Hemorajik İnme - İskemik İnme Ayırıcı Tanısında Hematolojik Parametrelerin ve Crp'nin Yeri

Role of Haematological Parameters and C-Reactive Protein in Discrimination of Ischemic and Hemorrhagic Stroke

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Öz

GİRİŞ ve AMAÇ: İnme, kardiyovasküler hastalıklar ve kanserlerden sonra üçüncü en yaygın ölüm nedenidir. CRP ve tam kan sayımı parametrelerinin iskemik ve hemorajik inmenin erken ayrımında rolü olup olmadığını araştırdık.

YÖNTEM ve GEREÇLER: Arşiv kayıtlarını kullanarak retrospektif bir çalışma yaptık. 5 Kasım 2015 ile 5 Kasım 2017 tarihleri arasında iskemik veya hemorajik inme tanısı alan hastalar çalışmaya dahil edilmiştir. Dahil edilen hastaların demografik verileri, temel semptom ve bulguları, bilgisayarlı tomografi ve manyetik rezonans görüntüleme sonuçları elde edildi. Hastaların trombosit sayısı, ortalama trombosit hacmi, hemoglobin konsantrasyonu, ortalama korpüsküler hacmi, beyaz küre sayısı ve C - reaktif protein sonuçları kayıt altına alınmıştır.

BULGULAR: Çalışmaya dahil edilen 100 hastanın 68'inde (% 68) iskemik inme vardı. Kalan 32 (% 32) hastaya hemorajik inme tanısı kondu. Kadınlarda ortalama yaş 75.35 ± 1.7, erkeklerde 71.06 ± 1.9 idi. Hemorajik inmeli hastalarda iskemik inmeli hastalara göre ortalama trombosit hacmi (p = 0,009) ve beyaz küre sayısı (p = 0,006) daha yüksekti ve istatistiksel olarak anlamlı çıkmıştır.

TARTIŞMA ve SONUÇ: Ortalama trombosit hacmi ve beyaz kan hücresi sayısı hemorajik inmede daha yüksek görünse de, daha bilgilendirici sonuçlar için daha ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: İnme, MPV, WBC

Abstract

INTRODUCTION: Stroke is the third most common cause of death after cardiovascular diseases and cancers. We investigated whether CRP and complete blood count parameters had a role for early differentiation of ischemic and hemorrhagic stroke.

METHODS: We performed a retrospective study by using archive records. Patients diagnosed with ischemic or hemorrhagic stroke between November 5, 2015 and November 5, 2017 were included in the study. Demographic data, main symptoms and signs, computerized tomography and magnetic resonance imaging results of included patients were obtained. Platelet count, mean platelet volume, hemoglobin concentration, mean corpuscular volume, white blood cell count and C - reactive protein results of the patients were noted.

RESULTS: Of 100 patients entering the study, 68 (%68) had ischemic stroke. The remaining 32 (%32) patients were diagnosed with hemorrhagic stroke. The mean age was 75.35 ± 1.7 for women and 71.06 ± 1.9 for men. Mean platelet volume (p= 0.009) and white blood cell count (p= 0.006) were higher and statistically significant in the patients with hemorrhagic stroke compared to those with ischemic stroke.

DISCUSSION and CONCLUSION: Even though mean platelet volume and white blood cell count seemed to be higher in hemorrhagic stroke, further studies are needed for more informative results.

Keywords: Stroke, MPV, WBC

INTRODUCTION

Stroke is a sudden onset of neurological deficit in which an acute injury occurs in the central nervous system following a vascular event including intracranial hematoma or cerebral infarction (1). There are two main types of stroke: ischemic and hemorrhagic. Hemorrhagic stroke is divided into two types as intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). Unilateral limb weakness and speech disturbance are the most common symptoms of stroke. Many other conditions such as somatoform disorders, migraine headache, seizure and hypoglycemia can mimic stroke (2).

