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Prognostic Value of the HALP Score for One-Year Mortality or Readmission in Patients Hospitalized with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Background

This study aimed to evaluate the prognostic significance of the hemoglobin-albumin-lymphocyte-platelet (HALP) score in predicting a composite outcome of all-cause mortality or chronic obstructive pulmonary disease (COPD)-related readmission within one year in patients hospitalized due to acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

Methods

In this retrospective cohort study, patients hospitalized for AECOPD at a tertiary care hospital between January 2023 and December 2024 were evaluated. 265 patients were included in the study. The HALP score was calculated using hemoglobin, albumin, lymphocyte, and platelet values at admission. The primary endpoint was defined as a composite of all-cause mortality or COPD-related readmission within one year after discharge. Independent prognostic factors were assessed using Cox proportional hazards regression, and event-free survival across HALP tertiles was compared using the Kaplan-Meier method.

Results

The mean age of the patients was 67.8 ± 8.3 years, and 77.4% were male. During the one-year follow-up, 128 patients (48.3%) experienced adverse clinical outcome. The HALP score was significantly lower in patients who experienced an adverse event than in those who did not [23.4 (27.3) vs. 31.1 (33.9); p = 0.02]. In multivariable Cox regression analysis, higher HALP scores were associated with a lower risk of the 1-year adverse clinical outcome (HR = 0.99; 95% CI: 0.98–1.00; p = 0.031), whereas long-term oxygen therapy was associated with an increased risk (HR = 1.78; 95% CI: 1.21–2.61; p = 0.003). One-year event-free survival differed significantly across HALP tertiles (log-rank p = 0.011), with the lowest event-free survival observed in the lowest HALP tertile.

Conclusions

In patients hospitalized for an AECOPD, a low HALP score, which is easily calculated from routine laboratory parameters, may serve as a practical prognostic marker that complements existing clinical and physiological assessments for long-term risk stratification.

Background

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung disease characterized by persistent and often progressive airflow limitation resulting from airway and/or alveolar abnormalities (1). COPD is one of the three leading causes of death worldwide (2). It represents a major cause of

global morbidity and mortality, with a significant and progressively increasing economic and social burden (3).

An acute exacerbation of COPD (AECOPD) is characterized by an acute worsening of respiratory symptoms that require additional treatment. Acute exacerbations represent a clinical state in which both systemic and local inflammatory burdens dramatically increase, often necessitating hospitalization (2). Hospitalization is associated with increased short- and long-term mortality, higher readmission rates, and substantial healthcare costs. Therefore, accurate early assessment of prognosis after an acute exacerbation is of major importance for identifying high-risk patients and planning appropriate follow-up strategies (3–5).

COPD is not merely an obstructive disorder confined to the lungs, but a complex disease state associated with persistent systemic inflammation (6). Previous studies have demonstrated associations between systemic inflammation and disease progression, comorbidities, and acute exacerbations. (7). Alongside systemic inflammation, the nutritional status of COPD patients is another important, yet frequently overlooked, factor that directly impacts symptom severity, length of hospital stay and overall survival (8).

The hemoglobin-albumin-lymphocyte-platelet (HALP) score is a novel biomarker calculated from hemoglobin, albumin, lymphocyte, and platelet values, which integrates inflammatory and nutritional status (9, 10). Previous systematic reviews and meta-analyses have reported that a low HALP score is an independent adverse prognostic factor in various solid-organ malignancies (11). Limited studies regarding the HALP score in COPD have reported that a lower HALP score is associated with intensive care unit (ICU) admission, as well as short- and long-term mortality in patients with AECOPD (8, 12). In a study conducted by Han et al. in COPD patients followed in the ICU due to acute exacerbation, a low HALP score was shown to be independently associated with ICU mortality (8). Another study found that the HALP score was associated with both 3-month and 1-year mortality in patients with AECOPD (12). Most studies of HALP in COPD have focused on mortality outcomes, whereas data on readmission remain limited. In particular, evidence regarding long-term composite outcomes combining mortality and COPD-related readmission is scarce.

The aim of this study was to evaluate the prognostic value of the HALP score at admission for one-year mortality or hospital readmission in patients hospitalized with AECOPD and to determine its independent contribution to predicting long-term adverse clinical outcomes.

Methods

Study Design and Ethical Approval

This single-center retrospective cohort study was performed at a tertiary training and research hospital specialized in chest diseases. The study protocol was approved by the Non-Interventional Research Ethics Committee of University of Health Sciences, İzmir Tepecik Training and Research Hospital (Date:

June 4, 2024; Decision No: 2024/05–07). The study adhered to the principles of the Declaration of Helsinki.

This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Inclusion Criteria

Patients hospitalized due to AECOPD at a tertiary chest diseases hospital between January 2023 and December 2024 were retrospectively screened for eligibility. The diagnosis of COPD was assessed based on clinical history and confirmed by a previously documented post-bronchodilator FEV_1/FVC ratio < 0.70 in the hospital information system.

