ORIGINAL RESEARCH

Evaluation of Cerebral Infarction by Carotid Doppler Ultrasound Combined with Cysteine, D Dimer, and Other Indexes

Yuliang Yin, MM; Letao Yu, BD

ABSTRACT

Background • Cerebral infarction, formerly known as ischemic stroke, refers to localized ischemic necrosis or softening caused by disorders of blood supply to the brain, ischemia, or hypoxia. Cerebral infarction is characterized by high mortality and morbidity. Therefore, early and accurate diagnosis of cerebral infarction is of great significance to the selection of treatment and prognosis of patients. Electrocardiogram (ECG) is the traditional method for diagnosing myocardial infarction. However, ECG diagnosis of myocardial infarction based on electrophysiological manifestations of cardiac electrostimulation can only indirectly reflect the anatomical lesions, and can not diagnose the lesions in special parts of the heart, so there are diagnostic limitations, there will be certain missed diagnosis and misdiagnosis.

Objective • Our study aimed to assess the effect of carotid Doppler ultrasound combined with cysteine, D dimer, and other indexes in the clinical diagnosis of cerebral infarction, in order to provide effective basis for early diagnosis and treatment of cerebral infarction patients

Design • This study was a retrospective study.

Setting • This study was carried out in First Affiliated Hospital, Anhui University of Science and Technology (Huainan First People's Hospital) from November 2020 to December 2022.

Participants • A total of 40 patients with cerebral infarction were selected as the observation group (OG). At the same time, 40 healthy people who underwent physical examinations were selected as the control group (CG). There were 21 males and 19 females in the OG. The age ranged from 59 to 76 years, with an average of (67.11±0.23) years. There were 23 males and 17 females in the CG. The age ranged from 58 to 77 years, with an average of (68.04±0.35) years.

Interventions • Both groups of subjects underwent carotid Doppler ultrasound examination to observe the number of carotid plaque formation, the carotid artery intimal thickness and the lumen diameter. Besides, serum homocysteine (Hcy) and cystatin C (Cys-C) levels of the subjects were detected by an automatic biochemical analyzer and supporting reagents. The serum high sensitivity C reactive protein (hsCRP) levels of the two groups were detected by immune turbidimetry. The plasma levels of D-dimer (D-D) and fibrinogen (FIB) were detected by immunoturbidimetric method. Receiver operating characteristic (ROC) curve was implemented to analyze the value of Color Carotid Doppler ultrasound combined with Hcy, Cys-C, hsCRP, D-D and FIB detection in diagnosing cerebral infarction.

Outcome Measures • (1) Carotid Doppler ultrasound can observe cardiac morphological changes from multiple angles and planes, and diagnose myocardial infarction according to the changes of ventricular wall structure caused by myocardial ischemia. It has the advantages of simple operation and high image quality. (2) The hemodynamic parameters of the bilateral common carotid artery and internal carotid artery, (3) Serum Hcy, Cys-C, and hsCRP levels, as well as plasma levels of D-D and FIB. Hcy is an independent risk factor for cardiovascular and cerebrovascular diseases, and the Hcy level is directly related to the pre-onset of cerebral infarction patients. Cys-C is an ideal endogenous marker to reflect the change of glomerular filtration rate. In recent years, it has been found that the interaction of Cys-C, Hcy and cathepsin is involved in the pathological process of cardiovascular diseases such as atherosclerosis, aneurysm and myocardial infarction. hsCRP can reflect left ventricular function, myocardial injury, inflammation and other conditions, which is helpful to evaluate the condition of cerebral infarction patients. D-D can reflect the coagulation function of the body, and its high expression can indicate that the body is in a state of hypercoagulation, accompanied by secondary hyperfibrinolysis, and is often used in the clinical diagnosis of cerebral infarction. FIB is an important factor contributing to atherosclerosis and plays an important role in the occurrence and development of cerebral infarction. (4) ROC curve results.

