

# Computed tomography imaging of early coronary artery lesions in stable individuals with multiple cardiovascular risk factors

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**OBJECTIVES:** To investigate the prevalence, extent, severity, and features of coronary artery lesions in stable patients with multiple cardiovascular risk factors.

**METHODS:** Seventy-seven patients with more than 3 cardiovascular risk factors were suspected of having coronary artery disease. Patients with high-risk factors and 39 controls with no risk factors were enrolled in the study. The related risk factors included hypertension, impaired glucose tolerance, dyslipidemia, smoking history, and overweight. The characteristics of coronary lesions were identified and evaluated by 64-slice coronary computed tomography angiography.

**RESULTS:** The incidence of coronary atherosclerosis was higher in the high-risk group than in the no-risk group. The involved branches of the coronary artery, the diffusivity of the lesion, the degree of stenosis, and the nature of the plaques were significantly more severe in the high-risk group compared with the no-risk group (all  $p < 0.05$ ).

**CONCLUSION:** Among stable individuals with high-risk factors, early coronary artery lesions are common and severe. Computed tomography has promising value for the early screening of coronary lesions.

**KEYWORDS:** Coronary atherosclerosis; Cardiovascular risk factor; CT imaging.

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## INTRODUCTION

Cardiovascular disease is determined not only by the severity of a single risk factor but also by multiple risk factors coexisting in an individual and the significant synergistic effects among them. With the increase in coexisting risk factors, the incidence of cardiovascular disease also increases. Early intervention for cardiovascular risk factors and early recognition of coronary artery lesions could reduce the incidence of coronary heart disease events (1–3).

Imaging examinations have significant value for the diagnosis of coronary heart disease (2,4). Selective coronary arteriography is a recognized “gold standard” for diagnosing coronary heart disease. However, it is an invasive examination and has some limitations, including relatively

high requirements for operators' technical skills, high risks, high examination costs, poor reproducibility, and certain operation contraindications and postoperative complications. In addition, selective coronary arteriography only determines the degree of artery stenosis based on the filling condition of contrast agents and cannot determine the nature of coronary atherosclerotic plaques. Therefore, its application in screening for coronary heart disease is limited (4–6). Multi-detector spiral computed tomography (MDCT) has become an important noninvasive method for the diagnosis of and screening for coronary heart disease. Newer technologies, such as 256-slice CT or 320-row detector CT, have emerged and have been used during coronary computed tomography angiography (7). The clinical application of 64-slice spiral CT is the most (almost universally) used platform for cardiac CT and can provide an accurate evaluation of the degree of stenosis of coronary atherosclerosis and the nature of coronary atherosclerotic plaques, thus playing an important role in the diagnosis and assessment of coronary heart disease. The applicability of 64-slice spiral CT in the diagnosis and risk assessment of coronary heart disease has obtained a certain degree of recognition (8–10).

To the best of our knowledge, the evaluation of early coronary atherosclerotic diseases in a high-risk population

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has scarcely been reported. In this study, we evaluated the degree of coronary atherosclerosis in a high-risk population using 64-slice spiral CT imaging and investigated the value of CT imaging for the early recognition of coronary atherosclerosis.

## METHODS

### Patient recruitment and exclusion criteria

The present study was performed at the First Affiliated Hospital of Guangxi Medical University from September 2010 to September 2011. The study was approved by the ethics committee of the hospital. Written informed consent was obtained from all of the participants. The patients who had more than three of the following risk factors were included in the high-risk group: hypertension (based on the 1999 WHO/ISH diagnostic standard); diabetes mellitus, impaired glucose tolerance, or impaired fasting glucose (based on the 1999 WHO diagnostic standard); total cholesterol (TC)  $\geq 6.22$  mmol/L, low-density lipoprotein (LDL)  $\geq 4.14$  mmol/L, high-density lipoprotein (HDL)  $< 1.04$  mmol/L and/or triglycerides (TG)  $\geq 2.26$  mmol/L; smoking; and body mass index (BMI)  $\geq 24$  kg/m<sup>2</sup> (1,11). Seventy-seven patients with three or more risk factors (high-risk group) and 39 controls (no-risk group) with none of the above cardiovascular risk factors were included.

