RESEARCH ARTICLE

Serum lipoprotein and RBC rigidity index to predict cerebral infarction in patients with carotid artery stenosis

Zhiwu Dong¹ | Qiang Guo² | Li Sun¹ | Feifei Li¹ | Aihong Zhao¹ | Jingfan Liu¹ |
Peipei Qu¹ | Qinghua Zhu¹ | Chunhai Xiao¹ | Fusheng Niu³ | Shuang Liang¹

¹Department of Laboratory Medicine, Jinshan Branch of Shanghai 6th People's Hospital Affiliated to Shanghai Jiaotong University, Shanghai, China

²Department of Ultrasound Medicine, Jinshan Branch of Shanghai 6th People's Hospital Affiliated to Shanghai Jiaotong University, Shanghai, China

³Department of Neurology, Jinshan Branch of Shanghai 6th People's Hospital Affiliated to Shanghai Jiaotong University, Shanghai, China

Correspondence

Zhiwu Dong, Department of Laboratory medicine, Jinshan Branch of Shanghai 6th People's Hospital Affiliated to Shanghai Jiaotong University, Shanghai, China.
Email: dongzw312@163.com

Funding information

the Shanghai Municipal Health and Family Planning Commission

Objective: This study aims to determine the risk factors and to predict the occurrence of cerebral infarction in patients with carotid artery stenosis.

Methods: Two hundred and one subjects with carotid artery stenosis were retrospectively selected from Jinshan Branch of Shanghai Sixth People's Hospital, 115 cases of which with cerebral infarction and 86 without it. Clinical tests were performed including coagulation indices, fasting glucose, serum lipid, and blood rheology. Logistic regression analyses were used to identify the risk factors. Regression model was established, and receiver operating characteristic (ROC) curve was applied to analyze its diagnostic value.

Results: Our data indicated that apolipoprotein AI (OR = 0.051, 95% CI: 0.009-0.295), lipoprotein (a) (OR = 1.003, 95% CI: 1.001-1.005), and RBC rigidity index (OR = 0.383, 95% CI: 0.209-0.702) were independent risk factors. Area under the curve (AUC) of the regression model = 0.78, with the sensitivity of 73.9% (95% CI: 64.9%-81.7%) and specificity of 69.2% (95% CI: 52.4%-83.0%). Prediction probability was determined while logistic regression score >0.748 defaulted as high-risk status. High-risk ratios were 80% in progressive cerebral infarction and 72% in nonprogressive cerebral infarction ($P > .05$), respectively, while significant differences were found when both compared with controls ($P < .001$).

Conclusions: We show herein that the regression model based on apolipoprotein AI, lipoprotein (a), and RBC IR is a promising tool to predict the occurrence of cerebral infarction in patients with carotid artery stenosis. However, identification of novel diagnostic markers for progressive cerebral infarction is still necessary.

KEYWORDS

apolipoprotein AI, blood rheology, cerebral infarction, lipoprotein (a), logistic regression analysis

1 | INTRODUCTION

The elderly are susceptible to a variety of cerebrovascular diseases. With the growing of the aging population in China, the incidence of the diseases has gradually increased, especially cerebral infarction, with high morbidity and mortality. The onset of ischemic cerebral infarction mainly attributes to a series of blood circulation disorders, leading to cerebral ischemic necrosis or brain tissue softening. Once

the ischemic cerebral infarction occurs, it develops rapidly and causes serious consequences if without timely and effective treatments. Although computed tomography (CT) and magnetic resonance image (MRI) have relatively high diagnostic values in cerebral infarction, the application of serological indicators is still an ideal approach for its prediction and diagnosis.^{1,2}

