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Original Article

A novel prognostic tool for predicting mortality in palliative care patients: HALP score

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Abstract

Objective: Patients who have high mortality are treated in Palliative Care Units (PCU). The prognostic data to be obtained in the initial evaluation of these patients is important for planning the most appropriate clinical approach. The prognostic role of hemoglobin, albumin, lymphocyte, and platelet (HALP) score was investigated in the study.

Methods: A total of 1,317 patients who received treatment in PCUs between January 2018 and December 2021 were included in this retrospective study. HALP scores of patients during admission to PCU were calculated. The patients were divided into two groups as discharge and mortality and HALP scores and other clinical characteristics of the two groups were compared. The relationship between HALP score and mortality was evaluated statistically.

Results: HALP score median of the mortality group (11.06) was lower than discharge group (21.36) ($p<0.001$). In the subgroup analysis made according to the presence of malignancy, it was found that the HALP score differed at significant levels between the discharge and mortality groups, regardless of malignancies ($p<0.005$). It was found in the regression analysis that the HALP score remained an independent predictor of mortality ($p=0.005$). In the receiver operating curve (ROC) Analysis, the optimal HALP score of patients was found to accurately predict mortality with a cut-off value of 20.51 with 77.7% sensitivity and 52.3% specificity ($p<0.001$). Having a HALP score of ≤20.51 during hospitalization was found to increase the probability of mortality 2.75 times.

Conclusion: The results showed that the HALP score could be a new prognostic tool to provide an effective mortality prediction in palliative care patients. The HALP score, along with other clinical data, may contribute to a more accurate prognostic prediction.

Keywords: HALP score, palliative care, prognostic tool.

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INTRODUCTION

There is a constant change in the age structure of the world population. Today, people are living longer and fertility levels are also decreasing. In parallel with this, the number and proportion of elderly people are constantly increasing in the world. On a global scale, the proportion of the elderly population aged 65 and over is expected to rise from 9.3% in 2020 to 16.0% in 2050 (1). Many elderly people who have serious chronic illnesses face complex health problems for which palliative care is indicated. Palliative care is a multidisciplinary approach aiming to prevent disease-related problems, relieve symptoms, reduce pain, support psychosocial needs, and increase the quality of life in patients who have diseases with high morbidity and mortality rates (2,3). The serious diseases with high morbidity and mortality are malignant diseases and geriatric diseases, human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) along with other non-malignant diseases such as congestive heart failure, cerebrovascular diseases, neurodegenerative diseases, and chronic respiratory failure (4,5). Malnutrition has an important place in these patients for whom palliative care is considered (6). Malnutrition is a common problem that can be seen in many chronic and severe diseases and is detected in 70-80% of cancer patients. It was also found that malnutrition has negative effects on survival and quality of life (7,8). As a negative acute phase marker, serum albumin can be used to evaluate the nutritional status of patients. Hypoalbuminemia may develop because of malnutrition, systemic inflammation, hypercatabolism, and increased cytokine secretion (9). The hemoglobin, albumin, lymphocyte, and platelet (HALP) score is a novel index showing systemic inflammation and nutritional status and can be easily calculated by peripheral blood cell counts and albumin values. A great deal of research has been conducted recently reporting that the HALP score can be used to predict prognosis and survival rates in cancer patients. A low HALP score was shown to be attributed to poor prognosis in several types of cancer, including bladder, stomach, esophageal, colorectal, and prostate cancers (10-14). However, the literature is lacking in studies that examine the effects of HALP score on mortality in a patient population consisting of patients who have malignancies and patients who are without malignancies, including different cancer types.

In the present study, the purpose was to investigate the role of the HALP score during the first hospitalization in the prediction of mortality in patients admitted to the Palliative Care Unit (PCU) for palliative care treatment.

