

The Relationship Between Complete Blood Count Parameters and Mortality in Early Period in Patients Diagnosed as Stroke in Emergency Service

Hüseyin Avni Demir*, Fikret Bildik, Tülin Gesoğlu Demir, Dikmen Çalışkan, Reyhan Şahnaoğlu, Ekim Özge Gökçe

DOI: 10.17944/mkutfd.786123

Hüseyin Avni Demir: Uzm. Dr., Sağlık Bilimleri Üniversitesi Mehmet Akif İnan Eğitim ve Araştırma Hastanesi, Şanlıurfa
Email: huseynavnidemir@yahoo.com
ORCID id: <https://orcid.org/0000-0003-2891-9345>

Fikret Bildik: Doç. Dr., Gazi Üniversitesi Tıp Fakültesi, Acil Tıp Anabilim Dalı, Ankara
Email: fbildik@hotmail.com
ORCID id: <https://orcid.org/0000-0003-2464-0232>

Tülin Gesoğlu Demir: Uzm. Dr., Şanlıurfa Eğitim ve Araştırma Hastanesi, Şanlıurfa
Email: trtulindemir@gmail.com
ORCID id: <https://orcid.org/0000-0002-9341-5525>

Dikmen Çalışkan: Uzm. Dr., Kepez Devlet Hastanesi, Antalya
Email: dikmenaliskan@gmail.com
ORCID id: <https://orcid.org/0000-0002-9015-5983>

Reyhan Şahnaoğlu: Uzm. Dr., Gazi Üniversitesi Tıp Fakültesi Hastanesi, Ankara
Email: dreyhansahna@yahoo.com
ORCID id: <https://orcid.org/0000-0002-7429-7033>

Ekim Özge Gökçe: Uzm. Dr., Etimesgut İlçe Sağlık Müdürlüğü, Ankara
Email: ekimozgegokce@gmail.com
ORCID id: <https://orcid.org/0000-0001-5742-7601>

Bildirimler/Acknowledgement

* Sorumlu Yazar/Corresponding Author

Çıkar Çatışması/Conflict of Interest

Yazarlar bu makale ile ilgili herhangi bir çıkar çatışması bildirmemişlerdir.

The authors declare that they have no conflict of interests regarding content of this article.

Maddi Destek/Financial Support

Yazarlar bu makale ile ilgili herhangi bir finansal destek bildirmemişlerdir.

The Authors report no financial support regarding content of this article.

Etik Beyan/Ethical Declaration

Yazarlar, çalışma için Keçiören Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulundan 13.01.2016 tarihli yazı ile izin alındığını, çalışmanın yürütülmesi esnasında Helsinki Beyannamesi 2013, ICMJ tavsiyeleri ile COPE'un Editör ve Yazarlar için Uluslararası Standartlarının yanısıra ilgili diğer biyoetik kılavuzların dikkate alındığını beyan etmişlerdir.

Permission was obtained from the Keçiören Training and Research Hospital Human Research Ethics Committee for this study with date 31.01.2016, and Helsinki Declaration rules were followed to conduct this study.

Geliş/Received: 27.08.2020

Düzeltilme/Revised: 13.09.2020

Kabul/Accepted: 24.10.2020

e-ISSN: 2149-3103

Web: <http://dergipark.org.tr/mkutfd>

Öz

Acil Serviste İnme Tanısı Alan Hastalarda Tam Kan Sayımı Parametreleri ve Erken Dönem Mortalite İlişkisi

Amaç: Akut iskemik inme, kalp hastalığı ve kanserden sonra en yaygın ölüm nedenidir. İskemik inmenin erken dönemindeki tam kan sayımı parametreleri arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntem: Çalışma geriye dönük arşiv çalışması şeklinde düzenlenmiştir. Acil servise başvuran ve iskemik inme tanısı alan hastalar dahil edilmiştir. Demografik bulgular, tam kan sayımı parametreleri, görüntüleme testleri, acilde kalış süresi, hastanede kalış süresi not edilmiştir.

Bulgular: Dört yüz yirmi iki hastanın ortalama yaşı $69,95 \pm 12,26$ yıldır. Hipertansiyon %68,5 oranıyla en sık görülen ek hastalıktır. İlk 7 günde ölüm oranı %2,1 iken ilk 30 günde %5,2 oldu. Nötrofil Lenfosit Oranının (NLO) ortalama değeri ilk 7 gün içinde ölen hastalarda anlamlı olarak daha yüksekti ($p = 0,013$). İlk 7 günde ölüm için 4,12 olarak belirlenen NLO cut-off değerinin duyarlılığı %77,8; özgüllüğü %68,5 idi. 30 gün içinde ölen hastaların Kırmızı Hücre Dağılım Genişliği (RDW) değerleri yaşayan hastalara göre istatistiksel olarak anlamlı düzeyde yüksek bulundu. Artan yaş, kalp yetmezliği ve atriyal fibrilasyon, erken ölüm için önemli risk faktörleri olarak bulundu.