Lipid consists of a group of natural biological molecules that are soluble in nonpolar solvents but not in water, such as fatty acids,

triacylglycerols, cholesterol, sphingolipids, phospholipids, and glycolipids. Lipid metabolism is the process of degradation and synthesis of lipids that make energy and produce structural or functional small molecules. Abnormal lipid metabolism frequently appears in a variety of vascular diseases which cause severe adverse outcomes or even prove fatal. Atherosclerosis is the most common risk factor in ischemic cerebral infarction, and abnormal lipid metabolism is closely associated with atherosclerosis.³ Apolipoprotein AI (apo AI) is the main carrier protein of high-density lipoprotein (HDL) that generally plays a key role for lowering blood lipid. A recent study reported that apo AI showed a lower level in patients with cerebral infarction compared with controls or even hemorrhagic stroke.⁴ HDL is usually recognized as a negative risk factor for cerebral infarction. HDL particles from stroke patients tend to have a larger volume, which contain significantly less apo AI.⁵ Low-density lipoprotein (LDL) can transport various lipid molecules, such as cholesterol, phospholipids, and triglycerides into endothelium, attracting macrophages and triggering atherosclerosis. Thus, high level of LDL is strongly associated with the increasing incidence of atherosclerosis. Lipoprotein (a) (Lp(a)) is a cholesterol-rich plasma lipoprotein that is similar to LDL including its roles. Many studies have shown that the elevation of Lp(a) is an important clue for the incidence of atherosclerosis and also the independent risk factor of cerebral infarction.⁶ Furthermore, serum Lp(a) from patients with cerebral infarction showed significantly higher level than those with cerebral hemorrhage.⁷ A previous study demonstrated that Lp(a) is associated with the incidence of some asymptomatic cerebral infarctions.⁸ Therefore, changes in blood lipid and lipoprotein levels are key events for the incidence of cerebrovascular diseases. The detection of relevant indices in aging population may benefit its early diagnosis and treatments.

Blood rheology is a discipline dedicated to evaluating the macroscopic blood flow properties that have been applied in the monitoring of cerebrovascular diseases. On account of the high incidence of vascular endothelial cell damage⁹ and the decrease in fibrinolytic activity, the abnormal blood rheology plays an important role in the onset and progression of cerebral infarction. Blood components including red blood cell (RBC), platelet (PLT), and fibrinogen (FIB) and their interactions contribute to the determination of the whole blood viscosity. Increased level of blood viscosity, one of the major indices in blood rheology, serves as a risk factor for cerebrovascular events.¹⁰⁻¹²

In this study, we identified the risk factors and established a predictive model for the early diagnosis of cerebral infarction in patients with carotid artery stenosis to improve its prevention and treatments.

2 | MATERIALS AND METHODS

2.1 | Study population

Two hundred and one patients with carotid artery stenosis (stenosis degree $\geq 30\%$ but not carotid occlusion) in Jinshan Branch of Shanghai 6th People's Hospital were enrolled in the study. One hundred and fifteen patients suffered from cerebral infarction, of which 45 cases with progressive cerebral infarction. Eighty-six noncerebral infarction patients with matched ages and related basic diseases during the

same time period were collected as controls. Inclusion criteria of the cerebral infarction group were as follows: (1) patients with ischemic cerebral infarction or cerebral infarction confirmed by clinical neurological examination or imaging diagnosis via CT or MRI with the diagnosis according to the World Health Organization criteria,¹³ excluding cerebral infarction caused by cardiogenic cerebral embolism, cerebral arteritis, and other causes, and (2) patients who had not taken any blood rheology or coagulation-related drugs within the prior 24 hours. The definition of progressive cerebral infarction was cerebral infarction with 48 hours or a week of progressive worsening in the course of conventional antithrombotic therapy. Exclusion criteria were patients with (1) malignant tumors; (2) a history of severe heart disease combined with cardiac infarction; (3) other severe liver and kidney dysfunctions; (4) cerebral hemorrhage; and (5) no history of cerebral infarction. Inclusion criteria of the control group were patients without a significant history of cerebrovascular diseases and with an imaging examination to exclude cerebral infarction.

2.2 | Ethical approval

We have complied with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects. The study protocol was approved by the Ethics Committee of Jinshan Branch of Shanghai 6th People's Hospital affiliated to Shanghai Jiaotong University. We have obtained informed consent from all the participants.

