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Atherosclerotic Burden of Cronaries in DM with MSCT

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Abstract

Background: Multiple studies have confirmed the extensive burden of coronary artery disease in cases with diabetes. Yet, no optimal assessment technique has been proposed for risk stratification of these populations. We performed this study to elucidate the impact of diabetes on the coronary atherosclerotic burden using Coronary Computed Tomography Angiography (CTTA).

Patients and methods: This cross-sectional study included 100 cases with coronary atherosclerosis that were divided into two groups; the non-diabetic group 63 cases, and the diabetic group 37 cases. All subjects were subjected to complete history taking, thorough physical examination, and routine preoperative investigations. Additionally, echocardiography and CCTA were done for all cases. Also, calcium score was calculated.

Results: The diabetic group displayed significant younger age. However, gender and body mass index did not significantly differ between the two groups. Although smoking prevalence was comparable in the study groups, both hypertension and dyslipidemia had significantly higher prevalence in the diabetic group. Most of the studies echocardiographic variables were comparable between the two groups. The diabetic cases showed a significant increase in both plaque and diseased vessel number. Obstructive lesions were more common in diabetic cases. Calcium score was significantly higher in the diabetic group compared to non-diabetics.

Conclusion: It is evident that diabetes is associated with a heavier atherosclerotic burden in the coronary arteries. Additionally, calcium score appears to be a reliable option for assessment of the severity of coronary atherosclerosis.

Keywords: Coronary artery disease; Diabetes mellitus; Coronary Computerized Tomography Angiography (CCTA)

Introduction

Not only in Egypt, but the incidence of diabetes mellitus is increasing around the world, and it is expected to increase in the upcoming years, which increases its socioeconomic impact on the governmental health services [1-3].

The patients suffering from Diabetes Mellitus (DM) show a greater prevalence of Coronary Artery Disease (CAD) and they are more liable to develop Myocardial Infarction (MI) compared to non-diabetic personnel. The possibility to develop either MI or coronary death in diabetic patients is similar to the subjects with previous positive history of MI [4].

Generally, diabetic patients having CAD experience atypical or blunted symptoms, which is secondary to diabetic autonomic neuropathy [5]. Also, there is also a debate about the optimum management plan between the European and American guidelines [6].

Coronary Computed Tomography Angiography (CCTA) has emerged as an effective non-invasive tool to diagnose coronary calcifications that usually occur prior to luminal stenosis or development of anginal symptoms. Also, CCTA showed high sensitivity in the detection of coronary stenosis [7,8].

The difference in coronary plaque burden could be the reason behind the increased rate and morbidity of that disease in the diabetic population. Thus, accurate assessment of coronary plaque burden would be of crucial importance for patient risk stratification [9,10].

To date, coronary artery calcium score has been applied to assess the degree of coronary atherosclerosis in cases diagnosed with diabetes and it revealed the presence of extensive atherosclerosis in such population [6,10-12].

The current study was performed to elucidate the impact of diabetes on the coronary atherosclerotic burden using CTTA.

Patients and methods

This is cross-sectional comparative study was conducted at computed tomography unit in cardiology department in police hospital, Cairo, Egypt, during the period between March 2019 to March 2020. This was done after gaining approval from the local ethical committee of Menoufia University. We included a total of 100 symptomatic cases (chest pain, dyspnea, fatigues, syncope, stable angina defined by according to canadian cardiovascular society [13], unstable angina defined by ESC guidelines [14] prepared for CCTA who were divided into two groups the first one included 63 non-diabetic subjects, and the second one included the remaining 37 cases who had diabetes mellitus type II [15].

We excluded cases with st elevation and non-st elevation myocardial infraction, renal impairment, previous history of coronary revascularization, contraindication to computed tomography (like contrast allergy), or atrial fibrillation from the current study.

Before participating in the study, all patients were informed about the procedures, aim, and drawbacks of each intervention. All subjects were subjected to complete history taking, detailed general examination, thorough cardiac examination (including blood pressure, heart rate, electro-cardiogram) and routine laboratory investigations (including blood sugar, glycosylated hemoglobin, cardiac enzymes and lipid profile). Additionally, transthoracic 2-D echocardiography was ordered to assess the ejection fraction and wall motion abnormalities. Echocardiography was performed using Hewlett Packard HP Sonos 5500 and Philips Envisor echo set using a 4 MHz transducer.

