Kerman University of Medical Sciences and Health Services
Scientific Research Journal
Journal of Kerman University of Medical Sciences
JKMU
Journal of Kerman University of Medical Sciences, 2017; 24(5): 360-367

Prognostic Value of Doppler Ultrasound Findings in Patients with Middle Cerebral Artery Ischemic Stroke

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Received: 12 June, 2017 Accepted: 13 December, 2017

ARTICLE INFO

Article type:
Original article

Keywords:
Doppler sonography
Stroke
Prognosis

Abstract

Background: There is still no finding available about malignant clinical course in patients with middle cerebral artery stroke. The aim of this study was to compare Doppler ultrasound findings in patients with malignant and non-malignant middle cerebral artery stroke in order to obtain its prognostic value in detecting malignant course.

Methods: This cross-sectional study was conducted on 40 patients with acute ischemic stroke in Shafa Hospital in Kerman, Iran, 2017. All patients were admitted within 24 hours of the onset of symptoms, and brain CT-scan was performed to confirm ischemic stroke. If more than 50% of the middle cerebral artery showed signs of hypo-density, it was considered as the massive MCA infarction (MMI), while others were excluded. In the first 24 hours, transcranial Doppler ultrasound was performed for all patients. Patients were then examined until discharge or death. In the case of fixed unilateral mydriasis in the clinical course or a displacement of more than 5 mm in septum pellucidum in the control CT-scan on days 3 to 7 (depending on the changes in the consciousness level), m-MCAI was diagnosed. Data were analyzed using SPSS.

Results: In the malignant cases, the mean PSV and MFV in MCA in the contralateral side of the lesion were significantly higher than those in the non-malignant cases. A significant increase in mean PSV and MFV in ACA in the contralateral side of the lesion was found in the malignant cases compared to the non-malignant cases (P=0.01). Significant difference was observed in terms of mean RI of ICA of contralateral side of the lesion between malignant and non-malignant cases (P=0.02).

Conclusion: Our study showed increase in PSV and MFV in MCA and ACA in the contralateral side of the lesion in cases that lead to malignancy, which can be helpful in early identification of cases that advance to malignancy.

Introduction

Cerebral stroke, with about 85% of ischemic cases, is a major cause of death and disability in adults (1). Middle cerebral artery (MCA) occlusion is one of the most common forms of ischemic stroke, and the frequency of Massive MCA Infarction (MMI) is up to 15% of the cases (2). About 50% of MMI cases have clinical course of malignant MCA infarction (m-MCAI) (3, 4), and due to the high rate of mortality without surgical intervention (80%), it is one of the deadliest cases of stroke (5-7). Surgical procedures, especially in the first 24 hours of a stroke, i.e., before their brain edema, are associated with a sharp reduction in mortality (5); however, such procedures require early detection of m-MCAI cases. Despite continuous advances in cerebral imaging, none of these methods have achieved this capability, and a part of research is dedicated to finding the ways that can identify m-MCAI cases before the completion of clinical image (2-5). Cerebrovascular Doppler ultrasound is a non-invasive and reliable method in the hemodynamic assessment of brain with different applications in patients with stroke and other cerebrovascular diseases (8). Some recent studies have addressed identification and evaluation of Doppler ultrasound findings in patients with MMI.

In a study on 4 patients with m-MCAI, it was found that ultrasound findings correspond with imaging, and ultrasound imaging of brain perfusion is a promising tool in the clinical assessment, early prognosis and therapy evaluation in the post-operative period (9).

Another study on 44 patients with m-MCAI reported that MCA blood flow velocity increased from about 42 cm/s on the first day to about 60 cm/s on the fourth day in the hemisphere with infarct before hemicraniectomy surgery (10).

In a study on 40 patients with ischemic stroke, the effects of venous and arterial thrombolytic therapy and continuous duplex ultrasound monitoring were compared. It was shown that symptomatic bleeding did not occur in the continuous duplex ultrasound monitoring cases, and good 90-day clinical outcome mRS= (0-2) was obtained in 70% of the patients, indicating the potential useful therapeutic effects of duplex ultrasound (11).