2.3 | Ultrasound examination

Ultrasound examinations were performed on the patients during hospitalization using S2000 system (Siemens Medical Solutions, Mountain View, CA, USA) equipped with a linear-array transducer of 5-12 MHz by 3 experienced ultrasound technicians (>3 years of experience in vascular ultrasound). The patients underwent ultrasound measurement including the left and right common carotid arteries, bifurcations, and internal carotid arteries. Diagnosis of carotid artery stenosis was determined by criteria recommended by the North American Society of Radiologists.¹⁴

2.4 | Clinical laboratory tests

Fasting venous blood sample (4 mL) was collected from the patients in the morning after being admitted in our hospital (before treatment) and the outpatients in the control group, followed by centrifuging at 1200 g for 10 minutes to collect the serum. The isolated serum was examined by ADVIA 2400 automatic biochemical analyzer (Siemens, Erlangen, Germany) to determine the fasting glucose (GLU, mmol/L) and lipid levels, including apo AI (g/L), apo B, (g/L), Lp(a) (mg/L), total cholesterol (TC, mmol/L), triglyceride (TG, mmol/L), low-density lipoprotein cholesterol (LDL-C, mmol/L), and high-density lipoprotein cholesterol (HDL-C, mmol/L). Five milliliters of heparin anticoagulant blood samples of each patient were used to detect hemodynamic parameters, including corrected whole blood viscosity at low/high shear

rate, whole blood viscosity at high shear rate (shear rates at 1 s, 5 s, 50 s, and 200 s, respectively), red blood cell (RBC) deformity index, RBC rigidity index (IR), RBC aggregation index, Casson's viscosity, and plasma viscosity using SA-6000 blood rheology analyzer (Succeeder, Beijing, China). Westergren's method was adopted to determine the erythrocyte sedimentation rate (ESR). Two milliliters of sodium citrate anticoagulant blood samples were centrifuged at 3000 rpm for 10 minutes, followed by detection of the coagulation indices (prothrombin time (PT, s), activated partial thromboplastin time (APTT, s), thrombin time (TT, s), D-dimer (DD, mg/L), and fibrinogen (FIB, g/L)) with the SYSMEX CA7000 coagulation analyzer (Sysmex, Kobe, Japan). All of the tests were strictly performed in accordance with the manufacturer's instructions as well as the clinical standard operating procedures (SOP).

2.5 | Statistical analysis

SPSS 19.0 software (SPSS Inc., Chicago, IL) was applied for the statistical analysis. Normally distributed data confirmed by the normality test are presented as mean $\pm$ standard deviation. Non-normally distributed data are presented using the median and quartile. Independent *t* test was used to compare the differences between 2 groups. Analysis of variance or a nonparametric test was used to compare the differences in multiple groups. Chi-square test or exact probability test was adopted for rate comparison. Logistic regression analysis was to study diagnosis-related factors in the study. $P < .05$ was considered to be a significant difference.

3 | RESULTS

3.1 | General information about the included patients

The mean ages of the patients in the control group and the cerebral infarction group were 71.86 ± 9.01 and 72.23 ± 9.47 years old, respectively, with no significant difference between the 2 groups ($P = .827$). The male-to-female ratios of the control and cerebral infarction groups were 59:27 and 89:26, respectively ($P = .162$). Hypertension and diabetes mellitus were found in 18 cases (15.6%) and 24 cases (20.8%) in cerebral infarction group, and they emerged in 13 cases (15.1%) and 20 cases (23.6%) in control group, respectively. There was

no significant difference between the 2 groups in respect of health risk behaviors (smoking and alcohol drinking) and concurrent diseases including diabetes, hypertension, and pulmonary disease as shown in Table 1 ($P > .05$).

3.2 | Establishment of the diagnostic model for cerebral infarction

Patients with nonprogressive cerebral infarction and progressive cerebral infarction were recruited in the cerebral infarction group, while patients without cerebral infarction were categorized into the control group. Univariate analysis was performed, and the results showed that apo AI, Lp(a), RBC deformity index, RBC rigidity index, corrected whole blood viscosity (WBV) at high shear rate, and whole blood shear rate (WBSR) at 200 s were significantly different between the 2 groups ($P < .05$). There was no significant difference between the groups concerning fasting glucose, coagulation indices, apo B, HDL-C, LDL-C, TC, TG, and ESR, nor in other hemodynamic parameters ($P > .05$). Multivariate logistic regression analysis showed significant differences ($P < .05$) regarding apo AI (OR = 0.051, 95% CI: 0.009-0.295), Lp (a) (OR = 1.003, 95% CI: 1.001-1.005), and RBC IR (OR = 1.383, 95% CI: 1.209-1.702), suggesting that the 3 indicators could be used as independent risk factors for the prediction of cerebral infarction (Table 2). Subsequently, based on the results of logistic regression analysis, the diagnostic model equation for the cerebral infarction was proposed to calculate the predictive probability of each patient.

