

## RESEARCH ARTICLE

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# Study on the levels of glycosylated lipoprotein in patients with coronary artery atherosclerosis

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**Background:** The main risk factors for atherosclerosis patients are not fully explained. The aim of this study was to analyze the levels of blood lipid and glycosylated lipoprotein in patients with coronary artery atherosclerosis and healthy individuals and to study the relationship between the glycosylated lipoprotein and atherosclerosis.

**Methods:** The study involved 200 patients diagnosed with myocardial infarction caused by coronary atherosclerosis as case group and 230 healthy individuals as control group. We analyzed and contrasted the levels of blood lipid and glycosylated lipoprotein between the different groups. In addition, we investigated the correlation between glycosylated low-density lipoprotein (G-LDL) and glucose levels.

**Results:** There is no statistical difference between the level of TG in case group and control group. The level of CHOL, HDL-C, and LDL-C in case group is significantly lower than that in control group (3.90 [3.23, 4.42] vs 5.16 [4.86, 5.77] [mmol/L]; 1.09 [0.83, 1.38] vs 1.46 [1.15, 1.80] [mmol/L]; 2.22 [1.68, 2.81] vs 2.95 [2.60, 3.27] [mmol/L]) ( $P < 0.05$ ). The level of GLU, HbA1c, G-HDL, and G-LDL in case group is significantly higher than that in control group (7.10 [5.68, 9.27] vs 4.84 [4.68, 5.07] [mmol/L]; 6.8 [6.3, 7.4] vs 5.9 [5.6, 6.1] [%]; 30.08 [25.04, 40.17] vs 22.95 [18.14, 27.06] [ng/mL], 6.26 [4.95, 7.50] vs 3.61 [2.66, 5.15] [ng/mL]) ( $p < 0.05$ ). The level of G-LDL in patients with coronary atherosclerosis was relevant with the level of GLU and HbA1c ( $r = 0.625, 0.706, P < 0.05$ ), and there was no relevance with LDL-C ( $r = 0.331, P > 0.05$ ).

**Conclusion:** Hyperlipidemia is not an important cause of coronary atherosclerosis. High glucose levels and glycosylated lipoprotein are of high importance in the development and progression of coronary atherosclerosis.

## KEYWORDS

coronary atherosclerosis, glycosylated lipoprotein, myocardial infarction

## 1 | INTRODUCTION

Acute myocardial infarction (AMI) is a severe case of myocardial cell hypoxia and necrosis caused by myocardial ischemia.<sup>1</sup> The mortality rate of AMI has increased significantly in recent years<sup>2</sup> and has become a major public health problem.<sup>3</sup> Coronary atherosclerosis

is one of the most typical pathophysiological signs of AMI. But the formation mechanism of atherosclerosis is not fully understood. The traditional risk factors for atherosclerosis are hyperlipidemia, hypertension, smoking, diabetes, obesity, and lack of physical activity.<sup>4</sup> In recent decades, some studies point out that modified lipoprotein plays an important role in atherosclerosis patients.<sup>5,6</sup>

Luo and He contributed equally to this work.

It is well-established that diabetes mellitus is an independent risk factor for atherosclerosis.<sup>7</sup> Several studies have demonstrated that patients with high glucose are at higher risk for atherosclerosis compared to people with normal glucose.<sup>8,9</sup> The 2015 U.S. Residents' Dietary Guidelines removed restrictions on residents' cholesterol intake. The Dietary Guidelines Advisory Committee (DGAC) is considered that the intake of cholesterol in the human body does not need to be taken into account, and it is recommended to control the intake of sugar.<sup>10</sup>

Therefore, we tested the hypothesis that high glucose might increase glycosylated lipoprotein levels and promotes atherosclerosis. The aim of this study was to investigate the clinical characteristics and the levels of lipid, glucose, and glycosylated lipoprotein of AMI patients in newly diagnosed atherosclerosis compared with control individuals.

