

■ Original Article

## Prognostic significance of neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, platelet/neutrophil ratio, and mean platelet volume in patients diagnosed with Hodgkin and Non-Hodgkin Lymphoma

*Hodgkin ve Non-Hodgkin Lenfoma tanılı hastalarda nötrofil/lenfosit oranı, trombosit/lenfosit oranı, trombosit/nötrofil oranı ve ortalama trombosit hacminin prognostik önemi*

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### Abstract

**Aim:** We aimed to show whether easily accessible NLR, PLR, PNR and MPV values can be used as prognostic markers in lymphoma subtypes and whether they can contribute to existing prognostic scoring systems.

**Material and Methods:** The records of all lymphoma patients between 2005-2019 were reviewed retrospectively. NLR, PLR, PNR and MPV values at the time of diagnosis were compared with Progression-Free Survival (PFS) and Overall Survival (OS) durations.

**Results:** PLR and NLR values in Marginal Zone Lymphoma (MZL) and PNR and MPV values in Diffuse Large B-cell Lymphoma (DLBCL) were found to be associated with prognosis and to have a direct effect on PFS and OS. Except for these parameters, we found that lactate dehydrogenase (LDH), MPV, age, stage and histological subtype had an effect on prognosis for all patients.

**Conclusion:** It has been concluded that PLR and NLR can be used as prognostic factors in MZL, whereas PNR and MPV can be used as prognostic factors in DLBCL, and that these values can be used as easily accessible methods in disease prognosis scores.

**Keywords:** lymphoma; prognostic score; pnr; mpv; pfs; os

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## Öz

**Amaç:** Kolay ulaşılabilir NLR, PLR, PNR ve MPV değerlerinin lenfoma alt tiplerinde prognostik belirteç olarak kullanılıp kullanılmayacağını ve mevcut prognostik skorlama sistemlerine ek katkı sağlayıp sağlayamayacağını göstermeyi amaçladık.

**Gereç ve Yöntemler:** 2005-2019 tarihleri arasında ki tüm lenfoma hastalarının kayıtları retrospektif olarak incelenmiştir. Tanı anında ki NLR, PLR, PNR ve MPV değerleri ile PFS ve OS süreleri karşılaştırılmıştır.

**Bulgular:** Marjinal zone lenfomada PLR ve NLR değerleri ve DBBHL'da da PNR ve MPV değerlerinin prognoz ile ilişkili olduğu, PFS ve OS üzerine doğrudan etkisi olduğu saptandı. Bu parametreler dışında tüm hasta grubu için LDH, MPV, yaş, evre ve histolojik alt tipin prognoz üzerinde etkili olduğunu saptadık.

**Sonuçlar:** Sonuç olarak PLR ve NLR Marjinal Zone lenfomada, PNR ve MPV'de DBBHL da prognostik faktör olarak kullanılabilir. Hastalık prognoz skorlarında kolay ulaşılabilir yöntemler olarak yerlerini alabilirler.

**Anahtar kelimeler:** lenfoma; prognoz skoru, pnr; mpv; pfs; os

## Introduction

Lymphomas are clinically and pathologically heterogeneous, clonal lymphoproliferative malignancies that usually originate from B cells [1]. Although various classification systems have been used to date, the World Health Organization classification of lymphoid neoplasms system, which was recently revised in 2016, is being used [2]. Known prognostic markers should be sought according to the lymphoma subtype of each patient whose diagnosis is confirmed. Prognosis scores (R-IPI, MIPI, IPS, FLIPI) developed for some common subtypes are used. The determination of prognosis helps to determine treatment management strategies such as choosing the best therapeutic treatment for the patient, predicting early relapse that may develop, and increasing stem cell transplantation plans. All these studies are also insufficient in predicting response to treatment [3]. There is a need for new easily accessible prognostic factors at this stage.

Peripheral blood leukocytosis, neutrophilia, lymphopenia and thrombocytosis may be seen in systemic inflammation. Many diseases such as cardiovascular diseases, cirrhosis and bipolar disorders have been shown to be associated with chronic inflammation [4, 5]. From this point of view, it is suggested that the values and ratios (NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, PNR: platelet-neutrophil ratio), which can be determined by fast and easily accessible full blood count, can be used as a marker of systemic inflammatory response and can be used to determine the prognosis of some diseases [6, 7]. There are many studies showing that it can be used as a prognostic marker in solid organ tumors such as breast, lung, hepatocellular, stomach, ovary and colorectal cancer [6, 8-12]. MPV (Mean Platelet Volume) is a parameter that increases in response to stress and is an indicator of platelet activation and

function[13]. It has been shown to be used as a prognostic marker in endometrial cancer [14]. In addition to all these studies, there are few studies in patients with Hodgkin Lymphoma, Follicular Lymphoma and Diffuse Large B-cell Lymphoma [15-19]. In this study, we aimed to show whether NLR, PLR, PNR and MPV values can be used as prognostic markers in different lymphoma types as well as to show whether it can contribute to existing prognostic scoring systems.