$$\text{logit}(p) = 0.003 \times [\text{Lp(a)}] + 0.970 \times \text{IR} - 2.967 \times [\text{apo AI}]$$

3.3 | Accuracy analysis of the regression model in the diagnosis of cerebral infarction

The receiver operating characteristic (ROC) curves of the regression model and independent indexes were drawn for the prediction of cerebral infarction. The areas under the curves (AUCs) of RBC IR, apo AI, and Lp(a) were 0.68, 0.71, and 0.61, respectively, which were lower than the established regression model score (LR): AUC = 0.782 (95% CI: 0.704-0.860) with better prediction results (Figure 1). According to the cutoff values, $\text{LR} > 0.748$, RBC

TABLE 1 Basic characteristics of the 2 groups of the subjects

	Control group (n = 86)	CI group (n = 115)	Statistic t/X ²	P
Age (y)	71.86 $\pm$ 9.01	72.23 $\pm$ 9.47	0.219	.827
Sex (male/female)	59/27	89/26	1.957	.162
Smoking	15 (17.4%)	26 (22.6%)	0.809	.368
Alcohol drinking	12 (13.9%)	17 (14.7%)	0.027	.869
Diabetes	20 (23.3%)	24 (20.8%)	0.164	.686
Hypertension	13 (15.1%)	18 (15.6%)	0.011	.917
Pulmonary disease	4 (5.1%)	13 (11.3%)	0.081	.776

CI, cerebral infarction.

Clinical indices	Univariate analysis		Multivariate analysis		
	P	OR (95% CI)	B	P	OR (95% CI)
Age (year)	.826	0.995 (0.956-1.036)			
Sex	.309	1.521 (0.678-3.414)			
D-dimer	.542	1.315 (0.545-3.169)			
Prothrombin time	.053	1.713 (0.992-2.959)			
Fibrinogen	.535	1.140 (0.753-1.728)			
Fasting glucose	.494	0.947 (0.812-1.106)			
Apolipoprotein AI	<.001	0.040 (0.007-0.210)	-2.967	.001	0.051 (0.009-0.295)
Apolipoprotein B	.401	0.519 (0.112-2.400)			
Lipoprotein a	.034	1.002 (1.000-1.005)	0.003	.046	1.003 (1.001-1.005)
Low-density lipoprotein	.384	1.200 (0.796-1.809)			
High-density lipoprotein	.12	0.399 (0.125-1.271)			
Total cholesterol	.201	0.792 (0.554-1.132)			
Total triglycerides	.074	0.773 (0.582-1.026)			
RBC deformity index	.004	1.001 (1.001-1.128)	-		
RBC rigidity index	.001	1.393 (0.230-1.672)	0.97	.002	1.383 (1.209-1.702)
RBC aggregation index	.216	1.429 (0.812-2.514)			
Casson's viscosity	.711	0.854 (0.372-1.963)			
Corrected WBV at low shear rate	.551	0.984 (0.935-1.037)			
Corrected WBV at high shear rate	.007	0.552 (0.357-0.852)	-		
WBSR at 1 s	.447	0.953 (0.841-1.079)			
WBSR at 5 s	.102	0.755 (0.539-1.058)			
WBSR at 50 s	.177	0.618 (0.307-1.243)			
WBSR at 200 s	.041	0.413 (0.177-0.963)	-		
ESR	.273	0.983 (0.952-1.014)			
K value of ESR equation	.117	0.987 (0.971-1.003)			
Plasma viscosity	.255	7.612 (0.230-251.663)			

ESR, erythrocyte sedimentation rate; CI, confidence interval; OR, odd ratio; WBSR, whole blood shear rate; WBV, whole blood viscosity.