To minimize selection and information bias, all eligible patients hospitalized during the predefined study period were screened using prespecified inclusion and exclusion criteria. Outcome ascertainment was based on electronic medical records and national health databases.

Exclusion Criteria

Patients without available spirometry or who did not meet spirometric criteria for diagnosis of COPD, those hospitalized for reasons other than acute exacerbation of COPD, and those lacking the necessary admission laboratory parameters required to calculate the HALP score were excluded from the study.

Study Size

No formal sample-size calculation was performed; the study included all eligible patients hospitalized with AECOPD during the predefined two-year study period.

COPD Exacerbation

An acute exacerbation of COPD was defined as a clinical condition requiring additional treatment because of worsening dyspnea, cough, and/or sputum volume or purulence beyond normal day-to-day symptom variation occurring over ≤ 14 days.

Data Collection

Demographic, clinical, and laboratory data were retrospectively obtained from the hospital electronic medical record system. These included age, sex, smoking status and smoking exposure in pack-years, body mass index (BMI), comorbidities, pulmonary function test parameters, use of long-term oxygen therapy (LTOT) and home noninvasive ventilation (NIV), and length of hospital stay. Complete blood

count, biochemical and arterial blood gas parameters obtained at admission were included in the analyses.

Charlson Comorbidity Index (CCI) with or without age component, was calculated for each patient to determine comorbidity burden (13).

Mortality data were verified using the national death notification system and electronic medical records. Data on COPD-related readmissions were obtained from electronic medical records and national personal health record system. One-year outcome status was ascertained through electronic medical records and national health databases; therefore, no patients were lost to follow-up for the primary outcome.

Pulmonary Function Testing

Spirometric measurements are performed in accordance with ATS/ERS guidelines by a certified respiratory technician with 5 years of experience (14). Spirometric measurements were performed using a ZAN 100 pulmonary function testing system (nSpire Health GmbH, Germany), in accordance with standard spirometry procedures. The device was calibrated regularly .

HALP Score

The HALP score, a multicomponent prognostic marker integrating nutritional and inflammatory status into a single index, was calculated from admission values using the following formula:

hemoglobin (g/L) × albumin (g/L) × lymphocyte count (10^9/L) / platelet count (10^9/L)

Adverse Clinical Outcome

The primary endpoint was defined as an adverse clinical outcome occurring within one year from the date of discharge. The adverse clinical outcome was a composite endpoint of all-cause death or COPD-related hospital readmission. Follow-up time was calculated from discharge to the date of the event, or to the end of the one-year follow-up period for patients without an event.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA).

The distribution of continuous variables was assessed visually using histograms and Q-Q plots and statistically using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed variables were expressed as mean ± standard deviation, whereas non-normally distributed variables were expressed as median (interquartile range [IQR]).

For comparisons between two groups, the independent-samples t-test was used for normally distributed variables, the Mann-Whitney U test for non-normally distributed variables, and the chi-square or Fisher exact test for categorical variables.

The HALP score was evaluated as a continuous variable in the primary analysis to avoid information loss and preserve statistical power. Patients were also categorized according to HALP tertiles to improve clinical interpretability, with categorical analyses performed as secondary analyses.

In the primary analysis, the association between HALP score and the one-year adverse clinical outcome was assessed using Cox proportional hazards regression. Candidate variables were initially examined using univariate Cox regression, and clinically relevant variables or those with $p < 0.10$ were considered for multivariable analysis. To minimize multicollinearity and overadjustment, closely related variables were not entered simultaneously. Albumin was excluded because it is a component of the HALP score. Among clinically related variables, pH was selected over $PaCO_2$ and LTOT over home NIV for inclusion in the final model. Results were reported as hazard ratios (HR) with 95% confidence intervals (CI). The multivariable analysis was performed using complete cases, and missing data were not imputed.

As a secondary analysis, patients were divided into HALP tertiles and event-free survival was evaluated across groups using the Kaplan-Meier method. Survival curves were compared using the log-rank test.

As an exploratory analysis, an optimal HALP cutoff of 36.4 was identified using maximally selected rank statistics. The stability of the derived cutoff was evaluated using 200 bootstrap samples. Given the substantial variability observed across bootstrap samples, the cutoff analysis was considered hypothesis-generating.

The proportional hazards assumption was assessed using Schoenfeld residuals, and multicollinearity was evaluated using variance inflation factors (VIFs). No relevant violations of these assumptions were identified.

A two-sided p value < 0.05 was considered statistically significant. No sensitivity analyses were performed.

Results

A total of 616 patients hospitalized at the tertiary care hospital with an International Classification of Diseases (ICD) diagnostic code for COPD between January 2023 and December 2024 were retrospectively screened. Patients without pulmonary function testing or who did not meet spirometric criteria for obstruction (n = 176), patients with COPD hospitalized because of lung cancer (n = 90), and patients with missing laboratory values (n = 85) were excluded, a total of 265 patients were included. (Fig. 1).

