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The efficiency of HALP score, neutrophil-lymphocyte ratio, and platelet-lymphocyte ratio in predicting mortality in intensive care patients

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ABSTRACT

Objective: The HALP Score, which is a combination of hemoglobin, albumin, lymphocytes, and platelets, is a new index that shows nutritional status and systemic inflammation, provides information about patient prognosis. In this study, we aimed to investigate the relationship of HALP score, platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR) and with poor prognosis in intensive care patients.

Material and Method: Our study was designed retrospectively on patients admitted from the emergency department (ED) to the intensive care unit (ICU). HALP scores, PLR and NLR values were calculated from the hemoglobin, albumin, lymphocyte, platelet and neutrophil values taken from the patients within 24 hours. One-week and three-month mortality were determined as poor outcomes. The relationship between results and poor outcomes was investigated.

Results: A total of 250 patients were included in the study. The median age of the patients was 72.5%, and 43.6% (n=109) were female. When the variables between survivors and non-survivors were compared, NLR was found to be significantly higher in non-survivors. In addition, there was a significant difference between the two groups in terms of both one-week and three-month mortality regarding age, albumin, lymphocyte, and thrombocyte values. When we analyzed the diagnostic performances of HALP Score, NLR, and PLR for one-week and three-month mortality, only NLR showed significant diagnostic performance. The optimal cut-off point for NLR for both one-week and three-month mortality was 8.22 (for one-week mortality: AUC=0.598, p=0.007; for three-month mortality: AUC=0.592, p=0.011).

Conclusion: It was observed that the HALP score was not an effective parameter in predicting prognosis in intensive care patients. It is thought that NLR has a significant relationship with one-week and three-month mortality and can be used as an effective parameter in the prediction of prognosis in intensive care patients.

Keywords: Intensive care, halp score, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio

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INTRODUCTION

Treating patients in intensive care units (ICU) and estimating mortality and morbidity has always been a challenging and critical issue for doctors. Therefore, various scoring systems have been developed for use in ICUs to predict the prognosis of patients and predict the severity of the disease (1-3). Some of the most common of these systems include Simplified Acute Physiology Score (SAPS II), Acute Physiology and Chronic Health Evaluation Score (APACHE II), Logistic Organ Dysfunction System (LODS) and Mortality Probability Model (MPM II). However, no consensus has yet been reached on which scoring system is the best for the discrimination of critically ill patients (2,4). The ideal scoring system should reveal the patient's prognosis best, and it should be easy to calculate.

General nutritional status, presence of inflammation, and susceptibility to atherosclerosis are important causes of mortality and prognosis in intensive care patients. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are valuable prognostic parameters that indicate the patient's overall immune strength against various stress factors and are used in the prognostic evaluation of several diseases, including community-acquired pneumonia, malignancies, acute pulmonary embolism, and myocardial infarction (5,6). In addition, recently, there are studies showing that an index

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called hemoglobin, albumin, lymphocyte, platelet (HALP) score reflects the general nutritional status and systemic inflammation of the patients. This score has been proven to be a useful prognostic factor in stomach, prostate, bladder and kidney malignancies and patients with an acute ischemic attack (7-11). Lymphocytes play a key regulatory role in inflammation. Platelet hyperactivity increases the risk for thromboembolism, atherosclerotic lesions and may cause abnormal thrombosis that exacerbates the inflammatory response (12). Hypoalbuminemia and anemia are indicators of malnutrition.

In this study, we investigated the prognostic role of HALP score, PLR, NLR and in patients admitted from the emergency department to the ICU.

