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Evaluation of extracranial carotid flow velocities with Doppler USG and its relationship with various risk factors in patients presenting with acute ischemic stroke: A clinical study conducted in Turkey

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ABSTRACT

Objective. The mechanism underlying the relationship between carotid flow velocities and stroke events remains unclear. This study aimed to reveal the relationship of flow velocity measurements with risk factors in patients with acute ischemic stroke.

Material and methods. A group of patients between the ages of 41-90 who applied to Mengücek Training and Research Hospital in the Eastern Anatolia Region of Turkey between 2014-2015 due to acute ischemic stroke were included. Groups with large artery atherosclerosis and small-vessel occlusion according to the Toast classification were included in the study. Brain tomography and magnetic resonance imaging, echocardiography, high-resolution color Doppler Ultrasonography examinations were performed. Internal carotid artery peak-systolic and end-diastolic flow velocity, common carotid artery peak-systolic and end-diastolic flow velocity, internal carotid artery peak systolic- common carotid artery peak-systolic velocity ratio and common carotid artery intima-media thickness were measured with Doppler Ultrasonography. The relationship between carotid flow velocities and brain infarction volume, comorbid factors, biochemical variables, left ventricular systolic -diastolic dysfunction was defined by using Statistical Package for Social Sciences version 21.0.

Outcomes. In acute ischemic stroke groups, a significant negative correlation between common carotid artery end-diastolic flow velocity and brain infarction volume, a significant positive relationship between common carotid artery peak-systolic velocity and smoking, a significant positive correlation between common carotid artery intima-media thickness and blood glucose and hba1c, a significant negative correlation between common carotid artery end-diastolic flow velocity and hypertension, a significant relationship between common carotid artery end-diastolic flow velocity and ischemic heart disease, an increase in cerebral infarction in patients with left ventricular systolic dysfunction and a decrease in Internal carotid artery peak-systolic flow velocity in patients with left ventricular diastolic dysfunction were detected.

Conlusions. In clinical practice, Doppler ultrasound is currently the main diagnostic tool for evaluating the diagnosis of carotid stenosis. In stenosis in the carotid artery system, it should be known as a basic rule that the flow velocity in the stenosis area increases, except for in severe stenosis and four basic measurements should be made to determine the degree of stenosis clearly. These measurements are peak systolic flow velocity (PSV), end-diastolic flow velocity (EDV), peak-systolic flow velocity ratio (ICA/CCA PSV). The purpose of sonographic evaluation of the extracranial cerebral arteries is to prevent bad sequelae and permanent deficits together with cerebral infarction.

Keywords: Stroke, Doppler Ultrason, Carotid Flow Velocities, Risk Factors

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INTRODUCTION

Stroke is the third most common cause of death and the primary cause of disability in the world [1]. Approximately 80% of strokes are of thromboembolic origin, and the source of the embolism is generally carotid arteries [2]. Early detection of pathological changes in carotid arteries will reduce morbidity and mortality due to stroke. For this purpose, Doppler ultrasonography can be used as a safe, non-invasive, accurate, and less time-consuming method in the diagnosis of carotid stenosis.

Carotid artery Doppler ultrasonography provides hemodynamic information about carotid and vertebral arteries [3]. The area, suspected of stenosis with color Doppler, is examined with pulse wave Doppler. In this way, the systolic flow velocity ratio can be calculated with the values obtained from the inside and the proximal part of the lesion. In stenosis in the carotid artery system, it should be known as a basic rule that the flow velocity increases in the stenosis area, except for in severe stenosis and four basic measurements should be made to determine the degree of stenosis clearly. These measurements are internal carotid artery peak systolic flow velocity (ICA PSV), internal carotid artery end-diastolic flow velocity (ICA EDV), common carotid artery peak-systolic flow velocity (CCA PSV), common carotid artery end-diastolic flow velocity (CCA EDV) and peak-systolic flow velocity ratio (ICA/CCA PSV) [4].

This study is a prospective observational clinical study. The relationship between flow velocity rates and co-morbidities, biochemical variables, and left ventricular diastolic-systolic dysfunction parameters were presented in acute stroke patients. The data were documented using the Statistical Package for Social Sciences version 21.0 software for Windows (IBM SPSS Statistics for Windows, version 21.0. Armonk, NY: IBM Corp.).

MATERIAL AND METHOD

Study design and patient consent

This study was conducted on 67 patients who were applied to Mengücek Training and Research Hospital in the Eastern Anatolia Region of Turkey between 2014 and 2015 due to acute ischemic stroke. 13 of them were excluded from the study due to cardiac, cerebral (brain edema, herniation, hemorrhagic transformation, decompression surgery etc.) sepsis, inability to comply with the examinations.

