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Original Article

Evaluation of the Relationship between Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score and Mortality in COPD Exacerbation

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SUMMARY

Background: Hemoglobin, albumin, lymphocyte, and platelet (HALP) scores are easily calculable markers that allow the evaluation of systemic inflammation and nutritional status. This study aimed to evaluate and compare the predictive power of HALP scores for 3-month and 1-year mortality in patients admitted to the emergency department with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

Methods: Hospital records of patients aged > 18 years who had been diagnosed with AECOPD in the emergency department (ED) and hospitalized were retrospectively reviewed. The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and HALP scores of the patients were analyzed. Three-month and 1-year mortality rates of the patients were evaluated.

Results: Mean age of the 957 patients were 70.6 ± 10.2 and 66.9% (n = 660) were male. The 3-month and 1-year mortality rates were 21.2% and 30.0%, respectively. For 3-month and 1-year mortality, the NLR and PLR were significantly higher and the HALP score was significantly lower in the mortality groups, and the HALP score was found to be a good predictor of 3-month and 1-year mortality.

Conclusion: HALP score is a potential prognostic index for patients with AECOPD. Increased NLR and PLR were associated with increased mortality in patients with AECOPD. The HALP score, NLR, and PLR can be used as important predictors of mortality in patients with AECOPD.

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, and treatable disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities. It is typically caused by significant exposure to noxious particles or gases, and influenced by host factors, including abnormal lung development.[1] Today, COPD, which has become the third cause of death worldwide, is responsible for 5.5% of all deaths.[2] Acute exacerbation of COPD (AECOPD) is characterized by sudden worsening of respiratory complaints, necessitating additional treatment.[3] AECOPD increases the severity and frequency of exacerbations, decreases physical activity, worsens lung function, increases hospitalization and mortality, and has adverse economic effects on both patients and the country.[4,5]

AECOPD is a systemic airway inflammatory state evidenced by an increase in inflammatory biomarkers. Advanced systemic inflammation is associated with poor clinical outcomes.[6]

Higher levels of inflammatory biomarkers have been associated with higher mortality in patients with COPD.[7–9] Blood biomarkers can reflect substances released from the lungs into systemic circulation, are easily measurable, and indicate COPD activity.[10] However, their current levels are still insufficient to assess the prognosis of COPD.

Anemia and hypoalbuminemia are indicators of malnutrition. Lymphocytes and platelets play a key role in systemic inflammation. In this study, we evaluated the relationship between a combination of these four markers and AECOPD.

The hemoglobin, albumin, lymphocyte, and platelet (HALP) score is used to evaluate the prognosis of various diseases; however, this study aimed to evaluate the significance of the HALP score in predicting 3-month and 1-year mortality in patients admitted to the emergency department with AECOPD.

2. Materials and methods

This retrospective study was conducted at the emergency department of atertiary hospital. Patients aged > 18 years who had previously been diagnosed with COPD and AECOPD in the emergency department and were hospitalized during the 12-month period were retrospectively identified from hospital records.

Hemoglobin, lymphocyte, neutrophil, platelet, and albumin levels were recorded from the tests performed using the blood collected during the emergency service application. Blood counts and biochemical parameters were measured using a hematology analyzer (CellDyn Ruby Hematology Analyzer, Abbott, IL, U.S.A.) and clinical chemistry analyzer (Architect *c*8000, Abbott, IL, U.S.A.), respectively. The neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratios (PLR) were calculated. The NLR was calculated by dividing the neutrophil count by the lymphocyte count. PLR was

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calculated by dividing the platelet count by the lymphocyte count. HALP score was calculated using the hemoglobin (g/dL) × albümin (g/L) × lymphocyte count (10^3/μL) / platelet count (10^3/μL) method.[11–13]

Poor prognosis was determined according to the 3-month and 1-year COPD-related mortality status of the patients. Data on patient mortality and general health status were obtained by examining patient files and hospital databases. In cases where data could not be obtained, telephone contacts were established with the patients.

The following patients were excluded: those with neoplastic and hematologic disorders, those undergoing immunosuppressive therapy, patients with congestive heart failure, liver dysfunction with deterioration in liver function tests and inflammatory markers, kidney dysfunction undergoing dialysis, or whose data could not be obtained.

This study was approved by the Eskişehir Education and Training Hospital of Medicine Non Interventional Clinical Research Ethics Committee (ESH/GOEK 2022/2). All procedures were performed in accordance with the ethical rules and principles of the Declaration of Helsinki.

