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Prognostic significance of inflammation scores in malignant mesothelioma

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Abstract. – OBJECTIVE: The relationship between inflammatory markers and survival in many cancers has been investigated previously. Inflammatory markers may also offer the possibility of predicting surveillance in patients with malignant mesothelioma. Our study seeks to enhance comprehension of how variables such as the nutritional status and inflammation indices of malignant mesothelioma patients impact the disease's progression and prognosis.

PATIENTS AND METHODS: This study included patients who were treated at the Erciyes University Medical Oncology Clinic between 2010 and 2022 and diagnosed with malignant mesothelioma. This is a retrospective single-center cohort study. Receiver Operating Characteristic (ROC) analysis was applied to determine the inflammation markers' optimal cut-off values with high sensitivity and specificity. Patients were categorized based on these values. The differences in overall survival (OS) and progression-free survival (PFS) between categorized groups were assessed using Log-rank curves and Kaplan-Meier tests. Multivariate analysis was performed using Cox regression analysis on statistically significant data. The relationship between inflammation markers and malignant mesothelioma survival was evaluated.

RESULTS: There are 115 patients in this study. Pre-treatment high neutrophil to lymphocyte ratio (NLR) (HR: 1.34, 95% CI: 1.12-2.83, *p*=0.04), high pan-immune inflammation value (PIIV) (HR: 2.01, 95% CI: 1.32-4.79, *p*=0.03), and high systemic inflammation response index (SIRI) (HR: 1.34, 95% CI: 1.2-2.78, *p*=0.04) were associated with poor OS. Conversely, high advanced lung cancer inflammation index (ALI) (HR: 0.73, 95% CI: 0.53-0.84, *p*=0.03) and high hemoglobin-albumin-lymphocyte and platelet (HALP) (HR: 0.67, 95% CI: 0.23-0.78, *p*=0.02) were associated with favorable survival.

CONCLUSIONS: Our study investigated the prognostic value of various inflammation markers in malignant mesothelioma patients and suggests that composite formulas like NLR, PIIV, SIRI, ALI, and HALP that incorporate CBC cells and nutritional parameters like albumin, height, and weight could more consistently and accurately predict malignant mesothelioma prognosis.

Key Words:

Advanced lung cancer inflammation index, Hemoglobin albumin lymphocyte and platelet score, Malignant mesothelioma, Pan immune inflammation value, Systemic inflammation response index.

Introduction

Malignant mesothelioma affects the serosal membranes of body cavities. The disease primarily affects the pleura (75%) and, less commonly, the peritoneum (25%). According to epidemiological data, the median survival of mesothelioma patients is approximately 12 months. Male gender, non-epithelioid histology, and advanced age are known as poor prognostic factors[1].

Malignant mesothelioma is a cancer type that often develops resistance to chemotherapy. The overall survival time can reach up to 12 months with cisplatin plus pemetrexed treatment. Later, it was realized that vascular endothelial growth factor (VEGF) is one of the main regulators of the disease, and bevacizumab was added to the treatment[2]. In recent years, immune checkpoint inhibitors have also shown efficacy in the treatment of malignant mesothelioma. Ipilimumab plus nivolumab treatment yielded better results, especially in non-epithelioid histology, compared to traditional chemotherapy[3]. However, due to cost and limited drug accessibility, many countries, including Turkey, still use platinum plus pemetrexed combination therapy as the standard first-line treatment.

Nutritional status is an important factor determining the prognosis of cancer patients. Previous studies[4,5] have shown that good nutritional status before treatment can enhance overall survival and progression-free survival. Chronic inflammation is also a significant factor in determining the prognosis of various cancer types, including malignant mesothelioma[4]. The advanced lung cancer inflammation index (ALI), initially described in lung cancer and subsequently evaluated in various

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cancers, is a prognostic biomarker indicating the patient's nutritional and inflammatory status[5]. Similarly, relationships have been found between survival and inflammation indices in various cancer types, including neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), platelet distribution width (PDW) to platelet count ratio (PPR), pan-immune inflammation value (PIIV), prognostic nutritional index (PNI), hemoglobin to red cell distribution width (RDW) ratio (HRR), systemic immune inflammation index (SII), lymphocyte to monocyte ratio (LMR), hemoglobin-albumin-lymphocyte and platelet (HALP) score and systemic inflammation response index (SIRI)[6-13]. While inflammation indices and their prognostic value have been investigated in various cancer types, the potential significance of certain inflammation indices in malignant mesothelioma has not been extensively studied. To our knowledge, the evaluated indices in malignant mesothelioma so far have been limited to PNI, NLR, and PLR.

In our study, we aim to better understand how factors such as nutritional status and inflammation indices of malignant mesothelioma patients influence the course and prognosis of the disease. Such research could contribute to developing treatment approaches and management strategies for patients. Results obtained through appropriate methodology and analysis can provide important information to improve the quality of life of cancer patients.

