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The relationship between oxidized low-density lipoprotein and related ratio and acute cerebral infarction

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Abstract

This study aimed to study the value of oxidized low-density lipoprotein (OX-LDL) and related ratio in the diagnosis of acute cerebral infarction and the classification of acute cerebral infarction.

Of the 129 patients enrolled in this study, 94 patients with acute cerebral infarction were assigned to the case group, and 35 healthy subjects were enrolled as control group (n = 35). And then the case group were divided into large-artery atherosclerosis (LAA) group (n = 61) and small-artery occlusion (SAO) group (n = 33) according to the TOAST classification standard. Plasma OX-LDL levels were determined by enzyme-linked immunosorbent assay. OX-LDL/total cholesterol (OX-LDL/TC), OX-LDL/high-density lipoprotein (OX-LDL/HDL), OX-LDL/LDL were calculated.

There were significant differences in OX-LDL, OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL in patients with acute cerebral infarction and those in control group ($P < .001$). The area under the receiver-operating characteristic curve of OX-LDL and related ratio was >0.7 ($P < .001$). There was a slight positive correlation between OX-LDL/TC and National Institutes of Health Stroke Scale score at admission ($r = 0.265$, $P = .039$) in the LAA group.

OX-LDL, OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL were closely related to acute cerebral infarction, especially with large atherosclerotic cerebral infarction. OX-LDL/TC can reflect the severity of acute cerebral infarction for LAA, but it cannot predict the short-term prognosis of acute cerebral infarction.

Abbreviations: ACS = acute coronary syndrome, AUC = area under the curve, CAD = coronary artery disease, DBP = diastolic blood pressure, ELISA = enzyme-linked immunosorbent assay, Hcy = homocysteine, HDL = high-density lipoprotein, hs-CRP = high-sensitivity c-reactive protein, LAA = large-artery atherosclerosis, LDL = low-density lipoprotein, NIHSS = NIH Stroke Scale, OX-LDL = oxidized low-density lipoprotein, ROC = receiver-operating characteristic, SAO = small-artery occlusion, SBP = systolic blood pressure, TC = total cholesterol, TG = triglyceride, UA = uric acid.

Keywords: acute cerebral infarction, arteriosclerosis, C-reactive protein, diagnosis, oxidized low-density lipoprotein, prognosis

1. Introduction

Stroke is the second leading cause of death (second only to ischemic heart disease) in the world, which accounts for about 9% of the all deaths. Acute ischemic stroke is the most common type of stroke, accounting for about 80% to 90% of all stroke.[1] Acute ischemic stroke refers to the interruption or severe reduction of cerebral arterial blood flow, and the lack of sugar

and oxygen to maintain the basic function of cells in corresponding brain tissues, resulting in the dysfunction of cell electrochemistry and metabolism and the production of cytotoxic products.[2] Head computed tomography(CT)/computed tomography angiography (CTA), cranial CT/CTA, conventional magnetic resonancemagnetic resonance imaging(MRI)/magnetic resonance angiography (MRA),[3] diffusion-weighted imaging,[4] perfusion-weighted imaging, arterial spin labeling perfusion, and diffusion tensor imaging-derived metrics[5] are objective imaging evidences for defining cerebral infarction.

Oxidative stress is the basic pathological mechanism of ischemic brain injury and reperfusion injury. Oxidative stress is caused by excessive production of free radicals, especially reactive oxygen radicals, and the imbalance between oxidation and antioxidant system further leads to oxidative damage.[6] The brain tissue is more vulnerable to be attacked by reactive oxygen than other tissues and organs, because of their low antioxidant enzymes activity, high concentration of oxidative lipid, high oxygen consumption, and more iron content.[7] Reactive oxygen species can cause tissue destruction and cell death through a variety of cellular effects, such as lipid peroxidation, protein denaturation, intracellular calcium release, and so on.[8] Oxidative stress can lead to cell apoptosis or death, or autophagy activation, and ultimately affect the volume of infarct.[9]

Oxidized low-density lipoprotein (OX-LDL) is the major serological marker of oxidative stress. The formation of OX-LDL by oxidative modification of LDL under reactive oxygen is a key

step in atherosclerosis. A large number of studies have shown that the level of plasma OX-LDL in patients with acute coronary syndrome (ACS) were significantly increased; thus, OX-LDL has diagnostic value for ACS.[10–12] Some studies have also shown that OX-LDL/total cholesterol (OX-LDL/TC), OX-LDL/high-density lipoprotein (OX-LDL/HDL), and OX-LDL/LDL were important indicators for predicting the risk of coronary heart disease, and the diagnostic value is superior to the traditional lipid markers.[13–15] Recently, it was reported that ox-LDL level is positively correlated with NIHSS score in patients with acute ischemic stroke.[16,17] But whether OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL also have important value and clinical significance in acute ischemic stroke is still unclear.

