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Quantification of atherosclerotic plaque volume in coronary arteries by computed tomographic angiography in subjects with and without diabetes

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Abstract

Background: Diabetes mellitus (DM) is considered a cardiovascular risk factor. The aim of this study was to analyze the prevalence and volume of coronary artery plaque in patients with diabetes mellitus (DM) *vs.* those without DM.

Methods: This study recruited consecutive patients who underwent coronary computed tomography (CT) angiography (CCTA) between October 2016 and November 2017. Personal information including conventional cardiovascular risk factors was collected. Plaque phenotypes were automatically calculated for volume of different component. The volume of different plaque was compared between DM patients and those without DM.

Results: Among 6381 patients, 931 (14.59%) were diagnosed with DM. The prevalence of plaque in DM subjects was higher compared with nondiabetic group significantly (48.34% *vs.* 33.01%, $\chi^2 = 81.84$, $P < 0.001$). DM was a significant risk factor for the prevalence of plaque in a multivariate model (odds ratio [OR] = 1.465, 95% CI: 1.258–1.706, $P < 0.001$). The volume of total plaque and any plaque subtypes in the DM subjects was greater than those in nondiabetic patients significantly ($P < 0.001$).

Conclusion: The coronary artery atherosclerotic plaques were significantly higher in diabetic patients than those in non-diabetic patients.

Keywords: Diabetes mellitus; Coronary artery disease; Plaque; Coronary CT angiography

Introduction

Diabetes mellitus (DM) is considered a cardiovascular risk factor, and the rate of cardiac events in people with diabetes is 2 to 3 fold higher compared with that in patients without DM.[1-4] Several investigations have indicated that DM patients without a history of cardiovascular events have a similar chance for myocardial infarction as compared to non-DM patients with previous coronary events.[1-4]

Coronary artery calcium (CAC) is a valuable method to assess coronary heart disease risk in diabetic patients.[5,6] However, little is known with insight into fully quantified plaque in patients with DM. Recent advancement in noninvasive computed tomography (CT)-based plaque imaging makes it possible to classify atherosclerotic plaque components and to quantify plaque volume.

There are few large cohort studies to fully quantified plaque component and volume in patients with DM.

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Methods

Ethical approval

The study was approved by the Ethics Committee of Fu Wai Hospital, and all patients provided informed consent for inclusion in the registry.

Patient population

We recruited 6676 consecutive patients referred for coronary CT angiography (CCTA) by their cardiologists between October 2016 and November 2017. Exclusion criteria were for the subjects who had insufficient clinical data ($n = 212$), non-diagnostic coronary images ($n = 45$), had an acute coronary syndrome ($n = 38$). Data of 6381 patients were collected for final analysis [Figure 1] and were divided into two groups ($n = 931$ patients with DM; $n = 5450$ without DM) according to the American Diabetes Association criteria.[7]

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CCTA scanning and image analysis

First, patients underwent non-enhanced scan to measure the calcium score. CCTA was performed, thereafter, using prospective electrocardiogram (ECG) gating. A double-head power injector was used to inject contrast media. The scanning parameters were as follows: 0.6 mm individual detector width; 280 ms gantry rotation time; 0.20 to 0.50 pitch; 200 to 250 mm field of view for raw image reconstruction. All the scans were analyzed on the workstation (ADW4.6, GE Healthcare, Milwaukee, WI, USA) by two radiologists. Calcium was defined as the presence of at least three pixels with a density of >130 HU. The coronary artery tree was segmented according to the modified American Heart Association classification. We classified coronary plaques by calcified and non-calcified components and quantified their volumes automatically according to Hounsfield unit thresholds.[8,9] Non-calcified plaque volume was further split by lipid and fibrous plaque volumes. Total plaque was summed up by different component plaque volume.

Clinical data

Obesity was defined as body mass index (BMI) greater than 30 kg/m^2. Hypertension was defined as systolic blood pressure >140 mmHg, diastolic blood pressure >90 mmHg, or antihypertensive medication use. Hypercholesterolemia was defined according to the National Cholesterol Education Program (NCEP) guidelines.[10] A family history of coronary heart disease was defined as a history of early coronary heart disease in the immediate family (father <55 years or mother <65 years).