Patients and Methods

This study included patients who were treated at the Erciyes University Medical Oncology Clinic between 2010 and 2022, diagnosed with malignant mesothelioma and had received at least 3 months of palliative chemotherapy in the metastatic stage. The study included 115 patients. Patient data, including age, gender, diagnosis, histology, stage at diagnosis, ECOG performance status, surgical history, history of radiotherapy, adjuvant/palliative chemotherapy history, pre-chemotherapy height, weight, complete blood count (CBC), and plasma biochemistry parameters, were retrospectively obtained from the medical records.

Definitions and Formulas

Calculations were performed using the CBC and plasma biochemistry parameters obtained from patients just before starting palliative chemotherapy. The following indices were calculated using the formulas provided:

NLR: Absolute neutrophil count (count/mm^3) / Absolute lymphocyte count (count/mm^3)

BMI (Body Mass Index): Weight/height^2 (kg/m^2)

ALI: Serum albumin (g/dL) x BMI / NLR

SII: NLR x Platelet count (count/mm^3)

PPR: PDW / Platelet count (count/mm^3)

PNI: [Serum albumin (g/dL) x 10] + [Absolute lymphocyte count (count/mm^3) X 0.005]

HRR: Hemoglobin (g/dL) / RDW

LMR: Absolute lymphocyte count (count/mm^3) / Absolute monocyte count (count/mm^3)

PLR: Platelet count (count/mm^3) / Absolute lymphocyte count (count/mm^3)

SIRI: NLR × Absolute monocyte count (count/mm^3)

PIIV: SIRI x Platelet count (count/mm^3)

HALP: [Hemoglobin (g/dL) × albumin (g/L) × Absolute lymphocyte count (/L)] / Absolute platelet count (/L).

Statistical Analysis

Descriptive statistics and statistical analysis of study variables were carried out using SPSS 22.0 software (IBM Corp., Armonk, NY, USA). In all statistical tests conducted with a 95% confidence interval, p-value<0.05 was considered statistically significant. Data with p<0.200, which could be clinically significant, were also included in the multivariate analysis.

Receiver Operating Characteristic (ROC) analysis was applied to determine the optimal NLR, ALI, SII, PPR, PNI, HRR, LMR, PLR, SIRI, PIIV, and HALP cut-off values with high sensitivity and specificity. Patients were categorized based on these values. The differences in overall survival (OS) and progression-free survival (PFS) between categorized groups were assessed using Log-rank curves and Kaplan-Meier tests. Multivariate analysis was performed using Cox regression analysis on statistically significant data. Analysis results were presented as medians (minimum-maximum), means, standard deviations, and hazard ratios (HR). In all statistical tests conducted with a 95% confidence interval, p-value<0.05 was considered statistically significant. Data with p<0.200, which could be clinically significant, were also included in the multivariate analysis.

Results

There are 115 patients in this study. Of these patients, 87 (75.7%) had malignant pleural mesothelioma, and 28 (24.3%) had malignant

peritoneal mesothelioma. The median age for the entire group was 64 years (range: 24-83). Eastern Cooperative Oncology Group Performance Status (ECOG-PS) was ≥2 in 13 (11.3%) patients. All patients were included in this trial at the metastatic stage and received palliative chemotherapy.

As first-line chemotherapy, 57 (49.6%) patients received cisplatin-pemetrexed, 47 (40.9%) received carboplatin-pemetrexed, 2 (1.7%) received cisplatin-pemetrexed-bevacizumab, and 9 (7.8%) received only pemetrexed treatment. Furthermore, 48 (41.7%) patients received 2 or more lines of palliative chemotherapy. The clinicopathological characteristics of the patients were reported in Table I. The area under the curve (AUC) values obtained through ROC analysis were as follows: NLR (0.72), ALI (0.75), SII (0.61), PNI (0.64), PPR (0.57), HRR (0.52), LMR (0.61), PLR (0.60), PIIV (0.70), SIRI (0.70), and HALP (0.73). ALI had a high AUC value. The optimal cut-off values were as follows: NLR (3.1), ALI (35.25), SII (854.3), PNI (48.3), PPR (0.03), HRR (0.31), LMR (3.36), PLR (206), PIIV (638), SIRI (1.78), and HALP (25.9). The best cut-off value for ALI was 0.75, with a sensitivity of 85% and specificity of 70%. Parameters were grouped as low and high based on the cut-off values.