Sonuç: Sonuç olarak, NLO ilk 7 gün içindeki mortalite ve RDW ilk 30 gün içindeki mortalite için prediktif olabilir. Kalp yetmezliği ve / veya atriyal fibrilasyon varlığı ve 65 yaş ve üstü, erken ölüm riskini arttırmaktadır.

Anahtar Kelimeler: İskemik İnme, Kırmızı Hücre Dağılım Genişliği, Nötrofil Lenfosit Oranı, Erken Mortalite

Abstract

The Relationship Between Complete Blood Count Parameters and Mortality in Early Period in Patients Diagnosed as Stroke in Emergency Service

Objective: Acute ischemic stroke is the most common cause of death after heart disease and cancer. We aimed to investigate the relationship between parameters of complete blood count in early period of ischemic stroke.

Material Method: The study was organized as a retrospective-archive study. Patients applied Emergency Department and diagnosed as ischemic stroke were included. Demographic findings, complete blood count parameters, imaging tests, duration time in the emergency, hospitalization time were noted.

Results: The mean age of 422 patients was 69.95 ± 12.26 years. Hypertension was the most common additional diseases, with the rate of 68.5%. While the mortality rate was 2.1% in the first 7 days, it was 5.2% in the first 30 days. The mean value of Neutrophil Lymphocyte Ratio (NLR) was significantly higher in patients who died within the first 7 days ($p = 0.013$). The sensitivity of NLR cut-off value, which was determined as 4.12 for death in the first 7 days, was 77.8% and specificity was 68.5%. Red Cell Distribution Width (RDW) values of patients who died within 30 days were found to be statistically significantly higher when compared to living patients. Increasing age, heart failure and atrial fibrillation were found to be significant risk factors for early mortality.

Conclusion: In conclusion, NLR can be predictive for mortality within the first 7 days and RDW for mortality within the first 30 days. The presence of heart failure and / or atrial fibrillation and the age of 65 and above increase the risk of early mortality.

Keywords: Ischemic Stroke, Red Cell Distribution Width, Neutrophil Lymphocyte Ratio, Early Mortality

1. INTRODUCTION

Stroke is defined by the World Health Organization as “findings that develop rapidly and last for 24 hours or more, or may result in death, due to focal or global impairment of cerebral functions” (1). Acute stroke is the most common cause of death after cancer and heart diseases in Turkey and all over the world. Stroke is also the major cause of morbidity and long-term disability in Europe. Since the mortality and morbidity rates of acute stroke are high, it is important to predict early mortality. In recent years, number of studies have been conducted with clinical findings, scoring systems, biochemical markers, and imaging methods to predict the mortality of coronary artery diseases, cancers, and strokes, which have high mortality. Some of the parameters used in these studies are neutrophil lymphocyte ratio (NLR), red cell distribution width (RDW) and mean platelet volume (MPV) (2-4). In this study, it was aimed to investigate the relationship between parameters of complete blood count which is an easily accessible, cheap, and fast test and early mortality in stroke.

2. MATERIAL AND METHODS

The study was conducted retrospectively between 2013 and 2015 with patients who were admitted to Gazi University Faculty of Medicine Adult Emergency Department and were diagnosed as ischemic stroke and hospitalized in the neurology department.

2.1. Collection of Data

Patients were included in the study by having data from patient records of the hospital data system. A study form was prepared for each patient and demographic data of all patients such as age, gender, additional diseases, and medications used were noted. Complaints, physical examination findings, hemoglobin (HGB), Hematocrit (HTC), Mean Corpuscular Volume (MCV), White Blood Cell (WBC), Platelet (PLT), Mean Platelet Volume (MPV), Red Cell Distribution Width (RDW), Neutrophil Lymphocyte Ratio (NLR) values and the imaging results of patients having Brain Computed Tomography (CT), Brain Magnetic Resonance (MR) and MR Angiography were noted.

All patients were divided into groups by applying Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification in terms of ischemic stroke etiologies. In addition, the duration of the stay in the emergency room, the length of hospitalization, status of death on the 7th and 30th day were noted. Death status of the patients who were discharged earlier than 30 days, was decided according to their re-admission. For patients who did not re-apply to the hospital, information about the death status was obtained by calling them from the hospital information database.

2.2. Inclusion and Exclusion Criteria

Patients who were over the age of eighteen, who were diagnosed with ischemic stroke by brain CT, brain MR or by the clinical findings, and those who were accepted as transient ischemic attack (TIA) were included in the study. Patients under the age of eighteen, patients with trauma on visit, patients with intracranial bleeding, patients with active neoplasia or bone marrow metastasis, having end-stage renal insufficiency or liver failure, presence of rheumatological disease, patients with immunosuppression / immunosuppressant drug use, patients using glucocorticoid drug, pregnant women, patients whose information could not be reached or who had missing information, were excluded from the study.

2.3. Statistical Analysis

The analysis of the data was performed with Statisti-

cal Package for the Social Sciences 21 (IBM SPSS Statistics 21®) version. Normality evaluation of continuous variables was done with Kolmogorov-Smirnov test. Non-parametric tests were used because of the variables were not compatible with the normal distribution. Arithmetic mean \pm standard deviation or median and minimum and maximum values were used in continuous variables according to their distribution structures. In the case of intergroup difference, Post-hoc statistics were used to determine which group the difference originated from. Statistical significance level was accepted as $p < 0.05$.

