

PROGNOSTIC RELATIONSHIP BETWEEN THE INFARCT VOLUME AND COMPLETE BLOOD COUNT IN ISCHEMIC CEREBROVASCULAR DISEASE

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ABSTRACT

Objectives: The aims of this study are to investigate a correlation between the infarct volume, Glasgow Coma Score (GCS) and some of the complete blood count (CBC) parameters such as leukocyte, lymphocyte, neutrophil, monocyte, platelet counts, red blood cell distribution width (RDW), platelet distribution width (PDW), and mean platelet volume (MPV) levels in patients with ischemic stroke and effectiveness of these parameters in predicting the prognosis.

Methods: The hospital records of 54 patients who admitted to our emergency department with a diagnosis of ischemic cerebrovascular disease between 01.01.2012 and 01.01.2011 were scanned retrospectively. Magnetic Resonance Imaging (MRI) was taken in the first 48 hours of the admission for all of the selected patients. Fifty healthy volunteers were enrolled in the study as the control group. The leukocyte, neutrophil, lymphocyte, monocyte, platelet counts, RDW, PDW, and MPV were compared between the two groups. Additionally these blood parameters and the infarct volume calculated with Diffusion MRI and GCS were compared in the patient group.

Results: In the patients group the MPV values were significantly higher than healthy volunteers ($p = 0.034$). There were no significant differences between the 2 groups in terms of other CBC parameters ($p > 0.05$). There was also no statistically significant difference between the checked parameters and the infarct volume and GCS ($p > 0.05$).

Conclusion: Our results suggest that MPV may be important in early diagnostic approach, but neither MPV nor the other CBC parameters have any prognostic significance in ischemic stroke.

Key words: Cerebral infarction, diffusion-weighted magnetic resonance imaging, infarct volume, blood cell count parameters, Prognosis

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Introduction

All over the world, stroke is the first most common cause of permanent disability, the second most common cause of dementia and the third most common cause of the mortality⁽¹⁾. Ischemic strokes account for the 87% of the stroke cases⁽²⁾. Platelets are known to play an important role in the pathogenesis of atherosclerotic complications. MPV is considered to be a good indicator of platelet function and it is shown to increase in diseases such as myocardial infarction and ischemic stroke which develop in the atherosclerotic basis⁽³⁾. Furthermore the inflammatory response also plays an important

role in secondary injury following ischemia and stroke. Leucocytes, including neutrophils and macrophages, are believed to contribute to inflammatory tissue injury in acute stroke^(4,5). Many reports have demonstrated leucocyte accumulation, initiation of thrombosis and exacerbation of ischemic brain injury after stroke^(6,7).

Lesion volume is believed to be an important parameter reflecting the primary pathological condition, and the extent of this pathological condition relates to neurological deficits and functional outcome⁽⁸⁾. Hence, infarct volume may serve as a predictor of the severity of neurological impairments such as paresis (i.e., neurological deficits) and func-

tional outcomes such as activities of daily living dependency after a stroke⁽⁹⁾.

The aims of this study are to investigate a correlation between the infarct volume, GCS and some of the CBC parameters such as leukocyte, lymphocyte, neutrophil, platelet counts, RDW, PDW, and MPV levels in patients with ischemic stroke and effectiveness of these parameters in predicting the prognosis.

Materials and methods

After approval of the hospital ethics committee, the files of 54 patients diagnosed with ischemic cerebrovascular disease according to the findings of physical examination and CT scan of the brain in Ankara Atatürk Training and Research Hospital Emergency Department between 01.01.2010 and 01.01.2011 were examined retrospectively. In this period, 174 patients with a presumptive diagnosis cerebrovascular disease was admitted to the emergency room. The patients who appropriate to the criteria defined by the American Heart Association in 2009 and the World Health Organization criteria was admitted as stroke.

The patients with comorbidities such as acute coronary syndromes, pulmonary embolism, acute renal failure, chronic renal failure which diagnosed simultaneously in the emergency department, the patients with a known thyroid disease and hematological disorders, the patients who were brought to the emergency room as cardiopulmonary arrest, patients with known or newly diagnosed cardiac thrombus were excluded from the study. The remaining 54 patients whom decisively diagnosed with cerebral MRI in with the first 48 hours enrolled in the study. Fifty healthy volunteers, without exclusion criteria and without doubt of stroke or transient ischemic attack, were included in the study as the control group.

Demographic data (age, gender), the complaint at admission, the application type, comorbid diseases, physical examination findings, GCS, duration of hospitalization, leukocyte, neutrophil, lymphocyte, monocyte, platelet, RDW, PDW, and MPV values obtained by CBC in the emergency room were recorded.