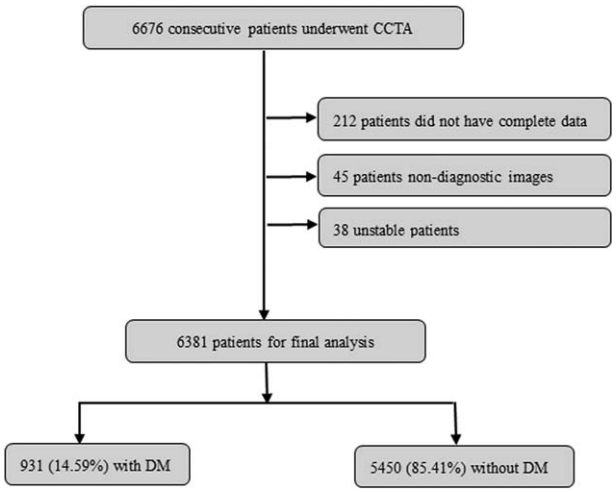

Figure 1: Flow chart of this cohort study recruiting 6676 consecutive patients who underwent coronary computed tomography angiography (CCTA). DM: Diabetes mellitus.

Statistical analysis

Mann-Whitney *U* test and Chi-square test were used to compare risk factors and different quantitative plaque component volumes between the nondiabetic and diabetic patients. Chi-square test was applied to compare the prevalence of plaque in different patients. Logistic regression was used to evaluate the association between diabetes and the prevalence of plaque. Statistical analyses were performed with SPSS version 19.0 (SPSS® Inc., Chicago, IL, USA).

Results

Overall, data of 6381 patients (3351 men and 3030 women) were collected for the final analysis, including 931 (14.59%) patients with DM, and 5450 (85.41%) without DM [Table 1]. The traditional cardiovascular risk factors were more pronounced in DM patients as compared to the non-DM patients except for presence of family history.

In Table 2, 2249 (35.25%) patients (450 DM patients and 1799 nondiabetic patients) had plaque detected on CCTA. The prevalence of plaque was significantly higher in DM subjects compared with nondiabetic group (lipid: 47.37% *vs.* 32.22%, fibrous: 48.23% *vs.* 33.00%, calcified: 37.92% *vs.* 24.97%, respectively, $P < 0.001$). Moreover, the prevalence of non-calcified plaque was significantly higher in the DM subjects (48.34% *vs.* 33.01%, $P < 0.001$) [Table 2, Figure 2]. In the univariate analysis, DM was a risk factor for plaque. DM remained an independent risk factor of the presence of plaques in a multivariate model (OR = 1.465, 95% CI: 1.258–1.706, $P < 0.001$) [Table 3)].

Plaque volumes ranged from 0 to 371.1 mm^3 (inter quartile range (IQR): 8.9 mm^3) in lipid plaques, from 0 to 2286.0 mm^3 (IQR: 92.0 mm^3) in fibrous plaques, and from 0 to 326.4 mm^3(IQR: 0.5 mm^3) in calcified plaques, respectively. The mean plaque volumes for lipid, fibrous and calcified plaques were significantly higher in the DM

Table 1: Baseline characteristics of all the 6381 consecutive patients underwent coronary computed tomography angiography.

Characteristics	Overall ($n = 6381$)	DM ($n = 931$)	Without DM ($n = 5450$)	Statistics	*P* values
Age (years)	55.4 ± 10.2	57.5 ± 10.0	55.0 ± 10.3	$t = 2.34$	0.019
Male, *n* (%)	3351 (52.52)	556 (59.72)	2795 (51.28)	$\chi^2 = 22.70$	<0.001
BMI (kg/m^2)	25.47 ± 3.21	26.31 ± 3.36	25.45 ± 3.41	$t = 7.15$	<0.001
Hypertension, *n* (%)	3188 (49.96)	549 (58.97)	2639 (48.42)	$\chi^2 = 35.38$	<0.001
Dyslipidemia, *n* (%)	2653 (41.58)	580 (62.30)	2073 (38.04)	$\chi^2 = 192.70$	<0.001
Family history, *n* (%)	2695 (42.23)	391 (42.00)	2304 (42.28)	$\chi^2 = 0.03$	0.886
Smoking, *n* (%)	2076 (32.53)	353 (37.92)	1723 (31.61)	$\chi^2 = 14.39$	<0.001
Chest pain, *n* (%)	2652 (42.56)	391 (42.00)	2261 (41.49)	$\chi^2 = 0.09$	0.774

DM: Diabetes mellitus; BMI: Body mass index.

