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Assessment of Risk Factors for Coronary Artery Disease and Severity by Coronary Computed Tomography Angiography Imaging

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Objective: To investigate the correlation between risk factors for coronary stenosis and the degree of coronary artery stenosis based on coronary computed tomography angiography (CCTA).

Methods: Two hundred seventy-eight patients with coronary artery disease who received treatment in our hospital between January 2020 and January 2021 were selected as the experimental group, and 100 healthy people who received physical examination in our hospital during the same period were selected as the control group (age and gender matched with the study group). The clinical data and CCTA data of the two groups of patients were collected and compared. Computed tomography fractional flow reserve (FFR_{CT}) values were calculated based on the CCTA data of the patients in the study group, risk factors for coronary artery stenosis were analysed and the correlation between the risk factors and CT flow reserve fraction was explored.

Results: The serum total bilirubin (BIL), apolipoprotein A (apoA), low-density lipoprotein cholesterol (LDL-C), uric acid, total cholesterol (TC) and mean platelet volume levels were higher in the experimental group than in the control group ($P < 0.05$). Unconditional logistic regression analysis showed that LDL-C, uric acid, TC, triglyceride, serum total BIL and apoA were independent risk factors for coronary heart disease ($P < 0.05$). Serum total BIL ($r = 0.27$), apoA ($r = -0.30$), uric acid ($r = -0.48$), TC ($r = -0.35$), triglyceride ($r = -0.73$) and LDL-C ($r = -0.65$) showed a negative correlation with FFR_{CT} values ($P < 0.05$). A positive correlation was detected between high-density lipoprotein cholesterol and FFR_{CT} values ($r = 0.37$, $P < 0.05$).

Conclusion: Triglycerides, LDL-C, uric acid, TC, serum total BIL and apoA are risk factors for coronary artery stenosis that should be closely monitored and receive active intervention in clinical practice.

Keywords: coronary heart disease, coronary artery stenosis, computed tomography angiography, risk factors, computed tomography fractional flow reserve

Introduction

Coronary heart disease (CHD) is a disease characterised by atherosclerotic lesions in the coronary arteries that induce stenosis or blockage of the vascular lumen. This condition can easily lead to myocardial ischaemia, hypoxia or necrosis, followed by chest pain, nausea, vomiting and other clinical symptoms.[1] Approximately one-third of patients die suddenly on the first attack.[2–7] Therefore, the prevention and early detection of CHD are vital.

Digital subtraction angiography is the gold standard for the diagnosis of coronary stenosis;[8] however, it is highly invasive, risky, costly and difficult for some patients to tolerate. With the development of electronic computed tomography (CT) imaging technology, coronary CT angiography (CCTA) has become the predominant test for clinical screening and diagnosis of CHD because it is convenient, non-invasive and has high sensitivity.[9] It has been reported that

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CCTA has good agreement with coronary angiography in assessing the degree of stenosis of the main coronary artery and secondary branches; however, in patients with arrhythmia, the evaluation of the degree of coronary stenosis by CCTA differs significantly from that by coronary angiography.[10] The CT fractional flow reserve (FFR_{CT}) technique is a non-invasive cardiac functional imaging technique that provides morphological and functional information about coronary arteries and accurately assesses coronary artery stenosis and haemodynamic changes.[11,12] In recent years, there have been many studies on the risk factors for CHD[13] but few on the influencing factors and correlation of coronary artery stenosis in patients with CHD. Investigating these factors will help strengthen the prevention and treatment of the disease and provide a reference for its early screening.

