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Predictors of Coronary Artery Disease in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Abundant evidence shows that patients with type 2 diabetes are at high risk for several cardiovascular disorders: coronary heart disease, stroke, peripheral arterial disease, cardiomyopathy, and congestive heart failure.

Aim: This study aimed to identify predictors of occurrence of coronary artery disease (CAD) in patients with type 2 diabetes mellitus.

Methods: This cross-sectional descriptive study was conducted on 100 patients with type 2 diabetes mellitus referred for coronary angiography with normal systolic function**,** no segmental wall motion abnormality and suspected CAD.

Results: It was found that 12% of cases had normal coronaries and 88% of cases had coronary artery disease. Only male sex, total cholesterol ≥ 150 mg/dL, HbA1c ≥ 7.0 and BMI ≥ 25.0 kg/m^2 were significant risk factors that increase the probability of having CA abnormality.

Conclusion: The main predictors of presenting the disease were male sex, total cholesterol ≥ 150 mg/dL, HbA1c ≥ 7.0 and BMI ≥ 25.0 kg/m^2. The high prevalence of obesity highlights the need to improve measures to prevent cardiovascular disease in this population.

Keywords: Risk factors, CAD, Diabetes mellitus, Obesity.

INTRODUCTION

Most people with type-2 diabetes are at risk for morbidity and death from cardiovascular disease. The patients nearly two- to three-fold increased risk of dying from ischemic heart disease or stroke, as well as the high frequency of other macrovascular sequelae like amputations or lower limb ischemia. There is a significant burden on patient health and a significant financial burden on the health care system. Identifying risk factors for cardiovascular disease that are increased in people with diabetes is very important for developing more potent preventative measures [(1)].

Although, it is widely acknowledged that hyperglycemia is the primary cause of diabetic microangiopathy, the significance of other risk factors for the condition is not as well established. Therefore, the amount of cardiovascular risk linked to hyperglycemia remains uncertain, as does the degree to which it is unaffected by other atherogenic variables [(2)].

While the primary cause of the cardiovascular risk in these patients is hypercholesterolemia, while other abnormalities of lipid metabolism, such as hypertriglyceridemia, decreased HDL-C, and altered LDL particle composition (smaller, more atherogenic, higher density), are more suggestive of diabetes. Furthermore, it's not evident which of these lipid abnormalities associated with diabetes better predicts the likelihood of cardiovascular disease. One of the known risk factors for cardiovascular disease is diabetes mellitus. Consequently, in order to prevent CAD in people who have type 2 diabetic mellitus (T2DM), it is imperative to precisely identify the high-risk factors and high-risk groups of CAD [(3)].

Diabetic patients have twice the risk of coronary artery disease (CAD) as people without the disease. Atherosclerosis is made worse by persistent hyperglycemia, which has a significant role in the development of cardiovascular disease. The primary mechanisms could be severe oxidative stress brought on by persistent hyperglycemia, increased levels of advanced glycation end products (AGEs) and endothelial cell dysfunction [(4)].

Therefore, creating a prediction model and identifying T2DM patients who are at high risk of CAD are the goals of this study. This model can be used to prevent some needless coronary angiography procedures. The nomogram has gained popularity as a forecasting tool in recent years. Medical personnel can more easily understand and use it. It can be applied quickly and easily in a clinical context. Key to primary prevention of CAD is the development and implementation of non-invasive screening technologies for people at high risk for early heart attacks. Thus, the purpose of the study was to determine risk factors for the development of CAD in people with type 2 diabetes.

PATIENTS AND METHODS

One hundred participants with type 2 diabetes mellitus were involved in this study & suspected coronary artery disease with no segmental wall motion abnormality in resting echocardiography who were referred for coronary angiography at Echocardiography Lab. and Catheterization Lab., Cardiology Department, Suez Canal University Hospital.

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Inclusion criteria: Patients with type 2 diabetes mellitus (Either recently diagnosed or previously diagnosed with DM on anti-diabetic drugs either insulin therapy or oral hypoglycemic drugs**)** referred for coronary angiography with normal systolic function (Normal range is 55% to 75%) [(5)], with no electrocardiographic or echocardiographic (segmental wall motion) abnormality and they were suspected by symptoms and risk factors to have CAD.

Exclusion criteria: Patients with prior myocardial infarction, revascularization, bundle branch block, atrial fibrillation or flutter, poor echocardiographic image quality, resting baseline echocardiography segmental wall motion abnormalities, pacemaker implantation, more than mild valvular heart disease and restrictive or dilated cardiomyopathy.

