ACTA ABP BIOCHIMICA POLONICA

Vol. 70, No 4/2023
911–917
https://doi.org/10.18388/abp.2020_6817

Regular paper

Value evaluation of serum (sdLDLc*HCYc)/HDLc ratio in the stability of intracranial arterial plaques in patients with acute cerebral infarction

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Background: We aimed to analyze the value of serum (sdLDLc*HCYc)/HDLc ratio in the stability of intracranial arterial plaques among patients with acute cerebral infarction. **Methods:** A retrospective analysis was conducted on 140 patients with acute cerebral infarction admitted to the neurology department and 101 healthy individuals for regular examinations in our hospital from 2013 to 2019, who were respectively allocated into the study group and the control group. Participants in both groups were measured for serum sdLDLc, HDLc, and HCYc using peroxidase method, enzyme-linked immunosorbent assay, and enzyme method, respectively. The laboratory indexes of the two groups were compared. The multivariate logistic regression analysis was done to analyze the influencing factors of the stability of intracranial artery plaque in patients with acute cerebral infarction. The value of high-density lipoprotein cholesterol (HDL-C), homocysteine, sdLDLc, (sdLDLc*HCYc)/HDLc in diagnosing the stability of intracranial artery plaque was also evaluated in patients with acute cerebral infarction. **Results:** There was no distinct difference in height, hypertension, diabetes, coronary heart disease, smoking history and drinking history between the two groups (P>0.05). The study group showed statistically significant differences in age, gender, weight, and BMI (P<0.05). The current study demonstrated no statistical difference in the levels of TG, low-density lipoprotein cholesterol (LDL-C), α-lipoprotein, and HCYc between the two groups (P>0.05). However, the levels of TC, HDL-C, sdLDLc, (sdLDLc*HCYc)/HDLc in the study group were significantly different when comparing with the control group (P<0.05). No statistically significant difference was found in the levels of TG, triglycerides, LDL-C, α-lipoprotein, and HCYc among patients with different degrees of stenosis in the study group (P>0.05). The level of HDL-C was significantly lower in cases of severe stenosis compared to no stenosis, mild stenosis and moderate stenosis, with severe stenosis showing the lowest levels; mild stenosis had lower levels than no stenosis, while moderate stenosis had lower levels than both no stenosis and mild stenosis (P<0.05). The levels of sdLDLc, (sdLDLc*HCYc)/HDLc exhibited a significant increase in cases of severe stenosis as compared tono stenosis, mild stenosis, and moderate stenosis. Furthermore, the levels of sdLDLc, (sdLDLc*HCYc)/HDLc were found to be higher in moderate stenosis as compared to no stenosis and mild stenosis. Similarly, the levels of sdLDLc, (sdLDLc*HCYc)/HDLc were observed to be higher in mild stenosis than no stenosis (P<0.05).The independent variables were set as the indicators with difference in single factor comparison, including age, gender, BMI, TC, LDL-C, HDL-C, HCYc, sdLDLc, (sdLDLc*HCYc)/HDLc. The dependent variable was the stability of intracranial artery plaque in patients with acute cerebral infarction. After variable selection, the results showed that the factors influencing the stability of intracranial artery plaque in patients with acute cerebral infarction were age, BMI, (sdLDLc*HCYc)/HDLc. The degree of plaque enhancement was used as a criterion to reflect the stability of plaque. ROC curve analysis showed that (sdLDLc*HCYc)/HDLc had a higher evaluation value for the stability of intracranial artery plaque than HDL-C, homocysteine, and sdLDLc in patients with acute cerebral infarction. **Conclusion:** The serum (sdLDLc*HCYc)/HDLc ratio was found to have potential in evaluating the stability of intracranial arterial plaques in patients with acute cerebral infarction.

Keywords: sdLDLc, HDLc, HCYc, acute cerebral infarction, stability of intracranial arterial plaques

Received: 25 April, 2023; revised: 29 July, 2023; accepted: 16 October, 2023; available on-line: 07 December, 2023

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Acknowledgements of Financial Support: This study was funded by Government-funded clinical excellence program (NO. ZF2023186).

