

Is Hemoglobin, Albumin, Lymphocyte, and Platelet Score a Prognostic Indicator in Metastatic Squamous Cell Lung Cancer?

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ABSTRACT

Aim: We aimed to determine the prognosis by using the HALP score as a prognostic marker in patients followed in our clinic due to metastatic lung squamous cell carcinoma (SCC).

Methods: The study retrospectively reviewed 35 patients diagnosed with metastatic lung SCC in our clinic between January 2015 and December 2022. Overall survival (OS) was calculated as the time from metastasis date to death or last follow-up. The HALP score was calculated using laboratory parameters at the time of metastasis, according to the formula [HALP = hemoglobin (g/L) × albumin (g/L) × lymphocyte count / thrombocyte count].

Results: Of the 35 patients included in the study, 28 were male (80%). There was no statistically significant association between the HALP score and gender ($p=0.735$), age groups ($p=0.862$), Eastern Cooperative Oncology Group performance status ($p=0.915$), receipt of palliative radiotherapy ($p=0.238$), and body mass index groups ($p=0.615$). In the overall cohort, the median OS was 18 months, while it was 14.4 months in the low HALP group and 20 months in the high HALP group.

Conclusion: Our study indicates that the HALP score could be a crucial prognostic marker for patients with squamous cell lung cancer. A lower HALP score is linked to a shorter OS.

Keywords: HALP score, lung cancer, squamous cell carcinoma

Introduction

Lung cancer stands as one of the most prevalent and fatal cancer types globally, with distinct categorizations into two main classes: small cell lung cancer (SCLC) and non-SCLC (NSCLC) [1,2]. Squamous cell carcinoma (SCC) is one of the most common subtypes of NSCLC and is characterized by its high potential for recurrence and metastasis, contributing significantly to its elevated mortality rates.

In lung cancer, the TNM classification system provides staging of the disease based on factors such as tumor size (T), lymph node involvement (N), and the presence of distant metastases (M). This classification system plays a significant

role in determining the prognosis of lung cancer [3]. However, in some cases, different prognoses may be observed even among patients with the same TNM stage. Therefore, research continues to identify new prognostic factors to better determine and improve prognosis.

Neutrophils, lymphocytes, platelets, hemoglobin, albumin, and C-reactive protein are primary laboratory parameters used in clinical practice to assess inflammation and nutritional status. These parameters are commonly investigated because they are cost-effective and readily accessible. Recently, researchers have tested a composite score, known as the HALP score, which combines several of these parameters, in various studies as a

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novel prognostic biomarker [4-10]. The HALP score is derived from the combination of indicators such as platelets and lymphocytes reflecting immune status, along with hemoglobin indicating anemia status, and albumin providing information about nutritional status.

In our study, our objective was to assess prognosis using the HALP score as a prognostic indicator in patients with metastatic lung SCC who are under follow-up at our clinic.

Methods

Study Design

From January 2015 to December 2022, we conducted a retrospective screening of patients diagnosed with lung cancer at our oncology clinic. Among these patients, individuals aged 18 and older who were initially diagnosed with early-stage lung SCC and subsequently developed metastasis were selected for inclusion in the study. Patients for whom medical records and hospital computer system data at the time of diagnosis were unavailable, as well as those with heart failure, inflammatory bowel disease, and those undergoing dialysis, were excluded from the study. A total of 35 patients were included in the analysis. Demographic and clinicopathological characteristics of the patients were retrieved and recorded from medical records and the hospital computer system. Overall survival (OS) was calculated as the time from metastasis date to death, or last follow-up date. The HALP score was calculated using laboratory parameters at the time of metastasis, prior to the initiation of chemotherapy, according to the formula [HALP = hemoglobin (g/L) × albumin (g/L) × lymphocyte count / thrombocyte count] [11]. The study was conducted in accordance with the principles of the Helsinki Declaration, and approval was obtained from the Ethics Committee of Ankara Etlik City Hospital (decision no: 2024-321, date: 08.05.2024).

Statistical Analysis

Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) Statistical Software (IBM SPSS Statistics version 22.0, IBM SPSS, USA). Descriptive analysis was used to present clinical and demographic data. Categorical and numerical variables were reported as frequency and percentage (n, %). Continuous variables were presented as mean±standard deviation when they exhibited a normal distribution; otherwise, they were presented as median (interquartile range). Survival analyses were conducted using the Kaplan-Meier method and log-rank test (univariate analysis), or Cox regression model (multivariate analysis). A p value <0.05 was considered statistically significant for all analyses.