During the one-year follow-up, 48 patients (18.1%) died and 101 patients (38.1%) were readmitted because of COPD. Twenty-one patients experienced both readmission and mortality during follow-up.

The mean age of the 265 included patients was 67.8 ± 8.3 years, and 205 (77.4%) were male. During one year of follow-up, 128 patients (48.3%) experienced adverse clinical outcome (readmission or death), while no event was observed in 137 patients (51.7%).

No significant differences were observed between-group differences in age, sex, smoking history, Charlson Comorbidity Index, pulmonary function test parameters, or body mass index.

In contrast, LTOT use was more frequent in the adverse outcome group (44.5% vs. 26.3%, $p = 0.002$). Similarly, home NIV use was significantly more common in patients who experienced an event (27.3% vs. 12.4%, $p = 0.003$).

Regarding laboratory parameters, neutrophil count ($p = 0.03$) and arterial blood gas $PaCO_2$ levels ($p < 0.001$) were significantly higher in the adverse outcome group, whereas serum albumin levels were lower ($p = 0.004$).

The median HALP score at admission was significantly lower in patients who experienced mortality or readmission within one year than in those who remained event-free [23.4 (27.3) vs. 31.1 (33.9), $p = 0.02$].

Detailed demographic, clinical, and laboratory characteristics of the patients are presented in Table 1.

Table 1
Baseline demographic, clinical, pulmonary function, and laboratory characteristics according to the 1-year adverse clinical outcome

Characteristic	Total population (n = 265)	No mortality or rehospitalization (n = 137)	Mortality or rehospitalization (n = 128)	P value
Age, years	67.8 ± 8.3	67.2 ± 8.46	68.3 ± 8.08	0.27
Male	205 (77.4)	105 (76.6)	100 (78.1)	0.88
Current smoker	125 (47.2)	71 (51.8)	54 (42.2)	0.25
Smoking exposure, pack-years	50 (21)	50 (20)	50 (25)	0.84
Any comorbidity	178 (67.2)	90 (65.7)	88 (68.8)	0.60
Hypertension	132 (49.8)	66 (48.2)	66 (51.6)	0.62
Diabetes mellitus	58 (21.9)	28 (20.4)	30 (23.4)	0.66
Coronary artery disease	69 (26)	33 (24.1)	36 (28.1)	0.49
Congestive heart failure	49 (18.5)	21 (15.3)	28 (21.9)	0.21
Peripheral vascular disease	4 (1.5)	0	4 (3.1)	0.053
Cerebrovascular disease	3 (1.1)	1 (0.7)	2 (1.6)	0.61
Dementia	1 (0.4)	0	1 (0.8)	0.48
Gastroesophageal reflux disease	10 (3.8)	3 (2.2)	7 (5.5)	0.21
Liver disease	1 (0.4)	1 (0.7)	0	1.00
Chronic kidney disease	14 (5.3)	4 (2.9)	10 (7.8)	0.10
Solid tumor	19 (7.2)	10 (7.3)	9 (7)	1.00
Charlson Comorbidity Index	4 (2)	4 (2)	4 (3)	0.07

Data are presented as mean ± standard deviation, median (interquartile range), or n (%), as appropriate. Units verified against the hospital laboratory report were used: hemoglobin, g/dL; hematocrit, %; leukocytes, neutrophils, lymphocytes, platelets, and eosinophils, ×10³/μL; glucose, urea, and creatinine, mg/dL; and C-reactive protein, mg/L. Cell-count values were rescaled from cells/μL to ×10³/μL without altering the underlying data. Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; CRP, C-reactive protein; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HALP, hemoglobin-albumin-lymphocyte-platelet; LTOT, long-term oxygen therapy; NIV, noninvasive ventilation; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; SaO_2, arterial oxygen saturation.

Characteristic	Total population (n = 265)	No mortality or rehospitalization (n = 137)	Mortality or rehospitalization (n = 128)	P value
Charlson Comorbidity Index (age-unadjusted)	2 (2)	1 (2)	2 (2)	0.16
LTOT	93 (35.1)	36 (26.3)	57 (44.5)	0.002
Home NIV	52 (19.6)	17 (12.4)	35 (27.3)	0.003
BMI	25.2 (7.6)	25.3 (7.6)	24.9 (8.2)	0.64
FEV_1, mL	1010 (500)	1040 (580)	1005 (458)	0.28
FEV_1, % predicted	38 (17)	40 (22)	37.5 (14)	0.27
FVC, mL	1960 ± 602	2018 ± 661	1900 ± 530	0.11
FVC, % predicted	57 ± 20	58.5 ± 15.8	56.0 ± 13.5	0.07
FEV_1/FVC, %	57 (17)	57 (17)	55 (16)	0.72
Hemoglobin, g/dL	13.0 ± 2.09	13.1 ± 2.04	12.8 ± 2.12	0.68
Hematocrit, %	39.8 ± 6.08	40.0 ± 5.85	39.5 ± 6.32	0.56
Leukocytes, ×10³/μL	10.17 (4.82)	9.85 (4.13)	10.535 (5.325)	0.12
Neutrophils, ×10³/μL	7.65 (4.5)	7.13 (4.105)	7.95 (4.71)	0.03
Lymphocytes, ×10³/μL	1.43 (1.325)	1.55 (1.33)	1.36 (1.248)	0.09
Platelets, ×10³/μL	259 (134.5)	249 (147)	269 (128)	0.57
Eosinophils, ×10³/μL	0.09 (0.205)	0.09 (0.2)	0.065 (0.218)	0.62
Glucose, mg/dL	130 (63)	132 (62)	128.5 (64)	0.54
Urea, mg/dL	39.3 (24.2)	38.7 (24.9)	40.7 (22.7)	0.32
Creatinine, mg/dL	0.83 (0.3)	0.86 (0.3)	0.82 (0.4)	0.36
Total protein, g/L	63.9 ± 6.43	64.3 ± 6.62	63.6 ± 6.28	0.49
Albumin, g/L	36.9 ± 4.95	37.7 ± 4.85	36.0 ± 4.92	0.004

