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RESEARCH

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Is HALP score a predictor of poor prognosis in patients with hematologic malignancies admitted to the intensive care unit?

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Abstract

Background The Hemoglobin, Albumin, Lymphocyte, Platelet Score (HALP) is a novel predictive biomarker that has surfaced in the literature in recent years. It has been applied to the prediction of many clinical outcomes related to different neoplasms. Each of these inflammatory and nutritional markers is taken into account by the HALP score, which provides an overall prognosis for patients with cancer.

Methods Retrospective data was collected on the demographics of patients hospitalized to our hospital's intensive care unit (ICU) for hematologic malignancies between January 2014 and March 2021. To measure the prognostic value of the HALP score, it was retrospectively calculated for patients with hematologic malignancies on the first day of ICU admission.

This study looked into the link between the HALP score and general prognostic characteristics because it has been suggested that the HALP score is a relevant prognostic marker.

Results Patients with an HALP score <37.10 had significantly higher APACHE II scores ($p < 0.001$). They also had significantly higher rates of qSOFA score ≥2 (89.3%), as well as statistically significantly higher rates of intubation (96%) and death (96.1%) ($p < 0.001$). Our study found that a HALP score <37.1 was associated with a 47.04-fold increase in mortality risk.

Conclusion In patients with hematologic malignancies, the prognosis is strongly correlated with the HALP score. When validated in large cohorts, the HALP score, APACHE II, and q SOFA scores, either individually or collectively, can be used to guide prognostic evaluation of patients and act as a reliable predictor of unfavorable clinical outcomes in patients with hematologic malignancies.

Keywords HALP score, Hematologic malignancy, Intensive care unit

Introduction

Hematologic malignancies (HM) are associated with significant morbidity and mortality, as well as a poor prognosis, due to treatment-related complications [1–3]. The rate of survival has increased recently due to the use of monoclonal antibodies, increased chemotherapy, and both autologous and allogenic bone marrow transplantation (BMT). Nevertheless, the use of rigorous treatment protocols, the toxicity of chemotherapy, severe or long-term immunosuppression, and graft-versus-host disease

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(GVHD) can result in major side effects that necessitate intensive care unit (ICU) care.

Sepsis or septic shock, acute respiratory distress syndrome (ARDS), and surgical care are the primary causes of ICU hospitalization [4]. For most HM patients, especially those who received allogenic or autologous BMT [4–6], mechanical ventilation (MV) significantly worsens the prognosis and is fatal [7–12]. Numerous variables, such as high acute physiology and chronic health evaluation-II (APACHE II) scores [1, 3–15], sepsis [1], and neutropenia [2], have been linked to a poor outcome among critically sick patients with HM admitted to the intensive care unit (ICU); nevertheless, the findings of published research have been inconsistent. Hematologists and critical care experts would find it easier to identify patients who could have benefited from intensive care unit therapy and to make treatment decisions if there was a clear characterization of the parameters linked to a catastrophic outcome.

However, the validity of sepsis criteria for patients with hematologic cancers remains unclear.

The indicators that can be utilized to forecast the mortality rate in patients with hematologic malignancies following admission to the intensive care unit are not yet evident, though. [16–18]. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score has been discovered to be a significant predictive factor for patients and is regarded as an easily calculable index of systemic inflammation and nutritional status. [19, 20]. However, it is unknown whether the HALP score is associated with poor outcomes in patients with hematologic malignancies admitted to the ICU. Against this background, this study sought to investigate the predictive significance of the HALP score in patients with hematologic malignancies in intensive care.

Materials and methods

The demographic characteristics of patients who were admitted to the ICU of our hospital for hematologic malignancies between January 2014 and March 2021 were retrospectively recorded. Comorbidities, including history of infectious diseases during the past month, renal failure, ischemic heart disease, lung diseases, liver diseases, cerebrovascular events, and diabetes mellitus were recorded. The study included patients aged 18 years or older with hematologic malignancies that were admitted to the ICU and investigated how the APACHE, qSOFA, and HALP scores on first day of ICU admission affected the prognosis. The study group was comprised of patients diagnosed with Acute Myeloid Leukemia (AML), Acute Lymphoblastic Leukemia (ALL), Myelodysplastic Syndrome (MDS), Non-Hodgkin Lymphoma (NHL) and Hodgkin Lymphoma (HL). Hematological and biochemical results of patients with hematologic malignancies on the first day of ICU admission were recorded. The HALP score was calculated as HALP = hemoglobin × albumin × lymphocyte/platelet [21]. The performance of HALP in predicting mortality was evaluated using ROC curves. Since the HALP score has been proposed as a significant prognostic marker, this study investigated the relationship between the HALP score and general prognostic parameters. The HALP score on the first day of ICU admission of patients with hematologic malignancies was retrospectively calculated to quantify its prognostic utility. The study received ethics committee approval from our center (E-10840098-772.02-7760).

