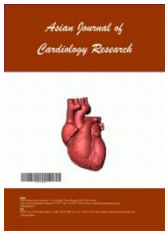

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Coronary Calcium Score in Mortality, Hospital Admissions with ACS and Need for Revasularization: A Retrospective Observational Study

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Objective: Cardiovascular disorders (CVD) are a leading cause of death in the world. Further, the identification of acute coronary syndrome (ACS) patients without any symptoms is a very crucial and important task. At present, the coronary artery calcium (CAC) scoring system has been developed to predict future risk of CVD. The present study is focused on the assessment of mortality, hospital admissions with ACS and need for revascularization on the basis of calcium score.

Methods: A retrospective observational study was conducted on the patients with stable angina or anginal equivalents like dyspnea on exertion history who visited Amrita Institute of Medical Sciences from January 2012 to December 2020 and underwent MDCT CAG and MDCT CAC assessment. Moreover, the patients with ACS such as unstable angina, NSTEMI or STEMI or who had undergone PTCA or CABG in past were excluded.

Results: A total of 459 patients were studied and the mean age of the study population was found 54.77±12.29 years. A total of 71% of patients were male and total of 8 patients had been found to develop ACS on follow up (NSTEMI or AWMI or IWMI). Furthermore, a total of 3 patients had severe coronary calcification while only 2 patients had mild and 2 patients moderate coronary calcification scores. These results showed that higher calcium score was associated with higher

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chances of ACS on follow up while number of patients requiring intervention (PTCA or CABG) were higher in moderate or severe coronary calcification group as compared to patients with zero or mild calcification group. Primary endpoint of mortality did not show any statistical difference between the all 4 groups.

Conclusion: It was concluded that the early detection of patients with CAD by calcium scoring system will help in the real time prediction of ACS and play a role in the management of healthy lifestyle.

Keywords: Cardiovascular disorders (CVD); acute coronary syndrome (ACS); multidetector computed tomography (MDCT); calcium score.

1. INTRODUCTION

Cardiovascular disorders (CVD) are the common causes of morbidity, debility and death across the world and approximately more than 17 million premature deaths are recorded every year [1]. Among of them, nearly about of half of the death occurred due to Coronary Artery Disease (CAD) [2]. India has a higher age-standardized CVD death rate *i.e.* 272 per 100 000 population as compared to the global average i.e. 235 per 100 000 population [3]. Air pollution, high blood pressure, diabetes, smoking, dyslipidaemia, obesity, atherogenic diet, inadequate physical exercise, low socioeconomic status, previous history of stroke and clinical conditions (heart failure, peripheral artery disease and chronic kidney diseases are the common etiological factor of the CVD [4,5,6]. It is necessary to diagnose patients at an early stage to get rid of these clinical conditions which is a most challenging task in the treatment and prognosis of CVD. At present, a risk factor (RF)- based approach is used for the identification of patients at increased risk for coronary events which includes limited predictive value and physical examination. However, these diagnostic procedures are not able to identify patients at an early stage, especially in patients with normal cardiac biomarkers and electrocardiograms (ECG) [5]. As a result, approximately 60% of patients with acute coronary syndrome (ACS) are discharged with a non-cardiac diagnosis [3 cross-refer 3] and increase a two-fold in mortality [4,6].

It is a very crucial task to identify the patient without any cardiac symptoms. However, approximately 65-80% of these future cardiac episodes can be identified by the "total risk scoring system" and the Framingham risk score (FRS) system is widely applied for the identification of asymptomatic patients [7,8]. Although FRS is used for the evaluation of risk factors namely age, gender, total cholesterol, high density lipoprotein cholesterol (HDL), smoking habits, and systolic blood pressure of the CAD of 10 years, it fails to detect most of the patient intended to develop future CAD episode [9,10,11]. To improve the assessment of future cardiac episodes coronary artery calcium (CAC) scoring system has been developed which exhibited good risk prediction level as compared to the traditional risk factors and revealed that the patients with high CAC burden (CAC scores ≥ 300 or 400) are more likely to have the risk of CAD [12,13]. Previously the CAC score was investigated by the electron beam computed tomography technique but is now completely closed due to its negative consequence on the health of patients [14] and at present multidetector computed tomography (MDCT) is the first choice of CAC evaluation. In MDCT CAC score is calculated by the tomography slices with 3 mm a thickness, acquired in synchrony with the electrocardiogram (ECG) at a predetermined moment in the R-R interval in the mid/late diastole [15], limited to the cardiac region, without overlapping, without the use of intravenous contrast medium. The Society of Cardiovascular Computed Tomography suggested that the < 1.5 mSv dose of radiation is a quite effective dose for capturing pictures [14] and calcification is diagnosed as areas of hyper attenuation of at least 1 mm2-with > 1Hounsfield units (HU) or ≥ 3 adjacent pixels [16]. A number of study has previously been conducted in various countries for the reproducibility and effectiveness of CAC score but presently there is lack of data recorded in India. The present study was focused on the evaluation of MDCT Calcium scoring impact on mortality, hospital admissions with ACS, need for revascularization in South India.