In another study on 50 patients with MCA or ICA artery occlusion who underwent intra-arterial interventions, the patients were followed up by transcranial Doppler ultrasound (TCD) a day after the intervention. In cases with poor clinical outcome (death or hemicraniectomy surgery), PI in MCA was significantly higher than the cases without poor clinical outcome after intra-arterial intervention (12).

Doppler ultrasound changes in patients with stroke are varied (9,10,13), and their value is not well defined yet. According to the above mentioned and by emphasizing the importance of this method in choosing a treatment for patients with ischemic stroke (14) and lack of study on the value of this method in the early detection of malignant cases, this study was designed to find an appropriate treatment for patients with stroke at the right time.

Materials and Methods

This cross-sectional descriptive analytical study was conducted on 40 patients with acute ischemic stroke in Shafa Hospital in Kerman during June 2015-April 2017. All patients had a stroke for the first time and were hospitalized in the first 24 hours of the onset of symptoms. Diagnosis was confirmed by brain CT scan and MRI (T1, T2 and DWI), and uncertain cases were excluded. Then all patients were visited by a cardiologist and cardiac evaluation including transthoracic echocardiography, and if necessary Transesophageal Echocardiography, was performed and those with embolic stroke were excluded. Patients with lacunar stroke, history of other disease such as blood disorder or vasculitis, history of taking medication (except medication for cardiac ischemia, diabetes, hypertension and hyperlipidemia) were also excluded from the study. CT scans were evaluated by a neurologist, and if more than 50% of the middle cerebral artery showed signs of hypodensity, it was considered as MMI, while the other cases were excluded (15). If the CT-scan results showed evidence of involvement of other areas or midline shift, the cases would be excluded from the study. For all patients, transcranial and extracranial cerebrovascular Doppler was performed using a bi-directional Doppler CW/PW connected to the Box Pro DWL (Sipplingen, Germany), in Doppler unit of Shafa hospital in Kerman. The device uses two separate 4-MHZ probes for common carotid arteries (CCA), internal carotid arteries (ICA), and a 2-MHZ probe to check anterior cerebral arteries (ACA), middle cerebral arteries (MCA), posterior cerebral arteries (PCA), vertebral arteries (VA), and basilar arteries (BA). Blood flow of arteries was checked in the standard depth and for each of the vessels listed, peak systolic velocity (PSV), mean flow velocity (MFV), pulsatility index (PI), and resistance index (RI) were calculated automatically by the device. Doppler parameters (PSV, MFV, PI and RI) of each patient, were separately measured for each artery on both sides. Patients who could not go under ultrasound imaging were excluded. For each patient, a data entry form containing demographic information (gender, age, history of hypertension, diabetes mellitus, hyperlipidemia, smoking and addiction) and other variables of the study was completed. The risk factors included the following: arterial hypertension (treated or systolic blood pressure >160 mmHg or diastolic pressure >90 mmHg after seventh day of stroke), hyperlipidemia [(history of hypercholesterolemia and/or fasting total cholesterol level >200 mg/dL or total triglyceride (TG) level > 200mg/dL or low-density lipoprotein (LDL) >130 mg/dL], hypertriglyceridemia (history of hypertriglyceridemia and/or fasting triglycerides level >180 mg/dL)], diabetes mellitus [(diagnosis according to the criteria of the National Diabetes Data Group (NDDG), smoking (more than 10 cigarettes per day for 6 months or during the recent year by any number of cigarettes), and opium addiction (consumption of opium in every day of the recent month) (16). The patients were followed up and assessed until discharge or death. In the case of fixed unilateral mydriasis in the clinical course or a displacement of more than 5 mm in septum pellucidum in the control CT-scan on days 3 to 7 (depending on the changes in the level of disorder of consciousness), m-MCAI was diagnosed (5). Finally, Doppler ultrasound findings of 20 patients with m-MCAI and 20 patients with MCAI who did not have malignant clinical course were compared. Data were analyzed using SPSS version 19. Descriptive statistics and statistical tests including independent t-test, Mann-Whitney and chi-square were applied. Statistical significant level was considered at P=0.05. This study was approved by the Ethics Committee of Kerman University of Medical Sciences (N: IR.Kmu.REC.1395.1010)