Data are presented as mean ± standard deviation, median (interquartile range), or n (%), as appropriate. Units verified against the hospital laboratory report were used: hemoglobin, g/dL; hematocrit, %; leukocytes, neutrophils, lymphocytes, platelets, and eosinophils, ×10³/μL; glucose, urea, and creatinine, mg/dL; and C-reactive protein, mg/L. Cell-count values were rescaled from cells/μL to ×10³/μL without altering the underlying data. Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; CRP, C-reactive protein; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HALP, hemoglobin-albumin-lymphocyte-platelet; LTOT, long-term oxygen therapy; NIV, noninvasive ventilation; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; SaO_2, arterial oxygen saturation.

Characteristic	Total population (n = 265)	No mortality or rehospitalization (n = 137)	Mortality or rehospitalization (n = 128)	P value
C-reactive protein, mg/L	27.9 (94.2)	25 (92.1)	30.4 (101.8)	0.48
Procalcitonin, ng/mL	0.14 (0.97)	0.20 (0.9)	0.10 (1.1)	0.72
pH	7.39 (0.07)	7.40 (0.06)	7.38 (0.06)	0.08
PaO_2, mmHg	56.5 (16.8)	56.4 (13.7)	57.9 (21.1)	0.08
$PaCO_2$, mmHg	47 (18)	44.1 (16.1)	51.3 (17.6)	< 0.001
SaO_2, %	89 (8.9)	88.8 (7.9)	89.2 (9.7)	0.28
HALP score	25 (30.6)	31.1 (33.9)	23.4 (27.3)	0.02
Length of hospital stay, days	7 (5)	6 (7)	8 (4)	0.06

Data are presented as mean ± standard deviation, median (interquartile range), or n (%), as appropriate. Units verified against the hospital laboratory report were used: hemoglobin, g/dL; hematocrit, %; leukocytes, neutrophils, lymphocytes, platelets, and eosinophils, ×10³/μL; glucose, urea, and creatinine, mg/dL; and C-reactive protein, mg/L. Cell-count values were rescaled from cells/μL to ×10³/μL without altering the underlying data. Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; CRP, C-reactive protein; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HALP, hemoglobin-albumin-lymphocyte-platelet; LTOT, long-term oxygen therapy; NIV, noninvasive ventilation; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; SaO_2, arterial oxygen saturation.

Univariate and multivariable Cox proportional hazards regression analyses were performed to identify factors associated with the one-year adverse clinical outcome.

To identify variables associated with the one-year adverse clinical outcome, univariate Cox proportional hazards regression analysis was first performed (Table 2). In univariate analysis, LTOT use (HR = 1.96; 95% CI: 1.38–2.78; p < 0.001), home NIV use (HR = 2.23; 95% CI: 1.51–3.29; p < 0.001), serum albumin level (HR = 0.94; 95% CI: 0.91–0.98; p = 0.001), $PaCO_2$ level (HR = 1.03; 95% CI: 1.01–1.04; p < 0.001), and HALP score (HR = 0.99; 95% CI: 0.98-1.00; p = 0.017) were significantly associated with the one-year adverse clinical outcome. The Charlson Comorbidity Index, FEV_1 % predicted, pH, neutrophil count, and lymphocyte count showed borderline significance at the p < 0.10 threshold for inclusion in the multivariable model. No significant association was observed between the adverse clinical outcome and age, sex, smoking exposure, or body mass index.