2. METHODS

This retrospective observational study was conducted during the period from January 2012 to December 2020 and followed up till April 2021

at Amrita Institute of Medical Sciences. Patients with atypical chest pain, stable angina and dyspnea on exertion were assessed for MDCT CAG and Calcium scoring assessment along with the baseline data such as age, gender, and comorbidities (hypertension, diabetes and dyslipidemia).

The MDCT CAC and MDCT coronary angiography (CAG) was performed using 256 slice Philips CT machine with ECG gating. CAC scoring was quantified by calculating calcium volume and its mass score by the Agatston method [16,17] where the area of calcified atherosclerosis (defined as an area with at least 1 mm^2 with a CT density >130 Hounsfield units [HU]) was multiplied by a density weighting factor and summed for the entire coronary artery tree using a 2.5-3.0 mm slice thickness CT dataset. Finally on the Basis of MDCT CAC score, patients were classified as 0 Agatston units= zero coronary calcification; 1-99 Agatston units= Mild coronary calcification; 100 to 399 Agatston units= Moderate coronary calcification; >400 Agatston units= severe coronary calcification.

The Statistical analysis was performed by STATA 11.2 (College Station TX USA). Chis square test for goodness of fit was used to evaluate the association between the age groups, gender, coronary artery involvement, diabetes, hypertension, dyslipidaemia, cardiac intervention, ACS on follow up and mortality with Severity of calcium involvement respectively and it's expressed as frequency and percentage. $P<0.05$ is considered as statistically significant.

3. RESULTS

3.1 Baseline Clinical Characteristics

A total of 459 patients were selected for the current study which included 12 years of children to 85 year old persons with a mean age of 54±12.29 years. All patients were divided into 6 age groups (≤30, 31-40, 41-50, 51-60, 61-70 & >70). Maximum patients i.e. 136 were recorded in Age group 51-60 followed by the 41-50, 61-70 and >70 i.e. 125, 98 and 48 respectively. In age group ≤ 30 all patients exhibited no calcium score while 10% of patients showed severe calcium score in age group of 61-70. In the case of mild calcium score, maximum (40%) of patients belonged to >70 age group followed by 61-70, 51-60 and 41-50 age group i.e. 32%, 26% and 21%. On other hand higher number (31%) of the patients was found in the <70 age group in case of moderate calcium score (Table1).

Gender pattern analysis revealed that out of 459 patients a total of 326 were male followed by 133 female. In the case of male patients, the maximum patients i.e. 166 (51%) were showed no calcium score followed by mild (93 or 77%), moderate (44 or 13%) and severe (23 or 7%). In terms of female patients similar trends were also recorded i.e. zero (103 or77%), mild (19 or 14%), moderate (10 or 8%) and sever (1 or 1%) coronary calcium scores which revealed that female patients had low coronary calcium score as compared to male patients (Fig. 1).

Calcium score analysis also showed that 39% of diabetics had zero coronary calcification as compared to non-diabetics while 30% of patients exhibited mild calcium scores followed by 22% patients. In the case of moderate calcium score 22% showed chance of CAD in the future where only 4% of patients had chance of CAD in the future due to their diabetic status. In case of hypertension history, maximum (44%) patients showed zero calcium score followed by mild (28%), moderate (19%) and severe (9%). In terms of dyslipidemia similar trend as diabetes and hypertension was recorded. Table 2 represents the comparative analysis of diabetes, hypertension and dyslipidemia with calcium scores.

