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Coronary Artery Calcium Score (CACS) – A Comparative Study in Diabetic and Non-Diabetic Patients

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Abstract

Introduction: Diabetes mellitus is a common metabolic disorder that shares the phenotype of hyperglycaemia[1]. Recently, diabetes has emerged as a leading cause of coronary heart disease[2]. Although, a variety of methods are available to assess CAD risk in diabetic patients, coronary artery calcium score(CACS) is most sensitive among all these methods. The CAC score is an independent predictor of the risk of major cardiovascular events. It has demonstrated superiority over the Framingham risk score, CRP level and carotid intima-media thickness[3].

Aims and objectives: To compare coronary artery calcium score among diabetics and non-diabetics and to observe the association of ECG changes and CACS score.

Methodology: All patients were assessed by clinical evaluation and investigations. CACS was calculated by using 128 slice single source CT-scan machine by the Agatston method.

Results: In the present study, 80 patients were taken, of which 40 were diabetic and 40 were non-diabetic. Majority of patients in the diabetic group 21 (52.5%) were in the age group of 51 - 60 years whereas in the non-diabetic group, age groups of 51 - 60 and 41 - 50 years were equal 17 (42.5%) in number. Among diabetics, 7 (17.5%) patients had CACS in mild category and 33 (82.5%) patients were in moderate-to-severe category. In non-diabetics, patients with CACS in mild category were 21 (52.5%) and in the moderate-to-severe category were 19 (47.5%). Among various age groups, the severity of CACS increased with increasing age. Proportion of patients having moderate-to-severe CACS score increased with increasing value of HbA1C (83.3% in 9 - 11% HbA1C category and 94.7% in >11% HbA1C category).

Conclusion: CACS is higher in diabetics than in non-diabetics and is usually associated with increased risk of CAD. CACS can be an important non-invasive investigation for early detection of CAD.

Key words: CAD, T2DM, CACS, CHD, DM.

Introduction

Diabetes is a chronic disease, caused due to insufficient production of insulin by the pancreas or when it cannot be utilised effectively at the cellular level. The prevalence of diabetes in the age groups between 20 to 70 years worldwide was estimated to be 8.9% in 2021 according to the International Diabetic Federation. The prevalence of diabetes is on an increasing trend as the number of adult diabetics is projected to rise from 382 million to 592 million as compare from 2013 to 2035. In 2013, 5.1 million people died because of complications of hyperglycaemia. Prevalence of CAD in diabetic patients is 21.4% (known diabetics 25.3% and newly diagnosed diabetics 13.1%). With an increasing incidence worldwide, DM and CAD are likely to be a leading cause of morbidity and mortality in the future[1].

Diabetes-related complications affect many organ systems which are responsible for most of the morbidity and mortality associated with the disease. More recently, diabetes has also been an important factor in the development of coronary heart disease (CHD). Diabetes associated complications usually do not appear until the second decade of hyperglycaemia. In contrast, diabetes-associated CHD risk, related in part to insulin resistance, may develop before hyperglycaemia is established[2]. Atherosclerosis is the major threat to macro-vascular complications in diabetics. Dyslipidaemia is highly corelated with atherosclerosis and up to 97% of diabetic patients are dyslipidaemic[4]. The coronary artery calcium score is a measurement of the amount of calcium in the walls of arteries that supply heart muscles. It is measured by taking a special CT scan of the heart. The scan shows the amount of hardening of arterial wall (caused by atherosclerosis). The results of the scan makes it possible to estimate the risk of a heart attack or stroke in the next 5 - 10 years.

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The main methods for the quantification of CAC score are, determination of the volume of calcium, and determination of the calcium mass score. These are the most widely used parameters, especially by the Agatston method, which is used for most of the studies and publications, involving risk stratification and is also the method mostly used in clinical practice. The calcium volume score and calcium mass score have shown better reproducibility[5]. In this study we compare CACS to assess CAD risk in diabetics.

Aims and objectives

- To compare coronary artery calcium score in diabetics and non-diabetics.
- To obsereve association of ECG changes with CACS score among diabetics and non-diabetics.