Table 2
Univariate Cox proportional hazards regression analysis of factors associated with the 1-year adverse clinical outcome

Characteristic	N	HR	95% CI	P value
Age, years	265	1.01	0.99–1.03	0.30
Sex	265			
Male		—	—	
Female		0.89	0.58–1.35	0.58
Smoking exposure, pack-years	265	1.00	1.00–1.01	0.56
Charlson Comorbidity Index (age-unadjusted)	265	1.15	0.99–1.33	0.07
BMI, kg/m²	265	0.99	0.96–1.02	0.38
LTOT	265			
No		—	—	
Yes		1.96	1.38–2.78	< 0.001
HALP score	265	0.99	0.98–1.00	0.017
Home NIV	265			
No		—	—	
Yes		2.23	1.51–3.29	< 0.001
pH	230	0.03	0.00–1.22	0.06
FEV_1, % predicted	265	0.99	0.97–1.00	0.06
Hemoglobin, g/dL	265	0.93	0.86–1.01	0.10
Neutrophils, $\times 10^{3/}\mu L$	265	1.04	1.00–1.08	0.06
Lymphocytes, $\times 10^{3/}\mu L$	265	1.00	1.00–1.00	0.08
Albumin, g/dL	265	0.94	0.91–0.98	0.001
$PaCO_2$ mmHg	230	1.03	1.01–1.04	< 0.001

HRs are derived from Cox proportional hazards regression. Em dashes indicate reference categories. Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; HALP, hemoglobin-albumin-lymphocyte-platelet; HR, hazard ratio; LTOT, long-term oxygen therapy; NIV, noninvasive ventilation; $PaCO_2$, arterial partial pressure of carbon dioxide.

To evaluate model validity, the proportional hazards assumption was examined using scaled Schoenfeld residuals. The global test indicated that the proportional hazards assumption was not violated (p = 0.070). However, findings suggesting a time-dependent effect were observed for LTOT, whereas the other covariates satisfied the proportional hazards assumption (p = 0.017).

In multivariable analysis, only LTOT use (HR = 1.78; 95% CI: 1.21–2.61; p = 0.003) and the HALP score (HR = 0.99; 95% CI: 0.98-1.00; p = 0.031) remained significantly prognostic markers. Accordingly, patients receiving LTOT had an approximately 78% higher risk of experiencing the adverse clinical outcome (Table 3).

Multivariable analysis showed that the HALP score was significantly associated with a lower risk of one-year mortality or hospital readmission (HR = 0.99; 95% CI: 0.98-1.00; p = 0.031). This finding indicates that each one-unit increase in the HALP score was associated with an approximately 1% reduction in the risk of the one-year adverse outcome. Age, sex, Charlson Comorbidity Index, FEV_1, and pH were not independent predictors in the multivariable model (Table 3).

Table 3
Multivariable Cox proportional hazards regression analysis of factors associated with the 1-year composite clinical outcome

Characteristic	**HR**	**95% CI**	**P value**
HALP score	0.99	0.98–1.00	0.031
Age	1.00	0.98–1.03	0.90
Sex			
Male	—	—	
Female	0.89	0.57–1.40	0.63
Charlson Comorbidity Index (age-unadjusted)	1.06	0.90–1.25	0.49
LTOT			
No	—	—	
Yes	1.78	1.21–2.61	0.003
FEV_1 (%)	0.99	0.97–1.01	0.22
pH	0.14	0.00–4.98	0.29

HRs are derived from Cox proportional hazards regression. Em dashes indicate reference categories. Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; HALP, hemoglobin-albumin-lymphocyte-platelet; HR, hazard ratio; LTOT, long-term oxygen therapy; NIV, noninvasive ventilation; $PaCO_2$, arterial partial pressure of carbon dioxide.

In the exploratory analysis using maximally selected rank statistics, an optimal cut-off value of 36.4 was identified for the HALP score. However, bootstrap resampling analysis revealed that this cut-off value exhibited marked variability. Therefore, it was decided not to use this cut-off value in confirmatory analyses, and it was interpreted solely as exploratory/hypothesis-generating. Consequently, the HALP score was handled as a continuous variable in the primary analyses of the study

Kaplan-Meier analysis demonstrated a significant difference in one-year event-free survival across HALP tertiles (log-rank p = 0.011). Patients in the highest HALP tertile had the highest probability of one-year event-free survival, whereas those in the lowest HALP tertile had substantially lower event-free survival. The intermediate HALP tertile lay between these two groups. Separation of the survival curves throughout follow-up supports the association between a low HALP score and the adverse clinical outcome (Fig. 2).

Discussion

In this study, a low HALP score at admission was significantly associated with the adverse clinical outcome comprising all-cause death or COPD-related hospital readmission within one year after discharge among patients hospitalized for an AECOPD. Each one-unit increase in the HALP score was associated with an approximately 1% reduction in the risk of the adverse clinical outcome. In supportive secondary analyses, Kaplan–Meier analysis stratified by HALP score tertiles demonstrated that patients in the lowest HALP tertile had the lowest one-year event-free survival, while those in the highest HALP tertile had the highest, with statistically significant differences between tertiles (log-rank p = 0.011). These findings suggest that the HALP score may be a readily available biomarker for long-term risk stratification after a COPD exacerbation requiring hospitalization.