Information and Methodology

Research Participants

A total of 278 patients (196 men and 82 women) with a first diagnosis of coronary artery stenosis between January 2020 and January 2021 were selected for the study and were included in the experimental group. Another 100 healthy individuals (62 men and 38 women) who received physical examinations at our hospital during the same period were assigned to the study's control group (No coronary heart disease, gender and age appropriate to the study group). The inclusion criteria were as follows: (1) based on the American Heart Association guidelines,[14] all patients in the study group met the diagnostic criteria for chronic CHD, and CCTA assessment of lesion stenosis of 50–90%; (2) patients aged 40–80 years old; (3) the heart rate can be controlled at <80 beats/min, without atrial fibrillation; (4) glomerular filtration rate of >60 mL/min; (5) New York Heart Association cardiac function classification of grade I–II; (6) The patients had no comorbidities of other organic cardiac diseases or diabetes mellitus; and (7) patients with complete clinical data. The exclusion criteria included: (1) patients with CT iodine contrast agent allergy; (2) CCTA images were not consistent with the diagnosis; and (3) women during breastfeeding or at childbearing age. Informed consent was obtained from the patients and their families, and the study was approved by the ethics approval committee of our hospital.

Research Methods

Coronary Computed Tomography Angiography Imaging Methods and Post-Processing

All patients underwent CCTA examination after admission. In this study, a GE 64-slice-volume CT system was used for scanning. Prior to scanning, the attendant precautions were explained in detail to the patients, who were instructed to exhale and hold their breath. The patient was placed in a supine position on the CT examination bed with both hands raised and was then connected to a chest cardiac conductance machine. The attending nurse was instructed to keep the venous indwelling needle in the elbow vein and to connect it to a high-pressure syringe.

The scanning conditions were as follows: tube voltage/current = 120 KV/500 mA; collimator width = 0.625 mm; pitch = 0.20 mm; scanning range was from the tracheal carina level to the cardiac diaphragm level. The non-ionic contrast agent, iohexol (350 mg/mL), was selected, with a total volume of 60–80 mL and an injection rate of 5 mL/s. Following the injection of the contrast agent, 40 mL of normal saline was injected at the same rate to flush the tube. The selected CT cardiac scanning mode was retrospective electrocardiogram-gated scanning, and a standard reconstruction algorithm was used for the plain scan and the image following the injection of the contrast agent. The total inspection time was approximately 14–18 min (Figure 1).

Computed Tomography Fractional Flow Reserve Analysis

The FFR_{CT} analysis was performed using deep learning software. After uploading the CCTA images to the software, the FFR_{CT} value of the coronary artery was automatically analysed and calculated. The distal end of the plaque was used as the measurement standard point (approximately 2–3 cm from the plaque) (Figure 2). The degree of coronary stenosis was reflected by the FFR_{CT} values. Here, $FFR_{CT} \leq 0.80$ was defined as significant hemodynamic stenosis. All measurements were completed independently by two or more attending physicians. When the difference between the two measurements was large, the measurement was retaken by a physician with the title of deputy director or above; otherwise, the mean value of the two measurements was taken as the final result.

