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Original Article

Clinical value of microemboli combined with cerebrospinal fluid inflammatory factor level monitoring in predicting recurrent stroke of middle cerebral artery stenosis

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Abstract: Objective: To evaluate the clinical value of microemboli combined with cerebrospinal fluid inflammatory factor level monitoring in the prediction of recurrent stroke in middle cerebral artery stenosis. Methods: This is a retrospective study. Patients (n=170) who were hospitalized in the Department of Neurology of the First People's Hospital of Jiangxia District from June 2019 to January 2021 with cerebral infarction or transient ischemic attack were included in the study. Among them, 85 patients with ischemic attack were divided into the non-recurrent stroke group (primary onset, n=40) and the recurrent stroke group (history of cerebral infarction or transient ischemic attack within 5 years prior to the onset, n=45). Routine blood biochemical tests were performed using the Olympus 5800 automated chemical analyzer. Cerebrospinal fluid levels of inflammatory factors (TNF-α, IL-6) were detected by ELISA kits. Special Doppler hyperintensities for microemboli in cerebral blood flow were tested by transcranial Doppler ultrasound. Results: The mean age, statins and LDL-C were higher in the recurrent stroke group than the non-recurrent stroke group (P<0.05). The levels of cerebrospinal fluid TNF-α, PCT, CRP and IL-6 in the recurrent stroke group were higher than the non-recurrent stroke group (P<0.05). The proportion of grade 0 microemboli in the recurrent stroke group was lower than the non-recurrent stroke group (P<0.05), and the proportion of grade 1, 2, 3, 4 and 5 microemboli was higher than the non-recurrent stroke group (P<0.05). The positive rate of microemboli in the recurrent stroke group was higher than the non-recurrent stroke group (P<0.05). The accuracy rate of microemboli combined with cerebrospinal fluid inflammatory factor level monitoring in the recurrent stroke group for the prediction of recurrent stroke due to middle cerebral artery stenosis was higher than that in the non-recurrent stroke group (P<0.05). Increased age, statin use, microembolization, and increased LDL-C, TNF-α, PCT, CRP and IL-6 levels were independent risk factors. Conclusion: Microemboli combined with cerebrospinal fluid inflammatory factor level monitoring can increase the detection rate of recurrent stroke in middle cerebral artery stenosis and prevent vascular events to a great extent.

Keywords: Microemboli, cerebrospinal fluid, inflammatory factors, cerebral artery stenosis, recurrent stroke

Introduction

Cerebrovascular diseases are becoming more and more common worldwide and they play an important role in the global morbidity and mortality [1-3]. According to reports, Asian people are more vulnerable to middle cerebral artery stenosis [4]. Despite many treatment measures, the incidence of stroke in invalids with middle cerebral artery stenosis is still high [5]. Ultrasound technology can also detect small circulating emboli by detecting embolic signals in ipsilateral middle cerebral artery stenosis using transcranial Doppler [6-8]. In this technique, it is usually necessary to record an audible, high-intensity embolic signal for 30 to 60 minutes, and small emboli can be detected with high diagnostic accuracy [9, 10]. A large number of publications in recent years have demonstrated that inflammatory factors make an important contribution to the development, progression and instability of atherosclerosis [11-13]. Atherosclerotic lesions in the cerebral arteries are associated with elevated cere brospinal fluid of inflammatory markers [14, 15]. The cells of atherosclerotic plaques are a

source of locally and systemically acting cytokine [16, 17]. IL-6 is one of the key mediators that limit the inflammatory process in atherosclerotic plaques. Infection and its associated immune response are also factors that determine the instability of atherosclerotic plaques. In recent years, studies in China and abroad have found that procalcitonin, (PCT) and C-reactive protein (CRP) have certain application value in the differential diagnosis of cerebrovascular diseases. The motivation for this study is that the balance of interactions between proinflammatory in atherosclerotic plaques seems to determine the disease, but the exact relationship is not clear and affects the development and implementation of clinical treatment protocols. The innovation of this study was to monitor the special Doppler high signal of microemboli in cerebral blood flow by transcranial Doppler ultrasound, and to analyze the risk factors of recurrent stroke with middle cerebral artery stenosis by Logistic binary regression. The clinical significance of this study is to research the clinical value of microembolus combined with cerebrospinal fluid inflammatory factor level monitoring in predicting recurrent stroke caused by middle cerebral artery stenosis, and to provide theoretical basis for clinical diagnosis of recurrent stroke.