54 patients participated in the study in accordance with the Helsinki Declaration guidelines and with written consent. Written informed consent was obtained from the first-degree relatives of the patients whose consent could not be obtained due to impairment of consciousness, severe paresis, speech impairment, and using disorder of the dominant extremity. The hospital management was informed. In addition, the study is not subject to ethics committee approval, patients signed consent for the diagnosis and treatment process. In the patient groups, whose ages range from 41 to 90 years, the groups with large artery atherosclerosis (LAA) and small-vessel occlusion (SVO), which are the subtypes of stroke, were evaluated as two separate groups according to the etiological TOAST stroke classification. Stroke due to other etiological reasons and stroke of unidentified cause and patients receiving thrombolytic therapy and/or undergoing thrombectomy and patients with subacute and/or chronic ischemic were excluded from the study. Anamnesis of each patient was taken. Brain BT, MR, ECHO and RDUS examinations were performed along with neurological examination. Age, gender, hyperlipidemia, smoking, hypertension (HT) (systolic blood pressure (SBP) ≥140 mmHg and diastolic blood pressure (DBP)≥90 mmHg), diabetes (DM) (fasting blood glucose: 70-105 mg/dl) were questioned. It is considered as Hba1c: 5.7-6.4: pre-diabetic, ≥6.5: diabetes. Clinical information such as cardiac disease findings or history, previous stroke, antiaggregant and anticoagulant use, and use of statins were recorded for all individuals. Venous blood samples were taken from the patients following an overnight fast for at least 12 hours after their admission to the hospital. Serum total cholesterol, high-density cholesterol (HDL), low-density cholesterol (LDL) and triglyceride (TG) were measured using standard procedures. The limit for normal values was considered as; total cholesterol <200 mg/dl, HDL> 40 mg/dl, LDL <130 mg/dl (under statin use) and TG <200 mg/dl.

Brain infarction volume measurement

In each patient, an unenhanced brain CT examination was performed twice, the first one was performed in the emergency department just before the treatment and the second one was performed in 8±2 days. The infarct volume calculation on CT, performed after 8 ± 2 days, was measured with a caliper by the largest diameter of the infarct (A), the largest vertical diameter (B), and summing the thickness of the visible slices of the lesion (C). Finally, the infarct volume was calculated according to the formula $0.5 \times A \times B \times C$.

Evaluation of IMT and calculation of flow velocities

The patients were evaluated in the supine position, using the Doppler Ultrasound (7.5-10.0 MHz probe, Toshiba Aplio 300) device to examine the distant and near walls of the arterial segments (common carotid, bifurcation and internal carotid arteries) by the radiologist with no information about

patient profiles. For carotid IMT measurement, a 1 cm segment was determined in the first 2 cm proximal region from the main carotid artery bulbus. In the measurements made from bilateral common carotid arteries, IMT value ≥1 mm and above was accepted as pathological. Pulse wave Doppler spectral analysis study was started for the area of suspected stenosis with color Doppler. PSV and EDV were measured at the ICA proximal and distal as well as at the CCA 2-4 cm below the bifurcation. For all participants, the scanning head was applied longitudinally for at least three cardiac cycles for blood flow velocity measurements. The highest velocity during systole was defined as PSV, and the lowest velocity during diastole was EDV. According to the Consensus Panel of the Ultrasound Radiologists Association, velocity calculations were made, including ICA PSV, ICA EDV, CCA PSV, CCA EDV and (ICA/CCA PSV) [5]. The criteria and velocity rates used in our study to measure the percentage of carotid stenosis are shown below:

1) ICA is considered normal when the ICA PSV is less than 125 cm/sec and no plaque or intimal thickening is seen sonographically. Additional criteria include the ICA/CCA PSV ratio 2.0 and ICA EDV 40 cm/sec.

2) ICA stenosis <50% is diagnosed when the ICA PSV is less than 125 cm/sec and plaque or intimal thickening is visible sonographically. Additional criteria include ICA/CCA PSV ratio 2.0 and ICA EDV 40 cm/sec.

3) When the ICA PSV is 125-230 cm/sec and the plaque is visible sonographically, 50-69% ICA stenosis is diagnosed. Additional criteria include the ICA/CCA PSV ratio 2.0-4.0 and ICA EDV 40-100 cm/sec.

4) ICA stenosis of less than 70% of ICA but less than near occlusion is diagnosed when visible plaque and lumen narrowing are seen in gray scale and color Doppler USG when ICA PSV is greater than 230 cm/sec. Additional criteria include ICA/CCA PSV ratio 4 and ICA EDV 100 cm/sec. The higher the Doppler parameter, the higher from the threshold of 230 cm/sec, the greater the probability of serious disease is considered to be.

5) In cases of near occlusion of ICA, velocity parameters may not be applicable as velocities may be high, low or undetectable. This diagnosis is primarily indicated by a markedly narrowed lumen in the color or spectral Doppler USG.

6) Complete occlusion of the ICA is suspected when there is no detectable patent lumen on gray scale USG and there is no flow with spectral, color Doppler USG [6].

Echocardiography application

All patients' data were collected with M-mode and 2-D images and color Doppler, PW Doppler (GE-VIVID 3s-RS PROB: 2.7-8.0 mhz) device by an experienced cardiologist who had no knowledge of patient profiles. PW Doppler echocardiography was used to measure peak early (E) and late (A) diastolic mitral flow velocities and DT (early filling deceleration time) values. The PW Doppler "cursor" was placed parallel to the LV exit path flow; IVRT (isovolumic relaxation time) values were measured. Echocardiographic measurements were made in accordance with the recommendations of the American Echocardiography Society [7].

The stroke patient with atrial fibrillation was excluded from the study because the E/A ratio could not be calculated.

