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Original Article

Assessment of Plaque Vulnerability in Diabetic and Non-Diabetic Patients with Coronary Artery Disease Using Multi-slice CT Angiography

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ABSTRACT

Background: Coronary artery disease [CAD] is a major determinant of the long-term prognosis among patients with diabetes mellitus [DM].

The aim of the work: The aim of this study was to investigate coronary plaque vulnerability using multi-slice computed tomography [MSCT-CA] coronary angiography in diabetic and non-diabetic patients.

Methods: 200 patients who underwent MSCT-CA were evaluated for the vulnerability of atherosclerotic coronary plaques. Patients were divided into Group I [100 patients with Type II DM] and Group II [100 non-diabetic patients].

Results: The DM group's mean age was greater [P 0.003]. In groups I and II, hypertension was present in 71% vs. 47%, and history of previous PCI was present in 6% vs. 0% [P values 0.001 and 0.029, respectively]; smoking history revealed a barely statistically significant difference [P 0.059], and the mean serum LDL-c level in the two groups was 154.25±34.11 vs. 191.66±16.829, respectively [P <0.001]. Positive remodeling of plaques [100% vs. 33%] and Napkin's ring [66% vs. 40%] and spotty calcification [45% vs. 35%] were more evident in the diabetic group than the non-diabetic group [P <0.001, <0.001, and 0.005, respectively]. Low-attenuation plaques were present [100% vs. 95%] in groups I and II with borderline statistical significance [P 0.059]. The most affected vessels in the diabetic group were the right coronary artery [RCA] and ramus intermedius [RI] at 36% and 13%, respectively [P <0.001], whereas the most affected vessel with severe luminal narrowing was the LAD [51% vs. 30%], which was more evident in the DM group than the non-DM group [P 0.002].

Conclusion: Vulnerable coronary plaques were more evident in the diabetic group compared to the non-diabetic group. Positive remodeling of plaques, Napkin's ring, spotty calcification, and severe luminal narrowing were the most significant signs of plaque vulnerability in the diabetic group.

Keywords: Diabetes Mellitus; Coronary Arteries Disease; MSCT Coronary Angiography; Plaque Vulnerability.

INTRODUCTION

In 2017, coronary artery disease [CAD] accounted for 46.2 % of the overall mortality in Egypt [1]. Patients with DM have plaques with larger necrotic cores, inflammation, and advanced coronary artery calcification [2]. The presence of DM was found to be a predictor of plaque progression despite very low levels of LDL-c [3].

The presence of vulnerable plaque features as detected by MSCT [positive remodeling, low attenuation, spotty calcification, and napkin's ring sign] may identify patients at increased risk for future ACS [4]. Studies on the identification and characterization of coronary atherosclerotic plaque stated that MSCT angiography allows for the determination of the degree of stenosis and has a strong correlation with intravascular ultrasound measurements [IVUS] [5].

THE AIM OF THE WORK

This work aimed to investigate and compare coronary plaque composition and vulnerability using MSCT coronary angiography in diabetic and non-diabetic patients.

PATIENTS AND METHODS

The current study included 200 patients who underwent MSCT coronary angiography with suspected CAD [based on the presence of symptoms, abnormal or inconclusive previous treadmill exercise electrocardiography [ECG], and/or nuclear testing]. All cases were evaluated for the vulnerability of atherosclerotic plaques. Patients were divided into two groups [according to presence and absence of DM]: group I, 100 patients with type II DM, and group II, 100 non-diabetic patients. The following patients were included; DM II and non-diabetics with suspected CAD with no contra-indications to MSCT. The following conditions were excluded; DM I, arrhythmia, Renal insufficiency, known allergy to contrast media, Pregnancy. The study was approved by the ethics committee for research involving human subjects at the Faculty of Medicine at Al-Azhar University. The referral for MSCT coronary angiography was based on the latest recommendations for cardiac computed tomography angiography according to ESC guidelines [2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes]. Full history taking, laboratory investigations [HbA1C, serum LDL-c, and S. creatinine], and a 12-lead electrocardiogram [ECG] were done. MSCT was performed using a Toshiba Aquilion 128-slice CT scanner.

All coronary arteries were evaluated at different phases of the cardiac cycle by the acquisition of thin slice sections [0.5 mm]. The heart rates of all patients were determined one hour before examinations. If the heart rate is > 75 BPM, the patient is given a beta-blocker agent orally [Metoprolol 50-100 mg].