Results • The number of carotid plaque formation in the OG was significantly higher compared to the CG ($P < .05$). The carotid artery intimal thickness in the OG was relatively elevated relative to the CG ($P < .05$). The lumen diameter was smaller in the OG compared to the CG ($P < .05$). The peak systolic velocity and end-diastolic velocity of the left and right common carotid artery and the left and right internal carotid artery in the OG declined compared to the CG, and the resistance index of the left and right common carotid artery and the left and right internal carotid artery in the OG was elevated compared to the CG ($P < .05$). The serum levels of Hcy, Cys-C, and hsCRP, as well as plasma levels of D-D and FIB in the OG, were elevated compared to the CG (<.05). The sensitivity and specificity of Color Carotid Doppler ultrasound combined with Hcy, Cys-C, hsCRP, D-D and FIB in the diagnosis of AMI were 0.919 and 0.817 respectively, significantly higher than that predicted by alone ($P < .001$).

Conclusions • Carotid Doppler ultrasound combined with cysteine, D dimer, and other indexes played an important role in the clinical diagnosis of cerebral infarction, which was worthy of promotion. Our experimental results provide an important basis for the clinical scientific application of Carotid Doppler ultrasound and myocardial marker detection, especially for those AMI patients with no abnormal changes in ECG and no obvious clinical symptoms, it can realize early diagnosis and timely treatment, and reduce the mortality of AMI. (*Altern Ther Health Med.* 2024;30(7):148-154).

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INTRODUCTION

Cerebral infarction is also called ischemic stroke, which refers to the loss of blood supply to local brain tissue, including blood vessels, glial cells, and nerve cells.[1] Cerebral infarction is divided into cerebral thrombosis, cerebral embolism, and lacunar infarction according to the different pathogenesis. Among them, cerebral thrombosis is the most common type of cerebral infarction, accounting for about

60% of all cerebral infarction.[2] This disease is prone to 50~60 years of age or older, males slightly more than females. It is often combined with arteriosclerosis, hypertension, hyperlipidemia or diabetes, and other risk factors or corresponding systemic non-specific symptoms.[3] The prodromal symptoms of cerebral infarction are not specific, some patients may have dizziness, temporary limb numbness, weakness, and other transient ischemic attack.[4] The related factors that induce cerebral infarction are occlusion diseases in extracranial or intracranial arteries that supply blood to the brain and fail to obtain timely and adequate collateral circulation so the metabolic need of local brain tissue is in short supply.[5] It has been reported that atherosclerosis is the main factor leading to cerebral infarction, and atherosclerosis is a chronic progressive disease caused by the continuous action of multiple factors, which makes it easy to induce systemic lesions in patients.[6] Electrocardiogram (ECG) is the traditional method for diagnosing myocardial infarction.[7] However, ECG diagnosis of myocardial infarction based on electrophysiological manifestations of cardiac electrostimulation can only indirectly reflect the anatomical lesions, and can not diagnose the lesions in special parts of the heart, so there are diagnostic limitations, there will be certain missed diagnosis and misdiagnosis.[8] Therefore, it is particularly important to find effective methods for early diagnosis and timely treatment of patients with cerebral infarction, thereby preventing further complications or reducing the economic burden on healthcare systems.

Carotid Doppler ultrasound is an effective method to detect carotid artery wall lesions.[9] It is helpful to determine the nature and stability of carotid atherosclerotic plaque in patients with ischemic cerebrovascular disease, determine the degree of carotid atherosclerosis and carotid artery stenosis and has advantages in showing the changes in the structure of the artery wall, which provides an objective basis for the early prevention and treatment of atherosclerosis.[10] Active treatment of atherosclerosis and carotid artery stenosis is of great significance for the prevention of ischemic stroke.[11]