Statistical analysis

Statistical analysis of the study was performed using Statistical Package for Social Sciences version 21.0 software for Windows (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp., USA). Normality assumption for quantitative variables was tested with Kolmogorov-Smirnov and Shapiro-Wilk tests. The explanatory statistics in the study were given as Mean±Standard deviation for quantitative variables providing normality assumption, Median (Min-Max) for quantitative variables not providing normality assumption and n (%) for categorical variables. Chi-square, Fisher Exact test, Fisher-Freeman-Halton exact test, Mann-Whitney U, Independent t test, One-way ANOVA, and Kruskal Wallis tests were used for univariate analysis of variables in the study depending on the type of variable and providing of assumptions. The Duncan Multiple Comparison test was used as a post hoc test to compare groups with significant differences in variables where normality assumption was provided, while Mann Whitney U tests were used as post hoc test in cases where normality assumption was not provided. Correlations between variables were determined with Spearman's Rho correlation coefficients. In all statistical analyzes, cases with a P-value below 0.05 were interpreted as statistically significant.

RESULTS

A total of 54 subjects participated in the study, 33 (61.1%) of them are women and 21 (38.9%) of them are men. The average age of the subjects is 74.33±12.87 years.

18 stroke patients out of 54 acute ischemic stroke patients participating in the study were included in the group of stroke caused by large artery atherosclerosis (LAA) and 36 of them were included in the group of stroke caused by small-vessel occlusion (CVO). When the infarct volume was calculated, volume of group 1 was measured as 80.06 (min20.0-max682.30) cm^3, the volume of group 2 was meas-

ured as 3.62 (min0.14-max24.10) cm^3. This value was considered statistically significant (p <0.000) (Table 1).

TABLE 1. Relationship between group 1 and group 2 with variables

	Group 1 (n=18)	Group 2 (n=36)	P
Glucose	136.72±63.129	117.67±33.38	0.151
Hba1c	6.86±2.19	6.85±1.83	0.977
T-Cholesterol	195.89±45.94	193.17±41.79	0.828
Ldl-chol	128.96±33.95	127.57±36.26	0.892
Hdl-chol	45.11±15.46	41.94±10.26	0.373
Triglyceride	160.0±33.97	133.79±13.30	0.392
SKB	149.72±21.03	144.64±22.43	0.427
DKB	90.0±11.88	90.0±11.40	1.000
Right CCA IMK	1.09±0.22	0.99±0.21	0.128
Left CCA IMK	1.07±0.21	1.03±0.18	0.409
Right ICA PSV	50(17-592)	57(0.0-150	0.259
Left ICA PSV	64.10±30.10	64.38±36.47	0.977
Right ICA EDV	17.20(0.0-97.0)	18.50(0.0-47.0)	0.287
Left ICA EDV	19(0.0-69.0)	18(0.0-54.0)	0.435
Right CCA PSV	53.24±17.90	60.91±19.72	0.171
Left CCA PSV	55.06±17.97	55.88±19.37	0.881
Right CCA EDV	11.02±6.58	13.52±5.76	0.158
Left CCA EDV	15.01±11.74	13.30±7.19	0.512
Brain infarction volume	80.06 (20.0-682.30)	3.62 (0.14-24.10)	0.000

Of the 54 patients, there was a total of 38 hypertension (HT) patients, including 16 (88.9%) HT in group 1 and 22 (61.1%) HT in group 2. This relationship was found to be statistically significant in both groups in terms of infarct volume (p <0.035) (Table 2). There was no significant correlation between other comorbid factors and ischemic subgroups.˝

A significant negative correlation was found between brain infarction volume and left CCA EDV (P <0.032). Left CCA EDV decreased as the infarction volume increased in patients with left cerebral infarction. The relationship between other variables and brain infarction volume was statistically insignificant (P> 0.05) (Table 3).

The effect of sex on the right CCA PSV values was found to be statistically significant (P <0.036). Right CCA PSV (65.20±22.88, p = 0.036) values of males were higher than females. In acute ischemic stroke patients participating in the study, it was observed that the right common carotid arteries were affected more in males than in females.

The effect of smoking on right and left CCA PSV values is statistically significant (P <0.05). Smokers had higher right CCA PSV (68.17±23.5, p = 0.026) and left CCA PSV (64.0±19.66, p=0.049) values than non-smokers. Both common carotid arteries of smoker patients with stroke were affected. According to these results, smoking is an effective factor on the CCA PSV variable.

TABLE 2. Relationship of group 1 and group 2 with comorbid factors, ICA/CCA PSV, E/A, EF

		Group 1	Group 2	P
Smoking	absent	11(61.1)	29(80.6)	0.188
	existent	7(38.9)	7(19.4)	
Statin	absent	15(83.3)	34(94.4)	0.319
	existent	3(16.7)	2(5.6)	
Diabetes	absent	9(50.0)	22(61.1)	0.436
	existent	9(50.0)	14(38.9)	
Coronerarter disease	absent	10(55.6)	22(61.1)	0.695
	existent	8(44.4)	14(38.9)	
Hypertension	absent	2(11.1)	14(38.9)	**0.035**
	existent	16(88.9)	22(61.1)	
Stroke history	absent	14(77.8)	28(77.8)	0.627
	existent	4(22.2)	8(22.2)	
Antiaggregan, anticoagulant use	absent	9(50.0)	16(44.4)	0.700
	existent	9(50.0)	20(55.6)	
Total Near Occlusion	absent	15(83.3)	30(83.3)	1.000
	existent	3(16.7)	6(16.7)	
Right ICA/CCA PSV	<50% stenosis	16(88.9)	32(88.9)	0.472
	50-69% stenosis	0(0.0)	2(5.6)	
	≥70 and above stenosis	2(11.1)	2(5.6)	
Left ICA/CCA PSV	<50% stenosis	16(88.9)	30(83.3)	0.440
	50-69% stenosis	2(11.1)	3(8.3)	
	≥70 and above stenosis	0(0.0)	3(8.3)	
EF	≥50	13(72.2)	32(88.9)	0.142
	<50	5(27.8)	4(11.1)	
E/A	≤2	6(33.3)	18(50.0)	0.245
	>2	12(66.7)	18(50.0)	

