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Original Article

Influencing factors of coronary artery stenosis in patients with stable coronary heart disease and a correlation analysis

Ming Zhao, Zhihao Guo, Guowei Jia, Rui Ma, Meili Li

Department of Cardiology III, Cangzhou Central Hospital, Cangzhou 061001, Hebei, China

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Abstract: Objective: To explore the relationship of the size and concentration of low density lipoprotein (LDL) particles and high density lipoprotein (HDL) particles and the coronary stenotic degree of stable coronary artery disease. Methods: Altogether 62 patients with coronary disease confirmed by coronary angiography treated in our hospital from March 2019 to March 2020 were selected as the observation group, and 62 healthy persons in the same period were chosen as the control group. The particle size of LDL and HDL protein complexes were measured and we then calculated the concentration ratio to explore the relationship between the two types of lipoprotein particles and the degree of coronary artery disease. The Gensini integral method and the lesion numbers were used to evaluate the coronary stenotic degree. Results: In comparison with the control group, the mean diameter of the average LDL particle in the observation group was smaller, but the type B ratio and Gensini score were higher (P<0.05). In comparison with the control group, the observation group had a higher Sd-LDL concentration ratio, as well as concentration of small-particle HDL, percentage of concentration of small-particle HDL in the whole HDL concentration and Gensini score (P<0.05). In comparison with the single-vessel disease group, the multi-vessel disease group had a smaller LDL concentration, as well as smaller large-particle HDL concentration and percentage of large-particle HDL concentration in the whole HDL concentration, and SD-LDL concentration ratio, small-particle HDL concentration, and percentage of small-particle HDL concentration in the whole HDL concentration and Gensini points were considerably higher (P<0.05). The Gensini score in the observation group showed negative correlations with LDL particle size (r=-0.375, P<0.05), and positive correlations with the concentration of large-particle HDL (r=0.301, P<0.05). Conclusion: The size and concentration of LDL and HDL are significantly related to the coronary stenotic degree in SCAD disease, suggesting that they play a role in the coronary stenotic degree.

Keywords: Low density lipoprotein particles, high density lipoprotein particles, stable coronary artery disease, coronary stenotic degree

Introduction

Stable coronary artery disease (SCAD), the most common type of coronary artery disease, refers to a common clinical disease in which atherosclerosis leads to organ lesions [1]. According to epidemiological statistics [2], the mortality rate of coronary artery disease in China has increased by 5.05% annually, which seriously affects the life and health of patients. The pathogenesis and principles of coronary artery disease are complex, with many risk factors. The stability of the plaque and coronary stenotic degree are fundamental for evaluating the prognosis of the disease [3]. In recent years, great progress has been made in the clinical treatment of dyslipidemia, such as regarding knowledge about the increase of high density lipoprotein cholesterol (HDLC), the decrease of low density lipoprotein cholesterol (LDLC), etc., but most people still have a high risk of getting cardiovascular disease. Related studies found that [4] large individual differences were discovered between the low-density lipoprotein (LDL) particles and the high-density lipoprotein (HDL) particles, which serve a critical role in the developmental process of coronary artery disease. A study found that [5] patients with coronary artery disease had less large HDL particles, compared to patients with non-coronary artery disease, but had more small HDL particles and LDL particles. At pres-

ent, there are few reports about this correlation with atherosclerosis. Therefore, in this study, 62 patients with coronary artery disease confirmed by coronary angiography in our hospital from March 2019 to March 2020, and 62 healthy persons with physical examination during the same period were selected to explore the relationship of the size and concentration of low density lipoprotein particles and high density lipoprotein particles and the degree of stable coronary stenotic coronary artery disease, aiming to find an index used to predict the degree of coronary artery stenosis in the future.

Materials and methods

General materials

A total of 62 patients with coronary disease confirmed by coronary angiography from March 2019 to March 2020 were selected as the observation group, and 62 healthy persons in the same period were chosen as the control group. In the control group, there were 35 males and 27 females aged from 42 to 78 years, with an average age of 58.92±9.89 years. In the observation group, there were 38 males and 24 females aged from 43 to 75 years, with an average age of 59.32±10.03 years. Inclusion criteria: (1) Patients in the observation group who were diagnosed in accordance with the *Guidelines for the Diagnosis and Treatment of Stable Coronary Heart Disease* of the European Society of Cardiology [6]; (2) Persons in both groups without any serious diseases of other organs; (3) Patients whose clinical data were complete. Exclusion criteria: (1) Patients with damage of heart, kidney, liver, lung and other organs; (2) Patients with autoimmune diseases or other central nervous system diseases; (3) Patients with myocarditis, congenital heart disease or acute coronary arterial syndrome; (4) Patients with cancer. The medical ethics committee of our hospital approved this study, and the patients and their families confirmed and signed an informed consent form.