Statistical analysis

Categorical variables were expressed in frequency and percentile. Bivariate analyses were performed, and associations between categorical variables were analyzed using the chi-square test of association. The Shapiro-Wilk test was used to determine whether the distribution of the data was normal. The Student's t-test was used for normally distributed variables to assess differences between 2 groups, and Mann Whitney U test was used for non-parametric variables. Receiver operator characteristic (ROC) curves were used to assess how well the HALP score performed in differentiating patients' mortality. Area under the curve (AUC) , sensitivity, and specificity were computed, along with their respective 95% confidence intervals (CI). Age, gender, certain clinical characteristics as well as laboratory results, and treatment methods were first analyzed using the univariate logistic regression and then, the variables include age, sex and BMI , the APACHE II and qSOFA scores along with the HALP score were analyzed using the stepwise multivariate Linear regression method . Each and every statistical test has two sides. Confidence intervals (CIs) were computed with a 95% level of accuracy since statistical significance was established at 5% (p 0.05). The optimal cutoff HALP, Apache II and qSOFA scores for differentiating mortality was defined as the point on the ROC curve closest to the 0% false-positive and 100% true-positive mark. IBM SPSS (Version 24.0, IBM SPSS, IBM Corp, Armonk, NY, USA) has been used for data coding, data cleaning, and analysis.

Results

Sociodemographic and clinical characteristics of the patients are presented in Table 1. It was determined that the frequency of sepsis (78.4%), the frequency of pneumonia (%43.2) and mortality (%82.2) were statistically significantly higher in men than in women. The median and interquartile ranges of the blood values of the patients on the first day of admission to the ICU are

Table 1 Sociodemographic and general characteristics of patients

	Total (*n*=121)	Male (*n*=74)	Female (*n*=47)	*p*
Age M [IQR]	60 [28]	58 [32]	62 [27]	0.269
BMI M [IQR]	26 [7.2]	25.1 [6.7]	27.6 [5.9]	0.107
Weight M [IQR]	72 [19]	73.4 [19]	69 [20]	0.104
Height M [IQR]	1.67 [0.14]	1.7 [1.09]	1.61 [1]	0.151
HALP M [IQR]	24.2 [52.7]	18.5 [37.1]	30 [76.2]	0.108
APACHE II M [IQR]	26 [11.2]	27 [17]	25 [9.4]	0.143
Length of ICU stay. days M [IQR]	5 [5]	5 [6]	5 [5]	0.157
Comorbidity n(%)				
None	29 (24.6)	21 (28,8)	8 (17,8)	0.078
1	36 (30.5)	16 (21,9)	20 (44,4)	
2	34 (28.8)	23 (31,5)	11 (24,4)	
3+	19 (16.1)	13 (17,8)	6 (13,3)	
Sepsis n(%)				
Yes	87 (71.9)	58 (78,4)	29 (61,7)	**0.047**
No	34 (28.1)	16 (21,6)	18 (38,3)	
Previous erythrocyte suspension replacement n(%)				
Yes	85 (72)	55 (75,3)	30 (66,7)	0.308
No	33 (28)	18 (24,7)	15 (33,3)	
qSOFA n(%)				
<2	22 (18.6)	13 (17,8)	9 (20)	0.767
≥2	96 (81.4)	60 (82,2)	36 (80)	
Pneumonia n(%)				
Yes	44 (36.4)	32 (43,2)	12 (25,5)	**0.048**
No	77 (63.6)	42 (56,8)	35 (74,5)	
Intubated n(%)	89 (74.2)	59 (79,7)	30 (65,2)	0.077
Extubated n(%)	31 (25.8)	15 (20,3)	16 (34,8)	
Dead n(%)	88 (73.3)	60 (82,2)	28 (59,6)	**0.006**
Alive n(%)	32 (26.7)	13 (17,8)	19 (40,4)	