Materials and methods

General information

This is a retrospective study. A total of 191 inpatients with cerebral infarction or TIA from June 2019 to January 2021 in the Department of Neurology of our hospital were selected. Among them, 21 patients were excluded, and 170 patients were included in the study. Then, 85 patients with ischemic attack were divided into the non-recurrent stroke group (primary onset, n=40) and the recurrent stroke group (history of cerebral infarction or transient ischemic attack within 5 years prior to the onset, n=45). The recurrence and non-recurrence groups were observed for 12 weeks. Prior to the study, authorization from the Ethics Committee of the First People's Hospital of Jiangxia District and informed consent from the patients and their licensors were obtained. The approval number of the ethics report is 2019-002.

Eligibility criteria

Patients were eligible if they were 40-80 years old, had recurrent stroke (the first diagnosis: "cerebral infarction" or "cerebral hemorrhage" with new neurological deficits), had aggravated initial symptoms and signs, had the first stroke over 1 month ago and had a narrowing of the middle cerebral artery and a stroke in the area of blood supply to the narrowed artery (revealed by computed tomography angiography). Intracranial arteries include intracranial internal carotid artery I-ICA, MCA, ACA, PCA, I-VA and BA.

Exclusion criteria

Patients were excluded if they were potential cardiogenic cerebral embolism patients and had pulmonary embolism or atrial septal and paradoxical aneurysm embolism, received thrombolysis, intravascular intervention or carotid endarterectomy in the acute phase, had ipsilateral extracranial carotid artery stenosis ≥50% according to carotid artery ultrasound examination, had progressive stroke, asymptomatic stroke (judged by neuroimaging), intracerebral hemorrhage (detected by head CT scan), severe cardiac, hepatic and renal insufficiency or stroke that lead to by non-atherosclerotic vascular stenosis, and were unable to participate in the study, those who could not accept stents (vascular stenosis or deformation, resulting in the inability of the catheter to reach the affected area, continuous multiple segments of stenosis or too long narrow segments, arterial occlusion), or those who did not want to receive stents.

Medical ethics statement

When patients were covered in the outpatient clinic, they all signed the informed consent form. This study followed the principles of the Declaration of Helsinki and was authorized by the Hospital Bioethics Committee.

Methodology

Follow-up observation

All invalids enrolled received standard treatment (100 mg/d aspirin or 75 mg/d clopidogrel, 20 mg/d atorvastatin calcium). Blood glu-

cose levels were controlled to adjust blood pressure (Extended Release Nifedipine Tablets or benazepril) in hypertensive patients. Patients with symptomatic stenosis were followed up regularly, at home or as out-patients. Duration of follow-up was from the point of enrollment in the study. All patients with cerebrovascular disease were followed up regularly by telephone once a month. The endpoints included primary endpoint (cerebral infarction and TIA), secondary endpoint (acute angina pectoris), and death due to various causes, and follow-up was terminated once an endpoint occurred.

The follow-up period was set from one day after discharge to one month after discharge. For the consideration of the safety of the subjects, if the subjects experience adverse events or abnormal laboratory tests, the researchers increased the number of follow-up visits to the subjects according to actual needs, namely unplanned follow-up visits. During the follow up, concomitant medications/treatments, adverse events, relevant examinations (including imaging examinations, etc.) were recorded. Follow-up frequency was set to once a week. The end point of follow-up was set at 1 month after discharge.

Laboratory and imaging evaluation

All patients underwent MRI, computed tomography angiography, complete blood count, blood chemistry, coagulation and electrocardiography. Baseline data included sex, stroke risk factors (hypertension, diabetes and smoking) and physical examinations.