ROC analysis was performed to determine the cut-off value for NLR. With this analysis, it was investigated whether NLR values higher than the determined threshold value could be a sign of poor prognosis for early mortality in patients diagnosed with stroke. The cut-off assessment for NLR was performed separately for both the first 7 days of mortality and the first 30 days of mortality.

Ethical Declaration

Ethical approval was obtained from Ankara Keçiören Training and Research Hospital Ethics Committee. with date 13.01.2016, and Helsinki Declaration rules were followed to conduct this study.

3. RESULTS

Of the 422 patients included in the study, 221 (52.4%) were male and 201 (47.6%) were female. The average age was 68.03 ± 12.07 in males and 72.05 ± 12.15 in females. The average age of women was statistically higher than that of men ($p < 0.001$). When the patients were evaluated according to the age ranges, it was seen that 2.1% ($n = 9$) were in the age group under the age of 45, and 10.2% ($n = 43$) in the age group of 85 and above. The rate of being in the 45-54 age group was statistically different in men and the rate of being in the age group 85 and above was statistically different in women ($p = 0.012$).

The patients were divided into two groups as aged 65 and above and aged below 65 years old. There were 139 patients (32.9%) who were under 65 years old and 283 patients (67.1%) 65 and over. There were 136 male (61.5%) and 147 females (73.1%) in the age group 65 and over. The ratio of women 65 years and older was significantly higher than that of men ($p = 0.011$).

Hypertension (HT) was the most common comorbid disease and was significantly higher in women ($p < 0.001$). Diabetes mellitus (DM), cerebrovascular disease (CVD), heart failure (HF), atrial fibrillation (AF), coronary artery disease (CAD), and hyperlipidemia (HPL) are other comor-

Table 1. Presence of additional diseases according to age groups

	< 65 years (n=139)		≥ 65 years (n=283)		p
	n	%	n	%	
DM	50	36.0	113	39.9	0.433
HT	77	55.4	212	74.9	<0.001
CVD	37	26.6	70	24.7	0.676
CAD	29	20.9	107	37.8	<0.001
HF	3	2.2	32	11.3	0.001
AF	2	1.4	46	16.3	<0.001
HPL	8	5.8	12	4.2	0.491
Others	34	24.5	101	35.7	0.020

bidities, with no difference in gender. A statistically significant difference was found in the age group 65 and above in terms of hypertension, coronary artery disease, heart failure and atrial fibrillation ($p < 0.001$) (Table 1).

Mean, standard deviation, median, minimum, and maximum values of the patients' complete blood count parameters were calculated. The mean RDW value was $16.13 \pm 8.12\%$ (median: 14%, smallest: 9.4%, largest: 113.3%); MPV was 9.13 ± 1.85 fL (median: 9.2, smallest: 1.2, largest: 17); NLR was 4.19 ± 3.67 (median: 2.94, smallest: 0.6, largest: 31.9). The mean RDW value of the cases was above the reference value range. Mean MPV value was determined within the reference value ranges. While, the mean female RDW (15.99 ± 6.32) was significantly lower than the men's (16.25 ± 9.47) ($p = 0.004$), mean female MPV (9.35 ± 1.87) was significantly higher than the male's (8.94 ± 1.81) ($p = 0.014$). There was no significant difference between NLR values by gender.

HGB and HTC parameters were lower in women than in men (both $p < 0.001$). The MCV, WBC, PLT and MPV parameters were not different in terms of gender ($p = 0.060$, $p = 0.903$, $p = 0.409$, $p = 0.186$, respectively).

In terms of age groups, HGB, HTC, WBC, PLT values were found to be significantly lower in those aged 65 and over ($p = 0.005$, $p = 0.016$, $p = 0.032$, $p = 0.001$, respectively). MCV, RDW and NLR averages were found to be significantly higher in those aged 65 and over ($p = 0.041$, $p < 0.001$ and $p = 0.030$; respectively). There was no significant difference in MPV values for both age groups.

Brain CT was done in 408 of the cases. No acute pathology was detected in 267 (65.4%) of these patients. Brain MR was performed on 374 patients. Diffusion restriction was not detected in 59 (15.8%) patients. 370 of the patients were evaluated by echocardiography, only 4 (1.1%) had intra atrial thrombus. 389 patients underwent carotid vertebral artery color doppler ultrasound (CVDUS) examination and 167 (42.9%) of them had plaque and atherosclerotic vessels.

Pathological CVDUS results (stenosis and occlusion of

50% or more in vessels) were significantly higher in male patients (27.7%) than in women (14.2%) ($p = 0.016$). While the rate of plaque and atherosclerotic vascular detection was 27.6% in patients under 65 years of age, it was 51.0% in patients 65 and older, and it was statistically significant ($p < 0.001$).