2.1. Statistical analysis

While summarizing the data, continuous variables with normal distiribution are shown as mean ± standard deviation, continuous variables that are not normally distributed are shown as median [interquartile range (IQR)], and categorical variables are shown as ratios. The normality of the data was evaluated using the Shapiro-Wilk test, and Levene's test was used to determine whether the group variances were homogeneous. The chi-square test was used to evaluate categorical variables. The Mann-Whitney U test was used to compare variables that were not normally distributed between the two groups. Receiver operating characteristic (ROC) curve analysis was used to evaluate the optimal cut off values, sensitivity, and specificity of HALP score. Statistical significance was set at $p < 0.05$ significant.

3. Results

In total, 957 patients with COPD were included in this study. Examination of the 3-month and 1-year mortality revealed that the death rates were 21.2% (n = 203) and 30.0% (n = 287), respectively.

The 3-month mortality status of the patients was evaluated. Median age of the survivor group patients were 70.5 (64.0–77.0) and 63.5% (n = 479) were male. Median age of the mortality group patients were 74.0 (66.0–82.0) and 70.4% (n = 143) were male. The mortality group was significantly older ($p < 0.001$); there were no statistical differences in terms of sex ($p = 0.060$). The mortality group had lower levels of HALP score (0.29 [0.17–0.51] for survivor group and 0.18 [0.12–0.36] for mortality group, $p < 0.001$ (data was shown as median [IQR])). The mortality group had higher neutrophil lymphocyte ratio (5.34 [3.19–10.17] for survivor group and 7.92 [4.59–13.37] for mortality group, $p < 0.001$ (data was shown as median [IQR])) and platelet lymphocyte ratio (168.73 [105.23–258.49] for survivor group and 204.80 [118.40–305.42] for mortality group, $p = 0.001$ (data was shown as median [IQR])). The laboratory results of these patients after 3 month follow-up period are shown in Table 1.

The mortality rate in patients diagnosed with COPD in the emergency department and whose parameters were evaluated were assessed at the end of one year. Median age of the survivor group patients were 70.0 (64.0–77.0) and 71.5% (n = 479) were male. Median age of the mortality group patients were 73.0 (64.0–80.0) and 63.1% (n = 181) were male. The HALP score of the mortality group was lower than that of the survivor group (0.29 [0.17–0.53] for survivor group and 0.22 [0.13–0.38] for mortality group, $p < 0.001$ (data was shown as median [IQR])). The mortality group had higher values of neutrophil lymphcyte ratio (5.33 [3.15–10.40] for survivor group and 5.33 [3.15–10.40] for mortality group, $p < 0.001$ (data was shown as median [IQR])) and platelet lymphocyte ratio (169.62 [105.05–260.19] for survivor group and 193.33 [117.75–293.33] for mortality group, $p = 0.008$ (data was shown as median [IQR])). The laboratory results of these patients after one year of follow-up are shown in Table 2.

Receiver operating characteristic (ROC) curve analysis was applied to evaluate the predictive value of the HALP score for the 3-month mortality of patients. The area under the curve (AUC) of the HALP score was 0.635 (95% confidence interval [CI], 0.590–0.679). The optimal cut off value was found as 0.2346, with a sensitivity of 62.9% and specificity of 64.5% (Figure 1a).

The ROC curve was used to determine the 1-year mortality predictive value of the HALP score in patients with COPD. The area under the curve (AUC) of the HALP score was 0.604 (95% CI, 0.565–0.642). The optimal cut off value was found as 0.2350, with a sensitivity of 63.0% and specificity of 56.4% (Figure 1b).

Table 1
The laboratory results of patients after 3 month follow-up.