Assessment of cerebral infarction and middle cerebral artery stenosis

MRI evaluation: Phased array coils were scanned using a SIEMENS 1.5T NOVUS MRI scanner. The scanning parameters were as follows: thickness of 5 mm, interval of 1 mm and matrix of 256×256. DWI SE-EPI axial view was TR 3400 ms, TE 98 ms, and single echo planar imaging was used to generate diffusion-sensitized gradient pulses in the X, Y, or Z directions with diffusion sensitivity coefficients (b-values) of 0 and 1000 seconds/mm^2.

Computed tomography angiography: 64-slice CT, intracranial and carotid computed tomography angiography (the upper edge of the aortic arch reaches the cranial bone), post-processing techniques, including VR, 3D-MPR, CPR and 3DMIP, were used to observe the degree of stenosis and occlusion of the arterial lumen and to quantitatively measure the lumen stenosis.

MRI and computed tomography angiogram images were tested by two deputy directors of imaging respectively, and the results were confirmed by two physicians. The North American Symptomatic Carotid Intima-media Test (NASCET) 9 was performed to calculate arterial stenosis rate. The extent of the stenosis was classified as mild (1%-39%), moderate (40%-69%), severe (70%-99%) and occlusive. The main recording parameters are as follows: ① Microemboli signal: signal identification-high signal above baseline, tilted in one direction; ② Number and classification of microemboli signals: positive results-the occurrence of microemboli signals within 10 seconds is considered as a positive standard. The criteria were as follows: grade i: no microemboli signal (negative); grade ii: 1-10 microembolic signals; grade iii: more than 10 but no “rain curtain”; grade iv: a “rain curtain” is formed.

Blood biochemical analysis

Blood samples were gathered 48 hours after the onset of ischemic stroke. Routine blood biochemical tests were performed using an Olympus 5800 automatic chemical analyzer (Olympus, Tokyo, Japan). CHOL, LDL-C, HDL-C, TG, Cr, AST, and ALT were assessed.

PCT, CRP, TNF-α and IL-6 were measured in cerebrospinal fluid

Cerebrospinal fluid samples were collected 2, 3, 4, 5, 6, and 7 days after the onset of ischemic stroke. Cerebrospinal fluid was centrifuged in an EDTA tube at room temperature at 3500 RPM for 15 min. Cerebrospinal fluid was collected and stored at -80°C. Serum concentrations of TNF-α and IL-6 were determined using enzyme immunoassay (ELISA) kits (human PCT ELISA Kits were purchased from Shanghai Beyotime Biological Company, China, lot No. 2020-050214; human CRP ELISA Kits were purchased from Shanghai Beyotime Biological Company, China, lot No. 2020-1366001; human TNF-α ELISA Kits were purchased from Shanghai Beyotime Biological Company, China,

Table 1. General information of patients ($\bar{x}$±sd)

Project	Non-recurrent stroke group (n=80)	Recurrent stroke group (n=90)	T/X^2	P
Age (years)	61.4±6.5	68.3±5.5	7.867	<0.001
Sex (n)			1.874	0.648
Male	48	52		
Female	32	38		
BMI (kg/m^2)	26.12±3.54	26.38±2.54	2.443	0.558
Smoking (%)	32 (40.00%)	36 (40.00%)	1.234	0.882
Hypertension (%)	44 (55.00%)	50 (55.56%)	1.947	0.948
Diabetes (%)	46 (57.50%)	52 (57.78%)	1.934	0.478
Statins	44 (55.00%)	46 (71.11%)	5.927	<0.001

Note: T test was used for age and BMI. The X^2 test was used for gender, smoking history, hypertension, diabetes and statins.

