

Original Article

Correlation between serum 25-hydroxyvitamin D level and coronary heart disease

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Abstract: Objective: To test the relationship between serum 25-hydroxyvitamin D[25(OH)D], interleukin-6 (IL-6), and the severity of coronary heart disease (CHD). Methods: A total of 150 patients with suspected myocardial ischemia presenting to our hospital from January 2018 to January 2020 were recruited. All patients underwent percutaneous coronary angiography (CAG). According to CAG results, they were divided into normal group (n=40) and CHD group (n=110). According to the coronary Gensini score, CHD patients were divided into 62 cases in the low-risk group (< 20 points), 31 cases in the moderate-risk group (20-40 points), and 17 cases in the high-risk group (> 40 points). The Gensini scores and serum 25(OH)D and IL-6 levels in each group were recorded, and the correlation between the serum 25(OH)D and IL-6 levels and the severity of the disease was analyzed. The Essen Stroke Risk Scale (ESRS) was evaluated and compared between the two groups. Results: The serum 25(OH)D, IL-6 level, and ESRS score in the CHD group and the normal group statistically differed ($P < 0.05$). In the CHD group, Gensini score, serum IL-6 level and ESRS score increased with the increase of coronary artery stenosis, and 25(OH)D level decreased with the increase of coronary artery stenosis, and all the differences were significant ($P < 0.05$). Pearson correlation analysis demonstrated that serum IL-6 levels in patients with CHD are positively correlated with the severity of the disease ($r=0.724$, $P < 0.001$), and 25(OH)D levels are in a negative relation ($r=-0.522$, $P < 0.001$). Conclusion: A decrease of serum 25(OH)D level and increase in IL-6 level in patients with CHD are associated with the severity of CHD. This may provide a reference for clinical diagnosis, treatment, and prognosis.

Keywords: Coronary heart disease, severity of disease, serum 25-hydroxyvitamin D, interleukin-6

Introduction

Coronary heart disease (CHD) is a leading cause threatening human life and health [1]. It is defined as myocardial ischemia, hypoxia, or necrosis as a result of stenosis or obstruction of the vascular lumen caused by coronary atherosclerosis [2]. The disease is a complex interplay of complicated pathogenesis and numerous etiologies, among which the atherosclerotic plaque is the pathophysiologic basis [3]. Recent studies have shown that [4] inflammatory cells infiltrate and secrete inflammatory cytokines strongly connected to the occurrence and development of atherosclerosis, such as serum high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6). Vitamin D is an essential trace element for the human body, and it has been reported to play an anti-arteriosclerosis role through the mediation of cellular vitamin D receptors, and has a vital impact on

the occurrence and development of various cardiovascular events [5]. 25-hydroxyvitamin D[25(OH)D] is a form of vitamin D, which is a clinical indicator that can be monitored. Currently, few trials have tested whether a strong correlation between the severity of coronary artery disease and 25(OH)D exists [6]. In view of this, the authors attempted to examine the correlation between the levels of 25(OH)D and IL-6 in patients with CHD and the severity of coronary artery disease.

Materials and methods

Participants

150 patients with suspected myocardial ischemia presenting to our hospital between January 2018 and January 2020 were enrolled. All patients underwent percutaneous coronary angiography. Among them, 82 were male pa-

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tients and 68 were female patients. Body mass index (BMI) was 20.54~29.76 kg/m²; 55 cases had a history of drinking, 67 cases had a history of smoking, and 90 cases had a history of hypertension. According to the results of coronary angiography, the patients were divided into normal group (40 cases) and CHD group (110 cases). The CHD group was divided into 62 cases in the low-risk group (< 20 points), 31 cases in the moderate-risk group (20-40 points), and 17 cases in the high-risk group (> 40 points) according to the Gensini score. The study was registered and carried out after obtaining ethical clearance.

Selection criteria

Participants who met the following were included: no serious mental illness; patients and their families voluntarily participated; normal cognitive, writing, and communication skills. Patients with severe infections, malignant tumors, liver and kidney dysfunction, autoimmune diseases, connective tissue diseases; rheumatic heart disease, cardiomyopathy, chronic heart failure, cerebrovascular diseases and peripheral vascular diseases; pregnancy and lactation; severe consciousness disturbance in the early stage; recent surgery, trauma, and burns; allergic to contrast agents or who were not suitable for coronary angiography (CAG) examination, or had unwillingness to participate were excluded.

