The Effect of Clinical Risk factors on Coronary Artery Remodeling in Diabetic Patients a Multi-Detector Computed Tomography Study.

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Coronary artery remolding index – T2DM, CTCA.

ABSTRACT
Background: Type two diabetes mellitus (T2DM) is a strong risk factor for coronary artery disease (CAD). It is associated with diffuse coronary atherosclerosis with different pattern of coronary artery remodeling. Numerous imaging studies have been done to understand the pattern of coronary remodeling in diabetic patients, comparing it with non diabetics.
Aim of study: To assess coronary artery remodeling in patients with T2DM by computed tomography coronary angiography (CTCA).
Patients and Methods: This observational cross-sectional study was held in Cairo University hospitals. It enrolled 530 Egyptian patients, whom underwent CTCA, during the period between January 2019 to January 2021. We studied 263 patients with T2DM and 267 served as non diabetic patients control group. Baseline anthropometric, clinical and CTCA features of diabetics were compared with those without diabetes.
Results: Diabetic patients were older than non diabetics (p value= 0.001). Hypertension, dyslipidemia, use of statin were more in diabetic group (p value= 0.047) (p value= 0.000) (p value= 0.000) respectively, and smoking was more in non diabetic group (p value= 0.037). Coronary remodeling index (RI) was less in diabetic patients (p value= 0.018), while no statistical significant difference between the two groups regarding the type of RI (p value= 0.082).
Coronary artery remodeling index was less in male patients, and in patients who presented with chest pain/SOB. Negative remodeling index pattern was more evident in diabetic patients on insulin and statin (p value= 0.041), (p value= 0.043), respectively.
Conclusion: Negative coronary artery remodeling in diabetics is associated with more insulin use, statin use.

Introduction

T2DM is a strong risk factor for CAD. It has 2-4 folds greater risk of developing CAD than non-diabetic patient 1,2, and associated with accelerated atherosclerosis3, diffuse distribution and multisite affection than individuals without DM 4,5

The prevalence of other risk factors like hypertension and dyslipidemia, in association with diabetes, accelerates the formation and propagation of atherosclerotic plaque in diabetic patients 6.

A focal compensatory change in vessel size in response to atherosclerotic plaque is termed as coronary artery remodeling, the increase in total vessel area proportional to plaque area, i.e. compensatory enlargement, is termed positive remodeling, in contrast, negative remodeling is reduction in vessel size at the lesion site compared to normal area of the vessel 7,8

To assess the coronary atherosclerosis, various imaging tools have been used, CTCA has emerged as a noninvasive technique for the detection of coronary artery disease and has demonstrated good accuracy for the detection of coronary artery stenosis and atherosclerotic plaques9,10. CTCA provides comparative atherosclerotic assessment tool with IVUS. Achenbach et al 2004, found that the cross-

sectional vessel areas measured in CTCA is correlated closely to the external elastic membrane area measured in IVUS 11.

Numerous imaging studies have been done to understand the pattern atherosclerotic disease in diabetic patients, comparing the atherosclerotic progression and the pattern of coronary artery remodeling between diabetic patient and non diabetic patients. In these studies, different pattern of coronary artery remodeling, either positive and negative remodeling, has been described in diabetic patients 12,13.

Methodology

This is an observational, cross-sectional study that enrolled 530 Egyptian patients who came for CTCA coronary angiography due to clinical purposes, during a period of 24 months, CTCA data sets of 2500 consecutive patients were reviewed and 530 data sets with high image quality and angiographically obstructive (more than 50%) lesions, located in proximal and mid coronary segments were selected and analyzed. We studied 263 patients with T2DM and 267 served as non diabetic patients control group, under age of 60 years. We excluded patients with known coronary artery disease, history of prosthetic valve implantation or valvular heart disease, atrial fibrillation, and history of contrast media allergies.

All enrolled patients have been subjected to full history taking and clinical examination with emphasis on demographic data, presenting symptoms, history of T2DM, hypertension, dyslipidemia, cigarette smoking: whether; current or non smokers, we measured body mass index (BMI), waist circumference (WC) with measurement of waist to height ratio (WHtR). WC was measured at the point midway between the iliac crest and the lowest lateral position of the rib cage. The measurements were performed according to the international guidelines 14.

Prior to CTCA assessment, all patients have been told to fast for 4-6 hours, computed tomography (CT) 64, 256, and 312 were used for all CT angiographic exams (Philips Medical Systems; Eindhoven, Netherlands).