The distribution of all patients according to TOAST groups were as follow: 41% ($n = 173$) Large Arterial Atherosclerosis, 23.7% ($n = 100$) Small Vascular Occlusion, 20.9% ($n = 88$) Cardio embolism, 14% ($n = 59$) Ischemic Stroke with unknown etiology and 0.5% ($n = 2$) Others. The frequency of large artery atherosclerosis and cardio embolism in the age group 65 and older was 43.5% and 24.7% and was statistically significantly higher ($p < 0.001$).

The mean of RDW and MPV values of TOAST groups were statistically different ($p = 0.034$ and $p = 0.037$). In comparison with post-hoc tests, there was a statistically significant increase in RDW values between those with only small vascular occlusion and cardio embolism ($p = 0.049$). There was a significant difference in MPV values between large arterial atherosclerosis and ischemic stroke with unknown etiology cases ($p = 0.02$).

The mean length of stay in emergency room was 59.48 ± 67.01 hours (median: 32), and mean hospital stay was 175.06 ± 387.02 (median: 71) hours. There was no significant difference between age and gender and length of stay in emergency room and hospitalization ($p = 0.295$, $p = 0.432$, respectively).

While the mortality rate was 2.1% ($n = 9$) in the first 7 days after stroke, the mortality rate was calculated as 5.2% ($n = 22$) in the first 30 days. There was no death in the first 7 days in the group under 65 years old. In the first 30 days, the mortality rate of cases in the age group 65 years and older was statistically significantly higher ($p = 0.004$). The average age of patients who died within the first 7 days and within the first 30 days was statistically higher than the average age of patients who lived within this period ($p = 0.043$ and $p < 0.001$, respectively). In patients with a history of heart failure and atrial fibrillation, the first 30 days death ratio were significantly higher ($p = 0.001$ and $p = 0.007$; respectively).

The NLR mean of the patient group who died in the first 7 days was significantly higher ($p = 0.022$). Although the average WBC of all patients was within the normal reference range in the first 30 days, the white blood cell values of the patients who died were found to be statistically significantly higher ($p = 0.027$). Also, RDW values of patients who died within the first 30 days were statistically significantly higher ($p = 0.013$). In the first 7 days after stroke, NLR cut-off was calculated as statistically significant ($p = 0.022$). The ROC area was 0.72 (Figure 1). NLR threshold value was

calculated as 2.97 with 100% sensitivity, 52% specificity. Although this sensitivity was 100% positive for this threshold in this patient group, the specificity was low in our opinion (52%), so we determined a different value. There was no value for which both were greater than 70%, therefore we determined the value closest to 70%. According to this, the threshold value was determined as 4.12 with the 77.8% of sensitivity and 68.5% of specificity (Table 2). NLR values equal to or higher than 4.12 were 77.8% sensitivity and 68.5% specificity for the first 7 days of mortality. Mortality rate was higher in the first 7 days in the group with NLR level 4.12 and higher ($p = 0.006$). According to NLR level 4.12, there was no difference between gender and NLR levels and between age and NLR levels ($p = 0.323$ and $p = 0.638$; respectively).

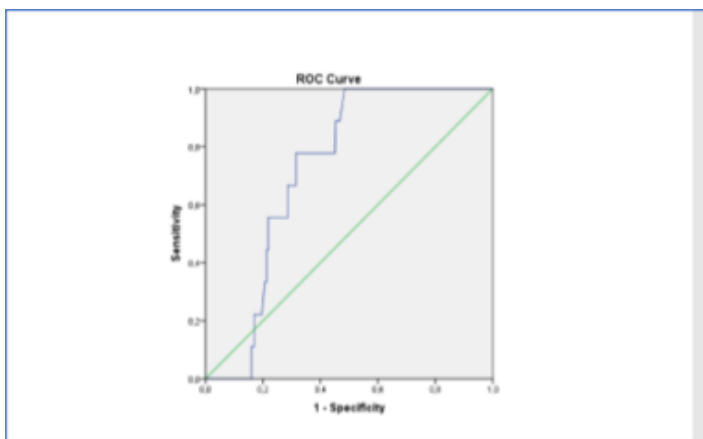


Figure 1. The ROC curve of NLR values for the mortality within the 1st 7 days

Table 2. NLR levels in whole study

NLR LEVELS		
	n	%
<4.12	285	67.5
≥4.12	137	32.5
Total	422	100

According to the NLR levels, there was no statistical difference between the length of emergency room stay and hospital stay ($p = 0.994$ and $p = 0.206$ respectively). The distribution of NLR levels according to the Brain CT results was statistically different ($p = 0.001$). This difference was due to the group with no acute pathology and cerebellar pathology. In cases without acute pathology, the ratio of having NLR lower than 4.12 levels were higher. Whereas the patients with cerebellar pathology, the ratio of having NLR equal or higher than 4.12 were higher. According to MR findings, the distribution of NLR levels was statistically different ($p < 0.001$). In cases within cerebral classification according to MR, the ratio of having NLR lower than 4.12 levels were higher. Whereas cases within cerebellar classi-

fication according to MR, the ratio of having NLR equal or higher than 4.12 were higher. NLR levels were not different according to the carotid Vertebral Doppler USG Classification and TOAST groups ($p = 0.129$ and $p = 0.989$; respectively). ROC analysis performed to determine NLR cut-off value in the first 30 days after stroke was not statistically significant ($p = 0.056$).