The aim of this study was to investigate the value of OX-LDL and related ratio (OX-LDL/TC, OX-LDL/HDL, OX-LDL/LDL) in the diagnosis and classification of acute cerebral infarction, and to investigate the correlation between OX-LDL and related ratio and the severity and short-term prognosis of acute cerebral infarction, so as to provide a new basis for the diagnosis and clinical classification of acute cerebral infarction, and provide a new target for the treatment of acute cerebral infarction.

2. Materials and methods

2.1. Research object

From December 2015 to December 2016, 94 hospitalized patients were confirmed with acute cerebral infarction by head CT and MRI after admission in the department of Neurology of Second Hospital of Hebei Medical University, were included in this study as a case group, including 74 males and 20 females, aged 40 to 85 years, and the average age was 61.29 ± 8.33 years. From December 2015 to December 2016, 35 healthy subjects confirmed by physical examination in the Second Hospital of Hebei Medical University was included as a control group, including 26 males and 9 females, aged 40 to 85 years, mean age 59.17 ± 10.07 years. The Ethics Review Board of our hospital approved this study (No: 2016008). The written informed consent was provided by all participants.

According to the TOAST classification criteria, the case group was further grouped into: large-artery atherosclerosis group (LAA) (61 cases); small-artery occlusion (SAO) (33 cases).

Inclusion criteria for case group: aged 40 to 85 years; onset within 72 hours; diagnosed as acute cerebral infarction based on clinical symptoms and head MRI of patients; compliance with the TOAST classification for the classification of atherosclerotic stroke and small arterial occlusive stroke; and signed informed consent.

Exclusion criteria for case group are: age <40 years or >85 years; the onset time of >72 hours; intracranial hemorrhage, venous sinus thrombosis, and other cerebrovascular diseases; received statins, antioxidants, hormone, or immunosuppressant drug therapy within 4 weeks before admission; acute myocardial infarction, atrial fibrillation, among others; severe liver and kidney dysfunction, heart failure, among others; pregnancy, trauma, infection, poisoning; tumor, blood system, and autoimmune diseases.

2.2. Clinical data

For case group, the age, sex, history (diabetes, coronary heart disease, among others), smoking history, and recent medication were collected at admission. And those baseline characteristics for control group were collected by their physical examination results. The blood pressure in both case group and control group

was measured by mercury sphygmomanometer, which was measured 3 times, taken the mean as the final blood pressure value. On the day of admission and at the time of discharge (2 weeks), neurological function for case group was assessed by the National Institutes of Health Stroke Scale (NIHSS). After taking fasting venous blood in both case group and control group, DXC800 automatic biochemical analyzer (Beckman,) was used to detect high-sensitivity C-reactive protein (hs-CRP), homocysteine (Hcy), TC, triglyceride (TG), HDL, LDL, and other biochemical indicators.

2.3. Plasma OX-LDL level detection

Double antibody sandwich direct enzyme-linked immunosorbent assay (ELISA) was used in this study. Microplates were coated with anti-human OX-LDL antibodies. Solidified anti-human OX-LDL antibody on the microplate was made to be in combination with OX-LDL in plasma samples. And then the unreacted plasma fraction was eluted. And the enzyme-labeled antibody was added to the enzyme substrate for color development; the light absorption value was measured at a wavelength of 450 nm. The content of OX-LDL in the sample was determined by the dosage response curve made from the calibration of the reaction in the same micro plate.