For CCTA, all examinations were carried out utilizing Toshiba Multislice Aquilion 320 system (Tokyo, Japan). Initially, a prospective non-enhanced coronary calcium scan was carried out, followed by CCTA. If the HR was ≥ 70 beats/min, extra oral ivabradine (7.5 mg two times per day 3 days before the examination) was commenced.

We defined calcium score as a dense area located in the coronary artery that exceeds the threshold of 130 Hounsfield units. For each patient, a total agatston score was recorded [16]. Moreover, an experienced CCTA observer visually assessed the presence of coronary plaques using axial images and curved multiplanar reconstructions. Both number and type of plaques (calcified, non-calcified, mixed) were noticed and recorded. Also, the number of diseased vessels was also evaluated.

We used SPSS software for mac for data collection and analysis. Data were either expressed in the form of number and percentage (for categorical data) or mean and standard deviation (for quantitative data). For the same previous category, median and range were used to describe non-parametric data. We used Chi-Square or Fischer's exact tests to compare two independent groups of categorical data. While comparing the quantitative data within two independent groups, independent samples t-test was used for parametric data and Mann Whitney test for non-parametric data. For all used statistical tests, the cut-off point below 0.05 for probability (P value) was considered to be statistically significant.

Results

The included cases had mean age of 56.57 and 50.54 years in the non-diabetic and diabetic groups respectively. Age was significantly younger in the diabetic group (p=0.001). However, no significant difference was reported between the two groups regarding gender, as males represented 55.6% and 64.9% of cases in both groups respectively. Likewise, BMI did not express any statistical difference between the two groups (26.54 kg/m2 and 26.68 kg/m2 in both groups respectively). As regard comorbidities, smokers represented 41.3% and 29.7% of cases in both groups respectively. However, both hypertension and dyslipidemia had significantly higher prevalence in the diabetic cases (p<0.05). These data are illustrated at Table 1.

	Non-diabetic (n = 63)	Diabetic (n=37)	P value
Age (years)	56.57 ± 7.96	50.54 ± 8.80	0.001
Gender			0.361
Male	35 (55.6%)	24 (64.9%)	
Female	28 (44.4%)	13 (35.1%)	
BMI (kg/m2)	26.54 ± 2	26.68 ± 2.46	0.764
Comorbidities			
Smoking	26 (41.3%)	11 (29.7%)	0.248
Hypertension	29 (46%)	26 (70.3%)	0.019
Dyslipidemia	32 (50.8%)	34 (91.9%)	<0.001

Table 1: Patient characteristics in the two groups.

The clinical presentation did not show any significant difference between the two groups, as atypical chest pain was the most common presentation in both groups (63.5% and 67.6% of cases in the two groups respectively). Other presentations included typical chest pain, dyspnea, fatigue and palpitation. NYHA class 2 and class 3 had higher prevalence in the diabetic group, while the non-diabetic group had higher prevalence of class 1. Table 2 illustrates these data.

	Non-diabetic (n=63)	Diabetic (n=37)	P value
Clinical presentation			0.063
Atypical chest pain	40 (63.5%)	25 (67.6%)	
Typical chest pain	6 (9.5%)	1 (2.7%)	
Dyspnea	6 (9.5%)	9 (24.3%)	
Fatigue	9 (14.3%)	0 (0%)	
Palpitation	3 (4.8%)	2 (5.4%)	
NYHA class			
1	32 (50.8%)	7 (18.9%)	0.006
2	27 (42.9%)	27 (73%)	
3	4 (6.3%)	3 (8.1%)	

Table 2: Clinical presentation and NYHA classification of the study groups. NYHA: New York Heart Association Classification

All of the studies echocardiographic variables were comparable between the two groups. However, ejection fraction showed a significant decrease in the diabetic group (59.59% *vs*. 61.41% in the non-diabetic group– p=0.001) whereas left ventricular internal diameter end systole showed a significant increase in the diabetic group (p=0.043). These data are further explained in Table 3.

