Original Article

The association of coronary non-calcified plaque loading based on coronary computed tomography angiogram and adverse cardiovascular events in patients with unstable coronary heart disease-a retrospective cohort study

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Background: Coronary computed tomography angiogram (CCTA) has the characteristics of non-invasive, high resolution, and can accurately determine the characteristics of tubular wall plaques. The non-calcified plaque loading of the coronary arteries is unstable and prone to shedding, leading to adverse cardiovascular events. However, few studies focused on the predictive value of non-calcified plaque loading for adverse cardiovascular events in patients with unstable coronary heart disease (CHD). The present study was conducted to investigate the association of coronary non-calcified plaque loading based on CCTA and adverse cardiovascular events in patients with unstable CHD.

Methods: A total of 206 patients with unstable CHD were collected and followed up for 1 year. The patients were divided into an observation group (n=56) and a control group (n=150) according to whether adverse cardiovascular events occurred or not. We analyzed the predictive value of coronary artery non-calcified plaque loading for adverse cardiovascular events in unstable CHD using receiver operating characteristic and multivariate logistics regression analysis.

Results: Compared with the control group, the non-calcified plaque volume in the observation group was increased (160.10±44.02 *vs.* 128.06±42.22 mm^3, P=0.000); non-calcified plaque loading increased (26.93%±7.98% *vs.* 21.46%±7.62%, P=0.000); carotid intima-media thickness increased (1.49±0.17 *vs.* 1.40%±0.18 mm, P=0.001); and left ventricular ejection fraction (LVEF) was significantly reduced (53.28%±7.39% *vs.* 58.02%±7.91%, P=0.000). Non-calcified plaque volume and non-calcified plaque loading have certain diagnostic value for recurrence of adverse cardiovascular events within 1 year (P<0.05). A non-calcified plaque volume >145.58 mm^3 is a risk factor for recurrence of adverse cardiovascular events (P<0.05).

Conclusions: Increased non-calcified plaque volume in patients with unstable CHD is associated with the development of adverse cardiovascular events in patients with unstable CHD.

Keywords: Unstable coronary heart disease (unstable CHD); coronary computed tomography angiography; non-calcified plaque loading; predictive value

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Introduction

Coronary atherosclerotic heart disease is currently one of the most clinically common cardiovascular diseases, mostly occurring in middle-aged and elderly people, and often leads to higher case fatality and disability rates (1,2). Unstable coronary artery disease is a more common manifestation of coronary heart disease (CHD), and its early prevention and diagnosis and treatment have become hot spots and difficulties in clinical practice. Although some scholars regarded interleukin-18 and high-sensitivity C-reactive protein as predictors of adverse cardiovascular events in CHD patients, these two indicators are not specific and can be increased in many diseases. In recent years, studies have found that coronary computed tomography angiogram (CCTA) has the characteristics of non-invasive, high resolution, and can accurately determine the characteristics of tubular wall plaques, which has high application value in the diagnosis of CHD (3,4). Coronary plaque loading can be divided into calcified plaque loading and non-calcification plaque loading, although calcified plaque loading also has a certain impact on coronary blood flow, but because the calcification plaque is relatively stable, it is not easy to fall off, so it does not often lead to myocardial infarction. However, non-calcified plaque loading is easy to fall off, non-calcified plaques account for the majority of the coronary plaques, its main component is cholesterol, the outer layer of non-calcific plaque only covers the fiber cap, so it is easy to fall off, leading to myocardial infarction (5-7). The present study was to investigate the association of coronary non-calcified plaque loading and adverse cardiovascular events in patients with unstable CHD. We present the following article in accordance with the STARD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-933/rc).

Methods

Participants

We retrospectively and continuously collected 206 patients with unstable CHD who were treated at the 74 Group Military Hospital of PLA Army from January 2018 to September 2020. The enrollment criteria were as follows: (I) unstable CHD; (II) CCTA had been performed; (III) age 18–80 years; and (IV) complete clinical data. The exclusion criteria were as follows: (I) acute pericarditis; (II) myocarditis; (III) electrolyte abnormalities; (IV) malignant tumors or serious cardiopulmonary, liver, kidney, and autoimmune diseases; and (V) pregnant and lactating women. All cases were followed up for 1 year and divided into an observation group (group with adverse events, n=56) and a control group (no adverse events, n=150). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of 74 Group Military Hospital of PLA Army (No. 2021087). Individual consent for this retrospective analysis was waived.