Kaplan-Meier analysis revealed a median PFS of 11 months and OS of 16 months for the entire group. Cox regression analysis was applied for univariate-multivariate analyses. In the multivariate analysis, advanced stage III-IV malign mesothelioma (p=0.001), high NLR value (HR: 1.33, 95% CI: 1.23-2.12, p=0.02), high PLR (HR: 1.21, 95% CI: 0.43-0.84, p=0.04), high PIIV (HR: 1.43, 95% CI: 1.14-4.21, p=0.03), and high SIRI (HR: 1.52, 95% CI: 1.23-3.23, p=0.02) were associated with poor PFS. On the other hand, high ALI (HR: 0.73, 95% CI: 0.37-0.89, p=0.001), high PNI (HR: 0.45, 95% CI: 0.21-0.78, p=0.02), and high HALP (HR: 0.73, 95% CI: 0.23-0.84, p=0.03) were associated with favorable PFS (Table II). In the multivariate analysis, factors such as sarcomatoid histology (p=0.025), advanced stage III-IV cancer (p=0.001), high NLR (HR: 1.34, 95% CI: 1.12-2.83, p=0.04), high PIIV (HR: 2.01, 95% CI: 1.32-4.79, p=0.03), and high SIRI (HR: 1.34, 95% CI: 1.2-2.78, p=0.04) were associated with poor OS. Conversely, high ALI (HR: 0.73, 95% CI: 0.53-0.84, p=0.03) and high HALP (HR: 0.67, 95% CI: 0.23-0.78, p=0.02) were associated with favorable OS (Table III).

In terms of histology, the median OS was 8 months for sarcomatoid histology and 15 months for epithelioid histology, with a statistically significant association (p=0.025). For the low NLR group, the median OS was 26 months compared to 12 months in the high NLR group; this is a statistically significant association (p=0.04) (Figure 1). In the high ALI group, the median

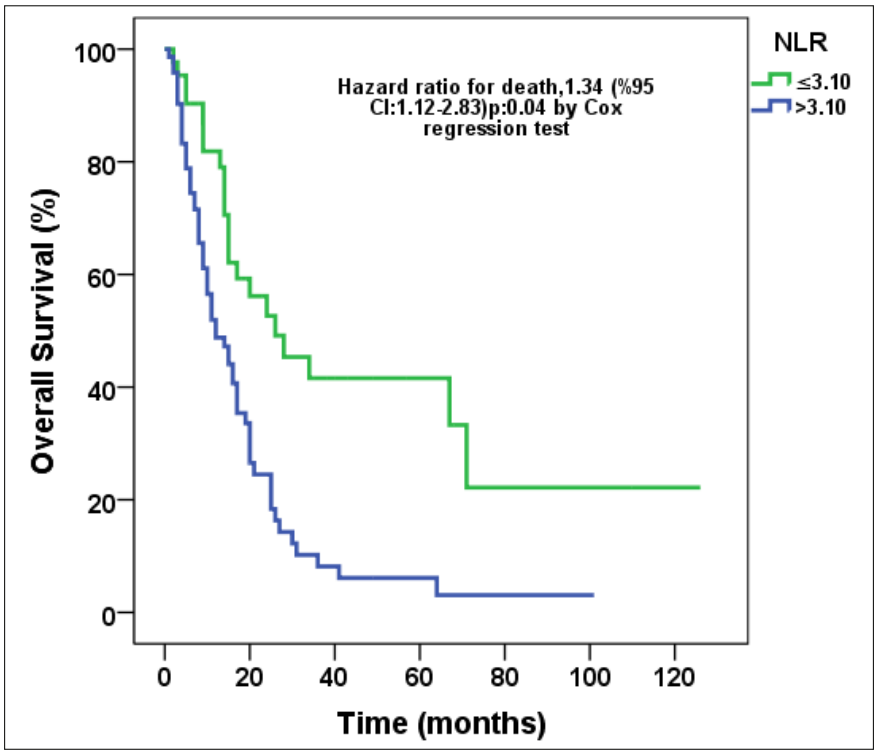

Figure 1. Overall survival outcomes according to NLR.

OS was 26 months compared to 12 months in the low ALI group, also displaying a statistically significant association (p=0.03) (Figure 2). For the low PIIV group, the median OS was 20 months compared to 12 months in the high PIIV group; this is also a statistically significant association (p=0.03) (Figure 3). The median OS was 20 months in the low SIRI group compared to 11 months in the high SIRI group, with a statistically significant association (p=0.04) (Figure 4).

Table I. Clinicopathological characteristics and inflammatory markers of patients.