TABLE 3. Relationship of brain infarction volume with carotid IMT and flow velocities

	Brain Infarction Volume
Right CCA IMK	0.169
Left CCA IMK	0.112
Right ICA PSV	-0.258
Left ICA PSV	-0.124
Right ICA EDV	-0.215
Left ICA EDV	-0.053
Right CCA PSV	-0.288*
Left CCA PSV	-0.116
Right CCA EDV	-0.243
Left CCA EDV	**0.032**

The presence of diabetes affects the right CCA IMT value (P <0.05). Right CCA IMT values of patients with acute ischemic stroke and diabetes were significantly higher than those without diabetes (P <0.05). Right CCA IMT values of those with diabetes are higher than left CCA IMT (1.10±0.18) values (p = 0.022).

Having coronary disease significantly affects the left CCA EDV values (P <0.05). Left CCA EDV (11 (0.0-29) values were found to be lower in patients with coronary artery disease than those not having it (p = 0.045). The presence of hypertension significantly affects the left CCA EDV (12.13±7.55, p = 0.026) value. Left CCA EDV values of patients with HT and stroke were found to be low. Left ICA PSV [47.45 (0.0-83), p = 0.013] values of patients with a previous history of stroke and recurrent stroke are affected (P <0.05). Left ICA PSV values were found to be low in 9 of 12 patients who had a history of stroke and had a recurrent stroke, and 9 patients had stenosis close to total occlusion in the left ICA. In the other 3 patients with total occlusion, flow could not be obtained.

The effect of antiaggregant and anticoagulant use on carotid flow velocities was statistically insignificant (p> 0.05) (Table 4).

The relationship between right CCA IMT and glucose is positive and statistically significant (P <0.05). A positive significant correlation was found between right CCA IMT and Hba1c values (P <0.01). There was a positive significant relationship between the right ICA PSV and Hba1c (P <0.05). The relationship between right ICA EDV and triglycerides is statistically significant (P <0.05). There was a positive correlation between TG high ischemic stroke patients and right ICA EDV. In stroke patients with diabetes and increased IMT thickness, a more right common carotid artery was affected, and there was a positive correlation between right ICA PSV and Hba1c (Table 5).

EF effect on the right ICA PSV values is statistically significant (P <0.05). When left ICA PSV mean velocity ratio (64 (17-211)) was compared with the right ICA PSV mean velocity ratio (42 (17-91)), it was seen that right ICA PSV of acute ischemic stroke patients with EF <50% was lower than left ICA PSV. In left ventricular systolic dysfunction (EF <50%) patient group admitted with acute ischemic stroke, left ICA PSV ratio increased compared to right ICA PSV.

The E/A ratio is significant in terms of right ICA PSV (47 (0-592) (P = 0.006) and left ICA PSV (49.5 (0-211)) values in acute ischemic stroke patients with left ventricular diastolic dysfunction. In the acute ischemic stroke group with E/A> 2, the right-left ICA PSV flow velocity was lower than in the stroke group without left ventricular diastolic dysfunction and it was statistically significant [Right ICA PSV (P = 0.006) left ICA PSV (P= 0.005)] (Table 6).

A significant correlation was found between the E/A groups of patients who had a previous history of stroke and had a recurrent stroke. In the group with the peak E (early diastolic mitral flow rate) /peak A (late diastolic mitral flow rate) (E/A) ≤2, the absence of a history of stroke was significant in patients with acute ischemic stroke. Left ventricular diastolic dysfunction (E/A>2) was detected in 11 patients of 12 patients who had a previous stroke, and this was statistically significant (P = 0.007). The difference between the EF groups in terms of brain infarction volume values was statistically significant. Brain infarction volume means value (45.69 (0.18-682.30)) increased in acute ischemic patients with EF<50% compared to those with brain infarction volume above EF≥50 (P <0.000) (Table 7).

DISCUSSION

Most strokes are based on an ischemic etiology caused by a sudden decrease in blood flow in a part of the brain. This is usually the result of embolization of a cerebral artery originating either from a lesion, most commonly from the carotid artery, or from the heart. Correct investigation and early diagnosis of carotid disease are of great importance for the prevention and treatment of stroke. Various imaging methods are currently used to view the carotid arteries. However, Doppler Ultrasound is predominantly used for routine evaluation and treatment decisions of carotid stenosis [5]. Velocity parameters were mostly chosen to detect 50%, 60%, 75% or 80% stenosis of internal carotid artery diameters and have led to recent recommendations for detecting major diseases of the carotid arteries. According to the results of the study of Hunink et al. an increase in ICA PSV of 2.3 msec or more indicates a 70% or more reduction in diameter. The validation study by Spencer et al showed that ICA EDV is a more important indicator as a standard reference (stenosis 75% or 80%) for using Doppler waveform analysis to rate the severity of internal carotid stenosis. It has also been proposed as a way of identify-

