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Malignant Melanoma: Clinicopathological Features and Prognostic Significance of Neutrophil-Lymphocyte Ratio

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Introduction: Malignant melanoma (MM) is a neoplasm characterized by high rates of metastasis and mortality. The aim of this study was to investigate the relationship of neutrophil-lymphocyte ratio (NLR) on prognosis and survival in MM, along with demographic and clinicopathological parameters.

Patients/Methods: A total of 107 patients; who were followed up in the Department of Medical Oncology, Faculty of Medicine, Eskişehir Osmangazi University in the period from the year 2010 to 2017 were evaluated retrospectively. The age and sex distribution of the patients; the levels of LDH, the neutrophil and lymphocyte counts, pathological parameters, and BRAF mutation status were examined along with their correlations with each other and the effects of these parameters on overall survival (OS) and disease-free survival (DFS) were investigated.

Results: Of the study patients; 86% were in the early stage and 14% were in the metastatic stage. Of the patients in Stage III; 65.2% (n: 23/107) had received adjuvant interferon treatment. Cutaneous involvement was common and the nodular MM were the predominant type. The most common sites of metastasis were respectively the lungs (64.7%), distant lymph nodes (40.4%), and the liver (39.2%). Of the 39 patients, for whom BRAF mutation status was investigated; BRAF V600 was positive in 53.8%. Median NLR was 1.97. All non-cutaneous MM cases were negative for BRAF ($p<0.0001$). No correlations were found between the presence of BRAF mutations and the following parameters including the levels of NLR and serum LDH, lymph node (LN) involvement, the disease stages, the pathologic parameters, and the distribution of age and sex. In the advanced disease stages, the incidences of high NLR and non-cutaneous MM were higher ($p=0.001$). A high NLR was found out to be correlated with advanced age ($p=0.008$), tumor ulceration ($p=0.011$), and the high mitosis rates in the tumor ($p=0.05$). Median OS was 13, 45, 84, 101 months for the advanced stage, stage III, stage II, and stage 0-I, respectively. A high NLR ($p<0.0001$), LDH levels ($p=0.04$), increased Breslow thickness ($p=0.01$), Clark levels ($p=0.01$), the number of mitosis ($p=0.02$), presence of ulcerations ($p=0.03$), and LN involvement ($p=0.04$) were significantly associated with a shorter OS duration. Median DFS was 40 months in stage II and 23 months in stage III. DFS was significantly shorter in patients with increased Breslow thickness ($p=0.01$), high Clark levels ($p=0.05$), a high number of mitosis ($p=0.02$), and LN involvement ($p=0.03$). Cox regression analysis revealed that the most significant parameters affecting OS were NLR (HR: 3.4, $p=0.04$) and the presence of a nodal disease (HR: 4.6, $p=0.01$). Nodal involvement was additionally found out to be the most significant predictor of recurrences (HR: 3.2, $p=0.03$).

Conclusion: NLR appears to be an additional biomarker to the classical ones for predicting prognosis. Patients with nodal involvement and high NLR should be closely monitored in the clinical practice. There is a need to prove the data, conducting large-scale studies.

Keywords: Clinicopathologic features, malignant melanoma, NLR

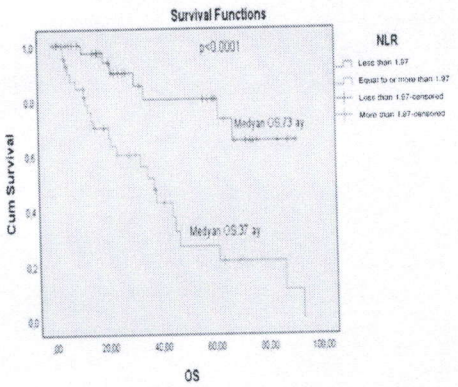


Figure 1. Change in the overall survival length in association with the neutrophil-lymphocyte ratio (Kaplan Meier analysis).

Table 1. Independent variables predicting death in the Cox multivariate analysis

Independent Variables	HR (Hazard Ratio)	p-value
Lymph node involvement	4.6 (1.2-16.8)	0.01
NLR	3.4 (1-11.9)	0.04
LDH	2 (0.5-7.9)	0.2
Breslow thickness	2.2 (0.6-8.2)	0.2
Gender	0.4 (0.08-2.9)	0.4
Number of Mitosis	0.3 (0.03-5.1)	0.4
Presence of ulcerations	0.4 (0.03-4.9)	0.4

Table 2. Independent variables predicting death in the Cox multivariate analysis

Independent Variables	HR (Hazard Ratio)	p-value
Lymph node involvement	3.2(1-10)	0.03
Number of Mitosis	2.3 (0.7-7.5)	0.1
Breslow thickness	1.9 (0.6-5.9)	0.2
LDH	0.4 (0.1-1.5)	0.2
NLR	1.6 (0.4-6.1)	0.4
Presence of ulcerations	0.9 (0.1-4.1)	0.8