Variables	Categories	N (%)	Median (min-max)
Age			64 (24-83)
Age	≤65	67 (58.3)	
	>65	48 (41.7)	
Gender.	Male	71 (61.7)	
	Female	44 (38.3)	
ECOG PS	0-1	102 (88.6%)	
	≥2	13 (11.3%)	
Mesothelioma type	Pleural	87 (75.7)	
	Peritoneal	28 (24.3)	
Histology	Epiteloid	88 (76.5)	
	Biphasic	21 (18.3)	
	Sarcomatoid	6 (5.2)	
Stage at diagnosis	I-II	25 (21.7)	
	III-IV	90 (78.3)	
Surgery	Yes	17 (14.8)	
	No	98 (85.2)	
Talc pleurodesis	Yes	66 (57.4)	
	No	49 (42.6)	
Chemotherapy	Adjuvant	6 (5.2)	
	Palliative	115 (100)	
Radiotherapy	Adjuvant	10 (8.7)	
	Palliative	30 (26.1)	
	No	75 (65.2)	
Cigarette history	Yes	48 (41.7)	
	No	67 (58.3)	
NLR	≤3.1	43 (37.4)	
	>3.1	72 (62.6)	
ALI	≤35.25	74 (64.3)	
	>35.25	41 (35.7)	
SII	≤104.3	60 (52.2)	
	>104.3	55 (47.8)	
PNI	≤48.3	77 (67)	
	>48.3	38 (33)	
PPR	≤0.03	53 (46.1)	
	>0.03	62 (53.9)	
HRR	≤0.31	74 (64.3)	
	>0.31	41 (35.7)	
LMR	≤3.36	57 (49.6)	
	>3.36	58 (50.4)	
PLR	≤206	46 (40)	
	>206	69 (60)	
PIIV	≤638	55 (47.8)	
	>638	60 (52.2)	
SIRI	≤1.78	58 (50.4)	
	>1.78	57 (49.6)	
HALP	≤25.9	71 (61.7)	
	>25.9	44 (38.3)	

ECOG PS: Eastern Cooperative Oncology Group Performance Status, NLR: Neutrophil to lymphocyte ratio, ALI: Advanced lung cancer inflammation index, SII: Systemic immune inflammation index, PNI: Prognostic nutritional index, PPR: Platelet distribution width to platelet count ratio, HRR: Hemoglobin to red cell distribution width ratio, LMR: Lymphocyte to monocyte ratio, PLR: Platelet to lymphocyte ratio, PIIV: Pan-immune inflammation value, SIRI: Systemic inflammation response index, HALP: Hemoglobin-albumin-lymphocyte and platelet.

Table II. Univariate and multivariate analysis results in terms of PFS.

Variables	Categories	Median PFS (Months)	Univariate analysis HR 95% CI	*p*-value	Multivariate analysis HR 95% CI	*p*-value
Age	≤65*	11				
	>65	11	1.2 (0.77-1.88)	0.41		
Gender.	Male*	11				
	Female	10	1.2 (0.78-1.89)	0.37		
Mesothelioma type	Pleural*	12				
	Peritoneal	5	2 (1.24-3.2)	**0.004**	1.6 (0.87-2.94)	0.124
Histology	Epiteloid*	11				
	Biphasic	11	1.25 (0.7-2.2)	0.44	0.71 (0.36-1.39)	0.32
	Sarcomatoid	7	2.1 (0.93-5.14)	0.072	2.1 (0.82-5.4)	0.12
Stage at diagnosis	I-II*	25				
	III-IV	10	2.67 (1.48-4.81)	**0.001**	2.97 (1.56-5.66)	**0.001**
NLR	≤3.1*	21				
	>3.1	10	2.2 (1.38-3.63)	**0.001**	1.33 (1.23-2.12)	**0.02**
ALI	≤35.25*	10				
	>35.25	25	0.44 (0.27-0.71)	**0.001**	0.73 (0.37-0.89)	**0.001**
SII	≤104.3*	10				
	>104.3	12	0.7 (0.45-3.18)	0.78		
PNI	≤48.3*	10				
	>48.3	25	0.39 (0.24-0.65)	**<0.001**	0.45 (0.21-0.78)	**0.02**
PPR	≤0.03*	14				
	>0.03	10	1.32 (0.48-1.17)	**0.21**	1.2 (0.57-4.32)	0.73
HRR	≤0.31*	10				
	>0.31	14	0.63 (0.39-1.01)	**0.05**	0.86 (0.46-1.61)	0.64
LMR	≤3.36*	10				
	>3.36	13	0.73 (0.27-1.32)	**0.06**	0.81 (0.35-3.96)	0.35
PLR	≤206*	14				
	>206	10	1.32 (1.15-2.19)	**0.01**	1.21 (0.43-0.84)	**0.04**
PIIV	≤638*	14				
	>638	9	1.91 (1.23-2.97)	**0.004**	1.43 (1.14-4.21)	**0.03**
SIRI	≤1.78*	12				
	>1.78	9	1.68 (1.08-2.6)	**0.02**	1.52 (1.23-3.23)	**0.02**
HALP	≤25.9*	10				
	>25.9	20	0.44 (0.27-0.71)	**0.001**	0.73 (0.23-0.84)	**0.03**

*Reference category. PFS: progression-free survival, NLR: Neutrophil to lymphocyte ratio, ALI: Advanced lung cancer inflammation index, SII: Systemic immune inflammation index, PNI: Prognostic nutritional index, PPR: Platelet distribution width to platelet count ratio, HRR: Hemoglobin to red cell distribution width ratio, LMR: Lymphocyte to monocyte ratio, PLR: Platelet to lymphocyte ratio, PIIV: Pan-immune inflammation value, SIRI: Systemic inflammation response index, HALP: Hemoglobin-albumin-lymphocyte and platelet.