	Non-diabetic (n = 63)	Diabetic (n=37)	P value
LA	3.50 ± 0.37	3.61 ± 0.48	0.192
AORTA (cm)	3.20 ± 0.27	3.22 ± 0.30	0.686
IVSD (cm)	1 ± 0.08	1.01 ± 0.08	0.894
LVPWD (mm)	1 ± 0.07	1 ± 0.08	0.894
LVIDD (cm)	3.93 ± 0.28	3.98 ± 0.29	0.379
LVIDS (cm)	3.09 ± 0.29	3.22 ± 0.35	0.043
EF (%)	61.41 ± 2.19	59.89 ± 2.08	0.001

Table 3: Echocardiographic parameters in the study groups. EF: Ejection fraction, LA: Left atrium, IVSD: Interventricular Septal End Diastole, LVIDd LVIDs: Left Ventricular Internal Diameter End diastole, LVIDs: Left Ventricular Internal Diameter End systole, LVPWD: Left Ventricular Posterior Wall Thickness End Diastole.

Diabetic cases had significantly increased plaques compared to non-diabetics (4 *vs*. 1 respectively, p<0.001). Also, the number of disease vessels increased significantly with diabetes (3 *vs*. 2 in the non-diabetic group, p<0.001). Calcified plaques were more prominent in the diabetic group, whereas soft plaques were predominant in the other group. Additionally, obstructive lesions were more prominent compared to the non-obstructive lesions (55.6% and 70.3% of cases in the non-diabetic and diabetic cases respectively). Nevertheless, statistical analysis showed significantly higher prevalence rate in the diabetic population. Table 4 summarizes these data.

	Non-diabetic	Diabetic	P value
	(n=63)	(n=37)	
Total plaque number	1 (0-9)	4 (0-13)	<0.001
Diseased vessel number	2 (0-4)	3 (0-4)	<0.001
Plaque type			
No plaque	22 (34.9%)	4 (10.8%)	<0.001
Calcified	11 (14.5%)	14 (37.8%)	0.001
Soft	21 (33.3%)	6 (16.2%)	0.009
Mixed	9 (14.3%)	13 (35.1%)	0.005
Lesion type			<0.001
Obstructive	35 (55.6%)	26 (70.3%)	
Non-obstructive	28 (44.4%)	11 (29.7%)	

Table 4: Plaque and lesion criteria in the study groups.

When it comes to the calcium score in the current study, it was significantly higher in the diabetic group compared to non-diabetics (210 *vs*. 165, respectively, p<0.001), as showed in Table 5.

	Non-diabetic	Diabetic	P value
	(n=63)	(n=37)	
Ca score	165 (27-565)	210 (78-576)	<0.001*

Table 5: Ca score in the study groups.

Discussion

Diabetes mellitus is a complex metabolic disorder correlated with an augmented possibility of microvascular and macrovascular disease. It has been characterized by remarkable advances in our understanding of the mechanisms [17]. It has been reported that Hyperglycemia and Insulin Resistance (IR) are commonly correlated with low-grade inflammation, oxidative stress, which triggers endothelial dysfunction and hence promotes atherogenesis. Additionally, type II DM is also associated with enhanced platelet and hemostatic functions [18]. The high atherosclerotic burden associated with diabetes has been demonstrated by CTTA and Calcium Score[19-22].

This study was carried out at police hospitals aiming to evaluate the difference of the atherosclerotic burden of coronary arteries between patients suffering from diabetes mellitus and non-diabetic patients by using CCTA. We included a total of 100 cases with coronary atherosclerosis that were divided into two groups; the non-diabetic group included 63 cases who had not had diabetes mellitus, and the diabetic group which included the remaining 37 cases who had diabetes.

In our study, the mean age of the included cases was 56.57% and 50.54% in the non-diabetic and diabetic groups respectively. Age was significantly older in the non-diabetic group (p=0.001). Malthesh et al. in their study among patients suffering from diabetes mellitus and non-diabetic cases presented with acute coronary syndromes, observed that the peak incidence of acute coronary syndrome in patients suffering from diabetes mellitus was in the 4th and 5th decade in comparison with the 5th and 6th decade in non-diabetics [23]. Contrarily, another study did not detect a significant difference between the 2 groups regarding age. The mean age of the included cases was 65.2 and 65.5 years in the diabetic and non-diabetic groups respectively [18].