It has been reported that abnormal serum homocysteine (Hcy) can lead to chronic damage of intradermal cells, resulting in lipid peroxidation and an abnormal increase in blood coagulation, increasing the risk of various cardiovascular and cerebrovascular diseases.[12] There is sufficient evidence to suggest that the increased plasma level of Hcy plays a role in the onset of cerebral infarction and could be exploited as an early diagnostic marker in cerebral infarction patients.[13] Therefore, hyperhomocysteinemia is also considered to be an important risk factor for cerebral infarction.[14] The amount of cystatin C (Cys-C) produced in human body is stable, and is not easily affected by age, sex, body weight and other factors.[15] At present, Cys-C is clinically recognized as an endogenous marker for evaluating glomerular filtration rate.[16] However, recent studies have found that Cys-C is closely related to cardiovascular diseases such as heart failure and hypertension, and mainly participates in the pathogenesis of heart failure through inflammatory response, oxidative stress, promoting atherosclerosis and other ways.[17] Besides, as an important indicator of clinical primary/secondary fibrinolysis, D-dimer (D-D) can be used as an important indicator for the diagnosis of cerebral infarction disease progression by relying on the characteristics of thrombotic lesions in cerebral infarction.[18] It has been documented that high-sensitivity C-reactive protein (hsCRP) is involved in the occurrence and development of inflammatory injury through activating complement and promoting coagulation, accelerating the release of active factors and other ways, and has a certain relationship with plaque instability, increasing the risk of cerebral infarction.[19] In addition, fibrinogen (FIB) belongs to the protein of coagulation function and is the core index in the process of coagulation. Under the action of thrombin, stable and insoluble fibrin clots are formed, and if the content increases, the body is in a hypercoagulable state.[20] Relevant literatures have demonstrated that the main factor of cerebral infarction is cerebral vascular occlusion caused by thrombosis, and most patients have abnormal coagulation and fibrinolysis.[21]

In this study, 40 patients with cerebral infarction were selected as the observation group (OG), including 21 males and 19 females, aged 59-76 years. At the same time, 40 healthy subjects aged 58 ~ 77 years old were selected as the control group (CG), including 23 males and 17 females. This study aims to evaluate the diagnostic efficacy of combining carotid Doppler ultrasound with specific blood biomarkers in detecting cerebral infarction.

METHODS

Participants

A total of 40 patients with cerebral infarction admitted to First Affiliated Hospital, Anhui University of Science and Technology (Huainan First People's Hospital) from November 2020 to December 2022 were selected as the OG. At the same time, 40 healthy people who underwent physical examinations were selected as the CG. There were 21 males and 19 females in the OG. The age ranged from 59 to 76 years, with an average of (67.11±0.23) years. There were 23 males and 17 females in the CG. The age ranged from 58 to 77 years, with an average of (68.04±0.35) years. There was no significant difference in clinical data between the two groups ($P > .05$). This study was conducted in accordance with ethical guidelines and approved by an ethics committee.

Inclusion criteria: (1) Patients with normal liver and kidney function; (2) signed informed consent; (3) No examination contraindications. Exclusion criteria: (1) Mental illness and cognitive impairment; (2) accompanied by malignant tumors; (3) Unable to communicate.

Procedures

Carotid Doppler ultrasound examination. Ultrasound examinations and related scores were performed independently by the same senior imaging physician. Color Doppler ultrasound diagnostic instrument, and high frequency linear array probe (instrument model Phillip

EPIQ5, Netherlands) were used. The range of probe frequency was 5-12 MHz. The sampling volume was set to 4 mm. The patient was instructed to lie flat on the pillow and slightly tilt his head back so that the neck was directly exposed. In the early stage, longitudinal scanning was performed on the outer edge of the sternocleidomastoid muscle and clavicle, and then 2-3 cm above the common cervical artery, carotid bifurcation, enlargement, and the beginning of internal carotid artery, 2-3 cm above the beginning of external cervical artery, and then counterclockwise transverse scanning was performed. The patient's carotid bifurcation, media thickness, and neck longitudinal section were probed, the highest position of the carotid artery was observed, and the presence of plaque, plaque location, plaque number, size, and other conditions were detected. The percentage of inner diameter stenosis of the concentric stenosis was detected to see the filling of the blood flow and the location of the stenosis obstruction.

Serum Hcy, cystatin C (Cys-C), and high sensitivity C reactive protein (hsCRP) levels determination. The subjects were fasted for 8 hours, and then the elbow venous blood was collected in the fasting state after getting up in the morning, and the volume was 3 mL. The centrifuge speed was controlled at 3000 r per minute, and the centrifuge treatment time was 10 minutes. The serum was separated and stored at -20°C. The serum Hcy and Cys-C levels of the subjects were detected by an automatic biochemical analyzer and supporting reagents. The serum hsCRP levels of the two groups were detected by immune turbidimetry. The instrument was a Siemens ADVIA1800 automatic biochemical analyzer (Germany).

Plasma levels of D-D and fibrinogen (FIB) determination. Blood samples of the two groups were collected into sodium citrate anticoagulant at a ratio of 9:1, mixed upside down, centrifuged at 3000 r/min for 10 min, and plasma was separated. Plasma D-D and FIB were tested by immunoturbidimetric method. An automatic hemagglutination instrument (Sysmex CS5100, Japan) was used for examination.