Finally, in the high HALP group, the median OS was 21 months compared to 15 months in the low HALP group, again with a statistically significant association (p=0.02) (Figure 5).

Discussion

Our study investigated the prognostic value of various inflammation markers in patients with malignant mesothelioma. Some of the parameters we evaluated had been previously examined in malignant mesothelioma patients. However, SII, PPR, HRR, LMR, PIIV, SIRI, and HALP parameters had not been previously studied for malignant mesothelioma.

Hypotheses previously put forth regarding the etiology of malignant mesothelioma suggested that inflammation could be a contributing factor to the disease. Therefore, it was thought that inflammation markers might play a role in predicting the prognosis of the disease. A previous meta-analysis[14] demonstrated that high NLR was identified as an adverse prognostic factor in malignant mesothelioma patients. Our study similarly found that elevated NLR was associated with poorer survival. For the low NLR group, the average survival was

Table III. Univariate and multivariate analysis results in terms of OS.

Variables	Categories	Median PFS (Months)	Univariate analysis HR 95% CI	*p*-value	Multivariate analysis HR 95% CI	*p*-value
Age	≤65*	16				
	>65	11	1.5 (1-2.2)	**0.04**	1.23 (0.75-2.01)	0.39
Gender.	Male*	15				
	Female	14	1.2 (0.81-1.82)	0.33		
Mesothelioma type	Pleural*	15				
	Peritoneal	12	1.5 (0.98-2.4)	**0.06**	1.25 (0.74-2.12)	0.39
Histology	Epiteloid*	15				
	Biphasic	14	1.3 (0.79-2.19)	0.28		
	Sarcomatoid	8	2.6 (1.11-6.18)	**0.02**	2.83 (1.13-7.05)	**0.025**
Stage at diagnosis	I-II *	20				
	III-IV	12	2.4 (1.44-4.29)	**0.001**	2.58 (1.44-4.64)	**0.001**
NLR	≤3.1*	26				
	>3.1	12	2.54 (1.32-3.15)	**0.001**	1.34 (1.12-2.83)	**0.04**
ALI	≤35.25*	12				
	>35.25	26	0.51 (0.33-0.79)	**0.003**	0.73 (0.53-0.84)	**0.03**
SII	≤854.3*	14				
	>854.3	15	0.92 (062-1.37)	0.71		
PNI	≤48.3*	12				
	>48.3	19	0.5 (0.32-0.78)	**0.003**	0.62 (0.3-1.26)	0.18
PPR	≤0.03*	16				
	>0.03	14	1.2 (0.45-.1.84)	0.31		
HRR	≤0.31*	14				
	>0.31	17	0.61 (0.39-0.95)	**0.03**	0.74 (0.42-3.95)	0.41
LMR	≤3.36*	12				
	>3.36	15	0.81 (0.73-2.12)	0.26		
PLR	≤206*	15				
	>206	13	1.61 (1.05-2.47)	**0.02**	1.32 (0.78-4.23)	0.43
PIIV	≤638*	20				
	>638	12	1.84 (1.22-2.76)	**0.003**	2.01 (1.32-4.79)	**0.03**
SIRI	≤1.78*	20				
	>1.78	11	1.66 (1.11-2.49)	**0.04**	1.34 (1.2-2.78)	**0.04**
HALP	≤25.9*	15				
	>25.9	21	0.48 (0.31-0.75)	**0.001**	0.67 (0.23-0.78)	**0.02**

*Reference category OS: Overall survival, NLR: Neutrophil to lymphocyte ratio, ALI: Advanced lung cancer inflammation index, SII: Systemic immune inflammation index, PNI: Prognostic nutritional index, PPR: Platelet distribution width to platelet count ratio, HRR: Hemoglobin to red cell distribution width ratio, LMR: Lymphocyte to monocyte ratio, PLR: Platelet to lymphocyte ratio, PIIV: Pan-immune inflammation value, SIRI: Systemic inflammation response index, HALP: Hemoglobin-albumin-lymphocyte and platelet.

26 months, while in the high NLR group, this duration was 12 months (p=0.04).

The relationship between PLR and malignant mesothelioma prognosis was examined in the literature. However, only one of these studies found a significant correlation between high PLR and poor OS, but it noted a limited sample size[15]. Although we had a larger patient group in this study, we could not find a significant relationship between PLR and OS (p=0.43). Nevertheless, high PLR was observed to be associated with poorer PFS (p=0.04).

Ebinç et al[16] reported in their study that a high PNI value was a favorable prognostic factor for malignant mesothelioma. Our study also associated a high PNI value with better PFS (p=0.02), although no significant relationship was found with OS (p=0.18). The sarcomatoid histology was linked to poorer OS compared to epithelioid histology (p=0.025), aligning with the literature[14].