## Material and Methods

This study was performed retrospectively from the medical records of patients who were followed up and treated for lymphoma (HL and NHL) in Antalya Training and Research Hospital. The records of all lymphoma patients between 2005-2019 were examined (n: 539). Because of the lack of hemogram values of 21 patients at the time of diagnosis, these patients were excluded and a total of 518 patients were included to the study. Demographic characteristics, histological subtypes, B symptom, stage, laboratory results, prognosis score according to histological subtype and disease status and life status were examined at diagnosis.

This study was approved by the Antalya Research and Training Hospital Clinical Research Ethics Committee dated 28.03.2019 and No 10/4. All procedures were carried out in accordance with the 2013 Helsinki Declaration.

## Statistical Analysis

Descriptive values of the obtained data were calculated as mean, SD median, minimum-maximum, number and % frequencies. The suitability of the data for normal distribution according to the groups examined was examined by Kolmogorov-Smirnov test. The relationships between the two categorical features were examined by Pearson Chi-square test or Fisher Exact



test, and changes in numerical properties were examined by independent samples t-test for normal distributed data, and Mann Whitney-U test for normal distribution. The relationship between prognosis development and ex-status and NLR, PLR, PNR and MPV measurements were examined with ROC curve and if significant correlation was found, the appropriate estimation value was found. Estimation was not calculated in non-significant relationships. OS and PFS times were compared with Log-Rank test and Kaplan Meier graph was plotted for each estimated value. The factors affecting OS and PFS durations were examined by multiple Cox regression model. SPSS 22.0 program was used in the calculations and statistical significance level was taken as  $P < 0.05$ .

## Results

518 lymphoma patients were included in the study. 227 of the patients were Diffuse Large B cell Lymphoma, 97 were Hodgkin Lymphoma, 68 were Follicular Lymphoma, 48 were Marginal Zone Lymphoma, 27 were Mantle Cell Lymphoma, and 51 were other Non-Hodgkin Lymphomas. The median age at the time of diagnosis was 59(18-88). 221 patients (42%) were female. The appropriate predictive value for NLR, PLR, PNR and MPV parameters in each diagnostic group and in all patients was investigated by ROC analysis. For NLR and PLR parameters, only significant results were obtained in ROC analysis in Marginal Zone Lymphoma subgroup ( $P=0.045$  for NLR area under the curve [AUC] value: 0.690, 95% confidence interval [CI]0.526–0.854) and  $P=0.047$  for PLR AUC value 0.688, 95% CI 0.516–0.860). There were no significant results for NLR and PLR in the other subgroups and in the whole patient group. Estimations were calculated as 1.86 for NLR and 148.95 for PLR.

For the PNR parameter, only significant predictive level was found in the DLBCL subgroup (41.64,  $P=0.018$  AUC value 0.405, 95% CI 0.326–0.485). ROC analysis for MPV parameter revealed significant but different predictive values in the DLBCL subgroup ( $P=0.036$  AUC value 0.584, 95% CI 0.505–0.663) and in all patients group ( $P=0.001$  AUC value 0.596, 95% CI 0.543.60.648).

Table 1 shows the comparison of demographic and laboratory results according to the predicted PNR and MPV values in the diagnosis subtypes of DLBCL patients. According to the table, gender distribution showed a significant difference in terms of PNR estimation value ( $P=0.027$ ). In the group with  $PNR < 41.65$ , males were found to be significantly higher. When the distribution of the stages according to PNR estimation value was examined, it was found that the rate of patients with stage 3-4 was significantly higher in the group with  $PNR < 41.65$

( $P=0.003$ ). The presence of B symptoms was significantly higher in the group with  $PNR < 41.65$  ( $P=0.023$ ). The proportion of patients with low prognosis score was found to be significantly higher in the group with  $PNR > 41.65$  ( $P=0.001$ ). Both age and LDH levels were significantly higher in patients with  $PNR < 41.65$  ( $P=0.003$  and  $P=0.001$ ). In contrast, the presence of Bulky lesion and hemoglobin mean values were not significantly different in patients with  $PNR < 41.65$  or higher ( $P=0.715$  and  $P=0.608$ ).