The exclusion criteria were as follows: patients with confirmed coronary heart disease who had received coronary stent implantation or coronary artery bypass graft; patients with grade 3 or 4 cardiac function according to the New York Heart Association (NYHA) functional classification; patients with atrial fibrillation or atrial premature beats and/or ventricular premature beats; patients with severe hepatic and renal insufficiencies; patients with severe respiratory insufficiency; pregnant women; patients with hyperthyroidism; and patients with iodine allergy.

### Assessment of metabolic parameters

Fasting venous blood samples were collected from all subjects in the morning. The sample detection and data report were completed by the Department of Laboratory Medicine at The First Affiliated Hospital of Guangxi Medical University. Blood lipids and glucose were detected using a Hitachi 7170A automatic biochemical analyzer. All required reagents were provided by Shanghai ZhiCheng Biological Technology.

### CT scanning

The examination was performed using a GE 64 Light Speed VCT-XT multi-detector CT scanner (USA). Post-processing was performed using the GE AW4.4 workstation for reconstruction. The subjects with a heart rate (HR) higher than 75 bpm were given 25 mg oral metoprolol 30 min before CT scanning. If subjects had  $\beta$ -blocker contraindications or unsatisfactory HR reduction after medication (higher than 70 bpm), the examination was not continued. The main CT parameters were previously described (8,9). The reconstruction of original images was based on the scanning data to obtain the corresponding R-R interval. The coronary CT angiogram (CTA) was reconstructed, and Cardiac IQ post-processing software was employed for evaluation.

### Evaluation of CT observations

The conditions of lesions in four major arteries in the coronary artery system were observed: the left anterior

descending branch (LAD), left circumflex artery branch (LCX), right coronary artery (RCA), and left main coronary artery (LMCA). Lesions involving the LAD, LMCA, and RCA were classified as single-branch lesions, double-branch lesions, and multi-branch lesions, respectively. Lesions involving more than two branches were classified as multi-branch lesions. A diffuse lesion was defined as a lesion with a length  $\geq 20$  mm and involving multiple sites in a single branch, which caused the entire or the majority of the involved blood vessels to be slender and stiff or slender and significantly tortuous. The quantification of the lesions followed the Society of Cardiovascular Computed Tomography (SCCT) recommendation on grading and plaque characteristics, as published (5). According to the percentage of the diameter with coronary stenosis, coronary artery stenosis was classified as grades 0–5: normal, 0: absence of plaque and no luminal stenosis; minimal, 1: plaque with  $< 25\%$  stenosis; mild, 2:  $25\%$ – $49\%$  stenosis; moderate, 3:  $50\%$ – $69\%$  stenosis; severe, 4:  $70\%$ – $99\%$  stenosis; occluded, 5.

After scanning, the original data were transferred to an AW4.4 workstation for post-processing using EDIT SECTION in Cardiac IQ to measure the lumen area (LA), the vascular ring area (VA), and the measured CT number of the plaque.

The plaque displayed in the CT images was evenly divided into four segments. CT values at four points randomly chosen on the image at the maximum intensity projection (MIP) plane (1 mm) of each segment were averaged to evaluate the nature of the plaque. The classification of coronary atherosclerotic plaques based on spiral CT values of plaques was adopted in this study: a CT value  $< 60$  HU indicated a soft plaque,  $60$ – $129$  HU indicated a mixed plaque, and  $\geq 130$  HU indicated a hard plaque (5,8,9).

### Statistical analyses

The results are expressed as the mean  $\pm$  SD for quantitative variables with normal distributions. Skewed parameters are presented as the median and range (min–max). Comparisons between the two groups were performed using Student's *t* test. The chi-squared test was utilized to compare other clinical features. Statistical analyses were conducted using SPSS 18.0 software (SPSS Inc., Chicago, IL). A two-tailed *p*-value  $< 0.05$  was considered statistically significant.

## RESULTS

There was no significant difference in age or gender between these two groups. In the high-risk factor group, there were 66 cases of hypertension (85.7%), 53 cases of diabetes mellitus (68.8%), 51 cases of dyslipidemia (66.2%), 33 cases with a history of smoking (42.9%), and 31 cases of overweight or obesity (40.2%). The differences in TG, HDL-C, fasting blood sugar (FBG), 2 h postprandial blood glucose (2hPBG), and body mass index (BMI) were statistically significant (all *p*  $< 0.05$ ) between the high-risk group and the control group, whereas LDL-C was similar between the groups (Table 1).