Table 2: The prevalence of plaque in patients with and without DM, *n* (%).

Plaque	Overall (*n* = 6381)	DM (*n* = 931)	Without DM (*n* = 5450)	χ^2	*P* value
Lipid plaque	2197 (34.43)	441 (47.37)	1756 (32.22)	80.82	<0.001
Fibrous plaque	2247 (35.21)	449 (48.23)	1798 (33.00)	80.92	<0.001
Calcified plaque	1714 (26.86)	353 (37.92)	1361 (24.97)	67.81	<0.001
Non-calcified plaque	2249 (35.25)	450 (48.34)	1799 (33.01)	81.84	<0.001
Any plaque	2249 (35.25)	450 (48.34)	1799 (33.01)	81.84	<0.001

DM: Diabetes mellitus.

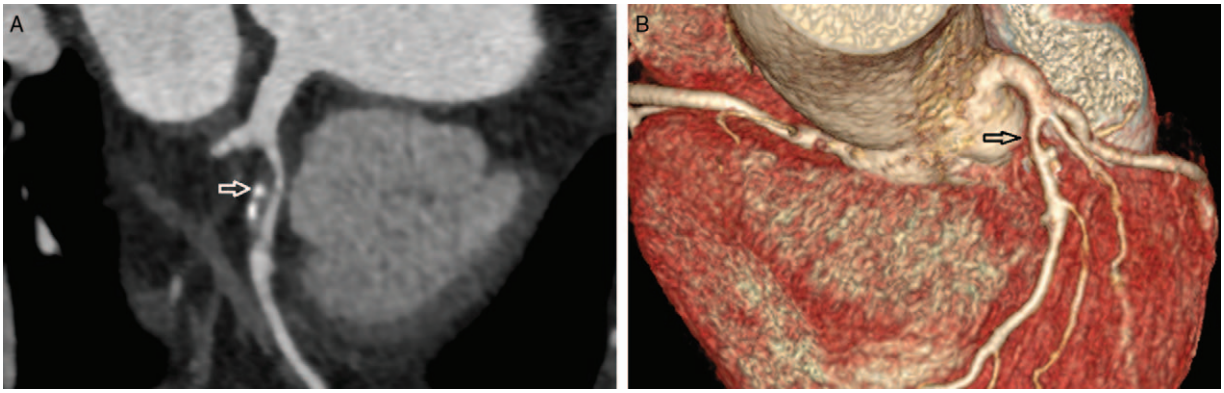

Figure 2: Maximum intensity projection (A) showed a mixed plaque (arrow) in the proximal anterior descending branch (LAD), volume rendering (B) showed the plaque caused more than 50% stenosis (arrow) in a 59-year-old female patient with diabetes mellitus (height: 1.60 m, weight: 60 kg).

Table 3: Logistic regression analysis between DM and the prevalence of plaque.

Plaque	Unadjusted Model		Adjusted Model	
	OR (95% CI)	*P* value	OR (95%CI)	*P* value
Lipid plaque	1.893 (1.644–2.179)	<0.001	1.463 (1.256–1.704)	<0.001
Fibrous plaque	1.892 (1.644–2.177)	<0.001	1.467 (1.259–1.708)	<0.001
Calcified plaque	1.836 (1.587–2.125)	<0.001	1.434 (1.224–1.680)	<0.001
Non-calcified plaque	1.890 (1.642–2.175)	<0.001	1.465 (1.258–1.706)	<0.001
Any plaque	1.890 (1.642–2.175)	<0.001	1.465 (1.258–1.706)	<0.001

DM: Diabetes mellitus; OR: Odds ratio.