2.4. Statistical methods

SPSS 22.0 (SPSS Inc, Chicago, IL) statistical software was used for statistical analysis. The measured data with normal distribution are expressed as mean±standard deviation, and the median (four percentile interval) is used for nonnormal distribution. If the normal distribution is satisfied, the independent-samples t test was used. The nonparametric test was used when the normal distribution is not satisfied. For comparison of multiple sets of data, if it conformed to the normality and variance homogeneity, the variance analysis was performed; if it did not subject to normality or variance homogeneity, Kruskal-Wallis H test was used. In addition, the SNK-q test was used to compare the differences after the analysis of variance. Pearson correlation analysis or Spearman rank correlation analysis was performed for the correlation analysis. Receiver-operating characteristic (ROC) curve was used to assess the diagnostic value of OX-LDL and related ratio in acute ischemic stroke. $P < .05$ indicates statistical significance.

3. Results

3.1. Comparison of the general data between the case group and the control group

There was no significant difference in sex ($P = .593$), age ($P = .228$), smoking history ($P = .58$), history of diabetes ($P = .319$) and coronary heart disease ($P = .248$), diastolic blood pressure ($P = .662$), uric acid ($P = .717$), TG ($P = .088$), and HDL ($P = .236$) between the case group and the control group. But there were significant differences in systolic blood pressure ($P = .032$), hs-CRP ($P = 0.003$), Hcy ($P < .001$), TC ($P = .02$), and LDL ($P = .007$) between the case group and the control group (Table 1).t

3.2. Comparison of OX-LDL and related ratio between the case group and the control group

There were statistical significances in the OX-LDL, OX-LDL/TC, OX-LDL/HDL and OX-LDL/LDL ($P < 0.001$) in the case group and those in the control group (Table 2). The value of OX-LDL,

Table 1

Comparison of baseline characteristics between case group and control group.

	Case group (n = 94)	Control group (n = 35)	P
Male/female (n)	74/20	26/9	.593
Age, y	61.29 ± 8.33	59.17 ± 10.07	.228
Smoking (%)	42.60%	37.10%	.58
Diabetes mellitus (n)	28.70%	20%	.319
CAD (%)	20.20%	11.40%	.248
SBP mmHg	149.30 ± 21.16	140.23 ± 21.10	.032
DBP , mmHg	86.09 ± 11.42	85.03 ± 14.09	.662
UA, μmol/L	293.49 ± 88.69	287.11 ± 88.94	.717
hs-CRP, mg/L	1.75 (0.88, 5.13)	0.90 (0.50, 1.70)	.003
Hcy, μmol/L	15.55 (12.68, 24.00)	12.90 (9.60, 16.10)	<.001
TC, mmol/L	4.50 ± 0.99	4.11 ± 0.76	.02
TG, mmol/L	1.32 (1.04, 1.88)	1.11 (0.83, 1.82)	.088
HDL, mmol/L	1.11 ± 0.25	1.17 ± 0.25	.236
LDL, mmol/L	2.89 ± 0.82	2.46 ± 0.67	.007

CAD = coronary artery disease, DBP = diastolic blood pressure, Hcy = homocysteine, HDL = high-density lipoprotein, hs-CRP = high-sensitivity c-reactive protein, LDL = low-density lipoprotein, SBP = systolic blood pressure, TC = total cholesterol, TG = triglyceride, UA = uric acid.

OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL in the diagnosis of acute cerebral infarction was evaluated by ROC curve. The area under the curve of OX-LDL was 0.807 ($P < .001$), which had the highest diagnostic value. The ROC curve results showed that when the optimal threshold value was 45.35 U/mL, the sensitivity was 64.9% and the specificity was 88.6%. The AUC of OX-LDL/TC, OX-LDL/HDL, OX-LDL/LDL, and Hcy were >0.7 ($P < .001$), and had better diagnostic value. Whereas the AUC of total cholesterol was 0.599, and there was no diagnostic value ($P = .083$); the AUC of LDL ($P = .013$) and hs-CRP ($P = .003$) was <0.7, and thus the diagnostic value were low. (Fig. 1, Table 3)

3.3. OX-LDL and related ratio in different stroke subgroups

OX-LDL, OX-LDL/TC, OX-LDL/HDL in LAA group and SAO group were all higher than those in control group, and the difference was statistically significant ($P < .05$). OX-LDL/LDL in LAA group was higher than the control group and there was significant difference ($P < .05$). There was no significant difference in OX-LDL/LDL between SAO group and control group ($P = .143$). OX-LDL and related ratios are also significantly different between LAA and SAO groups. ($P < .05$) (Fig. 2).