TABLE 4. Relationship between carotid flow velocities and co-morbid factors

		Right CCA IMK	Left CCA IMK	Right ICA PSV	Left ICA PSV	Right ICA EDV	Left ICA EDV	Right CCA PSV	Left CCA PSV	Right CCA EDV	Left CCA EDV
Sex	female	1.00±0.21	1.02±0.17	51(0.0-592)	57(0.0-126)	19(0.0-97)	20(0.0-69)	54.0±15.49	51.90±16.83	13.48±5.90	15.09±9.54
	male	1.07±0.23	1.08±0.21	65(17-113)	59(17-211)	18(0.0-38)	18(0.0-50)	65.20±22.88	61.43±20.48	11.45±6.34	11.96±7.58
	P	0.219	0.242	0.356	0.380	0.638	0.483	**0.036**	**0.068**	0.237	0.211
Smoking	absent	1.03±0.20	1.04±0.16	56(0.0-592)	56(0.0-211)	17.5(0.0-97)	17.5(0.0-69)	54.92±16.62	52.65±17.72	12.7±6.09	13.52±6.13
	existent	1.01±0.25	1.05±0.26	56(17-79)	69.5(17-135)	18.5(0.0-35)	20.5(0.0-48)	68.17±23.5	64.0±19.66	12.67±6.35	14.87±6.41
	P	0.765	0.812	0.969	0.203	0.968	0.573	**0.026**	**0.049**	0.991	0.630
Statin	absent	1.02±0.21	1.03±0.19	56(0.0-592)	58(0.0-211)	18(0.0-97)	18(0.0-69)	58.71±18.41	55.77±18.26	12.75±6.21	13.95±9.23
	existent	1.10±0.25	1.18±0.21	53(38-68)	64(44-135)	20(11-28)	16(12.7-48)	54.88±19.29	54.04±25.53	12.10±5.48	13.04±4.82
	P	0.459	0.110	0.858	0.633	0.800	0.964	0.677	0.846	0.822	0.828
Diabetes	absent	0.97±0.22	1.02±0.20	51(0.0-150)	57(0.0-126)	17(0.0-47)	18(0.0-54)	59.70±17.61	54.87±16.23	13.77±6.09	15.67±6.24
	existent	1.10±0.18	1.06±0.18	65(17-592)	64(32-211)	18(0.0-97)	18(0.0-69)	56.53±21.67	56.61±22.03	11.23±5.93	11.44±6.05
	P	**0.022**	0.457	**0.088**	0.377	0.624	0.972	0.556	0.739	0.133	0.084
Coronary artery disease	absent	0.99±0.22	1.03±0.19	57(17-592)	54.5(0.0-126)	18(0.0-97)	18(0.0-69)	62.75±16.63	58(0.0-95)	14(0.0-27)	14(6-51)
	existent	1.08±0.20	1.05±0.20	54(0.0-99)	63(33-211)	16.2(0.0-29)	19(7-51)	51.97±21.47	48.1(30-91)	11(4-27)	11(0.0-29
	P	0.118	0.695	0.718	0.089	0.312	0.408	0.043	0.701	0.662	**0.045**
Hypertension	absent	0.95±0.22	0.96±0.17	52.5(0.0-100)	57.5(30-126)	17.37(0.0-29)	20(9-51)	60.81±22.13	59.87±15.49	12.37±6.08	18±7.63
	existent	1.06±0.21	1.07±0.19	57.5(23-592)	58.5(0.0-211)	17(3-97)	17.5(0-69)	57.32±18.22	53.82±19.87	12.82±6.18	12.13±7.55
	P	**0.085**	**0.058**	0.324	0.762	0.992	0.622	0.550	0.283	0.806	**0.026**
Former stroke history	absent	0.92±0.27	1.06±0.18	56.5(0.0-592)	59.5(17-211)	17.5(0.0-97)	20(0.0-69)	57.6±19.31	54.85±18.57	12.85±6.09	14.04±6.10
	existent	1.05±0.19	0.98±0.21	55.5(17-84)	47.45(0.0-83)	18.5(0.0-38)	13.5(0.0-41)	60.78±19.98	58.26±19.95	12.12±6.36	13.26±6.48
	P	**0.061**	0.210	0.429	**0.013**	0.967	0.111	0.627	0.583	0.718	0.791
Antiaggregan, anticoagulant use	absent	1.02±0.20	1.04±0.18	57(0.0-592)	58(17-126)	19(0.0-97)	20(0.0-69)	59.52±20.14	53.96±19.63	13.52±6.31	14.48±6.23
	existent	1.03±0.23	1.04±0.20	56(17-99)	58(0.0-211)	16(0.0-29)	16(0.0-50)	57.35±18.87	57.04±18.17	11.98±5.93	13.35±7.69
	P	0.769	0.937	0.979	0.555	0.322	0.609	0.686	0.552	0.361	0.646

TABLE 5. The relationshipbetween carotid flow velocities and biochemical variables