M Median and IQR: Interquartile range [IQR:Q3–Q1]

presented in Table 2. It was observed that CRP levels were statistically significantly higher in female cases than in males (p<0.025). The performance of the HALP score in predicting mortality was evaluated based on ROC curves. The optimal cutoff value of the HALP was <37.10 units (Fig. 1). The AUC was 0.924 (95% CI 0.851–0.998), *p* value < 0.001, with a sensitivity of 91.3% and a specificity of 90.6%, The optimal cutoff value of the APACHE II was > 18.8 units. The AUC was 0.783 (95% CI 0.677–0.889), *p* value < 0.001, with a sensitivity of 94.7% and a specificity of 60%, The optimal cutoff value of the qSOFA was >0.5 units. The AUC was 0.666 (95% CI 0.542–0.790), *p* value=0.008, with a sensitivity of 89.9% and a specificity of 43.3%.

Table 2 Descriptive statistics of blood values on the first day of admission to the intensive care unit

	Total	Male	Female	*p*
WBC(leukocyte)	1.53 [10.43]	2,24 [10,43]	1.52 [10,58]	0.945
Albumin	2.85 [0.79]	2,88 [0.78]	2.7 [0,71]	0.189
HGB(hemoglobin)	8.3 [2.5]	8,35 [2.6]	8.3 [2]	0.473
PLT(platelet)	30 [44]	30,5 [46]	27 [36]	0.992
CRP	142.98 [296.44]	118,65 [237.13]	231.05 [287,33]	**0.028**
Procalcitonin	4.07 [19.47]	3,61 [23.47]	6.09 [14,06]	0.884
Creatinine	1.15 [1.04]	1,15 [1.37]	1.03 [0,84]	0.219
pH	7.39 [0.12]	7,39 [7, 13]	7.38 [0,1]	0.983
pO_2	88.2 [73.8]	92,4 [84.5]	82.4 [51]	0.111
Lactate	2.8 [2.5]	2,8 [2.9]	2.85 [1,95]	0.507
Base deficit	−2.3 [9.2]	-1,8 [9.7]	-3.05 [7,75]	0.654

M Median and IQR: Interquartile range (P75–P25)

The distribution of sociodemographic and comorbidities (Fig. 2) and clinical characteristics of patients was analyzed in two subsamples: patients with HALP scores <37.10 and those with HALP scores ≥37.10 (Table 3). Results showed statistically significant differences in the APACHE II scores, qSOFA scores, intubation rates, and mortality rates in the HALP subsamples ($p < 0.05$). Patients with HALP scores <37.10 had a significantly higher APACHE II score of 28 [IQR:14.91] ($p < 0.001$). Among patients with HALP scores < 37.10, the rate of qSOFA scores ≥2 was significantly high at 89.3%, the rate of intubation was 96% and the rate of mortality was 96.1% ($p < 0.001$).

Univariate LR analysis showed that gender, HALP, APACHE II, qSOFA scores, pneumonia, and intubation were statistically significant risk factors for mortality ($p < 0.05$). Males had 3.13 times higher mortality risk (95% CI: 1.35–7.23) compared to females ($p = 0.007$), and a HALP score < 37.1 was associated with a 47.04-fold increase (95% CI: 12.67–174.73) in mortality risk ($p < 0.001$), an APACHE II score ≥26 with an 5.25-fold increase (95% CI: 2.11–13.05) in mortality risk ($p < 0.001$), a qSOFA score ≥2 with a 7.55-fold increase (95% CI: 2.71–21.04) in mortality risk ($p < 0.001$), pneumonia with a 3.29-fold increase (95% CI: 1.23–8.80) in mortality risk ($p = 0.017$) and finally, intubation with a 1261.5-fold increase (95% CI: 110.28–14426.40) in mortality risk ($p < 0.001$).

Although univariate LR analysis found that gender, HALP, APACHE II, qSOFA scores, pneumonia, and intubation were significant variables, the stepwise multivariate LR (enter method) model investigating the combined effect of these same variables found no significant effect on mortality ($p > 0.05$) (Table 4).