Table 2

Comparison of OX-LDL and the ratio between case group and control group.

	Case group	Control group	P
OX-LDL, ,U/mL	57.59 ± 24.48	32.00 ± 14.18	<.001
OX-LDL/TC	12.70 (7.95, 17.34)	7.46 (5.38, 10.44)	<.001
OX-LDL/HDL	52.26 (33.13, 69.32)	24.88 (19.87, 40.37)	<.001
OX-LDL/LDL	18.91 (12.18, 24.44)	12.93 (8.68, 16.98)	<.001

HDL = high-density lipoprotein, OX-LDL = oxidized low-density lipoprotein, TC = total cholesterol.
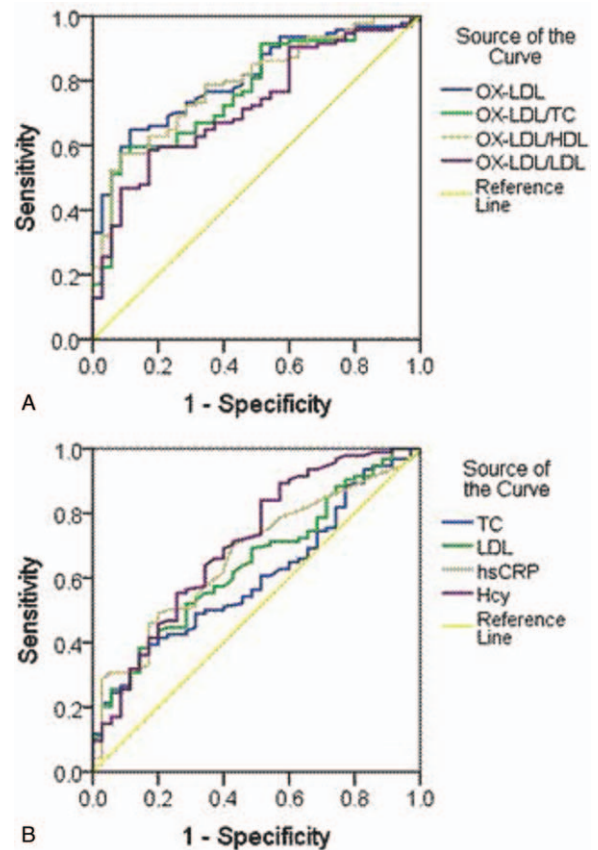

Figure 1. Receiver-operating characteristic curves for (A) OX-LDL and the ratio and (B) other plasma biomarkers (TC, LDL, hs-CRP, Hcy). Hcy = homocysteine, HDL = high-density lipoprotein, hs-CRP = high-sensitivity c-reactive protein, OX-LDL = oxidized low-density lipoprotein, TC = total cholesterol.

3.4. Correlation between NIHSS score and OX-LDL and related ratio in different stroke subtypes

Spearman correlation analysis showed that only OX-LDL/TC was slightly positively correlated with NIHSS score at admission in LAA group ($r = 0.265$, $P = .039$) (Fig. 3). There was no significant correlation between OX-LDL, OX-LDL/HDL, OX-LDL/TC, and NIHSS score at admission ($P > .05$) in LAA group. In the 2 groups, there was no significant correlation between OX-LDL and its ratio and NIHSS score at discharge ($P > .05$) in SAO group. In the 2 groups, there was no significant correlation between OX-LDL and its ratio and NIHSS score at discharge ($P > .05$) (Table 4).

3.5. Correlation of OX-LDL and related ratio with other biomarkers in the case group

In the case group, OX-LDL was positive correlated with hs-CRP ($r = 0.661$, $P < .001$), and had no significant deference with TC ($P = .939$), TG ($P = .258$), HDL ($P = .789$), LDL ($P = 0.849$), respectively. OX-LDL/TC was positively correlated with hs-CRP ($r = 0.533$, $P < .001$), and negatively correlated with TC ($r = -0.379$, $P < .001$), TG ($r = -0.206$, $P = .046$), HDL ($r = -0.244$, $P = .018$), and LDL ($r = -0.361$, $P < .001$). OX-LDL/HDL was positively correlated with hs-CRP ($r = 0.568$, $P < .001$), but negatively correlated with HDL ($r = -0.443$, $P < .001$). OX-LDL/

Table 3

Receiver-operating characteristic curves for OX-LDL and the ratio and other plasma biomarkers (TC, LDL, hs-CRP, Hcy).

