

## Research Article

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# Detection of Vulnerable Plaques in Middle-Aged and Elderly Patients With Coronary Heart Disease Complicated With Diabetes Mellitus By Combined Use of Coronary CTA, UA and APOB/A I ratio

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### Abstract

**Objective:** To explore the clinical value of 256-slice spiral CT coronary angiography combined with serum uric acid (UA) and apolipoprotein B/A I (ApoB/A I) ratio in detecting vulnerable coronary plaques (VP) in middle-aged and elderly diabetic patients.

**Methods:** 1. Patients hospitalized in the Department of Cardiology, Second Affiliated Hospital of Xuzhou Medical University from January 2016 to January 2018 with diabetes mellitus and coronary CTA diagnosed as coronary heart disease were divided into three groups according to the nature of plaque: 28 vulnerable plaque group, 30 mixed plaque group and 25 calcified plaque group. 26 patients with simple DM and without coronary plaque group were included as control group and other patients in DM group. Three groups were compared. 2. Record the general data of the subjects. All the subjects

were treated with UA, ApoA I, ApoB, FIB, FPG and TG after admission.

**Results:** There were significant differences in UA and ApoB/AI ratios among groups ( $P < 0.05$ ). Logistic regression analysis showed that FIB, ApoB, UA and ApoB/AI were independent risk factors for vulnerable plaques ( $P < 0.05$ ).

**Conclusion:** The ratio of UA to A poB/A I is an independent risk factor for vulnerable plaque in middle-aged and elderly patients with coronary heart disease and DM. The ratio of coronary CTA combined with UA and A poB/A I has important clinical value in predicting the vulnerability of plaque in middle-aged and elderly patients with coronary heart disease and DM.

**Keywords:** Coronary heart disease; Uric acid; Apolipoprotein B/A I ratio; Diabetes mellitus; Vulnerable plaque

## 1. Introduction

Cardiovascular disease is the leading cause of death worldwide. Coronary atherosclerotic heart disease (CAD) is the most common cardiovascular disease in clinic. Previous studies have found that diabetes is associated with more easily ruptured lipid plaques. Coronary artery disease with diabetes mellitus is characterized by multiple vessel lesions and diffuse lesions, unstable atherosclerotic plaques and much higher mortality than non-diabetic patients [2,3]. Elevated UA levels are associated with lipid-rich plaques, decreased coronary flow reserve, and impaired coronary microvessels, and are known risk factors. However, in the case of acute coronary syndrome, especially under current conditions, studies on the incidence and mortality of UA and long-term cardiovascular diseases are still limited [4]. In recent years, it has also been found that the ratio of ApoB and ApoB/A I is correlated with the occurrence of acute cardiovascular events. The ratio of ApoB and ApoB/A I is positively correlated with coronary artery score, and the correlation degree is higher than that of other lipid components. The 256-slice spiral CT used in this experiment is more accurate and widely used than the previous CT. It can evaluate the unstable plaque in middle-aged and elderly patients with coronary heart disease and

diabetes mellitus, and provide an important basis for preventing the occurrence of acute cardiovascular events and early clinical treatment of patients with coronary heart disease.

## 2. Materials and Methods

**Selected object** From January 2016 to January 2018, patients with diabetes mellitus and coronary heart disease diagnosed by CTA were enrolled in the Department of Cardiology, Second Affiliated Hospital of Xuzhou Medical University. According to the nature of plaque, they were divided into three groups: vulnerable plaque group (28 cases), mixed plaque group (30 cases) and calcified plaque group (25 cases). **Group comparison.** Selection criteria: Age (> 45 years old), in line with the diagnostic criteria of type 2 diabetes mellitus, coronary CTA showed at least one coronary artery stenosis (> 50%) and coronary atherosclerotic plaque. **Exclusion criteria:** (1) Heart valve disease, hypertrophic cardiomyopathy, thyroid disease, severe anemia, hemorrhagic diseases; (2) Infection, systemic immune diseases, tumors, the use of immunosuppressive drugs; (3) Severe liver and kidney diseases; (4) Patients with acute lung injury and pulmonary edema. **Contraindications to coronary CTA:** 1.1 (1) allergy to iodine-containing contrast media; (2) severe arrhythmia; (3) decompensated cardiac insufficiency; (4) severe liver and kidney dysfunction; (5) inability to lie flat and to cooperate with breath-holding.