## 2 | MATERIALS AND METHODS

### 2.1 | Subjects

Between December 2016 and December 2017, 389 Chinese patients diagnosed with acute myocardial infarction at the West China Hospital of Sichuan University. We enrolled 200 patients as case group. Inclusion criteria: The patients were first-episode acute myocardial infarction and had not been taking lipid-lowering drugs before. Imaging examination showed that the patient had coronary plaques and met the criteria for the diagnosis of acute coronary syndrome in the European Society of Cardiology (ESC) 2015.<sup>11</sup> Exclusion criteria: Patients with a previous history of myocardial infarction. Patients were with severe liver or kidney disease or malignancy. And incomplete medical records or patients who are unwilling to provide basic information were excluded.

At the same time, we enrolled 230 healthy people as control individuals. Inclusion criteria: People have no coronary heart

disease, chronic obstructive pulmonary disease, peripheral vascular disease, and severe liver and kidney disease history. Electrocardiogram and echocardiography showed cardiac function is normal.

### 2.2 | Laboratory measurements

We collected 5 mL of venous blood samples from participants after an overnight fast and centrifuged at 1600 g/min for 15 min. The samples were taken for measurement. Glycosylated hemoglobin (HbA1c) was measured by high-performance liquid chromatography (Tosoh, Tokyo, Japan). Fast plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured by hexokinase method (cobas 8000; ROCHE, Germany). Collection of samples and analysis were according to laboratory standard operating procedure and had CAP accreditation.

### 2.3 | Glycosylated lipoprotein measurement

All serum was stored at -20°C for glycosylated lipoprotein measurement. Glycosylated high-density lipoprotein (G-HDL) and glycosylated low-density lipoprotein cholesterol (G-LDL) were measured by ELISA (Human Gly-HDL/LDL ELISA Kit, bioTSZ, USA).

### 2.4 | Statistical analyses

All statistical analyses were performed by SPSS 20.0. A *P* value less than 0.05 was considered as statistically significant. Continuous data were presented as the mean ± standard if normally distributed, and non-normally distributed data were expressed as median and values of 25 to 75 percentiles. Categorical data were presented as percentage. To compare variables between two groups, *t* test was

	AMI patients	Control individuals	P-value
Number of subjects	200	230	
Male	146 (73%)	157 (68%)	0.283
Age (y)	65 (53, 74)	62 (51,69)	0.076
Heart rate (bpm)	83 (71, 101)	74 (64,86)	<0.001
SBP (mm Hg)	146 (130, 165)	120 (115,133)	<0.001
DBP (mm Hg)	86 (78, 96)	74 (69,83)	<0.001
Smoking	126 (63%)	136 (59%)	0.412
Hypertension	104 (52%)	28 (12%)	<0.001
Dyslipidemia	18 (9%)	17 (7%)	0.543
Diabetes	60 (30%)	19 (8%)	<0.001

**TABLE 1** Characteristics of study subjects

Values are expressed as the median (interquartile range) or percentage. For group comparisons, nonparametric Mann-Whitney tests are used for non-normally distributed variables. Categorical variables were compared using a chi-square test.

SBP, systolic blood pressure; DBP, diastolic blood pressure.

**TABLE 2** The levels of blood lipid and glucose in different groups

	Case group (n = 200)	Control group (n = 230)	P value
TG (mmol/L) <sup>a</sup>	1.36 (0.97, 2.15)	1.21 (0.94, 1.75)	0.235
TC (mmol/L)	4.42 ± 1.16	4.95 ± 0.84	<0.001
HDL-C (mmol/L)	1.12 ± 0.37	1.45 ± 0.39	<0.001
LDL-C (mmol/L)	2.68 ± 1.01	3.05 ± 0.75	0.004
FPG (mmol/L) <sup>a</sup>	7.85 (6.62, 10.09)	5.15 (4.85, 5.68)	<0.001
HbA1c (%) <sup>a</sup>	6.1 (5.8, 6.8)	5.7 (5.5, 6.0)	<0.001

Quantitative data of normal distribution are presented as the mean ± SD, and quantitative data of non-normal distribution are presented as median (interquartile range). <sup>a</sup>Non-normal distribution of continuous variables.

TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin.

used for normally distributed continuous data and Wilcoxon test for non-normally distributed data. Chi-squared test was used for categorical variables. Spearman correlation test was used for the levels of glycosylated lipoprotein and glucose or lipid.

### 3 | RESULT

#### 3.1 | Characteristics of study subjects

Among the 430 study subjects, 200 (46.5%) were AMI patients and 230 (53.5%) were control individuals. The clinical characteristics of them are presented in Table 1. Both AMI patients and control individuals had an equal sex and age distribution, whereas the AMI group had a strong predominance of hypertension and diabetes. The AMI patients had significantly higher heart rate, SBP, and DBP than control individuals ( $P < 0.001$ ).

#### 3.2 | Comparison of lipid and glucose levels between the subjects with and without coronary atherosclerosis

The clinical and laboratory characteristics of the studied subjects with and without coronary atherosclerosis are shown in Table 2. Both the case group and control group had an equal sex and age distribution. The levels of FPG and HbA1c in AMI patients were higher than in control individuals ( $P < 0.001$ ). Interestingly, there is no statistical difference between the level of TG in case group and control group. And the level of CHOL, LDL-C in patients with coronary atherosclerosis is lower than in control individuals.

#### 3.3 | The levels of glycosylated lipoprotein in study subjects

The G-LDL level in AMI patient was 30.08 (25.04, 40.17) (ng/mL) which was higher than that in the control individual 22.95 (18.14, 27.06) (ng/mL). The level of D-HDL had the same result (6.26 [4.95, 7.50] vs 3.61 [2.66, 5.15] [ng/mL]) (Figure 1).

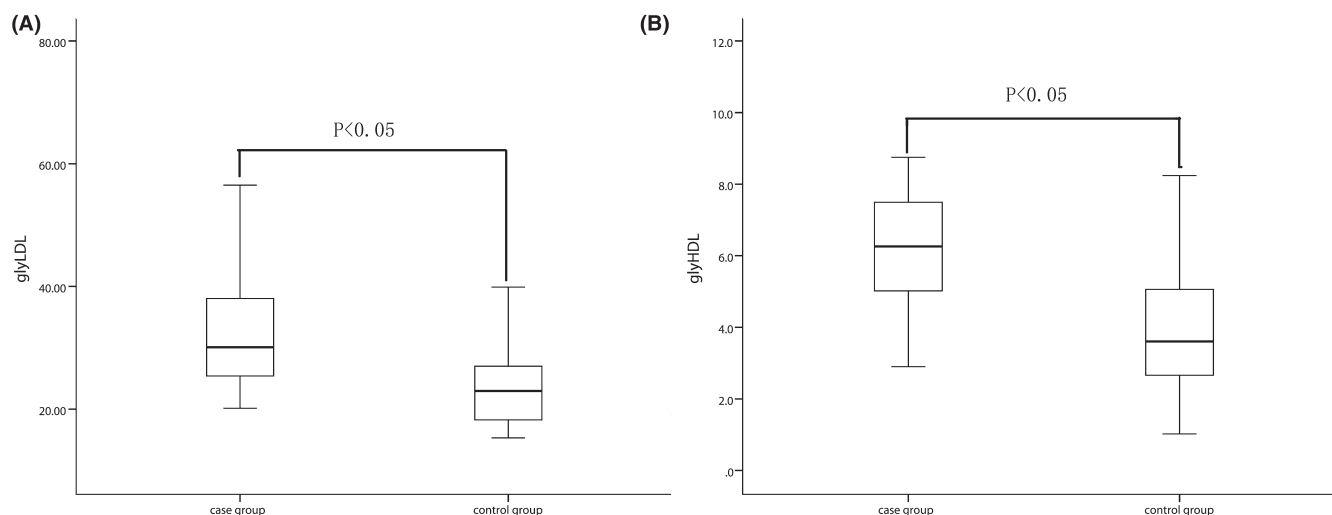
#### 3.4 | Analyses of G-LDL correlation with lipid and glucose in the coronary atherosclerosis group

The Spearman correlation analyses for G-LDL are shown in Table 3. The level of G-LDL is correlated with FPG and HbA1c levels ( $P < 0.05$ ). To the contrary, G-LDL level is independent of the level of LDL-C ( $P > 0.05$ ).