The relationship between malignant mesothelioma prognosis and SII, PPR, HRR, and LMR had not been previously investigated. However, in our study, no statistically significant correlation was found between these inflammation parameters and the prognosis of malignant mesothelioma.

While the relationship between ALI and malignant mesothelioma prognosis had been studied

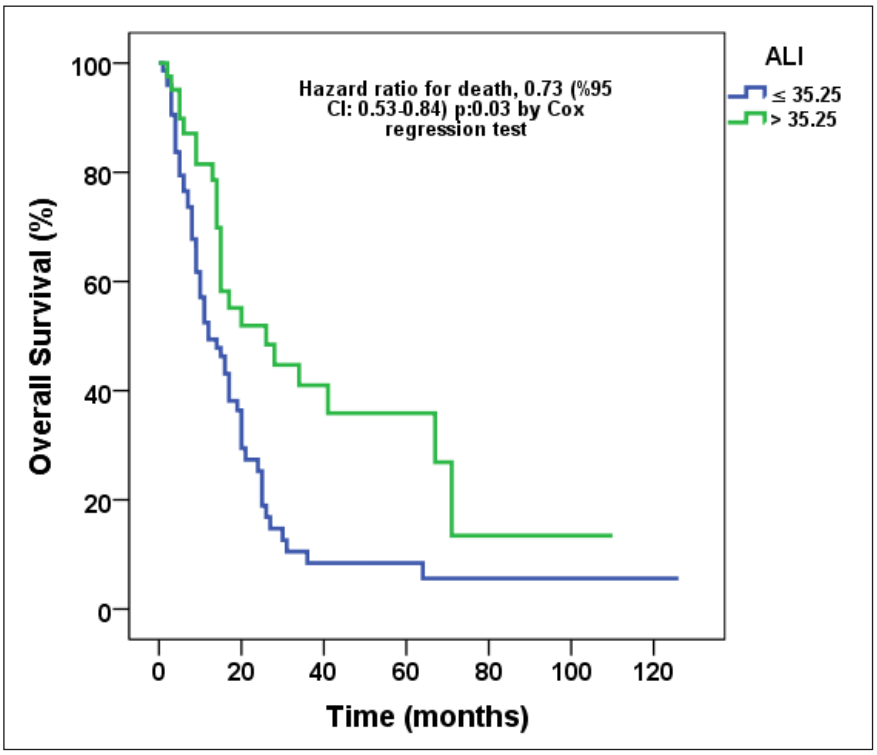

Figure 2. Overall survival outcomes according to ALI.

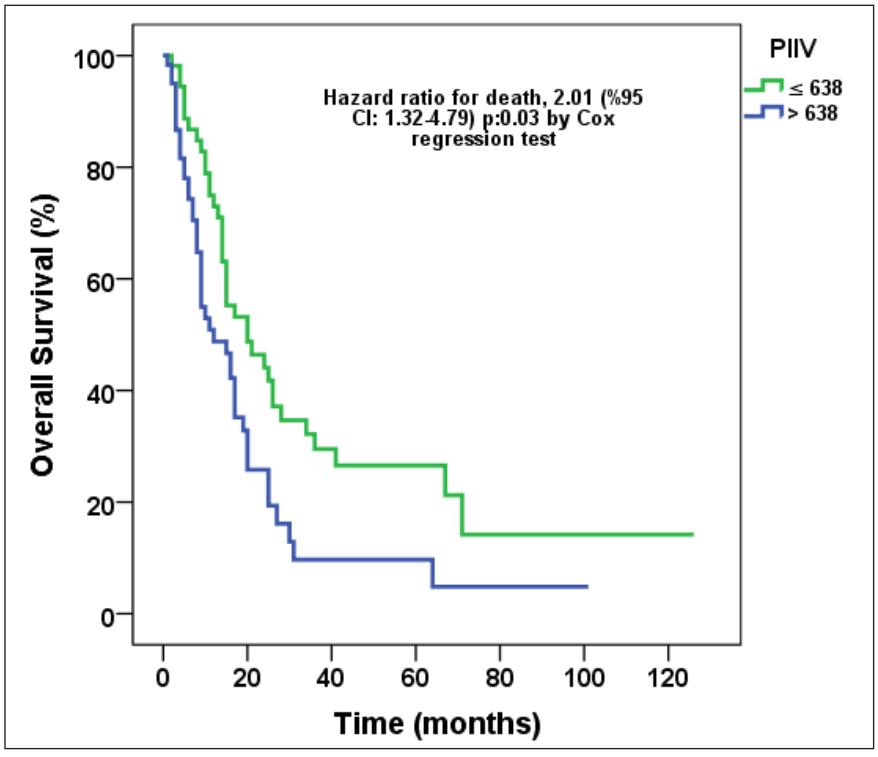

Figure 3. Overall survival outcomes according to PIIV.

before, no significant association had been found in a previous study[16]. Our study demonstrated that a high ALI was a good OS prognostic factor. In the low ALI group, the average survival was 12 months, whereas, in the high ALI group, it was 26 months (HR: 0.73, 95% CI: 0.53-0.84, p=0.03).