Table 1. Comparison of age distribution with calcium score

Age group	Zero	Mild	Moderate	Severe	Total	P-Value
≤30	11 (100%)	-	-	-	11	<0.001
31-40	40 (98%)	1 (2%)	-	-	41	
41-50	90 (72%)	26 (21%)	5 (4%)	4 (3%)	125	
51-60	79 (58%)	35 (26%)	16 (12%)	6 (4%)	136	
61-70	39 (40%)	31 (32%)	18 (18%)	10 (10%)	98	
>70	10 (21%)	19 (40%)	15 (31%)	4 (8%)	48	
Total	269	112	54	24	459	
Mean age 54.77±12.29						

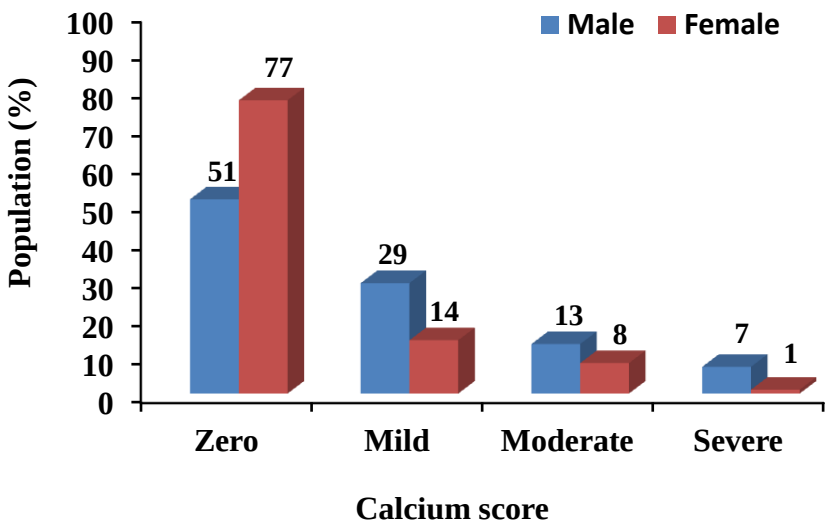

Fig. 1. Comparison of gender distribution with calcium score

Table 2. Comparison of diabetes, hypertension and dyslipidemia with calcium score

Comorbidities	Status	Zero	Mild	Moderate	Severe	Total
Diabetes	**Yes**	45 (39%)	35 (30%)	25 (22%)	11 (4%)	116
	No	224 (65%)	77 (22%)	29 (8%)	13 (4%)	343
Hypertension	**Yes**	80 (44%)	50 (28%)	43 (19%)	16 (9%)	180
	No	189 (68%)	62 (22%)	20 (7%)	8 (3%)	279
Dyslipidemia	**Yes**	120 (52%)	63 (28%)	29 (13%)	17 (7%)	229
	No	149 (65%)	49 (21%)	25 (11%)	7 (3%)	230

Table 3. Comparison of coronary artery involvement with calcium score

Comorbidities	Zero	Mild	Moderate	Severe	Total	P-Value
Normal	213	32	1	-	246	<0.001
Mild	51	57	30	9	147	
SVD	5	17	14	7	43	
DVD	-	3	9	4	16	
TVD	-	3	-	4	7	
Total	269	112	54	24	459	

**SVD= Small vessel disease, DVD= Double vessel disease, TVD= Triple vessel disease*

3.2 Coronary Calcification with MDCT - CAG Findings

A total of 269 patients were found with zero coronary calcification, out of which 231 patients had normal coronaries followed by mild CAD (51), single vessel disease (5) while there is no Double or Triple vessel disease were recorded on MDCT CAG. While in the case of mild coronary calcification, a total of 32 had mild coronary calcification with normal coronaries and 57 patients had mild CAD on MDCT CAG. Moderate coronary calcification showed only 1 patient had normal coronaries, while 14 and 9 patients had Single Vessel Disease and Double vessel disease, respectively. Severe coronary calcification revealed that no patient had normal coronaries, (Table 3). It finally revealed that patients with zero calcification had more tendency to have normal coronaries while patients with mild or moderate coronary calcification had mild CAD or Single vessel disease.

3.3 Correlation of ACS on Follow up with Calcium Scoring

A total of 8 patients developed ACS on follow up out of which 6 patients had anterior wall

myocardial infarction while only 1 patient had inferior wall myocardial infarction (IWMI) and 1 patient had Non-ST-elevation myocardial infarction (NSTEMI). Further, a total of 24 patients had severe coronary calcification, out of them 3 (12%) developed Anterior wall myocardial infarction (AWMI) on follow up. Moreover, in moderate calcification 1 patient found to have AWMI and 1 found to have IWMI in the future. Total of 112 patients with mild coronary calcification, 2 (1.7%) patients had ACS on follow up with 1 patient had NSTEMI and 1 had AWMI. Additionally, the total of 269 patients had zero coronary calcification out of which only 1 patient had developed AWMI on follow up (Table 4).