In the current study, no significant difference was noted between the two groups regarding gender (p=0.361). Males represented 64.9% and 55.6% of cases in the diabetic and non-diabetic cases respectively. Similarly, Bharath found among diabetics, there were 52.8% male patients and 47.2% female patients, similarly among non-diabetic group, 57.2% were males and 42.8% cases were females. Majority of the cases among both the groups were males [24]. A previous study has also reported that male gender is one of the main non-modifiable risk factors for CAD [25]. Both of the previous studies agree with our findings regarding the increased prevalence of CAD in males.

In our study, no significant difference was reported between the two groups regarding BMI (p=0.764). It had mean values of 26.46 kg/m2 and 26.54 kg/m2 in the diabetic and non-diabetic groups respectively. Similarly, Deseive and his associates reported no significant difference between the two groups regarding BMI (p=0.22). It had mean values of 28.3 kg/m2 and 28.7 kg/m2 in the diabetic and non-diabetic groups respectively [18].

In our study, smoking was reported by 29.7% and 41.3% of cases in the diabetic and non-diabetic groups respectively, with no significant difference between the two groups (p=0.248). Another study reported that smokers represented 18% of cases in both groups (p=0.54) [20]. Additionally, it has been recognized that smoking cigarette is a potent risk factor for development of CAD. Previous studies have found a significant correlation between smoking cigarette and atherosclerosis, MI and death from CAD [26].

In our study, there was an increased prevalence of dyslipidemia in the diabetic group versus the non-diabetic one (91.9% *vs*. 50.89% in both groups respectively (p<0.001). Similarly, Laimoud and his associates reported that the prevalence of hyperlipidemia was significantly higher in the diabetic group (84% *vs*. 39.4% of cases in the non-diabetic group (p=0.001) [27]. On the other hand, Rana and his associates reported no significant difference between diabetic and non-diabetic cases regarding the prevalence of hyperlipidemia (p=0.61). It was present in 70% of cases in both groups [20].

In our study, there was no significant difference between the 2 groups regarding the clinical presentation (p=0.063). Atypical chest pain was the commonest presentation in both groups (67.6% and 63.5% in diabetic and non-diabetic cases respectively). Other presentations included typical chest pain, dyspnea, fatigue, and palpitations.

Deseive and his associates reported no significant difference between the two groups regarding the presentation (p=0.52). Chest pain was the commonest complaint in both groups as it was reported by 33.3% and 38.3% of cases in both groups respectively, and that agreed with our results. Other presentations included abnormal stress test, dyspnea at exertion, along with arrhythmia [18].

In our study, the diabetic cases tended to have higher NYHA classification compared to non-diabetic subjects (p=0.006). This could be explained by the fact that diabetic cases had more extensive CAD that affected their performance status. Also, diabetes is associated with other systemic complications that have a negative impact on the general condition like its effect on the kidney and other blood vessels [28].

In our study, ejection fraction was significantly decreased in the diabetic group compared to non-diabetics (59.89% *vs*. 61.41% respectively, p=0.001). In another recent study, left ventricular ejection fraction was categorized in three groups accordingly normal (EF>50%) mild (EF between 40%-49%), moderate (EF<40%) and severe (EF<30%). It was observed that diabetic patients had more severe systolic dysfunction as compared to non-diabetic patients [24]. Malthesh et al. in their study reported that the Left ventricular dysfunction was relatively more common (46%) in diabetics than in non-diabetics (10%), these results were similar to the present study [23]. Conversely, Laimoud and his colleagues reported that there was no significant difference between diabetics and non-diabetics regarding EF (p=0.54). It had mean values of 58.52% and 59.42% in both groups respectively [27].

In our study, although there was no significant difference between the two groups regarding LVIDD (p=0.379), LVIDS showed a significant increase in the diabetic group (3.22 *vs*. 3.09 in non-diabetics p=0.043). In another study, no significant difference was detected between diabetics and non-diabetics regarding LVIDD, and that agrees with our findings. Nevertheless, the same study reported no significant difference between the two groups regarding LVIDS (3.16 *vs*. 3.15, p>0.05), and that contradicts with our findings [29].

