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Original Article

The relationship between the carotid atherosclerosis ultrasound parameters and the cardiac and endothelial functions of coronary heart disease patients

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Abstract: Purpose: This study aimed to discover the relationship between the carotid atherosclerosis ultrasound parameters and the cardiac and endothelial functions of coronary heart disease patients. Methods: 150 patients with coronary artery disease were divided into a single-branch group (one coronary artery with stenosis > 50%), a double-branch group (two coronary arteries with stenosis > 50%), and a multi-branch group (multiple coronary arteries with stenosis > 50%) based on the severity of each patient's coronary stenosis. Meanwhile, 50 healthy volunteers who were admitted to the hospital for routine health checks were recruited as the control group. This study tested the ultrasound parameters of carotid artery atherosclerosis among all the subjects in each group [common carotid artery sclerosis (β), carotid artery compliance (AC), elastic coefficient (Ep), pulse wave conduction velocity (PWVβ)], including the left ventricular end diastolic inner diameter (LVEDD), left ventricular ejection fraction (LVEF) and endothelial function parameters [endothelin-1 (ET-1), von Willebrand factor (vWF), and nitric oxide (NO)]. Results: The study found that the β, AC, Ep, PWVβ, LVEDD, LVESD, ET-1, and vWF levels of patients with coronary artery disease were all higher than the corresponding levels in the control group ($P < 0.05$). The values increased as the number of coronary artery branches with stenosis increased ($P < 0.05$). The LVEF and NO of the patients with coronary artery disease were lower than they were in the control group ($P < 0.05$). The LVEF and NO decreased as the coronary artery branches with stenosis increased ($P < 0.05$). The correlation analysis indicated that the ultrasound parameter of carotid atherosclerosis has a significant positive relation with the LVEDD, LVESD, ET-1, and vWF levels ($P < 0.05$) and a negative relation with the LVEF and NO levels ($P < 0.05$). Conclusion: The ultrasound parameter of carotid atherosclerosis, cardiac function, and endothelial function can be used for the early diagnosis of coronary heart disease.

Keywords: Coronary heart disease, carotid atherosclerosis, ultrasound, cardiac function, endothelial function, early diagnosis

Introduction

Coronary artery disease is short for coronary atherosclerotic heart disease. It begins when an abnormal lipid metabolism leads to the excessive deposition of lipids on the arterial intima, which causes vascular lumen stenosis or blockage and further leads to myocardial hypoxia ischemia or necrosis. Coronary artery disease is usually divided into stable coronary heart disease and acute coronary syndrome [1]. The basic pathology of the coronary heart disease includes the formation of coronary artery thrombosis and reduced myocardial blood supply. The formation of coronary artery thrombosis is caused by the formation of atherosclerotic plaques, which causes a thickening of the arterial walls, inflammation and fibrosis of the vessel walls, eventually leading to acute coronary syndrome [2]. Acute coronary syndrome is an unstable coronary artery disease. Coronary heart disease is commonly seen in the elderly, a disease that severely affects patients' lives. The current clinical diagnosis of coronary artery disease is mainly based on the clinical symptoms, ECG, cardiac color Doppler ultrasound and coronary artery ultrasound contrast [3]. However, most diag-

Table 1. General patient clinical data

Data	Single branch group	Double branch group	Multibranch group	Control group
Case	47	55	48	50
Age (years)	63.23±5.24	62.45±4.39	64.12±5.16	61.64±3.90
Sex				
Male	27	28	25	25
Female	20	27	23	25

nostic methods are complicated, and they cannot be widely promoted as routine components of physical examinations. Therefore, new indicators for the early diagnosis of coronary artery diseases are still needed. Published studies already document the characteristic changes in coronary artery sclerosis during the early stage of coronary artery disease. However, there are few studies on the relationship between carotid artery changes and disease progression [4]. Therefore, this experiment studies the relationships between carotid atherosclerosis ultrasound parameters and the cardiac and endothelial functions of patients with coronary heart disease. It aims to determine the functions' value in the early diagnosis of coronary artery disease from the perspective of the carotid atherosclerosis parameters.