4. DISCUSSION

In the present study, the mean value of Neutrophil Lymphocyte Ratio (NLR) was significantly higher in patients who died within the first 7 days. Also, Red Cell Distribution Width (RDW) values of patients who died within 30 days were found to be statistically significantly higher when compared to living patients. Increasing age, heart failure and atrial fibrillation were found to be significant risk factors for early mortality.

The mean age of our cases were 69.95 ± 12.26 years, like literature. Recent studies such as Yoneda et al. found the average age as 70 ± 11 , Reganon et al. as 65.3 ± 8.2 and Ntasisos et al. as 72 years (5-7). A study in which 2606 patients were evaluated showed that women had a more severe clinical stroke (mean age of 70 in females, and 65 in males) and more severe clinical outcomes (8). In the study of Demirci et al., It was found that the increase in stroke incidence with age was more prominent in women over 70 years old and this difference was statistically significant (9). In our study, mean stroke age of males was younger than female, this can be explained by atherosclerosis as it begins in males 10-15 years before the females.

Hypertension is a major risk factor for both ischemic stroke and intracranial bleeding. There is a constant, gradual, and consistent relationship between blood pressure and stroke risk. As blood pressure increases, the risk of stroke increases, even if it is not in the hypertensive range (10). In our study, hypertension was the most common comorbid disease, like other studies.

The inflammatory response plays an important role in secondary damage following stroke and ischemia. It is known that leukocytes contribute to secondary tissue damage in acute stroke. In many publications, leukocyte accumulation has been shown to increase ischemic tissue damage after stroke (6). In addition to leukocytes, it is known that platelets play a role in acute coronary syndromes and stroke pathogenesis developing in atherosclerotic basis. MPV is considered as a good indicator of platelet function (11). Additionally, there are some studies showing that RDW is elevated in patients with acute stroke and high levels of RDW in the acute phase of some diseases such as coronary artery disease, heart failure, kidney damage, and pneumonia, have been shown to be strongly associated with poor clinical outcomes (3).

Inflammation can affect both bone marrow and iron metabolism. Inflammatory cytokines may increase RDW by preventing red cell maturation in the bone marrow and allowing new and large reticulocytes to circulate early (12). In addition, although the role and importance of erythrocytes in hemostasis and fibrinolytic system is unclear, increased RDW rates may reflect the pro-coagulant state of erythrocytes (3). The RDW mean of 422 ischemic stroke patients in our study was 16.13%. Kara et al. found the mean of RDW as 14.7% in the patient group and 13.6% in the control group and stated that these results were statistically significant (13). Ramirez Moreno et al. conducted a case-control study investigating the relationship between RDW and ischemic stroke, and they found the RDW average as 14.48% (14). The data in our study were found to be higher than the reference values in parallel with the literature. The mean RDW of the women was significantly lower than the men. Söderholm et al. examined 26,879 patients in terms of RDW and stroke incidence, obtained similar data with our study (15). This may be related to the increased incidence of ischemic stroke due to higher incidence of large artery atherosclerosis in men. The mean RDW in the 65 age and older group was significantly higher than the group below 65 age. There was also a weak positive correlation between age and RDW.

There was no significant difference in the RDW values of the patients who died in the first 7 days compared to those who did not die, but the RDW values of the patients who died in the first 30 days were significantly higher than those who did not. Kim et al., showed that an increase of 1% in RDW, increased for poor functional results (OR: 1.222), early deaths (OR: 1.395) (3). This suggests that the severity of the mechanisms (inflammation, ischemia, increased oxidative stress) thought to increase RDW by affecting the bone marrow also affects the mortality of these patients.

Ntaios et al. found significant relation only between the cardioembolic group and RDW among the whole subtypes of stroke and RDW (7). We have not seen any other studies examining this relationship. In our study, RDW rates were found to be statistically significantly higher in strokes due to cardioembolic causes. This suggests that inflammation and oxidative stress occurring in cardiac problems causes stroke-related inflammation and oxidative stress contribute to higher RDW rates.

Platelets play a key role in the pathophysiology of ischemic stroke via thrombus formation after erosion or rupture of the atherosclerotic plaque. Larger platelets contain denser granules, are metabolically more active than small platelets, and have a high thrombotic potential. The relationship between stroke risk factors, classification, outcome, and MPV has been shown in many relevant studies (9). Arıkanoglu et al. found the mean MPV in ischemic stroke to be 8.6 ± 1.95 and stated that it was significantly

higher than the healthy control (16).

In a multicentric study by Tamer et al. no difference was found between MPV values in the control and the patient group (17). In our study, it was found as high as 9.13 ± 1.85 . The mean MPV of women was significantly higher than the men. Cho et al. found that MPV values were higher in women in their study with stroke cases in Korea (18). Similarly, in our study, it was found to be higher in women. This may be due to the older female patients. Slavka et al. determined increased vascular mortality above the MPV values of 11.01 (19). In our study, the MPV values were not found to be significantly different between those who died and survived in the first 7 days and in the first 30 days. Since we did not take control group in this study, no control-case comparison was made like these two studies. In addition, the times we accept in patients who die and live are different from those in these studies. It is thought that the differences in the data are due to these reasons. Arıkanoglu et al. stated that there was no significant difference between MPV values and TOAST groups (16).