Outcome Measures.

Carotid Doppler ultrasound measures: (a) number of carotid plaque formation, (b) intimal thickness (mm), (c) lumen diameter (mm).

Hemodynamic parameters: (a) systolic blood flow velocity (cm/s), (b) end-diastolic blood flow velocity (cm/s), (c) resistance index.

Blood biomarker levels: (a) Hcy (μmol/L), (b) Cys-C (mg/L), (c) hsCRP (mg/L), (d) D-D (μg/L), (e) FIB (g/L).

Statistical Analysis

SPSS 22.0 statistical software (IBM Co., USA) was used to process the data of Carotid Doppler ultrasound measures, hemodynamic parameters and blood biomarker levels. The measurement data were calculated as ($\bar{x} \pm s$), and a t test was performed. The count data was shown as [n (%)] in the table, and χ^2 test was performed. Receiver operating characteristic (ROC) curve was implemneted to analyze the value of Color Carotid Doppler ultrasound combined with Hcy, Cys-C, hsCRP, D-D and FIB detection in diagnosing cerebral infarction, and the area under the curve (AUC) was calculated. $P < .05$ was considered statistically significant.

Table 1. Comparison of Carotid Artery Characteristics Between Observation and Control Groups

Groups	n	Number of carotid plaque formation	Intimal thickness (mm)	Lumen diameter (mm)
Observation group	40	36 (90.00%)	1.22±0.13	4.48±0.39
Control group	40	10 (25.00%)	1.00±0.14	4.82±0.46
χ^2/t		34.58	7.28	3.57
P value		<.05	<.05	<.05

Table 2. Comparison of Hemodynamic parameter characteristics Between Observation and Control Groups

Group		Observation group (n = 40)	Control group (n = 40)	t	P value
Peak systolic blood velocity (cm/s)	Left common carotid artery	69.96±12.23	78.25±12.47	3	<.05
	Left internal carotid artery	58.71±11.16	65.39±12.04	2.57	<.05
End-diastolic blood flow velocity (cm/s)	Left common carotid artery	16.05±6.87	19.72±7.26	2.32	<.05
	Left internal carotid artery	17.83±8.02	21.92±8.53	2.21	<.05
Resistance index	Left common carotid artery	0.92±0.13	0.71±0.12	7.51	<.05
	Left internal carotid artery	0.87±0.14	0.63±0.15	7.4	<.05
Peak systolic blood velocity (cm/s)	Right common carotid artery	70.12±12.05	82.36±13.29	4.32	<.05
	Right internal carotid artery	59.34±11.16	67.47±11.98	3.14	<.05
End-diastolic blood flow velocity (cm/s)	Right common carotid artery	16.21±5.54	20.61±6.81	3.17	<.05
	Right internal carotid artery	18.03±7.97	22.85±8.42	2.63	<.05
Resistance index	Right common carotid artery	0.93±0.14	0.68±0.11	8.88	<.05
	Right internal carotid artery	0.85±0.13	0.57±0.14	9.27	<.05

RESULTS

Color Carotid Doppler ultrasound examination of the carotid artery in both groups

It was revealed in Table 1 that, the number of carotid plaque formation in the OG was significantly higher compared to the CG ($P < .05$). The carotid artery intimal thickness in the OG was relatively elevated relative to the CG ($P < .05$). The lumen diameter was smaller in the OG compared to the CG ($P < .05$).

Hemodynamic parameter characteristics of in both groups

It was revealed in Table 2 that, the peak systolic velocity and end-diastolic velocity of the left and right common carotid artery and the left and right internal carotid artery in the OG were declined compared to the CG, and the resistance index of the left and right common carotid artery and the left and right internal carotid artery in the OG was elevated compared to the CG ($P < .05$).

Serum levels of Hcy in both groups

It was indicated in Figure 1 that, the serum level of Hcy in the OG was enhanced in comparison with the CG ($P < .05$).