All scans were preceded by the non-contrast enhanced scan for coronary calcium score. In each patient, 70 mL of iodinated contrast is followed by 50 mL of normal saline solution. Contrast was given in two phases: the first phase was a test bolus in the ascending aorta [the scan delay was 12 seconds].

The second phase included the administration of the main contrast material, and images following the san were acquired after the scan to identify motion-free coronary artery images and affected vessels by motion and artefacts were discarded. Then the CT-acquired images were transferred to the Vitrea workstation for post-processing. The image data sets were analyzed using multi-planar reformatted images [axial, coronal, and sagittal views], curved multi-planar reformatted images [cMPR], thin-slab maximum-intensity projection images [thin MIP], and volume-rendered images [VRI].

Atherosclerotic plaque was defined as any clearly discernable structure larger than 1-2 mm that was assigned to the coronary artery wall in two perpendicular imaging planes. Remodelling index was obtained by dividing the vessel diameter at the plaque site by the diameter at the reference site. Positive remodeling was reported when the remodeling index was greater than 1.1. The plaque was referred to as a "low attenuation plaque" [LAP] with a radiodensity lower than the surrounding tissue. LAPs are classified according to density into vulnerable plaques with Hounsfield Units [HU] equal to or less than 30 HU and non-vulnerable plaques with HU greater than 30 HU.

The severity of luminal diameter stenosis was classified according to the percentage of luminal narrowing as absent [0%], mild [25–49%], moderate [50–69%], and severe [70–99%]. Coronary lesions in the diagonal branches, obtuse marginal branches, and posterolateral branches were considered to be part of the LAD, LCX, and RCA arteries, respectively. Depending on the dominance of the coronary artery, the

posterior descending artery was considered to be part of the RCA or LCX arteries. Coronary artery calcium was identified as a dense area in the coronary artery exceeding the threshold of 130 HU; accordingly, plaques were divided into calcific with more than 130 HU, non-calcified with less than 130 HU, or mixed with >50% of non-calcified plaque area.

Statistical analysis: All data were collected and statistically analyzed using Microsoft Office Excel 2010 and SPSS 22.0 for Windows. Categorical data were compared using the Chi-square test or Fisher's exact test when appropriate. A p-value less than 0.05 was considered statistically significant; and a p-value more than or equal to 0.05 was considered statistically insignificant.