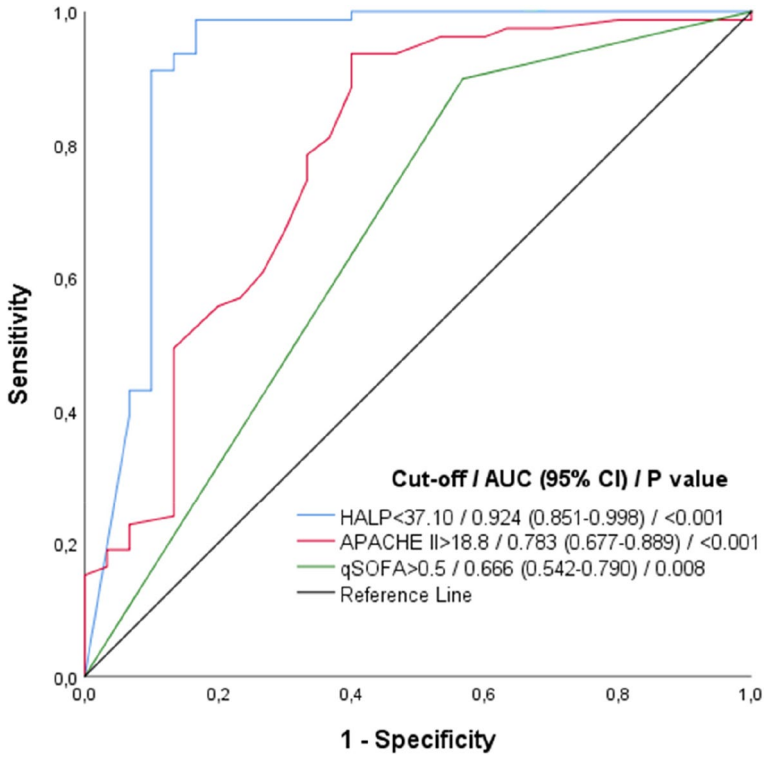

Fig. 1 The optimal cutoff value of the HALP score

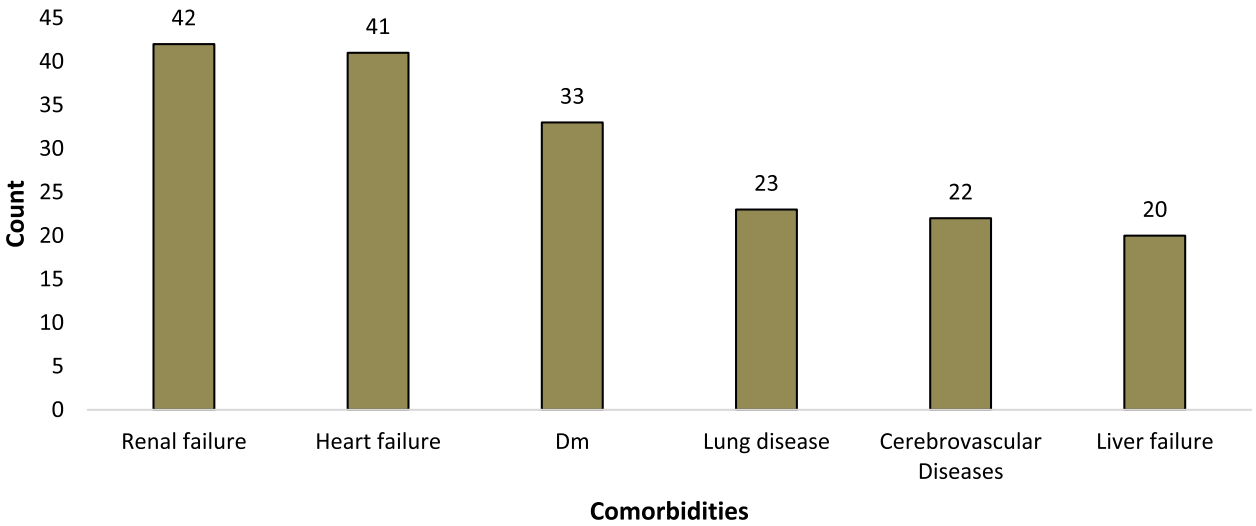

Fig. 2 Patients comorbidities distributions

Discussion

Patients with hematologic malignancies continue to experience high rates of morbidity and mortality in the ICU. Although there is sufficient evidence to define the predictors of ICU admission in this population or the predictors of survival in hospitalized patients with hematologic malignancies, predictors of mortality in patients with hematologic malignancies admitted to the ICU are poorly defined [22]. According to Vijenthira et al. [23], a combination of disease-related (acute leukemia and curative chemotherapy), laboratory-related (platelet count, albumin, and LDH), and physician-related characteristics