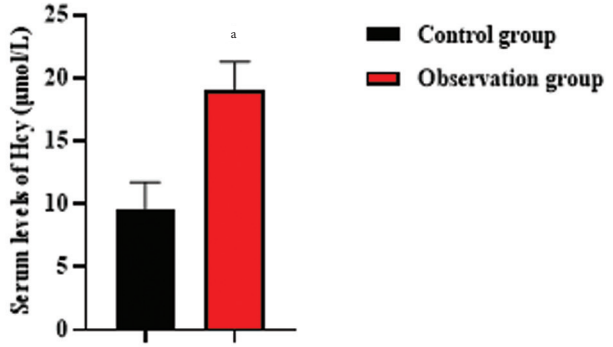
Serum levels of Cys-C in both groups

It was indicated in Figure 2 that, the serum level of Cys-C in the OG was increased in comparison with the CG ($P < .05$).

Serum levels of hsCRP in both groups

It was indicated in Figure 3 that, the serum level of hsCRP in the OG was enhanced in comparison with the CG ($P < .05$).

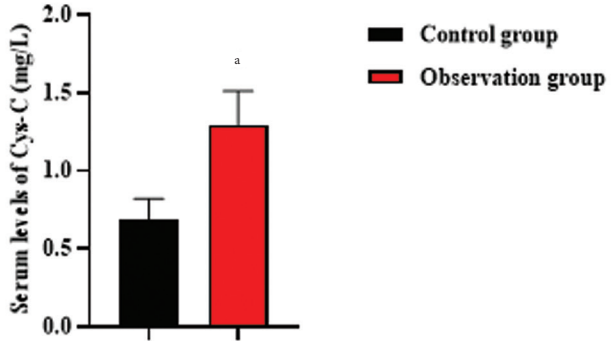
Figure 1. Serum Homocysteine (Hcy) Levels in Both Groups.



[a]$P < .05$.

Abbreviations: Hcy, homocysteine.

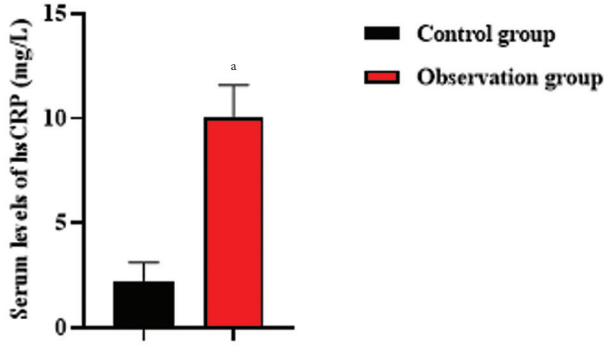
Figure 2. Serum Cystatin C (Cys-C) Levels in Both Groups.



[a]$P < .05$.

Abbreviations: Cys-C, cystatin C.

Figure 3 Serum High Sensitivity C Reactive Protein (hsCRP) Levels in Both Groups.



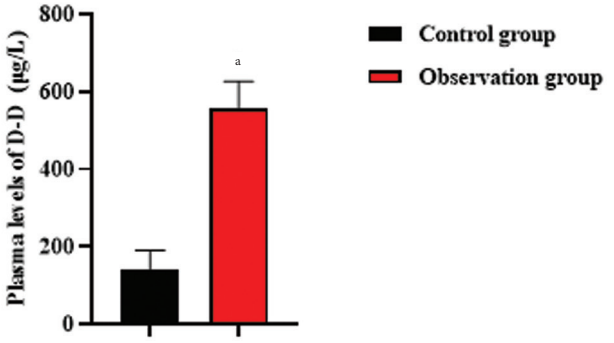
[a]$P < .05$.

Abbreviations: hsCRP, high sensitivity C-reactive protein.

Plasma levels of D-D in both groups

It was indicated in Figure 4 that, the plasma level of D-D in the OG was elevated in comparison with the CG ($P < .05$).

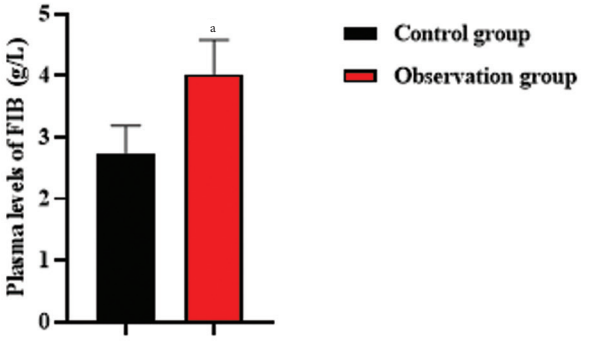
Figure 4 Plasma D-dimer (D-D) Levels in Both Groups.