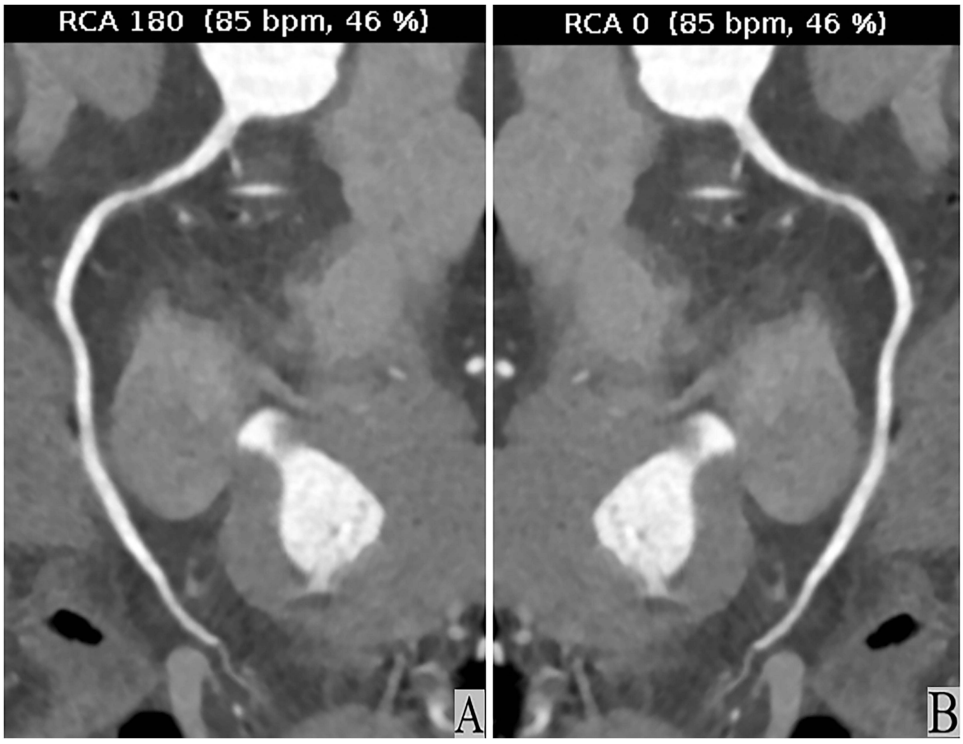

Figure 1 CCTA images of 2 patients with normal coronary artery. (**A**) Male 54 years old, CCTA showed multiple mixed plaques in the proximal right crown with 80% stenosis of the lumen; (**B**) Female 49 years old, multiple non-calcified plaques in the proximal-mid right main stem of the crown with 50% stenosis of the lumen.

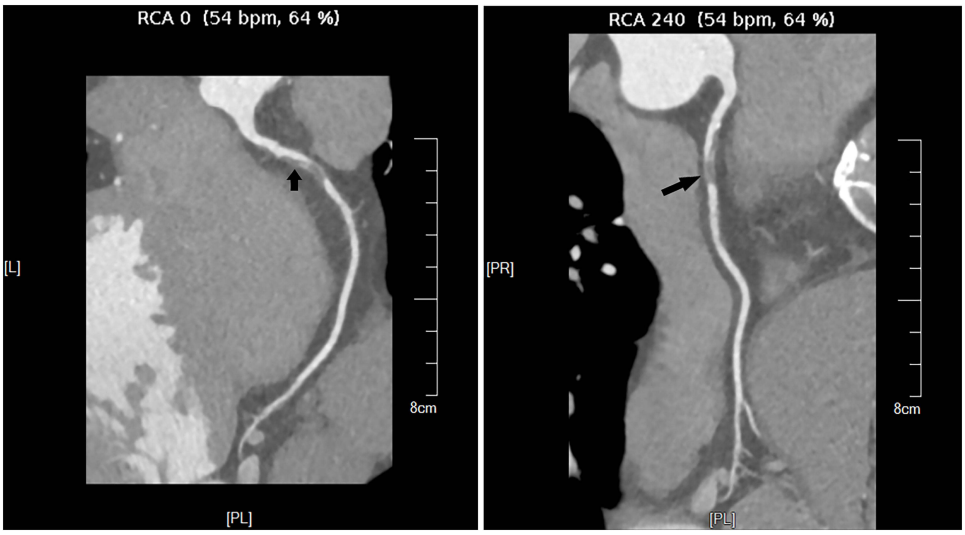

Figure 2 Examination results of a 55-year-old female patient with coronary artery disease. Arrowhead: Coronary CTA test showing calcified lesions in the proximal.

Determination of Risk Factor Indicators

Basic clinical information of the patients was collected after follow-up and basic data such as their age, gender, whether they were hypertensive (blood pressure 160/95 mmHg or above), whether they were smokers, and family history were recorded. Within 2 days of the CCTA examination, 15–20 mL of peripheral venous blood was collected from all patients. The patient's blood index levels were measured, including: total bilirubin (BIL, normal range: 3.42–20.05 μmol/L), apolipoprotein A (apoA, normal range: 1–1.6 g/L), high-density lipoprotein cholesterol (HDL-C, normal range: 1.16–1.42 mmol/L for men, 1.29–1.55 mmol/L for women), low-density lipoprotein cholesterol (LDL-C, normal

range: < 2.6 mmol/L), uric acid (normal range: 150–416 μmol/L in men and 89–357 μmolL in women), mean platelet volume (MPV, normal range: 7–11 fL), total cholesterol (normal range: < 6.0 mmol/L), triglycerides (normal range: <1.7 mmol/L).