Table 3 Socio-demographic and clinical characteristics of subsamples with HALP ≤ 37.10 ($n = 70$), and HALP > 37.10 ($n = 51$)

	HALP < 37.10	HALP > 37.10	*p*-value
Age M[IQR]	61.5 [30.5]	60 [28]	0.979*
BMI M[IQR]	25.8 [6.85]	26.3 [7.6]	0.652*
APACHE II M[IQR]	28 [14.91]	22 [10.46]	**<0.001***
Length of ICU stay. Days M[IQR]	5 [5.5]	5 [5]	0.620*
Comorbidity n(%)			
1	22 (29.3)	14 (32.6)	0.953+
2	22 (29.3)	12 (27.9)	
3+	13 (17.3)	6 (14)	
Sepsis n(%)			
Yes	56 (73.7)	31 (68.9)	0.571+
No	20 (26.3)	14 (31.1)	
Packed red blood replacement n(%)			
Yes	56 (74.7)	29 (67.4)	0.400+
No	19 (25.3)	14 (32.6)	
qSOFA n(%)			
<2	8 (10.7)	14 (32.6)	**0.003**+
≥2	67 (89.3)	29 (67.4)	
Pneumonia n(%)			
Yes	30 (39.5)	14 (31.1)	0.355+
No	46 (60.5)	31 (68.9)	
Intubated n(%)	72 (96)	17 (37.8)	**<0.001**+
Extubated n(%)	3 (4)	28 (62.2)	
Dead n(%)	73 (96.1)	15 (34.1)	**<0.001**+
Alive n(%)	3 (3.9)	29 (65.9)	

+ Chi Square test, *Mann–Whitney U test, M: Median and IQR: Interquartile range [IQR=Q3–Q1]

were the best predictors of ICU admission in hospitalized patients with hematologic malignancies. Using scoring systems can help forecast death risk and determine how an illness will progress. This study found gender, HALP, APACHE II, qSOFA scores, pneumonia, and intubation as statistically significant predictors of mortality, which is in line with the results of many previous studies that showed that multiple organ dysfunction, renal replacement therapy, vasopressor use, and high APACHE II and SOFA scores were the most common predictors of mortality [16, 24]. This study found that patients with an APACHE II score ≥26 had a 5.25-fold increase in mortality risk, while patients with a qSOFA score ≥2 had a 7.55-fold increase in mortality risk.

Although some studies [25, 26] have reported an association between body mass index, admission due to infection, disease histology, presence of leukemia, albumin, or comorbidity index score and the risk of death, our study did not find any significant relationship between the length of ICU stay, body mass index, red blood cell replacement and the HALP score.

The growing population worldwide results in an increased need for ICU support in connection with malignancy-related problems and treatment complications, with data showing high rates of ICU and in-hospital mortality for this patient group. Patients with hematologic malignancies in need for ICU admission have mortality rates that vary between 25% and 85% [27, 28]. In the present study, the mortality rate was found to be 73.3%, which may be because our institution is a bone marrow transplant center and receives more patients with relapsed and refractory disease.

Table 4 Univariate and multivariate logistic regression models evaluating the effects of factors on mortality

	Univariate LR Odds Ratio (95% CI)	*p*-value	Multivariate LR Odds Ratio (95% CI)	*p*
Age > 60	1.23 (0.54-2.77)	0.620	5,11 (0,47-55,18)	0,179
Sex (male)	3.13 (1.35-7.23)	**0.007**	2,87 (0,37-22,19)	0,313
BMI > Median = 26	0.76 (0.34-1.71)	0.507	1,66 (0,23-12,15)	0,619
HALP < 37,1	47.04 (12.67-174.73)	**<0.001**	4,45 (0,58-34,42)	0,152
APACHE > median = 26	5.25 (2.11-13.05)	**<0.001**	1,95 (0.23-16,35)	0,540
ICU stay > median = 5	1.16 (0.51-2.62)	0.719		
Comorbidity (1)	0.89 (0.34-2.36)	0.820		
Sepsis (1)	1.57 (0.65-3.77)	0.311		
RB replacement (1)	0.90 (0.35-2.29)	0.828		
qSOFA ≥ 2	7.55 (2.71-21.04)	**<0.001**	0.43 (0.02-7.70)	0.566
Pneumonia (1)	3.29 (1.23-8.80)	**0.017**	0.54 (0.06-4.48)	0.565
Intubation (1)	1261.50 (110.28-14426.40)	**<0.001**	612.1 (0.05-25190.14)	0.550

Bold values are statistically significant ($p < 0.05$)

Abbreviation: *CI* Confidence interval, *LR* Logistic Regression, and *BMI* Body Mass Index

(1) Means it is present.