Hospitalization for a COPD exacerbation represents an important turning point in the natural history of the disease. In a recent large meta-analysis including individual data from 65,945 patients, 365-day mortality and readmission rates after hospitalization for COPD exacerbation were reported as 10.9% and 32.1%, respectively (15). In the same study, the need for noninvasive mechanical ventilation and previous exacerbation-related hospitalizations were among the important determinants of adverse outcomes (15). In our study, when mortality and COPD-related readmission were evaluated as a composite endpoint, 48.3% of patients experienced an adverse clinical outcome within one year. This high event rate indicates that patients hospitalized for COPD exacerbations remain at substantial risk after discharge.

COPD is a complex disease associated with systemic inflammation, muscle loss, and nutritional impairment. Therefore, composite indices that integrate inflammatory and nutritional status may provide prognostic advantages. Indeed, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and albumin-based markers have been associated with COPD prognosis (16, 17). The HALP score combines hemoglobin, albumin, lymphocyte, and platelet parameters in a single formula and is a multicomponent,

next-generation index that simultaneously reflects systemic inflammation, immune response, and nutritional status (11).

The prognostic strength of the HALP score stems from the fact that its components holistically represent distinct aspects of COPD pathophysiology. Albumin, a negative acute-phase reactant, reflects chronic inflammation and reduced nutritional and physiological reserve (17, 18). In our study, albumin levels were significantly lower in the event group (36.0 ± 4.92 vs. 37.7 ± 4.85 g/L; p = 0.004; HR = 0.94; p = 0.001). Among the other components, lymphopenia reflects immune dysregulation, platelet count reflects systemic inflammatory activity, and hemoglobin reflects oxygen-carrying capacity and chronic disease burden (8, 12, 19). Combining these four parameters into a single index may provide a more comprehensive inflammatory-nutritional profile than individual biomarkers and may offer prognostic information about the patient's overall physiological reserve (11, 19, 20).

In one of the earliest key investigations examining the HALP score in COPD, Han et al. demonstrated that a low HALP score independently increased ICU mortality in 1,533 AECOPD patients in the intensive care unit (HR = 1.69; 95% CI: 1.14–2.53) (8). Yıldız and Ayyıldız reported that HALP predicted 3-month and 1-year mortality in patients hospitalized from the emergency department with AECOPD (12). Similarly, a recent study including 793 hospitalized patients with AECOPD found that a low HALP score was independently associated with in-hospital mortality and that a cutoff value < 16.84 provided discriminatory performance (AUC: 0.678) (20). In summary, the literature confirms a consistent relationship between low HALP scores and adverse prognosis across different follow-up durations and patient populations.

Our findings are also consistent with recently reported data on short-term readmission. Zheng and Li reported that HALP scores were lower in patients with AECOPD who were readmitted and that HALP was an independent predictor of 30-day readmission. They also reported that the HALP score decreased with increasing disease severity and could show greater discriminatory performance than CRP for predicting 30-day readmission (21). Using a one-year follow-up period and assessing mortality combined with COPD-related readmissions in our study supports the notion that HALP is not merely a short-term risk marker, but is also linked to long-term clinical trajectory.

One important challenge in the clinical use of HALP is that an optimal cutoff value has not yet been established. Previous studies have reported different HALP cutoff values depending on the patient population and endpoint (8, 20). Although an optimal cutoff of 36.4 was obtained using maximally selected rank statistics in the present study, bootstrap resampling showed that this value was unstable. Therefore, evaluating HALP as a continuous variable in the primary analysis and considering the cutoff analysis exploratory represents a more cautious methodological approach. Furthermore, the step-wise improvement in event-free survival from the lowest to the highest HALP tertile (log-rank p = 0.011) suggests that evaluating HALP as a continuous or graded risk marker may be more appropriate than relying on a single fixed threshold. Data suggesting that the association between HALP and mortality

may be nonlinear in the general population further support caution when defining a fixed universal cutoff value (19).

In our study, elevated $PaCO_2$ [51.3 (17.6) vs. 44.1 (16.1) mmHg; $p < 0.001$], home NIV use (HR = 2.23), and the need for LTOT (HR = 1.96), which may be considered markers of advanced disease, chronic hypoxemia, and hypercapnic respiratory failure, were associated with the adverse clinical outcome in univariate analysis. Previous studies have likewise shown that the need for ventilatory support and features of severe COPD are associated with increased risks of mortality and readmission after hospitalization (15). The persistence of LTOT as an independent risk factor in multivariable analysis (HR = 1.78; $p = 0.003$) should be interpreted as a marker of the underlying severe physiological impairment rather than as a direct adverse effect of the treatment itself.

One of the major strengths of our study is that, unlike previous HALP studies, it evaluated a clinically meaningful composite end point including mortality and COPD-related readmission during the one-year period after discharge rather than focusing only on short-term or in-hospital mortality. In contrast, our study differs substantially from previous reports in terms of its endpoint. Existing COPD studies have primarily evaluated in-hospital or short-term mortality (8, 12, 20). Yet, early and recurrent post-discharge hospital readmissions are both strong predictors of subsequent mortality and primary indicators of overall disease burden (22). Accordingly, our study used a composite clinical endpoint including not only mortality but also all-cause death or COPD-related readmission. Thus, we evaluated not only the association of the HALP score with survival, but also its role in predicting post-discharge disease burden and clinical instability. Second, HALP was evaluated not only using a categorical cutoff but also as a continuous variable in the primary analysis and by tertiles in the secondary analysis, thereby preserving statistical information and allowing assessment of a potential dose-response relationship.