Table 1. General characteristics of the patients

Variables		All Hospitalizations (n=1,317)
Gender	Male	692 (52.54%)
	Female	625 (47.46%)
Age (years)		79 (20-110)
Hospitalization duration (day)		10 (1-333)
Malignancy	Exists	287 (21.79%)
	None	1,030 (78.21%)
Mortality		358 (27.18%)

Table 2. Univariate comparisons of hospitalizations ending in discharge and mortality and multivariate binomial logistic regression results

Variables		Univariate Analysis			Multivariate Analysis			
		Discharge (n=959)	Mortality (n=358)	p	Coefficient (SE)	Wald	p	OR (95% CI)
Gender	Male	495 (51.62%)	197 (55.03%)	0.270				
	Female	464 (48.38%)	161 (44.97%)					
Age (years)		79 (20-103)	79 (30-110)	0.500				
Neutrophil count (10^9/L)		6.62 (0.02-51.3)	8.13 (0.02-42.91)	<0.001	0.043 (0.014)	10.144	0.001	1.044 (1.017-1.073)
Hemoglobin (g/L)		111.8±21.8	104.5±20.4	<0.001	0.088 (0.039)	5.029	0.025	1.092 (1.011-1.18)
Albumin (g/L)		33 (14-51)	25 (7-45)	<0.001	-1.83 (0.149)	150.603	<0.001	0.16 (0.12-0.215)
Lymphocyte count (10^9/L)		1.3 (0.2-10.34)	0.88 (0.1-3.41)	<0.001	-0.849 (0.160)	28.194	<0.001	0.428 (0.313-0.585)
Platelet count (10^9/L)		206 (15-1,532)	212.5 (2-1,266)	0.870	0.001 (0.001)	0.779	0.377	1.001 (0.999-1.002)
HALP score		21.36 (0.95-500)	11.06 (0.26-312.48)	<0.001	0.013 (0.005)	7.887	0.005	1.013 (1.004-1.023)
Hospitalization duration (days)		9 (1-333)	15 (1-207)	<0.001				
Malignancy	Exists	132 (13.76%)	155 (43.30%)	<0.001	1.305 (0.168)	60.151	<0.001	3.688 (2.652-5.129)
	None	827 (86.24%)	203 (56.70%)					

Abbreviations; *CI: Confidence interval, HALP: Hemoglobin, albumin, lymphocyte, and platelet, OR: Odds ratio, SE: Standard error*

MATERIALS AND METHODS

Approval for the study was obtained from the Hitit University Faculty of Medicine Clinical Research Ethics Committee (Decision no:2022-101, decision date:11.30.2022). Patients receiving palliative care treatments in the PCU of a tertiary education and research hospital constituted the study population. Patients treated in CPUs between January 2018 and December 2021 were included in the Study. Patients hospitalized in PCU were those with active malignancies who did not have the chance for medical and surgical treatment and those without any malignancies. All laboratory data, clinical characteristics, and medical history of the patients required for the study were retrospectively scanned by using the hospital's electronic database. Patients under the age of 18, with a known hematological disease, pregnancy and breastfeeding status, and those whose laboratory data on the first day of hospitalization required for the study and other patient data could not be reached, were excluded from the study. Then, the demographic/clinical characteristics of the patients (age, gender, length of hospital stay, presence of active malignancy, and mortality), hemoglobin, albumin, lymphocyte, platelet, and neutrophil values were recorded. The HALP score was calculated based on the hemoglobin, albumin, lymphocyte, and platelet values at the time of admission to the PCU and using the formula: Hemoglobin (g/L)×albumin×(g/L) lymphocyte count(/L) / platelet count(/L) (13). According to hospitalization results, patients were divided into two groups as those discharged from the hospital without death (the discharge group) and those discharged from the hospital because of death (the mortality group). These two groups were compared with statistical methods in terms of demographic characteristics, laboratory data, HALP score, and length of hospital stay. The relationship between HALP score and mortality was evaluated using statistical methods.

