IMPACT OF DIABETES DURATION ON CORONARY ATHEROMA BURDEN IN PATIENTS WITH LOW TO INTERMEDIATE PRETEST PROBABILITY FOR CORONARY ARTERY DISEASE: EVALUATION BY CORONARY CT ANGIOGRAPHY

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Abstract

Background: The risk of coronary artery disease (CAD) and CAD events is increased in those with diabetes mellitus (DM). When compared to individuals without diabetes, type 2 diabetics have a two- to four-fold higher risk of cardiovascular events. **Aim:** To use optical coherence tomography angiography to evaluate DM duration as a predictor of coronary atherosclerosis in patients presenting by chest pain with low to intermediate pre-test probability (PTP). **Methods:** This was a cohort observational study that used coronary CT angiography to assess the relationship between DM duration and coronary atherosclerosis in individuals presenting with low to intermediate PTP and chest pain. Depending on the length of DM, patients were divided into three equal groups: Group A with DM duration is less than five years, Group B with DM duration is five to ten years, and Group C with DM duration is more than ten years. **Results**: There were significant variations in the coronary computed tomography angiography (CCTA) results for coronary artery disease (CAD) and coronary artery calcium scores across the groups under study. Group C had a significantly higher prevalence of stenosis (≥50%) than groups A and B. While the vessels affected showed insignificant differences among the groups, the coronary artery calcium score was higher in group C compared to both A and B, with group B also exhibiting a significantly higher score than group A. Atheroma burden obstructive and segment involve scores were significantly elevated in group C compared to both A and B, with insignificant variation between groups A and B. The segment stenosis score was higher in groups B and C compared to group A, while being insignificant between B and C. There were differences between the groups in the parts of the left anterior descending, left circumflex, and right coronary arteries, with different patterns of importance in the proximal, mid, and distal parts. Group C experienced a significant higher incidence of major adverse cardiac and cerebrovascular events (MACCE) early in life compared to groups A and B. The best cutoff of burden thrombus score for prediction of stenosis and time for detection of obstructive coronary atheroma burden was >0, >7 years with 100%, 61.76% sensitivity, 100%, 66.67% specificity,

100%,79.7% PPV and 100%, 45.1%NPV respectively. **Conclusion:** Long-term diabetes was strongly correlated with a higher severity of coronary atheroma load. Individuals who had had diabetes for longer than ten years showed a dramatically greater frequency of severe adverse cardiovascular events, an increased atheroma burden, and significantly raised rates of coronary artery disease (CAD).

Keywords: Coronary Artery Disease; Coronary Atheroma Burden; Coronary CT Angiography; Diabetes; Pretest Probability.

Introduction

An elevated risk of incidents related to coronary artery disease is linked to diabetes mellitus (DM). Research based on a population has indicated that individuals with type 2 diabetes have two to four times more cardiovascular events than people without the disease (1).

All cardiovascular comorbidities, including peripheral vascular disease (PVD), systolic and diastolic heart failure, myocardial infarction (MI), and CAD, are influenced by diabetes mellitus. Regardless of CAD, it is linked to higher overall mortality rates in men and women of all ages and ethnic backgrounds (2).

Using the American Diabetes Association's 2010 criteria, type 2 diabetes was diagnosed. As to this specification, individuals who exhibit fasting glucose levels of 126 mg/dL, 48 mmol/mol or 6.5% for glycated haemoglobin (HbA1C), and/or post-challenge glucose levels (measured two hours following an oral glucose load of 75 g) of 200 mg/dL are classified as having diabetes (3).

Diabetics were also defined as patients who treated with insulin or oral hypoglycemic medications, or who had a history of type 2 diabetes that was recorded or self-reported. Any moment any of the aforementioned conditions were first satisfied was considered the start of diabetes. When the patient is being interviewed, and if the patient was unaware, through a direct medical record inquiry, the information regarding the development of diabetes was prospectively acquired for individuals with established type 2 diabetes. The amount of time a patient has had diabetes was determined by subtracting their present age from their age at onset (4).

The most frequent cause of death linked to diabetes mellitus and the most common type of damage to target organs is CAD. Investigations for a patient with stable CAD are focused on risk assessment, symptom management, and adverse event prevention (4).

