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# THE ROLE OF MEAN PLATELET VOLUME AND NEUTROPHIL LYMPHOSCYTE RATIO DETERMINING. EARLY MORTALITY IN STROKE PATIENTS

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#### Abstract

**Background:** The objective of this retrospective study was to determine the place of MPV and NLR in the assessment of the mortality within the first three months in patients, who were diagnosed with an acute cerebrovascular disease (ACD).

**Methods:** The patients who were hospitalized in the neurology service from our emergency service between the dates 01.01.2014 and 31.12.2014 were assessed retrospectively. The patients, who were followed up for 3 months, were divided into two groups as survived (Group 1) and exitus (Group 2). Mann-Whitney U test was used for statistically analysis. p<0.05 was accepted as significantly.

**Results:** The median MPV value was found that 10.30 (1,1) fL in group1 and 10.20 (0.8) fL in group 2. The median NLR value was found that 2.40 (2.2) fL in group1 and 2.86 (1.7) fL in group 2. There was no statistically significant difference between two groups for MPV and NLR.

**Conclusion:** We conclude that MPV and NLR did not have a role in the determination of the early mortality in stroke patients.

Key words: stroke, early mortality, NLR, MPV.

### Резюме

## РОЛЬ СРЕДНЕГО ОБЪЕМА ТРОМБОЦИТОВ И ОПРЕДЕЛЕНИЕ СООТНОШЕНИЯ НЕЙТРОФИЛЬНЫХ ЛИМФОЦИТОВ РАННЯЯ СМЕРТНОСТЬ У БОЛЬНЫХ ИНСУЛЬТОМ

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**Целью** настоящего ретроспективного исследования явилось определение места MPV и NLR в оценке смертности в течение первых трех месяцев у пациентов, которым был поставлен диагноз острого цереброваскулярного заболевания (ACD).

**Методы:** ретроспективно оценивались пациенты, госпитализированные в неврологическую службу нашей Службы неотложной помощи в период с 01.01.2014 по 31.12.2014. Пациенты, находившиеся под наблюдением в течение 3 месяцев, были разделены на две группы: выжившие (1-я группа) и умершие (2-я группа). Для статистического анализа использовался U-критерий Манна-Уитни. Р<0,05 был принят как значимый.

**Результаты:** медианное значение MPV было установлено, что 10.30 (1,1) fL в группе 1 и 10.20 (0,8) fL в группе 2. Медианное значение NLR было установлено, что 2,40 (2,2) fL в группе 1 и 2,86 (1,7) fL в группе 2. Статистически значимой разницы между двумя группами по MPV и NLR не было.

**Заключение:** мы пришли к выводу, что MPV и NLR не играли роли в определении ранней смертности у больных с инсультом.

**Ключевые слова:** инсульт, ранняя смертность, NLR, MPV.

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#### Түйіндеме

# ТРОМБОЦИТТЕРДІҢ ОРТАША КӨЛЕМІНІҢ РӨЛІ ЖӘНЕ НЕЙТРОФИЛЬДІ ЛИМФОЦИТТЕРДІҢ АРАҚАТЫНАСЫН АНЫҚТАУ. ИНСУЛЬТПЕН АУЫРАТЫН НАУҚАСТАРДАҒЫ ЕРТЕ ӨЛІМ-ЖІТІМ

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Осы ретроспективті **Зерттеудің мақсаты** жіті цереброваскулярлық ауру (ACD) диагнозы қойылған емделушілерде алғашқы үш ай ішінде өлім-жітімді бағалаудағы MPV және NLR орнын анықтау болып табылды.

**Әдістер:** ретроспективті түрде 01.01.2014-31.12.2014 аралығында біздің жедел жәрдем қызметінің неврологиялық қызметіне жатқызылған пациенттер бағаланды. 3 ай бойы бақылаудағы пациенттер екі топқа бөлінді: тірі қалғандар (1 топ) және өлгендер (2 топ). Статистикалық талдау үшін Манна-Уитни и-критериясы қолданылды. Р<0,05 маңызды ретінде қабылданды.

**Нәтижелер:** MPV медианалық мәні 10.30 (1,1) fL 1 топта және 10.20 (0,8) fL 2 топта анықталды. NLR медианалық мәні 2,40 (2,2) fL 1 тобында және 2,86 (1,7) fl 2 тобында анықталды. MPV және ҰЛР бойынша екі топ арасында статистикалық маңызды айырмашылық болған жоқ.

**Қорытынды:** біз инсультпен ауыратын науқастарда ерте өлім-жітімді анықтауда MPV және NLR рөл атқармаған деген қорытындыға келдік.

Түйінді сөздер: инсульт, ерте өлім, NLR, MPV.