Methods

Materials: From the medical records, the personal details of patients collected during physical examinations regarding gender, age, body mass index (BMI), diastolic blood pressure, systolic blood pressure, diabetes, hypertension, blood sugar, triacylglycerol (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDLC), high density lipoprotein cholesterol (HDLC), etc. were collected.

Collection of samples: Patients gave 8 mL of cubital venous blood on an empty stomach in the morning in hospital, and 4 mL was centrifuged and seperated at 2000 r/min. Then the supernatant was stored in a freezer at -80°C for later use, and all reagents were tested within 3 h. A direct method was used for measuring and confirming LDLC, HDLC and small dense low density lipoprotein (SD-LDL), enzyme assay was used for TC, and colorimetry for TG. The operation steps strictly obeyed the instructions.

Another 4 mL of venous blood was mixed into an ethylene diaminete traacetic acid (EDTA) anticoagulation tube, centrifuged at 3000 r/min for 10 minutes, and stored in a freezer at -70°C for testing. Blood plasma was added into the LDL particle kit and the HDL particle kit respectively, and was tested by the Lipoprint lipoprotein analyzer (Quantimetrix, USA). LDL particles consist of 7 isoforms. LDL-1-2 isoforms are large and light LDL particles, type A, are mainly responsible for the transportation of cholesterol; LDL-3-7 isoforms are small and dense LDL particles, namely type B. Compared with type A, type B LDL is more prone to oxidation, thus leading to cardiovascular diseases. HDL particles are composed of 10 isoforms, and HDL1-3 represent large particles HDL, HDL-4-7 are medium particles HDL, HDL-8-10 are small particles HDL.

Evaluation of coronary stenotic degree: Gensini score system was employed to quantitatively assess the severity of coronary artery stenosis, which was divided into six degrees: 1 point (1%-25%), 2 points (26%-50%), 4 points (51%-75%), 8 points (76%-90%), 16 points (91%-99%) and 32 points (100%). The scores of coronary stenosis were multiplied by the corresponding coefficient of the coronary artery lesion: left main × 5.0; anterior descending artery: proximal × 2.5, middle × 1.5, distal × 1.0; circumflex artery: proximal × 2.5, middle × 1.0, distal × 1.0; the proximal, middle and distal sections of the right coronary artery respectively × 1.0; small branch × 0.5, the final score showed the severity of coronary artery disease.

Table 1. Comparison of general materials

Item	Observation group (n=62)	Control group (n=62)	t/χ^2	*P*-Value
Gender (M/F)	38/24	35/27	0.300	0.584
Age (years)	59.82±10.03	59.72±10.06	0.055	0.956
BMI (Kg/m)	23.85±7.29	24.52±6.02	0.558	0.578
DBP (mmHg)	124.55±14.38	127.46±16.12	1.061	0.291
DBP (mmHg)	80.20±8.56	79.98±8.68	0.142	0.887
Diabetes (numbers)	41 (61.19)	26 (38.81)	7.306	0.007
Hypertension (numbers)	38 (63.33)	22 (36.67)	8.267	0.004
TG (mmol/L)	1.80±0.89	1.12±0.38	2.799	0.006
TC (mmol/L)	4.01±0.75	3.96±0.94	0.327	0.744
blood sugar (mmol/L)	5.93±1.80	5.70±1.84	0.704	0.483
LDL-C (mmol/L)	2.05±0.40	2.99±0.80	8.275	<0.001
HDL-C (mmol/L)	2.98±0.84	2.33±0.56	5.070	<0.001
Sd-LDL (mmol/L)	0.70±0.41	0.47±0.21	3.931	<0.001
Family history (yes/no)	12 (60.00)	8 (40.00)	0.945	0.329

Note: diastolic blood pressure = DBP, systolic blood pressure = SBP.

Statistical methods

SPSS 23.0 software was employed for statistically analyzing all data in this study. The measurement data were tested using a normality test, and the data conforming to a normal distribution was expressed by ($\chi \pm sd$), and the independent sample t test was conducted between groups and one-way analysis of variance among groups. The qualitative data were described by percentage and conducted using chi-square χ^2 test. The correlation between the two factors was analyzed by bivariate correlation. P<0.05 was considered statistically significant.

Results

Comparison of general materials

The general materials such as gender, age, BMI, diastolic blood pressure, systolic blood pressure, diabetes, hypertension, TG, TC, blood sugar, etc. were not statistically different (P>0.05), Significant differences were found in LDLC, HDLC, and SDLDL (P<0.05). See **Table 1**.