Statistical Analysis

Statistical analysis was performed using SPSS 19.0 and GraphPad Prism 5 (GraphPad Software) software. Count data were recorded in the form of composition ratios and rates, and comparisons between groups were performed using the chi-square (χ^2) test. Measurement data were recorded in the form of mean ± standard deviation, and comparisons between groups were made using a dual independent-sample *t*-test. Pearson's correlation analysis was used to explore the correlation between the risk factors for coronary stenosis. Non-conditional multiple logistic regression analysis was used to explore the risk factors for coronary atherosclerosis. A bilateral *p* value of <0.05 was considered statistically significant.

Results

Comparison of General Clinical Data

The age of the patients in the experimental group was 19–89 years old, with an average of 56.27 ± 12.31, and the age of the healthy control group was 23–78 years old, with an average of 59.86 ± 2.99. The average degree of vascular stenosis was 63.2%. There was no significant difference in age range, sex composition, hypertension, smoking composition or family history between the experimental group and the control group ($P > 0.05$), showing that the two groups were comparable. The collection of clinical laboratory indicators (measurement data) was in line with a normal distribution. The serum total BIL (14.51 ± 1.27 vs 10.26 ± 1.40 μmol/L), apoA (1.53 ± 0.16 vs 1.22 ± 0.22 g/L), LDL-C (2.71 ± 0.68 vs 2.29 ± 0.56 mmol/L), HDL-C (1.29±0.27 vs 1.27±0.24 mmol/L), uric acid (324.77 ± 90.11 vs 316.04 ± 74.27 μmol/L), TC (1.26 ± 0.74 vs 1.06 ± 0.38 mmol/L) and MPV (10.67 ± 1.06 vs 10.63 ± 0.96 fL) values were significantly higher in the experimental group than in the control group ($P < 0.05$). Triglyceride levels were lower in the experimental group than in the control group ($P < 0.05$). The difference in FFR_{CT} values between the two groups was statistically significant ($P < 0.05$) (Table 1).

Correlation Analysis Between Risk Factors and Computed Tomography Fractional Flow Reserve Values

Among the 278 patients with coronary artery stenosis participating in the study, 26 had FFR_{CT} values of >0.80 and 252 had FFR_{CT} values of <0.80. Pearson's correlation analysis of each risk factor and the FFR_{CT} values revealed that apoA ($r = -0.30$), uric acid ($r = -0.48$), TC ($r = -0.35$), triglyceride ($r = -0.73$) and LDL-C ($r = -0.65$) had a negative correlation ($P < 0.05$). Total serum bilirubin ($r = 0.27$) and HDL-C ($r = 0.37$) were positively correlated with FFRCT values ($P<0.05$). In the present study, there was no clear correlation between MPV and FFR_{CT} values (Table 2 and Figure 3).

Multiple Analyses of Coronary Heart Disease

Unconditional logistic regression analyses were performed using a FFR_{CT} value of <0.8 as the dependent variable, and factors that were statistically significant in one-way analyses and risk factors as independent variables. The results showed that LDL-C (odds ratio [OR] = 1.643, 95% confidence interval [CI] = 1.031–1.828, $P = 0.010$), uric acid (OR = 1.607, 95% CI = 1.419–2.031, $P = 0.018$), TC (OR = 2.128, 95% CI = 1.876–2.510, $P = 0.023$), triglycerides (OR = 1.509, 95% CI = 1.122–1.831, $P = 0.017$), serum total BIL (OR = 1.626, 95% CI = 1.419–1.956, $P = 0.034$), apoA (OR = 2.730, 95% CI = 2.513–3.210, $P = 0.008$) and HDL-C (OR = 0.690, 95% CI = 0.587–0.926, $P = 0.013$) were independent risk factors for CHD ($P < 0.05$) (Table 3).