	Glu	Hba1c	T-chol	LDL	HDL	Tg	Skb	Dkb
Right CCA IMT	0.297*	0.486**	0.100	-0.147	-0.169	0.164	0.125	-0.012
Left CCA IMT	0.243	0.248	0.135	-0.131	-0.001	0.013	0.175	-0.030
Right ICA PSV	0.306*	0.378**	0.250	0.047	0.099	0.194	0.021	0.008
Left ICA PSV	0.081	0.291*	-0.037	0.100	-0.141	0.090	-0.067	0.012
Right ICA EDV	0.076	0.153	0.233	0.045	-0.145	0.326*	0.070	0.002
Left ICA EDV	-0.062	0.119	0.039	0.018	-0.238	0.149	-0.044	-0.044
Right CCA PSV	-0.047	-0.151	0.067	-0.046	0.023	0.077	-0.117	0.082
Left CCA PSV	0.048	0.045	0.139	0.096	0.019	0.220	-0.262	0.024
Right CCA EDV	-0.101	-0.139	0.032	-0.081	-0.023	0.030	-0.108	-0.048
Left CCA EDV	-0.189	-0.158	0.022	0.120	-0.145	0.113	-0.198	-0.132
Brain infarct volume	0.054	-0.089	-0.062	-0.243	0.464**	-0.051	0.049	0.005

TABLE 6. Relationship of carotid flow velocity with EF and E/A in acute ischemic stroke patients

	EF			**E/A Ratio**		
	≥50	<50	p	≤2	>2	p
Right CCA IMT	1.02±0.22	1.03±0.20	0.957	1.0±0.19	1.05±0.23	0.453
Left CCA IMT	1.04±0.18	1.04±0.24	0.976	1.04±0.18	1.04±0.20	0.988
Right ICA PSV	57(0-592	42(17-91)	**0.043**	65.5(17-150)	47(0-592)	**0.006**
Left ICA PSV	57(0-135)	64(17-211)	0.523	70.5(30-135)	49.5(0-211)	**0.005**
Right ICA EDV	19(0-97)	14(0-35)	0.137	20(0-47)	16.2(0-97)	0.257
Left ICA EDV	18(0-69)	16(0-50)	0.754	20.5(0-51)	15(0-69)	0.143
Right CCA PSV	58.98±20.0	55.22±15.42	0.598	62.75±17.67	54.84±20.13	0.137
Left CCA PSV	56.76±18.86	49.88±18.09	0.320	58.0±18.9	53.7±18.72	0.408
Right CCA EDV	13.16±6.13	10.33±5.70	0.207	13.7±5.90	11.88±6.24	0.279
Left CCA EDV	13.98±8.91	13.33±8.31	0.844	15.41±8.9	12.64±7.96	0.258

TABLE 7. Relationship between co-morbid factors- brain infarction volume and EF, E/A

		EF			**E/A**		
		≥50	<50	P	≤2	>2	P
Smoking	absent	35(77.8)	5(55.6)	0.216	18(75.0)	22(73.3)	0.890
	existent	10(22.2)	4(44.4)		6(25.0)	8(26.7)	
Statin	absent	41(91.1)	8(88.9)	0.834	22(91.7)	27(90.0)	0.834
	existent	4(8.9)	1(11.1)		2(8.3)	3(10.0)	
Diabetes	absent	26(57.8)	5(55.6)	0.902	15(62.5)	16(53.3)	0.585
	existent	19(42.2)	4(44.4)		9(37.5)	14(46.7)	
Coronerarter disease	absent	28(62.2)	4(44.4)		15(62.5)	17(56.7)	0.783
	existent	17(37.8)	5(55.6)		9(37.5)	13(43.3)	
Hypertension	absent	15(33.3)	1(11.1)	0.253	9(37.5)	7(23.3)	0.369
	existent	30(66.7)	8(88.9)		15(62.5)	23(76.7)	
Stroke history	absent	34(0.0)	8(88.9)	0.665	23(95.8)	19(63.3)	**0.007**
	existent	11(24.4)	1(11.1)		1(4.2)	11(36.7)	
Anti aggregates, anticoagulants use	absent	21(46.7)	4(44.4)	1.000	13(54.2)	12(40.0)	0.300
	existent	24(53.3)	5(55.6)		11(45.8)	18(60.0)	
Brain infarct volume		6.25 (0.14-244.2)	45.69 (0.18-682.30)	0.000	5.31 (0.14-296)	6.79 (0.18-682.30)	0.144

ing a subgroup of patients at higher risk for cerebrovascular events. The peak end-diastolic velocity is largely dependent on the flow resistance and shows a greater elasticity than the peak systolic velocity. A lower CCA PSV reflects a high degree of stenosis in the internal carotid. The ICA/CCA (PSV) ratio has of-

ten been used to compensate for velocity changes resulting from cardiac output changes due to cardiac arrhythmia or myocardial function [3].