Volume was calculated by using apparent diffusion coefficient (ADC) maps which we created by using 'diffusion-weighted image' sequences with 5 mm thickness 1 mm gap. Restricted diffusion areas were matched with infarct volume, and possi-

ble T2 shining effects were excluded by using ADC mapping.

Complete blood count parameters which measured in the first blood tests from patients were included to study. Blood samples of both the patients group and the control group were included in ethylene diamine tetra Aceticacid blood (EDTA) tubes and analyzed in the first hour in Roche Sysmex X-2100 analyzer device.

Statistical analysis

The study was carried out with SPSS 15.0 statistical analysis software package. Compliance of the data with the normal distribution was evaluated with Kolmogorov-Smirnov test. Mann-Whitney U test was used for comparisons of continuous variables of the two groups which do not match the normal distribution; the data were expressed in median and 25-75% quarterly values. Student's t test was used for comparisons of the continuous variables of two groups with normal distribution the data were expressed as mean \pm standard deviation. Pearson's chi-square test was used for categorical data analysis; the data were expressed as numbers and percentages. Correlation analysis was performed by Spearman's method. $p < 0.05$ was considered statistically significant.

Results

Fifty-four patients and 50 healthy volunteers were included in the study. Thirty-three patients (54.1%) were male, 21 (45.9%) patients were female and mean age was 66.50 (min:60.00, max:70.75). There was no statistically significant difference between patients and healthy volunteers of gender and age ($p > 0.05$). Some demographic and laboratory data of the patients and healthy volunteers were presented in Table 1.

| | Patients* | Healty Volunteers* | p value |
|-----------------|------------------------|------------------------|---------|
| Age | 66.50 (60.00-70.75) | 70.50 (58.75-78.50) | 0.212 |
| Male sex | 33 (%54.1) | 28 (%45.9) | 0.597 |
| Leukocyte count | 8200 (6275-11500) | 8200 (6575-10150) | 0.747 |
| Platelet count | 248000 (205000-298250) | 221000 (200000-264250) | 0.180 |
| MPV | 9.64 \pm 1.06 | 9.23 \pm 0.88 | 0.034 |

Table 1. Patient and control group characteristics.

There was no statistically significant difference in terms of lymphocyte, neutrophil, monocyte, platelet and leukocyte counts and RDW and PDW values between the patients group and the control group ($p > 0.05$), whereas MPV values of the patients were significantly higher than healthy volunteers ($p = 0.034$).

The median value of infarct volumes of the group of patients in the MRI was 2927.5 (1,000 to 12,600). The value of GCS in the patients group was 14.44 ± 0.64 . The GCS was calculated as 15 for 26 patients (48.15%), 14 in 20 patients (37.03%), 13 in 8 patients (14.8%).

In the patients group, median lymphocyte count was 1750 (1400-2625), neutrophil count was 5050 (3625-6365), RDW value was 45.25 (41.63-47.73), respectively. The average value of PDW was 4.12 ± 1.60 , and monocyte was 717.41 ± 283.74 , respectively. There were no statistically significant correlations between infarct volumes and leukocyte ($p = 0.390$), neutrophil ($p = 0.383$), lymphocyte ($p = 0.204$), monocyte ($p = 0.842$), and platelet counts ($p = 0.273$), and RDW ($p = 0.087$), PDW ($p = 0.250$) and MPV values ($p = 0.958$) respectively.

A weak negative correlation between infarct volumes and GCS of the patients was defined ($r = -0.290$, $p = 0.034$), whereas there was no statistically significant correlation ($p > 0.05$) between GCS and leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts, and RDW, PDW, and MPV values.

Regarding patients' medical history 20 patients (37.0%) had diabetes mellitus, 35 patients had hypertension (64.8%), 9 patients had coronary artery disease (16.7%), 4 patients had atrial fibrillation (7.4%) respectively. Ten patients (18.5%) were smokers whereas only one (1.9%) was using alcohol. Ten patients (18.5%) had ischemic stroke before, while none had hemorrhagic stroke. There was no statistically significant correlation between medical history of the patients and infarct volumes (for all variables $p > 0.05$).

Regarding to the patients who had used drugs, 16 patients (29.6%) used aspirin, 6 patients (11.1%) used warfarin, 17 patients (31.5%) used oral antidiabetics, and 35 patients (64.8%) used antihypertensive drugs, respectively. There was no statistically significant correlation between using drugs and infarct volumes (for all variables $p > 0.05$).