Materials and methods

General patient clinical data

150 patients with coronary artery disease who were admitted into our hospital for treatment from January 2017 to December 2018 were recruited as the study cohort. The cohort included 80 males and 70 females. Also, 50 healthy volunteers who were admitted to the hospital during the same period for routine health checks were recruited as a control group, and this group included 25 males and 25 females. Inclusion criteria: (1) Patients diagnosed through color Doppler ultrasound or coronary angiography, (2) Patients with no history of acute myocardial infarction treatment, (3) Patients with at least one stenotic coronary artery > 50%, (4) Patients with no other serious diseases, such as cardiovascular diseases, abnormal liver function, or systemic diseases, and (5) Patients who signed the written consent form. Exclusion criteria: (1) Patients over 80 or less than 18 years old, (2) Patients who had a cerebral infarction within 6 months before their admission, (3) Patients with certain diseases, such as abnormal liver and kidney function, malignant tumors, severe infections, and immune system diseases, (4) Patients with rheumatic heart disease, heart valve disease, or other cardiovascular diseases, and (5) Patients lacking a complete medical history. This study was approved by the hospital ethics committee. The non-control group patients were divided into a single branch group (one coronary artery with stenosis > 50%), a double branch group (two coronary arteries with stenosis > 50%), and a multiple branch group (three or more coronary arteries with stenosis > 50%) based on the severity of each patient's coronary stenosis. The general clinical data of the patients with coronary artery disease and the healthy patients in the control group are shown in **Table 1**. There were 27 males and 20 females in the single branch group. The double branch group included 28 males and 27 females, and the multiple branch group had 25 males and 23 females. There were no significant differences in the gender distributions or ages of the patients in the various groups ($P > 0.05$).

Monitoring the patients' carotid atherosclerosis ultrasound parameters

All the patients were requested to undergo a carotid atherosclerosis ultrasound check. The patients needed to lie down and rest for 10 to 15 min before the examination. Then, the Philips iE33 color Doppler ultrasound diagnostic apparatus was utilized to determine the degree of bilateral common carotid artery sclerosis in each patient. The probe's frequency was 10 MHz. The carotid atherosclerosis ultrasound parameters include common carotid artery stiffness (β), carotid artery compliance (AC), the elastic coefficient (Ep), and the pulse wave velocity (PWVβ).

Monitoring the patients' cardiac function parameters

The Philips iE33 color Doppler ultrasound diagnostic apparatus was utilized to determine the patients' cardiac function parameters, including their left ventricular end-diastolic diameters (LVEDD), their left ventricular end-systolic

Table 2. A comparison of the patients' routine blood parameters

Blood routine parameters	Single branch group	Double branch group	Multibranch group	Control group
Total cholesterol (TC, mmol/l)	4.43±0.53*	4.64±0.54*	4.73±0.43*	3.88±0.41
Triglyceride (TG, mmol/l)	1.89±0.24*	2.04±0.54*	2.11±0.43*	1.57±0.29
LDL-cholesterol (LDL-C, mmol/l)	2.74±0.54*	2.78±0.33*	2.75±0.43*	2.21±0.29
HDL-cholesterol (HDL-C, mmol/l)	1.27±0.22	1.26±0.27	1.23±0.43	1.28±0.19
Uric acid (UA, μmol/l)	378.24±56.65*	371.43±66.53*	404.75±71.47*	283.36±44.22
Total bilirubin (TB, μmol/l)	13.43±2.25	11.87±2.33*	9.32±2.09*,#	15.46±3.45
Direct bilirubin (DB, μmol/l)	4.83±1.13	4.34±1.26*	3.35±1.27*,#	5.71±1.32

Note: *: compared with the control group, $P < 0.05$; #: compared with the single branch group, $P < 0.05$.

diameters (LVESD), and their left ventricular ejection fractions (LVEF).