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; sdLDLc, (sdLDLc*HCYc)/HDLc

INTRODUCTION

Currently, acute ischemic cerebral infarction stands as the most prevalent type of stroke, comprising over 75% of all stroke cases. This condition exhibits alarmingly high incidence and disability rates, and is prone to causing neurological function loss, thereby impinging not only upon daily quality of life of patients, but also their life safety (Edwards & Hughes, 2021; Shao *et al.*, 2022). A recent study has revealed that more than 25% of acute cerebral infarction cases arise from the rupture of unstable plaque caused by atherosclerosis, leading to thrombus formation (Kim *et al.*, 2013). The stability of intracranial atherosclerotic plaque is inextricably linked to factors such as plaque surface smoothness, ulcer formation, regularity, and presence of bleeding (Lu *et al.*, 2021; Tao *et al.*, 2021). Therefore, early detection of the nature and structure of intracranial atherosclerotic plaque

holds immense significance in predicting the occurrence of acute cerebral infarction.

The serum low density lipoprotein (LDL) level is acknowledged as the most important risk factor for atherosclerosis. But the determination of LDL level by conventional blood lipid detection methods fails to completely predict the risk of carotid atherosclerosis; some patients at a high risk of cardiovascular disease may have normal LDL level (Hartley *et al*., 2019). Based on previous research (QiaoZhen *et al*., 2019), LDL can be subdivided into several subtypes, from LDL1 to LDL7 using the Lipoprint lipoprotein classification detection system. The LDL1-2 lipoprotein is typically regarded as physiologically normal, as it fulfills the role of transporting cholesterol. Conversely, the LDL3-7 lipoproteins are deemed to be abnormal, as they manifest as small dense low-density lipoproteins (sdLDL) that exhibit heightened susceptibility to oxidative stress, possess diminished affinity for LDL receptors, demonstrate a protracted plasma half-life, and exhibit a greater inclination to penetrate the vascular wall, ultimately depositing plaque beneath the endothelium. The cumulative effect of these factors contributes to the development of cardiovascular and cerebrovascular diseases (QiaoZhen *et al*., 2019). Currently, copious studies are available to show that even if patients have normal LDL levels, an increase in the ratio of sdLDL in total LDL can still result in an increased risk of cardiovascular disease by more than three times (QiaoZhen *et al*., 2019). Therefore, sdLDL is considered an effective predictor of atherosclerosis. The clinical auxiliary diagnostic value of single biomarkers such as small dense low-density lipoprotein cholesterol (sdLDLc), homocysteine concentration (HCYc) and HDL-C concentration (HDLc) for cerebral infarction has been confirmed by many studies (Ishii *et al*., 2022; QiaoZhen *et al*., 2019; Santos *et al*., 2020), while the predictive value of (sdLDLc*HCYc)/HDLc in primary cerebral infarction is higher than that of a single biomarker, including sdLDLc, HCYc, and HDLc (Luo *et al*., 2022). Based on this, our study aimed to evaluate the value of serum (sdLDLc*HCYc)/HDLc ratio in the stability of intracranial arterial plaques in patients with acute cerebral infarction.

MATERIALS AND METHODS

Clinical data

A retrospective analysis was conducted on 140 patients with acute cerebral infarction admitted to the neurology department and 101 healthy individuals for regular examinations in our hospital from 2013 to 2019, who were allocated into the study group and the control group, respectively. In our hospital, about 100 cases of stroke patients are enrolled every year. Inclusion criteria: All patients met the diagnostic criteria for acute cerebral infarction established at the Fourth National Conference on Cerebrovascular Disease (Wang, 1996) in 1995, and were determined by intracranial high-definition magnetic resonance angiography; no oral or intravenous antibiotics, antiviral, non steroidal, or glucocorticoid drugs were administered within 14 days before the onset of the disease. Exclusion criteria were patients with serious infectious diseases; autoimmune diseases; malignant tumor diseases; diabetes; primary organ disorders, including heart, lung and other systemic diseases; new neurological deficits; other nervous system disease that may lead to neurological dysfunction, such as hereditary degenerative diseases of the central nervous system, tumors, encephalitis, demyelinating diseases, brain trauma, epilepsy, etc.

The study protocol was approved by the Ethics Committee of Hebei General Hospital. Informed consent was obtained from all the study subjects before enrollment. All methods were designed in accordance with the Declaration of Helsinki.