Statistical analysis

All statistical analyses were made with the IBM SPSS Statistics Made using Windows software (version 26; IBM Corp., Armonk, NY, USA). Descriptive statistics were reported by using numbers and percentages for categorical variables, mean ± standard deviation for normally distributed numerical variables, and median and minimum and maximum values in brackets for non-normally distributed numerical variables. The normal distribution of the data was checked with the Shapiro-Wilks test. Pearson's and Spearman's correlations were used between variables in accordance with the data distribution to evaluate the relationships between the variables. The comparison of the numerical measurements for two independent groups according to the study groups was made in accordance with data distribution and by using the Mann-Whitney U test for age, length of hospital stay, serum neutrophil, lymphocyte, platelet counts, albumin level, and HALP score, and student t-test was used for serum hemoglobin level only. The ratio comparisons of the categorical variables of gender and mortality distribution according to

Table 3. Comparison of HALP scores between discharge group and mortality group (with subgroup analysis for malignancy)

Variables		Discharge (n=959)	Mortality (n=358)	p
HALP score (All patients, n=1,317)		21.36 (0.95-500)	11.06 (0.26-312.48)	<0.001
Subgroups	No malignancy (n=1,030)	22.96 (0.96-336.07)	12.1 (1.03-195.62)	<0.001
	Malignancy exists (n=287)	13.9 (0.95-500)	9.85 (0.26-312.48)	0.002

Abbreviations; *HALP: Hemoglobin, albumin, lymphocyte, and platelet*

Table 4. HALP Score cut-off values for mortality prediction (with subgroup analysis for malignancy)

Variables		Cut-off	Diagnostic values					ROC analysis			Odds ratio	
			Sensitivity	Specificity	PPV	NPV	Accuracy	AUC(SE)	95% CI	p	OR (95% CI)	p
HALP score (All patients, n=1,317)		<20.51	77.4%	52.3%	37.7%	86.1%	59.1%	0.691 (0.017)	0.659-0.724	<0.001	3.756 (2.844-4.961)	<0.001
HALP score (subgroups)	No malignancy (n=1,030)	<19.62	73.9%	57.3%	29.8%	89.9%	60.6%	0.691 (0.021)	0.651-0.732	<0.001	3.800 (2.699-5.351)	<0.001
	Malignancy exists (n=287)	<12.02	58.1%	59.1%	62.5%	54.5%	58.5%	0.608 (0.033)	0.543-0.673	0.002	2.000 (1.248-3.204)	0.004

Abbreviations; *AUC: Area under curve, CI: Confidence interval, HALP: Hemoglobin, albumin, lymphocyte, and platelet, NPV: Negative predictive value, OR: Odds ratio, PPV: Positive predictive value, ROC: Receiver operating curve, SE: Standard error*

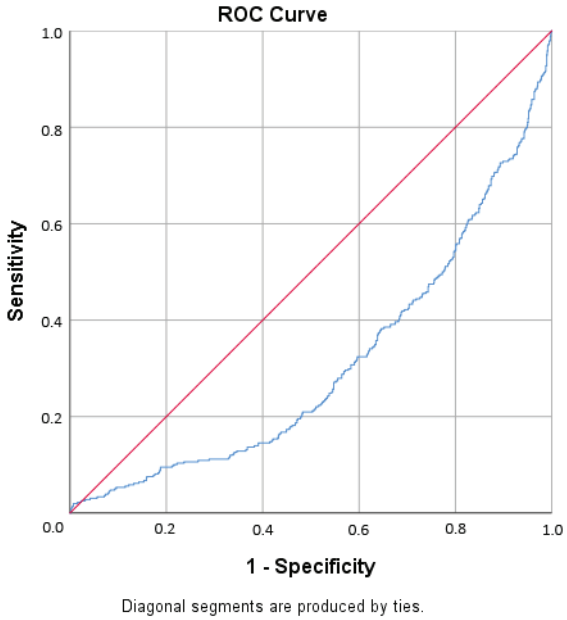

Figure 1. Receiver operating curve of HALP score (Whole group)