Discussion

With the introduction of new and different methods in the treatment of ischemic stroke, prompt diagnosis has gained importance. Thus, in order to define a correlation with the existence of ischemic brain injury, CBC parameters have been investigated, as well as many other biochemical markers.

Whether increased MPV and high platelet reactivity are markers of more severe stroke is still controversial. Greiseneger et al in their study including 455 patients with ischemic stroke found a significant relationship between MPV values of the patients three months after the incident and bad prognosis.³ In another study investigating MPV and NIHSS, it is reported that these 2 parameters are important indicators for predicting the prognosis⁽¹⁰⁾.

However, in the studies of O'Malley et al. and Ntaios et al. no significant relationship between MPV and stroke prognosis was found^(11,12). In our study MPV values of patients were significantly higher than in healthy volunteers, however we did not find any association between infarct volume and GCS and MPV. Therefore, we consider that MPV may have a predictive significance in the early period, but in the long-term it doesn't have a prognostic impact.

The number of circulating platelets shows a broad spectrum. It is shown to be an inverse relationship between platelet count and MPV^(3,11). Toghi et al. in their study with lacunar stroke patients, found a decrease in the PDW in the acute and sub-acute phases⁽¹³⁾. In our study there were no significant differences between the PDW values of patients and healthy volunteers. Furthermore we didn't find any relationship between the infarct volume and GCS and PDW. Therefore we think that PDW has no a predictive value in the early phase or a prognostic impact in the long term.

Studies with animal models have shown neutrophil invasion to atherosclerotic plaque. Neutrophils may facilitate plaque tearing by releasing proteolytic enzymes, arachidonic acid derivatives, and superoxide radicals⁽¹⁴⁾. Thus, increased number of neutrophils may not only indicate severity of the inflammatory condition in atherosclerotic patients but also instability of the atherosclerotic plaque⁽¹⁴⁾. In addition, increased numbers of leukocyte and neutrophils have been suggested to be indicators for severity of clinical symptoms, poor prognosis, mortality, and a larger infarct volume,

but in another study, it is reported that there is a relationship between GCS and white blood cell count, but has no prognostic value^(15,16,17).

In our study, we neither found a difference between the neutrophil and leukocyte counts of patients and healthy subjects, nor a correlation between these parameters and infarct volume and GCS. Given these results, we suggest that these parameters may not have any predictive value in the early phase, nor prognostic value in the late phase.

VCAM-1 is an adhesion molecule that is released from the endothelium and binds monocytes. Monocytes that bind to endothelium pass through to subendothelial area and accumulate here, and this accumulation precipitate atherosclerosis⁽¹⁸⁾. In a study conducted with transient ischemic attack and ischemic stroke patients with the number of monocytes was significantly higher in both groups⁽¹⁹⁾. In our study, did not find a significant difference between the numbers of monocytes of patients and healthy volunteers.

RDW has been traditionally used to differentiate types of anemia, specifically iron deficiency anemia. But, in many recent studies elevated levels of RDW are associated with poor prognosis in the setting of stable angina, acute myocardial infarction, heart failure, stroke, peripheral arterial disease, and older age, Although recent studies report a association between RDW and poor prognosis in cardiovascular disease, the mechanisms have not yet been fully understood^(20,21,22,23,24,25).

However, RDW may have a role in the pathogenesis by inflammation.²⁶ Possible mechanisms may include the fact that the higher levels of RDW may reflect an underlying inflammatory state which is related with poor outcomes and which leads to impaired erythrocyte maturation^(27,28). In our study, we did not observe any difference between the RDW values of patients and healthy volunteers, neither we find a correlation between these parameters and infarct volume and GCS. Therefore we suggest that RDW may not have any predictive value in the early phase, Nor prognostic value in the late phase.

Conclusion

As a result, regarding MPV, the significant difference between the patients and healthy volunteers, may indicate that MPV may be a diagnostic tool in early stages of ischemic stroke.

However, there were no significant differences between patients and healthy volunteers in terms of CBC parameters (leukocyte, neutrophil, lymphocyte, monocyte, platelet counts, RDW and PDW). This suggests that CBC parameters have no diagnostic value in early period of ischemic stroke. There were no significant difference between infarct volume which is the most important prognostic factor in ischemic stroke, GCS which also is an important factor and neither MPV nor other CBC parameters. This suggests that these parameters have no prognostic value in late period of ischemic stroke.

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Study limitations: Small number of patients and the lack of patients with GCS 12 and under

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