	AUC	SE	95% CI	*P*	TV	Sensitivity	Specificity
OX-LDL, U/mL	0.807	0.039	0.731–0.883	<.001	45.35	0.649	0.886
OX-LDL/TC	0.766	0.045	0.678–0.853	<.001	11.75	0.574	0.914
OX-LDL/HDL	0.792	0.042	0.710–0.873	<.001	46.64	0.574	0.914
OX-LDL/LDL	0.723	0.047	0.630–0.816	<.001	17.85	0.585	0.829
TC, mmol/L	0.599	0.053	0.496–0.703	.083	—	—	—
LDL, mmol/L	0.642	0.052	0.540–0.744	.013	3.01	0.415	0.829
hs-CRP, mg/L	0.668	0.051	0.569–0.768	.003	1.85	0.489	0.8
Hcy, μmol/L	0.705	0.053	0.601–0.810	<.001	11.95	0.84	0.486

AUC = area under the curve, CI = confidence interval, Hcy = homocysteine, HDL = high-density lipoprotein, hs-CRP = high-sensitivity c-reactive protein, OX-LDL = oxidized low-density lipoprotein, SE = standard error, TC = total cholesterol, TV = threshold value.

LDL was positively correlated with hs-CRP ($r = 0.476$, $P < .001$), and negatively correlated with TC, HDL and LDL ($r = -0.462$, $P < .001$; $r = -0.234$, $P = .023$; $r = -0.477$, $P < .001$) (Table 5).

4. Discussion

In this study, there were significant differences in plasma OX-LDL levels in patients with cerebral infarction and the control group, and this validated the previous results.[16,17] The AUC of OX-LDL was 0.807, which was significantly higher than that of traditional serological markers, such as TC, LDL, hs-CRP, and Hcy. When the optimal value of OX-LDL was 45.35 U/mL, the sensitivity was 64.9% and specificity was 88.6%. The results showed that there was no significant correlation between OX-

LDL and the degrees of neurological deficiency in LAA and SAO cerebral infarction. Uno et al[18] found that plasma OX-LDL concentration in patients with acute cerebral infarction was 2 times higher than the normal control group, the plasma concentration of OX-LDL reached the peak third days after attack, but the increase of OX-LDL was not corrected with the severity of neurological deficit in patients with acute cerebral infarction. It was found that elevated plasma OX-LDL levels in patients with cortical infarcts were significantly associated with infarct volume and baseline NIHSS scores; however, there was no correlation between the increase of OX-LDL and the severity of neurological deficits in patients with acute cerebral infarction.[19] Vibo et al[20] have found that acute-phase protein can predict the severity of acute cerebral infarction and poor prognosis, but
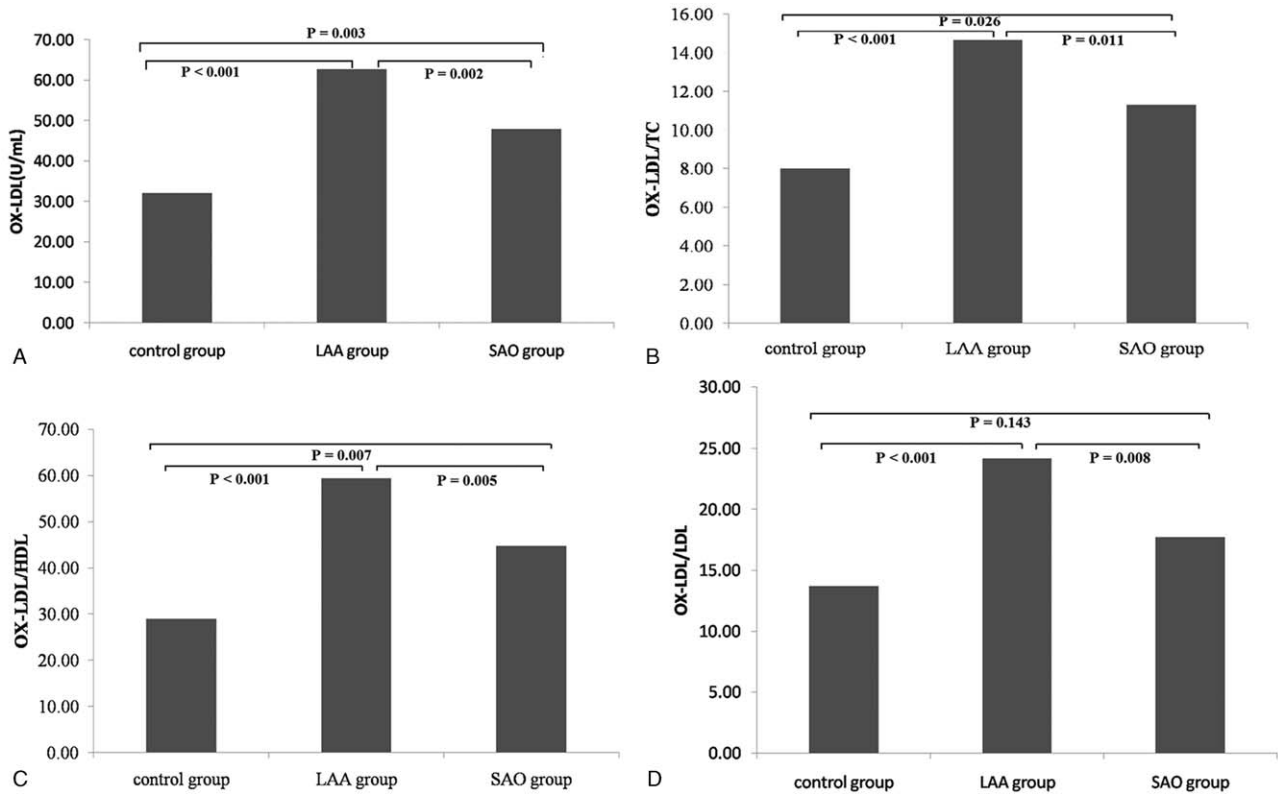