Methodology

This cross-sectional observational study was carried-out at the Departments of Medicine and Radiology, LLRM Medical College and SVBP Hospital, Meerut, Uttar Pradesh from October to December-2021. All diabetic patients with age 30 - 60 years with no symptoms of CAD admitted during the study duration and willing to take part in the study were included. Equal number of non-diabetic patients who were fulfilling the inclusion and exclusion criteria were included in the study. Informed consent was taken from all patients. The clearance was taken from Institutional Ethics Committee, LLRM Medical College (approval – SC-1/2021/A246, dated 27/12/2021). All procedures followed guidelines laid down by the Declaration of Helsinki (2013). All selected patients were interviewed and relevant investigations including ECG and CT scan were done. CACS was calculated for both diabetic and non-diabetic patients and ECG was used to assess CHD risk.

The method used for quantification of CAC score was the Agatston method[5].

Agatston method: The Agatston method is the most widely used method used for calculating coronary artery calcium score. It uses those lesions which have a density above 130 HU. Weighted sum of all the lesions is taken and the area of calcification is multiplied by a factor related to maximum plaque attenuation. Multiplication factors used were 130 - 199 HU, factor 1; 200 - 299 HU, factor 2; 300 - 399 HU, factor 3; and ≥400 HU, factor 4. The CAC score was done by CT, based on axial slices, using slice thickness of 3 mm, without any overlapping or gaps, limited to cardiac region, acquired in synchrony with the electrocardiogram prospectively, at a predetermined moment in the R-R interval, usually in the mid/late diastole, without the use of intravenous contrast medium[5].

The effective dose of radiation is usually low, typically less than 1.5 mSv, which is the recommended dose for use in image acquisition, according to the Society of Cardiovascular Computed Tomography. Calcification was identified as areas of hyper attenuation of at least 1 - 2 mm with >130 Hounsfield units (HU) or ≥3 adjacent pixels[5].

Inclusion criteria

- Covid-negative patient with type 2 Diabetes Mellitus for diabetic group and age, sex-matched non-diabetic patients for non-diabetic group.
- >18 years.
- Patients consenting to take part in the study.
- Asymptomatic for coronary artery disease at the time of presentation.

Exclusion criteria

Patients having CAD and hypertension, smokers, alcoholic, malignancy – multiple myeloma, lymphoma, malignancy of lung, breast, patients on thiazide diuretics, there with chronic renal failure, thyroid disease – hypothyroidism, hyperthyroidism, primary hyperparathyroidism, hypervitaminosis-D, critically ill patients, morbidly obese patients, and pregnant patients were excluded from study.

All data was compiled and analysed at the end of the study by applying appropriate statistical tests, using EPI info Software. Unpaired student T-test was applied.

Observation and results

Table I shows the demographic profile of patients of both diabetic and non-diabetic groups. Out of 40 diabetic patients, majority of 21 (52.5%) were in the age group of 51 - 60 years followed by 12 (30%) in 41 - 50 years and 7 (17.5%) in 31 - 40 years age group. Among non-diabetic patients, 17 (42.5%) were in 51 - 60 age group, 17 (42.5%) patients in 41 - 50 age group and 6 (15%) patients in 31 - 40 age group. In diabetic patients, 13 (32.5%) were males and 27 (67.5%) were females. Among 40 non-diabetic patients, 23 (57.5%) were males and 17 (42.5%) were females. There was no significant age and gender variation between both groups.

Fig. 1 is a bar graph showing distribution of CACS in diabetic and non-diabetic patients. Out of 40 diabetic patients, 7 (17.5%) had mild CACS and 33 (82.5%) had moderate-to-severe CACS. Out of 40 non-diabetic patients, 21 (52.5%) had mild score and 19 (47.5%) had moderate-to-severe score. We can see that diabetic patients had more severe CACS than the non-diabetic group. On statistical analysis, this difference of CACS score between diabetic and non

diabetic patients was found to be highly significant.