The gold standard for assessing stenosis of the coronary arteries anatomically and for obtaining crucial prognostic data is coronary angiography. Nevertheless, coronary angiography may underestimate the amount of plaque due to vascular remodeling and the disease's diffuse character. It does not reflect coronary flow reserve or intraluminal plaque burden (5).

Adjunctive use of intravascular ultrasound (IVUS) greatly facilitates the investigation of hazy areas on coronary angiograms which may be caused by calcium, thrombus, severe eccentric lesions or dissection. However coronary angiography is invasive procedure with

serious potential risks which include coronary artery dissection, stroke. MI, arrhythmias, vascular complications (pseudoaneurysm, arteriovenous fistula, arterial thrombosis, peripheral embolization), bleeding and even death (0.1% risk) (6).

Over the past ten years, cardiovascular CT has developed at a rapid pace, gaining new and extended applications for noninvasive evaluation of the heart, large arteries, and peripheral vasculature. Radiation and contrast dosages have been drastically lowered thanks to novel scanning methods and sophisticated multi detector CT (MDCT) scanners(7).

In contrast to coronary computed tomography angiography (CCTA), which is regarded as the gold standard, invasive angiography has demonstrated to be a very accurate noninvasive technique for imaging the coronary artery with high sensitivity (85% - 95%) and specificity (95% - 98%) (8).

In order to establish individualized post-test illness probabilities for a given patient, the interpretation of noninvasive cardiac tests needs clinicians to take the results of diagnostic tests and apply their pretest estimates (termed pretest probability, PTP) of the disease. Age, gender, and the type of symptoms are the main factors that determine PTP(9).

Patients with low to intermediate PTP benefit most from CCTA in the evaluation of CAD. Generally speaking, CCTA is a great modality for ruling out CAD because its negative predictive value is consistently strong in trials with success rates ranging from 95% to 100% (10).

So, we aimed to use coronary CT angiography to assess the relationship between DM duration and coronary atherosclerosis in patients with low to intermediate pre-test probability and chest pain.

Patients and methods

The present study included 150 cases aged ≥ 18 years old known to be type II DM and presented by chest pain with low to intermediate pretest probability (PTP) underwent coronary CT angiography. presenting to Cardiology department, Benha University hospital and Al Ahrar teaching hospita.

The patients gave their informed written consent. Each patient was given a code number and an explanation of the study's objectives. The Research Ethics Committee of the Benha University Faculty of Medicine gave its approval before the study could begin.

Exclusion criteria were patients with known CAD or history of MI or unstable angina (ECG shows ST-T wave changes or echocardiography shows regional wall motion abnormalities or positive cardiac troponin or positive stress ECG), above 80 beats per minute (BPM) in the heart rate, atrial fibrillation or frequent extrasystoles, contraindications to CCTA, contrast allergy, hyperthyroidism, pregnancy, renal impairment (eGFR < 30 ml/min/1.73 m^2), decompensated heart failure.

DM duration was used to separate patients into three equal groups :

Patients in Group A: had diabetes for at least five years.

Patients in Group B: had diabetes for five to ten years
Patients in Group C: had diabetes for at least ten years.
The low and intermediate PTP were detected by its major determinants which are age, gender, and the nature of symptoms.
≤15% Low PTP.
15-85% Intermediate PTP.
≥ 85% High PTP (11).

Methodology:

Each patient was subjected to the following: **Patient History:** Personal history: name, age, sex, height, weight, and BMI; family history: it was feasible to determine whether or not early coronary heart disease had been in the patients' family by asking them questions. Inquiries on the patients' history of stroke or transient ischemic attack (TIA) were also used to gather data present history: course of the disease and duration, past history of any medical condition or previous hospital admission, cardiovascular risk factors, such as smoking, diabetes, and hypertension, symptoms suggestive of cardiac disease. Routine laboratory investigations included: complete blood count (Hb, WBCs, Platelets), random blood sugar, kidney function testes (creatinine and urea), liver function tests (ALT, AST).

Full clinical examination: Comprehensive assessment of the cardiovascular system to look for any irregular heart sounds or murmurs, and general examination encompassing vital signs include blood pressure, temperature, pulse, and heart rate.

Electrocardiography (ECG): Twelve-lead surface ECG was done to all patients.