Table 2. Routine blood biochemical tests ($\bar{x}$±sd, mmol/L)

Project	Non-recurrent stroke group (n=80)	Recurrent stroke group (n=90)	T value	*P*-value
CHOL	6.08±0.52	6.12±0.54	2.937	0.838
LDL-C	2.54±0.31	3.26±0.28	8.928	<0.001
TG	1.82±0.29	1.89±0.26	1.028	0.278
HDL-C	1.19±0.37	1.18±0.15	1.082	0.788
hs-CRP	3.05±0.24	3.22±0.57	1.141	0.938

Note: T test was used for CHOL, LDL-C, TG, HDL-C, hs-CRP. CHOL: cholesterol; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; TG: triglyceride; hs-CRP: high-sensitivity C-reactive protein.

lot No. 2019-12120369; human IL-6 ELISA Kits were purchased from Shanghai Beyotime Biological Company, China, lot No. 2019-11063680). Absorbance values were obtained using a Sirio S spectrometer at 450 nm.

Detection of microemboli by transcranial Doppler ultrasound

Transcranial Doppler monitoring was performed using a transcranial Doppler sonographer equipped with a head rest and two 2 MHz probes. The patient was monitored by transcranial Doppler for 30 minutes while breathing room air, for up to 1 hour while breathing 100% oxygen through a one-way Hi-Ox mask at a rate of 8 L/min. The purpose of the oxygen inhalation was to remove nitrogen from the blood thereby preventing the formation of nitrogen bubbles that typically form in the cavitation and flow outside the valve. Oxygen monitoring was started 20 minutes after the start of oxygen inhalation.

Statistical analysis

The monitoring data were analyzed by statistical software SPSS 19.0. The results of data analysis were represented as mean ± standard deviation ($\bar{x}$±sd). Multigroup data analysis was founded on one-way ANOVA. LSD test was used for subsequent analysis. P<0.05 indicated a significant difference.

Results

Comparison of general data in patients

According to the general statistics of patients with middle cerebral artery stenosis, the average age of invalids in the non-recurrent stroke group was 61.38±6.48 years old, the ratio of men to women was 24:16, and the BMI was 26.12±3.54. In the recurrent stroke group, the average age was 68.32±5.47 years old, the ratio of male to female was 26:19, and the BMI was 26.38±2.54. The recurrent stroke group had 36 subjects with a history of smoking in the past three years, 50 with underlying hypertension and 52 had underlying diabetes. The mean age and history of statins in the recurrent stroke group were higher than those in the non-recurrent stroke group, but there was no difference in other general information (P>0.05). See **Table 1**.

Routine blood biochemical tests

Routine blood biochemical tests were performed using Olympus 5800 automatic chemical analyzer. LDL-C was higher in the recurrent stroke group than that in the non-recurrent stroke group (P<0.05), and CHOL, TG, HDL-C and hs-CRP were not statistically different between the two group (P>0.05). See **Table 2**.

Comparison of cerebrospinal fluid inflammatory factors

The levels of cerebrospinal fluid inflammatory factors (TNF-α and IL-6) were higher in the

Table 3. Levels of TNF-α in cerebrospinal fluid ($\bar{x}$±sd, pg/mL)

Groups	Non-recurrent stroke group (n=80)	Recurrent stroke group (n=90)	t value	*P*-value
2 days after stroke	1.26±0.12	1.87±0.15	8.937	<0.001
3 days after stroke	1.41±0.10	2.12±0.11	9.125	<0.001
4 days after stroke	1.57±0.08	2.30±0.05	15.267	<0.001
5 days after stroke	1.69±0.09	2.45±0.12	19.553	<0.001
6 days after stroke	1.42±0.10	1.89±0.11	12.029	<0.001
7 days after stroke	1.35±0.06	1.45±0.07	10.955	<0.001
F value	21.003	35.216	-	-
P-value	<0.001	<0.001	-	-

Note: F test was used for levels of TNF-α in cerebrospinal fluid. TNF-α, tumor necrosis factor-α.

