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The Role of C-RP / Albumin Ratio in The Diagnosis of Stroke and an Overview of the Factors Affecting Hemispheres

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Abstract

Objective: Stroke has an important in emergency room admissions. Co-morbidities can increase the risk of stroke. Infection markers can be used in the diagnosis of stroke. The incidence of stroke originating from the left hemisphere has been reported more than the right. To investigate the accuracy of this situation; We tried to examine our patients who applied to our Emergency Department with stroke symptoms.

Materials and Methods: In our study, 1049 patients who presented to our Emergency Department with stroke symptoms and were diagnosed with stroke after neurology consultation were included in our study within 2 years. It was recorded retrospectively whether there was a previous stroke, gender, history of additional disease, infarction region, hemorrhagic or ischemic infarction, whether the C-RP (C-Reactive Protein) / albumin value contributed to this situation was examined. Findings were analyzed with SPSS statistical program, Chi-square and Mann Whitney-U tests.

Results: Between 2015 and 2017, 1049 patient findings were evaluated. Hemorrhagic findings were found in 74 (7.05%) of these patients, and ischemic infarction in 975 (92.95%). 875 (83.4%) of these patients had additional disease. Stroke originating from the left hemisphere was detected in 502 (47.9%) patients. C-RP, albumin, C-RP/ albumin values did not differ significantly ($p > 0.005$) in the group with hemorrhage and infarction.

Conclusion: Patients with chronic diseases, especially hypertension, chronic artery disease, diabetes and a history of previous stroke are in the high-risk group in terms of stroke risk. For this, treatment method or risk reduction, measures should be taken before stroke develops.

Key Words: C-RP/Albumin value, Diabetes, Hypertension, Left Hemisphere Infarction, Stroke

Introduction

The most common cases in the emergency room, among the cerebrovascular diseases are stroke (cerebrovascular disease: CVD) patients. Stroke is symptoms seen as a result of blockage in the vessels leading to the brain. Considering the localization and termination patterns of stroke symptoms, 4 basic clinical pictures are encountered[1]:

1. **Transient Ischemic Attack**: It is a transient focal neurological deficit that starts suddenly, usually lasts 5-15 minutes and resolves completely within 24 hours.
2. **Reversible Ischemic Neurological Deficit**: Neurological symptoms are temporary, but lasts longer than 24 hours.
3. **Progressive Stroke**: Neurological deficit begins suddenly, progresses for hours or days, and remains continuous in a certain plateau. It often occurs as a result of active occlusive thrombosis of the major cerebral artery.
4. **Completed Stroke**: It is a clinical condition in which neurological deficit develops in less than 6 hours.

In the classification used in the TOAST "Trial of Org 10172 in Acute Stroke Treatment" study, etiology was included in addition to clinical findings[2].

- **a.** Large artery atherosclerosis (thrombosis or embolism).
- **b.** Cardioembolic.
- **c.** Small vessel occlusion (lacuna).
- **d.** Ischemic stroke due to other identified causes.
- **e.** Ischemic stroke of unknown cause.

The incidence of stroke has increased with the prolongation of life expectancy and the increase in the elderly population. Risk factors; It can be grouped under two headings, namely modifiable or non-modifiable (Table-1)[3]. Epidemiological studies conducted in recent years show that the mortality rate due to stroke has decreased. This situation is explained by the capture of even small ischemic areas with advanced imaging methods and the further development of clinical information. In addition, the treatment or regulation of modifiable risk factors plays a big role.

In stroke; Among the diseases that disrupt the vascular

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Table-1: Stroke risk factors

I. Non-modifiable risk factors	a. Age b. Sex c. Race d. Family history of stroke e. Genetic predispotion
II. Modifiable risk factors	**b. Less well documented**
a. Well documented	1. Metabolic syndrome
1. Hypertension	2. Alcohol or drug abuse
2. Smoking	3. Hyperhomocysteinemia
3. Diabetes or hyperglycaemia	4. Infectious diseases (C. Pneumonia, H.Pylori, CMV, periodontal diseases)
4. Cardiovascular Disease	5. Migraine
5. Carotid stenosis	6. High cholesterol
6. Atrial fibrillation	7. Sleep-disordered breathing
7. Hypercoagulability	
8. Dyslipidaemia	
9. Obesity	
10. Diet and nutrition	
11. Physical inactivity	
12. Oral contraceptive therapy	

*C. pneumonia: Clamidyadophila Pneumonia, H. Pylori: Helicobacter Pylori, CMV: Cytomegalovirus

wall structure in the long term, the most common chronic conditions we encounter are hypertension (HT), diabetes (DM), chronic artery disease (CAD). Acute changes in acute phase reactants such as CRP (C-Reactive Protein) or albumin also increase this risk.