While ischemic stroke accounts for approximately 80% of stroke cases, the remaining 20% of strokes are hemorrhagic (3). Although there are various etiological factors for stroke, hypertension, which is also a modifiable risk factor, is the underlying cause of the majority of the cases (4). Even though men seem to be under a greater risk for both ischemic and hemorrhagic stroke, women aged 35-44 and those aged ≥ 85 years have higher incidence of stroke than men (5). It is estimated that hemorrhagic stroke cases are more common in our country compared to the other countries and this is attributed to uncontrolled hypertension (6).

Non-contrast brain computerized tomography (CT) scan is the first imaging modality to be performed in diagnosing stroke. Brain CT scan, as an initial workup, is very useful for detection of intracerebral and subarachnoid hematoma and other causes mimicking stroke such as brain tumors. Moreover, in order to rule out a subtle intracranial hematoma, a CT scan of the head should be considered in patients with ischemic stroke, particularly in those being considered for administration of thrombolytic therapy. Despite its limited sensitivity at the early phase of ischemic stroke, CT scan can help in determining a number of ischemia signs such as acute hypodensity, loss of gray matter -white matter differentiation, obscuration of the lentiform nucleus, insular ribbon sign and hyperdense middle cerebral artery sign. Furthermore, non-contrast CT of the brain remains the first imaging choice in diagnosing stroke since it is fast, inexpensive and easily applicable. However, diffusion-weighted magnetic resonance imaging (MRI) has become the gold standard for diagnosis of acute ischemic stroke because of being more sensitive than CT (7).

In prior studies, many biochemical markers, including complete blood count (CBC) parameters, have been investigated in differential diagnosis of stroke types. CBC is one of the most ordered laboratory tests in medicine. CBC, which quantifies absolute numbers, sizes and percentages of white blood cells, red blood cells and platelets, are extensively used in the diagnosis, treatment and follow-up of many diseases. White blood cell count (WBC), hemoglobin (HGB), platelet count (PLT), mean platelet volume (MPV), mean corpuscular volume (MCV) are the most commonly used parameters in a CBC test (8). C-reactive protein (CRP), as a valuable acute phase reactant, has been assessed in some previous studies concerning hemorrhagic and ischemic stroke besides being used in the many other circumstances (9).

MATERIAL AND METHOD

This study was performed retrospectively by including patients diagnosed with ischemic stroke or hemorrhagic stroke following their admission to the emergency department of Abant Izzet Baysal University Faculty of Medicine in Bolu, Turkey between November 5, 2015 and November 5, 2017. Ethical approval of the study was obtained from Bolu Abant Izzet Baysal University Clinical Research Ethics Committee (Date: 01.12.2017, Number: 181). A total of 100 patients aged ≥18 were included in the study. All the patients underwent brain CT scan and/or diffusion-weighted MRI. Additionally, all the patients included in the study had both CBC and CRP results ordered during the admission. Age, gender, symptoms, physical examination findings, serum HGB, WBC, PLT, MCV, MPV and CRP levels and CT and/or MRI results of the all patients were collected.

Statistical analysis was performed using SPSS 22.00. Descriptive data was expressed by the number of patients (n), percent (%), median, interquartile range (IQR). The patients were divided into two groups as hemorrhagic stroke and ischemic stroke. Distribution of continuous variables was evaluated by Kolmogorov-Smirnov test. Chi-square test was used to compare

categorical variables. Student T test and Mann Whitney test were used to compare continuous variables. A p value less than 0.05 was considered statistically significant.

RESULTS

Of the patients, 68 (68%) were ischemic and 32 (32%) were hemorrhagic. There were 53 (53%) female and 47 (47%) male patients in the study. The mean age was 75.3 ± 1.7 in women, 71.0± 1.9 in men and the majority of the patients were in the 71-80 age group. The most common symptom was found to be unilateral limb weakness (Table 1).