### 4 | DISCUSSION

Atherosclerosis is a type of chronic progressive pathological process which lipids and blood components deposited in the arterial intima, smooth muscle cells and collagen fibrosis hypertrophied, necrosis and calcification and other degrees of lesions are involved.<sup>12</sup> AMI caused by coronary atherosclerosis has a high rate of recurrence, disability, and mortality, which seriously threatens the physical and mental health of middle-aged and elderly patients.<sup>3</sup> The mechanism of AS is not fully established. The traditional view is that hyperlipidemia, especially high LDL, is a major risk factor for the development of atherosclerosis.<sup>13</sup> However, some studies showed that blood lipid levels are not significantly related to atherosclerosis.<sup>14</sup> At present, most studies focused on the role of modified lipoprotein especially oxidized lipoprotein in atherosclerosis.<sup>15,16</sup> But investigations about the glucose and glycosylated lipoprotein in atherosclerosis were scarce. Therefore, we carried out this study to access the characteristics of AMI patients with atherosclerosis and tried to explore the risk factors in the development of atherosclerosis.

In this study, AMI patients and control individuals showed no significant differences in the level of TG. The level of CHOL and LDL-C in patients is lower than in control individuals. However, the level of FPG, HbA1c, and glycosylated lipoprotein is significantly higher in AMI patients than in control individuals. These findings are interesting and suggested that we need to fully recognize glucose level was important in the development of atherosclerosis. It is noteworthy that the G-LDL level only has associated with FPG and HbA1c, but independent of LDL. So glucose control is very important while lowering lipids.



**FIGURE 1** The levels of glycosylated lipoprotein in different groups. The G-LDL level (A) and G-HDL level (B) in AMI patients and control individuals. G-LDL, glycosylated low-density lipoprotein; G-HDL, glycosylated high-density lipoprotein; AMI, acute myocardial infarction

In recent years, the role of glucose metabolism in the development of atherosclerosis has received more and more attention.<sup>17,18</sup> On the one hand, hyperglycemia can directly act on vascular cells. It can promote the combination of modified lipoprotein and macrophage scavenger receptors to form foam cells which could promote the formation of atherosclerosis.<sup>19</sup> On the other hand, hyperglycemia can cause nonenzymatic reactions of glucose with longer-lived molecules, resulting in stable early glycosylation products. Then, they undergo a series of rearrangements, dehydration, and cleavage reactions to produce stable glycation end products, including G-LDL, G-HDL, and other glycosylated proteins.<sup>20</sup> Glycosylated lipoprotein also promotes lipoprotein oxidation.<sup>16</sup> LDL and HDL with glycosylated or oxidative modification cannot be combined with normal receptors due to structural changes.<sup>21</sup> Modified lipoproteins can only intake cells through the scavenger receptor and cannot downregulate scavenger receptor expression.<sup>22</sup> The modified lipoprotein can continuously ingest cells through the scavenger receptor, cause cholesterol accumulation, and eventually result in the formation of atherosclerosis.<sup>23</sup>

There were some limitations in our study, such as missing biochemical indexes, and missing information of diet and exercise. The

included patients were hospitalized patients, and there might be selection bias in the study. Next, we need prospective studies to evaluate the role of glycosylated lipoprotein in the assessment and prevention of atherosclerosis.

## 5 | CONCLUSION

In summary, the lipid level is not a major factor in the development of coronary atherosclerosis, and the level of modified lipoprotein is closely related to the development of coronary atherosclerosis. It is necessary to take action for glucose control while administering lipid-lowering therapy.

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**TABLE 3** The correlation analysis between G-LDL and the blood lipid and glucose<sup>a</sup>

	<i>r</i>	<i>P</i>
FPG	0.625	<0.05
HbA1c	0.706	<0.05
LDL-C	0.331	>0.05

FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; LDL-C, low-density lipoprotein cholesterol.

<sup>a</sup>Spearman's correlation test for correlation analysis.

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