In this study; We tried to examine how and why, which hemispheres are affected when patients with HT, DM, CAD and previous stroke have had a stroke, how the rates of CRP and albumin, which are among the infection markers, changed.

Materials and Methods

Our study included 1049 patients over 18 years of age who presented to the Emergency Service with stroke symptoms between January 1, 2015 and December 31, 2017, who were diagnosed with ischemic or hemorrhagic CVD by a neurologist, and whose radiological images were checked by a radiologist. The history and clinical findings of the patients were obtained retrospectively. The type of stroke was noted in patients with a CRP value above 5 mg / dl and an albumin value below 3.4 g / dl. Analysis was performed based on the hypothesis that the risk of stroke was increased in patients with chronic disease and a C-RP / albumin ratio> 1.7 (mean C-RP / albumin in all patients). In the descriptive statistics of the data, mean, standard deviation, median lowest, highest, frequency and ratio values were used. The distribution of variables was measured with the Kolmogorov Simirnov test. Mann Whitney-U test was used to analyze quantitative independent data. Chi-square test was used in the analysis of qualitative independent data. SPSS 27.0 program was used in the analyzes. p <0.05 was considered significant. The study was approved by the University of Health Sciences Haseki Training and Research Hospital Ethic Committee (19.12.2017/594).

Results

1049 patients with a diagnosis of stroke were included in our study. 436 of them (41.6%) were female, 613 (58.4%) were male. The average age of the patients was 67. Hemorrhagic in 27 (36.5%) of female patients, ischemic infarction in 409 (41.9%); In the male patients, 47 (63.5%) had hemorrhagic and 566 (58.1%) had ischemic infarction. In 657 patients (62.6%), the C-RP (C-Reactive Protein) value was significantly higher (5 mg /dl), 310 (47.2%) of these patients had a stroke originating from the left hemisphere. Hypoalbuminemia (3.4 g / dl) was found in 205 (19.5%) patients, 89 (43.4%) of these patients had stroke findings originating from the left hemisphere. In patients with hemorrhagic stroke, the C-RP value was 21.4 ± 44.1 (mean 6.8 mg / dl), albumin value 4.3 ± 4.4 (mean 3.9) g / dl; In patients with ischemic stroke, the C-RP value was 24.6 ± 45.1 (mean 6.6) mg / dl, and the albumin value was 4.2 ± 3.4 (mean 4) g / dl (Table-2).

Of the patients, 191 (18.2%) had previous CVD, 683 (65.1%) had HT, 247 (23.5%) had a history of chronic artery disease (CAD), and 335 (31.9%) had a history of DM (Some of the patients had more than one additional disease). Ischemic infarction in 179 (18.4%) of patients with previous CVD history, hemorrhagic infarction in 12 (16.2%); Ischemic infarction in 632 (64.8%) of HT patients, hemorrhagic infarction in 51 (68.9%); Ischemic infarction in 324 (33.2%) DM patients, hemorrhagic infarction in 11 (14.9%); Ischemic infarction was detected in 237 (24.3%) of CAD patients, and hemorrhagic infarction in 10 (13.5%) (Table-3).

In 502 (47.9%) patients in the left hemisphere, in 478 (45.6%) patients in the right hemisphere, in 38 (3.6%) patients in the other region (cerebellum, pons, corpus callosum), in 31 (3%) patients' bilateral lesion was detected (Table-4). Among the patients with left hemisphere lesions, 423 (49.9%) patients had ischemic infarction, and 79 (39.1%) patients had hemorrhagic infarction (p<0.05). We have detected left hemisphere stroke in 327 patients (47.9%) out of

Table-2: Demographic data and test results of the patients'