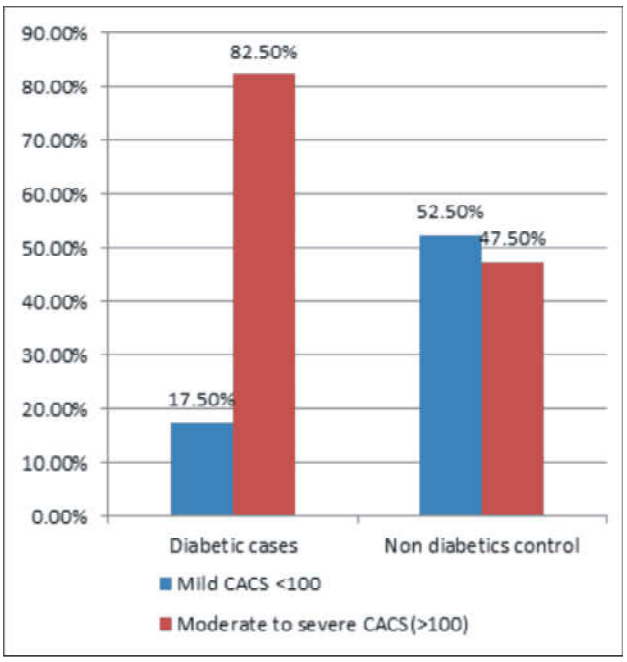

Fig. 1: *Distribution of CACS in diabetics and non-diabetics.*

Table I: Distribution of age and gender in diabetic and non-diabetic groups.

	Diabetic cases		Non-diabetic controls	
Age groups (years)				
18 - 40	7	17.5%	6	15%
41 - 50	12	30%	17	42.5%
51 - 60	21	52.5%	17	42.5%
Total	40	100%	40	100%
Gender				
Male	13	32.5%	23	57.5%
Female	27	67.5%	17	42.5%
Total	40	100%	40	100%

In Table II, CACS is shown in various age groups among diabetics and non-diabetics. In 18 - 40 years age group among diabetics, 57.1% of patients had moderate-to-severe CACS while among non-diabetics 33.3% were in moderate-to-severe category. On statistical analysis this difference was found to be insignificant. In 41 - 50 years age group, moderate-to-severe CACS was found in 83.3% and 64.7% among diabetics and non-diabetics respectively, but this difference was also insignificant. In older age group (51 - 60 years) most of the diabetic patients (90.5%) had moderate-to-severe CACS, whereas only 35.3% of non-diabetics had CACS >100. This difference in CACS among diabetics and non-diabetics was statistically highly significant (p = .001).

Table II: Mean level of CACS in different age groups among diabetic cases and non-diabetic controls.

	Diabetic			Non-Diabetic			Statistical analysis
Age Group	Mild (<100) No (%)	Modrate -to- severe (>100) No (%)	Total No	Mild (<100) No (%)	Modrate -to- severe (>100) No (%)	Total No	
18 - 40	3 (42.9)	4 (57.1)	7	4 (66.7)	2 (33.3)	6	$X^2 = 0.737$, P value = 0.39
41 - 50	2 (16.7)	10 (83.3)	12	6 (35.5)	11 (64.7)	17	$X^2 = 1.2219$, P value = 0.26
51 - 60	2 (9.5)	19 (90.5)	21	11 (64.7)	6 (35.3)	17	$X^2 = 12.710$, P value = **0.0003**
Total	7 (17.5)	33 (82.5)	40 (100%)	21 (52.5)	19 (47.5)	40 (100%)	$X^2 = 10.7692$, P value = **0.001**

In Table III, association of HbA1C and CACS was observed among diabetic patients. It was observed that in patients with HbA1C in the range of 7 - 9%, 66.7% of patients were having moderate-to-severe CACS. Proportion of patients having moderate-to-severe CACS increased with increasing value of HbA1C (83.3% in 9 - 11% HbA1C category and 94.7% in >11% HbA1C category). On statistical analysis this difference was not found to be significant.

Table III: Association of HbA1C with CACS among diabetic patients.

HbA1C	CACS		Total
	Mild	Modrate-to-Severe	
7 - 9	5 (33.3%)	10 (66.7%)	15
9 - 11	1 (16.7%)	5 (83.3%)	6
>11	1 (5.3%)	18 (94.7%)	19
Total	7 (17.5%)	33 (82.5%)	40

$X^2 = 4.578$, *P value = 0.101.*

Table IV: Association of ECG changes with CAC score in diabetics and non-diabetics.

Group	Diabetic group (n = 40)	Non-diabetic group (n = 40)	T-test (p value)
ECG changes No.(%)	14 (35%)	1 (2.5%)	$X^2 = 13.866$,
CACS (mean ± SD)	413 ± 79.1	136 ± 128.8	***P value <0.05***

Table IV shows the ECG changes found in both diabetic and non-diabetic group. Out of 40 diabetic patients, 14 patients had ECG changes, in these 14 patients mean CACS was 413 ± 79.1 and in non-diabetics only one patient was found to have ECG changes with a CACS of 136 ± 128.8, and the association between ECG changes in the two groups was statistically significant (p value < 0.05). It shows that ECG

changes were more in diabetic patients who had a high CACS (>200), as compared to non-diabetics – with only one patient having ECG changes.

