Coronary Artery Calcium Score as a Risk Enhancer in Pre-Diabetics

Dr. Vyom Mori[1], Dr. Arun Mohanty[2], Dr. Anurag Yadav[3], Dr. Aman Makhija[4], Dr. Bhuwanesh Kandpal[5], Dr. Arjun Sreekumar[6], Dr. J P S Sawhney[7], Dr. R R Mantri[8]

Abstract

Introduction: Among all the risk factors for atherosclerosis, diabetes is one that has a direct causal association with it, so it has been a focus in major primary prevention studies. The prediabetic population is considered at the same risk as non-diabetics as per the latest guidelines. By using the Coronary artery calcium score (CACS) which is a predictor of cardiovascular events, in this subset of people authors tried to analyse whether prediabetics can be treated the same as non-diabetics.

Methods: Patients undergoing CT coronary angiography with no major epicardial coronary artery obstruction were included and divided into three subgroups of non-diabetic, pre-diabetic and diabetic. Their CACS were measured and compared for any significance.

Results: A total of 300 patients were part of the study with 100 patients in each subgroup. The mean age of the population was 48 years. Lipid profile was significantly deranged in the non-diabetic and pre-diabetic subgroup as they were not on any therapy. CACS was 5.4 ± 37.37, 98.02 ± 300.89, 209.47 ± 277.61 in non-diabetic, pre-diabetic and diabetic subgroups respectively. The CACS was much higher in the pre-diabetic subgroup of people missing statistical significance by only a small margin.

Conclusion: From this observational study authors conclude that prediabetics are at much higher risk of adverse cardiovascular events than non-diabetics and so when it comes to primary prevention therapy, they should not be considered in the same risk category as non-diabetics.

Keywords: Primary prevention; risk modifier; atherosclerosis

Conflict of Interest: None declared

Sources of Support: None declared

[1] Senior Resident; [2] Professor, Department of Cardiology; [3] Professor, Department of Radiology; [4] Associate Professor; [5] Professor; [6] Senior Resident; [7] Professor; [8] Professor, Department of Cardiology, Sir Ganga Ram Hospital, New Delhi.

Corresponding Author: Dr.Vyom Mori, Department of Cardiology, Sir Ganga Ram Hospital, Old Rajinder Nagar, Delhi-110060, India. Email ID: vyommori@gmail.com

Introduction

Diabetes is considered a traditional risk factor for atherosclerotic vascular disease for a long, and if uncontrolled, it increases the risk manifold. Hence, for primary prevention of atherosclerosis in diabetics (age more than 40 years), all guidelines recommend for initiation of statin therapy.[1] For non-diabetics however, primary prevention is considered based on the online calculated risk score after evaluating various parameters. In this scoring system, certain risk enhancers are used to decide the need for therapy if patients have borderline risk score. Coronary artery calcium score (CACS) is one of the risk enhancers in guidelines for such a subset of people. CACS is widely studied in the population and for patients with a borderline risk score, CACS > 100 is considered as a marker for initiation of primary prevention therapy.[2] CACS > 100 is an established risk marker for major adverse cardiovascular events.[3-5] Even those patients with a score < 100 or with a score = 0, but progressively increasing in subsequent scans are considered at increased risk of major adverse events.[6-8] Pre-diabetes is a precursor of developing diabetes in the future if neglected. No guidelines recommend initiation of primary prevention therapy for pre-diabetes and are considered in the same risk category as non-diabetic.[9] In this study we have assessed CACS in diabetes, pre-diabetes and controls using Computed Tomography (CT) and tried to calculate the burden of atherosclerotic disease in pre-diabetic compared to other population. Our hypothesis was prediabetics have more atherosclerosis and so should be considered early for primary prevention.

Methodology

In this study, patients undergoing CT coronary angiography for chest discomfort were included. All patients with significant epicardial coronary artery disease i.e., >50% of luminal narrowing, were excluded from the study. Then patients were grouped into three subgroups of controls, pre-diabetic and diabetic depending on their history. Pre-diabetics were defined in our study as those with HbA1c of 5.9 to 6.4% and not on any glucose-lowering therapy. The demographic and lipid profiles were noted in all patients. Coronary artery calcium score was measured in these subgroups and comparison was done.

Statistical Analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then the non-parametric test was used.

Statistical tests were applied as follows:

1. Quantitative variables for comparing three groups were compared using ANOVA and Kruskal Wallis test (when the data sets were not normally distributed). For comparing two groups Independent t-test and Mann Whitney test (when the data sets were not normally distributed) was used.
2. Qualitative variables were correlated using the Chi-Square test.

