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RESEARCH ARTICLE

The association between the HALP score and survival in metastatic breast cancer patients treated with antibody–drug conjugates

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Abstract

Objective: The hemoglobin–albumin–lymphocyte–platelet (HALP) score is an inflammation and nutrition -based biomarker in various solid tumors; however, its prognostic value in patients with metastatic breast cancer treated with antibody–drug conjugates (ADCs) remain unclear. We aimed to evaluate the association between HALP score and overall survival (OS) in this patient population.

Materials and Methods: This retrospective cohort study included female patients with metastatic breast cancer treated with ADCs between December 2017 and October 2024. The HALP score was calculated from baseline hemoglobin, albumin, lymphocyte, and platelet values. Patients were categorized into low and high HALP groups according to the median HALP value. Survival was evaluated using the Kaplan–Meier method, with associations assessed through univariate and multivariate Cox regression models.

Results: A total of 111 female patients with metastatic breast cancer treated with ADCs were included in the analysis (median age, 51 years). The median HALP score was 30.1, and patients were stratified into low- and high-HALP groups. Overall survival was significantly shorter in the low-HALP group compared with the high-HALP group (median OS, 31.0 vs 76.0 months; $p < 0.001$). In multivariate analysis, a low HALP score remained independently associated with shorter OS (HR 3.03, 95% CI 1.67–5.47; $p < 0.001$).

Conclusion: The HALP score is an independent prognostic marker for overall survival in women with metastatic breast cancer treated with ADCs and may serve as a simple tool for risk stratification in this setting.

Keywords: metastatic breast cancer, antibody–drug conjugates, HALP score, overall survival, prognostic biomarker

Introduction

Breast cancer is the most commonly diagnosed malignancy among women worldwide and remains a leading cause of cancer-related mortality despite major therapeutic advances [1]. Although survival has improved with the development of targeted agents and novel systemic therapies, metastatic breast cancer remains incurable, with substantial heterogeneity in clinical outcomes. Identifying robust and clinically

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applicable prognostic biomarkers is therefore essential to refine risk stratification and optimize treatment strategies in this population.

Antibody–drug conjugates (ADCs) have reshaped the therapeutic landscape of metastatic breast cancer over the past decade. By selectively delivering highly potent cytotoxic payloads to tumor cells, ADCs such as trastuzumab emtansine (T-DM1), trastuzumab deruxtecan (T-DXd), and sacituzumab govitecan have emerged as effective treatment options, with evidence of survival benefit in defined breast cancer [2]. These findings have informed evidence-based treatment strategies in HER2-positive and triple-negative breast cancer (TNBC), supported by clinical trial data from early-stage and metastatic disease [3]. Prognostic assessment in patients receiving ADCs is commonly based on conventional clinical parameters, with increasing interest in biomarkers reflecting host-related factors.

Systemic inflammation, nutritional status, and immune competence are increasingly recognized as key determinants of breast cancer progression and survival [4]. Composite indices derived from routine laboratory parameters have therefore gained attention as pragmatic prognostic tools in oncology. The hemoglobin–albumin–lymphocyte–platelet (HALP) score integrates markers of anemia, nutritional reserve, immune function, and systemic inflammation into a single metric. A low HALP score has been associated with inferior survival outcomes in several solid tumors [5]; however, evidence regarding its prognostic value in metastatic breast cancer is limited, particularly in the contemporary era of ADC-based therapy.

Given the expanding use of ADCs and the lack of validated, easily accessible prognostic markers in this setting, clarifying the role of HALP in patients treated with ADCs is of clinical relevance. In this study, we aimed to evaluate the association between the HALP score and overall survival in women with metastatic breast cancer receiving ADCs in a real-world cohort.

Material And Methods

Study design and setting

This retrospective cohort study was conducted at Hacettepe University Faculty of Medicine, a tertiary academic center in Türkiye. Female patients with metastatic breast cancer who received ADCs therapy between December 2017 and October 2024 were evaluated. The study was performed in accordance with the Declaration of Helsinki and approved by the local institutional ethics committee. Due to the retrospective nature of the study, the requirement for informed consent was waived.

Patients

Adult female patients (≥18 years) with histologically confirmed metastatic breast cancer who were treated with at least three cycles of an ADCs including T-DM1 and T-DXd were eligible for inclusion. Patients were required to have available baseline laboratory data obtained prior to ADCs initiation, including hemoglobin, serum albumin, lymphocyte count, and platelet count. Patients with missing baseline laboratory values or incomplete follow-up data were excluded from the analysis.

Definiton of HALP score

HALP score was calculated using the following formula: HALP = (hemoglobin [g/L] × albumin [g/L] × lymphocyte count [/L]) / platelet count [/L]. Baseline laboratory values obtained closest to, and before, the initiation of ADC therapy was used for HALP score calculation.