### Библиографическая ссылка:

Altinbilek Ertugrul, Ozturk Derya, Algın Abdullah, Caltili Cilem, Calik Mustafa, Sahin Balkan, Kavalci Gulsum, Kavalci Cemil Роль среднего объема тромбоцитов и определение соотношения нейтрофильных лимфоцитов. Ранняя смертность у больных инсультом // Наука и Здравоохранение. 2019. 6 (Т.21). С. 30-33.

Altinbilek Ertugrul, Ozturk Derya, Algın Abdullah, Caltili Cilem, Calik Mustafa, Sahin Balkan, Kavalci Gulsum, Kavalci Cemil The role of mean platelet volume and neutrophil lymphoscyte ratio determining. Early mortality in stroke patients // Nauka i Zdravookhranenie [Science & Healthcare]. 2019, (Vol.21) 6, pp. 30-33.

Altinbilek Ertugrul, Ozturk Derya, Algın Abdullah, Caltili Cilem, Calik Mustafa, Sahin Balkan, Kavalci Gulsum, Kavalci Cemil Тромбоциттердің орташа көлемінің рөлі және нейтрофильді лимфоциттердің арақатынасын анықтау. Инсультпен ауыратын науқастардағы ерте өлім-жітім // Ғылым және Денсаулық сақтау. 2019. 6 (Т.21). Б. 30-33.

Introduction. Stroke is clinical findings with a sudden start which are formed as a result of pathological processes in which one or more blood vessels in the brain are involved, they last for 24 hours or longer, they can cause death, they have vascular origins and they are formed as a result of focal or global cerebral function disorder [3]. National Institute of Neurological Disorders and Stroke (NINDS) has defined cerebrovascular disease as a disease in which "an area of the brain is transiently or permanently affected by ischemia or bleeding and/or primer pathology of one or more blood vessels involving the brain [18].

Stroke occurs with 80-85% ischemic type and 15-20% hemorrhagic type [10]. Among the reasons for mortality, Stroke is the second after heart diseases and the first in terms of morbidity in the whole world [12].

Inflammation plays a main role in atherosclerosis [11]. White blood cell (WBC) count and subtypes of WBC are usually used as a inflammatory markers [6]. In these day, neutrophil to lymphocyte ratio (NLR) has used as a new biomarker of the systemic inflammation. It is an easily achieve and cheaper [6]. Previous studies reported that NLR was associated with poor outcomes and predict early mortality in patients with stroke [14,15].

Yu et al. reported in their study that the neutrophil/lymphocyte ratio (NLR) is a predictor for the short-term functional outcome in acute ischemic stroke [18]. However, in the same study, the investigators showed that high NLR was not significantly related to mortality and major disability. Gokhan et al. demonstrated that NLR was significantly increased in acute ischemic stroke patients, resulted in mortality [4]. Goyal et al. illustrated that the high NLR at the baseline was an independent predictor for the mortality within 3 months and symptomatic intracranial bleeding in diffuse vascular occlusions, which were treated with mechanic thrombectomy [5].

The objective of this retrospective study was to determine the place of MPV and NLR in the assessment of the mortality within the first three months in patients, who were diagnosed with an acute cerebrovascular disease (ACD).

**Material and Method.** A retrospective cross-sectional study including 179 adult patients was carried out after taking approval from institutional ethics committee. We retrospectively investigated patients who were hospitalized in the neurology service after being diagnosed with Stroke between January 1<sup>st</sup>, 2014 and December 31<sup>th</sup>, 2014. The files of patients who were diagnosed with Acute Ischemic Stroke were reached from the

hospital's automation system. The patients who were hospitalized in the neurology service with diagnosis codes of Vascular Syndromes of the Brain in Cerebrovascular Diseases according to ICD-10 coding system were included in the study. The patients who did not have Acute Ischemic Stroke (patients with subdural, epidural, intracranial hematoma, subarachnoid bleeding) were excluded.

The patients' age, gender, date of coming to the emergency service, hour of coming to the emergency service, symptoms, starting hour of the symptoms, detailed neurological examination (Glascow coma scale, cooperation, orientation, speaking, cranial nerves, motor functions, pathological reflexes, walking, cerebellar tests, presence of meninx irritation findings, response to light reflex, pupillary diameter), comorbid diseases (hypertension, DM, hyperlipidemia, sequel CVD), laboratory findings, brain tomography and magnetic resonance imaging results, echocardiography results and the patients' 3-month survival rates were recorded in data collection forms.

For statistical assessment, the data were uploaded to SPSS 20 program and analyzed. Descriptive statistics, averages, standard deviation and frequency tables were used as primary statistical analyses. Continuous variables were expressed as average ± standard deviation, median (interquartile range), while categorical data were expressed as n (patients number) and percentage (%). The patients, who were followed up for 3 months, were divided into two groups as survived (Group 1) and exitus (Group 2). For advanced analysis, Mann-Whitney U test was used. p<0.05 was accepted as significantly.