TABLE 2 Logistic regression analysis of risk factors for the incidence of cerebral infarction

IR > 4.239, apo AI < 1.36, and Lp(a) > 320.2 used as positive predictive values for the incidence of cerebral infarction, the sensitivity and specificity of the LR score were 73.9% (95% CI: 64.9%-81.7%) and 69.2% (95% CI: 52.4%-83.0%), respectively; the sensitivity and specificity for RBC IR, apo AI, and Lp(a) were 60.9% (95% CI: 51.3%-69.8%) and 71.8% (95% CI: 55.1%-85.0%), 84.4% (95% CI: 76.4%-90.5%) and 51.3% (95% CI: 34.8%-67.6%), and 33.9% (95% CI: 25.3%-43.3%) and 89.7% (95% CI: 75.8%-97.1%), respectively. The sum of sensitivity and specificity for LR was higher than the other 3 indicators, although apo AI had a better sensitivity and negative prediction value 52.6% (95% CI: 35.8%-69.0%) and Lp(a) possessed a better specificity and positive prediction value 90.7% (95% CI: 77.9%-97.4%) (Table 3).

3.4 | Role of the regression model in distinguishing cerebral infarction and progressive cerebral infarction

According to the positive cutoff values of the above indicators, the high-risk ratio of each patient at different stages of cerebral infarction was calculated. Among them, the high-risk ratio of the patients with nonprogressive cerebral infarction (72%) was lower than that of the patients with progressive cerebral infarction (80%), but there was no significant difference ($P > .05$); however, the high-risk ratios of these 2 groups were much higher than the control group (30.8%) ($P < .05$). Although apo AI exhibited the highest positive rates and Lp(a) the lowest positive rates among the 4 groups, LR score manifested the largest gap between progressive or nonprogressive cerebral infarction and

FIGURE 1 ROC curves of the established regression model, RBC IR, apo AI, and Lp(a). (A) ROC curve of the regression model: AUC = 0.782 (95% CI: 0.704-0.860); (B) ROC curve of RBC IR: AUC = 0.68 (95% CI: 0.58-0.77); (C) ROC curve of apo AI: AUC = 0.71 (95% CI: 0.61-0.81); and (D), ROC curve of Lp(a): AUC = 0.61 (95% CI: 0.51-0.71). The regression model shows a larger AUC than RBC IR, apo AI, and Lp(a)

TABLE 3 Accuracy analysis of regression model and 3 indices for the diagnosis of cerebral infarction

Variable	Regression model (LR)	RBC IR	Apo AI	Lp (a)
AUC (95% CI)	0.78 (0.704-0.86)	0.68 (0.58-0.77)	0.71 (0.61-0.81)	0.61 (0.51-0.71)
Cutoff value	>0.748	>4.239	<1.36	>320.2
Sensitivity (95% CI)	73.9 (64.9-81.7)	60.9 (51.3-69.8)	84.4 (76.4-90.5)	33.9 (25.3-43.3)
Specificity (95% CI)	69.2 (52.4-83.0)	71.8 (55.1-85.0)	51.3 (34.8-67.6)	89.7 (75.8-97.1)
Positive prediction (95% CI)	87.6 (79.4-93.4)	86.4 (77.0-93.0)	83.6 (75.6-89.8)	90.7 (77.9-97.4)
Negative prediction (95% CI)	47.4 (34.0-61.0)	38.4 (27.2-50.5)	52.6 (35.8-69.0)	31.5 (23.0-41.0)
Youden J	0.431	0.327	0.356	0.237

Youden J, Youden's index; AUC, area under the curve.

the control subjects, suggesting a promising clinical diagnostic value for the regression model. The comparison of the positive rates of the indicators was shown in Figure 2.