A p-value of <0.05 was considered statistically significant.

Results

A total of 300 patients with 100 patients in each subgroup of controls, pre-diabetic and diabetic. The mean

Table 1: Comparison of demographic characteristics between control, prediabetic and diabetic

Demographic characteristics	Control; group C (n=100)	Pre-diabetic; group P (n=100)	Diabetic; group D (n=100)	Total	P value
Age	47.33 ± 5.22	46.07 ± 5.28	50.33 ± 3.75	47.91 ± 5.08	0.003
Female	43.33%	33.33%	20%	32.22%	0.152
Male	56.67%	66.67%	80%	67.78%	
Smoking	23.33%	23.33%	26.67%	24.44%	0.942
HTN	30%	43.33%	73.33%	48.89%	0.003
BMI kg/m²	26.87 ± 2.93	27.86 ± 3.24	26.17 ± 3.82	26.97 ± 3.39	0.151
HbA1C	5.38 ± 0.15	6.03 ± 0.21	7.09 ± 0.98	6.17±0.92	<0.0001
Total Cholestrol (mg%)	192.83 ± 50.84	187.87 ± 38.62	148.7 ± 30.83	176.47 ± 45.08	0.0001
LDL(mg/dl)	123.4 ± 43.87	120.2 ± 35.22	91 ± 27.52	111.53 ± 38.64	0.0001
HDL(mg/dl)	41.2 ± 7.24	41.47 ± 11	34.8 ± 8.15	39.16 ± 9.37	0.0007
Non-HDL(mg/dl)	151.63 ± 50.29	146.4 ± 36.74	113.63 ± 30.14	137.22 ± 42.96	0.0007
Triglycerides(mg/dl)	149.1 ± 62.93	145.1 ± 53.48	111 ± 58.63	135.07 ± 60.32	0.009

age of the population was 47.91 ± 5.08 years (Table 1), the age difference was statistically significant between non-diabetic and diabetic but numerically the difference was small. Gender difference, history of smoking, BMI (body mass index) were not statistically significant. The incidence of hypertension was higher in the diabetic subgroup of people. HbA1C was higher in a diabetic subgroup of people. Lipid profile was found to be statistically higher in the non-diabetic and prediabetic subgroup as compared to the diabetic patients as they were on lipid-lowering therapies. 65% of the diabetic subgroup were on lipid-lowering therapies whereas, none of the patients in the non-diabetic and pre-diabetic subgroup was on these therapies. Total coronary artery calcium score (Table 2) was 15.4 ± 37.37, 98.02 ± 300.89, 209.47 ± 277.61 in the controls, pre-diabetics and diabetics respectively. Total CACS was highest in the diabetics, followed by pre-diabetics and the lowest in the control group suggesting that altered glucose metabolism increases the risk of atherosclerosis. The difference was statistically significant between the diabetic and pre-diabetic subgroups(p=0.02) but there was no statistical difference noted between the pre-diabetic and control groups(p=0.06). However, the absolute values of CACS were far higher in the pre-diabetic group of people.

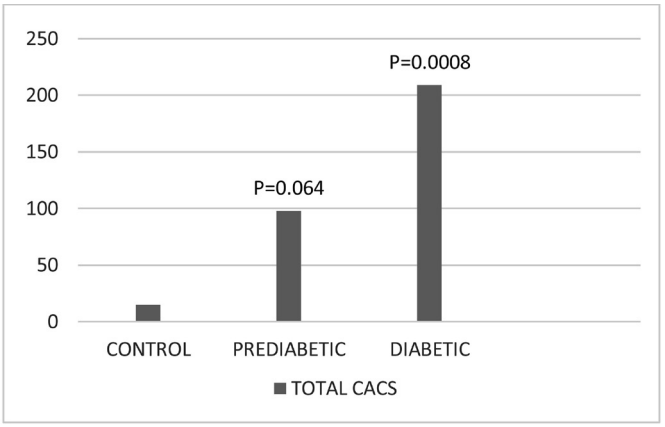

Figure 1: Comparison of Total coronary artery calcium score in diabetics, prediabetics and non-diabetics.