When the patients with DLBCL were examined according to the MPV estimation value, the distribution of those with normal platelet levels was found to be significantly higher in the group with  $PNR < 10.2$  ( $P=0.017$ ). In addition, the frequency of patients without progression was higher in the group with  $MPV < 10.2$  or less ( $P=0.040$ ). In terms of other demographic and laboratory measurements, no significant difference was found between those below and above the MPV estimation value (Table 1).

Table 2 shows the comparison of demographic and laboratory results according to the predictive values of PLR and NLR in the marginal group. When the table was examined, Bulky absence was found to be significantly more frequent in the group with a PLR estimation of less than 148.94 ( $P=0.003$ ). The frequency of those with high lymphocyte levels was significantly higher in the low PLR group, whereas the frequency of those with normal platelet levels was significantly higher in the PLR group ( $P=0.001$  and  $P=0.009$ ).

It was seen that the female ratio was higher in the NLR group ( $P=0.009$ ). The ratio of patients with high levels of lymphocytes was higher in the group with low NLR value ( $P=0.001$ ). Absence of bone marrow involvement was higher in the group with high NLR levels ( $P=0.020$ ). However, the incidence of non-progression was higher in the group with low NLR ( $P=0.028$ ) and significantly higher in the group with high NLR ( $P=0.040$ ). The relationship between both PLR and NLR levels with other measurements was not significant (Table 2).

The comparison of demographic and laboratory results according to MPV estimation value which is significant for evaluation in the whole patient group without differentiating according to diagnostic subtypes is given in Table 3. Significant differences in neutrophil and platelet distribution were observed among individuals below and above MPV estimation ( $P=0.011$  and  $P=0.001$ ). Accordingly, the ratio of patients with both neutrophil and platelet levels was found to be significantly higher in the MPV predictive value group 9.9 and below. It was found that there was no correlation between the high prognosis scores calculated especially for the subgroups and the MPV estimation value of the other results.

**Table-1.** The comparison of demographic and clinical features according to the predicted PNR and MPV values in patients with DLBCL †

Demographic and Clinical Condition		PNR≤41.65 (n=56)	PNR>41.65 (n=171)	P	MPV≤10.2 (n=177)	MPV>10.2 (n=50)	P
Gender	Female	19 (33.9)	87 (50.9)	0.027 <sup>a</sup>	82 (46.3)	24 (48)	0.834 <sup>a</sup>
	Male	37 (66.1)	84 (49.1)		95 (53.7)	26 (52)	
Stage	I&II	11 (19.6)	71 (41.5)	0.003 <sup>a</sup>	67 (37.9)	15 (30)	0.307 <sup>a</sup>
	III&IV	45 (80.34)	100 (58.5)		110 (62.1)	35 (70)	
Presence of Symptom B	Absent	12 (21.4)	65 (38)	0.023 <sup>a</sup>	61 (34.5)	16 (32)	0.745 <sup>a</sup>
	Present	44 (78.6)	106 (62)		116 (65.5)	34 (68)	
Presence of bulky mass	Absent	33 (58.9)	96 (56.1)	0.715 <sup>a</sup>	101 (57.1)	28 (56)	0.893 <sup>a</sup>
	Present	23 (41.1)	75 (43.9)		76 (42.9)	22 (44)	
Neutrophil (×103/mm3), median	<2000	4 (7.1)	16 (9.4)	0.001 <sup>a</sup>	14 (7.9)	6 (12)	0.544 <sup>a</sup>
	2000-7000	29 (51.8)	138 (80.7)		130 (73.4)	37 (74)	
	>7000	23 (41.1)	17 (42.5)		33 (18.6)	7 (14)	
Lymphocytes (×103/mm3), median	<1200	22 (39.3)	59 (34.5)	0.026 <sup>a</sup>	65 (37.7)	16 (32)	0.450 <sup>a</sup>
	1200-3100	26 (46.4)	104 (60.8)		98 (55.4)	32 (64)	
	>3100	8 (14.3)	8 (4.7)		14 (7.9)	2 (4)	
Platelet (×103/mm3), median	<150	24 (42.9)	9 (5.3)	0.001 <sup>a</sup>	21 (11.9)	12 (24)	0.017 <sup>a</sup>
	150-450	29 (51.8)	142 (83)		134 (75.7)	37 (74)	
	>450	3 (5.4)	20 (11.7)		22 (12.4)	1 (2)	
IPI Score	0-2	22 (39.3)	114 (66.7)	0.001 <sup>a</sup>	108 (61)	28 (56)	0.523 <sup>a</sup>
	3-5	34 (60.7)	57 (33.3)		69 (39)	22 (44)	
Bone Marrow Involvement	Absent	17 (65.4)	91 (90.1)	0.004 <sup>b</sup>	84 (86.6)	24 (80)	0.376 <sup>b</sup>
	Present	9 (34.6)	10 (9.9)		13 (13.4)	6 (20)	
Progression/relapse	Absent	20 (39.2)	97 (63.8)	0.002 <sup>a</sup>	96 (61.5)	21 (44.7)	0.040 <sup>a</sup>
	Present	31 (60.8)	55 (36.2)		60 (38.5)	26 (55.3)	
Age median		68 (37-88)	59 (18-88)	0.003 <sup>c</sup>	61 (18-88)	62 (27-84)	0.645 <sup>c</sup>
Hemoglobin g/dL median		12 (5-16.1)	11.9 (4.5-16)	0.608 <sup>c</sup>	11.8 (5-16)	12.2 (4.5-16.1)	0.775 <sup>c</sup>
LDH IU/dL median		397.5 (117-4099)	253 (117-1483)	0.001 <sup>c</sup>	273 (117-4216)	273 (128-1390)	0.525 <sup>c</sup>