4 | DISCUSSION

Circulating lipid and lipoproteins are extensively employed for prediction of the occurrence, development, and even transformation of

cerebral infarction.^{15,16} In this study, the univariate analysis showed no significant difference concerning HDL and LDL between cerebral infarction and the control group, implying that apo AI and Lp(a) might be more sensitive in the diagnose of cerebral infarction. Generally speaking, HDL particles are recognized as the good guy, while LDLs the bad for their opposite roles in the delivery of fat molecules. Interestingly, a recent report demonstrated that patients with ischemic stroke benefited from hyperlipidemia (fasting low-density lipoprotein cholesterol (LDL-C) level > 100 mg/dL (2.6 mmol/L), or >70 mg/dL (1.82 mmol/L)

FIGURE 2 Comparison of the positive rates of LR score, RBC IR, apo AI, and Lp(a) in the nonprogressive cerebral infarction, progressive cerebral infarction, and control groups. According to the cutoff values, LR > 0.748, RBC IR > 4.239, apo AI < 1.36, and Lp(a) > 320.2 as positive predictive values, the positive rate of high-risk ratio in the patients at different statuses of cerebral infarction was calculated. Among them, the positive rate of LR in patients with nonprogressive cerebral infarction (72%) was lower than the patients with progressive cerebral infarction (80%) to a certain extent, but no significant difference was found between them ($P > .05$). The positive rates of these 2 groups were much higher than the control (30.8%, $P < .05$). Among the 4 groups, apo AI presented the highest positive rates and Lp(a) had the lowest positive rates. Compared with the control subjects, the difference of LR scores was the largest in both progressive and nonprogressive cerebral infarction group. *** represents the comparison with the control group (cerebral infarction group vs control group; and progressive cerebral infarction group vs control group, $P < .001$)

with diabetes, heart disease, or other vascular disease) with a significantly lower mortality rate.¹⁷ Moreover, after acute cerebral infarction, low level of LDL-C predicted the increased rate of hemorrhagic transformation.¹⁵ Intriguingly, higher total cholesterol level presages a lower risk of death after acute ischemic stroke.¹⁸ Dependency and recurrence rates were significantly higher in the patients with lower TC (<4.07 mmol/L) than those with higher TC group.¹⁹ These data challenge the traditional point of views from many of the biologists and physicians. The unexpected role of the evildoers needs further investigations.

Studies on the changes in blood rheology in patients with cerebral infarction are also worthy of attention. Ten related studies have reported different degrees of changes in blood rheology related indicators in patients with cerebrovascular disorders. The blood rheological properties including enhanced whole blood viscosity, elevated erythrocyte aggregability, and decreased deformability were observed in patients with stroke compared to the healthy group.²⁰ During the ischemic cerebral infarction, RBCs encounter metabolic changes as well as the ultrastructural and morphologic alteration, leading to the accumulation of codocytes, stomatocytes, and echinocytes.²¹ Intriguingly, abnormal fibrin fibers and dense matted deposits (DMDs) tended to appear during thrombotic events, which are particularly resistant to fibrinolytic degradation. Under the scenario, RBCs change their shape and associate with the fibrin fibers, forming highly resistant clots that partially or entirely block the blood vessels.²²

The results of the multivariate analysis showed that RBC IR could be used as the independent risk factor for predicting the incidence of cerebral infarction. RBC IR is the main factor that affects RBC deformity, which indicates the RBC deformability in whole blood at a high shear state. Notably, hyperlipidemia can increase the area of the RBC membrane, thereby reducing the membrane mobility and RBC deformity to increase RBC IR,²³ undoubtedly leading to the onset of cerebral infarction. It was also reported that hyperlipidemia caused an increase in RBC osmotic fragility and decrease in their membrane elasticity compared with controls in high-fat diet rabbits.²⁴ Thus, blood rheology indicators could be used as important measurements for patients with cerebral infarction.

Numerous studies on the diagnosis of cerebral infarction have been conducted in recent years, mainly regarding blood coagulation,²⁵ blood lipid index,² blood rheology indices,²⁶ protein,²⁷ and cytokines.²⁸ However, few reports discussed the prediction models of cerebral infarction. In this study, we retrospectively analyzed blood rheology and blood lipid-related indicators. The data indicated that apo AI, Lp(a), and RBC IR were the risk factors of cerebral infarction. A regression model associated with these tests presented a preferable predictive and diagnostic value for cerebral infarction. This finding may promote the corresponding clinical research.