Results

In this study, 40 patients were examined. Nineteen patients (47.5%) were male, and 21 (52.5%) were female (Table 1). The mean age of the patients was 75.63 with SD= 9.75. The minimum and maximum age was 40 and 86 years, respectively. In 25 patients (62.5%), the ischemic lesion was observed in the right hemisphere, while in 15 (37.5%), was observed in the left hemisphere of the brain.

In the chi-square test, no statistically significant difference was found between malignant and non-malignant stroke groups in terms of frequencies of gender, smoking, high cholesterol, diabetes, history of drug addiction and side of lesion (Table 1).

Doppler Ultrasound Findings

The mean PSV in the MCA of the involved side was 90 m/s in the malignant cases and 78.65 in the non-malignant cases, and the difference was not significant (P=0.22), while the mean PSV in the MCA of the uninvolved side was 96.5 m/s in the malignant cases and 75.2 in the non-malignant cases, and the difference was significant (P=0.01). The mean PSV in the ACA of the involved side was 79.85 m/s in the malignant cases and 67.25 in the non-malignant cases, and the difference was not significant (P=0.13), while the mean PSV in the ACA of the uninvolved side was 78.9 m /s in the malignant cases and 58.4 in the non-malignant cases, and the difference was significant (P=0.01) (Table 2).

The mean MFV in the MCA of the involved side was 57.3 m/s in the malignant cases and 52 m/s in the non-malignant cases, and the difference was not significant, while the mean MFV in the MCA of the uninvolved side was 61 m/s in the malignant cases and 48 in the non-malignant cases, and the difference was significant (P=0.01). The mean MFV in the ACA in the involved side was not significantly different between the malignant and non-malignant cases (P=0.27), while the mean MFV in the ACA of the uninvolved side was 47 m/s in the malignant cases and 33 in the non-malignant cases, and the difference was significant (P=0.01) (Table 2).

In the study of mean PI in intra- and extracranial arteries in the involved side and the contralateral side in the malignant and non-malignant cases, no statistically significant relationship with MMI malignancy was found (Table 3).

In addition, except in ICA, no significant relationship was observed between mean RI and other intra- and extracranial arteries in both involved and uninvolved sides, and malignancy of MMI. The difference of RI in ICA in the malignant and non-malignant cases of the involved side was not significant (P=0.11), while, in the contralateral side of the lesion, its mean in the non-malignant cases was significantly higher (0.7) than that in the malignant cases (0.79) (Table 3).

Table 1. The comparison of gender, history of disease, and side of lesion frequencies in the malignant and non-malignant MMI.

		Stroke Malignancy			
		Malignant N (%)	Non-malignant N (%)	Total	P-value
Gender	Male	8 (40)	11(55)	19(47.5)	0.342
	Female	12(60)	(9(45)	21(52.5)	
Smoking	Smoker	8(40)	3(15)	11 (27.5)	0.077
	Non-smoker	12(60)	17(85)	29 (72.5)	
Hyperlipidemia	hyperlipidemic	5 (25)	2(10)	7 (17.5)	0.212
	Non-hyperlipidemic	15 (75)	18(90)	33(82.5)	
Diabetes	Diabetic	8 (40)	6(30)	14(35)	0.507
	Non-diabetic	12 (60)	14(70)	26(65)	
Hypertension	Hypertensive	9 (45)	9(45)	18(45)	1
	Non-hypertensive	11 (55)	11(55)	22(55)	
Addiction	Addict	(35)	9(45)	20(50)	0.519
	Non-addict	13 (65)	11(55)	20(50)	
Side of lesion	Right	11 (27.5)	14(35)	25(62.5)	0.342
	Left	9 (22.5)	6(15)	15(37.5)	

Table 2. The comparison between PSV and MFV indices of intra- and extracranial arteries in the malignant and non-malignant MMI.