METHODS

Clinical data

Clinical data of all participants, including age, gender, height, weight, BMI, hypertension, diabetes, coronary heart disease, smoking history, drinking history were collected.

Laboratory examination

After a 12-hour fast, 5 ml of venous blood of the study group was collected the following morning, and venous blood of the control group was also collected in the morning for physical examination. The serum was centrifuged for 10 min with a 3000 r/min high-speed centrifuge, and the supernatant was stored at –80°C for inspection. The experimental indicators were total cholesterol (TC), triglycerides(TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and other experimental indicators using AU680 automatic biochemical analysis system by Beckman Kurt. Serum sdLDLc was detected using enzyme-linked immunosorbent assay (ELISA) with a kit from Shanghai Enzyme-linked Biotechnology Co., Ltd. The reagent instructions for operation were strictly followed for quality control.

Intracranial high-definition magnetic resonance angiography

Using the HDX platform 3.0T MRI system (GE Healthcare, the US), multi-sequence MRI examinations were performed with application of an 8-channel standard coil. The HRMR scanning matrix was 320×256. The bright-blood technology was the first choice to perform three-dimensional time-of-flight magnetic resonance angiography, to clarify the location of the affected blood vessels after vascular reconstruction, and then use the black blood technology for multi-sequence scanning of intracranial diseased blood vessels. The scanning parameters were as follows: fast spin-echo T1-weighted imaging, fast spin-echo T2- weighted enhanced imaging, T1-weighted enhanced imaging, with repetition times of 567, 2883, and 567 ms, echo times of 15.8, 49, and 15.8 ms, and imaging field of view of 100 mm×100 mm, with a layer thickness of 2mm and a spacing of 2.5 mm. The T1-weighted variable flip angle 3D fast spin-echo sequence has a repetition time of 900 ms, an echo time of 5.6 ms, and a layer thickness of 0.5 mm. The enhanced examination was performed using MeglumineZapenate as the contrast agent. The participants were in travenously injected with contrast agent 5 minutes before scanning. The scanning parameters were the same as T1-weighted variable flip angle 3D fast spin-echo sequence. The completion time of the above sequence scanning was 30 to 40 minutes. IV contrast was used during MRI scanning

The assessment of intracranial responsible vessels included the degree of arterial stenosis and the characteristics of responsible plaques. Responsible blood vessels referred to the blood vessels that supplied responsible

Table 1. Comparison of clinical data

Indicator	Study group (n=139)	Control group (n=101)	χ^2/t	P
Age (year)	59.41±12.02	64 15±11.81	–3.044	0.003
Gender (male/female)	38/102	46/55	18.469	<0.001
Height (cm)	168.11±15.38	166.72±15.02	1.657	0.098
Weight (kg)	74.11±11.99	68.20±11.39	–4.045	<0.001
BMI (kg/cm^2)	26.14±3.23	24.52±3.71	–3.591	<0.001
Hypertension (n)	89	53	2.985	0.084
Diabetes (n)	40	19	3.023	0.082
Coronary heart disease	18	19	1.601	0.206
Smoking history	47	39	0.048	0.827
Drinking history	30	21	0.022	0.882
Degree of vascular stenosis (n)			–	-
Grade 0: no stenosis	23 (16.43)			
Grade 1: mild stenosis	26 (18.57)			
Grade 2: moderate stenosis	29 (20.71)			
Grade 3: severe stenosis	62 (44.29)			

lesions. If there was only one lesion in the blood vessel, the plaque at that lesion was considered the responsible plaque; if there were multiple diseased blood vessels, the plaque with the most severe vascular stenosis was the responsible plaque. According to the warfarin-aspirin symptomatic intracranial disease (WASID) method, the degree of stenosis of the responsible vessel was measured on the maximum intensity projection image of MRA. The degree of stenosis is divided into 5 levels: no obvious stenosis (0%), mild stenosis (1–49%), moderate stenosis (50–69%), severe stenosis (70–99%), and occlusion (100%).