Table 4. Levels of IL-6 in cerebrospinal fluid ($\bar{x}$±sd, pg/mL)

Groups	Non-recurrent stroke group (n=80)	Recurrent stroke group (n=90)	t value	*P*-value
2 days after stroke	2.24±0.16	4.55±0.28	9.272	<0.001
3 days after stroke	2.41±0.12	4.97±0.19	12.036	<0.001
4 days after stroke	2.53±0.13	5.12±0.17	17.667	<0.001
5 days after stroke	2.67±0.10	5.30±0.15	15.956	<0.001
6 days after stroke	2.22±0.10	4.61±0.19	11.251	<0.001
7 days after stroke	2.25±0.08	4.36±0.11	10.628	<0.001
F value	19.885	29.623	-	-
P-value	<0.001	<0.001	-	-

Note: F test was used for levels of IL-6. IL-6, interleukin-6.

Table 5. Levels of PCT in cerebrospinal fluid ($\bar{x}$±sd, μg/L)

Groups	Non-recurrent stroke group (n=80)	Recurrent stroke group (n=90)	t value	*P*-value
2 days after stroke	0.08±0.04	0.49±0.14	9.659	<0.001
3 days after stroke	0.14±0.03	0.53±0.09	11.923	<0.001
4 days after stroke	0.19±0.02	0.61±0.15	13.025	<0.001
5 days after stroke	0.27±0.04	0.73±0.10	16.112	<0.001
6 days after stroke	0.20±0.02	0.59±0.08	12.750	<0.001
7 days after stroke	0.11±0.02	0.52±0.04	10.539	<0.001
F value	15.657	22.526	-	-
P-value	<0.001	<0.001	-	-

Note: F test was used for levels of PCT in cerebrospinal fluid. PCT, procalcitonin.

recurrent stroke group than those in the non-recurrent stroke group (P<0.05). The cerebrospinal fluid inflammatory factors (PCT, CRP) levels were also higher in the recurrent stroke group than those in the non-recurrent stroke group (P<0.05). See **Tables 3**-**6**.

Microembolic classification ratio

Special Doppler hyperintensities of microemboli in cerebral blood flow were monitored by transcranial Doppler ultrasound, which showed the presence of air bubbles in the cerebral arteries. In addition to the visual output on the screen, a loud signal appeared in the audio output as each bubble passed through the patent foramen ovale. The proportion of grade 0 microemboli in the recurrent stroke group was lower than that in the non-recurrent stroke group (P<0.05), and the proportions of grade 1, 2, 3, 4 and 5 microemboli were higher than those in the non-recurrent stroke group (P<0.05). See **Figure 1**; **Table 7**.

Comparison of positive rates of microemboli

The positive rate of microemboli in the recurrent stroke group was higher than that in the non-recurrent stroke group (P<0.05). See **Table 8**.

Comparison of joint monitoring accuracy

The accuracy rate of microemboli combined with cerebrospinal fluid inflammatory factor level monitoring in the recurrent stroke group for the prediction of recurrent stroke due to middle cerebral artery stenosis was higher than that in the non-recurrent stroke group (P<0.05). See **Table 9**.

Independent risk factors for recurrent stroke

Results showed that increased age, statin use, microembolization, and increased LDL-C, TNF-α, and IL-6 levels were all independent risk factors for carotid stenosis. Sex, BMI, HDL-C, smoking history, CHOL, hyper-

Table 6. Levels of CRP in cerebrospinal fluid ($\bar{x}$±sd, mg/L)

Groups	Non-recurrent stroke group (n=80)	Recurrent stroke group (n=90)	t value	*P*-value
2 days after stroke	14.95±0.87	35.27±3.41	12.786	<0.001
3 days after stroke	16.02±0.91	37.52±2.29	15.127	<0.001
4 days after stroke	16.19±0.25	39.02±1.71	17.701	<0.001
5 days after stroke	16.52±0.62	38.85±2.16	19.962	<0.001
6 days after stroke	15.15±0.75	37.23±2.19	10.239	<0.001
7 days after stroke	41.32±2.57	35.56±3.13	11.627	<0.001
F value	25.639	36.870	-	-
P-value	<0.001	<0.001	-	-

Note: F test was used for levels of CRP in cerebrospinal fluid. CRP, C-reactive protein.