† Median [min-max] or frequency (%). a: Chi-Square test b: Fisher Exact test b: Mann Whitney-U test

**Table-2.** The comparison of demographic and clinical features according to the predicted PLR and NLR in patients with MZL †

Demographic and Clinical Condition		PLR<148.94 (n=29)	PLR≥148.94 (n=19)	P	NLR<1.85 (n=24)	NLR≥1,8571 (n=24)	P
Gender	Female	11 (37.9)	10 (52.6)	0.315 <sup>a</sup>	6 (25)	15 (62.5)	0.009 <sup>a</sup>
	Male	18 (62.1)	9 (47.4)		18 (75)	9 (37.5)	
Stage	I&II	6 (20.7)	5 (26.3)	0.732 <sup>a</sup>	3 (12.5)	8 (33.3)	0.086 <sup>a</sup>
	III&IV	23 (79.3)	14 (73.7)		21 (87.5)	16 (66.7)	
Presence of Symptom B	Absent	20 (69.0)	10 (52.6)	0.253 <sup>a</sup>	16 (66.7)	14 (58.3)	0.551 <sup>a</sup>
	Present	9 (31.0)	9 (47.4)		8 (33.3)	10 (41.7)	
Presence of bulky mass	Absent	28 (96.6)	11 (61.1)	0.003 <sup>b</sup>	22 (91.7)	17 (73.9)	0.137 <sup>b</sup>
	Present	1 (3.4)	7 (38.9)		2 (8.3)	6 (26.1)	
Neutrophil (×103/mm3), median	<2000	5 (17.2)	0 (0)	0.147 <sup>a</sup>	5 (20.8)	0 (0)	0.057 <sup>a</sup>
	Normal	19 (65.5)	16 (84.2)		15 (62.5)	20 (83.3)	
	>7000	5 (17.2)	3 (15.8)		4 (16.7)	4 (16.7)	
Lymphocytes (×103/mm3), median	<1200	3 (10.3)	10 (52.6)	0.001 <sup>a</sup>	2 (8.3)	11 (45.8)	0.001 <sup>a</sup>
	Normal	10 (34.5)	9 (47.4)		7 (29.2)	12 (50)	
	>3100	16 (55.2)	0 (0)		15 (62.5)	1 (4.2)	
Platelet (×103/mm3), median	<150000	13 (44.8)	2 (10.5)	0.009 <sup>a</sup>	10 (41.7)	5 (20.8)	0.282 <sup>a</sup>
	Normal	16 (55.2)	14 (73.7)		13 (54.2)	17 (70.8)	
	>450000	0 (0)	3 (15.8)		1 (4.2)	2 (8.3)	
Progression/relapse	Absent	11 (64.7)	4 (30.8)	0.065 <sup>a</sup>	10 (71.4)	5 (31.3)	0.028 <sup>a</sup>
	Present	6 (35.3)	9 (69.2)		4 (28.6)	11 (68.8)	
Age median		61 (20-84)	69 (38-78)	0.082 <sup>c</sup>	61 (18-88)	62 (27-84)	0.274 <sup>c</sup>
Hemoglobin g/dL median		11.8 (5-15.7)	9.6 (7.5-15.8)	0.343 <sup>c</sup>	11.8 (5-16)	12.2 (4.5-16.1)	0.040 <sup>c</sup>
LDH IU/dL median		196 (140-285)	207 [9-466]	0.696 <sup>c</sup>	273 (117-4216)	273 (128-1390)	0.893 <sup>c</sup>