Tablo 1. Demographic features and clinical characteristics according to stroke types

Variables		Ischemic stroke (n)	Hemorrhagic stroke (n)
Gender (M/F)		31/37	16/16
Age groups	31-40	1	2
	41-50	1	3
	51-60	5	6
	61-70	10	4
	71-80	23	11
	81-90	27	3
	≥91	2	2
Symptoms	Speech disturbance	14	4
	Unilateral limb weakness	40	12
	Unconsciousness	1	10
	Others	16	7

The mean HGB value of patients with ischemic stroke was 13.09 ± 0.27, while the mean HGB value of patients with hemorrhagic stroke was 13.08 ± 0.4. There was no statistically significant difference for HGB between the groups (p> 0.05). The mean WBC values in ischemic stroke and hemorrhagic stroke were 9.36 ± 0.35 and 11.71 ± 0.94, respectively. Accordingly, a statistically significant difference was determined between the groups for WBC count with a higher value in hemorrhagic stroke group (p <0.05). The mean

PLT value in ischemic stroke patients was 244.19 ± 12.02, while that in hemorrhagic stroke group was 241.68 ± 11.23. There was no statistically significant difference for PLT between the groups (p> 0.05). The mean MCV value of patients with ischemic stroke was 90.01 ± 0.81, while the mean MCV value of patients with hemorrhagic stroke was 89.11 ± 0.98. There was no statistically significant difference for mean MCV value between the stroke types (p> 0.05). The mean MPV value of patients with ischemic stroke was 8.11 ± 0.17, while the mean MPV value of patients with hemorrhagic stroke was 8.71 ± 0.33. The difference between the groups was found to be statistically significant (p <0.05). The mean MPV value in the hemorrhagic stroke patients was higher than that of the ischemic stroke patients. The mean CRP value of the patients with ischemic stroke was 43.66 (61.2). On the other hand, the mean CRP value in hemorrhagic stroke patients (n = 32) was 53.72 (27). Increased CRP levels were detected in both stroke types. However, there was no statistically significant difference between the groups (p> 0.05) (Table 2).

Tablo 2. Laboratory results according to stroke types

Laboratory Parameters	Ischemic stroke	Hemorrha gic stroke	*P value*
HGB (gr/dl)	13.09±0.27	13.08±0.42	0.98
WBC (10^3 /µL)	9.36±0.35	11.71±0.94	**0.006***
PLT (10^3 /µL)	244.19±12.02	241.68±11.23	0.89
MCV (fL)	90.01±0.81	89.11±0.98	0.51
MPV (fL)	8.11±0.17	8.71±0.33	**0.009***
CRP (mg/dL) (median-Interquartil range)	43. 66 (61.2)	53.72(27)	0.34

*: Significantly, HGB: Hemoglobin, WBC: White blood cell, PLT: Platelet, MCV: Mean corpuscular volume, MPV: Mean Platelet Volume, CRP:C-reactive protein.

DISCUSSION

In our study, we analyzed the role of complete blood count parameters and CRP in differentiating ischemic stroke and hemorrhagic stroke. Ultimately, it was concluded that MPV and WBC can be considered for usage in discrimination of stroke types.

MPV is a marker enlightening about platelet function and activation. In a study investigating the role of MPV as consequence of a link between thrombosis and inflammation, it has been revealed that MPV levels were inclined to be elevated in inflammatory diseases and thromboembolic diseases such as cerebrovascular event (10). In a study performed by Ha et al., the prognostic role of MPV in predicting ischemic stroke in patients with atrial fibrillation was researched. During 15- month follow-up, it was found that the mean MPV was 8.5 ± 1.0 fL and the percentage of stroke was higher in patients with higher MPV levels (11). However, in another study with ischemic and hemorrhagic stroke cases, no relation was detected between MPV level and stroke risk and prognosis. In the study, the mean MPV was found to be 8.73 (12). In our study, MPV level was 8.115 in the ischemic stroke group and 8.719 in the hemorrhagic stroke group. We determined higher mean MPV value in hemorrhagic stroke patients. However, conflicting results have been published before (19). We think that these incompatible results are highly likely because of insufficient numbers of studies regarding this subject. Moreover, MPV levels may increase in hemorrhagic stroke as expected in ischemic stroke.