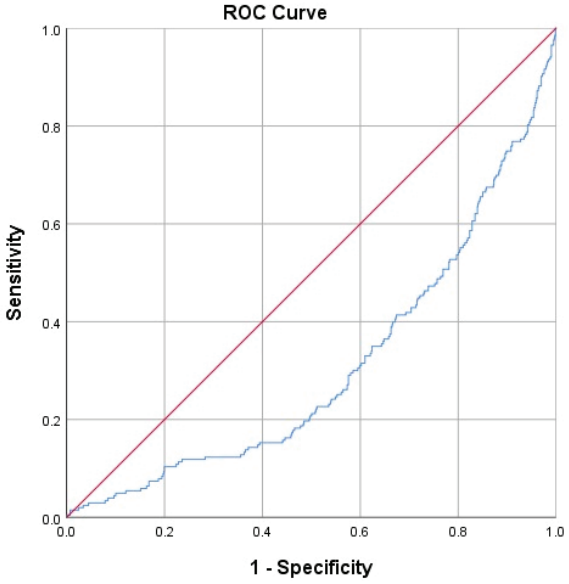

Figure 2. Reciever operating curve of HALP score (No malignancy group)

the study groups were evaluated by using the chi-square test. The predictive power of the HALP score in patients who had and who did not have malignancies was evaluated by performing subgroup analyzes according to the presence of malignancy. The receiver operating curve (ROC) analysis was performed according to the presence of mortality to show the distinctiveness of the HALP score, and optimal cut-off values were found for markers by using area under the curve (AUC) and Youden's index. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and precision values were calculated for these cut-off values. According to these cut-offs, the odds ratio values were found by calculating, and $p<0.05$ was accepted for statistical significance level.

RESULTS

A total of 1,317 patients whose data could be accessed were included in the study. A total of 692 (52.54%) patients were male and 625 (47.46%) were female in the whole group. The median age of the patients was 79 years, and the median length of stay was 10 days. There were 287 (21.79%) patients who had active malignancies in the whole group (Table 1). The median HALP score of all patients was calculated as 18.05.

Comparison of discharge and mortality groups

The patients were divided into two groups as the discharge group and the mortality group. No statistically significant differences were detected between the groups in terms of gender and age ($p=0.270$, $p=0.500$, respectively). The median length of stay was 9 days in the discharge group and 15 days in the mortality group. The hospitalization times of the patients in the group were longer at significant levels ($p<0.001$) (Table 2). When the laboratory examination results were examined, hemoglobin, albumin values, and lymphocyte counts were found to be lower and neutrophil counts were higher at statistically significant levels in the mortality group compared to the discharge group ($p<0.001$), but no significant difference was detected between the platelet counts ($p=0.870$). The HALP score median of the mortality group was lower at statistically significant levels compared to the discharge group (median HALP score=11.06, 21.36, respectively) ($p<0.001$) (Table 2).

A total of 13.7% of the patients who were discharged and 43.30% of patients who had mortality had active malignancies. Malignancy was higher in the patient group with a mortality outcome at statistically

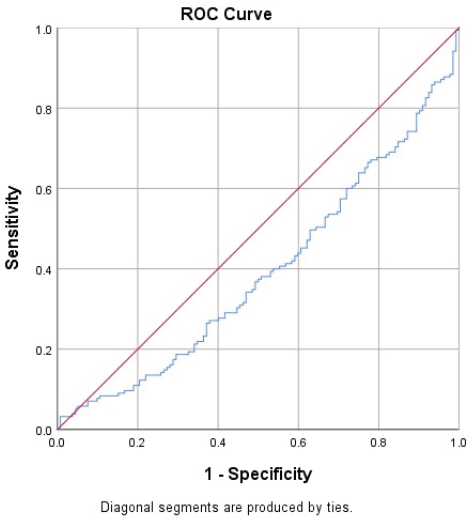

Figure 3. Receiver operating curve of HALP score (Malignancy group)

significant levels (p<0.001) (Table 2).