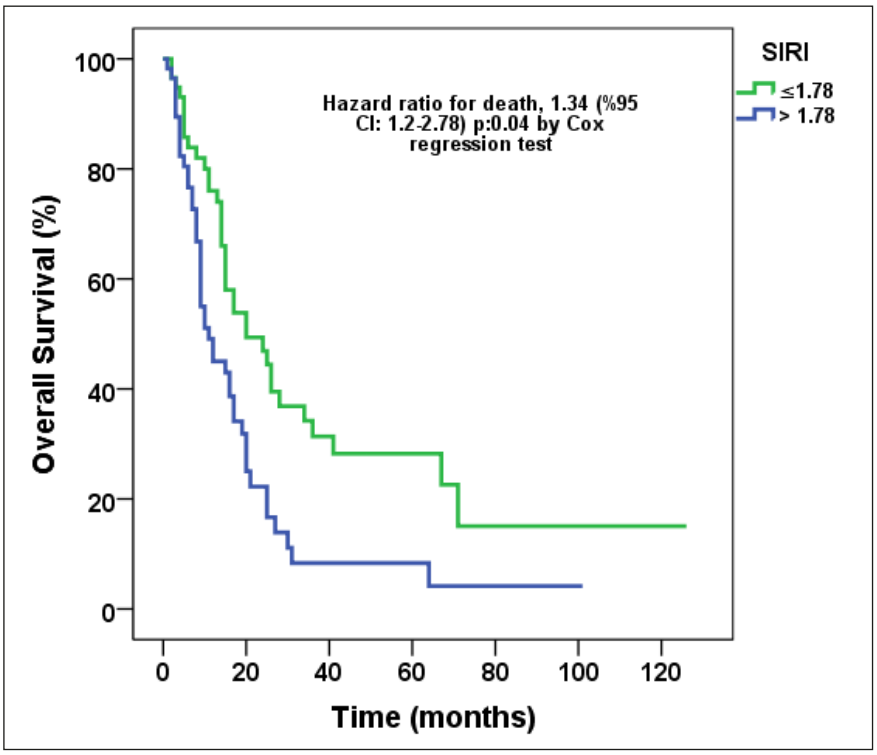

Figure 4. Overall survival outcomes according to SIRI.

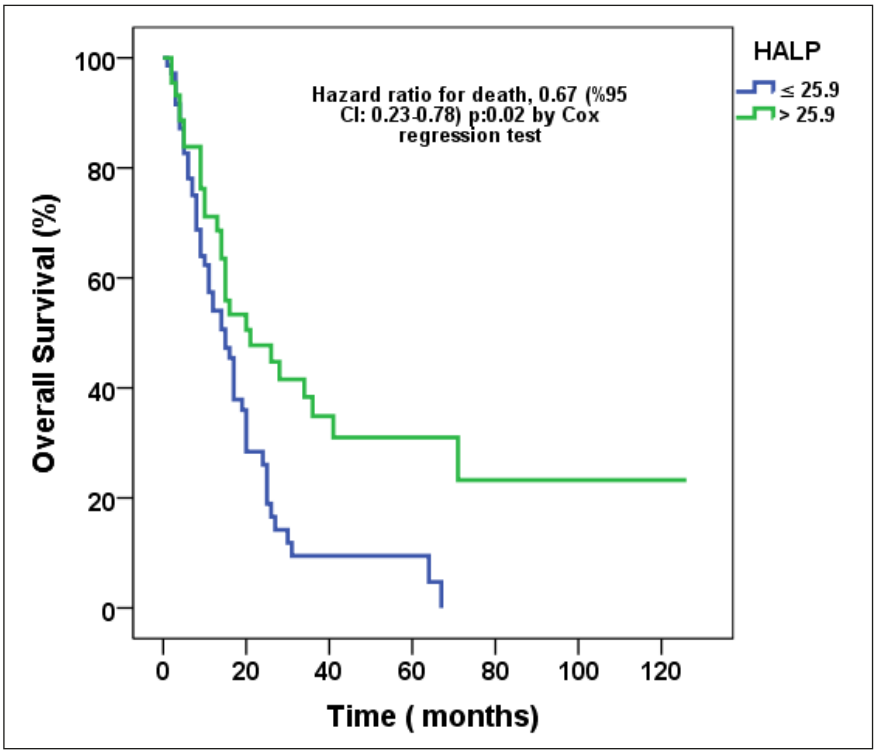

Figure 5. Overall survival outcomes according to HALP.