Outcome measures

The primary outcome of the study was overall survival (OS), defined as the time from initiation of ADC therapy to death from any cause or last follow-up. Patients who were alive at the time of last follow-up were censored.

Statistical analysis

Continuous variables were summarized as medians with interquartile ranges (IQRs), and categorical variables were expressed as frequencies and percentages. Comparisons between low and high HALP groups were

performed using the chi-square test or Fisher's exact test for categorical variables, as appropriate.

Patients were dichotomized into low- and high-HALP groups using the median HALP value as the cut-off. The median HALP value was used as the cut-off to ensure balanced group sizes and to reduce the risk of overfitting, particularly given the relatively limited sample size of the cohort. Overall survival was estimated using the Kaplan–Meier method, and survival differences between groups were compared using the log-rank test. Univariate and multivariate Cox proportional hazards regression analyses were performed to identify factors associated with overall survival. Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported. All statistical analyses were two-sided, and a p value <0.05 was considered statistically significant. Statistical analyses were conducted using IBM SPSS Statistics version 27.0.

Results

A total of 111 female patients with metastatic breast cancer treated with ADCs were included in the analysis. The median age was 51 years (IQR, 43–62). Baseline clinical and treatment characteristics stratified by HALP score are summarized in Table 1. Age distribution, ECOG performance status, body mass index, tumor type, and treatment regimen did not differ significantly between HALP groups. However, mortality was significantly higher in the low-HALP group compared with the high-HALP group (74.5% vs 69.6%, p = 0.009).

The median HALP score was 30.1, and patients were categorized into low (HALP <30.1) and high (HALP ≥30.1) groups.

Kaplan–Meier analysis showed that overall survival (OS) was significantly shorter in patients with low HALP scores compared with those with high HALP scores (median OS, 31.0 months [95% CI, 15.17–46.83] vs 76.0 months [95% CI, 25.88–126.12]; p < 0.001) (Figure 1). In univariate Cox regression analysis, ECOG performance status ≥1, low HALP score, and higher LDH levels were significantly associated with worse OS (Table 2). In multivariate analysis, low HALP score remained independently associated with shorter OS (HR: 3.03, 95% CI: 1.67–5.47; p < 0.001), along with ECOG performance status ≥1 (HR: 4.33, 95% CI: 1.81–10.36; p < 0.001) and higher LDH levels (HR: 1.003 per unit increase, 95% CI: 1.001–1.004; p < 0.001).

Table 1. Baseline clinical and treatment characteristics by HALP status

Variable	HALP score <30.1 n (%)	HALP score ≥30.1 n (%)	p value
Age category			0.853
<65 years	44 (80)	44 (78.6)	
≥65 years	11 (20)	12 (21.4)	
ECOG performance status			0.727
0	16 (29.1)	18 (32.1)	
≥1	39 (70.9)	38 (67.9)	
Body mass index (BMI)			0.580
Low	18 (32.7)	18 (32.1)	
Intermediate	21 (38.2)	17 (30.4)	
High	16 (29.1)	21 (37.5)	
Tumor type			0.723
Invasive ductal carcinoma	48 (87.3)	48 (85.7)	
Invasive lobular carcinoma	1 (1.8)	3 (5.4)	
Solid papillary carcinoma	2 (3.6)	1 (1.8)	
Mixed carcinoma	4 (7.3)	4 (7.1)	
Hormone receptor status			0.076
Negative	33 (60)	25 (44.6)	
Positive	22 (40)	31 (55.4)	
Disease progression	41 (74.5)	39 (69.6)	0.565
Death	32 (58.2)	19 (33.9)	0.009
Treatment regimen			0.562
Fam-trastuzumab deruxtecan	9 (16.4)	7 (12.5)	
Trastuzumab emtansine	46 (83.6)	49 (87.5)	

Data are presented as n (%).
Body mass index was categorized into low, intermediate, and high groups based on tertiles (33rd and 66th percentiles) of the study population.