In addition, many studies have shown that hypertension,^{29,30} diabetes,^{31,32} and other abnormal metabolism conditions are risk factors for patients with cerebral infarction. Most of the studies selected healthy volunteers as their controls, whereas we matched the relevant information in the control group before establishing the predictive model in this study to enhance the practicability of the model. Moreover, this study also focused on progressive cerebral infarction. Although the positivity varied in our model, it did not distinguish the progressive from nonprogressive cerebral infarction. More researches are required for identifying specific circulating biomarkers.

5 | CONCLUSION

Apo AI, Lp (a), and RBC IR were risk factors for the occurrence of cerebral infarction in patients with carotid artery stenosis. The regression model based on the indices represents high values of area under the curve (AUC), sensitivity, and specificity. The results highlighted a role for lipid metabolism and RBC deformability in the pathogenesis of cerebral infarction.

ACKNOWLEDGMENTS

This work was supported by grants from the Shanghai Municipal Health and Family Planning Commission (No. 20134240, No. 201640131).

ORCID

Zhiwu Dong <http://orcid.org/0000-0002-3792-9556>

REFERENCES

- Dong XL, Xu SJ, Zhang L, et al. Serum resistin levels may contribute to an increased risk of acute cerebral infarction. *Mol Neurobiol*. 2017;54:1919-1926.
- Ikeda K, Sawada M, Morioka H, et al. Clinical profile and changes of serum lipid levels in epileptic patients after cerebral infarction. *J Stroke Cerebrovasc Dis*. 2017;26:644-649.
- Zhou G, Li M, Zhu Y, Zhao J, Lu H. Cerebral venous sinus thrombosis involving the straight sinus may result in infarction and/or hemorrhage. *Eur Neurol*. 2016;75:257-262.
- Walsh KB, Hart K, Roll S, et al. Apolipoprotein A-I and paraoxonase-1 are potential blood biomarkers for ischemic stroke diagnosis. *J Stroke Cerebrovasc Dis*. 2016;25:1360-1365.
- Ortiz-Munoz G, Couret D, Lapergue B, et al. Dysfunctional HDL in acute stroke. *Atherosclerosis*. 2016;253:75-80.
- Tascilar N, Dursun A, Ankarali H, et al. Relationship of apoE polymorphism with lipoprotein(a), apoA, apoB and lipid levels in atherosclerotic infarct. *J Neurol Sci*. 2009;277:17-21.
- Wang D, Hu J, Ma Q, Ma J, Liu B. Correlation between biochemical indicators of blood lipid with cerebral vascular diseases. *Int J Clin Exp Pathol*. 2015;8:3022-3026.
- Fukunaga N, Anan F, Kaneda K, Nawata T, Saikawa T, Yoshimatsu H. Lipoprotein (a) as a risk factor for silent cerebral infarction in hemodialysis patients. *Metabolism*. 2008;57:1323-1327.
- Chen Y, Ge JW, Deng BX [A new rat model of cerebral infarction based on the injury of vascular endothelial cell]. *Chin J Integr Med*. 2005;11:195-200.
- Li RY, Cao ZG, Li Y, Wang RT. Increased whole blood viscosity is associated with silent cerebral infarction. *Clin Hemorheol Microcirc*. 2015;59:301-307.
- Furukawa K, Abumiya T, Sakai K, et al. Increased blood viscosity in ischemic stroke patients with small artery occlusion measured by an electromagnetic spinning sphere viscometer. *J Stroke Cerebrovasc Dis*. 2016;25:2762-2769.
- Song SH, Kim JH, Lee JH, Yun YM, Choi DH, Kim HY. Elevated blood viscosity is associated with cerebral small vessel disease in patients with acute ischemic stroke. *BMC Neurol*. 2017;17:20.
- Stroke-1989. Recommendations on stroke prevention, diagnosis, and therapy. Report of the WHO Task Force on Stroke and other Cerebrovascular Disorders. *Stroke*. 1989;20:1407-1431.