[a]$P < .05$.

Abbreviations: D-D, D-dimer.

Figure 5 Plasma Fibrinogen (FIB) Levels in Both Groups.



[a]$P < .05$.

Abbreviations: FIB, fibrinogen.

Table 3. Value of Color Carotid Doppler Ultrasound Combined with Hcy, Cys-C, hsCRP, D-D and FIB in the Diagnosis of AMI

Predictive factor	Area under the curve (AUC)	95% confidence intervals (CI))	Sensitivity	Specificity	*P* value
Hcy	0.820	0.750-0.889	0.772	0.623	<.001
Cys-C	0.780	0.705-0.854	0.754	0.615	<.001
hsCRP	0.838	0.774-0.906	0.789	0.637	<.001
D-D	0.783	0.708-0.849	0.758	0.629	<.001
FIB	0.806	0.716-0.835	0.743	0.518	<.001
Color Carotid Doppler ultrasound	0.856	0.812-0.928	0.808	0.783	<.001
Combination of six	0.908	0.831-0.945	0.919	0.817	<.001

Plasma levels of FIB in both groups

It was indicated in Figure 5 that, the plasma level of FIB in the OG was elevated in comparison with the CG ($P < .05$).

Value of Color Carotid Doppler ultrasound combined with Hcy, Cys-C, hsCRP, D-D and FIB in the diagnosis of AMI

Table 3 showed that the sensitivity and specificity of Color Carotid Doppler ultrasound combined with Hcy, Cys-C, hsCRP, D-D and FIB in the diagnosis of AMI were 0.919 and 0.817 respectively. AUC=0.908, significantly higher than that predicted by alone ($P < .001$).

DISCUSSION

Cerebral infarction is mainly due to cerebral blood supply disorders, leading to brain tissue hypoxia, and blood oxygen performance, causing brain softening.[22] In the early stage, the lipid attachment on the carotid intima forms the localized thickening of the intima, thus the plaque appears.[23] Plaque fibrosis, calcification, and internal echo enhancement are hard masses.[24] There are bleeding manifestations in the plaque, specifically irregular hypoechoic or mixed plaques. Combined with relevant domestic and foreign research literature, it is pointed out that atherosclerosis, especially internal carotid atherosclerosis, is an important cause of cerebral infarction.[25]

This clinical study found that the carotid artery intimal thickness in the OG was relatively elevated relative to the CG, and the lumen diameter was smaller in the OG compared to the CG, which was consistent with previous studies,[26] and further demonstrated that there is a certain internal relationship between the presence of severe irregular carotid plaque and cerebral infarction. Most clinical researchers have pointed out that hypoechoic plaque is the primary influencing factor leading to cerebral infarction and other intracranial ischemic and hypoxic diseases.[27]

Besides, the results of this study showed that the number of carotid plaque formations in the OG was higher than that in the CG. The probability of abnormal blood flow in the OG was higher compared to the CG, which showed that the diagnostic method of carotid Doppler ultrasound can intuitively present the basic situation of carotid artery plaque and artery stenosis in patients, and plays an important role in assessing the risk of cerebral infarction,[28] which was consistent with previous studies.[29] Carotid artery system is an important blood supply artery to the brain, which can supply the nutritional support required for the first 2/3 region of the brain. If the blood vessel wall of the blood supply system is plaque or narrow, it can directly lead to changes in cerebral hemodynamics and increase the risk of cerebral infarction.[30] The above ultrasonic imaging features can be used as important diagnostic indicators in clinic. Compared with health people, patients with cerebral infarction are more prone to carotid artery plaque and neck vascular stenosis.