Image reconstruction

Two data sets have been generated for each patient at various points in the cardiac cycle (40% and 75% of the R-R interval).

CTCA image analysis

Using a fixed image display setting, the region of maximum luminal narrowing, more than 50% stenosis, was identified visually and the outer vessel contour was manually traced for calculation of the cross-sectional vessel area 15-17. In addition, 2 cross-sectional vessel areas of reference segments were obtained. These reference segments, by definition, have been selected from 2 points, specifically 5 mm proximal and 5 mm distal to the area of maximal luminal constriction.

The analysis did not include segments whose luminal diameter was less than 2.0 mm. The remodeling index was then calculated by dividing the cross-sectional vessel area at the region of maximum luminal narrowing by the mean of the 2 reference areas. Positive coronary artery remodeling was defined as RI >1.05 and negative coronary artery remodeling as RI <0.95, according to previous CTCA and IVUS studies of coronary remodeling index measurement 18-20.

Results

This is an observational, cross-sectional study, 530 Egyptian patients underwent CT coronary angiography, 263 patients with T2DM and 267 non diabetic patients. Among the study cohort, males constitute 79.1% of the whole population, and mean of age was 53.42±6.74 years, more than 60% has hypertension, dyslipidemia and smokers. Chest pain/SOB was the main complaint, table 1.

CTCA Characteristics of the Study Population

The mean remodeling index was 1.1±0.26 among whole study population. Patients with positive remodeling were more than patients with negative remodeling, table 2.

Table 1 Baseline Demographic, Anthropometric Measures and Clinical Characteristics of Whole Population

Variables	Mean ± SD or Number (%)
Gender, Male (%)	419 (79.1)
Age (years)	53.42±6.74
Weight(kg)	85.3±13.8
Height (cm)	171.6±9.0
BMI (kg/m2)	29.1±5.2
WC (cm)	101.8±11.0
WC/height ratio	0.59±0.07
T2DM (%)	263 (49.6)
T2DM on insulin (%)	65 (24.7)
T2DM duration (years)	6.8±5.2
Hypertension (%)	318 (60)
Dyslipidemia (%)	340 (64.2)
Use of Statin (%)	298(56.2)
Diabetics on Statin (%)	168(63.9)
Smokers (%)	258 (48.7)
Chest pain/ SOB (%)	448 (84.5)
Check up	67 (12.6)
Palpitation	5(0.9)
Other complaints (%)	9 (1.7)
BMI, body mass index; kg, kilograms; m, meter; SOB, shortness of breath; T2DM, type 2 diabetes mellitus; WC, waist circumference	

Table 2 CTCA Characteristics of the Whole Population

Variables (Agatston Units)	Mean ± SD and or Number (%)
Remodeling Index	1.1±0.26
Positive Remodeling Index	1.27±0.18
Negative Remodeling Index	0.83±0.10
Patients with Positive Remodeling Index (%)	340 (64.2)
Patients with Negative Remodeling Index (%)	190 (35.8)
Diabetics with Positive Remodeling Index (%)	150 (57)
Diabetics with Negative Remodeling Index (%)	113 (43)
LAD (%)	400 (75.5)
RCA (%)	83 (15.5)
LCX (%)	46 (8.7)
LM (%)	1 (0.2)
CACs, coronary artery calcification score; ECC, LAD, left anterior descending artery; RCA, Right coronary artery; LCX; left circumflex Artery; LM, Left main artery	

Comparative Analysis

Anthropometric Clinical and Characteristics in Different Coronary Artery Remodeling Index Groups in Diabetic Patients

Negative remodeling index pattern was more evident in patients on insulin and statin, as shown in table 3.

Table 3 Comparison of Anthropometric Measurements and Clinical Characteristics between Remodeling Index Groups in Diabetic Patients

Variables	Positive RI (n= 150)	Negative RI (n= 113)	P value
	Mean ± SD or Number (%)		
Gender, Male	117(78)	87 (77)	0.84
Age (years)	53.9±6.3	55.2±5.6	0.08
BMI (kg/m2)	28.8±5.0	28.8±5.6	0.99
WC (cm)	102.1±9.3	99.8±11.7	0.05
WC/Height	0.59±0.063	0.58±0.07	0.097
Use of Insulin	30(20%)	35(31%)	0.041
Chest Pain/SOB	129(86)	105(92.9)	0.076
Check up	18(12)	6(5.3)	0.068
Palpitation	0(0)	1(0.9)	0.248

Smoking	67(44.7)	49(43.4)	0.83
Hypertension	94 (62.7)	75(66.4)	0.53
Dyslipidemia	103(68.7)	89 (78.7)	0.068
Use of Statin	88(58.7)	80(70.8)	0.043
BMI, body mass index; cm, centimeters; kg, kilograms; m, meter WC; waist circumference			

Correlations

Spearman's coefficients in diabetic patients a positive correlation between coronary RI and waist circumference (r =0.130, p =0.035), table 4.