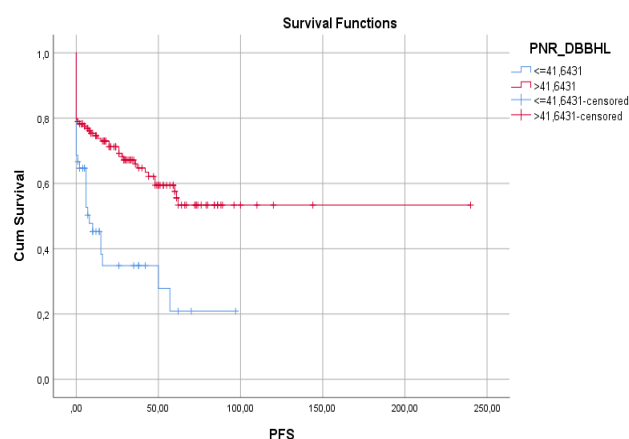
† Median [min-max] or frequency (%). a: Chi-square test b: Fisher Exact test c: Mann Whitney-U test

**Table 3.** The comparison of MPV estimation with demographic and laboratory data in all lymphoma patients †

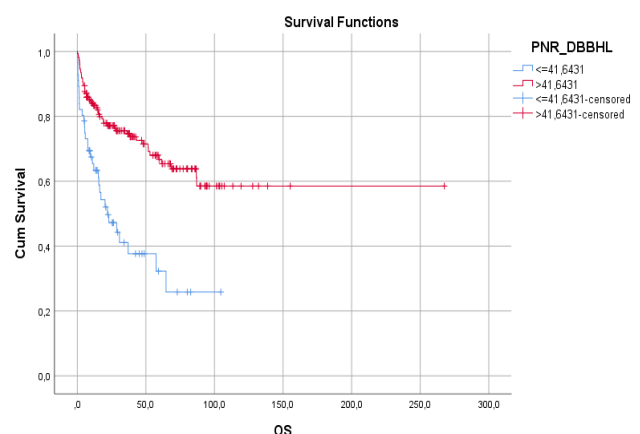
		MPV≤9.9 (n=364)	MPV>9.9 (n=154)	p
Gender	Female	152 (41.8)	69 (44.8)	0.522 <sup>a</sup>
	Male	212 (58.2)	85 (28.6)	
Lymphoma Subtypes	DLBCL	165 (45.3)	62 (40.3)	0.057 <sup>a</sup>
	FL	41 (11.3)	27(17.5)	
	HL	73 (20.1)	24 (15.6)	
	MZL	35 (9.6)	13 (8.4)	
	MCL	21 (5.8)	6(3.9)	
	Others	49 (13.4)	20 (12.9)	
Stage	I&II	106 (29.4)	47 (31.3)	0.671 <sup>a</sup>
	III&IV	254 (70.6)	103 (68.7)	
Presence of Symptom B	Absent	155 (43.1)	66 (44)	0.845 <sup>a</sup>
	Present	205 (56.9)	84 (56)	
Presence of bulky mass	Absent	243 (67.1)	101 (67.3)	0.964 <sup>a</sup>
	Present	119 (32.9)	49 (32.7)	
Neutrophil (×103/mm3), median	<2000	24 (6.6)	19 (12.3)	0.011 <sup>a</sup>
	Normal	257 (70.6)	114 (74)	
	>7000	83 (22.8)	21 (13.6)	
Lymphocytes (×103/mm3), median	<1200	127 (34.9)	40 (26)	0.072 <sup>a</sup>
	Normal	193 (53.0)	87 (56.5)	
	>3100	44 (12.1)	27 (17.5)	
Platelet (×103/mm3), median	<150000	45 (12.4)	35 (22.7)	0.001 <sup>a</sup>
	Normal	278 (76.4)	113 (73.4)	
	>450000	41 (11.3)	6 (3.9)	
Prognosis Score	Low	186 (62)	74 (62.2)	0.972 <sup>a</sup>
	High	114 (38)	45 (37.8)	
Progression/relapse	Absent	188 (61.6)	68 (51.9)	0.058 <sup>a</sup>
	Present	117 (38.4)	63 (48.1)	
Age median		58.5 (18-88)	61 (19-87)	0.953 <sup>b</sup>
Hemoglobin g/dL median		11.85 (5-17.2)	12.1 (3.7-16.1)	0.324 <sup>b</sup>
LDH IU/dL median		244.5 (93-4216)	241.5 (107-1390)	0.285 <sup>b</sup>

† Median [min-max] or frequency (%). a: Chi-square test b: Mann Whitney-U test

When the results of PFS and OS duration according to PNR estimation value determined by ROC analysis for DLBCL patients were examined, PFS and OS were found to be significantly longer in those above the predictive value (P=0.001&P=0.001). Kaplan Meier graphs are given in Figure 1A and 1B.