Observation indicators

The laboratory indexes of the two groups were compared. The multivariate logistic regression analysis was done to analyze the influencing factors of the stability of intracranial artery plaque in patients with acute cerebral infarction. The value of HDL-C), homocysteine, sdLDLc, (sdLDLc*HCYc)/HDLc in diagnosing the stability of intracranial artery plaque were also evaluated in patients with acute cerebral infarction.

Statistical analysis

We used SPSS 21.0 software to analyze the data and Excel to establish the database. The measurement data conforming to the normal distribution was expressed in $\bar{x}\pm$ s. Using one-way ANOVA, the overall comparison of the data of each group was performed. And the pairwise comparison of the data between groups and within groups was conducted by LSD method. Moreover, the counting data was expressed in percentage (%) and compared using chi-square χ^2 test. Multiple logistic regression analysis was used to analyze the influencing factors, with $P<0.05$ as the significant difference.

RESULTS

Comparison of clinical data

There was no distinct difference in height, hypertension, diabetes, coronary heart disease, smoking history and drinking history between the two groups ($P>0.05$). The study group showed statistically significant differences in age, gender, weight, and BMI ($P<0.05$) (Table 1).

Comparison of laboratory indicators

The current study demonstrated no statistical difference in the levels of TG, LDL-C, α-lipoprotein, and HCYc between the two groups ($P>0.05$). However, the levels of TC, HDL-C, sdLDLc, (sdLDLc*HCYc)/HDLc

Table 2. Comparison of laboratory indicators ($\bar{x}\pm$ s)

Indicator	Study group (n=139)	Control group (n=101)	t	P
TC (mmol/L)	4.36±1.16	4.65±1.14	2.202	0.029
TG (mmol/L)	1.71±1.87	1.71±0.96	1.281	0.200
HDL-C (mmol/L)	1.03±0.22	1.16±0.30	3.261	0.001
LDL-C (mmol/L)	2.80±0.86	3.00±0.82	–1.762	0.079
α-lipoprotein (mmol/L)	269.81±242.74	266.35±257.75	–0.411	0.681
HCYc(umol/L)	19.43±17.15	15.57±9.06	–1.795	0.073
sdLDLc(ng/dL)	8.13±6.62	5.59±3.63	–2.713	0.007
(sdLDLc*HCYc)/HDLc (%)	167.71±215.81	80.49±78.75	–3.477	0.001

Table 3. Comparison of laboratory indicators for different degrees of stenosis in the study group ($\bar{x}$± s)

Indicator	No stenosis (n=23)	Mild stenosis (n=26)	Moderate stenosis (n=29)	Severe stenosis (n=61)	*t*	*P*
TC (mmol/L)	4.39±0.16	4.36±0.13	4.34±0.18	4.35±0.15	0.508	0.677
TG (mmol/L)	1.71±0.27	1.72±0.21	1.68±0.25	1.69±0.23	0.171	0.916
HDL-C (mmol/L)	1.07±0.05	1.04±0.09*	1.01±0.07*#	0.96±0.11*#★	10.159	<0.001
LDL-C (mmol/L)	2.85±0.27	2.82±0.29	2.73±0.25	2.76±0.29	1.076	0.362
α-lipoprotein (mmol/L)	268.76±36.37	269.76±35.17	270.98±36.18	272.81±36.81	0.089	0.966
HCYc(umol/L)	21.51±1.93	21.56±1.87	21.65±1.76	21.87±2.01	0.286	0.835
sdLDLc(ng/dL)	8.01±0.21	8.71±0.71*	9.23±0.67*#	9.87±0.87*#★	41.639	<0.001
(sdLDLc*HCYc)/HDLc(%)	163.01±12.16	167.28±11.08*	172.18±12.01*#	178.82±12.98*#★	11.466	<0.001

Note: Compared with no stenosis (*P<0.05); compared with mild stenosis (#P<0.05); compared with moderate stenosis (★P<0.05).

in the study group were significantly different when comparing with the control group (P<0.05) (Table 2).