3.4 Correlation of Cardiac Interventions done with Calcium Scoring

A total of 418 patients were subjected to medical follow up, out of 459 total patients only 3 patients had undergone coronary artery bypass grafting (CABG) while 38 patients were subjected to Percutaneous transluminal Coronary Angioplasty (PTCA). Moreover, 15 patients with moderate calcium scores were found to have undergone PTCA followed by severe (11), mild (9). Table 5 represents a comparative assessment of cardiac intervention with calcium score.

3.5 Correlation of Mortality with Calcium Score

Mortality did not show any significant relationship with coronary calcification. A total of 3 patients were found dead during follow up while 2 patients had zero coronary calcification and only 1 patient had severe coronary calcification (Table 6).

4. DISCUSSION

The present study revealed that the patient with atypical chest pain, stable angina and dyspnea on exertion had 54.77±12.29 mean age and patients with <40 years of age had zero calcification score while > 70 years of age patients had mild to severe calcium scores which exhibited that the risk of ACS was increased with the age. Similar age and trends were also recorded in several published data [18,19] while an age of >55 years was also revealed in previous studies [20,21]. This study also revealed that males had higher calcium scores as compared to the female patients and a similar observation was also reported from the different countries [19,22,23]. The diabetic, hypertensive and dyslipidemia patients had higher coronary calcification scores and support the study conducted by a number of research groups [23,24,25].

Table 4. Comparison of ACS events on follow up with calcium score

Comorbidities	Zero	Mild	Moderate	Severe	Total	P-Value
NSTEMI	0	1 (0.89%)	0	0	1	<0.001
AWMI	1 (0.37%)	1 (0.89%)	1 (1.9%)	3 (12%)	6	
IWMI	0	0	1 (1.9%)	0	1	
No	268 (99.63%)	110 (98.21%)	52 (96.2%)	21 (88%)	451	
Total	269	112	54	24	459	

** NSTEMI= Non-ST-elevation myocardial infarction, AWMI= Anterior wall myocardial infarction, IWMI= Inferior wall myocardial infarction*

Table 5. Comparison of cardiac intervention done with calcium score

Comorbidities	Zero	Mild	Moderate	Severe	Total	P-Value
CABG	0	0	1 (2%)	2 (8%)	3	<0.001
PTCA	3 (1%)	9 (8%)	15 (28%)	11 (46%)	38	
Nil	266 (99%)	103 (92%)	38 (70%)	11 (46%)	418	
Total	269	112	54	24	459	

**CABG= Coronary Artery Bypass Grafting, PTCA= Percutaneous transluminal Coronary Angioplasty*

Table 6. Comparison of mortality with calcium score

Comorbidities	Zero	Mild	Moderate	Severe	Total	P-Value
Yes	2 (67%)	-	-	1 (33%)	3	0.128
No	267 (56%)	112 (24%)	54 (12%)	23 (5%)	456	
Total	269	112	54	24	459	

Additionally, this study revealed that the zero calcification score patients had high a tendency to have normal coronaries while patients with mild, moderate and severe coronary calcification scores had high chance to develop mild CAD, single vessel disease and double or triple vessel disease, respectively. Similar pattern were also recorded in several studies [26,27]. Moreover, it was also recorded that patients with moderate or severe coronary calcification had more chance to develop ACS as compared to patients with zero or mild coronary calcification scores on follow up. The low number of total ACS events occurred (1.7%) on follow up with MDCT CAG which was due to timely interventions (PTCA or CABG). Further, the current study did not show any correlation between mortality and coronary calcification score while Nasir et al. recorded a correlation between calcium score and mortality. In addition, both CAC scores >100 and ≥400 Agatston units were found associated with an increased risk of mortality by Rijlaarsdam et al [28]. In the present study have several limitations such as a heterogenous follow up period, single center design. Along with this, the inadequate information about the atherogenic diet, physical activity and socioeconomic status of the selected patients.

5. CONCLUSION

This study finally concluded that that demographic factors (age and gender) and risk factor (diabetes, hypertension and dyslipidemia) are the most predominant factor for the development of CAD. Furthermore, the patients with moderate or severe coronary calcification had higher chances of ACS on follow up and had higher need for revascularization. Above mentioned finding will helps in the real time prediction CAD and play role in the management of healthy lifestyle.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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