David S. Strosberg et al. found that the higher EDV in CCA, the less likely the ICA to have stenosis. They showed the sensitivity of CCA EDV in predicting 70% to 99%. Patent distal ICA will allow an increase in diastolic flow and thus CCA EDV by reducing distal vascular resistance (unlike ICA EDV, which is thought to be associated with a high-grade ICA when ICA stenosis is elevated) [8]. The study by Samar I. Essa et al showed that in elderly patients with large artery atherosclerosis, the lower diastolic rate (CCA EDV), as well as the increased risk of stroke and the prediction of cardiovascular events, significantly increased due to greater resistance in the intracranial vessels [9]. This study found a significant negative correlation between brain infarction volume and left CCA EDV in both groups in acute ischemic stroke patients, especially in the SVO group ($P < 0.05$). It was determined that the patients with acute ischemic stroke who participate in the study had more left carotid artery disease and accordingly left CCA EDV was lower than the right. The mechanism underlying the relationship between carotid flow velocities and stroke events remains unclear. A cross-sectional case-control study reported that patients with transient ischemic attacks or ischemic stroke had lower EDV than the control group, but they had similar PSV [10]. Chuang et al. found that CCA EDV is associated with the development of stroke. Taken together, these findings show that more attention should be paid to the role of CCA EDV in the development of cerebrovascular events. Carotid flow velocity, specifically CCA EDV, represents the subclinical atherosclerosis index and should be included in the assessment of cardiovascular disease and stroke risk. Increased common carotid artery (CCA) intima-media thickness (IMT) has been reported under various conditions, including hypertension, dyslipidemia, obesity, diabetes, smoking, ischemic stroke and cardiovascular disease. CCA-IMT is associated with changeable (e.g., blood pressure, blood cholesterol, smoking, diabetes and obesity) and unchangeable risk factors (age, sex, genes and currently unknown risk factor [11]. The onset of carotid atherosclerosis is characterized by an increase in vascular IMT, the progression of which leads to plaque formation and vascular narrowing. Increased CCA-IMT value reflecting systemic atherosclerosis creates a high risk for stroke [12]. In this study, a positive correlation between right CCA IMT and glucose, a positive significant correlation between right CCA IMT and Hba1c values, the relationship between right ICA EDV and triglycerides is statistically significant and a positive significant relationship between left ICA PSV and Hba1c were found. Diabetes and hypertension are important risk factors for coronary heart disease and stroke, and their main determinant is systemic atherosclerosis. These effects are clearly visible on the main arteries [13]. This is due to increased arterial stiffness and decreased arterial compliance caused by changes in the arterial wall such as aging, hypertension and diabetes, and this is also associated with increased wall thickness and arterial wall thickness resulting from increased collagen deposition with decreased elastin content in the intima-media content. These changes in elastin and collagen content are important effects on artery stiffness [9]. As a result, it shows that small change in lumen diameter is related to a large change in peak systolic velocity, slower velocities are not related to change in lumen diameter, but may be mainly associated with an increase in flow resistance [14]. Watanabe et al. found that in hypertensive patients, especially those with insulin resistance, the arterial stiffness of CCA increase according to hemodynamic criteria and they showed that these patients have lower rate of diastolic perfusion (CCA-EDV) than normotensive subjects by evaluating the hemodynamic changes in CCA and using Doppler ultrasound [15]. In this study, it was found that the presence of hypertension in acute ischemic patients significantly affects the left CCA EDV value of the patients. Left CCA EDV values of patients with acute ischemic stroke and hypertension were found to be low. In addition, a statistically significant relationship was found between hypertension and brain infarction volume in both stroke subgroup.

Smoking is associated with widespread changes in small arteries and arterioles, which are rarely seen in nonsmokers and independent of the atherosclerotic process [16]. H. Mahmoud S. Babiker found a strong significant relationship between smoking and carotid plaques as well as carotid artery hemodynamics. The data showed a strong linear relationship between smoking duration and the percentage of carotid stenosis increasing by 0.34% per year and the frequency of smoking and the degree of carotid stenosis increasing by 0.31% per unit frequency [17]. The results of this study also supported the findings of Mustafa [18], who suggested that smoking is associated with carotid artery morphological changes resulting from significant deterioration of arterial endothelial function. This atherogenic effect leads to variability of the blood flow rate within the CCA by increasing PSV and EDV proportionally and linearly. This study found that the effect of smoking on the right and left CCA PSV values was statistically significant, supporting other studies. Smokers had higher values for both right CCA PSV and left CCA PSV than nonsmokers. It revealed that smoking causes morphological changes in the carotid arteries and has a strong linear relationship with carotid artery hemodynamics.

Stroke-heart

Cardiac diseases are well-determined risk factors for ischemic stroke and cause approximately 25% of all events [19]. Both ischemic and arrhythmic electrocardiographic changes are common within the first 24 hours after acute ischemic stroke. A preclinical study has shown that catecholamine release after acute ischemic stroke causes prolonged cardiac dysfunction and remodeling. In relation to inflammatory outcomes after acute ischemic stroke, it is unclear whether it is the main factor for cardiac dysfunction or whether cardiac susceptibility before acute ischemic stroke affects poststroke cardiovascular events [20]. For stroke physicians, LV diastolic dysfunction has important clinical implications. It is hypothesized that left ventricular diastolic dysfunction has a direct impact on left atrial contractility and events that increase the likelihood of recurrent thromboembolism through intracardiac stasis. In particular, the presence of heart failure (HF) increases the risk of ischemic stroke. Patients with HF have a recurrent stroke incidence and higher mortality rates and may experience more severe strokes with a worse functional outcome. Markers of cardiac systolic dysfunction, such as left ventricular ejection fraction (LVEF), are also risk factors for ischemic stroke, regardless of the presence of clinical symptoms. In this study, the difference between the EF groups in terms of brain infarction volume values was found to be statistically significant. As the cerebral infarction volume mean value increased, the EF was found to be quite low <50%. In acute ischemic stroke patients, the previous stroke is the cause of left ventricular diastolic dysfunction [21]. Due to the complex pathophysiology of diastoline, a gold standard indicator for diastolic dysfunction was not designed. In this study, the E/A ratio was used and a significant relationship was found between stroke history and acute ischemic stroke. Left ventricular diastolic dysfunction was found in 11 of 12 patients who had a previous stroke, and this was statistically important.