	Ischemic Mean±SD/%	Hemorrhagic Mean±SD/%	Total Average n/%
Age	61.9±15.5	66.9±13.2	**67**
Gender F:	409/%41.9	27/%36.5	436/%41.6
M:	566/ %58.1	47/%63.5	613/%58.4
CRP	24.6±45.1	21.4±44.1	6.7
Albumin	4.2±3.4	4.3±4.4	3.9
CRP/Albumin	7.8±16.9	6.3±14.6	1.7

†*SD: Standard Deviation, F: Female, M: Male*

Table-3: Relationship between comorbidity and stroke type

Risk Factors	Hemorrhagic n	Ischemic n	p
DM	11 (14.9%)	324 (33.2%)	0.001
HT	51 (68.9%)	632 (64.8%)	**0.476**
CAD	10 (13.5%)	237 (24.3%)	0.035
CVD	12 (16.2%)	179 (18.4%)	**0.645**

Table-4: Statistical distribution table in stroke patients according to the affected area

Area	Ischemic	Hemorrhagic	p
Right	377 (44.5%)	101 (50%)	**0,183** x^2
Left	423 (49.9%)	79 (39.1%)	0,007 x^2
Bilateral	29 (3.4%)	2 (1%)	**0,109** x^2
Others	18 (2.1%)	20 (9.9%)	0,000 x^2

‡ *x^2: Chi-square test*

683 patients with HT, 125 patients (50.6%) among 247 with CAD,174 patients (51.9%) among 335 patients with DM, and 86 (45%) patients out of 191 patients with previous CVD history detected.

Discussion

The risk of stroke increases with age in all chronic diseases that cause vascular pathology, especially hypertension and diabetes. Increasing the patient's C-RP / Albumin ratio also contributes to this situation.

In a study by Janghorbani et al; 116,316 women were followed up for 26 years, if they had diabetes, what type they were, and whether they had CVD according to obesity and blood pressure. They found that patients with DM were at higher risk than patients without DM, and that Type 1 DM patients had 4 times more risk and those with Type 2 DM had 2 times more risk. They observed that those with a history of DM and HT were in the higher risk group[4]. Also, in our study, patients with DM were in the highest risk group.

Pathophysiology of cerebrovascular disease patients with diabetes has not been characterized, but both large and small blood vessels appear to be affected. Potential underlying mechanisms include excessive glycation, endothelial dysfunction, increased platelet aggregation, impaired fibrinolysis, and insulin resistance. Associated dyslipidemia and hypertension probably contribute. Decreased fibrinolysis with increased coagulation and platelet aggregation in diabetic patients; may increase the risk of large artery infarction[5]. To reduce the risk of diabetes-related stroke, treatment of glycemia, hypertension, dyslipidemia, and platelet aggregation should be considered together.

The most common modifiable risk factors are hypertension. It is a major risk factor for both ischemic and hemorrhagic stroke. The higher the blood pressure, the greater the risk of stroke [6]. This risk is significant especially in patients with diastolic pressure greater than 110 mm / Hg[7].

Taking blood pressure under control not only protects from the risk of stroke but also prevents damage to other target organs (congestive heart failure, kidney failure). All antihypertensive treatments have been found to reduce the incidence of stroke by 35-44%. It has been emphasized in the latest treatment guidelines that blood pressure should be <140/90 mm / Hg. It was even thought that patients with diabetes would be protected at a lower blood pressure level. However, a large part of society is either undiagnosed or inadequately treated for hypertension[8,9].

In patients with hypertension; Atherosclerosis is accelerated and leads to occlusion of the large artery or lipohyaline degeneration in small arteries[10,11,12]. In a study conducted in hypertensive rats; Sympathetic nerve density was found to be higher in the left hemisphere than in the right hemisphere[13]. It has been suggested that blood pressure increases in patients with acute stroke due to increased sympathetic activity. This vicious circle can lead to more blockage of the artery.

Zia et al. Found that hemorrhagic stroke was more common in hypertensive patients than ischemic stroke. In this study, it was reported that either systolic or diastolic pressure elevation was sufficient alone[14]. In our study, the opposite was the case among hypertensive patients. In other words, the number of patients who had ischemic stroke was higher than those who had hemorrhagic stroke.

The reason why patients with a history of HT seemed to have low risk in our study; that maybe because we do not know the blood pressure value at the time of admission to the hospital and whether they used long-term antihypertensive drugs.