Table 4 Correlation of Coronary Artery Remodeling with Clinical and CTCA Characteristics in Diabetic Patients

Variables	Coronary Artery Remodeling Index	
	Spearman Correlation	P value
Age	-0.058	0.346
BMI	0.03	0.594
WC	0.130*	0.035
WC/Height	0.119	0.055
BMI, body mass index; CACs, coronary artery calcification score; DM, diabetes mellitus; WC, waist circumference		

Discussion

This prospective cross - sectional study evaluated 263 patients with T2DM and 267 served as non diabetic patients control group. Hypertension and dyslipidemia were more prevalent in diabetics in comparison to non diabetics. This is consistent with other studies, Tsimihodimos et al 2018, concluded that prevalence and incidence of hypertension increases significantly in the presence of diabetes mellitus 21. Around 70% of diabetic patients in our study were dyslipidemics, and this figure agrees with the prevalence figure of dyslipidemia in diabetic patients in other studies22, which may explain also the reason behind much use of statin therapy in our diabetic group

Our study showed that diabetics tended to be fewer smokers, this finding is similar to finding from national survey of cardiovascular risk factors in diabetics in middle east country, Malekzadeh et al 2020, found that diabetics were fewer smokers in their survey 23, that may suggest that efforts for lowering the prevalence of smoking have been successful in controlling smoking habit among diabetic patients. We evaluated coronary artery remodeling by measuring coronary artery RI, we demonstrated that diabetic patients showed less expansive coronary remodeling when compared with non diabetics, this ties well with previous studies wherein diabetic patients tend to have vessel shrinkage. Jime´nez-Quevedo et al 2009, evaluated 237 coronary segments in diabetic patients, by serial IVUS study, they suggested that the progression of coronary artery disease in patients with type 2 diabetes may be mainly attributed to vessel shrinkage and this shrinkage is influenced by insulin requirements and metabolic control and is associated with more advanced coronary atherosclerosis 13. The less expansive remodeling described in diabetics in our study didn't be statistically significant to reach the threshold of negative remodeling (frank shrinkage) to state that negative remodeling was the pattern of

remodeling in our diabetic group.

Actually, our current results showed that both positive and negative remodeling patterns were seen in diabetic patients, these findings are matching to findings reported another study, Lawand et al 2017, they retrospectively analyzed 210 IVUS studies in 181 patients, 71% (n =128) patients were diabetics, in their study, positive remodeling index was observed in both diabetics and non diabetics, without significant difference (1.4 versus 1.3 respectively, p = 0.7)24.

Our finding demonstrated that patients with diabetics with negative remodeling are those with more insulin and statin use. This prominent constrictive wall remodeling among statin users is compatible with prior studies on the role of statin in modulation of the coronary artery remodeling. In PARADIGM study, Lee et al 2018, evaluated 1,079 coronary artery lesions in statin-naive patients (n = 474), and 2,496 coronary artery lesions were evaluated in statin-taking patients (n = 781). Compared with lesions in statin-naive patients, those in statin-taking patients displayed a slower rate of overall percent atheroma volume progression (1.76 ± 2.40% per year vs. 2.04 ± 2.37% per year, respectively; p = 0.002) but more rapid progression of calcified percent atheroma volume (1.27 ± 1.54% per year vs. 0.98 ± 1.27% per year, respectively; p < 0.001)25, thus, statin promotes coronary calcification and halt atherosclerotic progression. A recent study conducted by Smit et al 2020, studied 202 patients, whom underwent serial CTCA with a mean inter scan period of 6.2±1.4 years, to assess coronary artery disease progression defined as the absolute annual increase in total, calcified, and non calcified plaque volume by quantitative CTCA analysis, they found that male sex (β=1.676; P=0.009), diabetes mellitus (β=1.725; P=0.012), and statin use (β=1.498; P=0.046) showed an independent association with annual progression of calcified plaque26.

Conclusion

Negative coronary artery remodeling in diabetics is associated with more insulin use, statin use.

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