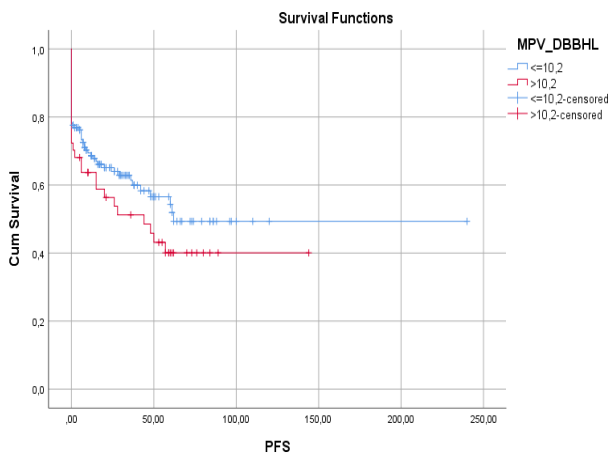


**Figure-1A.** PFS analysis according to PNR estimation in DLBCL

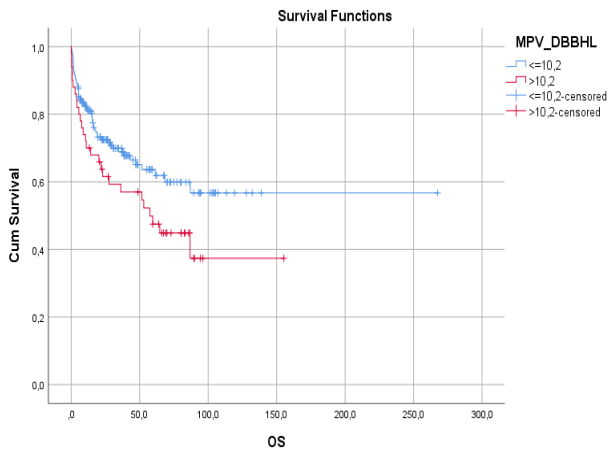


**Figure-1B.** OS analysis according to PNR estimation in DLBCL

When the results of PFS and OS duration according to MPV estimation value determined by ROC analysis for DLBCL patients were examined, there was no significant difference in PFS between MPV>10.2 and <10.2 (P=0.196), whereas OS was significantly shorter in patients with MPV>10.2 (P=0.048). Kaplan Meier graphs are given in Figure 2A and 2B.



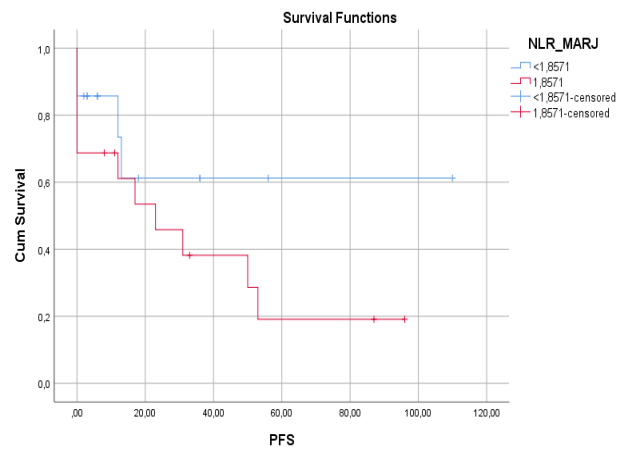
**Figure-2A.** PFS analysis according to MPV estimation in DLBCL



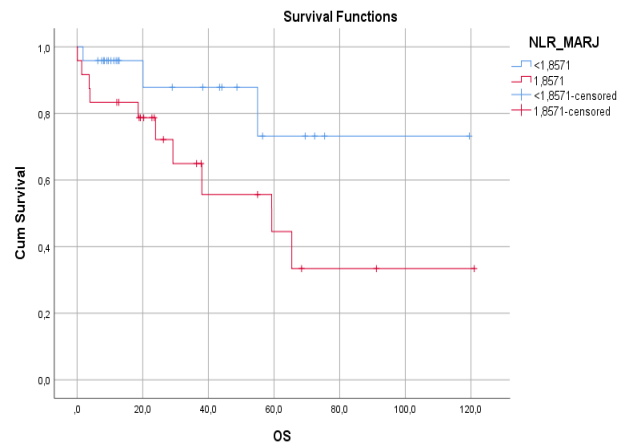
**Figure-2B.** OS analysis according to MPV estimation in DLBCL