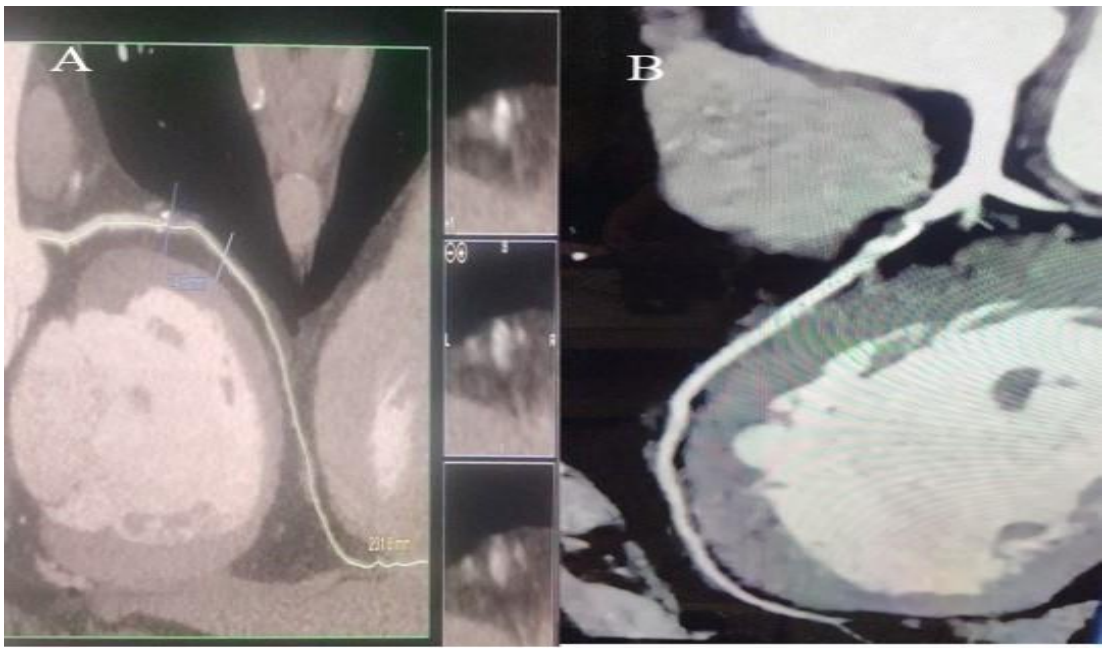

Figure [1]: Example of vulnerable plaques assigned on MSCT-CA: A: spotty calcium, LAP, and positive remodeling in a DM patient. B: Low attenuation plaque and positive remodeling in a non-diabetic patient

RESULTS

The demographic characteristics of the study population are summarized in Table 1. The mean age was 56.49±9.71 vs. 51.70±8.23 in groups I and II, respectively [P=0.003]. Hypertension was present [71% vs. 47%] in groups I and II, respectively [P 0.001]. History of previous PCI was 6% vs. 0% in groups I and II, respectively [P 0.029]. Family history of CAD, history of dyslipidemia, history of previous CABG, and CVS/TIA showed no statistically significant differences between both groups [P = 0.852, 1.000, 1.000, and 0.621, respectively]. History of smoking showed borderline statistical significance between both groups [P = 0.059].

The mean serum LDL-c level was higher in group I than in group II [191.66±16.829 vs. 154.25±34.11, respectively, P <0.001]. Higher levels of HbA1c in group I indicate poor control of DM, which could be a reasonable explanation for more plaque vulnerability in this group [P <0.001]. Table [2].

Resting ECG showed more ST-T changes in group I [54% vs. 39% in groups I and II, respectively] [P 0.033]. MVD [Multi-Vessel Disease] was more prevalent in the DM group [3% vs. 0%], whereas single vessel affection was more prevalent in the non-diabetic group [29% vs. 63%] [P <0.001 for both] [Table 3].

The most affected vessels in the diabetic group were RCA and RI [36% vs. 13% and 6% vs. 0%, respectively] in groups I and II [P 0.001 and 0.029]. In groups I and II, the incidence of LMCA, LAD, and LCX affection was 4% vs. 5%, 79% vs. 86%, and 10% vs. 9%, respectively] [P values 0.809, 1.000, and 0.193, respectively], as shown in Table 5.

Criteria of plaque vulnerability were compared in both groups, including positive remodeling, napkin's ring, plaque attenuation, and spotty calcification. Added to these criteria, plaque screening, total calcium score, plaque eccentricity, severity of luminal stenosis, and plaque type. Positive remodeling was present in 100% vs. 33%, napkin's ring was seen in 66% vs.

40%, and spotty calcification was also more prevalent in DM than non-diabetic patients [45% vs. 35%], with a statistically significant difference between both groups [P 0.005]. While low attenuation showed no statistically significant difference between both groups [100% vs. 95%, P 0.059] [Table 4].

The total calcium scoring mean was [118.61 ± 385.74 vs. 21.18 ± 44.10], and the presence of eccentric plaques was [87% vs. 73%] in groups I and II [P <0.001, <0.001, 0.010, and 0.013, respectively]. Mixed plaques were seen more in group I than group II [48% vs. 33%]; however, the difference was not statistically significant [P 0.087]. In contrast, non-calcific plaques were seen more in group II than in group I [46% vs. 61%], and the difference was not statistically significant between both groups [P 0.087]. Severe stenotic lesions were more prevalent in LAD [51% vs. 30%], LCX [25% vs. 3%], RCA [39% vs. 2%], and RI [4% vs. 0%] in groups I and II [P 0.002, <0.001, <0.001, and 0.045, respectively] [Table 5].