### 2.1 Methods

**2.1.1 General information** Clinical data including sex, age, smoking history, hypertension history and diabetes history were collected. ECG, color Doppler echocardiography and chest X-ray examination were performed after admission. All the participants were fasting (fasting for 12 hours) the next morning after admission to collect elbow venous blood. Liver function, renal function (including serum creatinine, urea nitrogen, uric acid, etc.), blood lipids (including triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, apolipoprotein A I, apolipoprotein B, etc.) and electrolytes were measured.

**2.1.2 Coronary artery CT** All subjects were scanned on GE revolution 256-slice spiral CT. During the scanning, patients were required to hold their breath for 10-12 seconds. The scanning parameters were

120 Kv:900 mA and the detector width was 0.6 mm. The rotational speed of the tube is 280 mS/week. The reconstruction thickness was 0.6 or 0.75 mm. The patients were taken in supine position and scanned from 1 cm below tracheal bifurcation to 2 cm below cardiac diaphragm. Before scanning, contrast agent (350 mg I/ml) was injected into elbow vein at a rate of 5.0 ml/s. Images are reconstructed immediately after the CT scanning is completed, and the scanning time image is automatically selected. All the original CT data are transmitted to the image workstation (GE ADW 4.6 workstation) for image processing. The reconstructed methods include surface reconstruction (CPR), maximum density projection (MIP), volume rendering (VR), and multi-plane reconstruction (MPR).

1.2.2 Completion of image analysis is based on the evaluation of two-dimensional transverse axis images and a variety of image reorganization methods, including MPRs, MIPs, cMPRs, VR and so on. If there are serious artifacts in the image and the blurred blood vessel display can not be used for evaluation, the case will be eliminated and not included in this experiment. Coronary artery was classified according to the severity of the most serious diameter stenosis: There was no plaque or stenosis (the stenosis rate was 0%). (2) Mild: plaque, stenosis < 25%. (3) Mild: 25%-49% stenosis. (4) Moderate: 50-74%. Stenosis may cause blockage of blood flow. Severe: 75-99%. Stenosis results in blockage of blood flow. Occlusion, 100% stenosis. One main vessel and branch stenosis (>50%) was considered to be pathological. In the reconstructed image, plaque is defined as a tissue with an area greater than 1 mm<sup>2</sup> between the outer and inner walls of the coronary artery.

Patch level analysis: Non-calcified plaque (NCP) is defined as plaque with calcified components less than 20% of the total plaque volume, and the average CT value of plaque is less than 130HU. Calcification is defined as mixed plaque (CP) between 20% and 80% of the total plaque volume. Calcified plaque is more than 80% of the total plaque volume and its CT value is more than 130HU. It is called calcified plaque (CP). Vulnerable plaques are defined as the following:

1. Positive reconstruction (PR): Positive reconstruction is defined as positive remodeling when the diameter of normal lumen measured is larger than the diameter of lumen measured (coefficient of remodeling is greater than 1.05). It indicates that plaque grows outward [6].
- Spot calcification (SC): Spot calcification is defined as a small dense (CT value < 130HU) plaque encapsulated by non-calcified plaques with a diameter less than 3 mm, suggesting that the plaque is unstable and that the possibility of acute myocardial infarction is high [7].
3. Napkin-ring sign (NRS): Napkin-ring sign are surrounded by high CT value plaques. High density ring in napkin ring

sign may be a new blood vessel or hemorrhage. Although the pathological mechanism is not clear, napkin ring sign is a high risk factor for plaque rupture. 4. Low CT attenuation: In non-calcified plaques, the CT value of some plaques is less than 30HU. It was found that low CT attenuation, napkin ring sign, positive remodeling and punctate calcification were associated with plaque rupture. Vulnerable plaques were classified as vulnerable plaques group, all calcified plaques were classified as calcified plaques group, all mixed plaques or mixed plaques and calcified plaques were classified as mixed plaques group. All images were analyzed by two senior radiologists. The inconsistent results were determined after consultation.

## 2.2 Statistical Method

All the data were processed by SPSS 22.0 software package. Normality test was used for the measurement. Data conforming to normal distribution were expressed by mean (+standard deviation). T test was used for comparison between the two groups, one-way ANOVA was used for comparison between groups, and non-parametric test was used for non-uniform variance. Non-normal data were represented by median (25th percentile, 75th percentile), and non-parametric tests were used for comparison between groups. The P values of non-parametric tests were adjusted. The counting data were expressed by the rate and the chi-square test was used in the statistical method. Statistically significant variables selected by univariate analysis were included in multivariate logistic regression analysis,  $P < 0.05$  considered that there was significant difference.