When the diagnoses were evaluated separately, the predictive values of NLR and PLR were obtained only for the MZL subgroup. NLR and PLR ratio were classified according to this value and PFS and OS durations were compared. When the results were examined, no significant difference was found in terms of PFS for  $NLR > 1.86$  and  $< 1.86$  ( $P=0.174$ ). On the other hand, OS was found to be significantly shorter in patients  $< 1.86$  ( $P=0.049$ ). There was no significant difference in PLR in terms of  $> 148.95$  and  $< 148.95$  PFS ( $P=0.432$ ). But it was found that OS was significantly longer in subjects who had a value below the estimation ( $P=0.045$ ). Kaplan Meier graphs are given in Figure 3A, 3B, 4A and 4B.

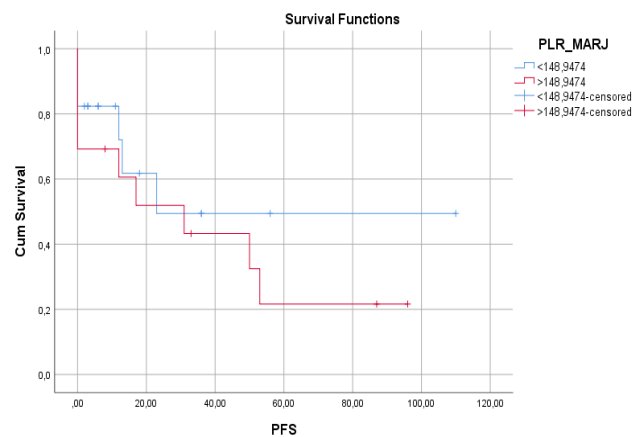
All patients were classified according to the ROC curve and the predictive value of MPV and compared for PFS and OS durations. It was determined that there was no significant difference in terms of PFS and OS duration in subjects with MPV values below and above 9.9 ( $P=0.362$  &  $P=0.070$ ).



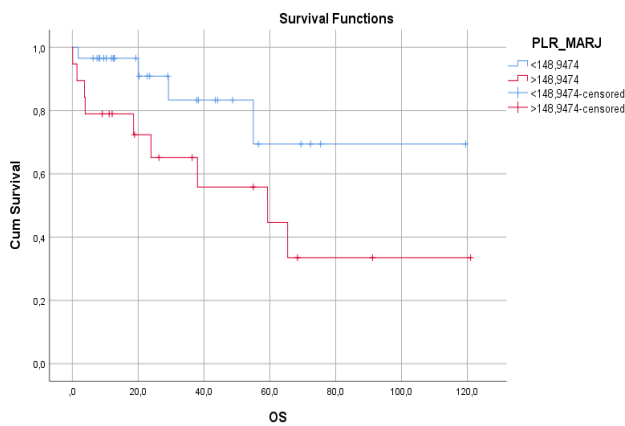
**Figure-3A.** PFS analysis according to NLR estimation in marginal zone lymphoma



**Figure-3B.** OS analysis according to NLR estimation in marginal zone lymphoma



**Figure-4A** PFS analysis according to PLR estimation in marginal zone lymphoma



**Figure-4B** OS analysis according to PLR estimation in marginal zone lymphoma

The effects of each of the factors such as gender, age, disease subtype, stage, symptom b, hemoglobin, platelet, lymphocyte, MPV, LDH, and bulky lesion presence were examined individually and uncorrected hazard ratio values were found. Factors without significant effect in these analyzes were not included in the multivariate Cox regression model. Others were modeled together to obtain corrected hazard ratio values. When the results were examined, it was observed that the risk of death increased 1.052 times significantly as age increased 1 year ( $p = 0.001$ ). The risk of death was found to be 0.519 times lower in patients with follicular diagnosis than those with DLBCL ( $P=0.030$ ). It was seen that the risk of death increased by 2,331 times compared to those with stage level 3-4 ( $P=0.001$ ). When LDH level increased by 1 unit, it was found that the prognosis development increased by 1,001 times ( $P=0.001$ ). When MPV level increased by 1 unit, the risk of death increased by 1,138 times ( $P=0.030$ ). Apart from these factors, the presence or absence of symptom B does not have a different effect on survival. Again, it was seen that increase or decrease in hemoglobin, platelet and lymphocyte levels did not significantly affect survival.