All participants were subjected to the following: **Complete history taking** [age, gender of the patient, history of smoking, diabetes mellitus, main cardiac symptoms, other endocrinal diseases, history of chronic diseases (hypertension, dyslipidemia, bronchial asthma, history of chronic renal failure, chronic liver disease), history of atrial fibrillation and other arrhythmias, history of valvular heart disease as demonstrated by echocardiography, and history and symptoms of PVD. Measurements of height, weight, BMI, waist circumference and blood pressure at presentation. ECG, and laboratory testing should all be part of a comprehensive assessment (lipid profile, serum triglycerides, serum creatinine, estimated GFR, BUN, serum electrolytes, and HbA1c).

Echocardiographic Assessment:

A conventional echocardiographic study was carried out using a commercially available system (Philips Ultrasound field Service Company, EPIQ 7 Q lab version 10.8.5 machine). The standard views parasternal long, short axis, apical 2 and 4 chamber views at rest [To assess left ventricular fractional shortening percentage, left ventricular end-systolic and end-diastolic diameters, left atrial diameter, the thickness of the interventricular septum (IVS), the posterior wall (PW) and any valvular lesions].

Ethical approval:

An informed written consent was obtained from patients. The study was approved by Faculty of Medicine, Suez Canal University (Alaa 4243 IRB). This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were processed, tabulated, and statistically assessed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 28.0 (IBM Corp., Chicago, USA, 2021). The Shapiro-Wilk test was used to confirm the normalcy of the quantitative data, which were represented as mean ± SD (standard deviation) and the lowest and maximum of the range. Then, the ANOVA test and independent t-test (two independent groups) were used for comparison. Fisher's exact test was used to compare qualitative data that were expressed as a number and a percentage. The Bonferoni test was employed in post hoc analysis. A ROC curve was employed to assess how well the GLS score performed in diagnosing CA abnormalities. Using logistic regression, one may determine the independent risk factors that lead to a CA anomaly. A p-value ≤ 0.05 was regarded as significant.

RESULTS

One hundred participants with type 2 diabetes were involved in the study. It was found that 12% of cases had normal coronaries and 88% of cases had coronary artery disease (Figure 1).

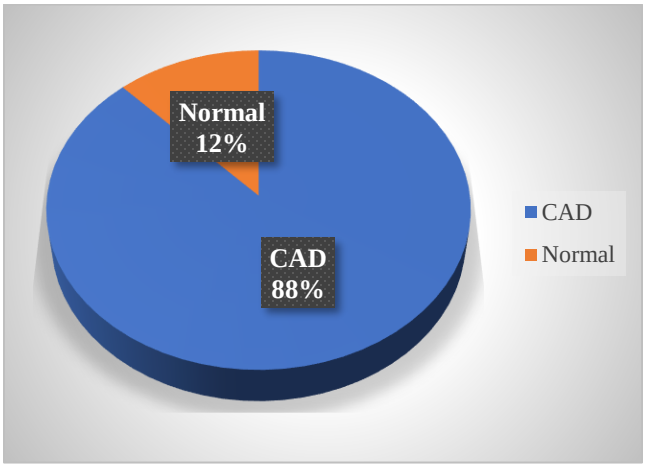

Figure (1): Prevalence of CAD in patients with type 2 DM.

Table (1) showed that BMI was statistically significantly higher in cases with abnormal CA findings. CA abnormality was significantly more frequent in males than in females. Otherwise, there were no statistically significant differences according to CA abnormality regarding other demographic characteristics.

Table (1): Comparison according to CA abnormality regarding demographic characteristics

Variables		Total (n=100)	CA findings		p-value
			Abnormal (n=88)	Normal (n=12)	
Age (years)	**Mean ± SD**	58.3±8.8	58.9±8.6	54.4±9.7	^0.101
	Range	38.0–77.0	38.0–77.0	38.0–68.0	
BMI (kg/m^2)	**Mean ± SD**	27.9±2.5	28.1±2.4	26.3±2.6	**^0.013***
	Range	22.0–36.0	24.0–36.0	22.0–30.0	
Duration of DM (years)	**Mean ± SD**	11.2±7.0	11.6±7.2	7.8±4.4	^0.074
	Range	1.0–30.0	1.0–30.0	1.0–15.0	
Gender (per raw)	**Male**	38 (38.0%)	37 (97.4%)	1 (2.6%)	**§0.027***
	Female	62 (62.0%)	51 (82.3%)	11 (17.7%)	
Smoking		17 (17.0%)	16 (18.2%)	1 (8.3%)	§0.685
Hypertension		88 (88.0%)	77 (87.5%)	11 (91.7%)	§0.999
Dyslipidemia		100 (100.0%)	88 (100.0%)	12 (100.0%)	NA
Atrial fibrillation		0 (0.0%)	0 (0.0%)	0 (0.0%)	NA

BMI: Body mass index.