This retrospective study investigated the prognostic significance of the HALP score as a novel index in patients with hematologic malignancies admitted to the ICU, and found significantly higher APACHE II scores in patients with HALP scores <37.10 calculated on the first day of admission to ICU. We also found that the traditional risk factors, APACHE II and q SOFA, improved discrimination power for mortality risk.

The HALP score has been demonstrated in recent research to be a useful prognostic marker in patients with cancer [20, 29] and to function as an indicator of inflammation and nutritional status in patients [19, 30, 31]. Lymphocytes lessen inflammation, whereas anemia and thrombosis increase it [32]. Contrarily, serum albumin is thought to be a marker of nutritional status and, in some studies, may also be a marker of the degree of autoinflammation and disease. [33]. The four hematological parameters stated above are combined to get the HALP score. Increased HALP scores were linked to a lower risk of death and stroke recurrence at 90 weeks in a prospective research by Tian et al. [33], and 1 year after the beginning of stroke, the HALP score was regarded as a robust indication of stroke. In a previous study that was comparable to this one, Kittinun et al. discovered that in a cohort of 1588 patients with locally advanced cervical cancer (LACC) receiving radiotherapy or chemoradiotherapy, a lower HALP score was an independent predictor of worse oncologic outcomes [34, 35]. Also, a similar study showed that the HALP score was a significant prognostic predictor not only in patients who could be operated early on but also in LACC patients who received only adjuvant therapy [36]. Many studies have shown that nutritional status and inflammatory response play a central role in the progression of cancer [37, 38]. The superiority of the HALP score over other scoring systems is derived from its combination of hematologic and biochemical parameters and its ability to provide clinical information about nutritional status. Thus, an increase in albumin, lymphocyte and hemoglobin levels was associated with good prognosis, and an increase in platelet levels was associated with poor prognosis. In conclusion, patients with a high HALP score were shown to have a better prognosis [39, 40], a result that was confirmed in our study. Similar studies have successively shown a similar positive association in pancreatic, esophageal, bladder and small cell lung cancers [19, 41]. The present study found that a HALP score <37.1 was associated with a 47.04-fold increase in mortality risk. A low pretreatment HALP score is a reliable and negative prognostic biomarker for survival outcomes in patients with hematology patients.

Limitation

This study has several limitations. Firstly, it has biases inherent to its retrospective, single-center design. Secondly, the HALP score was not collected in a public database of individuals with hematological malignancies. Thirdly the fact that it is the first to look into the use of the HALP score in patients with hematologic malignancies admitted to the ICU, that it was conducted in a single center with a small number of patients, and that it only calculated the HALP score at the time of admission without monitoring changes over time. Multicenter cohort studies are required to validate these findings.

Conclusion

HALP score may be a valuable prognostic marker for hematology patients. Integrating this minimally invasive and easily accessed biomarker into current hematologic practice might be helpful in risk stratification.

In patients with hematologic malignancies, the prognosis is strongly correlated with the HALP score. When validated in large cohorts, the HALP score, APACHE II, and q SOFA scores, either individually or collectively, can be used to guide prognostic evaluation of patients and act as a reliable predictor of unfavorable clinical outcomes in patients with hematologic malignancies. In conclusion, patients with a high HALP score were shown to have a better prognosis. By virtue of being a strong prognostic indicator, HALP shows potential in guiding the way in informing when clinicians should use in their practice.

Future studies should focus on optimizing the HALP score as well as if doing so improved outcomes.

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Authors' contributions

SS contributed to the conception and design of the work, drafted the work, and revised it. BT shared in the acquisition and analysis of data, shared in writing the manuscript, drafted the work, and revised it. All authors read and approved the final manuscript.

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Availability of data and materials

The authors agree with sharing, copying, and modifying the data used in this article, even for commercial purposes, so long as appropriate credit is given, and possible changes are indicated.

Declarations

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Istanbul Medipol University of Medical Sciences, Istanbul, Turkey

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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