## Discussion

This study is the first in the literature because it evaluates all lymphoma patients and subtypes separately and also investigates parameters such as NLR, PLR, PNR and MPV in a single study. There are various prognosis scores (R-IPi, MIPI, IPS, FLIPI) used in lymphoma subtypes. Prognosis scores consist of parameters such as age, hemoglobin level, stage and LDH level. When evaluated comparatively with OS and PFS, we found that the parameters we studied may be part of prognosis scores in some subtypes.

Inflammation is known to play a role in the development of many cancers and has an impact on disease progression, angiogenesis and treatment resistance [20-22]. The result of this is that inflammation affects OS in patients. Neutrophils are important markers of inflammatory response. They increase in response to inflammation in cancer. While platelets increase with neutrophils, there is a suppression of lymphocytes responsible for immune response [23]. It was thought that NLR can be used as a prognostic marker from this relationship and many studies have been conducted. Studies other than solid organ tumors for the effect of NLR on PFS and OS are usually of the subtypes of DLBCL [16, 19, 24]. The effect of NLR on MZL has never been studied. In our study, we found that having  $NLR > 1.86$  significantly shortened OS although not associated with PFS. Although not in lymphoma patients, Kelkitli et al. showed that the relationship between NLR height and decreased PFS and OS in MM patients [25]. The prognostic value of NLR was also investigated in many solid organ tumors and positive results were obtained [8-10]. In our study, we found that NLR was insufficient to show PFS and OS in patients with other subtypes except MZL. There are different results in this regard in the literature. Wang et al. found that NLR elevation was not associated with PFS, but was associated with OS in patients with DLBCL [19]. In studies conducted by Ho et al. including DLBCL studies and Romano et al. including HL studies, they showed that NLR was unrelated to PFS and OS [24, 26]. The results of these two studies are parallel to our study.

Studies on PLR are not as common as NLR. In our study, we found that having  $PLR > 148.95$  significantly shortened OS even though it was not only associated with PFS in MZL. Seo et al. found a significant relationship with PFS in their study with MZL, but there was no data about OS in this study [27]. Reddy et al. found significant results between 2-year PFS and PLR in HL patients and no information was given about OS [18]. In addition to these studies, Ni et al. found that PLR had a significant relationship with PFS in DLBCL, but not with OS [28].

In our study, in the analysis for PNR, PFS and OS were seem to be significantly shorter in those with  $PNR < 41.64$  in the DLBCL subtype. Platelets and neutrophils are cells that are expected to increase in inflammation. The prognostic significance of the rates of increase in this rate was investigated. However, it should be kept in mind that the disease may be thrombocytopenia due to bone marrow involvement. It is known that bone marrow involvement in lymphoma patients is considered to be stage-4 and is associated with poor prognosis. In our study, bone marrow involvement was found to be significantly higher

in the group with  $PNR < 41.64$  ( $P = 0.004$ ). There are no studies related to prognosis associated with PNR in the literature. Mercier and Voutsadakis found PNLR to be significantly associated with PFS and OS in their study of colorectal cancer [29]. Choi et al. found that thrombocytopenia is associated with low PFS and OS in peripheral T cell lymphoma [30]. In our study, platelet levels of those with  $PNR < 41.64$  were found to be significantly lower than those with  $PNR > 41.64$ .

MPV value increases in response to stress [13]. The increase in stress has suggested us that it can be used as a prognostic marker in newly diagnosed lymphomas. In our study, we found OS to be significantly shorter in patients with DLBCL with  $MPV > 10.2$ . We could not find any relationship between PFS and MPV. When all patients were evaluated as a whole, no significant correlation was found between the predictive value for MPV and PFS and OS. However, when we look at 5-year survival, it is seen that 1 unit increase in MPV value was found to cause 1,138-fold increase in mortality risk. In a study by Zhou et al., it was found that MPV was associated with OS in parallel with our study in patients with DLBCL diagnosis [18]. Rupa-Matysek et al. showed that VTE also increased due to the increase in MPV, but OS regressed significantly [31].

The weakness of the study is that it is monocentric and includes very few patients, especially subtypes such as CNS lymphoma and T-cell lymphoma. Multinational and multicenter simultaneous study will have more meaningful results. In addition, there is no common predictive value for the parameters we investigate. Each retrospective study has its own value and it is very difficult to standardize them. A recent study showed that values such as NLR and PLR may vary according to age [32]. This makes it difficult to determine a common value for all patients.

## Conclusion

It has been concluded that PLR and NLR can be used as prognostic factors in MZL, whereas PNR and MPV can be used as prognostic factors in DLBCL, and that these values can be used as easily accessible methods in disease prognosis scores.

## Declaration of conflict of interest

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