Table [1]: Demographic criteria of the study population

Possible risk factors or associated conditions	Group I [N =100]	Group II [N =100]	P value [Sig <0.05]
Age	56.49±9.71	51.70±8.23	0.003
Family history of CAD	18 [18%]	17 [17%]	0.852
Smoking	45 [45%]	32 [32%]	0.059
Hypertension	71 [71%]	47 [47%]	0.001
Dyslipidemia	32 [32%]	32 [32%]	1.000
Previous CABG	5 [5%]	5 [5%]	1.000
Previous PCI	**6 [6%]**	0 [0%]	0.029
CVS/TIA	**3 [3%]**	1 [1%]	0.621

Table [2]: Key LAB findings in groups I and II

Laboratory results	Group I [N =100]	Group II [N =100]	P value [Sig <0.05]
Serum LDL [mg/dl] [Ref: 100–129]	191.66±16.829	154.25±34.11	<0.001
Serum creatinine [mg/dl] [Ref: 0.8–1.4]	1.06±0.22	0.96±0.15	0.003
Serum HbA1c [%] [Ref: <6.5]	7.93±1.15	5.79±0.78	<0.001

Table [3]: Extent of CAD in both groups

Extent of CAD	Diabetics [N =100]	Non-diabetics [N =100]	P value [Sig <0.05]
Single vessel	29	63	<0.001
Two vessels	42	29	
Three vessels	26	8	
Multiple vessels	3	0	

Table [4]: Criteria of plaque vulnerability in both groups

Plaque characterization	Diabetic group [N=100]	Non-Diabetic group [N=100]	P-value [Sig.<0.05]	Odds ratio	Relative Risk
Low attenuation	100	95	0.059	1.0526	1.005
Positive remodeling	100	83	**<0.001**	**1.88**	**1.88**
Napkin's Ring	66	40	**<0.001**	**1.84**	**1.4**
Spotty calcifications	54	35	**0.005**	**2.18**	**2.18**

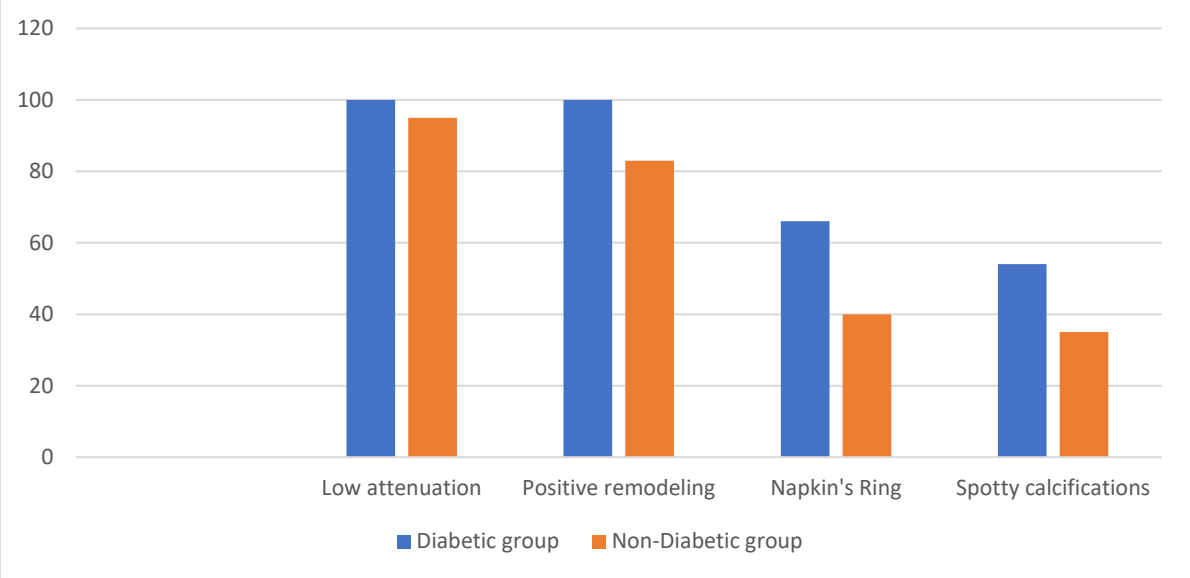

Figure [2]: Clustered columns demonstrating distribution of plaque vulnerability characteristics in diabetic and non-diabetic patients

