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Effectiveness of neutrophil/lymphocyte, lymphocyte/MPV and platelet/MPV ratios in the classification and mortality prediction of acute stroke

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ABSTRACT

Objective: The aim of this study is to investigate whether Neutrophil / lymphocyte (NLR), Lymphocyte / MPV (mean platelet volume) (LMR) and thrombocyte / MPV (PMR) ratios obtained from the complete blood count, can be used as an effective marker in acute stroke for determining the prognosis and subtype of stroke.

Material and methods: Patients admitted to the emergency department with acute stroke symptoms between January 1, 2020 and December 31, 2020 were evaluated retrospectively. The patients were divided into two groups as hemorrhagic or ischemic cerebrovascular disease (CVD) according to the radiological findings. NLR, LMR and PMR ratios were calculated. The last diagnosis and hospitalization information were recorded and their 28-day mortality status was evaluated.

Results: A total of 764 patients were included in the study. The median age of the patients included in the study was 68 (IQR 25-75: 59-78) and 404 (52.9%) of the patients were male. In the analysis performed; it was observed that the LMR, NLR and PMR levels were significantly different in those who developed mortality on the 28th day ($p = 0.009$), ($p = 0.002$), ($p = 0.026$). In addition, only the NLR level was found to be significantly different in the ischemic group ($p < 0.001$).

Conclusion: We think that in cases with stroke, NLR, LMR and PMR levels can be used in predicting the prognosis of this disease. Also, NLR is significantly higher in ischemic stroke, and also significant in terms of showing that CVD type is hemorrhagic or ischemic.

Keywords: Emergency department, cerebrovascular disease, hematological parameters, stroke

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INTRODUCTION

Stroke is an important cause of morbidity and mortality worldwide (1). Despite all urgent approaches and treatments, mortality still ranges between 20-30% (2). Prevention of mortality is associated with rapid diagnosis, effective use of imaging methods, and availability of vital interventions such as thrombolytic or interventional procedures, especially in emergency services, which are the first application area.

In the presence of acute cerebrovascular disease (CVD), it is only possible to distinguish the current clinic from ischemic or hemorrhagic cerebrovascular disease after the availability of imaging methods. Every patient who admitted with acute stroke clinic are being evaluated as a thrombolytic or thrombectomy candidate and effective diagnostic procedures are completed within the time when the decision for treatment is required.

Blood parameters such as complete blood count, biochemistry and coagulation tests obtained at the first evaluation in the emergency department are important in the presence of cerebrovascular disease in terms of treatment decision, supportive treatment or determining the existing additional pathology.

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However, a detailed examination of complete blood count parameters can make important contributions to the emergency physician in the evaluation process of the patient. The usage of hemogram parameters in the differential diagnosis of CVD as ischemic or hemorrhagic type can accelerate the functioning of emergency services and may allow appropriate triage for patients, especially at the decision point of stroke procedures like thrombolytic therapy or surgical intervention.

There are publications stating that neutrophil functions and neutrophil infiltration, which are an important part of the systemic inflammatory response, affect the results of ischemia (3). Studies have shown that neutrophil migration and systemic inflammatory response play a role in the repair of the blood-brain barrier regardless of the size of the infarct site (4). In the presence of strokes, a decrease in the total neutrophil count is observed (4). Neutrophil//lymphocyte ratio (NLR) is an important systemic marker of inflammation (5-7). Due to it is easy access, it can be easily used in patients who are suspected of stroke. Increased NLR can be used to predict prognosis in patients with stroke (8, 9).

Mean platelet volume (MPV) indicates the size of platelets and is associated with platelet function and activation. There are many studies related to its role in thrombosis and inflammation (10). In blood count results, the two most featured indicators regarding platelets are thrombocyte count and MPV. Platelet average volume is 7.8-11.0 fl. High MPV is considered in terms of coronary heart disease and stroke risk (10).

Our study aims to evaluate the effectiveness of NLR, lymphocyte/MPV ratio (LMR) and thrombocyte/MPV ratio (PMR) in the classification of acute CVD diagnosis and its place in mortality prediction.

MATERIAL AND METHODS

Patients who were admitted to the Health Sciences University, Bursa Yuksek Ihtisas Training and Research Hospital Emergency Department with acute stroke symptoms and diagnosed with CVD within a 1-year period between January 1, 2020 and December 31, 2020 were retrospectively analyzed. Written approval was obtained from the ethics committee of our hospital during the planning phase of our study (2011-KAEK-25 2021/01-16).