Comparison of laboratory indicators for different degrees of stenosis in the study group

No statistically significant difference was found in the levels of TG, triglycerides, LDL-C, α-lipoprotein, and HCYc among patients with different degrees of stenosis in the study group (P>0.05). The level of HDL-C was significantly lower in cases of severe stenosis compared to no stenosis, mild stenosis and moderate stenosis, with severe stenosis showing the lowest levels; mild stenosis had lower levels than no stenosis, while moderate stenosis had lower levels than both no stenosis and mild stenosis (P<0.05). The levels of sdLDLc, (sdLDLc*HCYc)/HDLc exhibited a significant increase in cases of severe stenosis as compared to no stenosis, mild stenosis, and moderate stenosis. Furthermore, the levels of sdLDLc, (sdLDLc*HCYc)/HDLc were found to be higher in moderate stenosis as compared to no stenosis and mild stenosis. Similarly, the levels of sdLDLc, (sdLDLc*HCYc)/HDLc were observed to be higher in mild stenosis than no stenosis (P<0.05) (Table 3).

Multivariate logistic regression analysis of factors affecting the stability of intracranial arterial plaques in patients with acute cerebral infarction

The independent variables were set as the indicators with difference in single factor comparison, including age, gender, BMI, TC, LDL-C, HDL-C, HCYc, sdLDLc, (sdLDLc*HCYc)/HDLc. The dependent variable was the stability of intracranial artery plaque in patients with acute cerebral infarction. After variable selection, the results showed that the factors influencing the stability of intracranial artery plaque in patients with acute cerebral infarction were age, BMI, and (sdLDLc*HCYc)/HDLc. (Table 4).

The value of HDL-C, homocysteine, sdLDLc, (sdLDLc*HCYc)/HDLc in diagnosing the stability of intracranial artery plaque in patients with acute cerebral infarction

The degree of plaque enhancement was used as a criterion to reflect the stability of plaque. ROC curve analysis showed that (sdLDLc*HCYc)/HDLc had a higher evaluation value for the stability of intracranial artery plaque than HDL-C, homocysteine, and sdLDLc in patients with acute cerebral infarction, as shown in Table 5 and Fig. 1.

DISCUSSION

Acute cerebral infarction is a life-threatening ischemic cerebrovascular disease that poses a significant threat to human health worldwide. The incidence of the condition has increased from 1.89% in 2012 to 2.19% in 2016, with a climbing disability rate with the passage of time. Acute cerebral infarction is deemed to be the leading cause of death and disability in adults in China (Zhang & Qin, 2022). Intracranial atherosclerosis accounts for

Table 4. Multivariate logistic regression analysis of influencing factors on the stability of intracranial arterial plaques in patients with acute cerebral infarction

Variable	β	SE	Waldx²	OR (95%CI)	*P* value
Age	-.033	0.014	5.787	0.971(0.945-0.998)	0.032
Gender	0.420	0.157	7.204	2.318(1.255-4.282)	0.226
BMI	0.108	0.045	5.718	1.114(1.020-1.218)	0.017
TC	0.004	0.442	0.000	1.004(0.422-2.389)	0.993
HDL-C	-0.499	0.843	0.350	0.607(0.1163.167)	0.554
LDL-C	-.400	0.594	0.453	0.670(0.209-2.148)	0.501
Homocysteine	0.010	0.012	0.747	1.010(0.987-1.034)	0.387
sd-LDL	0.112	0.033	11.48	1.119(1.049-1.194)	0.411
Hypertension	-.279	0.154	3.275	0.572(0.313-1.047)	-.152
Diabetes	-.304	0.175	3.018	0.544(0.274-1.081)	-.145
(sdLDLc*HCYc)/HDLc	0.004	0.002	6.725	1.004(1.001-1.007)	0.010

Table 5. The value of HDL-C, homocysteine, sdLDLc, (sdLDLc*HCYc)/HDLc in diagnosing the stability of intracranial artery plaque in patients with acute cerebral infarction

ROC model	Area	Standard error	95% wald	Cut-off value	Sensitivity	Specificity
HDL-C	0.6232	0.0377	0.5493	≤1.03mmol/L	0.751	0.701
Homocysteine	0.5678	0.0371	0.4950	≥19.43μmol/L	0.763	0.722
sdLDLc	0.6022	0.0360	0.5316	≥8.13ng/dL	0.789	0.746
(sdLDLc*HCYc)/HDLc	0.6313	0.0357	0.5613	≥167.71%	0.853	0.817

about 46.6% of cerebral infarction patients in China (Chu & Liu, 2021). The stability of intracranial artery plaque is highly associated with acute cerebral infarction. Earlier research indicated that high resolution magnetic resonance (HRMR) intracranial artery wall imaging was able to effectively assess the size, shape and stability of intracranial atherosclerotic plaque. The degree of plaque enhancement and intra plaque hemorrhage are greatly related to intra-plaque hemorrhage and plaque stability, but serum markers fail to effectively reflect the stability of intracranial atherosclerotic plaque (Xie *et al.*, 2022).