MATERIAL AND METHOD

A retrospective design was used in the study, and it was approved by Balıkesir University Clinical Researchs Ethics Committee (Date: 08.09.2021, Decision No: 2021/182). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study consisted of 250 patients who presented to Balıkesir University Faculty of Medicine Emergency Service for various reasons between January 2020 and May 2021 and were later admitted to the ICU. All patients over the age of 18 who presented to the emergency department as an outpatient or were brought by ambulance and were admitted to the ICU after the examination and follow-up were included in the study without any exclusion criteria. Patients who had missing laboratory data and were referred to an external center during their follow-up were excluded from the study. Blood counts were analyzed using an autoanalyzer (Beckman Coulter Hematology Analyzer LH780). All serum biochemical parameters were tested using an automated biochemical analyzer (Beckman Coulter Chemistry Analyzer AU680). Hemoglobin, albumin, lymphocyte, platelet, and neutrophil values of the patients taken within 24 hours were analyzed. HALP score and NLR and PLR values were calculated based on these values. HALP score was calculated using the following formula: hemoglobin (g/L) × albumin (g/L) levels × lymphocyte count (/L)/platelet count (/L) (7,8,13). NLR was obtained by dividing the neutrophil count by the lymphocyte count, and PLR was obtained by dividing the platelet count by the lymphocyte count. Poor outcomes were considered as our patients' one-week or three-month mortality.

Statistical Analyses

Shapiro-Wilk test was used to test the normality of variables. Continuous variables with normal distribution were expressed as mean ± standard deviation, and comparisons between two independent groups were performed with independent samples t-test. Non-normal variables were expressed as median (minimum-maximum) values, and comparisons between two independent groups were performed with the Mann-Whitney U test. Receiver operating characteristics (ROC) curve analysis was performed to evaluate and compare the performances of diagnostic markers. Youden J index was used to obtain an optimal cut-off value, and related sensitivity, specificity, positive predictive, and negative predictive values were given. Binary logistic regression analysis was performed to detect the risk factors for in-hospital mortality. The significance level was taken as $\alpha = 0.05$. Two-tailed hypothesis tests were used. Statistical analyses were performed with IBM SPSS Statistics version 23.0 (IBM Corp., USA) and MEDCALC VERSION 12.3.0.0.

RESULTS

250 patients were included in our analysis. The median age of the patients was 72.50 (min-max: 25.00-96.00) years, and 43.60% (n=109) of them were female. One-week and three-month mortality rates were 34.40% (n=86) and 55.60% (n=139), respectively. When we compared the variables between survivals and non-survivals, NLR was significantly lower in the survival group than the non-survival group, both for one-week and three-month mortality. Also, there was a significant difference in terms of age, albumin, lymphocytes, and platelets between the two groups, both for one-week and three-month mortality (**Table 1, Table 2, Figure 1**).

Table 1. Comparison of patient characteristics in terms of one-week mortality

Variables	Survivor	Non-survivor	p value
Patients, n	164	86	-
Age (yr)[&]	72.00 (25.00-96.00)	75.00 (44.00-94.00)	**0.037**
Gender[#]			0.686
female	70 (42.68)	39 (45.34)	
male	94 (57.31)	47 (54.65)	
Neutrophils (10^9/L)[&]	9.35 (0.20-25.00)	10.50 (1.10-28.30)	0.347
Albumin (g/L)*	31.70±5.97	29.73±6.06	**0.014**
Hemoglobin (g/L)*	120.92±21.20	121.09±20.66	0.951
Lymphocytes (10^9/L)[&]	0.70 (0.10-42.30)	0.60 (0.10-7.80)	**0.008**
Platelets (10^9/L)[&]	263.00 (37.00-1205.00)	219.00 (40.00-589.00)	**<0.001**
HALP score[&]	10.65 (0.98-328.87)	10.57 (0.00-86.92)	0.380
NLR[&]	11.22 (0.25-135.00)	14.17 (1.92-82.00)	**0.011**
PLR[&]	335.00 (6.71-3012.50)	324.00 (32.50-1796.67)	0.706

Data given as *mean±standard deviation, &median (minimum-maximum) or #n (%)