Hcy is an important intermediate metabolite of cysteine and methionine.[31] Studies have shown that the damage mechanism of the high level of Hcy on vascular endothelial cells is to improve the adhesion and aggregation function of platelets, thereby accelerating atherosclerosis and thrombosis, leading to lumen stenosis or even occlusion, and increasing the risk of cerebrovascular disease.[32] The results of this study showed that the serum Hcy level of the OG was higher relative to the CG. Likewise, many studies have supported that elevated plasma Hcy levels indicate a strong and modifiable risk factor for ischemic stroke.[33] It may be due to that atherosclerosis is an independent risk factor for inducing cardiovascular and cerebrovascular events, and the increase of Hcy level predicts the progression of cerebral infarction.[34] Therefore, Hcy can be used as a reference index of high value in the diagnosis and prediction of short-term prognosis of cerebral infarction, and its mechanism is that Hcy can block NO secretion from endothelial cells, induce continuous contraction of vascular smooth muscle, accelerate the generation of superoxide and peroxide, lead to or exacerbate hypoxia-induced vascular endothelial cell injury, and increase the risk of thrombosis.[35] Hcy damages vascular endothelial cells and stimulates the growth of vascular smooth muscle cells, and the damage caused by both blocks the blood flow pathway.[36] At the same time, Hcy stimulate the proliferation of blood vessels and cardiac smooth muscle cells, and participate in the generation of atherosclerosis.[37]

Cys-C is an inhibitor of cysteine protease, which can be produced by almost all nucleated cells in the body and secreted into the blood continuously, and the concentration in the blood is relatively stable.[38] It freely passes through the glomerular filtration membrane, but almost all of it is reabsorbed and decomposed by the proximal tubule. When the renal function is only mildly damaged, its sensitivity is higher than that of the traditional serum creatinine, and it is a new indicator of renal function.[39] It has been reported that Cys-C is involved in the inflammatory response in the body and the occurrence and development of cardiovascular and cerebrovascular diseases.[40] Other studies have shown that the abnormal increase of Cys-C level is closely related to the occurrence and development of cerebrovascular diseases.[41] The mechanism of serum Cys-C increase is that Cys-C in cerebrospinal fluid of patients with cerebral infarction enters the blood circulation through the blood-brain barrier of the lesion, resulting in the increase of blood Cys-C level. At the same time, cerebral infarction accompanied by brain edema leads to neuro-endocrine disorders, resulting in abnormal renal function, decreased glomerular filtration rate, and decreased blood Cys-C excretion through urine.[42] Cys-C can interfere with the phagocytosis and chemotaxis of granulocytes, promote the release of inflammatory factors, and participate in the occurrence of arteriosclerosis.[43] Previous study has proved that the combination of carotid artery color Doppler ultrasonography with Cys C plasma levels is of great clinical value in the diagnosis and treatment of arteriosclerotic cerebral infarction.[44] Similarly, the results of our research displayed that the serum level of Cys-C in the OG was increased in comparison with the CG, which implied that Cys-C may be involved in vascular injury and inflammatory reaction, participate in the formation of atherosclerosis, and have a close relationship with the occurrence and development of acute cerebral infarction. In line with our finding, a previous study has indicated that the level of Cys-C in patients with lacunar cerebral infarction increases with the aggravation of cognitive impairment, and high Cys-C is an independent risk factor of cognitive impairment in patients with lacunar cerebral infarction.[45]

According to relevant studies, there is a close relationship between the increase of hsCRP level and cerebral infarction, which is mainly manifested in the accelerated release of tissue factors by monocytes, resulting in the disorder of coagulation

and fibrinolysis system of the body.[46] Once the collective inflammatory reaction occurs, hsCRP will activate the complement system, and damage the vascular intima, resulting in atherosclerosis. hsCRP can increase vascular permeability, make vascular smooth muscle sclerosis appear hyperplasia phenomenon, and expand arteriosclerosis plaque, promote white blood cells to release protease, resulting in rupture of thrombus fibrous cap, and then form thrombosis.[47] Patients with cerebral infarction will have a series of changes in coagulation function indicators before thrombosis, including platelets, coagulation, as well as anticoagulation.[48] Consistently, our study found that patients with cerebral infarction harbored higher hsCRP levels than healthy people. In addition, it has been reported that hsCRP level is closely related to the occurrence of cerebral infarction,[49] which supports our findings.

