ORIGINAL RESEARCH

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Association of Whole Blood Viscosity and Severe Extracranial Carotid Artery Stenosis

Adnan Burak Bilgiç[1], Çetin Kürşad Akpınar[2]

[1]University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Neurology, İstanbul, Turkey
[2]Samsun University Faculty of Medicine, Department of Neurology, Samsun, Turkey

Abstract

Objective: Carotid artery stenosis (CAS) is not only an important risk factor for cerebrovascular events but also can indicate generalized atherosclerosis. Hemorheological parameters are altered in CAS and chronic cerebrovascular disorders as well, but it is controversial whether hemorheological parameters could be markers of stenosis or atherosclerosis.

Materials and Methods: We studied 154 patients with extracranial internal carotid artery stenting for symptomatic or asymptomatic severe CAS. Hematocrit total protein values of the patients included in the study were calculated using the De-Simone constant formula, low shear stress (LSR) and high shear stress (HSR).

Results: No statistically significant difference was found between the whole blood viscosities (LSR, HSR) of asymptomatic and symptomatic patients with carotid artery stenting (p=0.234, p=0.165).

Conclusion: Although hemorheological parameters are impaired in both CAS and chronic cerebrovascular disorders, the severity of stenosis cannot be detected based on hemorheological parameters. Our investigation suggests that the alteration of hemorheological parameters could indicate carotid atherosclerosis.

Keywords: Carotid artery stenosis, hematocrit, viscosity, carotid artery stenting

Introduction

The relationship between age, gender, blood pressure, total cholesterol, low-density lipoproteins and high-density lipoproteins, triglyceride levels, smoking, fibrinogen concentration, whole blood viscosity (WBV), and cerebrovascular diseases has been reported [1-5]. Blood viscosity level in patients with small artery occlusion was higher than in other stroke subtypes with large artery atherosclerosis or cardioembolism [6,7]. Flow resistance is proportional to blood viscosity and inversely proportional to vessel diameter; thus, flow resistance is markedly increased in narrow vessels such as stenotic lesions or small perforating arteries [6,8]. This is only a hypothesis, and whether blood viscosity affects large arteries other than small vessels has not been proven. In addition, there are few studies showing that WBV can also correlate with the degree of carotid artery stenosis (CAS) in both symptomatic and asymptomatic patients [9-11].

CAS that is defined by a stenosis of ≥70 (high-grade) CAS in the region of the bifurcation of the extracranial internal carotid artery, is a major risk factor for ischemic stroke [12].

It is not clear whether alterations in blood rheology are the late consequences of cerebrovascular events or markers of carotid atherosclerosis. Several studies have investigated the connection between hemorheological parameters and stenosis of carotid arteries, but their methods of hemorheological measurements and patient classification according to stenosis were different. In this study, we decided to compare the acute clinically significant stenosis with non-significant stenosis.

Address for Correspondence: Adnan Burak Bilgiç, University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Neurology, İstanbul, Turkey
Phone: +90 216 542 32 32 **E-mail:** bilgicadnan0@gmail.com **ORCID-ID:** orcid.org/0000-0002-5216-1573
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Materials and Methods

A total of 154 consecutive patients with severe extracranial internal CAS who underwent endovascular carotid artery stenting between January 2018 and December 2021 were included in this study. The severity of the stenosis (≥70%) was detected by Doppler ultrasonography and/or computed tomography angiogram and was confirmed by the American Symptomatic Carotid Endarterectomy Trial formula. Both symptomatic (acute stroke or tia) and asymptomatic patients were evaluated.

The inclusion criteria were; age between 18 and 80 years, having no history of coronary and peripheral artery diseases, no history of malignancy, rheumatological diseases, and alcohol. Other patients were excluded from the study.

Ethics committee approval was obtained from the Ethics Committee of Samsun University, Samsun Training and Research Hospital with dated 26.05.2021 and decision number 2021/10/15. Informed consent was obtained from all patients included in the study.

Calculation of Whole Blood Viscosity

Hematocrit and total protein values were calculated using the De-Simone constant formula, low shear stress (LSR) and high shear stress (HSR) [5].

For HSR calculation: (0.12 × HCT) + 0.17 (TP - 2.07)

For LSR calculation: (1.89 × HCT) + 3.76 (TP - 78.42)

Statistical Analysis

Statistical analysis was performed with IBM SPSS statistical software version 26. Data are expressed as mean standard deviation. Differences between categorical variables were investigated with the chi-square test. Difference among groups for variables that were considered a normal distribution with Shapiro-Wilk test was evaluated by One-Way ANOVA and Dunnett post-hoc tests. Non-parametric Mann-Whitney U test was used for non-normal distribution variables. Significance level was defined as $p<0.05$.

Results

One hundred fifty four patients were included in the study; 43 (27.9%) were female and 111 (72.1%) were male. The mean age was 67.8±9 years. According to DSA, patients with stenosis of 70% or more were divided into two groups; symptomatic and asymptomatic. Seventy eight (50.6%) of patients constituted the symptomatic patient group. Demographic characteristics and biochemical parameters (albumin, total protein, etc.) are shown in Table 1. There was no statistically significant difference in demographic and biochemical data between symptomatic and asymptomatic patients (p=0.791).