Transthoracic Echocardiography (TTE): All patients underwent TTE using commercially available machines. A 2D, M-mode and Doppler images were obtained and interpreted. Using two-dimensional (2-D), M-mode, and Doppler echocardiographic techniques, images were obtained with the patient either in the left lateral position or supine. EACVI protocols were followed in acquiring images in the left parasternal long axis (LAX) view, apical 4, 3, and 2-chamber views.

Coronary computed tomography angiography CCTA: A dual-source CT (DSCT) (Somatom definition, Siemens Healthcare, Forchheim, Germany) or a 64-slice MDCT (Light Speed VCT 64; GE Healthcare, Milwaukee, WI, USA) was used for the procedure. The following scan protocols are available on all CT scanners: The 64-slice MDCT scan procedure includes the following parameters: 350 ms for the gantry rotation period, 0.2 for the pitch, 100–120 kV for the tube voltage (based on BMI), and 600 mAs for the tube current. The collimation of the slice is 64 × 0.625 mm. There was less radiation exposure when the ECG-triggered tube current modulation was turned on.

All patients' heart rates were recorded one hour before to tests. Patients who did not have a contraindication to beta-blockers were given 40–80 mg if their heart rate was greater than 75 beats per minute, the oral betablocker propranolol hydrochloride (indenol @ 40 mg/tablet). Just prior to the scan, a 0.5 mg sublingual dosage of nitroglycerin was given.

A contrast medium procedure with two phases was employed to modify the scan time. All patients received nonionic iso-osmolar contrast medium intravenously; a test bolus approach was used to provide a 10 ml dose of the agent at a rate of 5 ml/s. Then, to perform angiography, 60 ml of the same contrast agent were administered at a 6 ml/s flow rate. With a rigorous adherence to the rules established by the Society of Cardiovascular Computed Tomography, coronary segments were visually scored for the presence of coronary plaque using a 16-segment coronary artery model in an intent-to-diagnose manner.

Plaques with a lumen narrowing of < 50%, non-obstructive (0% luminal stenosis), the degree of luminal diameter stenosis was classified into three categories: mild, moderate, or obstructive (plaques with maximal stenosis ≥ 50%). It was believed that obstructive CAD was present in the posterolateral, obtuse marginal, and diagonal branches of the right coronary artery, left circumflex artery, and left anterior descending artery, respectively. A number of coronary CT angiographic scores were employed to evaluate the degree and volume of coronary artery disease (12).

Software specifically designed for this purpose was used to evaluate the CACS. A thick area of the coronary artery that exceeds the 130 HU cutoff has been recognized as coronary artery calcium (13).

The amount of plaques in the total coronary tree with > 50% stenosis was determined as the atheroma burden obstructive score (ABOS) (14).

No matter how much luminal stenosis there is in any one coronary artery segment, the total number of segments containing plaque (minimum = 0; maximum = 16), was used to determine the segment involvement score (SIS) (15).

The total area of coronary artery plaque was measured using the Segment Stenosis Score (SSS). Based on the degree of obstruction of the coronary luminal diameter, each coronary segment was categorized as having no to severe plaque (i.e., scores ranging from 0 to 3). The total score, which varied from 0 to 48, was then calculated by adding the extent ratings of each of the 16 segments (16).

Statistical analysis

IBM©, Armonk, NY, USA provided SPSS v28 for the statistical study was used. Quantitative non-parametric data were presented as median and interquartile range (IQR), and the Kruskal-Wallis test with Mann Whitney test was used to compare each group. Qualitative variables were represented as frequency and percentage (%) and were studied using the Chi-square test. Both the post hoc Tukey test and the ANOVA (F) test were used to assess quantitative parametric data. The standard deviation (SD) and mean of the results were given. Major adverse cardiac and cerebrovascular events (MACCE) time to occurrence was plotted using the Kaplan-Meier curve. If the P-value is less than 0.05, it is considered significant.