## 3 Results

3.1 Patients with coronary heart disease and DM were divided into vulnerable plaque group, mixed plaque group and calcified plaque group according to the nature of plaque, and the control group was set up. There were 28 cases in vulnerable plaque group, with an average age of 64.29 (+9.28) years, 15 males (53.57%) and 30 mixed plaque groups, with an average age of 64.33 (+8.50) years, 17 males (56.67%) and 25 calcified plaque groups, with an average age of 62.08 (+8.67) years, 14 males (56%) and 26 controls, with an average age of 60.31 (+7.54) years and 15 males (57.7%). There were no significant differences in gender, age, smoking history, hypertension history, FPG, TG, TC and HDL-C between vulnerable plaque group, mixed plaque group, calcified plaque group and control group ( $P >$

0.05). There were significant differences in UA and ApoB/A I ratios among groups (P < 0.05). There was significant difference in FIB between vulnerable plaque group and calcified plaque group and control group (P < 0.05). There was significant difference in LDL-C level between vulnerable plaque group and control group (P < 0.05). There was significant difference in ApoA I between vulnerable plaque group and control group (P < 0.05). ApoB level in vulnerable plaque group was significantly higher than that in calcified plaque group and control group (P < 0.05). ApoB level in mixed plaque group was significantly higher than that in control group (P < 0.05) (Table 1).

Index	Gender	Age	Smoking	Hypertension
control group (n=26)	15 (57.7)	60.31±7.54	8 (30.8)	17 (47.2)
Calcified plaque group (n=25)	14 (56.0)	62.08±8.67	8 (32.0)	16 (64.0)
Mixed plaque group (n=30)	17 (56.7)	64.33±8.50	10 (33.3)	20 (66.7)
Vulnerable plaque group (n=28)	15 (53.6)	64.29±9.28	9 (32.1)	18 (64.3)
Statistic	0.103	1.403	0.042	3.371
P	0.992	0.246	0.998	0.338

Index	FIB (g/L)	FPG (mmol/L)	TG (mmol/L)	TC (mmol/L)	HDL-C (mmol/L)
control group	3.06 (3.0, 3.44)	7.14 (5.73, 9.94)	1.62 (1.48, 1.90)	4.78±0.85	1.16±0.43
Calcified plaque group	3.12 (2.53, 3.78)	8.42 (6.65, 9.43)	1.88 (1.23, 2.26)	4.82±0.81	1.14±0.28
Mixed plaque group	3.39 (3.0, 3.81)	8.17 (6.61, 9.16)	1.48 (1.32, 2.76)	4.80±1.11	1.12±0.27

Vulnerable plaque group	3.76 (3.46, 4.01)	7.94 (6.61, 9.16)	1.68 (1.01, 2.21)	4.91±0.93	1.12±0.27
Statistic	15.884	2.091	0.999	0.118	0.074
P	0.001	0.554	0.802	0.949	0.949

Index	LDL-C (mmol/L)	ApoAI (g/L)	ApoB (g/L)	UA (µmol/L)	ApoB/AI ratio
control group	2.89±0.56	1.23 (1.02, 1.35)	0.82±0.13	288.50±47.88	0.70±0.13
Calcified plaque group	2.90±0.84	1.07 (0.96, 1.29)	0.89±0.16	325.96±55.00*	0.82±0.19*
Mixed plaque group	3.11±0.88	1.07 (1.00, 1.20)	1.00±0.24*	366.87±66.24**	0.92±0.21**
Vulnerable plaque group	3.41±0.81**	1.01 (0.91, 1.10)	1.10±0.19** 30.159	403.07±65.33** △	1.09±0.18**△
Statistic	2.587	14.362	12.431	18.779	22.880
P	0.011	0.002	0.000	0.000	0.000

\*\*" means that compared with the control group,  $P < 0.05$ ; Compared with calcified plaque group, the expression of was  $P < 0.05$ . "Delta" means that compared with mixed plaque group,  $P < 0.05$ .

**Table 1:** Comparison of indicators in different plaque groups.

### 3.2 Single factor regression analysis of various indicators and vulnerable plaque

3.2.1 The vulnerable plaques were grouped and analyzed by single factor regression: there was no significant difference between gender, age, smoking history, hypertension history, FGB, TG, TC, HDL-C and vulnerable plaque ( $P > 0.1$ ), FIB, LDL-C, ApoB, UA and ApoB/A I ratio were risk factors for vulnerable plaques ( $P < 0.1$ ) (Table 2).