According to their smoking habits, they were divided into two groups as current smokers and non-smokers. The smoker ratio was 29.9 %.

Comorbidities such as diabetes mellitus (DM) and hypertension (HT) are shown in Table 2. Stenting was applied to the right internal carotid in 83 (53.9%) patients. Re-stroke was seen in 11 (7.1%) of all patients within the last 6 months (Table 2).

WBV was not statistically significant between the symptomatic and asymptomatic groups (Table 3). The effect of gender on LSR (p=0.097), HSR (p=0.084), and stenosis grade (p=0.912) was not statistically significant. The effects of DM and HT on LSR (p=0.106), HSR (p=0.063), and the degree of stenosis (p=0.272) were not statistically significant. Both group LSR (p=0.774), HSR (p=0.903), and degree of stenosis (p=0.927) did not differ between smokers and non-smokers. The side of the carotid artery stenting on LSR (p=0.772), HSR (p=0.901), and stenosis grade (p=0.165) was not statistically significant.

Table 1. Demographic data

	Total	Minimum	Maximum	Mean	Standard deviation
Degree of carotid artery stenosis	154	70.0	99.0	84.8	10.5
Age	154	48.0	82.0	67.8	9.0
Haematocrit	154	23.2	49.4	38.4	4.9
Total protein	154	3.5	8.6	6.7	0.7
Albumin	154	1.8	5.1	3.8	0.5
LDL	154	24.0	211.0	107.0	43.7
HDL	154	14.0	120.0	42.1	11.9
Triglyceride	154	37.0	799.0	173.2	126.6
Total cholesterol	154	73.0	363.0	178.4	55.09
Total	154				

LDL: Low-density lipoprotein, HDL: High-density lipoproteins

Table 2. Risk factors and stroke recurrence

Risk factors	Yes	No	Total
Smoking	46 (29.9%)	108 (70.1%)	154
Hypertension	154 (100%)	0	154
Diabetes mellitus	58 (37.7%)	96 (62.3%)	154
Re-stroke after carotid stenting	11 (7.1%)	143 (92.9%)	154

Table 3. LSR and HSR rates in the both groups

	Symptomatic group	Asymptomatic group	p value
WBV at LSR (0.5/s-1)	46.5±13.4	45.3±10.4	0.234
WBV at HSR (208/s-1)	16.5±0.7	15.1±0.9	0.165

WBV: Whole blood viscosity, HSR: High shear stress

There was no statistical difference between LSR (p=0.464), HSR (p=0.413), and stenosis grade (p=0.726) values in patients who had and did not have a stroke after stenting.

Discussion

Our study is the first to investigate WBV in asymptomatic and symptomatic severe CAS. Previous investigations showed increased hematocrit levels, WBV, and plasma viscosity in stenosis in patients with chronic cerebrovascular diseases, but in acute stroke, no differences were found in hematocrit and WBV [11,13,14]. Only plasma viscosity was higher in patients with severe CAS [11]. Our results in our study were similar to those in the literature.

Prior findings suggested that red blood cell deformability and WBV may be potential markers of atherosclerotic plaque formation in patients after three months of acute stroke [15]. There are several studies claiming that WBV and hematocrit levels may predict intima-media thickness (IMT), early phase atherosclerosis, and the progression of stenosis [14-17]. The studies found a correlation between hematocrit and IMT [17], between WBV and early phase atherosclerosis [14,17].

Studies showed an association between active or ex-smokers and hemorheological disturbances such as increased hematocrit, WBV, fibrinogen, deteriorated red blood cell aggregation, and deformability [14,17-19]. Our results suggest that active smoking is a relevant factor, but past history smoking does not play a significant role in hemorheology [19].

Our study results show no statistical association between WBV and severe CAS, but cerebrovascular events themselves play a remarkable role.

Multicentre and prospective studies are needed in large populations to better characterize the relationship between severe CAS and WBV.

Study Limitations

The modest sample size, retrospective, non-randomized, and single-center study are important methodological shortcomings. WBV was not validated by accurate measurement of viscosity using a viscometer. The extrapolation formula that we used in our study has been validated and used in several other studies, but direct comparison of estimated and directly measured WBV in this patient population may strengthen our results and serve precision. In addition, other hemorheological factors that may affect blood viscosity, such as platelet and erythrocyte aggregability and rigidity, were not evaluated.

Conclusion

To our knowledge, this is the first study to evaluate the relationship between WBV and stenosis in patients with severe CAS. Results of our study showed that increased WBV, LSR, and HSR were not significantly clear in patients with symptomatic and asymptomatic stenosis.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the Ethics Committee of Samsun University, Samsun Training and Research Hospital with dated 26.05.2021 and decision number 2021/10/15.

Informed Consent: Informed consent was obtained from all patients included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.B.B., Concept: Ç.K.A., Design: A.B.B., Data Collection or Processing: A.B.B., Analysis or Interpretation: Ç.K.A., Literature Search: A.B.B., Writing: A.B.B.

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