Table 2. Comparison of patient characteristics in terms of three-month mortality

Variables	Survivor	Non-survivor	p value
Patients, n	111	139	-
Age (yr)[&]	71.00 (25.00-96.00)	75.00 (44.00-94.00)	**0.005**
Gender[#]			0.877
female	49 (44.14)	60 (43.17)	
male	62 (55.86)	79 (56.83)	
Neutrophils (10^9/L)[&]	9.30 (0.20-19.30)	9.70 (1.10-28.30)	0.223
Albumin (g/L)*	32.72±5.54	29.67±6.13	**<0.001**
Hemoglobin (g/L)*	122.06±21.61	120.11±20.49	0.467
Lymphocytes (10^9/L)[&]	0.70 (0.10-42.30)	0.60 (0.10-7.80)	**0.041**
Platelets (10^9/L)[&]	264.00 (76.00-1205.00)	236.00 (37.00-719.00)	**0.004**
HALP score[&]	10.51 (0.98-328.87)	10.71 (0.00-86.92)	0.223
NLR[&]	11.00 (0.25-135.00)	14.36 (1.92-83.33)	**0.012**
PLR[&]	340.91 (6.71-3012.50)	322.83 (32.50-2000.00)	0.774

Data given as *mean±standard deviation, &median (minimum-maximum) or #n (%)

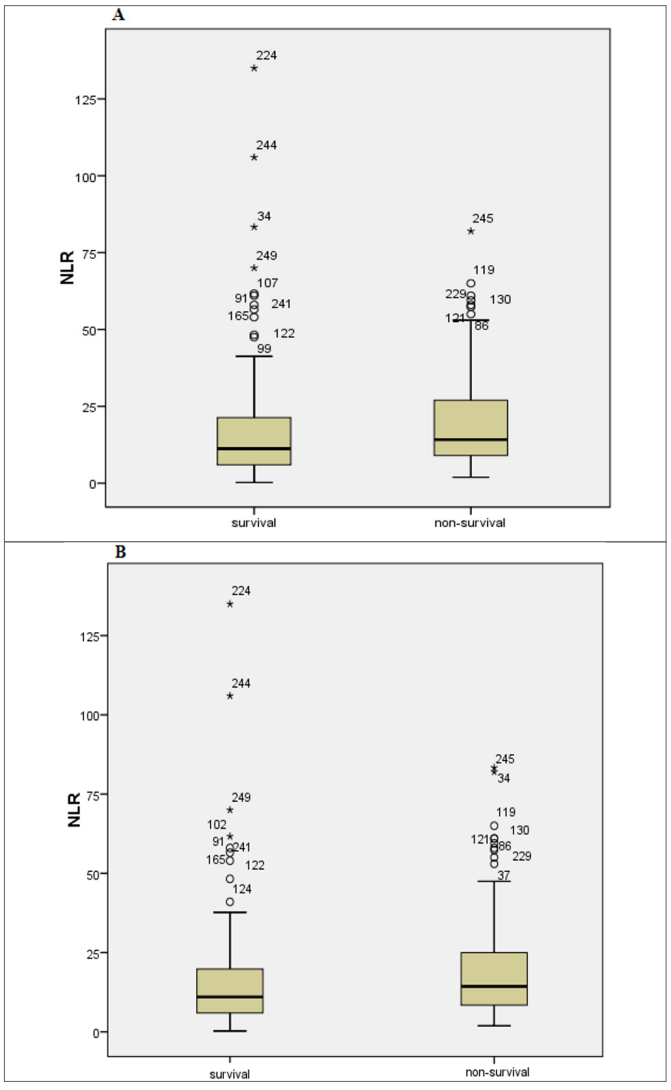

Figure 1. Box-plots for NLR in **A)** one-week survivals and non-survivals, **B)** three-month survivals and non-survivals. Outliers and extreme values are marked with ° and *, respectively.

When we examined the diagnostic performances of HALP score, NLR, and PLR for one-week and three-month mortality, only NLR showed a significant diagnostic performance. Optimal cut-off value was 8.22 for NLR both for one-week and three-months mortality (for one-week mortality: AUC=0.598, p=0.007; for three-month mortality: AUC=0.592, p=0.011) (**Table 3, Table 4**).