Figure 2. Comparison of OX-LDL (A) and the ratio in control group, LAA group and SAO group. Comparison of OX-LDL/TC (B), OX-LDL/HDL (C), OX-LDL/LDL (D), in control group, LAA group and SAO group. HDL = high-density lipoprotein, hs-CRP = high-sensitivity C-reactive protein, LAA = large-artery atherosclerosis, OX-LDL = oxidized low-density lipoprotein, SAO = small-artery occlusion, TC = total cholesterol.
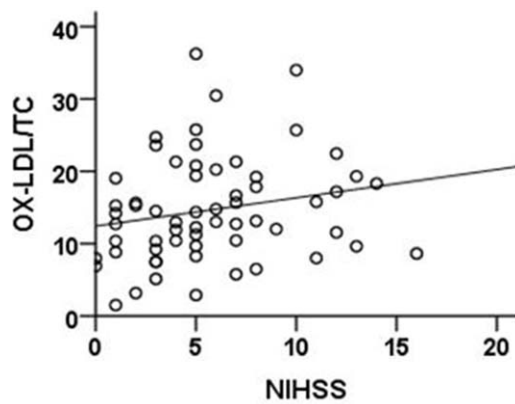
Figure 3. Relationship between plasma OX-LDL level and NIHSS assigned at admission. NIHSS = National Institutes of Health Stroke Scale, OX-LDL/TC = oxidized low-density lipoprotein/total cholesterol.

Table 5

The correlation between OX-LDL and the ratio and other factors (hs-CRP, Hcy, TC, TG, HDL, LDL).

		OX-LDL	OX-LDL/TC	OX-LDL/HDL	OX-LDL/LDL
hs-CRP, mg/L	r	0.661	0.533	0.568	0.476
	P	.000[†]	0.000[†]	0.000[†]	0.000[†]
Hcy, μmol/L	r	0.069	0.124	0.058	0.143
	P	0.511	0.236	0.576	0.170
TC, mmol/L	r	−0.008	−0.379	−0.149	−0.462
	P	0.939	0.000[†]	0.152	0.000[†]
TG, mmol/L	r	−0.118	−0.206	0.010	−0.177
	P	0.258	0.046[*]	0.921	0.087
HDL, mmol/L	r	−0.028	−0.244	−0.443	−0.234
	P	0.789	0.018[*]	0.000[†]	0.023[*]
LDL, mmol/L	r	0.020	−0.361	−0.108	−0.477
	P	0.849	0.000[†]	0.299	0.000[†]