This study is the first to demonstrate the relationship between ALI and malignant mesothelioma prognosis. The association of ALI with cancer prognosis was shown in the literature. A meta-analysis[5] found that low ALI was associated with poor OS in various cancer patients, including lung

malignancy, colorectal malignancy, head and neck malignancy, and lymphoma. Low body weight, malnutrition, and hypoalbuminemia have been linked to persistent systemic inflammation. BMI and albumin have been validated as effective prognostic indicators for cancer patients. ALI combines these relevant markers and provides prognostic insights for cancer patients. As a composite index involving both inflammation status (NLR) and nutritional status (BMI and albumin), ALI might have superior discriminatory capabilities compared to other biomarkers and continue to be an effective inflammatory prognostic factor. This study is the first to demonstrate the relationship between ALI and malignant mesothelioma prognosis.

Meanwhile, PIIV and SIRI have been investigated as prognostic markers in various cancers[17]. In a meta-analysis[18] investigating breast cancer patients, high PIIV values were associated with poor OS. Their effects on malignant mesothelioma prognosis had not been explored before, and our study is the first to investigate this relationship. We found a significant relationship between high PIIV values and poor OS (HR: 2.01, 95% CI: 1.32-4.79, p=0.03).

Similarly, the relationship between SIRI and malignant mesothelioma prognosis had not been previously investigated, and our study is the first to investigate this relationship as well. We found a significant relationship between high SIRI values and poor OS (HR: 1.34, 95% CI: 1.2-2.78, p=0.04). SIRI is a newly proposed index based on circulating immune cells that can evaluate the balance of inflammatory and immune responses by reflecting interactions between neutrophils, monocytes, and lymphocytes in the tumor microenvironment. Numerous studies[19-21] have shown SIRI's predictive value for prognosis in different tumor types. A high SIRI value often indicates a poor prognosis and can provide guidance in clinical management.

Thrombocytes can play a significant role in tumor growth and metastasis through various pathways. They can interact with circulating tumor cells to form a thrombus, weakening the immune system's defense against tumor cells. Additionally, activated platelets can release various growth factors contributing to tumor spread and development[22].

Similarly, monocytes can be linked to cancer prognosis. M2 macrophages derived from monocytes, in particular, can influence processes such as angiogenesis, invasion, and immune suppression through molecules like VEGF, tumor necrosis factor-alpha (TNF-alpha), and interleukin (IL)-10. Neutrophils have also been associated with tumor development through mechanisms like the production of reactive oxygen species and the release of stimulating chemokines[23].

The PIIV score is a calculation method that includes various cell types in the immune system to reflect the inflammatory pressure more accurately. By incorporating all pro-inflammatory cells, hematological parameters, and albumin levels, the PIIV score is formulated. Therefore, there is a biological basis for the PIIV score, and it might provide better risk stratification than other indices like NLR or PLR. A recent study[24] created the PIIV score using data from two separate phase III clinical trials and found it to be a significant prognostic parameter for both PFS and OS, surpassing other hematology-based indices.

Several studies[25] have previously shown a correlation between low HALP scores and poor prognosis in various cancer types. However, the relationship between malignant mesothelioma prognosis and the HALP scores had not been explored in the literature. This study is the first to investigate the relationship between the HALP score and malignant mesothelioma prognosis. We found a significant relationship between low HALP score and poor OS in malignant mesothelioma patients (HR: 0.67, 95% CI: 0.23-0.78, p=0.02). While numerous clinical pieces of evidence support the notion that a low HALP score is an adverse prognostic factor for patients with cancer, the specific mechanisms by which the HALP score affects cancer prognosis remain largely uncharted. We can explore this by examining the four components of the HALP score. Pre-treatment low hemoglobin levels are a common clinical feature in cancer patients and can contribute to hypoxia, potentially leading to cancer progression and therapeutic resistance[26]. Clinical studies[27] have closely linked anemia with poor survival. Additionally, serum albumin is another crucial component. Serum total protein levels are essential indicators reflecting the host organism's inflammation levels and nutritional status. Hypoalbuminemia can adversely affect immune system function and lead to poor oncological outcomes[28].

Conclusions

Our study investigated the prognostic value of various inflammation markers in malignant mesothelioma patients and suggests that composite formulas like PIIV, SIRI, ALI, and HALP that incorporate CBC cells and nutritional parameters like albumin and BMI could more consistently and accurately predict malignant mesothelioma prognosis.

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Ethics Approval
The study was conducted following the principles of the Declaration of Helsinki and reviewed and approved by the Bioethics Committee of the Medical University of Erciyes (Date: 22.02.2023, No.: 2023/144).

Informed Consent
Written informed consent was obtained from each patient.

Conflict of Interest
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors' Contributions
Concept: E.M.; design: E.M., M.I.; data collection or processing: E.M.; analysis or interpretation: E.M., M.I.; literature search: E.M., M.I.; writing: E.M.

Availability of Data and Materials
The datasets generated during and/or analyzed during the current study are available in the Erciyes University Medical Oncology Department Database repository.

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