Comparison of the size and concentration of LDL particles and HDL particles

No difference was detected in medium-particle HDL concentration and the percentage of the medium-particle HDL concentration in the HDL concentration between the two groups (P>0.05). In comparison with the control group, the observation group had a smaller mean diameter of the average LDL particle, and higher type B ratio and higher Gensini score (P<0.05). In comparison with the control group, the observation group had a lower large-particle HDL concentration and lower percentage of large-particle HDL concentration in the HDL concentration, higher small-particle HDL concentration and higher percentage of the small-particle HDL concentration in HDL concentration (P<0.05). See **Table 2**.

The relationship of the size and concentration of LDL particles and HDL particles and the severity of coronary artery disease between the two groups

The observation group had less LDL particles, less of a concentration of large-particle HDL and lower percentage of the concentration of large-particle HDL in the whole HDL concentration in both the single-vessel disease group and the multi-vessel disease group in comparison of the control group. In comparison of the control group, the observation group had a higher Sd-LDL concentration ratio, higher concentration of small-particle HDL, as well as percentage of the concentration of small-particle HDL in the whole HDL concentration and Gensini score (P<0.05). In comparison with the single-vessel disease group, the multi-vessel disease group had smaller LDL concentration as well as large-particle HDL concentration, lower percentage of large-particle HDL concentration in the whole HDL concentration, while the SD-LDL concentration ratio, small-particle HDL concentration, and the percentage of small-particle HDL concentration in HDL concentration and Gensini points were considerably higher (P<0.05); See **Table 3**.

The relationship of other factors and the severity of coronary artery disease

In the observation group, both single-vessel and multi-vessel disease group had higher diabetes, hypertension ratio and triacylglycerol (TG) levels than those in the control group (P<0.05). See **Table 4**.

Table 2. Comparison of the size and concentration of LDL particles and HDL particles

Group	Observation group (n=62)	Control group (n=62)	*t*	*P*
Size of average LDL particle (Å)	259.78±3.42	266.02±4.28	8.968	<0.001
LDL isoform (A/B, %)	27.33/72.67	53.30/46.70		<0.001
Gensini score (score)	51.03±20.39	30.75±17.64	5.923	<0.001
Large-particle HDL concentration (mg/L)	103.45±46.27	144.37±49.89	4.735	<0.001
Medium-particle HDL concentration (mg/L)	221.31±75.64	219.88±75.51	0.105	0.916
Small-particle HDL concentration (mg/L)	125.04±65.78	88.13±34.97	3.901	<0.001
Large-particle HDL concentration/HDL concentration (%)	23.08±8.43	31.20±7.90	5.534	<0.001
Medium-particle HDL concentration/HDL concentration (%)	50.78±6.77	50.02±8.62	0.546	0.586
Small-particle HDL concentration/HDL concentration (%)	19.23±6.92	28.78±12.53	5.253	<0.001

Table 3. The relationship of the size and concentration of LDL particles and HDL particles and the severity of coronary artery disease in the two groups

Group	Control group (n=62)	single-vessel disease (n=24)	multi-vessel disease (n=38)
Size of average LDL particle (Å)	268.02±3.84	265.51±3.55[a]	263.02±3.30[a,b]
Sd-LDL concentration ratio (%)	9.65±4.68	11.46±8.50[a]	16.82±10.46[a,b]
Large-particle HDL concentration (mg/L)	162.20±48.29	127.48±43.38[a]	93.37±41.89[a,b]
Small-particle HDL concentration (mg/L)	86.02±32.4	110.04±43.78	132.13±65.97
Large-particle HDL concentration/HDL concentration (%)	33.02±8.82	28.08±7.43	22.20±6.22
Small-particle HDL concentration/HDL concentration (%)	17.83±5.35	19.23±6.92[a]	28.78±12.53[a,b]
Gensini score (Points)	0	22.30±16.15	58.69±32.77[b]

Note: a means the comparison with the control group (P<0.05); b means the comparison with the single-vessel disease group (P<0.05).

Table 4. The relationship of other factors and the severity of coronary artery disease

Group	Control group (n=62)	single-vessel (n=24)	multi-vessel (n=38)
Diabetes (numbers, %)	12 (19.35)	15 (62.25)[a]	30 (78.95)[a,b]
Hypertension (numbers, %)	17 (27.42)	19 (79.17)[a]	18 (47.37)[a]
TG (mmol/L)	1.88±0.92	1.40±0.70[a]	1.12±0.42[a,b]

Note: a means the comparison with the control group (P<0.05); b means the comparison with the single-vessel disease group (P<0.05).