The changes in the composition of LDL-Care are particularly pivotal in the progression of acute cerebral infarction. However, LDL-C is heterogeneous. The diameter of LDL-C main peak particles obtained by non-denaturing gradient gel scanning can be subdivided into LDL-C A with high cholesterol content, high density and large volume (diameter peak ≥25.8nm) and LDL-C B with low cholesterol content, high density and small volume (diameter peak <25.8nm), that is, small dense low-density lipoprotein cholesterol (sdLDLc) (Kanonidou, 2021). The latest research (Huang & Gu, 2021)asserted that, sdLDLc had a stronger atherogenic ability than LDL-C, and has been included in the newly discovered important risk factors for cardiovascular and cerebrovascular disease recommended by the adult treatment group of the National Cholesterol Education Program. sdLDLc is correlated with the number of atherosclerotic plaques and carotid stenosis caused by atherosclerotic plaques (Ikezaki *et al.*, 2020). Ikezaki and others (Ikezaki *et al.*, 2020) depicted that sdLDLc had a significant impact on

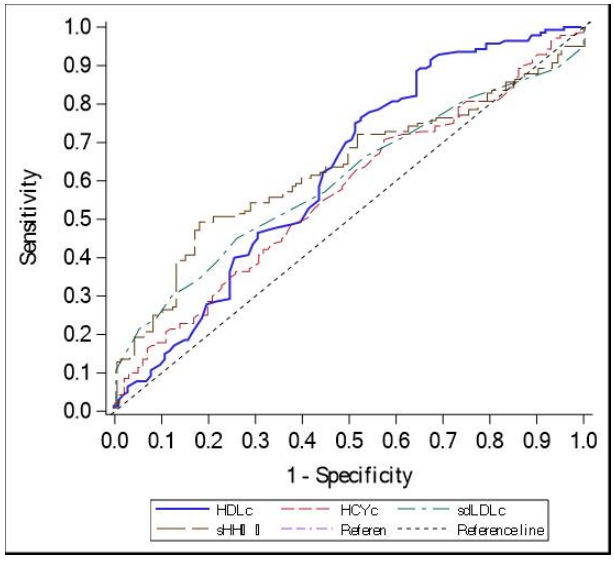

Figure 1. ROC curve of HDL-C, homocysteine, sdLDLc, (sdLDLc*HCYc)/HDLc in diagnosing the stability of intracranial artery plaque in patients with acute cerebral infarction.