The binomial logistic regression analysis that was made to evaluate the differences between the groups classified 79.4% of the model cases as statistically significant [$\chi^2(4)=423.901$], p<0.001]. In the multivariate analysis, neutrophil, hemoglobin, albumin, lymphocyte, HALP score, and malignancy excluding platelet count were still independent predictive factors of mortality (for platelet, p=0.377, p=0.001, p=0.025, p<0.001, p<0.001, p=0.005, p<0.001, respectively). It was also found that a 1-unit decrease in the HALP score increased the probability of mortality by 1.3% [Exp(B)=1.013, 95% CI (1.004-1.023), p=0.005]. The presence of malignancy increased the probability of mortality 3.69 times [Exp(B)=3.688, 95% CI (2.652-5.129), p<0.001] (Table 2).

When subgroup analysis was made according to the presence of malignancy, in patients without malignancies, the median HALP score was 22.96 in patients who resulted in discharge and 12.10 in patients that resulted in mortality (p<0.001). In patients who had malignancy, the median HALP score was 13.90 in patients who were discharged and 9.85 in patients who had mortality (p=0.002). With or without malignancy, the HALP score differed between patients who had discharge and mortality (Table 3).

The prognostic value of HALP score in predicting mortality

To find the optimal value that best represented the ability of the HALP score to predict mortality in patients who were included in the study [AUC(SE)=0.691 (0.017), 95% CI (0.659-0.724), p<0.001]. The cut-off value of the HALP score was found to be 20.51 with 77.7% sensitivity, 52.3% specificity, 37.7% PPV, 86.1% NPV, and 59.1% test accuracy [OR=3.756, 95% CI (2.844-4.961), p<0.001] (Table 4 and Figure 1). When subgroup analysis was performed, ROC analysis was made to find the optimal value that best represented the ability of the HALP score to predict mortality in 1030 patients who were without malignancies [AUC(SE)=0.691 (0.021), 95% CI (0.651-0.732), p<0.001]. The cut-off value of the HALP score was found to be 19.62 with 73.9% sensitivity, 57.3% specificity, 29.8% PPV, 89.9% NPV, and 60.6% test accuracy [OR 3.8, 95% CI (2.699-5.351), p<0.001]. ROC analysis was also made for 287 patients who had a history of malignancy to find the optimal value that best represented the ability of the HALP score to predict mortality [AUC(SE)=0.608 (0.033), 95% CI (0.543-0.673), p=0.002]. The cut-off value of the HALP score was 12.02 with 58.1% sensitivity, 59.1% specificity, 62.5% PPV, 54.5% NPV, and 58.5% test accuracy [OR=2.000, 95% CI (1.248-3.204), p=0.004] (Table 4, Figures 2 and 3).

According to the analysis of the study data, the HALP score was found to be successful in predicting mortality in patients receiving palliative care treatments in PCUs, and a HALP score of 20.51 and below at the time of hospitalization increased the probability of mortality approximately 2.75-fold. Similarly, it was found that a HALP score of 19.62 and below was detected in patients who were without malignancies increased the probability of mortality 2.8-fold, and a HALP score of 12.02 and below increased the probability of mortality approximately 2-fold in patients who had malignancy (Table 4).

The relationship between HALP score and length of hospitalization

The median length of hospital stay was found to be 11.5 days in patients who had a HALP score of 20.51 and below, and 8 days in patients who had a HALP score above 20.51. Statistically significant differences were detected in the groups in this respect (p<0.001).

A multivariate linear regression analysis was made by including gender, age, presence of malignancy, and HALP score to evaluate the relationship between the length of stay and other variables. The model was statistically significant [$R^2=0.02$, F (4.1312)=6.637, p<0.001]. Although age and presence of malignancy lost their significance for the duration of hospitalization (p=0.738, p=0.377, respectively), it was found that HALP score and gender remained independent determining factors in the multivariate analysis (p<0.001, p=0.009, respectively). A 10-unit decrease in HALP scores prolonged hospitalization by approximately 1 day [B=0.096, 95% CI (-0.140, -0.051), p<0.001].