In a study by Yamori et al. with rats; They showed that the lesion was more in the left hemisphere in 1278 patients (73.4%) out of 1740 patients. The most prominent feature of these patients is that they are in the group with high blood pressure. In another similar study, they emphasized that hypertension, human blood factors, vascular wall disorder, and hypoxia factors may cause a risk for ischemic or hemorrhagic stroke[15]. In our study, in all patients with chronic diseases especially HT; the Left area lesion rate was higher than other area lesions.

According to TOAST criteria, HT and DM indirectly cause cardioembolic due to small and large vessel pathologies; It is the source of more than one etiology. Furthermore, patients with previous CVD also have existing vascular pathologies, they have a high risk for recurrent stroke.

C-RP is an acute-phase protein synthesized in hepatocytes in response to pro-inflammatory cytokines during infectious processes. It can be used as a biomarker of acute inflammation in ischemic stroke and atherothrombotic diseases. C-RP most likely recognizes the phospholipid com-

ponents of damaged cells and foreign pathogens and binds to phosphocholine, affecting the pathophysiological process of the inflammatory process[16]. Chang et al. found the C-RP count to be significantly higher in patients with ischemic stroke compared to controls[17]. We also found a similar finding in our study. Hypoalbuminemia, on the other hand, is an acute phase response associated with inflammation and oxidative stress. Various studies have shown a relationship between hypoalbuminemia and increased C-RP levels. It has been reported that it correlates with poor prognosis in patients with previous ischemic stroke. In a study, an improvement in the neurological deficit was observed when albumin therapy was administered following the formation of an acute intracortical hematoma[18]. Also, in our study; Hypoalbuminemia was more prominent in patients with ischemic stroke.

According to our study, patients with DM and CAD history are seen in a higher risk group for stroke, compared to patients with a history of HT and previous CVD. This situation; The limited number of our patients, the inability to check the patients' application and follow-up vitals, whether they receive treatment for their chronic diseases or stable in terms of these chronic diseases; whether smoking history or other diseases that cause vascular pathology such as heart disease or hyperlipidemia may have been caused. However; among HT, CAD, and DM patients, the number of patients with stroke originating from the left hemisphere was determined more than the patients with stroke in the other area.

The further occurrence of cerebrovascular pathology on the left side may be due to hemodynamic effects related to the specific anatomy of the carotid vessels. While the right common carotid artery originates from the brachiocephalic trunk (usually at right angles to the flow of the innominate artery), the left one arises directly from the aortic arch and runs in a more even line with the ascending aorta. There is a different flow in both arteries. In this case, energy transfer in the left carotid artery is greater than the right one, and left-sided stroke is more common. In hypertensive patients, this condition becomes more severe, and the incidence of ischemic or hemorrhagic stroke increases[19, 20, 21].

In 90% of individuals; speech, understanding of spoken and written language is controlled by the left hemisphere; thus, the left hemisphere is dominant in most adults[22]. The non-dominant hemisphere (usually the right hemisphere) is excelling in musical abilities, art, emotional intelligence, recognizing people from their faces, locating, and orientation (abstract skills that cannot be expressed in space and time). One of the more common causes of left hemisphere stroke cases is that the symptoms are pronounced from the outside. The relatives of the patients notice the symptoms and bring the patient to the hospital earlier. The most common of these findings is aphasia. Right hemisphere-originated stroke cases have unclear symptoms such as unilateral neglect, space and time disorientation[23].

Study Limitations

Since our study was retrospective, some limitations were determined: symptoms, vital signs, general condition of the patients during hospitalization, and follow-up after discharge could not be performed. In addition, conditions such as smoking and a history of hyperlipidemia, which also cause vascular pathology, could not be examined because they were not recorded. It is also unknown whether they have been treated for their chronic diseases.

Conclusion

In this study, we tried to examine which hemispheres are affected more during stroke and which underlying conditions cause this, in line with the data we have.

In CVD patients; Which hemisphere is affected also affects the patient's risk of disability in the long term. Precautions should be taken before the disease develops for stroke, which affects the individual and the national economy with its care and long-term treatment. For this, changeable risk factors should be focused on, problems such as lifestyle changes, access to healthy and natural food, and treatment of chronic diseases should be resolved.

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