Discussion

The COVID-19 pandemic has accelerated the interest and investment of health systems in remote care and digital technology. Digital technology will continue to progress and will continue to be applied in many aspects, such as

Table 1 Comparison of General Clinical Data

	Experimental Group	Control Group	t/χ^2	*p*
Number of cases (n)	278	100	–	–
Age (year)	56.27±12.31	59.86±2.99	9.42	0.612
Male [n (%)]	196 (70.50)	62 (62.00)	1.73	0.073
Hypertension [n (%)]	126 (45.32)	48 (48.00)	2.364	0.326
Composition ratio of smoking [n (%)]	169 (60.79)	54 (54.00)	0.97	0.64
Body mass index (Kg/m^2)	28.6±3.4	24.8±3.5	12.29	0.059
Family history [n (%)]	122 (43.88)	39 (39.00)	0.83	0.083
Glomerular filtration rate (mL/min)	88.18±7.48	92.43±8.49	9.201	0.051
Total serum bilirubin (μmol/L)	14.51±1.27	10.26±1.40	3.319	0.008
Apolipoprotein A (g/L)	1.53±0.16	1.22±0.22	9.203	0.005
High-density lipoprotein cholesterol (mmol/L)	1.29±0.27	1.27±0.24	1.017	0.013
Low-density lipoprotein cholesterol (mmol/L)	2.71±0.68	2.29±0.56	1.943	0.022
Uric acid (μmol/L)	324.77±90.11	316.04±74.27	5.228	0.006
Mean platelet volume (fL)	10.67±1.06	10.63±0.96	0.973	0.023
Total cholesterol (mmol/L)	1.26±0.74	1.06±0.38	0.512	0.043
Triglyceride (mmol/L)	1.02±0.35	1.08±037	1.118	0.012
CT fractional flow reserve value				
>0.80	26 (9.35)	86 (86.00)	47.03	0.003
<0.80	252 (90.65)	14 (14.00)		

Table 2 Correlation Between Risk Factors and CT-FFR Value

Variables	r	*p*
Low-density lipoprotein cholesterol (mmol/L)	−0.65	0.012
Uric acid (μmol/L)	−0.48	0.027
Total cholesterol (mmol/L)	−0.35	0.022
Triglyceride (mmol/L)	−0.73	0.031
Total serum bilirubin (μmol/L)	0.27	0.043
Apolipoprotein A (g/L)	−0.30	0.010
High-density lipoprotein cholesterol (mmol/L)	0.37	0.009
Mean platelet volume (fL)	0.002	0.732

diagnosis, rehabilitation and treatment, especially in patients with cardiovascular diseases.[14,15] Studies have shown that mobile technology-based solutions have a good therapeutic effect on such diseases.[16,17] For example, FFR_{CT} technology can reduce the threshold of green, safe and accurate screening (stenosis), reduce unnecessary invasive interventional examination and avoid missed diagnosis and treatment of some patients, thus promoting the development of hierarchical