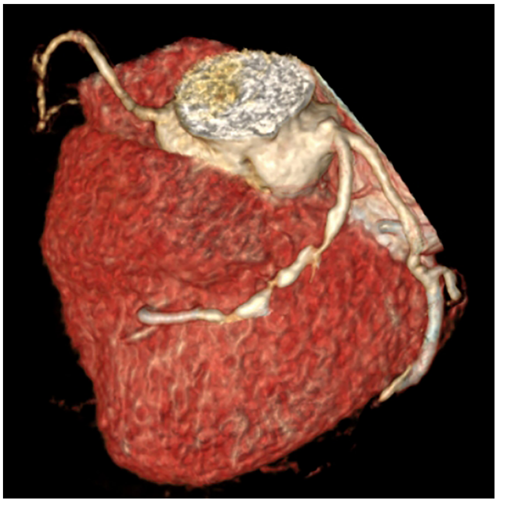

Figure 1 Diagram of three-dimensional reconstruction of coronary arteries (multiple coronary stenoses can be seen from the figure).

CCTA examination

A Siemens Dual Source Spiral CT (Siemens, Erlangen Germany) was used to perform CCTA. The parameter settings were as follows: tube voltage 120 kV, current 80 mA, pitch 0.15–0.21 mm, scanning time 7–11 s, and thickness 0.620 mm, speed 0.25 s/rpm. Contrast medium was injected intravenously through the elbow using a high-pressure syringe, and 85–90 mL of Ultravist (Bayer HealthCare, Berlin, Germany) and 40 mL of normal saline were injected at a rate of 4.5–5.5 mL/s, and then scanned. The collected primary data were transferred to the workstation for image reconstruction and analysis of blood vessel stenosis and plaque nature. Non-calcification loading of coronary arteries was determined as follows: calculate the non-calcified plaque volume, vascular volume, non-calcifying plaque loading, non-calcification plaque loading = non-calcified plaque volume/vascular volume (*Figure 1*).

Table 1 Comparison of general information [n (%) or mean ± SD]

Grouping	Observation group (n=56)	Control group (n=150)	t/χ^2 value	P value
Gender (male)	30 (53.57%)	84 (56.00%)	0.097	0.755
Diabetes	35 (62.50%)	73 (48.67%)	3.129	0.077
Hypertension	42 (75.00%)	80 (53.33%)	7.927	0.005
History of smoking	26 (46.43%)	68 (45.33%)	0.019	0.888
Alcoholism	30 (53.57%)	76 (50.67%)	0.138	0.710
Average age (years)	64.23±3.56	63.53±3.67	1.229	0.221
Average course (years)	8.34±5.34	7.86±5.26	0.580	0.562
Average BMI (kg/cm^2)	30.26±4.23	29.78±4.17	0.732	0.465

Smoking history: ≥1 cigarette per day for 1 year, or the total amount of smoking ≥360 cigarettes per year; alcoholism: drinking ≥2 times a week, liquor ≥50 mL each time, or beer ≥500 mL each time. SD, standard deviation; BMI, body mass index.

Data collection

The following data were collected: (I) general information such as age, gender, body mass index (BMI), hypertension, diabetes, history of alcoholism, smoking history, and disease history. (II) Non-calcified plaque volume, vascular volume, and non-calcifying plaque loading. (III) Carotid intima-media thickness and left ventricular ejection fraction (LVEF).

Diagnostic method

Adverse cardiovascular events: all the patients were followed up for 1 year after surgery, an adverse cardiovascular event was defined if the patient experienced angina, cardiac insufficiency, occasional malignant arrhythmias, malignant arrhythmias, recurrent myocardial infarction, heart failure, or cardiac arrest.