		PSV		MFV	
	Stroke Malignancy	Mean (SD)	Pv	Mean (SD)	P-value
Affected_side_CCA	Malignant	45.2(14.75)	0.79	17.55(7.02)	0.18
	Non-malignant	44(14.38)		15(4.75)	
Affected_side_ICA	Malignant	50.75(20.01)	0.20	27.9(13.31	0.06
	Non-malignant	41.95(23.34)		19.95(12.22)	
Affected_side_MCA	Malignant	90.4(31.01)	0.22	57.3(21.27)	0.43
	Non-malignant	78.65(28.38)		52.1(20.52)	
Affected_side_ACA	Malignant	79.85(26.83)	0.13	46.65(20.1)	0.27
	Non-malignant	67.25(24.34)		39.65(19.67)	
Affected_side_PCA	Malignant	60.8(17.52)	0.82	33.9(13.64)	0.89
	Non-malignant	59.15(27.67)		34.5(14.66)	
Affected_side_VA	Malignant	65.1(14.12)	0.89	34.1(11.63)	0.84
	Non-malignant	66.05(27.96)		34.85(11.68)	
RI_BA	Malignant	64.85(17.85)	0.30	37.7(13.45)	0.14
	Non-malignant	57.95(22.58)		31.35(13.72)	
Opposite_side_CCA	Malignant	50.9(15.57)	0.08	20.05(6.43)	0.11
	Non-malignant	43.3(11.66)		17.1(4.89)	
Opposite_side_ICA	Malignant	44.55(11.39)	0.23	25.35(7.13)	0.42
	Non-malignant	54.1(33.72)		22.55(13.74)	
Opposite_side _MCA	Malignant	96.5(28.86)	0.01	61.05(17.43)	0.01
	Non-malignant	75.2(19.12)		48.8(12.67)	
Opposite_side _ACA	Malignant	78.9(26.08)	0.01	47(17.39)	0.01
	Non-malignant	58.4(21.49)		33(17.46)	
Opposite_side _PCA	Malignant	56.2(19.23)	0.67	32.05(12.4)	0.60
	Non-malignant	53.6(19.37)		29.75(15.13)	
Opposite_side _VA	Malignant	64(19.56)	0.85	37.05(17.62)	0.72
	Non-malignant	65.25(24.01)		35.4(11.31)	

Table 3. The comparison between PI and RI indices of intra- and extracrania arteries in the malignant and nonmalignant MMI.

		PI		RI	
	Stroke Malignancy	Mean (SD)	P-value	Mean (SD)	P-value
Affected_side_CCA	Malignant Non-malignant	2.55(1.04) 2.59(1.34)	0.90	0.87(0.12) 0.98(0.43)	0.30
Affected_side_ICA	Malignant Non-malignant	1.43(0.44) 1.94(1.09)	0.06	0.72(0.12) 0.79(0.15)	0.11
Affected_side_MCA	Malignant Non-malignant	1.01(0.26) 1.04(0.3)	0.76	0.62(0.1) 0.63(0.1)	0.80
Affected_side_ACA	Malignant Non-malignant	1.31(0.57) 1.51(0.9)	0.42	0.7(0.15) 0.75(0.16)	0.34
Affected_side_PCA	Malignant Non-malignant	1.48(0.71) 1.28(0.44)	0.28	0.73(0.16) 0.71(0.13)	0.70
Affected_side_VA	Malignant Non-malignant	1.49(0.7) 1.38(0.63)	0.62	0.7(0.15) 0.7(0.13)	0.86
RI_BA	Malignant Non-malignant	1.31(0.58) 1.51(0.72)	0.35	0.7(0.13) 0.78(0.18)	0.09
Opposite_side_CCA	Malignant Non-malignant	2.28(0.85) 2.11(0.8)	0.52	0.96(0.46) 0.87(0.11)	0.39
Opposite_side_ICA	Malignant Non-malignant	1.35(0.44) 1.94(1.45)	0.08	0.7(0.1) 0.79(0.15)	0.02
Opposite_side _MCA	Malignant Non-malignant	0.98(0.21) 1.1(0.89)	0.53	0.61(0.08) 0.61(0.11)	0.95
Opposite_side _ACA	Malignant Non-malignant	1.24(0.43) 1.55(0.77)	0.12	0.69(0.13) 0.76(0.17)	0.16
Opposite_side _PCA	Malignant Non-malignant	1.35(0.44) 1.59(0.77)	0.24	0.76(0.15) 0.77(0.16)	0.86
Opposite_side _VA	Malignant Non-malignant	1.24(0.52) 1.4(0.713)	0.42	0.67(0.12) 0.69(0.15)	0.62