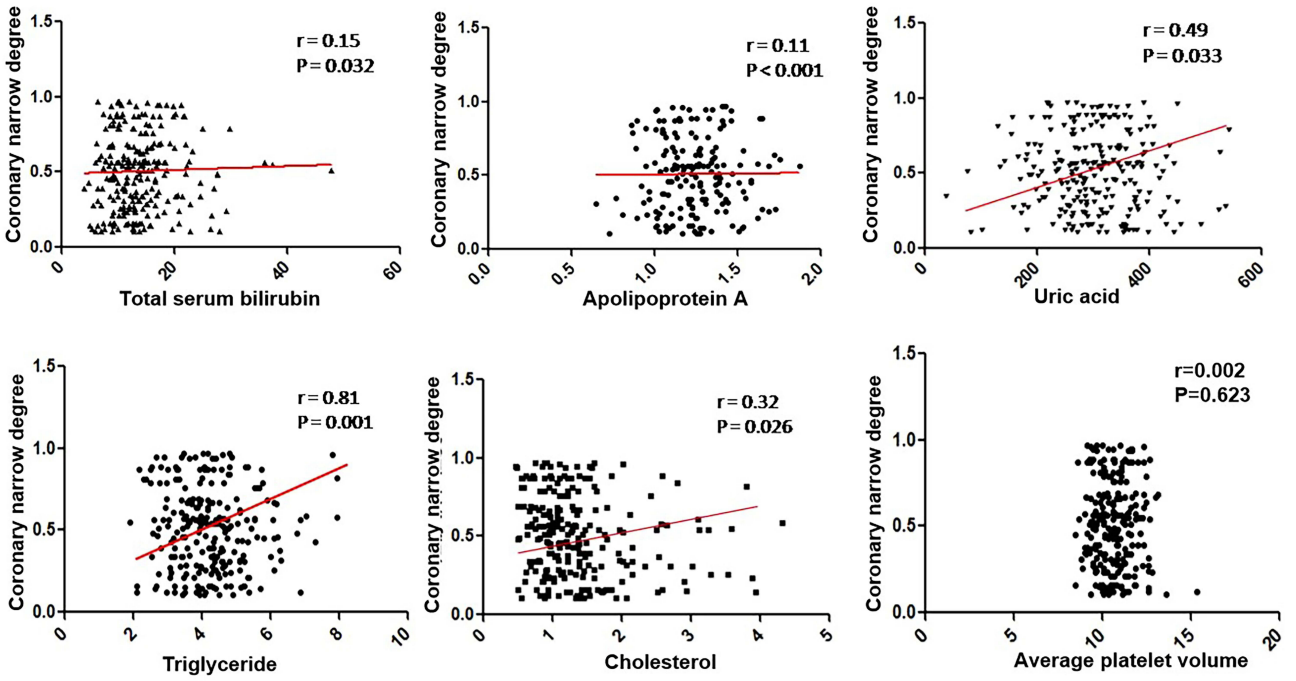

Figure 3 The correlation between risk factors and the degree of coronary artery stenosis.

diagnosis and treatment. At the same time, it can predict the curative effect of surgery and expand the application range of coronary function technology.[13]

In this study, logistic multiple correlation analysis revealed that LDL-C, uric acid, TC, triglycerides, serum total BIL and apoA are risk factors for coronary stenosis. The above results suggest that many risk factors are closely related to the occurrence and development of CHD. Deng et al[18] found a significant causal relationship between LDL-C, uric acid and CHD, which is consistent with the results of the present study. Shaya et al[19] identified LDL-C as an independent risk factor for CHD events. Based on the quantification of CHD, the present study further illustrates LDL-C relationship with the occurrence and development of coronary atherosclerosis, which has been confirmed by existing research. Clinical studies on FFR_{CT} have confirmed that FFR_{CT} has good diagnostic efficacy for CAD, with a sensitivity and specificity of more than 80%.[20] However, there is no complete FFR_{CT} database study in China, and there are few related clinical studies. In this study, there was a positive correlation between HDL-C and FFR_{CT} values. This is consistent with the findings of Wang et al.[21]

Table 3 Multiple Logistic Regression Analysis Between Risk Factors and CT-FFR Value

Variables	Partial Regression Coefficient (β)	Standard Error (SE)	OR value	95% CI	*p* value
Low-density lipoprotein cholesterol (mmol/L)	0.656	0.200	1.643	1.031–1.828	0.010
Uric acid (μmol/L)	0.442	0.315	1.607	1.419–2.031	0.018
Total cholesterol (mmol/L)	0.775	0.227	2.128	1.876–2.510	0.023
Triglyceride (mmol/L)	0.742	0.241	1.509	1.122–1.831	0.017
Serum total bilirubin (μmol/L)	0.437	0.347	1.626	1.419–1.956	0.034
Apolipoprotein A (g/L)	0.431	0.254	2.730	2.513–3.210	0.008
High-density lipoprotein cholesterol (mmol/L)	0.509	0.219	0.690	0.587–0.926	0.013