Table (2) showed that Total cholesterol and HbA1c were the only laboratory findings with statistically significant differences in cases with abnormal CA findings.

Table (2): Comparison according to CA abnormality regarding laboratory findings

Variables		Total (n=100)	CA findings		p-value
			Abnormal (n=88)	Normal (n=12)	
Total cholesterol (mg/dL)	**Mean±SD**	172.5±20.6	174.9±19.0	154.7±23.6	**^0.001***
Triglycerides (mg/dL)	**Mean±SD**	102.6±20.7	104.3±12.0	90.8±15.3	^0.157
LDL (mg/dL)	**Mean±SD**	88.2±11.8	88.6±11.1	84.9±16.4	^0.463
HDL (mg/dL)	**Mean±SD**	52.5±7.3	52.5±7.5	52.8±5.5	^0.875
HbA1c (%)	**Mean±SD**	7.9±1.6	8.2±1.4	5.7±1.0	**^<0.001***
Creatinine (mg/dL)	**Mean±SD**	0.97±0.21	1.0±0.2	1.0±0.2	^0.841
BUN (mg/dL)	**Mean±SD**	17.3±3.7	17.7±4.7	14.0±2.5	^0.075
Potassium (mmol/L)	**Mean±SD**	3.9±0.4	3.9±0.4	4.0±0.4	^0.584

^Independent t-test. *Significant. LDL: HDL stands for high density lipoprotein, BUN stands for blood urea nitrogen, and HbA1c is for glycated hemoglobin.

Figure (2) showed **coronary angiography findings among the studied cases**. Only 12.0% of subjects had normal coronaries, another 20% had mild disease while the majority had significant CAD (56% underwent PCI, 10% underwent CABG and 2% had ectatic vessels).

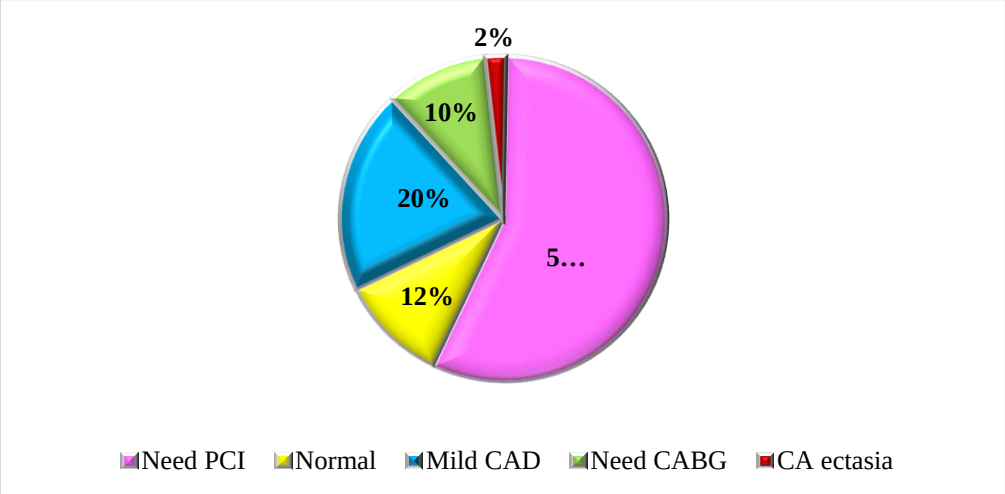

Figure (2): Coronary angiography findings among the studied cases

Table (3) showed that after studying different factors using logistic regression, only male sex, total cholesterol ≥ 150 mg/dL, HbA1c ≥ 7.0 and BMI ≥ 25.0 kg/m^2 were independent risk factors that increase the probability of having CA abnormality.

Table (3): Logistic regression for factors affecting having CA abnormality

Factors	B	SE	p-value	Odds ratio (95% CI)
Male sex	3.08	1.39	**0.027***	1.43 (21.87–334.50)
Total cholesterol ≥150 mg/dL	2.61	0.89	**0.004***	2.36 (13.60–78.47)
HbA1c ≥7.0	2.48	0.96	**0.010***	1.83 (11.91–77.41)
BMI≥25.0 kg/m^2	2.10	0.99	**0.033***	1.18 (8.20–56.83)
Constant	-2.50	1.00	**0.013***	

β: Regression coefficient. SE: Standard error. CI: Confidence interval. *Significant.