Variables	Survivor group (n = 754)	Mortality group (n = 203)	p value
Age, year*	70.5 (64.0–77.0)	74.0 (66.0–82.0)	0.000
Gender, male, n (%)	479 (63.5%)	143 (70.4%)	0.060
pH*	7.34 (7.29–7.39)	7.30 (7.22–7.39)	0.000
pCO2, mmHg*	53.8 (44.7–66.8)	56.7 (43.4–72.1)	0.125
pO2, mmHg*	32 (24.8–42.3)	35.1 (24.9–55.0)	0.009
Lactat, mmol/L*	1.5 (0.9–2.4)	2.3 (1.3–3.2)	0.000
HCO3, mmol/L*	26.1 (23.8–29.6)	25.2 (20.8–30.2)	0.013
Hemoglobin, g/dl*	13.1 (11.4–14.9)	11.6 (10.2–13.9)	0.000
Albumin, g/L*	3.9 (3.6–4.2)	3.6 (3.2–4.0)	0.000
Leukocyte count, 10^3/μL*	11.2 (8.6–14.9)	12.5 (9.1–16.8)	0.029
Neutrophil count, 10^3/μL*	8.26 (6.04–11.56)	9.63 (6.79–14.18)	0.000
Lymphocyte count, 10^3/μL*	1.49 (0.96–2.14)	1.24 (0.71–1.82)	0.000
Platelet count, 10^3/μL*	255.0 (194–316)	254.0 (176–354)	0.891
NLR (neu/lym)*	5.34 (3.19–10.17)	7.92 (4.59–13.37)	0.000
PLR (plt/lym)*	168.73 (105.23–258.49)	204.80 (118.40–305.42)	0.001
HALP score*	0.29 (0.17–0.51)	0.18 (0.12–0.36)	0.000

* Data given as median (Interquartile range); Mann-Whitney U Test was applied.
HALP: hemoglobin, albümin, lymphocyte, platelet; NLR: neutrophil lymphocyte ratio; PLR: platelet lymphocyte ratio.

Table 2
The laboratory results of patients after 1 year follow-up.

Variables	Survivor group (N = 670)	Mortality group (N = 287)	p value
Age, years*	70.0 (64.0–77.0)	73.0 (64.0–80.0)	0.001
Gender, male, n (%)	479 (71.5%)	181 (63.1%)	0.010
pH*	7.34 (7.29–7.39)	7.31 (7.24–7.39)	0.000
pCO2, mmHg*	53.7 (44.5–65.4)	56.6 (43.8–72.4)	0.027
pO2, mmHg*	31.5 (24.7–41.9)	35.7 (25.5–50.6)	0.000
Lactat, mmol/L*	1.4 (0.9–2.3)	2.1 (1.3–3.2)	0.000
HCO3, mmol/L*	26.0 (23.8–29.4)	26.0 (22.1–31.0)	0.633
Hemoglobin, g/dl*	13.2 (11.3–15.1)	11.7 (10.4–14.0)	0.000
Albumin, g/L*	3.9 (3.6–4.2)	3.7 (3.3–4.1)	0.000
Leukocyte count, $10^3/\mu L$*	11.1 (8.6–14)	12.1 (9.1–16.5)	0.025
Neutrophil count, $10^3/\mu L$*	8.3 (6.0–11.6)	9.50 (6.8–13.60)	0.000
Lymphocyte count, $10^3/\mu L$*	1.49 (0.96–1.49)	1.35 (0.85–1.87)	0.010
Platelet count, $10^3/\mu L$*	254.5 (194.0–316.0)	258.0 (191.0–346.0)	0.534
NLR (neu/lym)*	5.33 (3.15–10.40)	7.16 (4.21–10.90)	0.000
PLR (plt/lym)*	169.62 (105.05–260.19)	193.33 (117.75–293.33)	0.008
HALP score*	0.29 (0.17–0.53)	0.22 (0.13–0.38)	0.000

* Data given as median (interquartile range); Mann-Whitney U Test was applied.
HALP: hemoglobin, albumin, lymphocyte, platelet; NLR: neutrophil lymphocyte ratio; PLR: platelet lymphocyte ratio.