Median progression-free survival (PFS) was 7.0 months (95% CI, 3.26–10.74) in the low-HALP group and 12.0

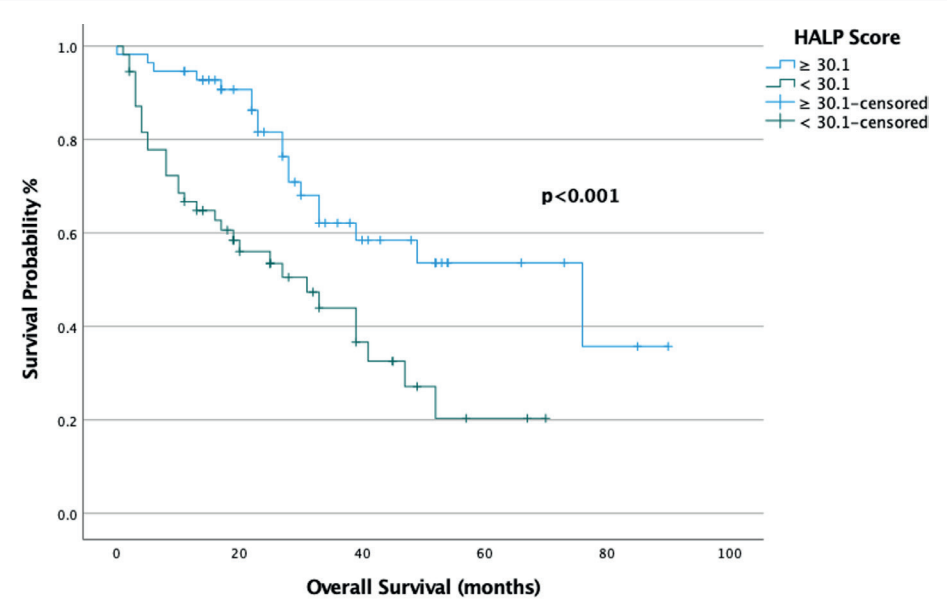

Figure 1. Kaplan–Meier analysis demonstrates overall survival stratified by HALP score (<30.1 vs ≥30.1)

Table 2. Univariate and multivariate cox proportional hazards analyses for overall survival

Variable	Univariate HR (95% CI)	p value	Multivariate HR (95% CI)	p value
Age (≥65 vs <65 years)	1.77 (0.95–3.30)	0.068	1.84 (0.97–3.49)	0.059
ECOG performance status (≥1 vs 0)	5.70 (2.41–13.45)	<0.001	4.33 (1.81–10.36)	<0.001
HALP (low vs high)	2.56 (1.43–4.59)	0.001	3.03 (1.67–5.47)	<0.001
LDH (per 1-unit increase)	1.003 (1.002–1.004)	<0.001	1.003 (1.001–1.004)	<0.001

Abbreviations: HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HALP, hemoglobin–albumin–lymphocyte–platelet score; LDH, lactate dehydrogenase.
Multivariate hazard ratios were adjusted for age, ECOG performance status, HALP score, and LDH.

months (95% CI, 6.74–17.26) in the high-HALP group. The median PFS for the overall cohort was 7.0 months (95% CI, 5.41–8.59). The difference in PFS between HALP groups was not statistically significant (p = 0.359) (Figure 2).

Discussion

In this study, we found that the HALP score was independently associated with overall survival in metastatic breast cancer patients treated with ADCs. The HALP score reflects multiple dimensions of host physiology, including anemia, nutritional status, immune competence, and systemic inflammatory response. These factors are increasingly recognized as important determinants of outcomes in patients with advanced cancer, complementing tumor-related characteristics and treatment-specific variables.

Previous research has also suggested a potential role of the HALP score as a predictive biomarker in gastrointestinal malignancies, where higher HALP values were associated with improved response to neoadjuvant chemotherapy in patients with gastric and gastroesophageal junction adenocarcinomas [6]. In another study, the HALP score was shown to have prognostic value in patients with metastatic castration-resistant prostate cancer treated with abiraterone or enzalutamide, with lower HALP scores associated with shorter progression-free and OS [7].

