similar to CRP. Using the combination of NLR, PLR and MLR increased diagnostic accuracy.[14] In a retrospective study, Liao et al., among predictors including NLR, only MLR was a risk factor for in-hospital mortality. In addition, increased ELR (Eosinophil-Lymphocyte ratio) was excessively associated with decreased in-hospital mortality.[15] In our study, NLR is significant predictors of mortality. The result of our study supports these studies in the current literature.

In a retrospective study conducted by Doğanay et al., the usability of NLR, PLR and MLR as prognostic indicators in patients with COPD was evaluated. SOFA score was found to be associated with mortality in COPD patients in ICU. Additionally, in cases with mortality, NLR, PLR, MLR were statistically significantly higher than in cases without mortality. Also revealed that there was a positive correlation of both NLR and MLR with SOFA score.[16] Similar to our study, in this study, SOFA is more significant in predicting mortality than NLR.

### Limitations

Small sample size might reduce the likelihood of the available findings to reflect actual outcomes. In addition, the retrospective study design mostly hampers consideration of many confounding factors, which may influence observed patient outcomes. In addition, septic patients were not excluded from the study.

### Conclusion

SOFA score and NLR were found to be higher in deceased patients. In ICU follow-up, SOFA score and NLR can be examined together to early detect critically COPD patients and predict mortality.

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### Conflict of Interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

### Compliance of Ethical Statement

The study received ethical approval from the Local Ethics Committee of the Health Sciences Scientific Research Ethics Board (Sağlık Bilimleri Bilimsel Araştırmalar Etik Kurulu) on October 22, 2024 (Approval No: 2024-17/147).

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### Author Contributions

GC provided that planning, writing, translating and statistical analysis. OÇ helped with collecting patients' data and writing. EC, SK, MKÖ, MET, DT, DSP, KMG, MB, EEK, GY, ŞSK and HÖ helped collect patients' data.

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