Pikija et al. found that the attenuated MPV values were associated with large vessel infarcts (20). In our study, MPV values were found to be significantly different in the large artery sclerosis group. This may be due to the presence of large sensitive atheroma plaques in the intracranial arteries and their bifurcation regions, and large platelets with high thrombotic potentials for thrombus formation. The difference between the results of the studies above may be due to the use of different criteria in stroke subgroups, as well as the measurement method differences and the small number of patients.

In the pathophysiology of ischemic stroke, the inflammatory response has an important place in every stage, from the early stages of brain cell death to post-ischemic tissue repair stages. The inflammatory response in the cerebral injury site promotes ischemic brain damage and accelerates impairment in brain function. As a result of the systemic inflammatory response, leukocytes accumulate in the ischemic brain tissue. Three to six days after stroke, lymphocytes appear in ischemic tissue later than leukocytes (6-12 hours) (21). High neutrophil counts were associated with poor prognosis in stroke patients over a 3-month period, and stroke patients with low lymphocyte counts were found to have a poor one-week clinical prognosis (22). In recent studies, early mortality was found to be associated with high NLR values (2,23). In the study of Tokgöz et al. increased infarct volume was significant for early mortality and NLR showed a positive correlation with infarct volume (24). Similarly, in our study, it was observed that the ones who died within the first 7 days were statistically significantly higher. This suggests that deaths in the first 7 days are mostly related to stroke severity. Tokgöz et al. accepted

the 4.81 NLR value as a cut-off and made short-term mortality calculations accordingly. They showed that this value has 94.7% sensitivity, 70.5% specificity and 98.9% negative predictive value for short-term mortality (24). As a result of the analyzes made in our study, 4.12 value was accepted as cut-off. Sensitivity was 77.8% and specificity was 68.5%. The reason for this difference may be due to the exclusion of lacunar infarcts in the study of Tokgöz et al.

Belen et al. found that high blood pressure values correlated with high NLR values in their study on resistant hypertensive patients (25). This may be due to the atherosclerotic process and inflammatory process developing secondary to increased vascular wall resistance. Patients with a large amount of infarction that can be seen in early-stage CT in stroke patients may develop proportionally more inflammatory responses in the brain tissues and increase NLR (23), and conversely, patients who are considered to have relatively smaller infarcts without acute pathology will be low in NLR values.

According to the Brain CT Classification, NLR was found in the group with a higher rate of <4.12 in patients without acute pathology and in patients with cerebral diffusion restriction in MRI. This can be explained by the small volume of infarct or lacunar infarction. In patients with cerebellar pathology in brain CT and diffusion MR, the NLR has higher rate of ≥ 4.12 . In the literature, there was no study investigating the relationship between cerebellar infarction and NLR. This may be due to the blood flow of the cerebellum arising from the posterior circulation and the large infarct volume.

Huang et al. found the duration of hospitalization of stroke patients was 13.9 ± 14.1 days, Zhao et al. as 11 days and Gökhan et al. as 11.16 ± 5.57 days, all were like ours (21,23,26). The length of hospital stay of the patients is related to the policies of the clinic as well as the clinical symptoms of the patient. However, Jain et al. reported the stay time in the emergency room as 332 minutes and Kıyan et al. as 21.5 ± 30.5 hours (27,28). Akhtar et al. found that 29.5% of the patients stayed in the emergency room for less than 8 hours and 70.4% of them stayed for more than 8 hours. There was a reduced risk of complications, shorter hospitalization, discharge with better prognosis, and fewer in-hospital mortality rates in the group that remained in the emergency room for less than 8 hours, compared to the group that remained for more than 8 hours (29). Long emergencies stay times of stroke patients increase hospital stay and in-hospital mortality, as well as increase hospital cost (21). In terms of cost, we think that these patients should be admitted to the appropriate departments quickly in terms of rapid onset of patient rehabilitation, especially in terms of reducing the emergency crowd.

In our study, the mortality rate was 2.1% in the first 7

days, while the mortality rate was 5.2% in the first 30 days. Nakibuuka et al. showed the mortality rate as 6.3% in the first 7 days and as 26.8% in the first 30 days (30). Ganesh et al. performed a study on 319,972 stroke patients, they determined the 30-day mortality rate as 12.7% (31). In our study, the presence of patients with lacunar infarction may have reduced these rates. In addition, it can be thought that the differences in the health services levels of the countries where the studies are conducted, and the characteristics of the patients included are relevant.

There are some limitations in our study. First, it includes the limitations of retrospective studies. The data were collected based on the reliability of the hospital database. Since it was a retrospective study, the absence of our control group in terms of complete blood count values was a limitation for us. The fact that the study is single centered constitutes an important limitation in terms of spreading the results across the country. Patients were evaluated for 7- and 30-days mortality, longer observations could yield different results. Also, patients did not classify according to the hospitalization to service or to the intensive care unit. The treatments given were not evaluated. Finally, the causes of mortality of the patients were not investigated, their primary outcome was considered as a whole cause of mortality.