Results

The current study was carried out on 150 cases known to be type II DM and presented by chest pain with low to intermediate pretest probability underwent coronary CT angiography. Baseline characteristics (age, sex, weight, height, and BMI) and comorbidities (hypertension, hyperlipidemia, family history of CAD and current smoker) were insignificantly different between both groups. Table 1

Regarding the medication use, aspirin use, diabetes management by lifestyle modification and hypertensive medication by CCB and diuretics were significantly different among the studied groups. The groups under study did not exhibit significant differences in the use of statins, oral hypoglycemic medicines for managing diabetes, insulin, or both, and beta blockers for treating hypertension. In comparison to group A, although total cholesterol was much higher in both groups B and C, there was no significant difference between them. Group B had significantly lower triglycerides than group A, while group C had significantly lower triglycerides than both groups together. There was no statistically significant difference in LDL between groups B and C and group A, despite the fact that LDL was significantly lower in the latter. Nevertheless, there was no appreciable variation in HDL amongst the research groups. **Table 2**

Significant differences ($P<0.001$) were found when examining the CCTA data for coronary artery disease (CAD) and coronary artery calcium scores among the groups under study. Stenosis ≥50% was notably more prevalent in group C compared to groups A and B. While the vessels affected showed insignificant differences among the groups, the coronary artery calcium score was markedly higher in group C compared to both A and B ($P<0.001$, 0.003), with group B also exhibiting a significantly higher score than group A ($P=0.039$). Additionally, group C's atheroma load obstructive and segment involve scores were substantially higher than those of groups A and B ($P<0.05$), while group A and group B's values varied insignificantly. Groups B and C had significantly higher segment stenosis scores than group A ($P=0.040$, 0.007), but there was no statistically significant difference between B and C. Specifically, differences were found between the groups in the segments of the LAD, LCX, and RCA arteries, with different significant patterns in the proximal, mid, and distal parts. **Table 3**

The incidence of MACCE was significantly higher in Group C compared to groups A and B ($P<0.001$). Table 4

The incidence of MACCE was significantly higher and earlier in group C compared to group A and compared to group B. Table 5

The best cutoff of burden thrombus score for prediction of stenosis and time for detection of obstructive coronary atheroma burden was >0, >7 years with 100%, 61.76% sensitivity, 100%, 66.67% specificity, 100%,79.7% PPV and 100%, 45.1%NPV. Table 6 Figure 1.

Discussion

The application of CCTA in evaluating CAD becomes most advantageous for patients whose pretest probability (PTP) is low to intermediate of the disease. Its remarkable negative predictive value, consistently reaching 95% to 100%, positions CCTA as an exceptional tool for ruling out CAD, thereby offering clinicians a valuable means of individualized post-test disease probability calculation based on pretest estimates (17).

Our study found that Significant differences were observed ($P<0.05$) in the medication use across the analyzed groups for aspirin, diabetes treatment through lifestyle modification, and hypertension therapy by CCB and diuretics. For statins, there was no significant variation across the groups that were tested insulin, oral hypoglycemic medicines for managing diabetes, and beta blockers for treating hypertension.

Kim et al. reported that there were significant differences ($P<0.05$) in medication use, diabetes management, aspirin, hypertensive medicine, and diuretics across the examined groups, which aligns with our findings. There were no appreciable differences between the groups under study in terms of statin and beta blocker treatment for hypertension(18).

In our study, regarding the CCTA CAD findings, CAD findings was significantly different among the studied groups, CAD by stenosis ≥ 50% was more prevalent in group C compared to groups A and B. There were no notable differences between the groups under study and the affected vessels. Group B's score was substantially higher than group A's ($P=0.039$), while group C's coronary artery calcium score was significantly greater than that of groups A and B ($P<0.001$, 0.003). Although there was no appreciable difference between groups A and B, group C's atheroma load obstructive and segment involve values were significantly higher than those of groups A and B ($P<0.05$). Although there was no statistical difference in the segment stenosis score between groups B and C, it was significantly higher in both groups B and C as compared to group A ($P=0.040$, 0.007).

In addition, Kim and colleagues found that longer diabetes duration was associated with higher rates of obstructive coronary artery disease and lower rates of normal coronary arteries, ($P < 0.001$). Compared to patients with diabetes lasting 5 years or 5–10 years, those with diabetes lasting more than 10 years had significantly higher coronary artery calcium scores, atheroma load obstructive, segment involve scores, and segment stenosis scores ($P < 0.001$) (18).