In a study, 1302 patients who suffered from ICH were retrospectively analyzed and it was determined that the WBC count was elevated at the time of admission. However, it was concluded that higher WBC levels were inversely associated with bleeding expansion. It was suggested that the occurrence of the inflammation in regulating coagulation cascade following bleeding is the probable cause (13). In another study performed with patients diagnosed with ischemic stroke, increased WBC levels have been shown to be associated with relapse of the disease, increased risk for both death and other thromboembolic diseases such as acute coronary syndrome. It has been though that increases in WBC count may be caused by stroke-related inflammation or concomitant infections (14). In our study, WBC levels in patients with hemorrhagic stroke were found to be higher compared to patients with ischemic stroke. It is known that leukocytosis occurs in intracranial hematoma. This may be related to the fact that leukocytes interact with platelets in modulating coagulation.

In a comprehensive study consisting 8013 patients with ischemic and hemorrhagic stroke, the impact of HGB levels on mortality was investigated. Lower HGB concentrations have been determined in a significant portion of stroke patients included in the study and this has been found to be associated with increased mortality risk (15). In another study performed by Tanne et al. the relationship between HGB concentration and prognosis and mortality of patients with ischemic and hemorrhagic stroke was evaluated. In the study, no significant association was found between stroke types for HGB levels. In addition, it has been suggested that both low and high concentrations of HGB lead to similar results in terms of mortality and the relationship is not linear (16). In our study, no significant difference was found between ischemic stroke and hemorrhagic stroke for HGB levels.

In a study aiming to characterize platelet functions in patients presenting with ischemic stroke, it was concluded that platelets are hyperresponsive in ischemic stroke and dual antiplatelet therapy may be beneficial for these patients (17). In another study inquiring the relationship between platelet dysfunction and prognosis in ICH patients, it was suggested that low platelet count or platelet dysfunction are

highly possible to be associated with poor outcomes including hematoma expansion in these patients (18). A prospective study performed with 692 patients with ischemic and hemorrhagic stroke revealed that MPV could be used as an important predictor in the prognosis of ischemic stroke and low PLT count can be considered as a predictor in hemorrhagic stroke (19). In our study, mean PLT levels were found to be similar in both ischemic stroke and hemorrhagic stroke groups without statistically significant difference.

The relationship between red blood cell parameters and the mortality of ischemic stroke was investigated in a study and it has been revealed that MCV can be used as a marker in predicting mortality (20). Söderholm et al. have reported that MCV levels decreased in stroke patients. It has been supposed that this was probably resulting from lower erythrocyte turnover and higher erythrocyte lifespan (21). In our study, it was investigated whether MCV would have a role in distinguishing between hemorrhagic stroke and ischemic stroke and no significant difference was found in MCV levels between the groups.

The role of high-sensitive CRP in predicting mortality risk within 3 months after ischemic stroke was evaluated in a study and high CRP levels were shown to be associated with higher mortality rates. It has been asserted that high CRP levels after ischemic stroke are due to concomitant inflammation after brain injury (22). Di Napoli et al. performed a study and inferred that elevated CRP levels were associated with increased mortality risk in patients with ICH (23). The relationship of CRP levels with coronary artery disease, stroke and mortality has been analyzed in a study and it has been revealed that high CRP concentrations can be used to predict ischemic vascular diseases (24). In our study, CRP levels didn't differ between ischemic stroke and hemorrhagic stroke. CRP levels were found to be increased in both types of stroke. Although CRP

levels were detected higher in the ischemic stroke type, no statistically significant difference was seen.

CONCLUSION

In our study, we determined that WBC and MPV levels were higher in hemorrhagic stroke compared to ischemic stroke. However, there are several prior studies suggesting different results than ours. Therefore, we believe that large sample studies are required to provide more accurate outcomes.

Limitation of Study

Disadvantages of retrospective and single center studies

Conflict of Interest

The authors declare no conflict of interest

Author Contribution

MK, CK, BOT design of study, interpretation of results, preparation of manuscrip

Availability of data of materials the authors declare that no data have been fabricated or manipulated (including images) to support the conclusions. The authors declare that no data, text, or theories by others are presented as if they were the authors own.

Ethical approval Ethical approval was granted by the Human Research Ethics Committee of Izzet Baysal University.

Human rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical

standards.

Informed consent For this retrospective study, informed consent is not required.

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