Patient data were obtained by scanning patient cards and patient epicrisis registered in the hospital automation system. Age, gender, chronic disease history, anticoagulant or antiaggregant drug use status of the patients were recorded. Patients were divided into two groups as hemorrhagic or ischemic cerebrovascular disease according to brain computed tomography and brain magnetic resonance imaging findings obtained after the first evaluation.

The neutrophil/lymphocyte ratio, lymphocyte/MPV ratio and thrombocyte/MPV ratios were calculated based on the hemogram examinations taken at the initial evaluation in the emergency service.

The last diagnosis and hospitalization information of the patients were recorded and their 28-day mortality status was evaluated. Patients under 18 years of age, patients with a history of previous cerebrovascular disease, presence of trauma, active malignancy were excluded from the study. Patients who presented with symptoms of the stroke but were evaluated as a transient ischemic attack due to no evidence of ischemic or hemorrhagic cerebrovascular disease on brain imaging were excluded from the study.

Statistical analysis: The data of the study were analyzed using SPSS 22.0for Windows (SPSS Inc., Chicago, IL, USA) software. Descriptive statistics were expressed as mean ± standard deviation or median values while categorical variables were expressed as numbers and percentage (%).

Kolmogorov-Smirnov test was used for the normality distribution of the data. The significance of the difference between the groups in terms of continuous numerical variables where parametric test statistics assumptions were met was examined with Student's t test, while the significance of the difference in terms of continuous numerical variables in which parametric test statistics assumptions were not met was evaluated with the Mann Whitney U test. Variables that may be effective in mortality were evaluated using the "enter" method in logistic regression analysis. $p < 0.05$ was considered statistically significant. Results were presented at 95% confidence interval.

RESULTS

The files of 1452 patients who were admitted to the emergency department with a stroke clinic within 1 year were retrospectively scanned. Of the remaining 1452 patients, 688 were excluded from the study for various reasons (Figure 1). A total of 764 patients were included in the study.

While the median age of the patients included in the study was 68 (IQR 25-75: 59-78), 404 (52.9%) of the patients were male. Also, 621 (81.3%) of the patients had comorbid diseases, while the most common additional disease was hypertension in 514 (67.3%) patients. Ischemic CVD was detected in 651 patients (85.2%), while mortality developed in 28 days in 70 (9.2%) patients (Table 1).

The mean LMR value of the patients was found to be 0.22 ± 0.13, the mean NLR value as 4.40 ± 4.50, and the mean PMR value as 25.50 ± 9.90 (Table 2). Mann Whitney U test was performed to investigate whether there was a difference between the LMR, NLR and PMR levels of the patients and the mortality on the 28th day.

As a result of this test, it was seen that the LMR, NLR and PMR levels were significantly different in those who developed mortality on the 28th day, respectively [($p = 0.009$), ($p = 0.002$), ($p = 0.026$)] (Table 3).

In the Mann Whitney U test conducted to investigate whether there is a difference between the LMR, NLR and PMR levels of the patients and the SVO type, it was found that the NLR level was significantly different in the ischemic group ($p < 0.001$) (Table 4).

In the logistic regression analysis performed to evaluate whether the variables of gender, comorbidities, antiaggregant and anticoagulant use status were an independent risk factor for mortality, it was found that the variables were not an independent risk factor. (Table 5)

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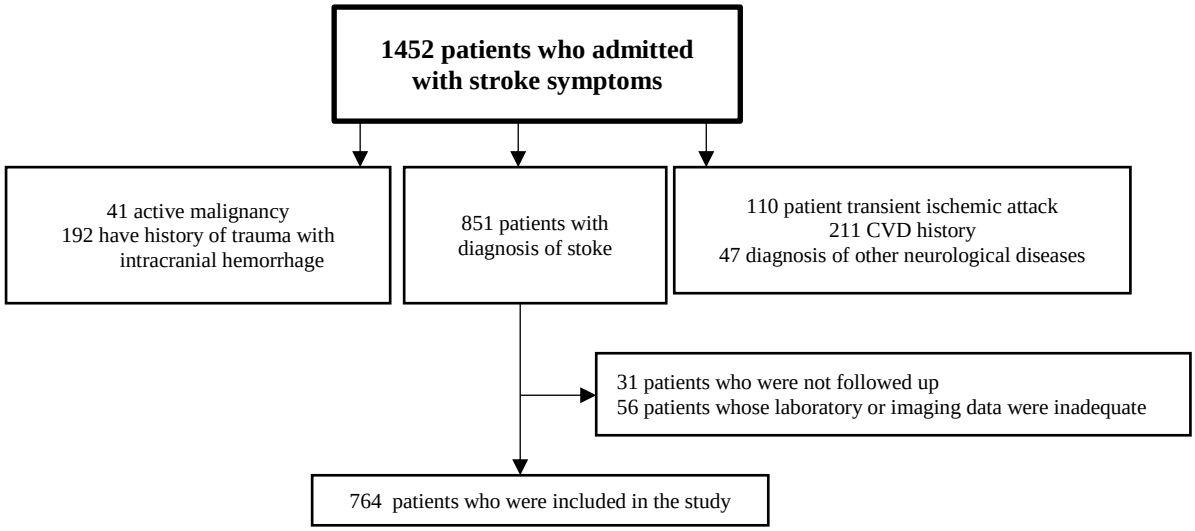

Figure 1. Identifying the cohort.