DISCUSSION

Most cancer patients who have no chance of surgical and medical treatment and patients who have non-cancer diseases such as chronic inflammatory diseases, cerebrovascular diseases, neurodegenerative diseases, and chronic respiratory failure are followed and treated in PCUs. Many of these patients also have impaired nutrition because of their diseases. High mortality is an expected result in this patient population with comorbidities. Reliable mortality markers predicting the overall survival of patients are very important for clinicians to make informed treatment decisions and to inform patients and/or their relatives more accurately.

The HALP score is a novel index whose prognostic value was investigated in many cancer types, but its prognostic

role in patients receiving palliative care treatments has not yet been investigated. In the present study, the role of the HALP score was investigated as an indicator of nutrition and inflammation in predicting mortality in PCU patients. It was found that there was a correlation between low HALP scores and mortality in patients receiving palliative care. It was also found that patients who had low HALP scores had longer hospital stays. If our results are confirmed by further studies, The HALP score can make a significant contribution to improving mortality prediction accuracy for clinicians working in PCU when combined with clinicians' own clinical experience and estimates.

The HALP score is a novel index of systemic inflammation and nutritional status (15). Although low hemoglobin and increased platelet count, which are the parameters that make up this score, may exacerbate inflammation, lymphocytes reduce inflammation (16). Serum albumin, however, is considered an indicator of nutritional status, and hypoalbuminemia may develop in cases of systemic inflammation and malnutrition (9, 17). Many previous studies showed that parameters indicating nutritional and inflammation status, including hemoglobin, albumin, lymphocyte, and platelet values, have very important roles in cancer survival (18-21). Liu et al. reported that elevated serum albumin reduced the risk of mortality by 45% in patients who have non-metastatic breast cancer (22). Present study results also showed that neutrophil count, hemoglobin and albumin value, and lymphocyte count may be independent prognostic factors for mortality prediction. Our results confirmed previous study results. Combinations of these hematological parameters, such as neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), and platelet-lymphocyte ratio (PLR), were shown to predict prognosis more accurately than one single parameter (23,24). However, it was also suggested that the HALP score, which is created by combining hematological parameters with albumin, is one of the best prognostic determinants among hematological parameters in some cancers. In a study conducted by Cong et al, the HALP score was found to be a significant independent prognostic factor when compared with the prognostic indices NLR and PLR in esophagus carcinoma (12). Again, another recent study conducted by Guo et al. in patients who had metastatic prostate cancer revealed that the HALP score has a higher predictive ability for cancer prognosis than NLR and PLR (14). The common characteristics of our patients in PCU were that they had an inflammatory disease and/or their nutrition was impaired. We also found that the HALP score was similar to that of our patient population. The present study was planned by predicting that it could be an ideal prognostic index for estimating mortality. Present study results showed that the HALP score can be successful in predicting mortality in patients receiving palliative care, confirming our prediction.

Recent studies also show that the HALP score is a predictive index for the survival of many solid cancer patients including gastric (11), colorectal (13), pancreatic (19), kidney (25), and bladder (10) cancers. A low HALP score was found to indicate a poor prognosis in these studies. The prognostic role of the HALP score was also investigated in patients who had chronic inflammatory diseases and/or malnutrition in PCUs where malignant and non-malignant patients coexist. It was shown in the present study that the HALP score can predict mortality in the entire group of patients receiving palliative care, in the group of patients who are without malignancies, and in the group of patients who have malignancies. According to the present study results, it was concluded that the HALP score is a prognostic index independent of malignancy in patients receiving palliative care. To the best of our knowledge, the present study is the first in the literature to show that the HALP score can be successful in predicting mortality in patients who have and who do not have malignancies followed up in PCUs.

Studies investigating the prognostic role of HALP score in non-cancer conditions are very limited. Tian et al. showed that a high HALP score in patients who have acute ischemic strokes is associated with a reduced risk of recurrent stroke and death (15). Also, Han et al. conducted a recent study and found that low HALP scores in acute exacerbations of chronic obstructive pulmonary disease patients were associated with an increased risk of intensive care unit mortality (26). Akbaş et al. showed that the preoperative HALP score is an independent marker in determining malignant etiologies in patients operated on for acute mechanical bowel obstruction (27). The present study also showed that a low HALP score may be associated with mortality in the patient group without malignancy and supported the results of very few other studies conducted with this patient group.