Methods

All patients underwent CAG using the Seldinger puncture method through the radial artery, and each coronary artery stenosis was assessed using Gensini scoring method: The calculation method: (1) Based on the gain coefficient and integral product of the lesion, descending branch and right coronary artery anterior, distal, middle, circumflex, distal, anterior descending branch of one of the obtuse edge, the first and second diagonal branch ×1; left ventricular posterior branch ×0.5; close to the cross section ×2.5 roundabout branch; roundabout branch opening ×3.5; middle anterior descending branch ×1.5; proximal anterior descending branch ×2.5; left main lesion ×5 were calculated. According to the degree of stenosis: 1 point was interpreted as ≤ 25%; 2 point as > 25% and ≤ 50%; 4 point as > 50% and ≤ 75%; 8

point as > 75% and ≤ 90%; 16 point as > 90% and ≤ 99%; 32 points as > 99% and ≤ 100%. ③ The total Gensini points were the sum of the above points. Patients with over 50% stenosis of more than one right coronary artery, left circumflex artery, left anterior descending artery, and left main trunk were diagnosed as CHD. Double-blind method was applied to assess by specialist clinicians in our hospital. The total score of 1-20 points was interpreted as the low-risk group, > 20-40 points as the moderate-risk group, and > 40 points as the severe-risk group.

Medical history collection and index testing: Medical history collection: Patients were investigated using a face-to-face questionnaire after obtaining the informed consent form, including gender, age, hypertension, diabetes, and other medical history. Index test: After admission, 3 ml of venous blood (without jaundice, hemolysis, and lipemia) was taken 12 hours before operation in the early morning prior surgery, placed in an EDTA anticoagulation tube, and sent to the hospital inspection center to detect total cholesterol (TC) and triglyceride (TG), low-density lipoprotein cholesterol (LDL-c) and high-density lipoprotein cholesterol (HDL-c). Roche automatic electrochemiluminescence immunoassay analyzer was applied to detect the serum 25(OH)D of all participants. Serum IL-6 levels were determined by double antibody sandwich enzyme-linked immunosorbent assay. The Essen Stroke Risk Scale (ESRS) was evaluated and compared between the two groups. The operation was in strict line with kit instructions.

Statistical methods

The present study was done by SPSS25.0 statistical package. The measured data conforming to the normal distribution were expressed as mean ± standard deviation, and independent sample t-test and one-way analysis of variance were adopted to examine whether the significant differences existed between and among groups. Counted data were given as rate, and χ^2 test and correlation analysis were employed to determine the differences between the groups and the correlation. One-way ANOVA was used to compare multiple groups. Significance was declared at a *P* value of < 0.05. Graphics were plotted by GraphPad prism 8.

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Table 1. Comparison of general information of the two groups of patients

Group	n	gender		age	hypertension	history of smoking	history of drinking	TC (mmol/L)	TG (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)
		male	female								
normal group	40	22	18	58.87±10.16	23	18	15	4.67±0.68	1.75±0.18	2.81±0.66	1.27±0.15
CHD group	110	60	50	65.42±8.94	67	49	40	4.69±0.67	1.81±0.19	3.36±0.67	1.28±0.15
X ² /t			0.781	-3.824	0.142	0.002	0.016	-0.147	-1.63	-4.474	-0.39
P			0.963	0.001	0.706	0.961	0.898	0.883	0.105	0.002	0.697

Table 2. Comparison of serum 25(OH)D and IL-6 levels between the normal group and CHD group

Group	n	25(OH)D (ng/mL)	IL-6 (pg/L)	ESRS score
normal group	40	29.46±3.97	7.97±2.30	1.42±0.81
CHD group	110	15.24±1.83	23.03±6.03	2.46±1.31
t		29.812	15.369	4.699
P		< 0.01	< 0.01	< 0.01

Table 3. Comparison of serum 25(OH)D and IL-6 levels in patients with low, medium, and high risk groups