The proximal section of the LAD artery revealed a substantial rise ($P<0.001$) when group C was compared to groups A and B, and a significant increase ($P=0.005$) when group B was compared to group A. While there was no significant difference in the mid segment between groups B and C, it was significantly higher in both B&C ($P=0.002$, 0.001) than in group A. There was no significant difference between groups A and C and the distal segment was significantly higher in both ($P<0.001$) when compared to group B. Group B had significantly more segments than group A ($P<0.05$), whereas group C had significantly more proximal, mid, and distal LCX artery segments than groups A and B

(P<0.05). Although there was no significant difference between the two groups, group C's proximal and mid parts of the RCA artery were significantly larger than those of groups A and B (P<0.001). Group B had a much higher distal segment than group A, while group C had a significantly greater distal segment than both groups combined (P<0.001).
According to Pathak et al.'s study, patients whose DM duration was more than ten years had a substantially greater incidence of Triple Vessel Disease/Multivessel sickness (64.7% vs. 35.3%, P < 0.001) compared to those whose DM duration was less than ten years (19).
Sheng et al.'s study found no differences in the distribution of culprit vessels (LAD, LCX, and RCA) among the three groups (20).
According to the results of the current investigation, Group C had a significantly greater incidence of MACCE than Groups A and B (P<0.001). Furthermore, Group C saw a significantly higher prevalence of MACCE at an earlier age than either Group A or Group B.
This was in line with the findings of **Noh et al.** who found that patients with severe CAS (50–69% luminal narrowing) and prolonged diabetes duration (≥10 years) had a considerably higher difference in MACE incidence (p < 0.001) (21).
Additionally, patients with pre-DM and DM in the **Gao et al.** trial had a significantly greater incidence of MACE (10.8%, 16.1%, 19.4%; p = 0.003) in comparison to the NG group (22).
According to Guo et al.'s study, patients with diabetes had a substantially greater incidence of MACE than patients without diabetes (adjusted hazard ratio [HR] 1.32, 95% confidence interval [CI] 1.09-1.61, p = 0.005) (23).
The current study had provided a cutoff value of DM duration to predict obstructive coronary atheroma which was 7 yrs with sensitivity = 61.76% and specificity = 66.67%. We defined obstructive coronary atheroma by ABOS ≥1 and SSS ≥3(ABOS ≥1 means that there is one or more coronary segment has obstruction more than 50%, SSS ≥3 means that there is one or more coronary segment has significant obstruction). By compination of the two scores by these value we can get an accurate detection of the obstructive coronary atheroma burden.
As far as we are aware, only a small number of research have looked at how long diabetes has been present on the severity of CAD and assess how long diabetes has been present as a predictor of patients' coronary atherosclerosis who come with chest pain. Examine the length of diabetes mellitus in relation to coronary atherosclerosis in patients who are experiencing chest pain.

Conclusion

Finally, our study shows a strong correlation between a lengthier course of diabetes and a greater severity of coronary atheroma burden in patients presenting with chest discomfort and a low to intermediate pretest likelihood for CAD. Patients whose diabetes had been present for more than ten years showed dramatically greater the frequency of significant

adverse cardiovascular events, increased atheroma burden, and significantly raised rates of coronary artery disease (CAD).

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Author contribution

Authors contributed equally in the study**.**

Conflicts of interest

No conflicts of interest

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Table 1: Baseline characteristics and medical history of the studied groups

	Group A (DM duration ≤5 years) (n=50)	Group B (DM duration 5-10 years) n=50)	Group C (DM duration ≥10 years) (n=50)	P value
Age (years)	56.36 ± 6.77	57.54 ± 6.74	59.1 ± 7.17	0.141
	45 - 69	45 - 70	47 - 75	
Sex	30 (60%)	34 (68%)	32 (64%)	0.707
	20 (40%)	16 (32%)	18 (36%)	
Weight (Kg)	73.24±2.12	73.46±1.74	73.98±1.78	0.136
	70 - 77	70 - 76	70 - 77	
Height (cm)	1.66±0.06	1.65±0.06	1.66±0.06	0.530
	1.55 - 1.75	1.55 - 1.75	1.55 - 1.75	
BMI (Kg/m^2)	26.84±2.2	27.07±2.06	26.82±2.2	0.816
	23.39 - 31.24	23.51 - 31.63	23.84 - 31.22	
Hypertension	18 (36%)	22 (44%)	25 (50%)	0.366
Hyperlipidemia	18 (36%)	24 (48%)	28 (56%)	0.131
Family history of CAD	0 (0%)	2 (4%)	3 (6%)	0.235
Current smoker	16 (32%)	17 (34%)	19 (38%)	0.431

BMI: body mass index, CAD: coronary artery disease, *: statistically significant as P value <0.05, P1: p value between groups A& B, P2: p value between groups A& C, P3: p value between groups B& C.