**Results.** A total of 179 patients were included in the study. Of those patients, 105 were men, while 74 (41.4%) were women and the youngest patient was 28 years old, while the oldest was 92 years old (Table1). The mean age of patient was 65.7±15.2 years. The mortality rate was

found as 13.8% in this study. When the patients' referral complaints were assessed, the most common complaint of referral was loss of strength with 45.3% (Table1). Clinical and demographic information of the patients are summarized in the table 1.

The median MPV value was found that 10.30 (1,1) fL in group1 and 10.20 (0.8) fL in group 2. The median NLR value was found that 2.40 (2.2) fL in group1 and 2.86 (1.7) fL in group 2. There was no statistically significant difference between two groups for MPV and NLR (p>0.05). The patients' laboratory results were shown in table 2.

Table 1.

Demographic data of patients.

Demographic data of patients.				
Variable	Range	n (%)		
Age group	18-34	5 (2.8%)		
	35-49	21(11.6%)		
	50-64	55(30.4%)		
	65-79	58(32.0%)		
	≥80	42(23.2%)		
Admission time	0-1h	27(14.9%)		
	2-3h	49(27.1%)		
	4-5h	28(15.5%)		
	6-11h	23(12.7%)		
	12-23h	14(7.7%)		
	≥24h	40/22.1%)		
Admission clock	08:00-15:59	78(43.1%)		
	16:00-23:59	82(45.3%)		
	00:00-07:59	21(11.6%)		
Complaint	speaking disorders	80(44.2%)		
	loss of strength	82(45.3%)		
	aphasia	8(4.4%)		
	sight disorders	10(5.5%)		
	other	25(13.8%)		

Table 2. Labratory findings according to groups

Variable	Group 1	Group 2	p value
Age (years)	65.5 (25)	79 (16)	0.001*
Gender (female/male)	60/96	15/10	0.07
MPV (fL)	10.30 (1,1)	10.20(0.8)	0.64
Platelet (/µL)	245500(105000)	252000 (86000)	0.27
Hematocrit (%)	39.95(6.4)	64.60(9.4)	0.001*
White blood cell (/µL)	8000 (2900)	9000 (3400)	0.40
Neutrophil (/µL)	5000 (2500)	4600 (2600)	0.34
Lymphocyte (/µL)	1900 (1300)	1600 (1200)	0.312
NLR	2.40 (2.2)	2.86 (1.7)	0.113

MPV: Mean platelet volume, NLR: Neutrophil to lymphocyte ratio. \*:p<0.05 Group 1=Early mortality (-), Group 2= Early mortality (+)

**Discussion.** In our study, we found out that only the age and hematocrits level were related to an early mortality. We observed that the early mortality rate was high among the elderly patients and patients with low hematocrits level. In literature, there are still disputes about hemogram parameters stroke pathogenesis. However, Yigit et al have suggested that anemia is a risk factor for repeated episodes of ischemic stroke in patients with malignancy [17]. Low hematocrit levels may increase mortality due to impaired oxygenation of tissues.

Kocaturk et al reported that age is related to mortality [9]. Gokturk et al. found that age is not related to early mortality [4].

In our study, age was found related to mortality. We suggest that cause of increased mortality atherosclerosis and comorbid diseases develop with increased age.

MPV is a parameter that reflects the average size of thrombocytes in circulation. Platelet volume is an indicator of platelet function and activation [1]. Bigger platelet contain more granule and they synthesize vasoactive and prothrombotic substances such as thromboxane A<sub>2</sub>, ADP more. There are some views that platelets with bigger volume ease the formation of thrombus in vascular bed since they are more active [13]. Karabacak et al. says that in their studies MPV was significantly higher in patients with

hypertensive emergency and hypertensive urgency when compared with control subjects [7] and in patients with CO poisoning [8]. Duman et al. found that MPV was significantly higher in patients with pulmonary thromboembolic disease when compared with control [2]. In our study, MPV was not related to the early mortality.

In our study, although the NLR was high in the group with early mortality, there was no statistically significant difference between the two groups. Kocatürk and his colleagues published recently a new study and showed that there was a correlation between NLR and anterior circulation infarct and between NLR and early mortality within three months, as well [9]. Likewise, Goyal et al. reported that there was a significant correlation between NLR and high mortality rate [5]. We believe that there is a need for further studies to determine the role of NLR in the early mortality.

In our study, it was found that DM, HT, etc. comorbid diseases were not related to early mortality. Gokhan et al reported that only DM was associated with mortality [4]. Kocatürk et al reported that only atrial fibrillation was associated with mortality [9]. Yu et al. reported that comorbid diseases were not associated with early clinical outcomes [18]. Our results support Yu et al.