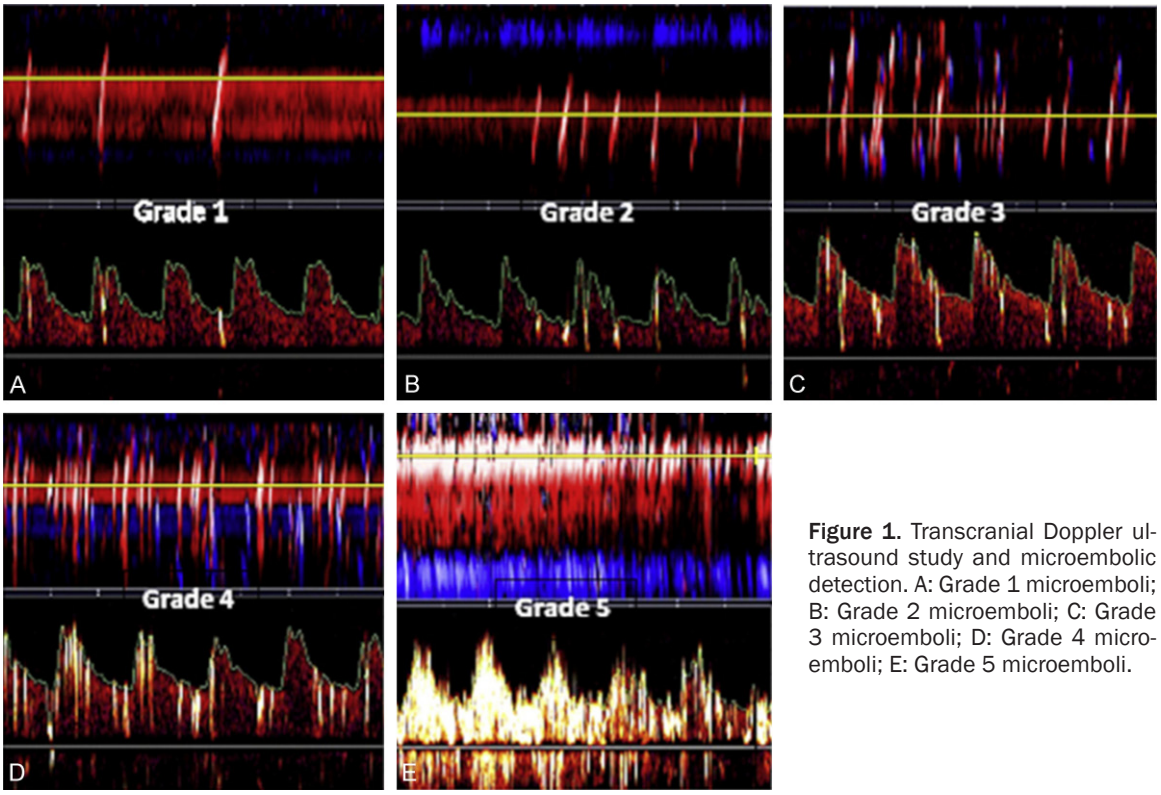

Figure 1. Transcranial Doppler ultrasound study and microembolic detection. A: Grade 1 microemboli; B: Grade 2 microemboli; C: Grade 3 microemboli; D: Grade 4 microemboli; E: Grade 5 microemboli.

tension, diabetes, TG, and hs-CRP were not risk factors. See **Table 10**.

Discussion

The relevant factors affecting the prognosis of invalids with symptomatic middle cerebral artery stenosis were analyzed in this study. It was shown that sex, smoking, hypertension and diabetes in the recurrent stroke group were not different from those in the non-recurrent stroke group. This indicates that the research subjects included in this study are relatively homogeneous. A study followed 569 patients found that 106 invalids (19.0%) had cerebral infarction with severe arterial stenosis, while ≥70% of the patients had the high risk of stroke, and the risk for women was increased. There was no effect on stenosis site or antithrombotic drug pretreatment. Logistic regression found that diabetes was significantly associated with stroke recurrence, making it known that patients with diabetes mellitus associated with cerebral artery stenosis were more likely to have stroke recurrence and are a high-risk population worthy of attention by clinicians.