Index	B	Wald	Exp(B)	95% CI for EXP(B)	P
Sex (n,%)	-0.130	0.087	0.878	0.370~2.081	0.767
Age (Year)	0.036	2.117	1.037	0.988~1.088	0.146
Smoking (n, %)	0.02	0.000	1.002	0.399~2.515	0.997
Hypertension (n, %)	-0.350	0.613	0.704	0.293~1.94	0.434
FIB (g/L)	1.728	13.034	5.629	2.203~14.384	0.000
FGB (mmol/L)	-0.023	0.066	0.977	0.817~1.168	0.797
TG (mmol/L)	0.000	0.000	1.000	0.660~1.514	0.999
TC (mmol/L)	0.136	0.326	1.146	0.718~1.828	0.568
HDL-C (mmol/L)	-0.192	0.073	0.825	0.205~3.317	0.787
LDL-C (mmol/L)	0.727	5.829	2.070	1.147~3.736	0.016
ApoAI (g/L)	-0.425	7.849	0.654	0.486~0.880	0.005
ApoB (g/L)	0.461	13.911	1.586	1.245~2.022	0.000
UA (µmol/L)	0.017	16.777	1.017	1.009~1.025	0.000
ApoB/AI ratio	0.658	20.951	1.931	1.457~2.559	0.000

**Table 2:** Univariate Regression Analysis of Indicators and Vulnerable Plaques in DM Group

3.2.2 The statistical variables FIB, LDL-C, UA and ApoB/AI ratio in univariate analysis were introduced into binary logistic regression analysis, the results showed that FIB, ApoB, UA and ApoB/AI were independent risk factors for vulnerable plaques (P < 0.05) (Table 3).

Index	B	Wald	Exp(B)	95.0% C.I. for EXP(B)	P
FIB (g/L)	1.430	6.624	4.179	1.406~12.415	0.010
LDL-C (mmol/L)	0.576	2.379	1.779	0.856~3.698	0.123
ApoB (g/L)	0.377	0.012	1.459	1.122~1.897	0.005
UA (µmol/L)	0.619	9.709	1.015	1.005~1.024	0.002
ApoB/AI ratio	0.329	13.676	1.856	1.337~2.577	0.000

**Table 3:** Multivariate Logistic Regression Analysis of High Risk Indicators of Vulnerable Plaques

**Discussion**

Diabetes mellitus is one of the risks of coronary heart disease. Diabetic patients are prone to metabolic abnormalities, which greatly increases the risk of coronary heart disease. In addition to diabetes, other risk factors of coronary heart disease include gender, age, smoking history, hypertension, dyslipidemia, family history of cardiovascular disease, etc.

[9]. The presence of vulnerable plaques is an important cause of acute cardiovascular events in patients with coronary heart disease. Therefore, this study aims to evaluate the stability of coronary plaques in elderly patients with coronary heart disease and diabetes mellitus by combining coronary CTA with serum UA and ApoB/AI ratio, so as to reduce the occurrence of acute cardiovascular events in elderly patients with diabetes mellitus.

Many large-scale epidemiological investigations have shown that the characteristics of lipid metabolism disorders in diabetic patients are low HDL cholesterol level, high LDL cholesterol level, high triglyceride, postprandial lipidemia, etc. [10]. In this study, we found that triglyceride levels in patients with coronary heart disease and diabetes mellitus were significantly higher than those in patients with coronary heart disease alone, which was consistent with the above findings. Adipose tissue has been proved to synthesize and secrete a large number of bioactive substances, such as plasminogen activator inhibitor (PAI-1), adiponectin, tumor necrosis factor (TNF $\alpha$ ), leptin, IL-6 [11]. Diabetes mellitus is a chronic inflammatory disease, and atherosclerosis is also a chronic inflammatory process. Endothelial damage initiates a series of subsequent reactions and ultimately forms atherosclerotic plaques. A large number of experiments have proved that the expression of many inflammatory factors in patients with coronary heart disease, diabetes mellitus, diabetes mellitus and coronary heart disease increased, such as C-reactive protein, tumor necrosis factor, IL-6, P-selectin, cell adhesion molecules and so on. This study found that the level of fasting blood sugar in vulnerable plaque group was significantly higher than that in non-diabetic group ( $P < 0.001$ ). A large number of epidemiological data show that diabetic patients with coronary heart disease are higher than non-diabetic control group of the same sex and age, about 2 times higher in male patients and 4.5 times higher in female patients. Therefore, the blood sugar level of patients should be strictly controlled in clinic to reduce the unstable factors of coronary heart disease plaque. Ishizaka et al. [12] also showed that elevated UA level was an independent risk factor for atherosclerosis. Liu Wei et al. [13] also showed that UA level in unstable coronary plaque group was significantly higher than that in stable coronary plaque group and control group, suggesting that the continuous and significant increase of UA level plays an important role in monitoring and identifying elderly patients with coronary heart disease. This study also confirmed that UA levels in vulnerable plaque group and mixed plaque group were significantly higher than those in calcified plaque group, and UA levels in vulnerable plaque group were also significantly higher than those in mixed plaque group. UA was an independent predictor of plaque instability, which was consistent with previous studies. This study also found that UA level in vulnerable plaque group of elderly patients with coronary heart disease was significantly higher than that of non-diabetic patients, because this experiment is a small sample experiment, the number of studies is too small, there may be deviation, so further experiments are needed. For the treatment of high UA, people need to pay attention to it. At present, there are few clinical studies on the treatment of UA. One study confirmed that 600 mg/d allopurinol can improve myocardial ischemia and improve the activity tolerance of patients with angina pectoris [14]. Johnson et al. [43] found that patients receiving allopurinol after coronary artery bypass grafting had improved cardiac function and reduced mortality. Han Yan et al. [15] also showed that the percentage of fibre lipid volume in left main coronary plaque in high ApoB/AI ratio group was significantly higher than that in low level group, and the percentage of fibre tissue volume was significantly lower than that in low level group. Multivariate linear regression analysis showed that: ApoB/AI ratio was positively correlated with the volume percentage of fibrolipid tissue in left main plaque and negatively correlated with the volume