Table 1: Demographic characteristics of patients

		Total		Ischemic CVD		Hemorrhagic CVD	
		Frequency n	Percent %	Frequency n	Percent %	Frequency n	Percent %
Gender	Female	360	47,1	305	46,9	55	48,7
	Male	404	52,9	346	53,1	58	51,3
Additional Disease History	Yes	621	81,3	542	83,3	79	69,9
	No	143	18,7	109	16,7	34	30,1
HT	Yes	514	67,3	441	67,7	73	64,6
	No	250	32,7	210	32,3	40	35,4
DM	Yes	191	25,0	175	26,9	16	14,2
	No	573	75,0	476	73,1	97	85,8
CAD	Yes	167	21,9	149	22,9	18	15,9
	No	596	78,0	502	77,1	95	84,1
CRF	Yes	16	2,1	16	2,5	0	0
	No	748	97,9	635	97,5	113	100,0
Others	Yes	34	4,5	31	4,8	3	2,7
	No	730	95,5	620	95,2	110	97,3
Antiaggregant use	Yes	187	24,5	173	26,6	14	12,4
	No	577	75,5	478	73,4	99	87,6
Anticoagulant use	Yes	38	5,0	32	4,9	6	5,3
	No	726	95,0	619	95,1	107	94,7
Final status	Neurology clinic admissions	538	70,4	510	78,3	28	24,8
	Neurosurgery clinic admissions	65	8,5	0	0,0	65	57,5
	İntensive care unit admissions	29	3,8	11	1,7	18	15,9
	Stroke Unit admissions	132	17,3	130	20,0	2	1,8
28-Day mortality	Exitus	70	9,2	44	6,8	26	23,0
	Alive	694	90,8	607	93,2	87	77,0
Total		764	100,0	651	100,0	113	100,0

CVD: Cerebrovascular disease, **HT:** Hypertension, **DM:** Diabetes mellitus, **CAD:** Coronary artery disease **CRF:** Chronic renal failure

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Table 2: Laboratory values of patients

	Total			Ischemic CVD			Hemorrhagic CVD		
	n	Mean	Std. Dvt	n	Mean	Std. Dvt	n	Mean	Std. Dvt
Wbc	764	9,87	4,24	651	9,61	4,13	113	11,35	4,57
Neutrophil	764	6,85	3,33	651	6,57	3,03	113	8,45	4,39
Lymphocyte	764	2,17	1,12	651	2,18	1,04	113	2,13	1,52
Platelet	764	247,41	76,55	651	246,62	76,25	113	251,98	78,46
MPV	764	9,98	1,23	651	10,01	1,24	113	9,81	1,14
Lymphocyte/MPV	764	0,22	0,13	651	0,22	0,13	113	0,22	0,16
Neutrophil/MPV	764	4,40	4,50	651	4,04	3,80	113	6,48	7,00
Platelet/MPV	764	25,50	9,89	651	25,36	9,94	113	26,32	9,64

CVD: Cerebrovascular disease, **MPV:** Mean platelet volume

Table 3: Analysis of variables with 28-day mortality with Mann- Whitney U Test

	28-day Mortality	n	median (IQR: 25th-75th percentiles)	p value
LMR	Survival	694	0.20(0.14-0.29)	p<0.05
	Mortality	70	0.18(0.11-0.23)	
	Total	764	0.20(0.14-0.28)	
NLR	Survival	694	2.85(1.89-4.73)	p<0.05
	Mortality	70	4.24(2.16-8.28)	
	Total	764	2.92(1.90-5.10)	
PMR	Survival	694	19.13(24.70-30.50)	p<0.05
	Mortality	70	17.29(21.75-28.28)	
	Total	764	24.30(18.95-30.39)	

LMR: Lymphocyte/Mean Platelet Volume Ratio, **NLR:** Neutrophil/ Lymphocyte Ratio **PMR:** Platelet/ Mean Platelet Volume Ratio

Table 4: Analysis of variables with cerebrovascular disease type with Mann-Whitney U Test