Table 7. Microembolic classification (n (%))

Projects	Non-recurrent stroke group (n=80)	Recurrent stroke group (n=90)	χ^2 value	*P*-value
Level 0	68 (85.00%)	40 (44.44%)	15.839	<0.001
Level 1	6 (7.50%)	10 (11.11%)	3.837	<0.001
Level 2	4 (5.00%)	12 (13.33%)	6.849	<0.001
Level 3	2 (2.50%)	8 (8.89%)	8.532	<0.001
Level 4	0 (0.00%)	12 (13.33%)	9.826	<0.001
Level 5	0 (0.00%)	8 (8.89%)	10.937	<0.001

Note: The X^2 test was used for microembolic classification.

Table 8. Positive rate of microemboli (n (%))

Groups	Positive rate of microemboli (%)
Non-recurrent stroke group (n=80)	12 (15.00%)
Recurrent stroke group (n=90)	50 (55.56%)
χ^2 value	6.038
P-value	<0.001

Note: The X^2 test was used for the positive rate of microemboli.

Table 9. Accuracy rate of joint monitoring

Groups	Accuracy (%)
Non-recurrent stroke group (n=80)	14 (17.50%)
Recurrent stroke group (n=90)	80 (88.89%)
χ^2 value	9.762
P-value	<0.001

Note: The X^2 test was used for the accuracy rate of joint monitoring.

Table 10. Independent risk factor for recurrent stroke

Projects	B	95% CI	SE	*P*-value
Age	1.238	1.026-1.487	0.458	<0.001
Statins	2.839	1.728-4.027	0.928	<0.001
Microembolus	1.567	1.016-2.067	1.698	<0.001
LDL-C	4.875	2.458-8.569	1.263	<0.001
TNF-α	5.369	2.637-9.528	1.148	<0.001
IL-6	6.514	3.458-11.561	1.534	<0.001

Note: The logistic test was used for independent risk factor for recurrent stroke. LDL-C: low density lipoprotein cholesterol; TNF-α: tumor necrosis factor-α; IL-6: interleukin-6.

In terms of intervention treatment, there was no obvious difference between regular or irregular use of antihypertensive and antiplatelet drugs in the two groups, indicating that the population in the region had compliance with control treatment. The statistical results showed that the number of patients who used statins irregularly in the recurrent stroke group was higher than that in the non-recurrent stroke group, showing irregular use of statins go hand in hand with the recurrence of stroke, which was one of the key reasons for the recurrence of stroke [18]. This result is not consistent with other relevant studies [19]. This indicates that the regular use of statins is very important, that is, medication compliance is a key factor affecting treatment efficacy. This may be due to differences in stenosis severity and patient adherence to different interventions. Researchers have shown that long-term use of statins can decrease the progression of stroke [20], delay the progression of atherosclerosis and even reduce the stenosis of already existing atherosclerosis. All findings were affirmed in coronary arteries. In one study, patients were observed to take atorvastatin 40 mg/d orally for 6 months until the completion of the second MRI. By the end of the study, 58% of patients had improved arterial stenosis, 38% had no change, and in 4% of patients, the condition deteriorated. Another study has shown that lower LDL cholesterol can decrease the risk of stroke recurrence [21]. This result suggested that if symptoms of ischemia are caused by arterial-arterial embolism due to unstable plaques, pharmacotherapy to stabilize plaques and reduce plaque shedding during the recovery phase should be further enhanced.

Previous studies have found that inflammatory markers (TNF-α, IL-6) are raised in patients with atherosclerosis. TNF-α is an inflammatory factor produced by macrophages. In the study, significantly higher cerebrospinal fluid concentrations of TNF-α and IL-6 were found in patients in the recurrent stroke group as compared with the non-recurrent stroke group. The severity of cerebral arterial stenosis is correlated with TNF-α and IL-6 levels. Other reports also demonstrated an association between high cerebrospinal fluid IL-6 and TNF-α concentrations and the presence of unstable plaques evaluated on ultrasound [25, 26]. One study has found that IL-6 is involved in the development of atherosclerosis, and cerebrospinal fluid IL-6 level is an independent predictor of the development of early atherosclerotic lesions. Another study found that the cerebrospinal fluid IL-6 of the cerebral artery stenosis group was higher than

that of the control group, and the cerebrospinal fluid IL-6 level of the symptomatic stenosis group was higher than that of the asymptomatic stenosis group. The importance of TNF-α and IL-6 in the progression of atherosclerotic lesions has also been demonstrated.