Discussion

This study aimed to compare Doppler ultrasound findings in MMI patients with malignant and non-malignant clinical course.

Three findings were obtained in this study. First, the mean PSV in the MCA in the contralateral side of the lesion was significantly higher in the malignant cases compared to the non-malignant cases. The mean MFV in this artery in the contralateral side of the lesion was also significantly higher in the malignant cases compared to the non-malignant cases. Since according to the formula, increase in PSV directly increases the MFV, it can be attributed to increase in MFV. Our second finding is a significant increase in mean PSV of ACA in the contralateral side of the lesion in the malignant cases compared to the non-malignant cases, while mean MFV in ACA in the contralateral side of the lesion was significantly increased in the malignant cases compared to the non-malignant cases. The last finding is a significant difference in the mean RI in ICA in the contralateral side of the lesion between the malignant and non-malignant cases. However, it should be noted that although the two above values have statistically significant difference, but they are in the range of normal values for this indicator.

Increase in PSV and the subsequent increase in MFV in ACA and MCA in the contralateral side of the lesion in the malignant cases can be attributed to the compensatory increase in the blood flow in the affected side caused by atherothrombotic occlusion. This might be a useful marker for predicting malignancy of MMI; however, further studies are needed in this regard.

Transcranial Doppler is a non-invasive and available method that is currently the main screening method for cerebral arterial stenosis in patients with stroke, and if be able to predict the course of disease in patients with MMI, it can greatly help in identifying high-risk cases and, thereby, in finding better treatment and possibly prevention that may reduce the mortality and morbidity. Our findings showed increased PSV and MFV in MCA and ACA in the contralateral side of the lesion in cases with malignant course. However, the value of these findings cannot be definitively determined.

Although a number of studies have been conducted to find factors that predict the course of malignancy in patients with MMCAI using blood markers (2), electroencephalography (15), evoked potentials (17), imaging modalities such as DWI-MRI (18) and PET scan (4), but no study has been conducted to examine the ultrasound Doppler indicators in these patients and to find predictors of malignancy using these indicators. Studies have mostly focused on post-craniectomy hemodynamic condition (9) or changes in sonographic indices in cerebral edema and increased intracranial pressure (18,19,20).

One of the limitations of this study is that wave morphology, which can greatly help understand the hemodynamic condition of cerebral arteries, was not addressed. Another limitation is that the exact location of stenosis or thrombosis, which in different parts of the arteries can have different effects on vascular hemodynamics and, therefore, on the sonographic indices, was not determined in this study.

Conclusion

The present study showed an increase in PSV and MFV in MCA and ACA in the contralateral side of the lesion in cases that took malignant course, which can be helpful in early identification of cases that advance to malignancy.

Acknowledgments

Authors would like to gratitude the Neurology Research Center of Kerman University Of Medical Sciences for supporting this project.

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