Monitoring the patients' endothelial function parameters

5 ml of morning fasting venous blood was taken from each patient. Then, the serum was separated from the blood by centrifugation. The endothelial function parameters included endothelin-1 (ET-1), the von Willebrand factor (vWF), and nitric oxide (NO). The ET-1 was measured using ET-1 ELISA detection kits (Abcam). The vWF was measured using von Willebrand factor (vWF) ELISA detection kits (Abcam). The NO was levels were measured using nitric oxide detection kits (made by Shanghai Biyuntian Biotechnology Co., Ltd.). In all cases, we followed the kits' instructions.

Statistical analysis

SPSS 17.0 was utilized for the statistical analysis. We used t tests to compare the measurement data between groups. We used χ^2 tests to compare the count data between groups. Pearson correlation analyses were used to test the correlations between the parameters. $P < 0.05$ was considered statistically significant.

Results and analysis

Comparison of the general data

No significant differences were found among the various groups with respect to gender or age ($P > 0.05$, **Table 1**).

A comparison of the routine blood parameters of the different groups of patients

There was no significant difference in the HDL-C levels between the patients with coronary artery disease and the heathy subjects ($P > 0.05$). The TC, TG, LDL-C, UA, TB, and DB levels in the patients with coronary artery disease were significantly higher than of the corresponding levels in the healthy subjects ($P < 0.05$). However, there were no differences in the routine blood parameters among the patients with different degrees of coronary stenosis (**Table 2**).

A comparison of the ultrasound parameters of carotid atherosclerosis in the various groups of patients

The results of the parameter comparison show that the carotid atherosclerosis ultrasound parameters β, AC, Ep, and PWVβ of the coronary artery disease patients were significantly higher than the corresponding levels in the control group patients ($P < 0.05$). The carotid atherosclerosis ultrasound parameters significantly increased as the number of branches of stenotic coronary arteries increased ($P < 0.05$) (**Table 3**).

A comparison of the patients' cardiac function parameters

The cardiac function parameter tests showed that the cardiac function parameters LVEDD and LVESD of the patients with cardiac artery disease were significantly higher than they were in the control group ($P < 0.05$). Also, they increased as the branch numbers of stenotic coronary arteries increased ($P < 0.05$). However, the LVEF levels in the patients with coronary artery disease were significantly lower than they were in the control group. Also, the level decreased as the branch numbers of stenotic coronary arteries increased ($P < 0.05$) (**Table 4**).

Table 3. The patients' ultrasound parameters of carotid atherosclerosis

Ultrasound parameters of carotid atherosclerosis	Single branch group	Double branch group	Multibranch group	Control group
β	6.21±0.62[c]	8.26±0.88[b]	10.18±0.96[a]	5.11±0.76[d]
AC (mm^2/kPa)	0.71±0.06[c]	0.82±0.09[b]	1.00±0.07[a]	0.54±0.07[d]
Ep	131.75±17.27[c]	160.54±21.73[b]	193.37±22.11[a]	111.24±13.32[d]
PWVβ (m/s)	6.28±0.71[c]	8.42±0.84[b]	11.33±1.15[a]	4.17±0.90[d]

Note: Different lower-case letters (a, b, c, d) in the table indicate significant differences between the groups (P < 0.05).

Table 4. The patients' cardiac function parameters

Cardiac function parameters	Single branch group	Double branch group	Multibranch group	Control group
LVEDD (mm)	60.26±5.88[c]	66.03±7.07[b]	73.34±7.26[a]	55.21±6.36[d]
LVESD (mm)	51.18±5.28[c]	55.27±5.42[b]	61.54±5.46[a]	44.24±4.23[d]
LVEF	0.56±0.05[b]	0.52±0.03[c]	0.47±0.04[d]	0.61±0.06[a]

Note: Different lower-case letters (a, b, c, d) in the table indicate significant differences between the groups (P < 0.05).