Statistical analysis

The data analysis was conducted using the software SPSS 26.0 (IBM Corp., Armonk, NY, USA), and P<0.05 indicated that the difference was statistically significant (two-sided). The measured data of both groups of patients were in line with the normal distribution, and the differences between the two groups were analyzed by independent sample t-test. The differences of counting data between the two groups were analyzed by chi-square test; The diagnostic value of coronary non-calcified plaque loading parameters for adverse cardiovascular events was analyzed by receiver operating characteristic (ROC) curve test. Risk factors for adverse cardiovascular events in patients with unstable CHD were investigated using multivariate logistics regression analysis.

Results

Comparison of general data of patients between the two groups

The proportion of hypertensive patients in the observation group was significantly higher than that in the control group (75.00% *vs.* 53.33%, P=0.005). There was no significant statistical difference in other general clinical data between the two groups (P>0.05) (*Table 1*).

Comparison of non-calcified plaque loading in coronary arteries between the two groups

Compared with the control group, the non-calcified plaque volume of the cases in the observation group was significantly increased (160.10±44.02 *vs.* 128.06±42.22 mm^3, P=0.000). Non-calcified plaque loading was significantly increased (26.93%±7.98% *vs.* 21.46%±7.62%, P=0.000) (*Table 2*).

Comparison of LVEF and carotid intima-media thickness between the two groups

Compared with the control group, the carotid intima-media thickness of the observation group was significantly increased (1.49±0.17 *vs.* 1.40±0.18 mm, P=0.001) and LVEF was significantly reduced (53.28%±7.39% *vs.*

Table 2 Comparison of coronary non-plaque loading in patients between the two groups (mean ± SD)

Grouping	Observation group (n=56)	Control group (n=150)	*t* value	P value
Non-calcified plaque volume (mm^3)	160.10±44.02	128.06±42.22	4.791	0.000
Vascular volume (mm^3)	600.87±60.60	603.97±57.77	0.339	0.735
Non-calcified plaque loading (%)	26.93±7.98	21.46±7.62	4.529	0.000

SD, standard deviation.

Table 3 Comparison of LVEF and carotid intima-media thickness between the two groups (mean ± SD)

Grouping	Observation group (n=56)	Control group (n=150)	*t* value	P value
Carotid intima-media thickness (mm)	1.49±0.17	1.40±0.18	3.389	0.001
LVEF (%)	53.28±7.39	58.02±7.91	3.895	0.000

LVEF, left ventricular ejection fraction; SD, standard deviation.

Table 4 The diagnostic value of different indicators for the recurrence of adverse cardiovascular events within 1 year in patients with unstable CHD

Variables	AUC	SE	P value	95% AUC	Optimal diagnostic cut-offs
Non-calcified plaque volume (mm^3)	0.698	0.041	0.000	0.618–0.778	145.58 mm^3
Non-calcified plaque loading (%)	0.688	0.040	0.000	0.609–0.767	23.40%
Carotid intima-media thickness (mm)	0.641	0.042	0.002	0.558–0.725	1.515 mm
LVEF (%)	0.336	0.041	0.000	0.256–0.417	56.57%

CHD, coronary heart disease; AUC, area under the curve; SE, standard error; LVEF, left ventricular ejection fraction.

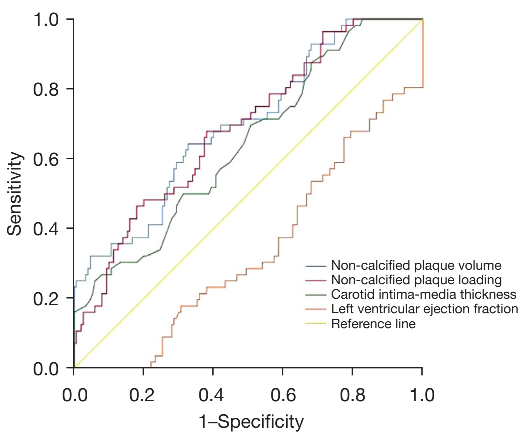

Figure 2 The diagnostic value of different indicators for the recurrence of adverse cardiovascular events within 1 year in patients with unstable CHD. CHD, coronary heart disease.

58.02%±7.91%, P=0.000) (*Table 3*).

Diagnostic value of different indicators for recurrence of adverse cardiovascular events in patients with unstable CHD within 1 year

Non-calcified plaque volume, non-calcified plaque loading, carotid intima-media thickness, and LVEF all had certain diagnostic value for adverse cardiovascular events that recur within one year in patients with unstable CHD (P<0.05) (*Table 4* and *Figure 2*).