In addition to aging, with ischemia or myocardial disease, left ventricular (LV) relaxation slows down and thus leads to a decrease in the vacuum effect of the LV, which leads to a decrease in E rate, to a compensatory increase in A rate (E/A <1). As LV compliance decreases and stiffness increases, the left atrial pressure (LAP) rises to maintain cardiac output. These results in a high E velocity (E/A> 1) and a shortened premature filling time [22]. Right ICA PSV and left ICA PSV values were significant in patients with an E/A ratio >2 who presented with acute ischemic stroke. ICA PSV flow velocity was lower than that in the stroke group without left ventricular diastolic dysfunction, and it was statistically significant [23]. Carotid flow velocity may underlie the relationship between cerebral blood flow and ischemic heart disease. Cerebral blood flow is approximately 30% lower in patients with severe heart failure than in a healthy age group matched the control group [24].

In addition, low cerebral flow velocity has also been associated with the poor cardiac function [25]. In advanced stage diastolic dysfunction, when the preload increases, atrial contraction, that is the contribution of the atrium to the diastole, decreases, and the E/A ratio increases due to the decrease in A velocity [26]. Few studies have explored the relationship between carotid flow velocities and ischemic heart disease. Studies have shown that lower carotid flow velocity may be associated with cardiac dysfunction and atherosclerosis [27,28]. These studies showed that low carotid blood flow velocity is associated with arteriosclerosis, which increases the risk of heart structure and function impairment and ischemic heart disease.

Low diastolic carotid flow velocity (CCA-EDV) may indicate lower shear stress (mechanical shear force exerted by blood flow on vessels, cross pressure) that may promote atherosclerosis. Shear stress is caused by blood viscosity and blood flow velocity; therefore, it is highly correlated with the blood flow velocity. In our study, a significant relationship was found between left CCA EDV values and ischemic heart disease (IHD) in acute ischemic stroke patients with IHD. It was statistically demonstrated that patients with coronary artery disease had lower left CCA EDV than those without IHD and left carotid interna were affected more.

LIMITATION OF THE STUDY

Although these criteria were used, positioning of the patient during carotid Doppler examination in some cases of acute ischemic stroke was resulted in difficulty. Large calcified plates covered the examination area due to posterior acoustic shadowing. Carotid arteries could not be evaluated properly in patients with high carotid bifurcation. Cardiac arrhythmia, aortic valve insufficiency, carotid dilatation or a aneurysm could cause underestimation of the degree of stenosis, while king in the carotid vessels, severe stenosis or occlusion to the opposite side of the tortuosity could cause the stenosis to be overestimated.

CONCLUSION

Approximately half (55-60%) of ischemic strokes are due to the embolism originating from the carotid arteries, and therefore the purpose of sonographic evaluation of the extracranial cerebral arteries is to prevent bad sequelae and permanent deficits together with cerebral infarction. Therefore, in clini-

cal practice, doppler ultrasound is currently the main diagnostic tool for evaluating the diagnosis and treatment decisions of carotid diseases, and the follow-up of patients is heavily dependent on ultrasound findings. This study aims to identify the patients at risk of stroke by revealing the risk factors associated with carotid flow velocity variables measured by Doppler ultrasonography in patients with acute ischemic stroke and to initiate preventive measures in high-risk patients. This study may have a demo feature for stroke studies to be performed with a single parameter and more participants in stroke subgroups of important topics emerging for future studies, and the most striking parameter in this study is the clear relationship between velocity variables and cardiac dysfunction.

The main highlights of the study:

1. When acute ischemic stroke patients are evaluated with Doppler USG, there is a significant negative correlation between common artery end-diastolic flow velocity (CCA-EDV) and brain infarction volume.

2. When acute ischemic stroke patients are evaluated with Doppler USG, there is a significant positive correlation between common carotid artery peak-systolic flow velocity (CCA-PSV) and smoking.

3. There is a significant positive significant relationship between CCA IMT and blood glucose and Hba1c.

4. There is a significant negative correlation between the common artery end-diastolic flow velocity (CCA-EDV) and the factor of hypertension.

5. Patients with acute ischemic stroke with left ventricular diastolic dysfunction above the E/A> 2 have a low internal carotid artery peak systolic flow velocity (ICA-PSV). Accompanying left ventricular diastolic dysfunction has been observed in patients with acute ischemic stroke who previously had a stroke. Did these stroke patients have a previous attack on the basis of diastolic dysfunction or did the stroke occur after the triggering of acute ischemic stroke? Large-scale studies are needed to find an answer to the question.

6. In acute ischemic stroke patients with left ventricular systolic dysfunction (EF) <50%, the brain infarction volume is large.

7. There is a significant relationship between CCA EDV values and IHD in acute ischemic stroke patients with ischemic heart disease (IHD). CCA EDV value is lower in patients with IHD than those without. Low diastolic carotid flow velocity (CCA-EDV) may indicate lower shear stress, which can promote atherosclerosis.

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