5. CONCLUSION

In conclusion, NLR can be predictive for mortality within the first 7 days and RDW for mortality within the first 30 days. Additionally, the presence of heart failure and / or atrial fibrillation and the age of 65 and above increase the risk of early mortality. We suggest that these parameters may be used as predictors of mortality in stroke. Thus, knowledge of mortality predictors would lead the emergency team to decide earlier for treatment and admission to appropriate departments in terms of rapid onset of patient rehabilitation, especially in terms of reducing the emergency crowd.

REFERENCES

1. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke; a journal of cerebral circulation*. 2013;44(7):2064-89. <https://doi.org/10.1161/STR.0b013e318296aeca>
2. Celikbilek A, Ismailogullari S, Zararsiz G. Neutrophil to lymphocyte ratio predicts poor prognosis in ischemic cerebrovascular disease. *Journal of Clinical Laboratory Analysis*. 2014;28(1):27-31. <https://doi.org/10.1002/jcla.21639>
3. Kim J, Kim YD, Song TJ, Park JH, Lee HS, Nam CM, et al. Red blood cell distribution width is associated with poor clinical outcome

- in acute cerebral infarction. *Thrombosis and Haemostasis*. 2012;108(2):349-56. <https://doi.org/10.1160/TH12-03-0165>
4. Li B, Liu X, Cao ZG, Li Y, Liu TM, Wang RT. Elevated mean platelet volume is associated with silent cerebral infarction. *Internal Medicine Journal*. 2014;44(7):653-7. <https://doi.org/10.1111/imj.12454>
 5. Yoneda Y, Okuda S, Hamada R, Toyota A, Gotoh J, Watanabe M, et al. Hospital cost of ischemic stroke and intracerebral hemorrhage in Japanese stroke centers. *Health Policy*. 2005;73(2):202-11. <https://doi.org/10.1016/j.healthpol.2004.11.016>
 6. Reganon E, Vila V, Martinez-Sales V, Vaya A, Lago A, Alonso P, et al. Association between inflammation and hemostatic markers in atherothrombotic stroke. *Thrombosis Research*. 2003;112(4):217-21. <https://doi.org/10.1016/j.thromres.2003.12.008>
 7. Ntaios G, Gurer O, Faouzi M, Aubert C, Michel P. Red cell distribution width does not predict stroke severity or functional outcome. *International Journal of Stroke: Official Journal of The International Stroke Society*. 2012;7(1):2-6. <https://doi.org/10.1111/j.1747-4949.2011.00609.x>
 8. Arrich J, Mullner M, Lalouschek W, Greisenegger S, Crevenna R, Herkner H. Influence of socioeconomic status and gender on stroke treatment and diagnostics. *Stroke; A Journal of Cerebral Circulation*. 2008;39(7):2066-72. <https://doi.org/10.1161/STROKEAHA.107.506147>
 9. Demirci S, Yalciner BZ, Bakac G, Dayan C, Aysal F, Baybas S. İnmelerde tekrarlayıcılığı etkileyen risk faktörleri. *Düşünen Adam Psikiyatri ve Nöroloji Bilimleri Dergisi*. 2010;23:38-43. <https://doi.org/10.5350/DAJPN2010230106>
 10. Polovina M, Potpara T, Giga V, Stepanovic J, Ostojic M. Impaired endothelial function in lone atrial fibrillation. *Vojnosanitetski Pregled*. 2013;70(10):908-14. <https://doi.org/10.2298/VSP110429016P>
 11. Arevalo-Lorido JC, Carretero-Gomez J, Alvarez-Oliva A, Gutierrez-Montano C, Fernandez-Recio JM, Najarro-Diez F. Mean platelet volume in acute phase of ischemic stroke, as predictor of mortality and functional outcome after 1 year. *Journal of stroke and cerebrovascular diseases: the official journal of National Stroke Association*. 2013;22(4):297-303. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2011.09.009>
 12. Ku NS, Kim HW, Oh HJ, Kim YC, Kim MH, Song JE, et al. Red blood cell distribution width is an independent predictor of mortality in patients with gram negative bacteremia. *Shock*. 2012;38(2):123-7. <https://doi.org/10.1097/SHK.0b013e31825e2a85>
 13. Kara H, Degirmenci S, Bayir A, Ak A, Akinci M, Dogru A, et al. Red cell distribution width and neurological scoring systems in acute stroke patients. *Neuropsychiatric disease and treatment*. 2015;11:733-9. <https://doi.org/10.2147/NDT.S81525>
 14. Ramirez-Moreno JM, Gonzalez-Gomez M, Ollero-Ortiz A, Roa-Montero AM, Gomez-Baquero MJ, Constantino-Silva AB. Relation between red blood cell distribution width and ischemic stroke: a case-control study. *International Journal of Stroke: Official Journal of The International Stroke Society*. 2013;8(6):E36. <https://doi.org/10.1111/ijss.12091>
 15. Soderholm M, Borne Y, Hedblad B, Persson M, Engstrom G. Red cell distribution width in relation to incidence of stroke and carotid atherosclerosis: a population-based cohort study. *PloS One*. 2015;10(5):e0124957. <https://doi.org/10.1371/journal.pone.0124957>
 16. Arikanoglu A, Yucel Y, Acar A, Cevik MU, Akil E, Varol S. The relationship of the mean platelet volume and C-reactive protein levels with mortality in ischemic stroke patients. *European Review for Medical and Pharmacological Sciences*. 2013;17(13):1774-7.
 17. Tamer D, Fevzi Y, Deniz AE, Cemil K, Fatih B, Cihat Y, et al. The value of serum mean platelet volume in ischaemic stroke patient. *JPMA The Journal of the Pakistan Medical Association*. 2013;63(12):1509-10.
 18. Cho SY, Jeon YL, Choi SK, Suh JT, Lee HJ, Park TS. Mean platelet volume in Korean patients with acute ischemic stroke: a gender difference. *Platelets*. 2013;24(1):75-6. <https://doi.org/10.3109/09537104.2012.658109>
 19. Slavka G, Perkmann T, Haslachner H, Greisenegger S, Marsik C, Wagner OF, et al. Mean platelet volume may represent a predictive parameter for overall vascular mortality and ischemic heart disease. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2011;31(5):1215-8. <https://doi.org/10.1161/ATVBAHA.110.221788>
 20. Pikija S, Cvetko D, Hajduk M, Trkulja V. Higher mean platelet volume determined shortly after the symptom onset in acute ischemic stroke patients is associated with a larger infarct volume on CT brain scans and with worse clinical outcome. *Clinical Neurology and Neurosurgery*. 2009;111(7):568-73. <https://doi.org/10.1016/j.clineuro.2009.04.002>
 21. Zhao L, Dai Q, Chen X, Li S, Shi R, Yu S, et al. Neutrophil-to-Lymphocyte Ratio Predicts Length of Stay and Acute Hospital Cost in Patients with Acute Ischemic Stroke. *Journal of Stroke and Cerebrovascular Diseases*. 2016;25(4):739-44. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2015.11.012>
 22. Kim J, Song TJ, Park JH, Lee HS, Nam CM, Nam HS, et al. Different prognostic value of white blood cell subtypes in patients with acute cerebral infarction. *Atherosclerosis*. 2012;222(2):464-7. <https://doi.org/10.1016/j.atherosclerosis.2012.02.042>
 23. Gokhan S, Ozhasenekler A, Mansur Durgun H, Akil E, Ustundag M, Orak M. Neutrophil lymphocyte ratios in stroke subtypes and transient ischemic attack. *European Review for Medical and Pharmacological Sciences*. 2013;17(5):653-7.
 24. Tokgoz S, Keskin S, Kayrak M, Seyithanoglu A, Ogmegul A. Is neutrophil/lymphocyte ratio predict to short-term mortality in acute cerebral infarct independently from infarct volume? *Journal of Stroke and Cerebrovascular Diseases*. 2014;23(8):2163-8. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2014.04.007>
 25. Belen E, Sungur A, Sungur MA, Erdogan G. Increased Neutrophil to Lymphocyte Ratio in Patients With Resistant Hypertension. *Journal of Clinical Hypertension*. 2015;17(7):532-7. <https://doi.org/10.1111/jch.12533>
 26. Huang YC, Hu CJ, Lee TH, Yang JT, Weng HH, Lin LC, et al. The impact factors on the cost and length of stay among acute ischemic stroke. *Journal of Stroke and Cerebrovascular Diseases*. 2013;22(7):e152-8. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2012.10.014>