Several limitations should also be considered. First, because of the retrospective, single-center design, selection bias and unmeasured confounding cannot be completely excluded. Second, the HALP score was calculated only from laboratory values obtained at admission; temporal changes in HALP during hospitalization or during a stable period were not evaluated. Third, HALP components may be affected by acute infection, inflammation, hydration status, medications, and comorbidities. Finally, the instability of the HALP = 36.4 cutoff in bootstrap analysis limits its use as a definitive clinical threshold. Therefore, our findings require validation in prospective, multicenter, and larger cohorts.

Conclusions

This study demonstrates that a low HALP score at admission is independently associated with the adverse clinical outcome comprising one-year mortality or COPD-related readmission after discharge in patients hospitalized for an acute exacerbation of COPD. The ability to calculate HALP easily from routine complete blood count parameters and serum albumin without additional cost or specialized laboratory testing is an important clinical advantage. Our findings suggest that the HALP score may be a simple prognostic marker that complements existing clinical and physiological assessments for

identifying high-risk patients after a COPD exacerbation requiring hospitalization. However, optimal cutoff values should be established and its prognostic performance validated in independent prospective cohorts before incorporation into clinical decision-making.

Abbreviations

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ATS, American Thoracic Society; AUC, area under the curve; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; ERS, European Respiratory Society; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HALP, hemoglobin–albumin–lymphocyte–platelet; HR, hazard ratio; ICD, International Classification of Diseases; ICU, intensive care unit; IQR, interquartile range; LTOT, long-term oxygen therapy; NIV, noninvasive ventilation; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; SaO_2, arterial oxygen saturation; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; VIF, variance inflation factor.

Declarations

Ethics approval and consent to participate

The study was approved by the Non-Interventional Research Ethics Committee of the University of Health Sciences, İzmir Tepecik Training and Research Hospital (June 4, 2024; decision no. 2024/05-07) and was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study.

Consent for publication

Not applicable. No identifiable individual participant information is presented.

Availability of data and materials

The datasets analyzed during the current study are not publicly available and cannot be shared because of patient confidentiality.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

TS, ÖÖ, MK, and GP contributed to the study conception. TS, ÖÖ, and MK collected the clinical data. TS and ÖÖ analyzed and interpreted the data and drafted the manuscript. ÖÖ, a biostatistician, supervised the statistical analysis. All authors reviewed and approved the final manuscript and agree to be accountable for all aspects of the work, including its accuracy and integrity.