the composition of carotid artery plaque cells. HCYc is an intermediate product of the methionine cycle. High levels of HCYc can promote the proliferation of smooth muscle cells, damage vascular endothelial cells, and affect the oxidation of LDL. It can activate platelets to increase platelet adhesion, promote thrombosis, cause arterial congee, and also reduce the bioavailability of nitric oxide, inhibit fibrin degradation, platelet aggregation, and promote atherosclerosis (Wang *et al.*, 2021). Based on Yang and others (Yang *et al.*, 2019) the severity of carotid atherosclerotic plaque in type 2 diabetes patients complicated with cerebral infarction was higher than that in simple diabetes patients, and the level of serum HCYc was positively correlated with the degree of carotid atherosclerosis, which may be involved in its occurrence and development. α-lipoprotein level is determined by genes and is an LDL-like protein composed of apolipoprotein (apo) A covalently continuous apoB-100. Lp(α) is believed to be involved in the occurrence of atherosclerosis, which is greatly related to thrombosis and fibrinolysis damage (Dai *et al.*, 2019). However, limited clinical research exists on the value evaluation of serum (sdLDLc*HCYc)/HDLc ratio in the stability of intracranial arterial plaques in patients with acute cerebral infarction. Our study showed that the age, gender, weight, and BMI of the study group differed from the control group (P<0.05), indicating that patients diagnosed with acute cerebral infarction exhibited a higher prevalence among the female population, alongside elevated weight and BMI, while their age was comparatively younger. But the small sample size may contribute to the biased results. In our study, the levels of TC, HDL-C, sdLDLc, (sdLDLc*HCYc)/HDLc in the study group were significantly different as compared to the control group (P<0.05), suggesting that the levels of TC, HDL-C in patients with acute cerebral infarction decreased, and the levels of sdLDLc, (sdLDLc*HCYc)/HDLc increased. Gu and others (Gu *et al.*, 2017)showed that HDL-C levels and TC/HDL-C ratios may effectively predict the severity of intracranial vascular stenosis. Similarly, another study (Zhang *et al.*, 2020) depicted that sdLDLc could effectively evaluate the severity of acute cerebral infarction in elderly patients. According to our study, the level of HDL-C was significantly lower in cases of severe stenosis compared to no stenosis, mild stenosis and moderate stenosis, with severe stenosis showing the lowest levels; mild stenosis had lower levels than no stenosis, while moderate stenosis had lower levels than both no stenosis and mild stenosis (P<0.05). The levels of sdLDLc, (sdLDLc*HCYc)/HDLc exhibited a significant increase in cases of severe stenosis as compared to no stenosis, mild stenosis, and moderate stenosis. Furthermore, the levels of sdLDLc, (sdLDLc*HCYc)/HDLc were found to be higher in moderate stenosis as compared to no stenosis and mild stenosis. Similarly, the levels of sdLDLc, (sdLDLc*HCYc)/HDLc were observed to be higher in mild stenosis than no stenosis (P<0.05). It was suggested that the levels of HDL-C, sdLDLc, (sdLDLc*HCYc)/

HDLc varied in patients with acute cerebral infarction of different stenosis degrees. The more severe the stenosis degree, the lower the level of high-density lipoprotein cholesterol, and the higher the levels of sdLDLc, (sdLDLc*HCYc)/HDLc.