Group	n	25(OH)D (ng/mL)	IL-6 (pg/L)	ESRS score
high-risk group	17	13.24±1.37	30.81±7.66	2.56±1.01
moderate-risk group	31	14.59±1.41	22.38±4.59	2.11±0.89
low-risk group	62	16.12±1.56	21.23±4.33	1.89±0.41
F		28.627	24.439	6.501
P		< 0.01	< 0.01	0.002

Results

General data in the CHD group and the normal group

The age and the LDL-C levels in the CHD group and the normal group differed significantly ($P < 0.05$). We found no significant difference with regard to other general information ($P > 0.05$), see **Table 1**.

25(OH)D, IL-6 and ESRS score in the CHD group and the normal group

Higher levels of serum D (25(OH)D) and IL-6 in the CHD group were observed than the normal group, ESRS score was lower than CHD group, and the difference reached significance ($P < 0.05$, **Table 2**).

25(OH)D, IL-6 levels and ESRS score in low-, medium- and high-risk groups

The difference in serum 25(OH)D, IL-6 levels and ESRS score of the three groups reached statistical significance ($P < 0.05$). Additionally, a higher level of IL-6 and ESRS score in the

high-risk group compared to the low- and medium-risk groups was observed; in contrast the 25(OH)D level was lower ($P < 0.05$). See **Table 3**.

Correlation between Gensini scores and serum 25(OH)D and IL-6 levels in CHD patients

Figure 1A, 1B present that the Gensini score ranged from 2 to 176 points. Serum 25(OH)D and coronary artery Gensini score were in a negative correlation ($r = -0.522$, $P \leq 0.001$, and IL-6 levels were positively connected to coronary artery Gensini score ($r = 0.724$, $P < 0.01$).

Discussion

CHD patients often exhibit symptoms such as chest tightness, chest pain, and others, and this poses a serious threat to health [8, 9]. Currently, drug treatment is the main option in clinical practice, which can better stabilize the condition. The prognosis of CHD is strongly associated with the severity of disease [10]. The assessment of the severity of CHD is usually carried out with large or invasive equipment, which is traumatic, time-consuming, expensive, and poorly accepted by patients [11]. In view of this, the urgency to seek a reliable and convenient serologic detection method is highlighted to enhance the efficiency of clinical diagnosis and help patients quickly assess prognosis.

Vitamin D is one of the main trace elements required by the human body [12]. With changes in modern living standards and dietary structure, and reduction of sunshine time and outdoor activities, problems arise such as lack of vitamin D [13]. As a steroid hormone, 25-OH-VitD can stimulate the activity of osteoclasts and

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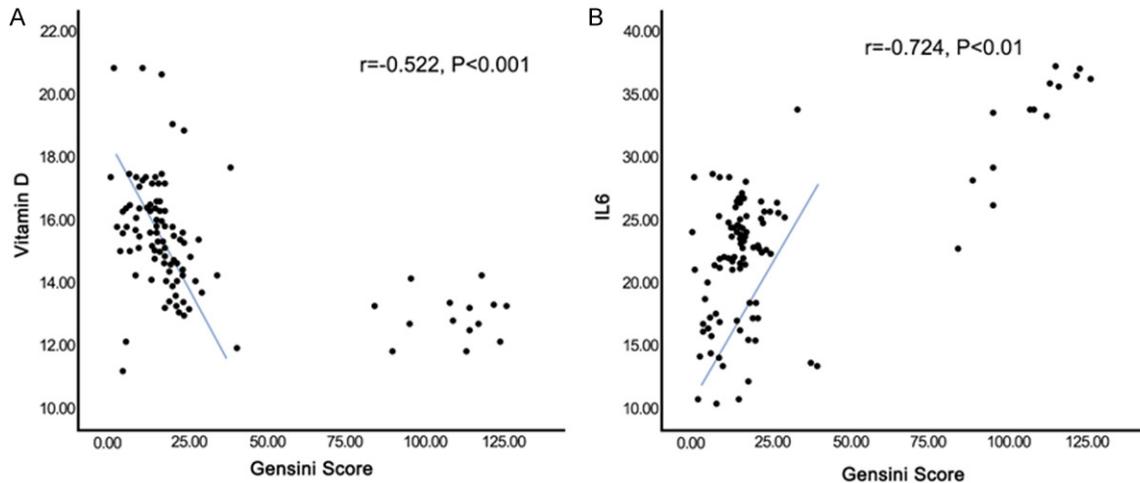