Table 3. ROC curve analysis results for HALP score, NLR, and PLR

	Accuracy index	HALP score	NLR	PLR
One-week mortality	AUC	0.534	0.598	0.515
	p-value	0.383	0.007	0.704
	Cut-off value	≤6.02	>8.22	>165.56
	Youden J index	0.093	0.201	0.072
	Sensitivity (95% CI)	32.56 (22.80-43.50)	82.35 (72.60-89.80)	85.88 (76.60-92.50)
	Specificity (95% CI)	76.83 (69.60-83.10)	37.80 (30.40-45.70)	21.34 (15.30-28.40)
Three-month mortality	AUC	0.545	0.592	0.511
	p-value	0.222	0.011	0.774
	Cut-off value	≤6.03	>8.22	>780
	Youden J index	0.125	0.157	0.105
	Sensitivity (95% CI)	32.37 (24.70-40.80)	76.09 (68.10-82.90)	19.57 (13.30-27.20)
	Specificity (95% CI)	80.18 (71.50-87.10)	39.64 (30.50-49.40)	90.99 (84.10-95.60)

AUC: Area under the curve, CI: Confidence interval

We performed binary logistic regression analysis with the backward conditional method by entering the significant variables and gender into the model to predict both one-week and three-month mortality, respectively. NLR was added to the model after it was categorized according to its optimal cut-off value obtained from ROC curve analysis. In the first model (p<0.001 for Omnibus test), age, albumin, platelets, and NLR (>8.22/≤8.22) were the remaining variables. Platelets and NLR were found to be statistically significant risk factors for one-week mortality. An NLR value of >8.22 increased the risk for one-week mortality 2.568 times, whereas a one-unit increase in the platelets level decreased the risk for one-week mortality 0.996 times.

In the second model (p<0.001 for Omnibus test), age, albumin, platelets, and NLR (>8.22/≤8.22) were the remaining variables. Age, albumin, platelets, and NLR were found to be statistically significant risk factors for three-month mortality. An NLR value of >8.22 increased the risk for three-month mortality 1.823 times, whereas a one-unit increase in age increased the risk for three-month mortality 1.032 times, a one-unit increase in albumin level decreased the risk for three-month mortality 0.924 times, and a one-unit increase in platelets level decreased the risk for three-month mortality 0.998 times (**Table 4**).

Table 4. Results of logistic regression analyses

Variables	One-week outcome				Three-month outcome			
	p value	OR	95% CI for OR		p value	OR	95% CI for OR	
			Lower	Upper			Lower	Upper
Age	0.082	1.021	0.997	1.044	0.004	1.032	1.010	1.055
Albumin	0.097	0.960	0.915	1.007	0.001	0.924	0.881	0.970
Platelets	0.002	0.996	0.993	0.998	0.045	0.998	0.996	1.000
NLR (RC: ≤8.22)	0.005	2.568	1.323	4.982	0.041	1.823	1.024	3.248

OR: Odds ratio, CI: Confidence interval, RC: Reference category

DISCUSSION

In this study, we examined the prognostic prediction of HALP score in intensive care patients. HALP score is a new index that combines hemoglobin, albumin levels with lymphocyte and thrombocyte counts and has been recently reported to show prognosis in various cancer and stroke patients. No significant relationship was found between HALP score and the prognosis of intensive care patients in our study, but a significant relationship was found between albumin, lymphocyte, and platelet values and mortality when the values were examined individually. Regarding HALP score and NLR and PLR values in our study, only NLR was found to be associated with one-week and three-month mortality.

ICUs are hospital units that have a high mortality rate, where critically ill patients are hospitalized. In some studies in the literature, various intensive care mortality rates have been reported (Karagöz et al. (14), 44.7%; Altaş et al. (15), 57%; Kutlucan et al. (16), 46.8%). Similar to the literature, in our study, too, one-week and three-month mortality rates were found to be 34.4% and 55.6%, respectively. Age is one of the important factors affecting the prognosis in intensive care patients. It is known that advanced age is closely associated with mortality in intensive care patients (14,16). We also found the mean age of non-surviving patients to be significantly higher than those who survived.