Table 5. The relationship of the Gensini score, LDL particles and HDL particles in the observation group

Item	r	P
Size of average LDL particle (Å)	-0.375	<0.001
Large-particle HDL concentration (mg/L)	0.301	<0.001

The relationship of the Gensini score, LDL particles and HDL particles in the observation group

The results of correlation analysis showed that the Gensini score in the observation group showed negative correlation with LDL particle size (r=-0.375, P<0.05), and positive correlation with the concentration of large-particle HDL proteins (r=0.301, P<0.05). See **Table 5** and **Figures 1**, **2**.

Discussion

SCAD mainly refers to the stable stage of ischemic cardiomyopathy, stable angina pectoris and acute coronary syndrome. In general, patients with this disease are under a relatively stable condition, but some patients with severe coronary stenosis are more likely to be at risk of acute cardiovascular events [7, 8]. There are a great many risk factors inducing the disease, which can be divided into non-adjustable factors and adjustable factors. Due to the poor control of adjustable factors and the continuous increase of non-adjustable factors, major

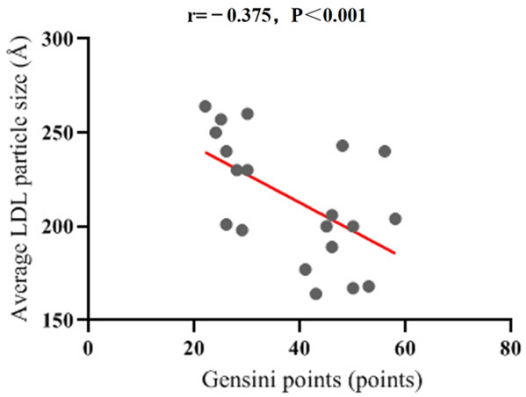

Figure 1. Correlation analysis of Gensini score and LDL particle size in the observation group.

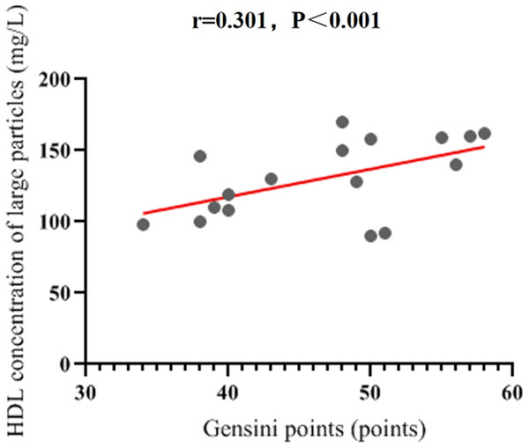

Figure 2. Correlation analysis of Gensini score and large-particle HDL concentration in the observation group.

adverse cardiovascular events may happen to patients with SCAD once again [9]. Some studies [9] have discovered that LDLC is a critical risk factor that induces coronary artery disease, and reducing LDLC level effectively lowers the risk and mortality of coronary artery disease. However, recent studies have found [10, 11] that there are considerable individual differences in LDL particles, and that the risk of atherosclerosis for patients with different concentrations of LDL sub-fractions of cholesterol and same LDL-C concentration differs. Some studies have also shown [12] that HDL particles are closely related to their functions, and the different sizes are critical to the process of atherosclerosis, not only as a suggestive index for lipid-lowering therapy, but also as an early landmark of atherosclerosis of patients with cardiovascular and cerebrovascular diseases. It is seen that, in addition to the level of LDLC and HDLC, attention needs to be paid to the physicochemical properties of the LDL and HDL proteins.

LDL is composed of particles with different densities, size and chemical components. The dense distribution of LDL sub-type is related to the coronary stenotic degree, with a critical role in the level of coronary artery disease [13]. More studies have found that [14], the risk of coronary artery disease is correlated to SDLDL or LDL type B, and lipid-lowering drugs reduce the risk of coronary artery disease by decreasing the level of Sd-LDL. The main test methods of LDL isoforms are nuclear magnetic resonance, density gradient ultra-centrifugation, non-denatured gradient gel electrophoresis, etc. Because of different test methods, there are differences in the classification of LDL isoforms [15]. Meanwhile, both the measurement of LDL subtypes and LDL peak particle size, and the absolute plasma concentration of LDL particles are of the same great clinical significance for disease risk assessment. HDL, a kind of heterogeneous lipoprotein, consists of preβ1-HDL, preβ2-HDL, HDL-2 and HDL-3 and other components in different sizes and subtypes [16]. In the traditional view, HDL-C is of great importance in adjusting cholesterol. It can not only promote reverse cholesterol transport (RCT) to directly protect the arterial wall, but also eliminates atherosclerotic plaque [17]. In patients with coronary artery disease or hyperlipidemia, when HDL3 of small particles increases and HDL2 of large particles decreases, it means that the RCT process is blocked. At present, relevant clinical studies have confirmed [18] that HDL particles are closely related to their functions, and show an important significance in the process of atherosclerosis. The heterogeneous particles and different subcomponents could lead different functions. The anti-arteriosclerosis function of HDL particles is not only related to the value of HDL-C, but more importantly, is related to the function of HDL particles. Studies have shown [19] that large-particle HDL shows a strong anti-arteriosclerosis function, but reports such as from Mazer et al [20] indicate that the relative size of HDL particles can be replaced with the ratio of HDL-C/apo-A1, revealing different functions of HDL particles. In this study, we showed that in