subjects than those in the nondiabetic patients (lipid plaques: IQR: 25.2 mm^3*vs.* 6.3 mm^3, $P < 0.001$; fibrous plaques: IQR: 171.7 mm^3*vs.* 73.0 mm^3, $P < 0.001$; calcified plaques: IQR: 5.3 mm^3*vs.* 0.1 mm^3, $P < 0.001$). Similar findings between the DM and non-DM groups were also observed for non-calcified and total plaque volume (IQR: 210.2 mm^3*vs.* 85.6 mm^3, $P < 0.001$; 222.2 mm^3*vs.* 91.8mm^3, $P < 0.001$) [Figure 3, Table 4].

Discussion

In this cross-sectional study, we found significant higher prevalence of coronary plaques and consistently higher plaque volumes of all the detected compositions among the patients with DM as compared to those without DM, which was consistent with previous studies.[11,12]

Although prior studies have rejected the theory of equivalency of diabetes with CAD,[13] the harm that diabetes does to cardiovascular system still cannot ignore.[14,15] The calcification score is only a quantification of calcified plaques, but in diabetic patients, there are a large number of non-calcified plaques in coronary arteries.[16] It has been shown that overall coronary plaque burden is a better predictor of future cardiovascular events.[17] In the past, the quantitative analysis of coronary artery plaque mainly relied on intravascular Ultrasound (IVUS).[18] Compared to IVUS, CT is also good at quantifying plaque, and can be used to study large populations.[19]

We found the prevalence of any plaque in DM subjects was remarkably high (48.34%), and DM was an independent risk factor. Pundziute *et al*[20] demonstrated in patients with diabetes, the segment of coronary artery plaque increased significantly. In a postmortem study, Burke *et al*[21] showed that patients with DM have a larger total and distal plaque.