27. Jain M, Damania D, Jain AR, Kanthala AR, Ganti L, Jahromi BS. Does prolonged length of stay in the emergency department affect outcome for stroke patients? *The Western Journal of Emergency Medicine*. 2014;15(3):267-75. <https://doi.org/10.5811/westjem.2013.8.16186>
28. Kıyan S, Öz Saraç M, Ersel M, Aksay E, Yürüktümen A, Musalar E, et al. Retrospective Analysis of 124 Acute Ischemic Stroke Patients Who Attended To The Emergency Department In One Year Period. *JAEM* 2009;8:3.
29. Akhtar N, Kamran S, Singh R, Cameron P, Bourke P, Khan R, et al. Prolonged Stay of Stroke Patients in the Emergency Department May Lead to an Increased Risk of Complications, Poor Recovery, and Increased Mortality. *Journal of Stroke and Cerebrovascular Diseases*. 2016;25(3):672-8. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2015.10.018>
30. Nakibuuka J, Sajatovic M, Nankabirwa J, Ssendikadiwa C, Furlan AJ, Katabira E, et al. Early mortality and functional outcome after acute stroke in Uganda: prospective study with 30 day follow-up. *SpringerPlus*. 2015;4:450. <https://doi.org/10.1186/s40064-015-1252-8>
31. Ganesh A, Lindsay P, Fang J, Kapral MK, Cote R, Joiner I, et al. Integrated systems of stroke care and reduction in 30-day mortality: A retrospective analysis. *Neurology*. 2016;86(10):898-904. <https://doi.org/10.1212/WNL.0000000000002443>