Table 5. The patients' endothelial function parameters

Endothelial function parameters	Single branch group	Double branch group	Multibranch group	Control group
ET-1 (ng/l)	57.25±5.65[c]	83.64±7.42[b]	117.53±13.26[a]	34.32±3.11[d]
vWF (%)	94.32±9.58[c]	153.32±14.75[b]	188.53±21.15[a]	68.53±5.37[d]
NO (μmol/l)	80.54±7.47[b]	63.22±6.48[c]	46.64±5.09[d]	96.24±7.32[a]

Note: Different lower-case letters (a, b, c, d) in the table indicate significant differences between the groups (P < 0.05).

A comparison of the endothelial function parameters in the various groups

The endothelial function test results showed that the endothelial function parameters EF-1 and vWF in the patients with coronary artery disease were significantly higher than they were in the control group (P < 0.05). Also, the levels increased as the branch numbers of stenotic coronary arteries increased (P < 0.05). However, the NO levels in the patients with coronary diseases were significantly lower than they were in the control group. The levels decreased as the branch numbers of stenotic coronary arteries increased (P < 0.05) (**Table 5**).

The correlation analysis of the different parameters

Pearson correlation analyses were used to test the correlation between the various parameters. There was a significant positive correlation among the four ultrasound parameters of carotid atherosclerosis (P < 0.05). Also, the carotid atherosclerosis ultrasound parameters had a significant positive correlation with LVEDD, LVESD, ET-1, and vWF (P < 0.05). However, LVEF had a significant correlation with NO (P < 0.05) (**Figure 1**).

Discussion

Coronary atherosclerosis is the pathological basis of coronary artery disease. Previous studies have shown that coronary atherosclerosis mainly occurs in the carotid arteries of coronary heart disease patients [5, 6]. The carotid artery is normally superficial, so it is easy to obtain ultrasound images with a high resolution. Therefore, determining the correlation between the carotid atherosclerosis parameters and the progression of coronary artery disease can help facilitate the clinical diagnosis [7]. Most patients with coronary artery disease have cardiac function issues. Also, the changes in some cardiac function parameters such as LVEDD, LVESD, and LVEF correlate with the severity of the disease and myocardial ischemia [8]. In addition, the vascular endothelial dysfunction gets involved in the pathological changes resulting from coronary artery disease. Endothelial function markers are used to determine the disease progression in clinical practice [9]. ET-1 is an important factor in the adjustment of cardio-