HALP score is a newly defined, valuable index that shows the patient's systemic inflammation and nutritional status. In this index, the general well-being of the patient is assessed based on hemoglobin, albumin, lymphocyte, and platelet values. A high HALP score is associated with longer survival (8,11,13). Anemia is a common condition in intensive care patients. The relationship between low hemoglobin levels and low quality of life has been demonstrated in randomized controlled studies (17). Serum albumin has often been used to assess nutritional status and visceral protein synthesis. Lymphocytes play a key role in inflammation. Excess platelet and hyperactivity can lead to thromboembolism and atherosclerotic lesions. HALP score, which is used to evaluate all these factors together, can give us important information about the prognosis of the patient. Peng et al. (18) showed a significant correlation between HALP score and survival in patients with bladder cancer. Feng et al. (19) stated that HALP score was an independent prognostic index in patients with esophageal cancer. Tian et al. (11) showed that HALP score was associated with 90-day and 1-year mortality in patients with stroke. Xu et al. (13) stated that HALP score was a good predictor of postoperative survival and recurrence in patients with pancreatic cancer. However, in our study, unlike the literature, HALP score did not yield significant results in terms of prognosis in intensive care patients. High albumin and lymphocyte levels showed a significant relationship with survival. However, high levels of platelet were observed in patients who survived, while low platelet levels were expected according to the HALP score. We think that we obtained an insignificant HALP score due to this situation.

PLR is recognized as a new marker in many systemic inflammatory diseases (20). PLR and NLR are indicators of the general immune response to various stress stimuli and play an important role in the prognostic assessment of a number of diseases, including community-acquired pneumonia, malignancies and myocardial infarction (5,6). Altaş et al. (15) showed that high PLR was associated with mortality in patients hospitalized in the ICU with the diagnosis of pneumonia. In addition to these, Yea et al. (21) showed that the PLR value was a significant marker for mortality in chronic obstructive pulmonary disease. However, in their study on patients with sepsis, Bıyıklı et al. (22) found no significant relationship between PLR and mortality. Although PLR is a low-cost, easy-to-use marker in intensive care conditions, similar to the Bıyıklı et al. (22), no significant relationship was found between PLR and mortality in our study, either.

NLR is an inflammatory biomarker that can be used as an indicator of systemic inflammation. It is obtained with a simple method using laboratory tests routinely performed in the hospital without additional cost. NLR has been shown to be closely associated with mortality and prognosis in many diseases (23). Gharebaghi et al. (24) (in ICU patients with sepsis), Liu et al. (25) (in sepsis patients), and King et al. (25) (in COVID-19 patients) showed that NLR was an effective marker. Altas et al. (15) reported 81.3% sensitivity, 77.1% specificity, and 11.3% cutoff value for NLR and stated that it was a good

parameter in the estimation of mortality in intensive care patients. Consistent with the literature, in our study, too, a significant correlation was found between NLR value and one-week and three-month mortality. Optimal cut-off value was 8.22 for NLR both for one-week and three-months mortality and the values were found as AUC=0.598, p=0.007 for one-week mortality and AUC=0.592, p=0.011 for three-month mortality.

CONCLUSION

The HALP score and PLR value were not found to be good predictors of prognosis in intensive care patients. It is thought that NLR has a significant relationship with one-week and three-month mortality and can be used as an effective parameter in the prediction of prognosis in intensive care patients.

Limitations

Since our study was retrospective and data were obtained from patients treated with a single treatment modality, our results may have a selection bias. Our data sample was small. Patients who were referred to an external center were excluded from the study as their mortality could not be determined. Therefore, these limitations could potentially limit the accuracy of our results. We think that our study should be supported by additional prospective, multicenter studies.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Balıkesir University Clinical Researchs Ethics Committee (Date: 08.09.2021, Decision No: 2021/182).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

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