- Grant EG, Benson CB, Moneta GL, et al. Carotid artery stenosis: gray-scale and Doppler US diagnosis—Society of Radiologists in Ultrasound Consensus Conference. *Radiology*. 2003;229:340-346.
- Yang N, Lin M, Wang BG, et al. Low level of low-density lipoprotein cholesterol is related with increased hemorrhagic transformation after acute ischemic cerebral infarction. *Eur Rev Med Pharmacol Sci*. 2016;20:673-678.
- Xu T, Zhong C, Peng Y, et al. Serum 25-hydroxyvitamin D deficiency predicts poor outcome amongst acute ischaemic stroke patients with low high density lipoprotein cholesterol. *Eur J Neurol*. 2016;23:1763-1768.
- Yeramaneni S, Kleindorfer DO, Sucharew H, et al. Hyperlipidemia is associated with lower risk of poststroke mortality independent of statin use: A population-based study. *Int J Stroke*. 2017;12:152-160.
- Markaki I, Nilsson U, Kostulas K, Sjostrand C. High cholesterol levels are associated with improved long-term survival after acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2014;23:e47-e53.
- Zhao W, An Z, Hong Y, et al. Low total cholesterol level is the independent predictor of poor outcomes in patients with acute ischemic stroke: a hospital-based prospective study. *BMC Neurol*. 2016;16:36.
- Tikhomirova IA, Oslyakova AO, Mikhailova SG. Microcirculation and blood rheology in patients with cerebrovascular disorders. *Clin Hemorheol Microcirc*. 2011;49:295-305.
- Swanepoel AC, Pretorius E. Scanning electron microscopy analysis of erythrocytes in thromboembolic ischemic stroke. *Int J Lab Hematol*. 2012;34:185-191.
- Pretorius E, Lipinski B. Thromboembolic ischemic stroke changes red blood cell morphology. *Cardiovasc Pathol*. 2013;22:241-242.
- Radosinska J, Vrbjar N. The role of red blood cell deformability and Na, K-ATPase function in selected risk factors of cardiovascular diseases in humans: focus on hypertension, diabetes mellitus and hypercholesterolemia. *Physiol Res*. 2016;65(Suppl 1):S43-S54.
- Abdelhalim MA, Moussa SA. Biochemical changes of hemoglobin and osmotic fragility of red blood cells in high fat diet rabbits. *Pak J Biol Sci*. 2010;13:73-77.
- Shi D, Xia T, Feng H, Cheng Q. Evaluating the diagnostic value of vWF:Ag, D-D and FDP in patients with acute cerebral infarction using ROC curves. *Exp Ther Med*. 2014;7:1573-1577.
- Mercuri M, Ciuffetti G, Robinson M, Toole J. Blood cell rheology in acute cerebral infarction. *Stroke*. 1989;20:959-962.
- Luger S, Witsch J, Dietz A, et al. Glial fibrillary acidic protein serum levels distinguish between intracerebral hemorrhage and cerebral ischemia in the early phase of stroke. *Clin Chem*. 2017;63:377-385.
- Qian L, Yuanshao L, Wensi H, et al. Serum IL-33 Is a novel diagnostic and prognostic biomarker in acute ischemic stroke. *Aging Dis*. 2016;7:614-622.
- Wang Y, Xu J, Zhao X, et al. Association of hypertension with stroke recurrence depends on ischemic stroke subtype. *Stroke*. 2013;44:1232-1237.
- Gorgui J, Gorshkov M, Khan N, Daskalopoulou SS. Hypertension as a risk factor for ischemic stroke in women. *Can J Cardiol*. 2014;30:774-782.
- Arboix A, Rivas A, Garcia-Eroles L, de Marcos L, Massons J, Oliveres M. Cerebral infarction in diabetes: clinical pattern, stroke subtypes, and predictors of in-hospital mortality. *BMC Neurol*. 2005;5:9.
- Tziomalos K, Spanou M, Bouziana SD, et al. Type 2 diabetes is associated with a worse functional outcome of ischemic stroke. *World J Diabetes*. 2014;5:939-944.

How to cite this article: Dong Z, Guo Q, Sun L, et al. Serum lipoprotein and RBC rigidity index to predict cerebral infarction in patients with carotid artery stenosis. *J Clin Lab Anal*. 2018;32:e22356. <https://doi.org/10.1002/jcla.22356>