Results

Analysis was conducted on 35 patients who met the inclusion criteria. Among them, 28 patients (80%) were male. Every patient had a smoking history. Out of the total, 25 patients (71.4%) had an Eastern Cooperative Oncology Group (ECOG)

performance status score of 0-1, while 17 patients (48.6%) received palliative radiotherapy (RT). The average levels of hemoglobin, albumin, lymphocytes, and platelets were found to be 11.97±1.81 g/dL, 3.76±0.76 g/dL, 3.26±2.87×10⁹/L, and 299.40±100.25×10⁹/L, respectively. The clinicopathological and laboratory characteristics of the patients were presented in Table 1.

There was no statistically significant association between the HALP score and gender (p=0.735), age groups (p=0.862), ECOG performance status (p=0.915), receipt of palliative RT (p=0.238), and body mass index (BMI) groups (p=0.615). The relationship between the HALP score and patient characteristics is presented in Table 2.

In the entire cohort, the median OS was 18 months. However, in the low HALP group, it was 14.4 months, whereas in the high HALP group, it was 20 months. Subgroups were compared in terms of OS. In the univariate analysis, no statistically significant difference was observed in terms of OS among age groups (p=0.747), BMI groups (p=0.072), gender (p=0.104), and receiving palliative RT (p=0.146). However, there was a statistically significant difference among HALP groups (p=0.04) (Figure 1). In the multivariate analysis, where parameters with a p-value below 0.1 were included, the statistical significance of the difference between HALP groups persisted (p=0.032). The results of both univariate and multivariate analyses are summarized in Table 3.

Discussion

Lung cancer is the most common cause of cancer-related deaths [1]. NSCLC constitutes the majority of lung cancers, with SCC having a higher incidence of recurrence and metastasis with

Table 1. Clinicopathological and laboratory characteristics of 35 patients with metastatic squamous cell lung cancer

| Characteristics | Values |
|--|-----------------|
| Age [median (range)] | 66 (45-81) |
| Gender (n, %) | |
| Female | 7 (20%) |
| Male | 28 (80%) |
| ECOG performance status (n, %) | |
| 0-1 | 25 (71.4%) |
| 2 | 10 (28.6%) |
| Palliative RT (n, %) | |
| Yes | 17 (48.6%) |
| No | 18 (51.4%) |
| Hemoglobin (mean±SD, g/dL) | 11.97±1.81 |
| Albumin (mean±SD, g/dL) | 3.76±0.76 |
| Lymphocyte (mean±SD, 10⁹/L) | 3.26±2.87 |
| Platelet (mean±SD, 10⁹/L) | 299.40±100.25 |
| BMI (mean±SD) | 24.98±3.45 |
| HALP score [median (range)] | 34.1 (7.1-93.2) |
| ECOG: Eastern Cooperative Oncology Group, RT: Radiotherapy, SD: Standard deviation, BMI: Body mass index | |

in this category. The poor prognosis and elevated treatment expenses linked to lung SCC patients have under scored the growing necessity for novel prognostic factors in this patient population.

The HALP score is a comprehensive score derived from factors reflecting immune status, such as platelets and lymphocytes, along with indicators providing information about nutrition, such as hemoglobin and albumin. Previous studies have indicated a relationship between immunity, nutrition, and cancer survival [12-15].

Table 2. Distribution of patients according to HALP score in subgroups

| Features | HALP low n (%) | HALP high n (%) | p value |
|--------------------------------|-------------------|--------------------|---------|
| Gender | | | |
| Female | 4 (22.2) | 4 (22.2) | 0.735 |
| Male | 14 (77.8) | 14 (77.8) | |
| Age group | | | |
| <67 | 9 (50) | 8 (47.1) | 0.862 |
| ≥67 | 9 (50) | 9 (52.1) | |
| ECOG performance status | | | |
| 0-1 | 13 (72.2) | 12 (70.6) | 0.915 |
| 2 | 5 (27.8) | 5 (29.4) | |
| Smoking | | | |
| No | 0 (0) | 0 (0) | |
| Yes | 18 (100) | 17 (100) | |
| Paliative RT | | | |
| No | 11 (61.1) | 7 (41.2) | 0.238 |
| Yes | 7 (38.9) | 10 (58.8) | |
| BMI group | | | |
| Low | 10 (55.6) | 8 (47.1) | 0.615 |
| High | 8 (44.4) | 9 (52.9) | |