As shown in Tables 2–4, the patients with multiple coronary risk factors had a higher incidence of coronary atherosclerosis. The degrees of stenosis at the LAD, LCX, LMCA, and RCA were significantly more severe in the high-risk group compared with the control group (all *p*  $< 0.05$ ). The nature of the plaques at the LAD, LCX, LMCA, and RCA



were all significantly different between the two groups (all  $p < 0.05$ ).

## DISCUSSION

In this study, the lesions in coronary arteries were more significant in the high-risk group than in the control group. The results indicated that the incidence of lesions in all coronary artery branches, the number of involved coronary artery branches, and the incidence of diffuse lesions were all higher in the high-risk population than in the no-risk population. These findings are consistent with the pattern that the accumulation of multiple risk factors increases the incidence of cardiovascular diseases.

The recognized major risk factors for cardiovascular disease can be divided into variable risk factors and independent risk factors. The former include hypertension, smoking, diabetes mellitus, dyslipidemia, overweight, and obesity, whereas the latter include age and gender. With the increased incidence of each major cardiovascular risk factor, high-risk populations with multiple risk factors have also expanded, and the number of risk factors accumulating in the high-risk population has increased accordingly (1–3,12–14). Our results reflect this trend.

Coronary artery stenosis caused by atherosclerosis is a major coronary artery lesion in coronary heart disease. MDCT not only can effectively detect the origin and spatial position of each coronary artery branch but also has high

sensitivity and specificity in measuring stenotic severity. Previous studies have confirmed the diagnostic value of the 64-slice spiral CT coronary angiography for coronary artery stenosis. MDCT represented by 64-slice spiral CT has been extensively applied in the clinic. Because of its various merits, such as fast scanning speed, minimal damage, and high temporal and spatial resolution, this technology has become an important noninvasive diagnostic and screening method for the evaluation of coronary artery lesions (4–10,15,16). In this study, the incidence of the lesions at each branch of the coronary arteries was higher in the study group; in particular, the incidence of multiple-branch lesions (40.3%) was much higher than that of single-branch lesions. The incidence of diffuse lesions in the high-risk group was seven times that of the control group. The degrees of stenosis and the nature of the plaques at the LMCA, LAD, LCX, and RCA were more significant in the high-risk group compared with the control group. Our study indicated that in addition to a single risk factor, the accumulation of multiple risk factors is also associated with the severity of coronary artery stenosis.

The detection of CAC through noninvasive medical imaging technologies is important for the diagnosis and risk assessment of coronary heart disease (17). The nature and components of plaques according to CT values showed a very good correlation with the IVUS results (18). In the present study, the incidence of soft plaques and mixed plaques at all coronary artery branches was higher in the

**Table 1** - Clinical and biochemical characteristics of the study participants.

Variables	No-risk group (n = 39)	High-risk group (n = 77)	p-value
Gender (M/F)	22/17	57/20	0.054
Age (years)	57 ± 12	60 ± 12	0.140
BMI > 24 kg/m <sup>2</sup>	0	31	<0.001
BMI (kg/m <sup>2</sup> )	21.71 ± 2.39	26.65 ± 3.24	<0.001
Diabetes (%)	0	53	<0.001
Dyslipidemia (%)	0	51	<0.001
Hypertension (%)	0	66	<0.001
Smoking (%)	0	33	<0.001
FBG (mmol/L)	4.83 ± 0.56	6.76 ± 2.90	<0.001
2hPBG (mmol/L)	6.05 ± 1.21	11.65 ± 3.71	<0.001
TG (mmol/L)	1.09 ± 0.47	2.78 ± 3.16	<0.001
HDL-C (mmol/L)	1.50 ± 0.33	1.18 ± 0.39	<0.001
LDL-C (mmol/L)	2.76 ± 0.92	2.78 ± 1.11	0.926

**Table 2** - Lesions of the LMCA, LAD, LCX, and RCA between the two groups.

Variables	No-risk group (n = 39)	High-risk group (n = 77)	p-value
LAD	14	44	0.031
LCX	6	28	0.019
LMCA	4	20	0.048
RCA	10	42	0.003
Diffuse lesions	1	63	<0.001