Table 2: Medication use and Lipid profile of the studied groups

	Group A (DM duration ≤5 years) (n=50)	Group B (DM duration 5-10 years) n=50)	Group C (DM duration ≥10 years) (n=50)	P value	
Aspirin	16 (32%)	27 (54%)	27 (54%)	**0.039***	
Statin	32 (64%)	28 (56%)	34 (68%)	0.450	
Diabetes management					
Lifestyle modification	19 (38%)	10 (20%)	6 (12%)	**0.007***	
Oral hypoglycemic agents	21 (42%)	17 (34%)	15 (30%)	0.442	
Insulin	3 (6%)	5 (10%)	8 (16%)	0.265	
Both oral hypoglycemic agents & insulin	26 (52%)	28 (56%)	27 (54%)	0.923	
Hypertensive medication					
Beta blocker	5 (10%)	6 (12%)	9 (18%)	0.475	
CCB	6 (12%)	13 (26%)	18 (36%)	**0.020***	
Diuretics	19 (38%)	25 (50%)	45 (90%)	**<0.001***	
Total cholesterol (mg/dL)	171.46 ±16.61 142 - 199	189.94±17.02 160 - 220	196.24±24.68 160 - 239	**<0.001***	**P1<0.001*** **P2<0.001*** P3=0.140
Triglycerides (mg/dL)	154.5±15.68 130 - 179	146.3±14.12 120 - 170	128.86±13.07 110 - 149	**<0.001***	**P1=0.007*** **P2<0.001*** **P3<0.001***

HDL (mg/dL)	48.04±6.49	49.46±7.94	46.16±7.09	0.074	----
	35 - 60	35 - 60	35 - 60		
LDL (mg/dL)	103.04±18.01	84.12±14.78	82.5±16.4	**<0.001***	**P1<0.001* P2<0.001*** P3=0.605
	70 - 130	60 - 110	60 - 114		

CCB: calcium channel blocker, HDL: high density lipoprotein, LDL: low density lipoprotein, *: statistically significant as P value <0.05, P1: p value between groups A& B, P2: p value between groups A& C, P3: p value between groups B& C.

Table 3: CCTA CAD findings of the studied groups

	Group A (DM duration ≤5 years) (n=50)	Group B (DM duration 5-10 years) n=50)	Group C (DM duration ≥10 years) (n=50)	P value	
CAD findings					
Normal	24 (48%)	14 (28%)	10 (20%)	**<0.001***	----
Non-obstructive (1–49%)	18 (36%)	25 (50%)	14 (28%)		
CAD by stenosis ≥ 50%	8 (16%)	11 (22%)	26 (52%)		
Vessels affected					
1VD	6 (12%)	9 (18%)	12 (24%)	0.538	----
2VD	5 (10%)	3 (6%)	14 (28%)		
3VD or LM disease	7 (14%)	12 (24%)	22 (44%)		
Coronary artery calcium score					
Mean± SD	148.76±220.3	247.44±250.4	416.04±296.32	**<0.001***	**P1=0.039* P2<0**