Table 2: Comparison of coronary artery calcium score between control, prediabetic and diabetic

Coronary artery calcium score	Control; group C (n=100)	Pre-diabetic; group P (n=100)	Diabetic; group D (n=100)	Total	P value
Total CACS	15.4 ± 37.37	98.02 ± 300.89	209.47 ± 277.61	107.63 ± 247.91	0.001 D vs P:0.027 D vs C:0.0008 P vs C:.084
LAD score	20.78 ± 59.27	26.68 ± 92.18	123.56 ± 211.35	57.01 ± 143.92	0.028 D vs P:0.055 D vs C:0.014 P vs C:0.350
LCX score	1.83 ± 7.57	2.38 ± 11.8	9.4 ± 19.58	4.53 ± 14.17	0.032 D vs P:0.040 D vs C:0.038 P vs C:1
RCA score	2.8 ± 8.72	57.52 ± 210.79	23.49 ± 62.58	27.94 ± 127.65	0.020 D vs P:0.208 D vs C:0.004 P vs C:0.196

Discussion

This observational study showed that the total coronary artery calcium score is higher in diabetics, followed by pre-diabetics and then the control group (Figure 1). Thus insulin resistance, altered glucose levels have a causal association with atherosclerosis. However, the difference between control and pre-diabetics was not statistically significant but was numerically higher than the control group. The significance was missed by only a marginal difference. CACS represents the extent of atherosclerotic burden in the coronary artery and is a risk for future major adverse events. Thus, the pre-diabetics subgroup has a higher CACS and thus, are at increased risk of cardiovascular events in the future compared to non-diabetics. It is also evident that pre-diabetics have a higher incidence of a deranged lipid profile than diabetics as they are usually not on any lipid-lowering therapies. The lipid-lowering therapies in pre-diabetics have been associated with mildly increased risk of diabetes in future but the benefit provided with its use outweighs the risk. [10] Hence, the authors suggest that the pre-diabetic subgroup should be appropriately treated with lifestyle modifications and early initiation of primary prevention therapy. Moreover, as in our study group, the pre-diabetics constitute a younger population so an earlier intervention would benefit them immensely.

Limitations of the study are the age difference was statistically significant and might have increased the atherosclerotic burden in the population, but this difference was numerically a very small number. This is only an observational study with a small number of study group so it can only be hypothesis-generating and can also be a reason for the differ-

ence missing statistical significance. A major study in the pre-diabetic subgroup is required to further substantiate this observation that early initiation of primary prevention therapy can prevent future events.

Conclusion

From this observational study, the authors concluded that the pre-diabetic subgroup of patients has a relatively higher calcium score and hence, are predisposed to cardiovascular events. Their risk assessment should not be as same as non-diabetics. CACS should be considered early in this subset so that they can be better risk stratified. Early and aggressive management of these patients could reduce morbidity and mortality associated with coronary atherosclerosis.

References:

1. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, *et al*; ESC Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J. 2020*;41(1):111-188.
2. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, *et al*. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation. 2019*;140(11):e596-e646.
3. Vliegenthart R, Oudkerk M, Hofman A, Oei HH, van Dijck W, van Rooij FJ, *et al*. Coronary calcification improves cardiovascular risk prediction in the elderly. *Circulation. 2005*;112(4):572-7.
4. Yano Y, O'Donnell CJ, Kuller L, Kavousi M, Erbel R, Ning H, *et al*. Association of Coronary Artery Calcium Score vs Age With Cardiovascular Risk in Older Adults: An Analysis of Pooled Population-Based Studies. *JAMA Cardiol. 2017*;2(9):986-994.
5. Kavousi M, Desai CS, Ayers C, Blumenthal RS, Budoff MJ, Mahabadi AA, *et al.* Prevalence and Prognostic Implications of Coronary Artery Calcification in Low-Risk Women: A Meta-analysis. *JAMA. 2016*;316(20):2126-2134.
6. Raggi P, Callister TQ, Shaw LJ. Progression of coronary artery calcium and risk of first myocardial infarction in patients receiving cholesterol-lowering therapy. *Arterioscler Thromb Vasc Biol. 2004*;24(7):1272-7.
7. Budoff MJ, Young R, Lopez VA, Kronmal RA, Nasir K, Blumenthal RS, *et al*. Progression of coronary calcium and incident coronary heart disease events: MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol. 2013*;61(12):1231-9.
8. Budoff MJ, Hokanson JE, Nasir K, Shaw LJ, Kinney GL, Chow D, *et al*. Progression of coronary artery calcium predicts all-cause mortality. *JACC Cardiovasc Imaging. 2010*;3(12):1229-36.
9. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, *et al*; ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J. 2020*;41(2):255-323.
10. Maki KC, Diwadkar-Navsariwala V, Kramer MW. Statin use and risk for type 2 diabetes: what clinicians should know. *Postgrad Med. 2018*;130(2):166-172.