PCT, as an emerging laboratory test in recent years, can roughly estimate the type of infectious pathogens in the early stage, evaluate the severity of infection, guide drug use and determine the prognosis, which has been increasingly recognized in clinical practice. When there is systemic bacterial infection, the body can have multiple organ failure syndrome, systemic inflammatory response syndrome and abnormally increased cerebrospinal fluid PCT concentration, and the degree of increase is related to the severity of the infection and the prognosis of the disease course. As one of the most commonly used acute phase-reaction proteins, CRP begins to increase at 6-8 h after infection and peaks at 24-48 h. It can reach hundreds or even thousands of times of the normal level. After the infection is eliminated, CRP content drops sharply and can return to normal within 1 week. After antibiotic treatment, CRP drops rapidly as the infection is controlled, and it can drop to 50% of the original concentration within 1 d. Therefore, a series of measurements during the course of the disease can provide valuable information for disease progression, early detection of complications, and treatment monitoring. In our study, significantly higher cerebrospinal fluid concentrations of PCT and CRP were found in invalids in the recurrent stroke group as compared with those in the non-recurrent stroke group.

In asymptomatic carotid artery embolization studies, the presence of embolic signals ipsilateral to the stenotic carotid artery increased the risk of future stroke by approximately sixfold compared with subjects without embolic signals [22-24]. Researchers from asymptomatic carotid artery embolization studies executed a meta-analysis and other asymptomatic carotid stenosis studies and found in a pooled analysis of nearly 1000 invalids that positive embolic signals had similar predictive power for ipsilateral stroke. However, the pathogenesis of symptoms and the instability of plaques are acute. This is why the time period from determination of cytokine level to onset of symptoms could have some significance in assessing the detected cytokine level, although there is no significant correlation between the measured cytokine level and the time elapsed since cytokine development. Symptoms (longer than 14 days) were found. Surgery for internal carotid artery stenosis is performed within two weeks after the onset of clinical symptoms due to stenosis, in order to maximize the prevention of vascular events. Surgical treatment for symptomatic cerebral artery stenosis two weeks after symptoms and asymptomatic cerebral artery stenosis brings less benefit. The characteristics of cerebral artery stenosis (stenosis over 70% and plaque morphology, and the presence of ulceration or hypoechoic structure of plaques on the surface) are more common in the symptomatic stenosis group in comparison with the asymptomatic stenosis group [27, 28]. These results found the usefulness of transcranial Doppler features of cerebral arterial stenosis instability in assessing the risk of clinical symptoms in invalids with cerebral arterial stenosis [29, 30].

We have found the role of PCT, CRP, TNF-α, IL-6 and microemboli in the pathogenesis and instability of recurrent stroke lesions in middle cerebral artery stenosis, and we hope that drugs that affect the measured cytokine concentrations may inhibit the progression of atherosclerosis. Experimental and clinical studies on the treatment of atherosclerosis and its complications with anti-cytokine drugs (TNF-α) have been reported.

For the credibility of the results, including more patients would be better. Also, there was no long-term follow-up of the patients and no prognostic data for cerebral artery stenosis. Besides, the cerebral arteries, the vertebral and basilar arteries also play a key role in ischemic stroke [31, 32]. If more studies were conducted on the vertebral and basilar arteries, we might systematically assess the role of microemboli combined with cerebrospinal fluid inflammatory factor level monitoring in recurrent stroke due to middle cerebral artery stenosis.

In summary, microemboli combined with cerebrospinal fluid inflammatory factor level monitoring can increase the detection rate of recurrent stroke due to middle cerebral artery stenosis and prevent vascular events to a great extent.

Disclosure of conflict of interest

None.

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