ECOG: Eastern Cooperative Oncology Group, RT: Radiotherapy, BMI: Body mass index

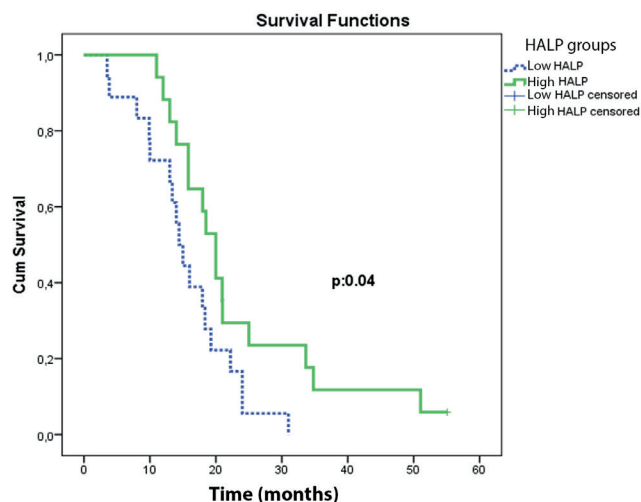


Figure 1. Comparison of HALP groups in terms of overall survival

Anemia, characterized by low levels of hemoglobin, is often prevalent in cancer patients and has been linked to resistance to RT and chemotherapy, consequently indicating a poor prognosis [16]. Research has demonstrated that low serum albumin levels indicate the nutritional status of cancer patients and are associated with a poor prognosis [17,18].

Numerous studies have demonstrated the involvement of the inflammatory microenvironment in cancer development, where lymphocytes and platelets play crucial roles [19,20]. Lymphocytes play a crucial role in the anti-tumor immune response by impeding the proliferation of tumor cells. Lymphopenia, which is prevalent among patients with advanced cancer, acts as a prognostic indicator for both OS and disease-free survival [20]. Platelets contribute to this microenvironment by releasing factors that facilitate tumor invasion and angiogenesis [21]. Based on these studies, it has been established that high levels of serum albumin, hemoglobin, and lymphocytes confer an advantage to cancer patients, whereas elevated platelet levels are associated with a disadvantage. Consequently, the HALP score, integrating these parameters, has emerged as a novel prognostic index in cancer [4,22,23].

In our study, we employed the HALP score as a prognostic index for patients monitored due to metastatic lung SCC, examining its correlation with disease prognosis. Our findings revealed poorer survival in the low HALP score group ($p=0.04$). Similar to our study, Zhai et al. [5] (2021) conducted an analysis on patients with NSCLC who underwent radical lung resection. Their findings revealed that patients with a high HALP score exhibited better OS compared to those with a low HALP score

Table 3. Analysis of prognostic factors in terms of overall survival

| Features | Univariate analysis | | Multivariate analysis | |
|---------------------|---------------------|---------|-----------------------|---------|
| | HR (95% CI) | p value | HR (95% CI) | p value |
| HALP groups | | | | |
| HALP low | 0.47 (0.23-0.97) | 0.04 | Ref | 0.032 |
| HALP high | | | 0.45 (0.22-0.93) | |
| Age groups | | | | |
| <67 | 0.89 (0.45-1.76) | 0.747 | | |
| ≥67 | | | | |
| BMI groups | | | | |
| Low | 0.52 (0.25-1.06) | 0.072 | Ref | 0.057 |
| High | | | 0.50 (0.24-1.02) | |
| Gender | | | | |
| Male | 2.06 (0.86-4.93) | 0.104 | | |
| Female | | | | |
| Paliative RT | | | | |
| No | 0.60 (0.30-1.20) | 0.146 | | |
| Yes | | | | |

CI: Confidence interval, HR: Hazard ratio, RT: Radiotherapy

($p < 0.001$). Wei et al. [7] (2022) obtained similar results in their study on NSCLC patients undergoing adjuvant chemotherapy. Our study stands out from the other two studies due to its exclusive inclusion of patients with squamous cell lung cancer and its specific focus on those in the metastatic stage.

Study Limitations

There are several limitations to our study. Firstly, it was conducted at a single center with a limited sample size, potentially limiting the generalizability of our findings and impacting the reliability of our results. Secondly, our study utilized a retrospective design, which may have resulted in missing data during the data collection process. Lastly, our study's findings are constrained in their ability to establish causal relationships and require validation by other studies. Nevertheless, despite these limitations, our study underscores the potential significance of the HALP score in predicting prognosis among lung cancer patients.

Conclusion

In summary, our study indicates that the HALP score could play a crucial role in predicting the prognosis of patients with squamous cell lung cancer. Lower HALP scores have been linked to decreased OS. Nonetheless, broader and prospective studies are required to validate and generalize these results. It's essential to acknowledge the limitations of this study and future research should thoroughly assess these prognostic factors.

Ethics

Ethics Committee Approval: The study was conducted according to the principles of the Declaration of Helsinki, and approval was obtained from the Ethics Committee of Ankara Etlik City Hospital (decision no: 2024-321, date: 08.05.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ö.D., Y.D., E.Ç., T.E., Concept: Ö.D., Design: Ö.D., Y.D., T.E., Data Collection or Processing: Ö.D., Y.D., E.Ç., Analysis or Interpretation: Ö.D., Y.D., Literature Search: Ö.D., Writing: Ö.D.

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