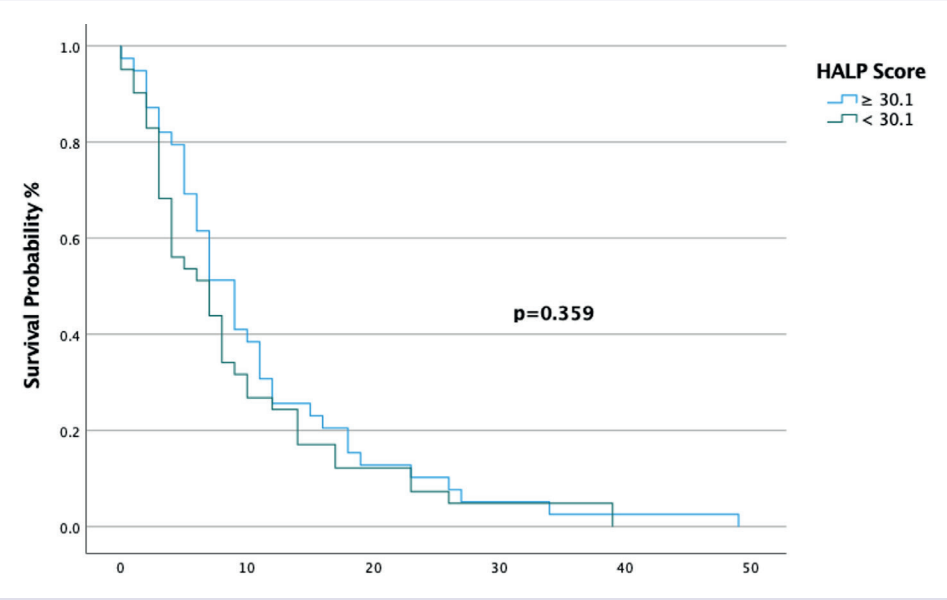

Figure 2. Kaplan–Meier analysis demonstrates progression-free survival stratified by HALP score (<30.1 vs ≥30.1)

In breast cancer, the prognostic relevance of the HALP score has also been demonstrated in large surgical cohorts, where preoperative HALP was independently associated with both overall and progression-free survival, supporting the role of inflammation–nutrition composite indices in breast cancer prognosis [8]. In another breast cancer cohort, lower HALP scores were associated with more aggressive disease characteristics, including a higher rate of axillary lymph node involvement, suggesting that inflammation–nutrition composite indices may reflect tumor burden and disease severity [8].

ADCs have become an important component of treatment across multiple subtypes of metastatic breast cancer. HER2-targeted ADCs such as trastuzumab emtansine and trastuzumab deruxtecan as well as TROP-2–targeting agents such as sacituzumab govitecan, have demonstrated significant improvements in survival outcomes in several landmark clinical trials, expanding treatment options in both HER2-positive and HER2-low disease as well as triple-negative and hormone receptor–positive breast cancer [9].

The need for predictive biomarkers in ADC therapy has been highlighted in recent studies, where multivariate gene-expression–based models such as ADC treatment response scores were shown to predict overall survival across different tumor types and ADC targets, beyond target expression alone [10]. In this context, our findings suggest that simple, routinely available host-related indices such as the HALP score may provide complementary prognostic information in patients treated with ADCs.

Our finding that HALP score was associated with overall survival but not PFS is consistent with previous studies. In a cohort of patients with metastatic head and neck cancer, HALP score was associated with OS but not with PFS [11]. Similarly, another study in extrapulmonary neuroendocrine carcinomas reported no significant relationship between HALP score and PFS [12]. These findings support the hypothesis that immunonutritional indices such as HALP may be more strongly related to long-term survival outcomes than to short-term tumor progression.

This study has several limitations. Its retrospective, single-center design and relatively small sample size may limit generalizability. HALP score was assessed only at baseline, and treatment heterogeneity among different ADC regimens may have influenced outcomes. Although ADCs are typically administered in later lines of therapy in our setting, detailed information regarding the exact line of treatment was not uniformly available and could not be included in the analysis. In addition, certain factors that may influence the components

of the HALP score, such as systemic inflammatory markers (e.g., C-reactive protein), infection status, and cachexia, could not be evaluated in this study. Due to the retrospective design, these variables were not uniformly available, and CRP measurements were not routinely performed in all patients at baseline, resulting in substantial missing data. Therefore, these parameters could not be reliably incorporated into the analysis. Nevertheless, the HALP score is a composite biomarker reflecting systemic inflammation, nutritional status, and immune function, and may partially capture the biological impact of these unmeasured factors. Additionally, although all patients had metastatic breast cancer, detailed information on metastatic burden (such as the number of metastatic sites or tumor load) was not consistently available due to the retrospective design. Prospective studies with external validation are needed to confirm these findings.

Conclusion

Low HALP scores were independently associated with shorter OS in women with metastatic breast cancer treated with antibody–drug conjugates. The HALP score may serve as a simple and accessible prognostic marker for risk stratification in this setting.

Author contributions

Conception: M.T., O.B., D.C.G., S.A.; Design: M.T., O.B., M.Ş., Y.Y., D.C.G., S.A.; Data acquisition: M.T., O.B., M.Ş., Y.Y., E.N.C.; Data analysis: M.T., O.B., D.C.G.; Data interpretation: M.T., O.B., D.C.G., S.A.; Drafting of the manuscript: M.T., O.B., M.Ş., Y.Y., E.N.C., D.C.G.; Critical revision of the manuscript: D.C.G., S.A. All authors reviewed the results, approved the final version of the manuscript, and agreed to be accountable for all aspects of this study.

Ethical approval

This study was approved by the Hacettepe University Health Sciences Research Ethics Committee (SBA 25/650). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest

The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Generative AI statement

The authors declare that no generative AI or AI-assisted technologies were used in the writing or preparation of this study.

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