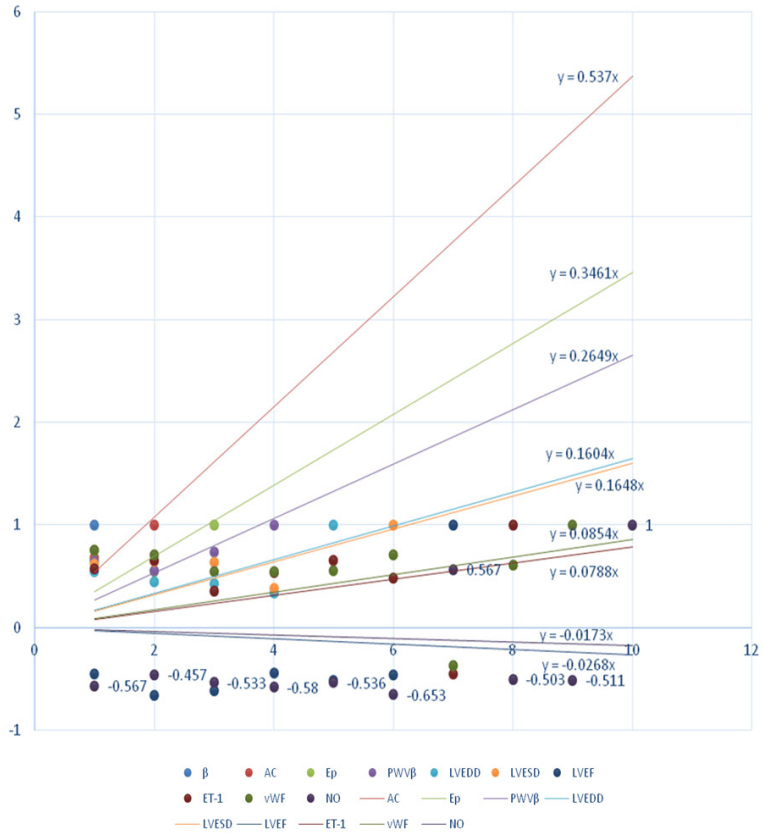

Figure 1. The Pearson correlation analysis.

vascular function, and it is synthesized and secreted by vascular endothelial cells. Elevated ET-1 levels can cause strong vasoconstriction and myocardial ischemia [10]. vWF is a type of glycoprotein that is involved in the synthesis of the vascular endothelium. A large amount of vWF is released into the bloodstream when a blood vessel gets damaged [12]. As a protective factor for vascular cells, NO can be synthesized by vascular endothelial cells, and NO regulates the vascular smooth muscles, relaxes the blood vessels, reduces the free radical damage, and inhibits inflammatory cell adhesion [13]. Therefore, this study explored the changes in the three types of parameters mentioned above among patients with coronary heart disease and their correlations.

This study initially compared the routine blood parameters between patients with coronary artery disease and healthy patients. We found that there was no significant difference in the HDL-C levels between the patients with coronary artery disease and the healthy patients. However, the TC, TG, LDL-C, UA, TB, and DB levels of the patients with coronary artery disease were significantly elevated compared to the health patients. There were no differences in the routine blood parameters of the patients with different degrees of coronary stenosis. This indicates that the routine blood parameters can reflect patients' health status to some extent, but they cannot be used as sensitive markers of coronary artery disease.

We found that the β, AC, Ep, and PWVβ levels of patients with coronary artery disease were significantly improved after testing the patients' carotid atherosclerosis ultrasound parameters, cardiac function parameters, and endothelial function parameters. This shows that the above parameters can directly indicate a change in the carotid atherosclerosis in patients with coronary artery disease [5]. The cardiac function parameters of patients with coronary artery disease, such as LVEDD and LVESD, are significantly higher than they are in healthy people. The LVEF of patients with coronary artery disease is significantly lower than it is in healthy people. This result is consistent with the findings of a previous study [6]. The endothelial function parameters of patients with coronary artery disease, ET-1 and vWF, are significantly higher than they are in healthy people. The NO levels of patients with coronary artery disease are lower than they are in healthy people. This indicates that the above endothelial function parameters are involved in the pathogenesis of coronary artery disease [10]. The above three parameters are closely related to the severity of the disease [14-17]. The more severe the disease is, the higher the abnormality of each index is [18-20]. This indicates that the above three parameters can diagnose coronary artery disease at an early stage. The correlation

analysis indicates that the carotid atherosclerosis ultrasound parameters have a significant positive relation with LVEDD, LVESD, ET-1, and vWF and a negative relation with LVEF and NO. This shows that the combined measurement of the above three parameters may benefit the early diagnosis.

In summary, this study has comprehensively measured the differences in the carotid atherosclerosis ultrasound parameters, cardiac function parameters, and endothelial function parameters between patients with coronary artery disease of different severities and healthy people. We found that the above three parameters can reflect the severity of coronary artery disease. We found a significant correlation between the parameters. Therefore, this study indicates that the combined measurement of the above three parameters are a new direction for the early diagnosis of coronary artery disease.

Disclosure of conflict of interest

None.

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