	CVD	n	median (IQR: 25th-75th percentiles)	p value
LMR	Ischemic	651	0.20(0.14-0.28)	p>0.05
	Hemorrhagic	113	0.18(0.12-0.27)	
	Total	764	0.20(0.14-0.28)	
NLR	Ischemic	651	2.81(1.89-4.61)	p=0.000
	Hemorrhagic	113	4.17(1.98-8.45)	
	Total	764	2.92(1.90-5.10)	
PMR	Ischemic	651	24.09(18.84-30.13)	p>0.05
	Hemorrhagic	113	25.21(19.71-32.51)	
	Total	764	24.30(18.95-30.39)	

CVD: Cerebrovascular diseae **LMR:** Lymphocyte/Mean Platelet Volume Ratio, **NLR:** Neutrophil/ Lymphocyte Ratio **PMR:** Platelet/ Mean Platelet Volume Ratio

Table 5: Analysis of variables with logistic regression

	p value	Exp(B)	95% C.I.for EXP(B)	
			Lower	Upper
Gender	>0.05	0,712	0,430	1,177
Additional disease history	>0.05	0,469	0,175	1,258
Antiaggregant use	>0.05	1,231	0,623	2,433
Anticoagulant use	>0.05	3,639	0,784	16,905

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DISCUSSION

Stroke is still an important cause of mortality and long-term morbidity, despite the rapid development of diagnostic methods and the development of aggressive treatment methods. Ischemic stroke is approximately 80% of cases in acute CVD (**11, 12**). In our study, the rate of ischemic stroke is similar to the literature, and similar to the studies, male gender was predominantly affected (**12, 13**). Hypertension, smoking, diabetes, obesity, physical inactivity and atrial fibrillation have been identified as important risk factors in the development of strokes and recurrent stroke (**14**). In our study, 81.3% of our patient group had comorbid diseases, and especially 67.3% of hypertension was found, and its importance as the main risk factor is demonstrated. While comorbidities, anticoagulant or antiaggregant drugs used, or sex are important risk factors for the development of stroke, in line with the data in our study, they were not considered as independent risk factors in the prediction of stroke mortality.

It is known that leukocytes play a role in the development of tissue damage in acute ischemic stroke. This inflammatory response, which is characterized by an increase in neutrophil count and a decrease in lymphocyte ratio, can be easily evaluated with the N/L ratio. NLR has been found to be associated with severe and widespread coronary artery disease and stroke (**10**).

It was emphasized that in cases with high NLR at the first admissions of stroke patients cardioembolic causes among the etiological factors should be investigated in more detail (**15, 16**). NLR can be used as a simple, easy and independent marker for predicting mortality in patients with acute ischemic stroke (**17, 18**).

In our study, NLR was found to be significant in determining stroke prognosis in accordance with the literature. Especially when evaluated together with the etiology of CVD, NLR is significantly higher in ischemic stroke, and it can be a guide in terms of whether CVD is hemorrhagic or ischemic. In the study of Kakhi et al. Investigating the change of NLR towards the etiology of stroke, similar to our study, it is emphasized that ischemic stroke is higher than hemorrhagic stroke (**19**). In hemorrhagic stroke, high levels of NLR have been found to be particularly effective in predicting 90-day mortality (**20, 21**).

MPV is an important indicator showing platelet function and activation. Large platalets can synthesize more prothrombic factors, so high MPV values have been detected in stroke and cardiovascular diseases and have been associated with poor outcomes and mortality (**22, 23**). MPV, which we evaluated with thrombocyte/MPV and lymphocyte/MPV, was found to be significant in predicting prognosis when evaluated proportionally, but did not differ when cerebrovascular disease was ischemic or hemorrhagic.

CONCLUSION

As a result, NLR is widely used in predicting prognosis of various diseases today. However, we first emphasized that LMR and PMR can be used in predicting the prognosis of acute stroke diseases.

As a result of these data we have obtained, we think that the NLR, LMR and PMR levels obtained from the hemogram, which is a simple and easy to obtain parameter simultaneously with radiological imaging methods, can be used in the prognosis prediction of this disease. At the same time, NLR is significantly higher in ischemic stroke and it is significant in terms of showing that SVH is ischemic or hemorrhagic.

Limitations: Our study was conducted retrospectively and in a single center. For this reason, there may be a loss of patient data at the point of access. Due to the intensity of the Covid-19 pandemic, insufficient data in the patient files increased the number of patients excluded from the study relatively. It is known that the thrombocytes gain volume while the blood taken for MPV value measurement we used in our study is kept in EDTA tubes. The blood samples taken in our study were measured in as little as four hours, but as in other studies, no time-dependent correction was made.

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Ethical issues: All authors declare originality of research.

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