The stability of carotid atherosclerotic plaque in elderly patients with acute cerebral infarction was linked to factors such as age, HCYc (Bai & Wang, 2021). Another study suggested that elevated levels of LDL-C and HCY-C were risk factors that affected the stability of carotid plaques in patients with acute cerebral infarction (Hansha *et al.*, 2022). Detecting and controlling the abovementioned indicators in clinical practice may help stabilize the carotid plaques in patients with acute cerebral infarction, thereby improving their prognosis. Our study showed that the influencing factors for the stability of intracranial arterial plaques in patients with acute cerebral infarction included age, BMI, (sdLDLc*HCYc)/HDLc, which was consistent with the above results. We further analyzed the value of HDL-C, homocysteine, sdLDLc, (sdLDLc*HCYc)/HDLc in diagnosing the stability of intracranial artery plaque in patients with acute cerebral infarction. The results revealed that (sdLDLc*HCYc)/HDLc exhibited a higher value in evaluating the stability of intracranial artery plaque in patients with acute cerebral infarction than HDL-C, homocysteine, and sdLDLc. (sdLDLc*HCYc)/HDLc consists of three components, encompassing their respective effects. The precise reasons are described as follows: (1) The formation of sdLDLc is related to the metabolism of VLDL rich in triacylglycerol. Cholesterol ester transporter protein (CETP) and hepatic lipase (HL) exert important roles in the formation of sdLDLc. When VLDL increases, especially when triglycerides in the core exchange with cholesterol esters in the LDL core, the proportion of cholesterol esters in the LDL decreases, and the proportion of triglycerides gradually increases. When triglycerides in the LDL reach a certain concentration and pass through the liver, they are hydrolyzed by hepatic lipase to remove triacylglycerol. The entire exchange process continuously reduces the diameter of LDL particles, increases density, forms sdLDLc, and the level of triacylglycerol increases. The active exchange process positively generates sdLDLc. During the development of atherosclerosis, sdLDLc is deposited in a certain part of the artery wall through the vascular endothelial gap, which is then taken up by monocyte macrophages, where lipids gradually accumulate and transform into foam cells. The above changes are mainly due to the presence of chondroitin sulfate proteoglycan (CSPG) in the extracellular matrix of tunica intima cells, which can combine with lipoproteins to form complexes, thus prolonging the residence time (Choi & Lee, 2022). In addition, some studies demonstrated that the structure of ApoB in sdLDLc may change, and sdLDLc was difficult to clear in the circulation, so there were more opportunities for sdLDLc to enter tunica intima (Zhou *et al.*, 2020). The abovementioned results highlight the fact that sdLDLc is closely related to atherosclerosis. (2) HCYc is one of the initiating factors of atherosclerosis. Under the environment of high concentration of HCY, vascular oxidative stress reaction generates free radicals, which reduces the function of endothelial cells. Endothelial cells enter the death process ahead of time. The process can also inhibit the regeneration of endothelial cells, reduce the number of endothelial cells, with lipid deposition and fibrosis in the excess space. Moreover, HCYc has an impact on a variety of cytokines, cyclins and cellular active substances, thus damaging the vascular wall, causing the protection and proliferation of vascular smooth muscle cells. Finally, the development of ischemia and hypoxia contributes to the vascular fibrosis, hardening and thickening the blood vessel. The impairment of the vascular wall leads to the aggregation of fibrin and platelets in the damaged vascular wall, ultimately contributing to the development of arterial atherosclerosis. HCYc can cause abnormalities in lipid metabolism, increase LDL-C levels, and produce oxidative reactions, resulting in cholesterol accumulation in the blood vessel wall. It also reduces the anti-atherosclerotic function of HDL-C in the blood vessels, where the role of endothelial cells in clearing cholesterol slows down, and then deposits under the vascular endothelium. The accumulated cholesterol gradually increases, ultimately forming arteriosclerosis (Lv *et al.*, 2022). In addition, HCYc is able to cause abnormal platelet function and alter the activity of coagulation factors V and X, leading to platelet aggregation and abnormal coagulation function, and ultimately inducing cerebrovascular disease (Liu *et al.*, 2019). (3) HDLc, as a receptor for cholesterol, mediates the flow of cholesterol from the intima of the arterial wall and transports it to the liver for metabolism through its interaction with the receptor, thereby reducing cholesterol levels in the plasma and preventing the occurrence of arteriosclerosis. HDLc has demonstrated the ability to prevent atherosclerosis *via* inhibiting the oxidation of LDL, which also participates in the reverse transport of oxidized LDL, reducing the damage caused by oxidized LDL. Additionally, HDLc inhibits monocyte cell adhesion and infiltration into the tunica intima and stimulates endothelial cell repair and proliferation. It can also inhibit the proliferation of vascular smooth muscle cells induced by growth factors and other mechanisms. Lastly, it exhibits property of anti-platelet aggregation, safeguarding against thrombosis (Woo *et al.*, 2020; Yin *et al.*, 2021).

CONCLUSION

The patients with acute cerebral infarction showed reduced levels of TC and HDL-C, and elevated levels of sdLDLc, (sdLDLc*HCYc)/HDLc. Age, BMI, (sdLDLc*HCYc)/HDLc were the influencing factors for the stability of intracranial arterial plaque in patients with acute cerebral infarction, of which (sdLDLc*HCYc)/HDLc exhibited superior value in diagnosing the stability of intracranial arterial plaque in such patients. However, there are a few shortcomings in this study. We noted that the participants in control group were not selected based on the age and gender of patients with acute cerebral infarction, resulting in a certain bias in the general data. Further multi-center studies are needed to determine the risk factors for intracranial arteriosclerosis in patients with acute cerebral infarction based on their age.

Declarations

Ethics approval and consent to participate. The study protocol was approved by the Ethics Committee of Hebei General Hospital. Informed consent was obtained from all the study subjects before enrollment.

Consent for publication. Not applicable.

Availability of data and material. The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests. The authors declare that they have no competing interests.

Authors' contributions. HY H and RS D contributed to the conception and design of the study; XX, YJ

L, HS C, LZ, SQ C,YL, TK W and NM performed the experiments, collected and analyzed data; HY H and RS D wrote the manuscript; HY H and RS D revised the manuscript. All authors reviewed and approved the final version of the manuscript.

Acknowledgements. None.

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