Numerous studies[22,23] have shown that different risk factors play different roles in coronary atherosclerosis. Research has also found that obesity, a family history of CHD and vitamin D supplementation are closely associated with this disease.[24–26] Messina et al[27] reported a link between serum cholesterol levels and the incidence of CHD. When serum cholesterol increases, blood viscosity also increases, leading to slow blood flow. In addition, TC tends to adhere to damaged vessel walls and accelerate thrombosis. Lakshmanan et al[22] explored the mechanisms involved in atherosclerosis and found that the condition was negatively associated with brachial artery flow-mediated dilatation, a surrogate marker of systemic endothelial dysfunction. Therefore, the clinical risk of CHD can be evaluated by detecting the above indicators.

In the present study, the correlation between the above risk factors and the severity of CHD was analysed, and the causal relationship between each risk factor and coronary atherosclerosis was considered. The degree of coronary artery stenosis was negatively correlated with serum total BIL, apoA, uric acid, TC, triglycerides and LDL-C and positively correlated with HDL-C. Li et al[28] found a mutually reinforcing relationship between LDL-C and high uric acid levels, with the latter promoting LDL-C oxidation and lipid peroxidation. As the uric acid level increases, oxygen free radicals also increase, which promotes and participates in the inflammatory response and induces platelet aggregation, ultimately leading to thrombosis.[29] Zhang et al[30] showed that the peroxidation of LDL-C led to a decrease in vascular endothelial antioxidant capacity, vascular endothelial dysfunction and the formation and development of atherosclerosis. Therefore, in the prevention and treatment of CHD, LDL-C and uric acid are worthy of attention.

Yoshida H et al[31] believe that for elderly patients with CHD, maintaining LDL-C levels can significantly reduce the incidence of cardiovascular adverse events and delay the progression of the disease. When the levels of LDL-C, apoA, TC and triglycerides in serum are low, HDL-C also decreases by varying degrees;[32] these results are different from the results of the present study. This may be because the present study included fewer patients and did not divide them into different age groups for analysis. Another study on the correlation between HDL-C, LDL-C and CHD showed that high levels of serum HDL-C can reduce the risk of CHD caused by LDL-C.[33] This is consistent with the results of the present study. In addition, a cross-sectional study of patients with acute coronary syndromes in northern Iran found that female patients were significantly older and had a higher mortality rate than their male counterparts, suggesting that gender may also be an influential factor.[34]

This study has some limitations. First, the sample size is small, and there may be some bias in the extrapolation of the results. In future research, we will further expand the sample size and conduct more in-depth research. Second, the evaluation indices used in the analysis were single and relatively simple. In future research, we will select more suitable evaluation indices, such as white blood cell count and platelet distribution width – which can be added to haematological factors – and inflammatory indices, such as the neutrophil-to-lymphocyte ratio and the levels of hypersensitive C-reactive protein. Third, bias may have emerged due to the age differences within the patient groups, potentially affecting the nature of coronary artery lesions and thus the results of the corresponding study. Further studies need to control for factors such as age, sex and the nature of coronary artery lesions to reduce study bias. Finally, the present study failed to follow up on the patients' survival. Hence, future studies should further explore the predictive value of related factors for patients with coronary artery stenosis.

Conclusion

Triglycerides, LDL-C, uric acid, TC, serum total BIL and apoA are risk factors for coronary stenosis. They should be closely monitored and receive active intervention in clinical practice. The results of this study have a certain reference value for the clinical treatment and prognosis of coronary artery disease.

Data Sharing Statement

All data generated or analyzed during this study are included in the article.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Central War Zone General Hospital of Wuhan. Informed consent was signed by all participants in this study.

Consent for Publication

Participants consented to have their images published.

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Disclosure

All of the authors had no any personal, financial, commercial, or academic conflicts of interest separately.

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