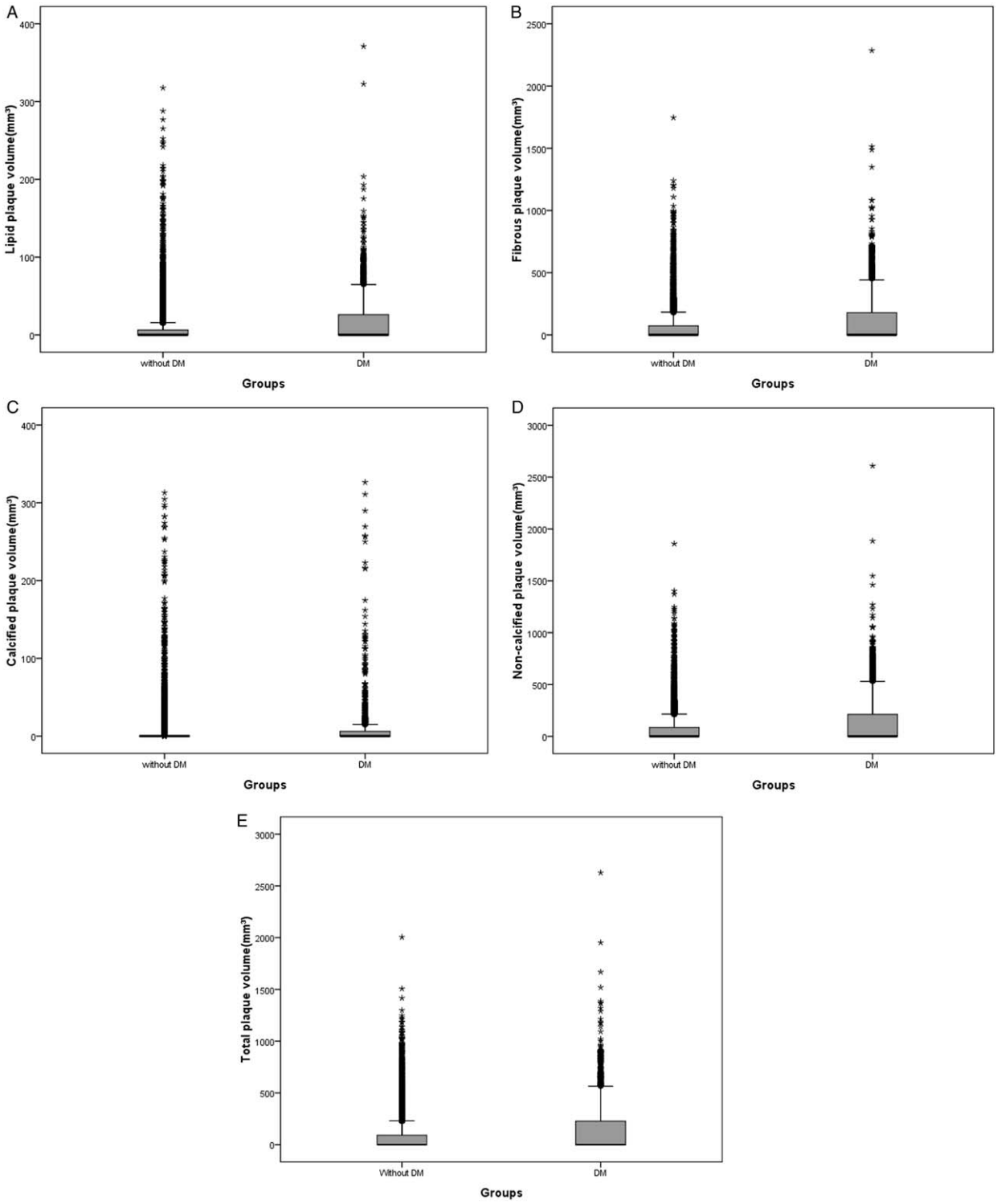

Figure 3: The quantified plaque volume in patients with and without DM. The lipid plaque volume (A), fibrous plaque volume (B), calcified plaque volume (C), non-calcified (D) and total plaque volume (E) in diabetic subjects were significantly greater than non-diabetic patients ($P < 0.001$). DM: Diabetes mellitus.

Previous study had also looked at the components of coronary plaque in patients with DM.[22] We found significantly greater calcified plaque volume in the DM patients than in the nondiabetic patients. As shown in a recent meta-analysis study of symptomatic patients without known CAD, calcifications assessed through CT scans are more frequent in patients with DM.[23] Similarly, patients with diabetes were also found to have a higher calcified plaque burden in their coronary arteries by the Multi-Ethnic Study of Atherosclerosis (MESA).[24] Previous study had also found a significant increase in the necrotic core and inflammatory cells of coronary plaque in diabetic patients.[25-28] Such plaque was vulnerable plaque that could lead to acute events. In this study, we also found

Table 4: The quantified plaque component and volume in patients with and without DM.

Plaque volume	Minimum	25%	Median	75%	Maximum	*z*	*P* value
Lipid plaque						−9.930	<0.001
DM	0	0	0	25.2	371.1		
Without DM	0	0	0	6.3	317.7		
Fibrous plaque						−9.748	<0.001
DM	0	0	0	171.7	2286.0		
Without DM	0	0	0	73.0	1745.8		
Calcified plaque						−8.472	<0.001
DM	0	0	0	5.3	326.4		
Without DM	0	0	0	0.1	313.0		
Non-calcified plaque						−9.797	<0.001
DM	0	0	0	210.2	2608.7		
Without DM	0	0	0	85.6	1857.6		
Total plaque						−9.752	<0.001
DM	0	0	0	222.2	2627.3		
Without DM	0	0	0	91.8	2005.0		

DM: Diabetes mellitus.

the volumes of lipid plaque and fibrous plaque was significantly higher in DM patients.

Study limitations

High-risk characteristics in the diabetic population may be partially influenced by daily glucose fluctuation and may be found already in patients with an impaired glucose tolerance.[29] However, in our study, we cannot fully exclude impaired glucose tolerance without overt diabetes mellitus in our non-DM group as oral glucose tolerance testing was not performed routinely. An autopsy study demonstrated an association between DM duration and the extent of atherosclerosis and myocardial lesions,[30] so the duration of DM should be considered in the future studies.

In conclusion, the coronary artery atherosclerotic plaques were significantly higher in diabetic patients than those in non-diabetic patients.

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Conflicts of interest

None.

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