Range		0 - 863	0 - 900	0 - 860		**.001***
Median (IQR)		31 (0-236.5)	219 (0-377.7)	435 (160.2-649.5)		**P3=0 .003***
Atheroma burden obstructive score						
Mean± SD		0.63±0.7	0.8±0.72	1.1±0.69	**0.005***	P1=0.229
Range		0 - 2.04	0 - 2.07	0 - 2.6		**P2=0 .001***
Median (IQR)		0.47 (0-1.15)	0.79 (0-1.34)	1.18 (0.79-1.50)		**P3=0 .038***
Segment involve score						
Mean± SD		1.62±1.99	1.98±1.66	2.92±2.09	**0.002***	P1=0.328
Range		0 - 7	0 - 5	0 - 7		**P2=0 .002***
Median (IQR)		1 (0-3)	2 (0-3)	3 (1-4)		**P3=0 .014***
Segment stenosis score						
Mean± SD		2.26±3.37	3.72±3.65	4.84±5.76	**0.020***	**P1=0 .040***
Range		0 - 13	0 - 13	0 - 24		**P2=0 .007***
Median (IQR)		0 (0-3)	3 (0-6)	3 (1-5)		P3=0.249
LAD artery	**Proximal**	0.88±0.17	0.98±0.18	1.38±0.44	**<0.001***	**P1=0 .005***
		0.61 - 1.2	0.71 - 1.29	0.73 - 2.08		**P2<0 .001***
						P3<0 .001*
	Mid	0.46±0.23	0.62±0.26	0.67±0.34	**0.009***	**P1=0 .002***
		0.11 - 0.85	0.06 - 1	0.12 - 1.2		**P2=0 .001***
						P3=0.428
	Distal	0.10±0.1	0.04±0.02	0.11±0.01	**<0.001***	**P1<0 .001***
		0.01 - 0.7	0.01 - 0.07	0.1 -		P2=0.

				0.13		323 **P3<0 .001***
LCX artery	**Proximal**	0.46±0.2	0.56±0.28	0.68±0.31	**<0.001***	**P1=0 .040* P2<0 .001* P3=0 .048***
		0.12 - 0.82	0.16 - 1	0.23 - 1.2		
	Mid	0.06±0.02	0.11±0.03	0.21±0.06	**0.009***	**P1<0 .001* P2<0 .001* P3<0 .001***
		0.03 - 0.12	0.06 - 0.15	0.1 - 0.3		
	Distal	0.23±0.1	0.29±0.1	0.34±0.09	**<0.001***	**P1=0 .002* P2<0 .001* P3=0 .009***
		0.06 - 0.4	0.1 - 0.46	0.21 - 0.5		
RCA artery	**Proximal**	0.26±0.13	0.3±0.08	0.46±0.15	**<0.001***	P1=0.071 **P2<0 .001* P3<0 .001***
		0.12 - 0.5	0.15 - 0.4	0.21 - 0.69		
	Mid	0.26±0.09	0.28±0.07	0.47±0.16	**0.009***	P1=0.076 **P2<0 .001* P3<0 .001***
		0.12 - 0.4	0.15 - 0.39	0.2 - 0.7		
	Distal	0.16±0.03	0.22±0.04	0.36±0.08	**<0.001***	**P1<0 .001* P2<0 .001* P3<0 .001***
		0.12 - 0.2	0.15 - 0.29	0.22 - 0.5		

CCTA, coronary computed tomography angiography; CAD, coronary artery disease; VD, vessel disease; LM, left main; LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery, *: statistically significant as P value <0.05, P1: p value between groups A& B, P2: p value between groups A& C, P3: p value between groups B& C.

Table 4: Incidence of MACCE the studied groups

	Group A (DM duration ≤5 years) (n=50)	Group B (DM duration 5-10 years) n=50)	Group C (DM duration ≥10 years) (n=50)	P value
Yes	5 (10%)	12 (24%)	30 (60%)	**<0.001***
No	45 (90%)	38 (76%)	20 (40%)	

DM: diabetes mellitus, MACCE: major adverse cardiac and cerebrovascular events, *: statistically significant as P value <0.05.

Table 5: Incidence of MACCE for 1-year outcome in the studied groups

	Mean	SE	95% CI for the mean
Group A (DM duration ≤5 years)	11.480	0.227	11.036 to 11.924
Group B (DM duration 5-10 years)	11.100	0.279	10.553 to 11.647
Group C (DM duration ≥10 years)	8.420	0.341	7.752 to 9.088

SE: standard error, CI: confidence interval, DM: diabetes mellitus, MACCE: major adverse cardiac and cerebrovascular events.

Table 6: Diagnostic accuracy of burden thrombus score for prediction of stenosis and time for prediction of obstructive coronary atheroma burden

	Cutoff	Sensitivity	Specificity	PPV	NPV	AUC	95% CI	P value
burden thrombus score for prediction of stenosis	>0	100	100	100	100	1.00	0.976 to 1.000	**<0.001***
time for prediction of obstructive coronary	>7	61.76	66.67	79.7	45.1	0.670	0.588 to 0.744	**<0.001***

atheroma burden								

PPV: positive predictive value, NPV: negative predictive value, AUC: area under the curve, CI: confidence interval, *: statistically significant as p value <0.05.