DISCUSSION

In the past sixty years, echocardiography has become a widely used and essential method for identifying and evaluating coronary heart disease (CHD). Visual identification of endocardial wall motion abnormalities and assessment of left ventricular (LV) ejection fraction are the primary methods that enable the echocardiographic evaluation of regional myocardial function, which is a critical step in the diagnosis and treatment of ischemic heart disease [(6)].

A history of ischemic disease, elevated LDL-C, inadequate management of hyperglycemia, and obesity are strongly and independently associated with cardiovascular risk, which is the risk of peripheral artery disease, coronary heart disease, or stroke, according to a prospective study conducted on a group of Spanish diabetic patients with hypercholesterolemia [(7)].

In the currents study, it was found that 12% of cases had normal coronaries and 88% of cases had coronary artery disease (20% had mild CAD, 56% need PCI & 10% need CABG). After studying different factors using logistic regression, only male sex, total cholesterol ≥ 150 mg/dL, HbA1c ≥ 7.0 and BMI ≥ 25.0 kg/m^2 were independent risk factors that increase the probability of having CA abnormality. The greatest predictor of cardiovascular illness was a prior history of ischemic heart disease, which was linked to a four-fold increased chance of developing new ischemic episodes [(8)]. Additional study on diabetic patients with ischemia in the past have also shown increased rates of morbidity and mortality, which is consistent with our findings. This emphasises how important it is to keep atherogenic variables under rigorous control in these patients [(9)].

A higher prevalence of microangiopathy in the past, such as pathologic albuminuria or diabetic retinopathy, were noted in patients who had a cardiovascular event while being monitored [(10)].

A growing body of research, drawing from pathophysiology, epidemiology, and clinical trials, implies that in people with diabetes, one important risk factor for the onset of cardiovascular disease is hyperglycemia. Furthermore, even at concentration ranges that may be regarded as normal or moderately increased, these most recent investigations have shown that HbA1c is a reliable indicator of cardiovascular risk. In light of this research, patients who experienced a cardiovascular disease episode were more likely to have high HbA1c concentrations both at baseline and throughout follow-up. Values of 7.5% or above were linked to a 2-fold increased chance of experiencing such events. Conversely, it has been shown that controlling hyperglycemia, as seen by a drop in HbA1c levels, reduces the chance of developing heart disease. For every 1% reduction in HbA1c, The UK Prospective Diabetes Study found that people with type-2 diabetes had a 14% and 12% lower risk of myocardial infarction or stroke respectively [(11)].

In our study, only total cholesterol ≥ 150 mg/dL can be considered as an independent risk factor for ischemic event. Otherwise, elevated LDL-C and TGs, or reduced HDL-C did not show any independent link to cardiovascular risk. Patients in another trial who had excess LDL-C (>=135 mg/dL) at follow-up were three times more likely to have an ischemic incident compared to patients with lower levels. The lipid factor that most reliably predicted cardiovascular risk was LDL-C. When LDL-C was included in the statistical model, it was found that triglycerides, HDL-C, the ratio of total cholesterol to HDL-C, and non-HDL cholesterol were not independently linked with cardiovascular risk. Triglycerides have a strong inverse relationship with HDL-C levels and a large degree of within-individual variability, which could account for their contentious prognostic value in relation to cardiovascular disease [(4)].

The significance of total cholesterol to HDL-C and non-HDL cholesterol ratios in the diabetic population for the prognosis of cardiovascular disease has been demonstrated by two recent studies particularly in those with hypertriglyceridemia. An increasing body of studies has demonstrated the benefits of statin therapy in lowering LDL-C in the diabetic population, especially for people whose cholesterol levels are within reference ranges or only slightly elevated [(12)].

Because of these results, statin therapy is now advised for all diabetic individuals who have a heightened risk of cardiovascular disease, even if they do not have

raised cholesterol levels. On the other hand, whereas low HDL-C and hypertriglyceridemia are more prevalent in the diabetic community than excess LDL-C, there is a dearth of information about their ability to predict the risk of cardiovascular disease or the effectiveness of treatment [(13)].

While losing weight helps to better control hyperglycemia, obesity exacerbates diabetes in those who already have it and raises the risk of the condition developing. According to the study's findings, obesity poses a significant risk for cardiovascular disease in people with type-2 diabetes and has predictive value that is unrelated to other atherogenic factors.

CONCLUSION

The main predictors of presenting the disease were male sex, total cholesterol ≥ 150 mg/dL, 7.0 for HbA1c and 25.0 kg/m^2 for BMI. The high rate of obesity in this population emphasizes the need for better cardiovascular disease prevention strategies.

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