Also, another result of the present study was that the HALP score was associated with the length of hospital stay of patients. A low HALP score at the time of hospitalization was an indication that patients would stay in the hospital longer, which showed a novel and different aspect of the HALP score that had not been demonstrated in previous studies. It can provide useful data for estimating the length of stay of the patients accurately, informing the patients and their relatives correctly, planning the hospital bed circulation correctly, and predicting the hospital costs.

Many elderly people are affected by multimorbidity, which means the co-existence of multiple chronic conditions that require palliative care (28), and there is increased mortality in these people (29). Researchers also aimed to develop various markers and tools to predict prognosis and mortality in patients receiving palliative care. The prognostic value of the Palliative Prognostic (PaP) Score (30), Palliative Prognostic Index (PPI) (31), Palliative Performance Scale (PPS) (32), Feliu Prognostic Nomogram (FPN) (33), and modified Glasgow Prognostic Score (mGPS) (34) was investigated in patients who have malignancies undergoing palliative care. It was shown that these are successful prognostic tools in determining the prognosis in palliative care patients with malignancies (30-34). In the present study, the effectiveness of the HALP score was demonstrated as a novel prognostic tool that can predict successful mortality in palliative care patients. The difference between the present study from other studies was that our patient population consisted of patients with and without malignity. Available prognostic tools demonstrated successful mortality prediction in patients who have malignancy. However, the HALP score showed a significant difference from other prognostic tools by showing that it could predict mortality successfully in both the malignant patient group and the non-malignant patient group.

It also uses a combination of available prognostic tools, clinical characteristics, and/or biomarkers, which consist of subjective evaluations covering symptoms and signs with various scales. Biomarkers are objective parameters using the results of various blood tests. The PaP score is calculated by using four subjective and two objective parameters, PPI five subjective, PPS seven subjective, and FPN two subjective and three objective parameters. The mGPS is the only prognostic tool that uses only two objective parameters and is calculated without using any subjective parameters (35,36). The HALP score used in our study is an index calculated by the combination of four objective parameters. Our results also showed that the HALP score may be the second prognostic tool that can be calculated by using only objective parameters among the tools developed so far for predicting prognosis in palliative care patients. Although they are proven to be effective and good prognostic markers, it is possible to face some difficulties in the routine use of these tools because of their subjective characteristics and their relatively complex scoring systems. The HALP score can provide clinicians with a significant advantage in practical use because it has completely objective characteristics and can be easily calculated with simple tests. The strength of the present study was that it was conducted with a sufficient number of patients.

Limitations:

However, the study also had several limitations. It had a retrospective design, some patient data could not be included in the study because they were not available, and the study was conducted based on data from a single center. Larger, multicenter, and prospective studies are needed to confirm the findings of the present study.

CONCLUSION

Prognostic data that can predict timely and accurate mortality is essential for optimizing palliative care and planning the most appropriate therapeutic program for clinicians interested in palliative care. Although various prognostic tools were developed to predict the prognosis of patients who have malignancy receiving palliative care, their clinical use is different. With the results of the present study, the HALP score was shown to be a novel prognostic tool that can successfully predict mortality independent of malignancy in patients receiving palliative care in PCUs. We believe that the HALP score, patients' clinical characteristics, and other prognostic tools, will make a significant contribution to a more accurate prognostic prediction when combined with the clinician's survival prediction. We recommend the calculation of the HALP score, closer follow-up of patients who have low HALP scores, and planning of more intensive support/treatments to prevent mortality in patients with or without malignancy hospitalized in PCUs for palliative care. Future studies should focus on testing the accuracy of current prognostic tools, including the HALP score, in different patient cohorts and comparing these with each other, as well as finding new prognostic factors.

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