**Conclusion.** We found that our patients' hemogram parameters were within normal limits. We conclude that MPV and NLR did not have a role in the determination of the early mortality in stroke patients.

**Limitations:** The most important limitation of this study is that it is retrospective. Another limitation is that it contained data from a single center

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#### References:

- 1. Bath P.M., Butterworth R.J. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis. 1996; 7(2): 157-61.
- 2. Duman A., Dagli B., Turkdogan K.A., Kapci M., Kuruoz G., Akoz A. Diagnosis of pulmonary embolism in patients mean platelet volume, neutrophil / lymphocyte ratio and platelet / lymphocyte ratio 's foresight. Medicine Science 2016; 5(4): 1002-4
- 3. *Go S., Worman D.J.* Stroke Syndromes. In: Tintinalli JE (eds). Tintinalli's Emergency Medicine. A Comprehensive Study Guide. 8<sup>th</sup> ed. McGraw-Hill;2016: NY, p.1142-1155
- 4. Gokhan S., Ozhasenekler A., Mansur Durgun H., Akil E., Ustündag M., Orak M. Neutrophil lymphocyte ratios in stroke subtypes and transient ischemic attack. Eur Rev Med Pharmacol Sci. 2013;17(5):653-7.

- 5. Goyal N., Tsivgoulis G., Chang J.J., Malhotra K., Pandhi A., Ishfaq M.F. et al. Admission Neutrophil-to-Lymphocyte Ratio as a Prognostic Biomarker of Outcomes in Large Vessel Occlusion Strokes. Stroke 2018;49(8):1985-1987.
- 6. Horne B.D., Anderson J.L., John J.M., Weaver A., Bair T.L., Jensen K.R., et al. Intermountain Heart Collaborative Study Group Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005; 45:1638–1643
- 7. Karabacak M., Dogan A., Turkdogan A.K., Kapci M., Duman A., Akpinar O. Mean platelet volume is increased in patients with hypertensive crises. Platelets. 2014;25(6):423-6.
- 8. Karabacak M., Varol E., Turkdogan K.A., Duman A., Akpinar O., Karabacak P. Mean Platelet Volume in Patients With Carbon Monoxide Poisoning. Angiology 2014; 65(3:) 252-6.
- 9. Kocaturk O., Besli F., Gungoren F., Kocaturk M., Tanriverdi Z. The relationship among neutrophil to lymphocyte ratio, stroke territory, and 3-month mortality in patients with acute ischemic stroke. Neurological Sciences 2019;40:139–146
- 10. Lewandowski C., Barsan W. Treatment of acute ischemic stroke. Ann Emerg Med. 2001; 37: 202-16.
- 11. Libby P., Ridker P.M., Maseri A. Inflammation and atherosclerosis. Circulation 2002; 105:1135–1143
- 12. Mathers C.D., Ma Fat D., Boerma J.T. The Global Burden of Disease: 2004 Update. Geneva, World Health Organization, 2008. Available from. https://www.who.int/healthinfo/global\_burden\_disease/GBD report 2004update full.pdf. last access date:08.11.2019
- 13. Park Y., Schoene N., Harris W. Mean platelet volume as an indicator of platelet activation: methodolojical issues. Platelets. 2002; 13(5-6): 301-6.
- 14. Tokgoz S., Kayrak M., Akpinar Z., Seyithanoğlu A., Güney F., Yürüten B. Neutrophil lymphocyte ratio as a predictor of stroke. J Stroke Cerebrovasc Dis 2013; 22:1169–1174
- 15. Xue J., Huang W., Chen X., Li Q., Cai Z., Yu T., Shao B. Neutrophil-to-lymphocyte ratio is a prognostic marker in acute ischemic stroke. J Stroke Cerebrovasc Dis 2017;26(3):650–657
- 16. Whisnant J.P., Basford J.R., Bernstein E.F., Cooper E.S., Dyken M.L., Easton J.D., et al. Special Report From The National Institute of Neurological Disorders and Stroke. Classification of Cerebrovascular Diseases III. Stroke. 1990; 21: 637-76.
- 17. Yigit M., Sogut O., Yigit E., Turkdogan K.A., Kaplan O., Dur A., et al. The relationship between anemia and recurrence of ischemic stroke in patients with Trousseau's syndrome: A retrospective cross-sectional study. Turk J Emerg Med. 2016; 16(2): 65-8.
- 18. Yu S., Arima H., Bertmar C., Clarke S., Herkes G., Krause M. Neutrophil to lymphocyte ratio and early clinical outcomes in patients with acute ischemic stroke. J Neurol Sci. 2018;387:115-118. doi: 10.1016/j.jns.2018.02.002.

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