D-D is the fragment produced by the degradation of crosslinked fibrin by the fibrinolytic system, and its production requires two elements, namely, the generation of crosslinked fibrin + the generation of fibrinolytic enzyme.[50] The increase of DD indicates the activation of the coagulation system and secondary fibrinolytic initiation. Plasma D-D level can reflect secondary fibrinolytic function, which can be used as an evaluation index of thrombosis, fibrinolytic enhancement, and thrombolytic therapy effect.[51] Its detection principle is that the anti-D-D monoclonal antibody is coated on the latex particles, and the antigen-antibody reaction occurs when it comes into contact with the plasma D-D, and then the aggregation of latex particles occurs.[52] D-D also activates monocyte to secrete the proinflammatory cytokines such as interleukin-6, and the increased inflammatory response may contribute to the stroke severity and affect the prognosis of cerebral infarction.[21] The results of this study showed that the plasma D-D level of patients in the OG was higher compared to the CG, suggesting the formation and degradation of fibrinogen in patients with cerebral infarction. Consistently, Tomoyuki Ohara et al. have indicated that high D-D levels can also provide clues for the cause of stroke and may be helpful in treatment decision-making of secondary stroke prevention.[53]

FIB is a protein synthesized and secreted by hepatocytes, which is an important coagulation factor in the body and an acute phase response protein.[54] The increase of FIB level is often a nonspecific reaction of the body, which can be increased by inflammation, infection, and trauma. FIB is an important factor contributing to atherosclerosis and plays an important role in the occurrence and development of cerebral infarction.[55] On the one hand, plasma FIB is involved in the whole process of atherosclerosis formation, which can make endothelial cells migrate and degenerate, and can also make smooth muscle cells proliferate and hypertrophy.[56] On the other hand, plasma FIB is an important factor of the blood coagulation system and a cofactor of platelet aggregation. The increase of plasma FIB level can promote the formation of local thrombosis.[57] FIB is involved in the damage of the arterial endothelium and the accumulation of lipids in the intima of the artery, leading to chronic inflammation of the artery wall and the gradual formation of atherosclerosis.[58] However, FIB and its degradation products promote the maintenance of blood hypercoagulability, induce the reversible aggregation of red blood cells, and thus restrict the flow of blood, which is one of the important reasons that eventually lead to the formation of atherosclerosis thrombosis.[59] At the same time, the incidence of plaque rupture is also significantly increased in patients with high plasma FIB level.[60] In line with the above data, our research displayed that the plasma level of FIB in the OG was elevated in comparison with the CG. Moreover, a meta-analysis has indicated that FIB is associated with an increased risk of ischemic stroke,[61] providing evidence to support our results.

In addition, our study indicated that the sensitivity and specificity of Color Carotid Doppler ultrasound combined with Hcy, Cys-C, hsCRP, D-D and FIB in the diagnosis of cerebral infarction were significantly higher than that predicted by alone. It could be seen that the combined diagnosis of cerebral infarction was more effective, and it was speculated that the reason may be related to the fact that the combined diagnosis of the two methods can provide imaging and molecular biological diagnosis results for the clinic at the same time.

Therefore, patients with cerebral infarction had higher carotid artery intimal thickness, lower lumen diameter, higher number of carotid plaque formations, higher probability of abnormal blood flow, as well as incrased levels of Hcy, Cys-C, hsCRP, D-D and FIB. Color Carotid Doppler ultrasound provides important help for clinical diagnosis and screening of cerebral infarction, but in the case of non-transmural cerebral infarction, Color Carotid Doppler ultrasound cannot clearly show dysmokinesis of the ventricular wall, and a definitive diagnosis cannot be made for small infarcts. The combination of Color Carotid Doppler ultrasound and Hcy, Cys-C, hsCRP, D-D and FIB can greatly improve the specificity and accuracy of single diagnosis.

However, the shortcomings of this study lie in the small sample size and limited sample sources, which may lead to certain selection bias. Therefore, the diagnostic value of Carotid Doppler ultrasound combined with Hcy, Cys-C, hsCRP, D-D and FIB in patients with cerebral infarction still needs to be further verified by large-scale sample studies in the future. Our study will further investigate the relation between Carotid Doppler ultrasound combined with Hcy, Cys-C, hsCRP, D-D and FIB and the prognosis of cerebral infarction patients.

CONCLUSIONS

Carotid Doppler ultrasound combined with cysteine, D dimer, and other indexes played an important role in the clinical diagnosis of cerebral infarction, which was worthy of promotion.

DATA AVAILABILITY STATEMENT

Original data from this study is available from the corresponding author upon reasonable request.

AUTHORS' DISCLOSURE STATEMENT

All authors declare that they have no conflicts of interest related to the study.

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