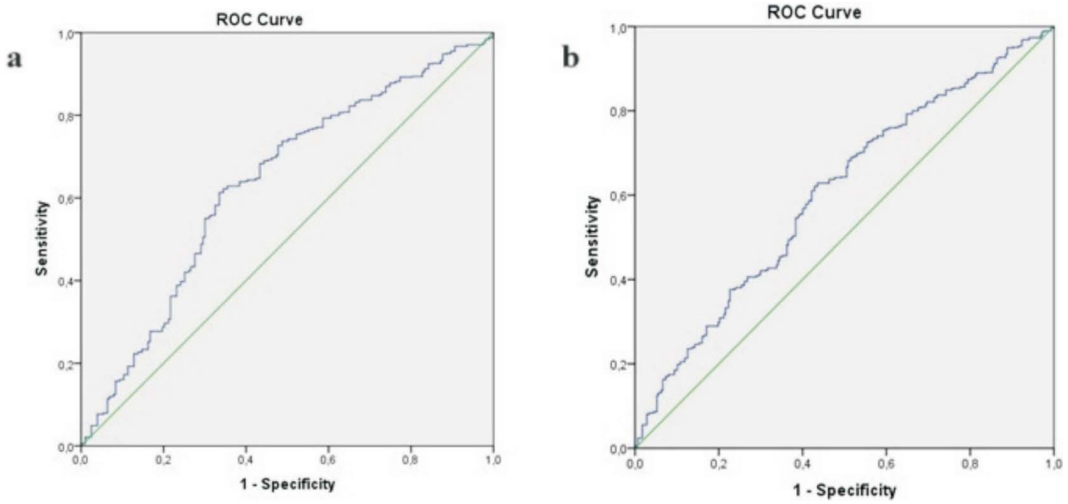

Figure 1. (a) The ROC curve analysis of HALP score on 3-month mortality of the patients. The area under the curve (AUC) of the HALP score was 0.635 (95% confidence interval [CI], 0.590–0.679). (b) The ROC curve analysis of HALP score on 1-year mortality of the patients. The area under the curve (AUC) of the HALP score was 0.604 (95% CI, 0.565–0.642).

4. Discussion

AECOPD is an acute condition frequently encountered in patients with COPD, which worsens symptoms by impairing lung function and increasing mortality.[14] Monitoring the levels of a simple biomarker that can accurately predict the complications and poor outcomes that may develop in AECOPD is important for the treatment of patients and proper use of medical resources.

Exacerbation of COPD occurs due to airway inflammation and an increase in immune modulators.[15] Increased biomarker levels indicate that the disease is more severe and carries a higher risk of mortality.[16]

The HALP score is useful in determining the prognosis of many diseases. This study investigated its potential usefulness to identify the risk of mortality in patients with AECOPD. The results indicate that a low HALP score at admission is associated with increased mortality rates at 3 months and 1 year.

According to recent studies, HALP score is an indicator of inflammation-nutritional status in many diseases[11,17] and an effective parameter in determining the prognosis of multiple patients with cancer.[12,13,18,19] Low hemoglobin levels can trigger inflammation via several pathological mechanisms.[20] In patients with COPD, increased levels of activated neutrophils and lymphocytes are associated with poor clinical outcomes and increased mortality.[21] Several studies have shown that thrombocytosis is associated with increased morbidity and mortality in patients with COPD.[22,23] Serum albumin level is a biomarker of nutritional status. Additionally, some studies have shown that albumin levels indicate inflammation and disease severity in acute diseases.[24] It is generally believed that inflammation and nutritional status are closely associated with the prognosis of patients with COPD.[7,25]

Studies that focused on patients with cancer and ischemic stroke revealed that the HALP score is closely associated with the prognosis, and low HALP scores are indicators of poor outcome and high mortality.[12,13,19,26–28] Our analysis revealed that HALP scores were lower in the 3-month and 1-year mortality groups than in the survivor group, similar to the literature. This shows that the HALP score can be used in patients presenting with COPD exacerbation to monitor prognosis and detect possible mortality in the early period.

In our study, apart from the HALP score, we also investigated the values of NLR and PLR values, which are frequently studied in patients with COPD, to determine prognosis. NLR is an indicator of

systemic inflammation and is associated with prognosis and mortality in many diseases.[29] The PLR is a newly detected marker for many systemic inflammatory diseases.[30] Previous studies have found that high NLR and PLR values are associated with poor outcomes and mortality in patients with AECOPD.[25] Tests for determining both NLR and PLR values are inexpensive and easily available in emergency department settings. We found a significant relationship between NLR and PLR values and mortality, similar to the literature. In our study, the NLR and PLR values were higher in the 3-month and 1-year mortality groups than in the survivor group. This indicates that NLR and PLR indices, akin to the HALP score, can be used to monitor the prognosis of patients presenting with COPD exacerbation and detect possible mortality at an early stage.

5. Conclusion

Decreased HALP scores and increased NLR and PLR values were important indicators for evaluating the 3-month and 1-year mortality in patients with AECOPD. Using these parameters, the response to treatment and the survival of patients with AECOPD can be monitored inexpensively and conveniently in clinical practice. These results suggest that in the emergency department setting, the HALP score in conjunction with the NLR and PLR values can be used as novel prognostic predictors of mortality in patients with AECOPD.

6. Limitations

This study had some limitations. Our study was conducted retrospectively, and the sample size was small. Because our data were obtained from patients followed-up at a single center and treated with a single treatment modality, our results may have a selection bias. Patients for whom data could not be obtained were excluded because their mortality could not be determined. These limitations can potentially limit the accuracy of the results. We believe that our study should be supported by additional prospective multicenter studies with larger sample size.

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