comparison of the control group, the observation group had a smaller mean diameter of the average LDL particles, but a higher type B ratio and a higher Gensini score. The observation group had lower concentration of large-particle HDL and a lower percentage of the concentration of large-particle HDL in the whole HDL concentration, compared to the control group. However, the observation group had a higher concentration of small-particle HDL and higher percentage of the concentration of small particle HDL in the whole HDL concentration. According to a foreign study [21], an increase in SDLDL concentration and a smaller diameter of LDL particles can predict the probability of future cardiovascular events in patients with stable coronary artery disease. In this study, the results showed that the observation group had less LDL particles, lower concentration of large-particle HDL and lower percentage of the concentration of large-particle HDL in the whole HDL concentration in both the single-vessel disease group and the multi-vessel disease group in comparison with the control group. In comparison of the control group, the observation group had a higher Sd-LDL concentration ratio, higher concentration of small-particle HDL, higher percentage of the concentration of small-particle HDL in the whole HDL concentration and Gensini score. In comparison with the single-vessel disease group, the multi-vessel disease group had smaller LDL concentration, lower large-particle HDL concentration and lower percentage of large-particle HDL concentration in the whole HDL concentration; while the SD-LDL concentration ratio, the small-particle HDL concentration, and the percentage of small-particle HDL concentration in HDL concentration and Gensini points were considerably higher, indicating that the decrease in LDL particles and the rise in small or large HDL concentration were able to promote the progression of coronary artery disease. Through the correlation analysis, the results showed that the Gensini score in the observation group showed negative correlations with LDL particle size and positive correlation with the concentration of large-particle HDL; indicating that LDL particle size, SDLDLC level and large-particle HDL concentration can express the severity of coronary artery disease, and may be a standard of CAD disease evaluation.

In conclusion, the degree of coronary stenotic in SCAD is related to the size and concentration of LDL and HDL particles, negatively related to the size of LDL particles, and positively related to the concentration of large-particle HDL. Sd-LDL is a part of LDL with a small proportion of cholesterol and alcohol components and a large proportion of protein (mainly apoB); the increase of Sd-LDL elevates the risk of coronary heart disease and myocardial infarction [22]. In the case of normal LDL levels, due to increased Sd-LDL, heart disease may still occur. Increased TG has received more attention for its effect of dysfunctional sclerosis. TG may have a certain relationship with lipoprotein oxidation modification, Sd-LDL production, and HDL-c reduction. High TG can also promote blood hypercoagulability, and further increases the risk of arteriosclerosis and the risk of arteriosclerosis [23]. The mechanism of Sd-LDL-induced arteriosclerosis and coronary heart disease is more complicated. It is generally believed that Sd-LDL has a low affinity for LDL receptors. The residual time in the blood is prolonged, which makes it easier for larger and lighter LDL particles to enter the arterial wall; Sd-LDL is more sensitive to oxidative modification, and has strong binding with arterial wall proteoglycans [22]. This study shows that the increase in Sd-LDL is accompanied by abnormalities in other lipid components. The occurrence of coronary heart disease is the result of multiple factors, and the size and concentration of LDL and HDL are correlated with the degree of coronary artery stenosis in SCAD patients, which are considered as one of the indicators to predict the degree of coronary artery stenosis. This study had a small sample size, without collecting the history of statin use, and lacks a representation of other issues, which results in certain information bias and possible differences in results. In the follow-up research, it is necessary to expand the sample size and look for further prospects.

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Disclosure of conflict of interest

None.

Address correspondence to: Ming Zhao, Department of Cardiology III, Cangzhou Central Hospital, No. 16, Xinhua West Road, Yunhe District, Cangzhou 061001, Hebei, China. E-mail: itszhaoming@163.com

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