Hcy = homocysteine, HDL = high-density lipoprotein, hs-CRP = high-sensitivity c-reactive protein, OX-LDL = oxidized low-density lipoprotein, r = correlation coefficient, TC = total cholesterol, TG = triglyceride.
[*] $P < .05$.
[†] $P < .001$.

plasma OX-LDL levels cannot. Plasma OX-LDL is closely related to acute cerebral infarction, which can reflect the level of oxidative stress in patients with acute cerebral infarction.[18,21] Plasma OX-LDL is closely related to the occurrence of acute cerebral infarction, and has a good diagnostic value. The relationship between OX-LDL and the degree of neurological deficit in cerebral infarction is still unclear and further study is needed.

In this article, the relationship between OX-LDL/TC, OX-LDL/HDL, OX-LDL/LDL, and acute cerebral infarction was studied for the first time. Unlike studies of Uno et al,[19] it was found that OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL in patients with cerebral infarction were higher than those in control group, and there were statistical significance. OX-LDL/TC (AUC = 0.766, $P < .001$), OX-LDL/HDL (AUC = 0.792, $P < .001$), and OX-LDL/LDL (AUC = 0.723, $P < .001$) have a good diagnosis value (AUC > 0.7). There was a slight positive correlation between OX-LDL/TC and NIHSS score at admission ($r = 0.265$, $P < .05$) in LAA group. It has been proved that OX-LDL/LDL can be used as an indicator to reflect the degree of LDL oxidation, and OX-LDL/LDL is closely related to coronary heart disease, which is helpful to assess the risk of coronary heart disease[22]; this is consistent with the results in this article.

Nordin et al[23] found that OX-LDL/TC value of acute myocardial infarction group is higher than that in the normal control group and hyperlipidemia group, and the plasma OX-LDL levels between acute myocardial infarction group and hyperlipidemia group were not statistically significant. Thus, it was considered that LDL is better than OX-LDL in predicting the risk of acute myocardial infarction. According to the analysis of ROC curve, Johnston et al[13] found that OX-LDL/HDL had important diagnostic value in coronary artery disease, better than lipoprotein-related phospholipase A2. OX-LDL/LDL, OX-LDL/HDL, OX-LDL/LDL may be good biomarkers for pediction and diagnosis of acute cerebral infarction. OX-LDL/TC can reflect the severity of acute cerebral infarction to some extent.

Large and small artery occlusion stroke are the most common type of ischemic stroke, accounting for 45%[24] of all ischemic stroke. Studies have shown that plasma OX-LDL level is particularly associated with large atherosclerotic stroke.[20,25] Guldiken et al[26] found that the plasma OX-LDL level in patients of LAA group was significantly increased, and it was higher than that of SAO group and control group, and serum interleukin-6 in SAO group was higher than that of LAA group and healthy control group; therefore, it suggests that oxidative stress is the main pathological mechanism of LAA type of ischemic stroke; inflammation may play a major role in the occurrence and development of SAO ischemic stroke. The results of this study showed that OX-LDL, OX-LDL/TC, and OX-LDL/HDL in LAA group and SAO group were higher than those in the control group and the difference was statistically significant ($P < .05$). OX-LDL/LDL in LAA group was higher than control group and

Table 4

The correlation between OX-LDL and the ratio and NIHSS at admission and discharge in LAA group and SAO group.

			OX-LDL	OX-LDL/TC	OX-LDL/HDL	OX-LDL/LDL
LAA group	NIHSS score at admission	r	0.208	0.265	0.201	0.24
		P	.108	.039[*]	.121	.063
	NIHSS score at discharge	r	0.241	0.22	0.191	0.192
		P	.064	.09	.145	.141
SAO group	NIHSS score at admission	r	−0.116	−0.064	−0.114	−0.1
		P	.519	.721	.527	.581
	NIHSS score at discharge	r	−0.151	−0.115	−0.121	−0.149
		P	.402	.526	.504	.408

HDL = high-density lipoprotein, LAA = large-artery atherosclerosis, NIHSS = National Institutes of Health Stroke Scale, OX-LDL = oxidized low-density lipoprotein, r = correlation coefficient, SAO = small-artery occlusion, TC = total cholesterol.
[*] $P < .05$.

there was significant difference ($P < .05$). But there was no significant difference in OX-LDL/LDL between SAO group and control group ($P > .05$). OX-LDL, OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL in LAA group were significantly higher than those in SAO group ($P < .05$). Research showed that OX-LDL, OX-LDL/TC, OX-LDL/HDL, and OX-LDL/ LDL were helpful to detect the correct cause of ischemic stroke. OX-LDL and related ratio were correlated with ischemic brain stroke, especially closely related to large artery atherosclerotic stroke.