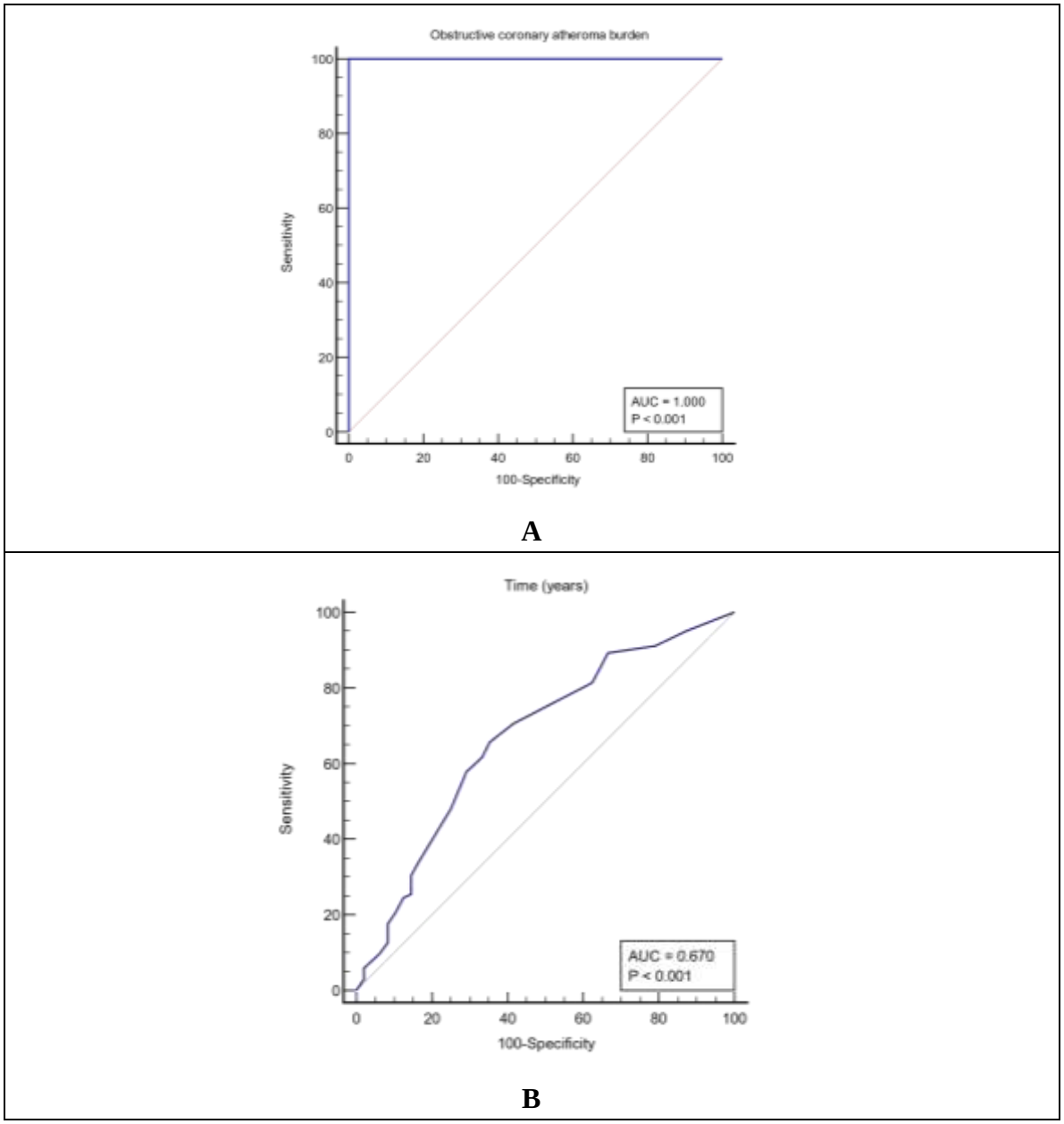

Figure 11: ROC curve analysis of (A) burden thrombus score for prediction of stenosis (B) time for detection of obstructive coronary atheroma burden