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Figures

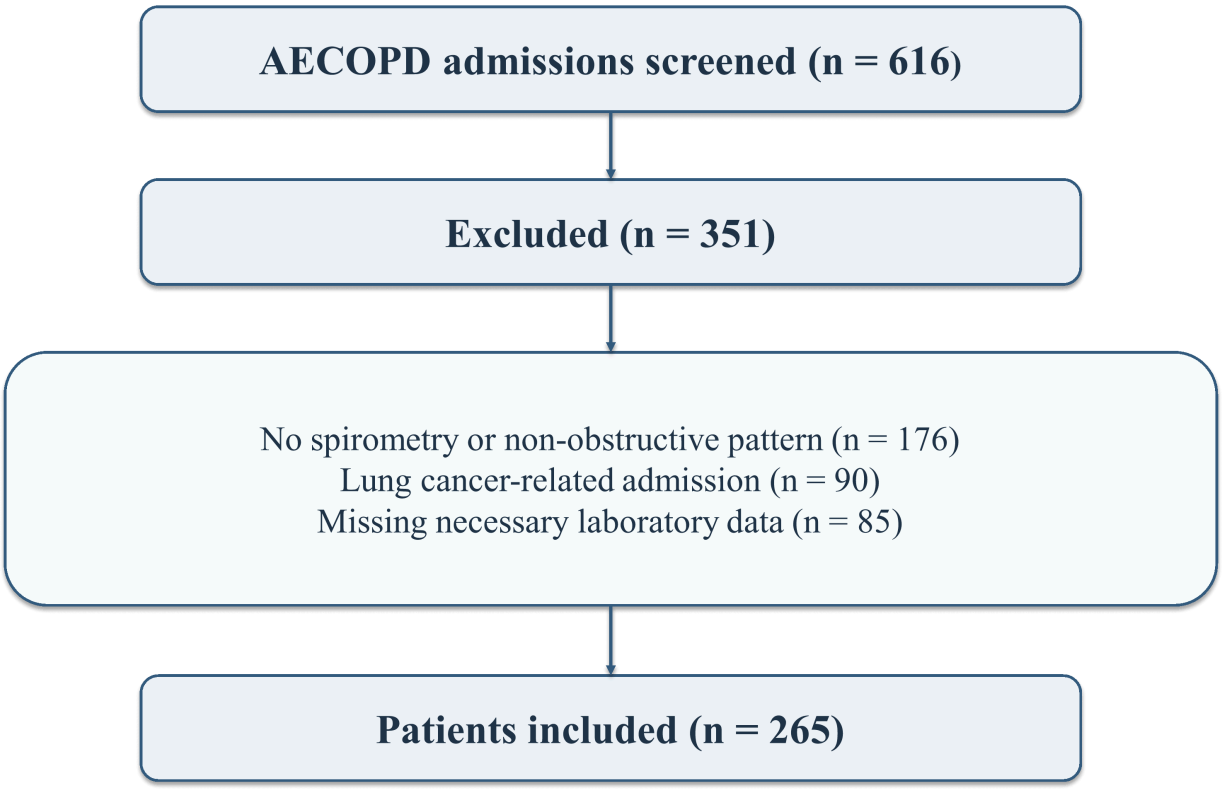

Figure 1

Patient-selection flow diagram

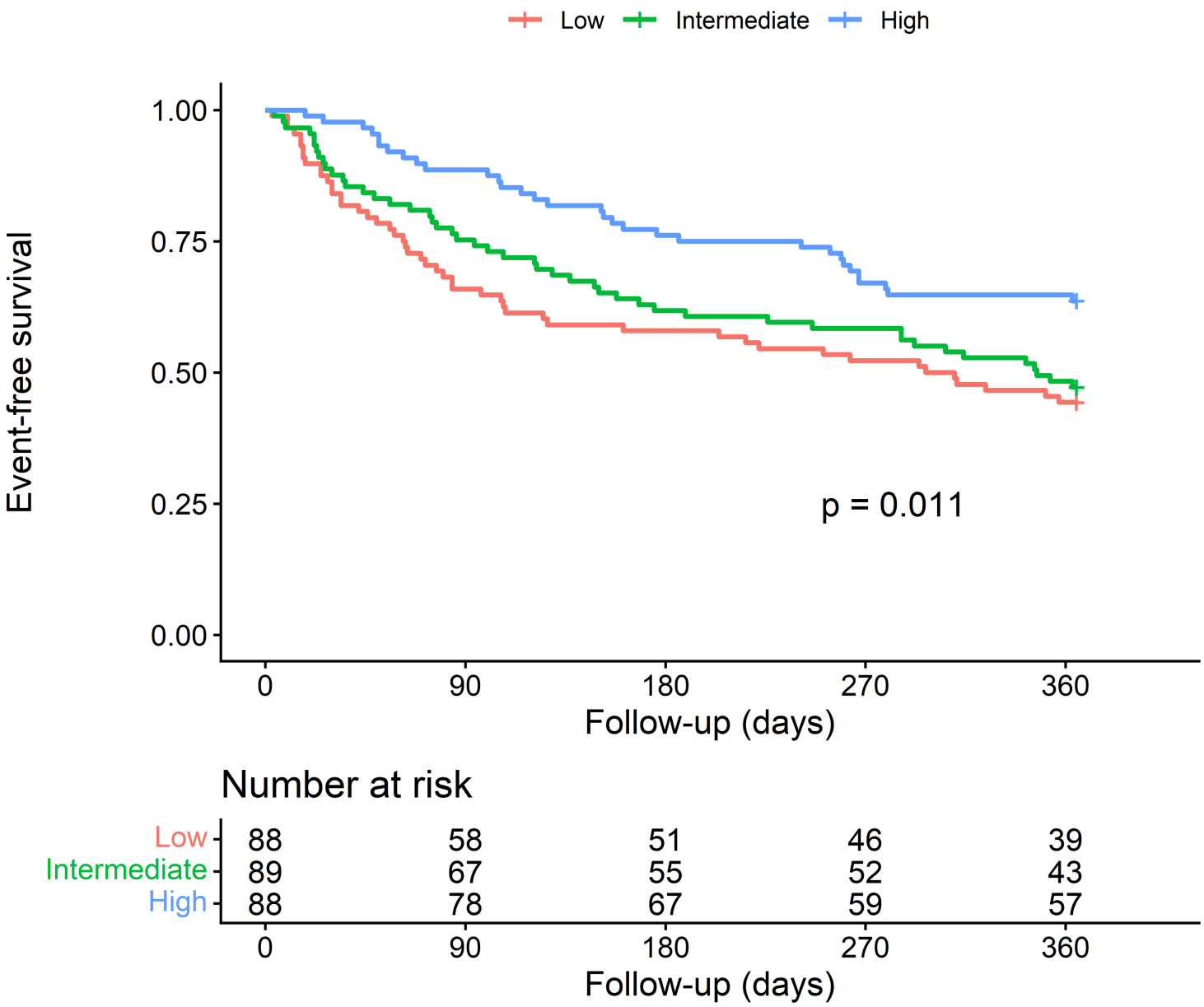

Figure 2

One-year event-free survival curves according to HALP tertiles.