**Table 3** - The degree of coronary artery stenosis between the two groups.

Variables	No-risk group (n = 39)				High-risk group (n = 77)			
	Normal-Minimal (n)	Mild (n)	Moderate (n)	Severe (n)	Normal-Minimal (n)	Mild (n)	Moderate (n)	Severe (n)
LAD	32	5	2	0	38**	16	12*	11*
LCX	37	1	0	1	56**	12*	5	4
LMCA	39	0	0	0	65*	7*	4	1
RCA	33	5	1	0	57	7	19*	4

Comparison with the control group: (\*)  $p < 0.05$ , (\*\*)  $p < 0.001$ .

**Table 4 - Atherosclerotic plaques between the two groups.**

Variables	No-risk group (n = 39)				High-risk group (n = 77)			
	Normal (n)	Soft (n)	Mixed (n)	Hard (n)	Normal (n)	Soft (n)	Mixed (n)	Hard (n)
LAD	25	9	3	2	33*	13	21*	10
LCX	33	2	1	3	49*	12	10*	6
LMCA	35	4	0	0	57**	7	10*	3
RCA	30	4	2	3	36**	15	20**	6

Comparison with the control group: (\*)  $p < 0.05$ , (\*\*)  $p < 0.001$ .

high-risk population than in the no-risk population. The control and high-risk groups had similar incidences of hard plaques at both the LCX and RCA, but the incidence of hard plaques at the LMCA and LAD in the high-risk population was higher than that in the no-risk population.

The clinical assessment of an individual with suspected stable coronary artery disease (CAD) is usually complemented by noninvasive tests. Cardiac computed tomography angiography (CCTA) has broadened the options for the assessment of CAD patients and is a potentially beneficial alternative for individuals with an intermediate or low pretest likelihood of disease (PLD). The cost-effectiveness of different diagnostic strategies in suspected stable coronary artery disease as well as seven diagnostic strategies were well assessed. Among the strategies, CCTA is the most cost effective in symptomatic patients with suspected stable coronary disease and a PLD of  $\leq 50\%$ . In high-risk patients, immediate invasive coronary angiography appears to be the most cost-effective strategy. In all pretest likelihoods of disease, strategies based on ischemia appear to be more expensive and less effective compared with those based on anatomical tests. The use of CCTA is a cost- and time-effective strategy for the evaluation of low-risk ( $< 30\%$  CAD prevalence) acute chest pain patients in the emergency department and can be used for the safe exclusion of acute coronary syndrome (19,20).

Hypertension, smoking, diabetes mellitus, dyslipidemia, overweight, and obesity are all major variable risk factors of coronary heart disease (1,11). The incidence of coronary artery lesions in the high-risk population with multiple risk factors is significantly higher than in the control population. Biochemical measurements of cardiovascular risk factors are more convenient and cost less than coronary CT. Sixty-four-slice spiral CT coronary artery scanning can effectively detect coronary artery lesions in patients with multiple cardiovascular risk factors, indicating its high clinical value for the early diagnosis of coronary disease in high-risk populations (15,16).

The incidences of various risk factors, such as hypertension, dyslipidemia, and diabetes mellitus, all increase with age. Because age and gender are important independent risk factors of coronary heart disease, a full understanding of the impacts of age and gender on coronary heart disease and other risk factors is important for the prevention and treatment of coronary heart diseases. Therefore, active intervention to improve the variable cardiovascular risk factors in clinical practice can play a pivotal role in the prevention and treatment of coronary heart diseases. A combination of regular exercise, healthy diet, smoking avoidance, and weight maintenance was associated with lower coronary calcium incidence, slower calcium progression, and lower all-cause mortality over 7.6 years (21). In addition to the impacts of the severity of each single risk

factor on the risk of cardiovascular disease, we should also pay attention to the importance of the presence of multiple risk factors in a single individual.

## AUTHOR CONTRIBUTIONS

Yang X was responsible for the study design and the manuscript preparation. Huang H, Zeng ZY and Zhang J collected and analyzed the data. Liu H was the principal investigator of the study and was responsible for the study design and manuscript finalization. All authors read and approved the final manuscript.

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