Discussion

According to the Framingham study, risk of cardiovascular mortality in men with diabetes is twice, and four times in women with diabetes when compared to non-diabetic population. Risk of developing acute myocardial infarction is fifty per cent higher in diabetic men whereas risk is 50% in women living with diabetes[5]. In diabetics, along with the characteristic pattern of increased triglyceride and decreased HDL cholesterol, abnormalities are seen in the structure of lipoprotein particles. Predominately small and dense form of LDL is found in diabetic patients. These small LDL particles are more atherogenic than large LDL particles. Both insulin deficiency and insulin resistance promote dyslipidaemia by increasing oxidation, glycosylation and by triglyceride enrichment of lipoprotein. All these factors contribute to increased atherogenicity in a diabetic patient[6]. Therefore, measurement of CACS by electron beam tomography has been shown to be a powerful predictor of coronary heart disease in asymptomatic diabetic patients, which can enhance prediction of adverse cardiovascular events early.

In the present study, we enrolled 80 patients, out of which 40 patients were diabetic and 40 non-diabetic. Maximum number of patients in both groups were between the age group of 50 to 60 years. A similar finding was seen in a study by Subhashish Agarwal *et al*[7], in whose study maximum patients were also in the age group of 61.4 years with a mean SD of 9.1. In the present study, in the diabetic group, 13 were male (32.5%) and 27 were female (67.5%); and in the non-diabetic group, 23 males (57.5%) and 17 females (42.5%). Similar findings were also seen by Agarwal *et al*[7]. It was observed in the present study that diabetic patients had higher CAC score as compare to non-diabetics. A similar study was also conducted by Elkeles *et al* which included measurement of CACS by electron beam tomography. They observed that only 23% patients among type 2 diabetics had low CACS[8].

In the present study it was observed that in older age group (51 - 60 years) most of the diabetic patients (90.5%) had moderate-to-severe CACS, whereas only 35.3% of non-diabetics had CACS >100. This difference in CACS among diabetic and non-diabetic patients was statistically highly significant (p = .001). Yuichiru Yano *et al* also found higher risk of coronary heart disease with increased CACS with increasing age[9].

Proportion of patients having moderate-to-severe CACS increased with increasing value of HbA1C (83.3% in 9 - 11% HbA1C category and 94.7% in >11% HbA1C category). Jing Yu *et al* observed that an increase in 1% of HbA1C was related to a 24% increase of CACS progression risk (HR = 1.24, 95% CI: 1.21 to 1.28) leading to statistically significant result[10].

In our study 14 patients in the diabetic group had ECG changes in which CAC score in comparison to the non-diabetic group was significantly high ($p < 0.05$). Similar study was done by Zhu *et al* which included five hundred eighty-eight outpatients with suspected CAD comprising 208 diabetic and 380 non-diabetic patients. Coronary artery plaque and CAC scores were measured; it showed that the diabetic group had significantly higher CAC scores in LAD than that in the non-diabetic group[11]. Elkeles *et al* observed that type 2 diabetic and non-diabetic subjects who had undetectable coronary artery calcification were observed to have similar mortality. On the contrary those subjects who have high CACS were found to have high cardiovascular risk. Thus not all those with type 2 diabetes are at similar cardiovascular risk[8].

Conclusion

Diabetes is characterised by high cardiovascular mortality. In diabetes, multi-vessel coronary atherosclerosis is often present before ischaemic symptoms occur and before treatment is instituted. A delayed recognition of various forms of cardiovascular diseases worsens the prognosis and survival in diabetics. Thus measurement of coronary artery calcium score (CACS) has been shown to be a powerful predictor of coronary heart disease events in asymptomatic diabetic subjects, especially among older age groups and patients with higher value of HbA1C. Hence, CACS can be used as a non-invasive test for early detection of the risk of CAD in diabetics.

Recommendation

- Since CACS of diabetics was significantly higher, it is recommended that CACS should be used for assessing the risk of occurrence of CAD among diabetics, so that sudden cardiac death can be avoided. CACS being a non-invasive procedure, can be used as a screening procedure for high-risk patients to predict coronary heart disease.
- A large study of multicentric origin is needed in order to get stabilised and quantified exact co-relation. This study is a modest attempt to assess CACS as a risk of CAD in diabetics.

Limitation

The limitation in this study is that it was a cross-sectional

study, so follow-up of patients could not be done and the sample size was small (80) because study was done during COVID era.

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