Table [5]: Screening of other plaque criteria in both groups

Plaque characterization			Diabetic group [N=100]	Non-Diabetic group [N=100]	P-value [Sig.<0.05]
Calcium score			118.61±385.74	21.18±44.10	**0.010**
Type of plaque	Calcific		6%	6%	0.087
	Mixed Calcific		48%	33%	
	Non-Calcific		46%	61%	
Eccentricity	Eccentric		87%	73%	**0.013**
	Concentric		13%	27%	
Degree of stenosis	LAD	Absent	6%	13%	**0.002**
		Mild	10%	25%	
		Moderate	33%	32%	
		Severe	51%	30%	
	LCX	Absent	62%	91%	**<0.001**
		Mild	3%	1%	
		Moderate	10%	5%	
		Severe	25%	3%	
	RCA	Absent	44%	87%	**<0.001**
		Mild	5%	4%	
		Moderate	12%	7%	
		Severe	39%	2%	
	RI	Absent	94%	0%	**0.045**
		Mild	0%	0%	
		Moderate	2%	0%	
		Severe	4%	0%	

DISCUSSION

According to our results, as regards the risk factors, hypertension as an effective risk factor was more prevalent in the DM population than in the non-diabetic population, showing a statistically significant difference; the average age of diabetic patients was higher compared to the non-diabetic population [Although the age group were not previously determined in the study for each group]; smoking history for both groups, however, exhibited marginally statistically significant differences between both groups; and **p**rior PCI revealed a statistically significant difference, which was in concordance with **Esteghamati *et al.*** [6]. There were also no statistically significant differences between the diabetic and non-diabetic groups for positive family history, history of dyslipidemia, history of CABG surgery, or prior CVS or TIA, which was in discordance with the same study. Most patients had at least one cardiovascular risk factor [hypertension, smoking, DM, and high cholesterol].

In our study results, the HBA1C level in the diabetic group was high, suggesting that poor DM control may have an impact on the pathology of increased plaque vulnerability. Also, the mean LDL-c levels in the DM group were greater than those in the non-diabetic group, showing highly statistically significant differences between both groups, which was also indicating that a large sector of the study population had dyslipidemia; however, many were giving a negative history of dyslipidemia, recommending dyslipidemia screening in all diabetic patients with CAD even if they are asymptomatic. These results were in correlation with **Shenouda *et al***. [7].

In our study, we found that the MVD pattern is higher in the diabetic group and showed a statistically significant difference between the two groups, which means that DM tends to affect a larger number of vessels in CAD if compared to non-DM patients. This is in accordance with **Zand Parsa *et al.*** [8].

In our study, we discovered that the RCA and RI were the most affected vessels with vulnerable plaques, which was also consistent with **Dar *et al.*** [9].

There was also a statistically significant difference between DM and the non-diabetic groups in the degree of luminal narrowing of the LAD and RI but not in the degree of luminal narrowing of the LCX and RCA, which was in discordance with **Tesche *et al.*** [10] and **Zhang *et al***. [11].

As regards plaque vulnerability characters, between DM and the non-diabetic groups, there were statistically significant differences in positive remodeling and napkin's ring, and this is in correlation with **Reddy *et al.*** [12]. There were no statistically significant changes in low attenuation between DM and the non-diabetic groups, which was in discordance with the same study. It was also noticeable that spotty calcification was more prevalent in the DM group than the non-diabetic group, showing a statistically significant difference. Poor glucose control can cause intimal and medial calcification in the form of spotty calcification, according to **Tomizawa *et al.*** [13].

As regards plaque analysis and calcium scoring in both groups, between the DM and the non-diabetic groups, calcium score and plaque eccentricity exhibited statistically significant differences, and this is in accordance with **Budoff *et al.*** [14] **and Kwon *et al.*** [15]. There was also no statistically significant difference between the diabetic and non-diabetic groups with regard to the type of plaque.

Limitations: The majority of selected patients were at moderate to high risk of having CAD, so some of the results could be affected by bias. Also, IVUS, which is considered the gold standard for studying plaque composition, was not used. Future large-scale studies are recommended, as the limited size of the study population may affect the final result.

Conclusion: In diabetic patients with long history of the disease and moderate risk of CAD, MSCT angiography is recommended for the identification of CAD extent, severity and risk stratification. MSCT angiography has a great ability to determine atherosclerotic plaque composition and vulnerability in diabetic and non-diabetic patients which could limit the major dependence on Unnecessary invasive modalities. Also, it obviously can help in the early detection of high-risk patients, early prevention and management either with medical treatment or elective intervention, and prevent acute events, this may help in decreasing the Mortality and morbidity for both DM and CAD.

Disclosure: None to be disclosed

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