The level of plasma OX-LDL increased in patients with acute ischemic stroke; this indicated that OX-LDL was closely related to the occurrence of acute ischemic stroke. In this study, we found that OX-LDL, OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL were not correlated with the NIHSS score of patients discharged from hospital ($P > .05$). Uno et al[19] found that the plasma OX-LDL level in the cerebral infarction group was significantly correlated with the baseline NIHSS score, but was not related to the modified Rankin score at 1 month after cerebral infarction. This is in agreement with our results to some extent. Vibo et al[20] also found no correlation between plasma OX-LDL and prognosis of cerebral infarction in clinical trials. A study of long-term prognosis in 1025 elderly patients with coronary heart disease showed no correlation between OX-LDL, OX-LDL/LDL, and 9-year mortality in patients with coronary heart disease.[27] Tsai et al[28] have shown that high levels of plasma OX-LDL was an independent risk factor for poor prognosis in acute ischemic stroke at 3 months, and the incidence of adverse prognosis in ischemic stroke can be increased by 9% for every 1-U/L increase of OX-LDL.

The results showed that OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL were closely related to the changes of blood lipid levels, which could reflect the abnormal lipid levels. OX-LDL and related ratio were positively correlated with hs-CRP. It was shown that CRP was an independent risk factor for predicting mortality of cerebral infarction.[29] Combined detection of plasma levels of hs-CRP and OX-LDL can improve the sensitivity and specificity for predicting the prognosis of patients with ACS.[30] CRP can promote the release of soluble LOX-1 from macrophages, promote the adhesion of monocytes to endothelial cells through LOX-1, and enhance the ability of macrophages to recognize and endocytosis OX-LDL.[31] OX-LDL can upregulate the expression of CRP through THP-1 macrophage insulin-like growth factor 2 pathway.[32] Zhang et al[33] found that OX-LDL and hs-CRP were positively correlated; OX-LDL and hs-CRP can directly lead to the occurrence of inflammatory reaction. However, some clinical studies had found that OX-LDL was not associated with hs-CRP in patients with coronary heart disease.[34,35]

This study has some limitations. First, the sample is small; this study included 94 patients with cerebral infarction; the patients were not grouped according to the location and size of the infarct site and whether they combined with other vascular disease; and the subtypes of cerebral infarction in this study only involved large artery atherosclerosis and arteriolar occlusion stroke. Second, this article mainly assesses the degree of neurological impairment according to the NIHSS score. The patients with cerebral infarction are mostly mild and moderate, but not serious. Third, compared with conventional CT, perfusion CT[36] can target the lesion more accurately. Time-resolved imaging of contrast kinetics MRA[37,38] is a reliable noninvasive tool for assessing head and neck arteriovenous malformations. We will then conduct further correlations between routine or advanced imaging findings and clinical and laboratory findings.[39]

5. Conclusions

The levels of OX-LDL, OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL were significantly increased in patients with acute cerebral infarction, and OX-LDL and related ratio had good early diagnostic value for acute cerebral infarction. OX-LDL, OX-LDL/TC, OX-LDL/HDL, and OX-LDL/LDL were closely related to the atherosclerosis and arterial occlusive stroke in the TOAST classification. OX-LDL/TC can reflect the severity of acute cerebral infarction in patients with atherosclerotic stroke, but it could not predict the short-term prognosis of acute cerebral infarction. OX-LDL was positively correlated with hs-CRP, which was closely related to the pathogenesis of acute cerebral infarction.

Author contributions

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Supervision: Dan He, Xiangjian Zhang.
Validation: Dan He, Xiangjian Zhang.
Visualization: Baosheng Fu, Dan He, Xiangjian Zhang.
Writing – original draft: Zhen Yan, Baosheng Fu, Dan He.
Writing – review & editing: Dan He.

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