percentage of fibrous tissue in left main plaque, suggesting that the level of ApoB/AI ratio was correlated with the vulnerability of left main plaque evaluated by IVUS-VH. For patients with stable angina pectoris treated with statin, the ratio of ApoB/A I was positively correlated with the percentage of fibrolipid tissue volume of left main coronary plaque evaluated by IVUS-VH, negatively correlated with the percentage of fibrous tissue volume. The ratio of ApoB/A I had certain predictive value for the vulnerability of left main coronary plaque. Zhu Jie et al. [16]. For 190 patients with acute coronary syndrome, ApoB/A I ratio can be used as a predictor of the occurrence and development of acute coronary syndrome. This study found that the ratio of ApoB/AI in VP group was higher than that in non-vulnerable plaque group, whether in diabetes mellitus group or simple coronary heart disease group. Therefore, clinical attention should be paid to reducing the level of apolipoprotein B in order to stabilize the plaque and reduce the probability of acute cardiovascular events.

In this experiment, GE revolution 256-slice spiral CT is a super high-end CT. Compared with traditional CT, Revolution CT achieves an all-round breakthrough in time resolution, spatial resolution, wide coverage, low dose and energy. Especially for the rapid imaging of cardiovascular system, without the restriction of spontaneous movement of respiratory muscles and heart rate, coronary CT scan can be achieved under any condition, which greatly improves the success rate of coronary CT examination [17]. A retrospective study using coronary angiography as the gold standard confirmed that in patients with acute coronary syndrome, the positive rate of CTA in identifying ruptured plaques was 77.7% [18]. A prospective study of 1168 subjects by Nadjiri et al. [19] confirmed that: Positive weight adequacy, low CT attenuation and napkin ring were independent predictors of major adverse cardiovascular events, and the volume of low CT attenuation was strongly correlated with adverse cardiovascular events. In a meta-analysis, the total volume, remodeling index and low CT attenuation of non-calcified coronary plaques in ACS patients were higher than those in stable angina pectoris patients, and the incidence of adverse cardiovascular events in ACS patients with high-risk plaques was much higher than those with stable plaques.

This study found that the ratio of UA and ApoB/AI can predict the stability of plaque well. Because of its advantages of non-invasive, convenient detection, relatively low price, fast, safe and good repeatability, UA and ApoB/AI can be widely carried out. Therefore, the detection of these serological markers and their dynamic evolution is helpful for early judgment of high-risk ACS population, guidance of risk stratification, determination of effective intervention measures and judgment of therapeutic effect, and has broad prospects. At the same time, the application of coronary CTA can more accurately identify patients with VP and further consolidate the diagnosis results. The limitations of this study are that the time is short, the sample size is small, the results may be biased, UA and apolipoprotein may be affected by many factors, which may affect the results of the study. Although coronary CTA can detect the nature of plaque more accurately, the diagnosis of coronary CTA is based on subjective judgment, which may lead to some deviation due to subjective reasons. In addition, the small diameter of the lumen may lead to missed diagnosis of high-risk plaques, so these situations should be avoided in clinical research.

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