Risk factors for recurrence of adverse cardiovascular events in patients with unstable CHD within 1 year

Multivariate logistics regression analysis showed that the

Table 5 Risk factors for recurrence of adverse cardiovascular events within 1 year in patients with unstable CHD

Variables	B value	S.E.	Wald	P value	Exp(B)	95% CI
Non-calcified plaque volume >145.58 mm^3	1.206	0.346	12.134	0.000	3.340	1.695–6.584
Carotid intima-media thickness >1.515 mm	0.701	0.351	3.979	0.046	2.015	1.012–4.010
LVEF <56.57%	0.978	0.351	7.737	0.005	2.658	1.335–5.294
Hypertension	0.758	0.375	4.080	0.043	2.135	1.023–4.456
Constant	−4.411	1.017	18.825	0.000	0.012	–

CHD, coronary heart disease; S.E., standard error; CI, confidence interval; LVEF, left ventricular ejection fraction.

non-calcified plaques volume >145.58 mm^3, the carotid intima-media thickness >1.515 mm, the LVEF <56.57%, and hypertension were risk factors for recurrence of adverse cardiovascular events within 1 year in patients with unstable CHD (P<0.05) (*Table 5*).

Discussion

With the change of people's lifestyle, unstable CHD has gradually become an important disease that threatens human life and health. Clinically, the degree of vascular stenosis in coronary angiography is mostly used as the "gold standard" for diagnosing CHD. However, some patients have still experienced adverse cardiovascular events despite the absence of arterial stenosis, and further autopsy results have revealed the presence of a large number of arterial plaques in such patients, so the early diagnosis and intervention of unstable CHD has also gradually attracted attention (8-10). Our study explored the diagnostic value of non-calcified plaque loading in adverse cardiovascular events in patients with unstable CHD. The results showed that non-calcified plaques volume and the non-calcified plaques loading had certain diagnostic value for the recurrence of adverse cardiovascular events within 1 year in patients with unstable CHD (P<0.05). Multivariate logistics regression analysis showed that non-calcified plaques volume >145.58 mm^3, carotid intima-media thickness >1.515 mm, the LVEF <56.57%, and hypertension were risk factors for recurrence of adverse cardiovascular events within 1 year in patients with unstable CHD (P<0.05).

The CCTA is a noninvasive imaging method that has emerged in recent years, which accurately and clearly shows the coronary arteries and ventricular wall. The current literatures report that CCTA plays an important role in the diagnosis of coronary atherosclerotic disease (11-13). Myocardial infarction due to coronary plaque shedding is an important cause of adverse cardiovascular events. Coronary plaque loading can be divided into calcified plaque loading and non-calcified plaque loading; calcified plaque is relatively stable and does not detach easily, and non-calcified plaque does detach easily, resulting in adverse cardiovascular events (14-16). In addition, when non-calcified plaque loading increases, it can also lead to coronary artery stenosis, resulting in insufficient myocardial blood supply, which in turn leads to myocardial remodeling, and can eventually lead to adverse cardiovascular events. In addition, the ROC curve analysis of this study showed that the diagnostic value of non-calcified plaque volume and loading for the recurrence of adverse cardiovascular events within 1 year in unstable CHD patients was comparable to that of carotid intima-media thickness, LVEF, hypertension, and so on. The carotid intima-media thickness, LVEF, and hypertension have been confirmed to be good predictors of adverse cardiovascular events (17-20), which indicates that the use of CCTA to measure the volume and loading of non-calcified plaques is of good value in diagnosing adverse cardiovascular events that recur within 1 year in patients with unstable CHD.

In summary, CCTA measurement of coronary non-calcified plaque loading can be used as a predictor for adverse cardiovascular events in patients with unstable CHD.

Limitations

This study had some limitations including that it was a retrospective clinical study and failed to explore the formation mechanism of non-calcified plaque loading. Moreover, the sample size is relatively small.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-933/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-933/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-933/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of 74 Group Military Hospital of PLA Army (No. 2021087). Individual consent for this retrospective analysis was waived.

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