In the current study, increased prevalence, extent, and severity of CAD for DM individuals were remarkably consistent across patient, vessel, and segment-based comparisons (not shown in tables). The number of diseased vessels increased significantly in the diabetic group compared to non-diabetics (3 *vs*. 2 respectively p<0.001). Likewise, another recent study reported that the median number of lesions per patient was 3 in the diabetic group *vs*. 1 in the non-diabetic group, with a significant difference between the two groups (p=0.01) [18].

Bharath and Gosavi also reported in their recent study that the prevalence of double vessel and three vessel disease was significantly higher in the diabetic group compared to the non-diabetic group (28.8% and 21.2% *vs*. 22% and 15.6% of cases in the two groups respectively p=0.03) [24]. Moreover, Malthesh et al. in their study reported that the incidence of triple vessel disease in diabetics was much higher (44%) compared to non-diabetics (16%). The incidence of double vessel disease was slightly higher (26%) compared to nondiabetics (20%) [23].

In the current study, obstructive lesions were significantly more common in the diabetic group (p<0.001). It was encountered in 70.3% and 55.6% of cases in the diabetic and non-diabetic groups respectively. In accordance with our findings, Deseive et al. reported that obstructive lesions were significantly more common at the diabetic group (50.9% *vs*. 38% of cases in the non-diabetic cases p=0.02) [18]. Reda et al. reported that obstructive lesions were present in 40% of cases in the diabetic group, while it was present only in 20% of non-diabetic cases (p=0.026) [6]. Furthermore, Rana et al. also confirmed the previous findings as obstructive lesions were detected in 37% of the diabetic cases *vs* 27% of cases in the non-diabetic group [20].

In our study, the total number of plaques was significantly higher in the diabetic group (p<0.001). It had median values of 4 and 1 in the diabetic and non-diabetic groups respectively. Another study confirmed the prevalence of high plaque burden and stenosis percent in association with diabetes [27]. Also, Lawand et al. confirmed the previous findings [30].

In the current study, there was a significant difference between the two groups regarding plaque type (p<0.05). Calcified plaques were the commonest in the diabetic group (37.8%), whereas soft plaques were the commonest in the non-diabetic group. The current literature reports conflicting results about the nature of coronary plaques in diabetes. Nicolli et al. reported that such lesions contained higher calcium and lower lipid content in diabetic cases compared to non-diabetics [31]. On the other hand, Farhan et al. negated any significant difference regarding plaque composition between diabetic and non-diabetic population [32].

When it comes to the Ca score in our study, it was significantly elevated in the diabetic group compared to non-diabetics (210 *vs*. 165 p<0.001). The results of the current study are in agreement with the results of other researchers, who have showed that diabetic individuals had higher prevalence and extent of calcium around the coronary vasculature compared to non-diabetics [33,34]. Other researchers found that diabetic patients had a significant increase in Coronary Artery Calcification (CAC) scores (>400) compared with age and gender matched non-diabetic controls [35].

In an additional study, Calcium Score was significantly higher in diabetic patients as it had a mean value of 124.1 compared to. 44.9 in non-diabetics (p<0.01) [18]. Another Egyptian study also reported that Ca score was significantly elevated in cases with type II diabetes (123), while it had mean values of 2 and 3 in type I diabetes and controls respectively (p=0.005) [6]. Furthermore, Natali et al. reported that the included diabetic cases had significantly higher atherosclerotic disease score when compared to non-diabetics (352 units *vs*. 211 units p<0.0001, respectively) [36].

Our results disagreed with that reported in the south bay heart watch study who reported that baseline calcium score failed to predict the risk in diabetic cases while it succeeded in the non-diabetic group [37,38].

The present study indicates that calcium scoring is an integral part of the evaluation of patients referred for coronary CT. Calcium scoring is a more sensitive noninvasive tool for the assessment of CAD. In patients with high calcium scoring, significant CAD is suspected. The correlation between calcification with MSCT and angiography is also needed.

A large number of patients should be included in further studies to assess the relation between calcium scoring, diabetes and the severity of CAD.

Conclusion

All in all, it is evident that diabetes is associated with a heavier atherosclerotic burden in the coronary arteries. Additionally, Ca score appears to be a reliable option for assessment of the severity of coronary atherosclerosis.

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