Figure 1. Correlation between serum 25(OH)D and Gensini score, and IL-6 level and Gensini score. Note: A. Correlation between serum 25(OH)D and Gensini score; B. Correlation between IL-6 level and Gensini score.

osteoblasts and promote the absorption of phosphorus and calcium by the intestinal mucosa through the clinical evaluation of vitamin D storage capacity [14]. The correlation between serum 25-OH-VD and cardiovascular disease currently remains controversial. Studies reported [15] that vitamin D deficiency can increase the odds of a variety of vascular diseases, and may even be directly involved in the formation and progression of atherosclerotic plaque. The authors compared the laboratory indicators of patients with CHD and patients without, and found that the serum 25-OH-VD level of patients with CHD was demonstrably lower when compared to the patients without CHD. This is in conformity with a previous trial [16]. Insufficient vitamin D can result in increased renin-angiotensin-aldosterone system activity and angiotensin II activity, influencing the changes in systolic blood pressure and left ventricular hypertrophy, and ultimately leads to cardiovascular events [17].

The findings of the current study demonstrated that the LDL-C level was completely higher in the CHD group when compared with the normal group ($P < 0.05$). This highlights a definite correlation between abnormal lipid metabolism and the occurrence of CHD. We further found that the serum 25(OH)D levels decreased gradually from the low-risk group, to the intermediate-risk group, to the high-risk group, while the IL-6 levels and ESRS score showed a gradual increasing trend. It is assumed that the serum 25(OH)D and IL-6 levels of CHD patients may be

closely associated with severity. This could result from the following reasons. Atherosclerosis involves the formation of atherosclerotic plaques on blood vessel walls, mainly manifested as inflammation, smooth muscle cell hyperplasia, neointimal hyperplasia, and cell fibrosis [18]. Activated endothelial cells can further promote the infiltration of immune cells such as macrophages and neutrophils by up-regulating chemokines and inflammatory factors, thereby promoting endothelial cell dysfunction and endothelial cell apoptosis, and ultimately advancing atherosclerosis [19]. In contrast, 25(OH)D can promote the production of nitric oxide by activating endothelial nitric oxide synthase in endothelial cells, further reduce or avoid the oxidative stress to vascular endothelial cells, and ultimately plays an important role in the occurrence and development of atherosclerosis. Importantly, Pearson correlation analysis revealed that serum 25(OH)D level is in a negative correlation with the severity of CHD, while IL-6 level is positively associated. This indicates that with a continuous decrease of 25(OH)D and the gradual increase of IL-6 level, the severity of CHD gets worse. This is presumably because the lack of 25(OH)D can stimulate the proliferation of vascular smooth muscle cells, promote their migration to the intima, and further affect the regulation of vascular tension, resulting in atherosclerosis. Generally, increased plasma IL-6 levels are related to vascular endothelial cell damage. When the level of IL-6 increases to a certain level, it will cause coro-

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nary artery spasm, which will damage endothelial cells and further promote atherosclerosis [20]. Of note, high levels of IL-6 can accelerate the process of atherosclerosis by stimulating the proliferation of smooth muscle cells. This study shows that decreased serum 25(OH)D, and increased IL-6 level are related to the severity of CHD, which can provide references for clinical diagnosis, treatment and prognosis of CHD. The study did not conduct multivariate analysis and did not explore whether serum 25(OH)D and IL-6 levels are independent risk factors for CHD; thus further analysis is required to provide a strong basis for clinical diagnosis and treatment of CHD patients.

In conclusion, the levels of 25(OH)D and IL-6 in patients with CHD are strongly associated with its severity. Also, IL-6 is perceived as a risk factor for the continued deterioration of CHD. Taken together, these have the potential to provide a reference for diagnosis and treatment of CHD.

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Disclosure of conflict of interest

None.

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