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Original Research Article

Study of estimation of coronary artery calcium by multi-slice spiral CT scan in post myocardial infarction cases

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ABSTRACT

Background: Strong relationship has been demonstrated between the presence of occlusive CAD and coronary artery calcification (CAC) detected at autopsy, fluoroscopy and computed tomography (CT scan). CT scan quantifies the relative burden of CAC deposits as a marker of atherosclerosis. Study explored utility of multi-slice spiral CT scan for detection of CAC in post myocardial infarction cases.
Methods: Fifty-one post myocardial infarction cases were enrolled in the study. Detailed clinical history was recorded in every case regarding age, sex, history of risk factors for CAD like systemic hypertension, diabetes mellitus, smoking and family history of CAD. Every case was evaluated for fasting and postprandial blood sugar and fasting lipid profile. Body mass index (BMI) was also calculated. Coronary artery calcium was estimated in each patient by multi -slice spiral CT scan. Conventional angiography was also undertaken in 18 patients. Co-relation of coronary calcium with different age groups, sex, risk factors, electrocardiography and angiography was drawn.
Results: Out of 51 cases scanned, 40 cases (78.4%) had detectable CAC. In 30 cases (58.8%), CAC score ranged from 1 to 100 (mild score); 6 cases (11.8%) had score between 101-400 (moderate score) while in 4 cases (7.8%) CAC score was more than 400 (severe score %). For detection of angiographically detectable disease, the sensitivity of multi-slice CT was 100% and the specificity was 33.3%.
Conclusions: CAC is a valid measure of atherosclerotic plaque burden and is recommended as a screening tool for demonstrating significant atherosclerosis in susceptible subjects.

Keywords: Coronary artery calcium, Myocardial Infarction

INTRODUCTION

Cardiovascular disease accounts for approximately 12 million deaths annually and is the commonest cause of deaths globally. Lately, the problem is assuming epidemic proportions more rapidly in the developing world.[1] Coronary artery disease (CAD) among Asian Indians has been found to be more severe, diffuse and associated with serious complications and increasing mortality at a younger age.[1]

Coronary artery calcium (CAC) is temporally related to vascular inflammation and the demise of lipid-laden macrophages.[2] Since calcium is deposited only in the atherosclerotic plaques and not in the normal vessels, and since atherosclerosis is a diffuse process, a high coronary calcium burden reflects the presence of more extensive coronary atherosclerosis. Hence higher coronary calcium scores have been postulated to be associated with the presence of significant CAD and future risk of adverse coronary events. Moreover, coronary calcium deposition

may represent a type of plaque instability, namely plaque rupture.[3]

Prospective epidemiological studies have established the association between major risk factors and the development of clinical CAD. However it has been estimated that these risk factors fail to explain up to 50% of CAD mortality and morbidity.[4] Given the scope of global illness burden due to cardiovascular disease, there is need for new strategies for the prevention of coronary artery disease (CAD).[5] Strong relationship has been demonstrated between the presence of occlusive CAD and coronary artery calcification detected at autopsy, fluoroscopy and computed tomography.[6] Computed tomography (CT) provides exquisite, high resolution imaging of the body and heart (and vascular system in general). It quantifies the relative burden of CAC deposits as a marker of atherosclerosis.

With the present study, we attempted to explore utility of multi-slice spiral CT scan for detection of CAC in post myocardial infarction cases and also study CAC score correlation with various risk factors, region of myocardial infarction by ECG diagnosis and with coronary angiography.

METHODS

Hospital based prevalence study conducted in Department of Medicine and Department of Radiology, Tertiary care centre in central India. The total duration of this study was one and half years.

Inclusion criteria

- Patients who had suffered myocardial infarction in recent past
- Myocardial infarction (MI) as diagnosed by ECG.

Exclusion criteria

- Patients who had undergone coronary angioplasty and stenting
- Refusal to give written consent.

Fifty-one post myocardial infarction cases were enrolled in the study as per mentioned selection criteria. Detailed clinical history was recorded in every case regarding age, sex, history of risk factors for CAD like systemic hypertension, diabetes mellitus, smoking and family history of CAD. Every case was evaluated for fasting and postprandial blood sugar and fasting lipid profile. Body mass index (BMI) was also calculated.

Coronary artery calcium was estimated in each patient by multi -slice spiral CT scan. The mean and median times between myocardial infarction and cardiac CT imaging were 31 and 35 days respectively (range 6 - 60 days). Coronary calcifications were quantified using the Agatston score.[7] Four absolute coronary score (CS) were considered: Zero, mild score (1 - 100), moderate score (101- 400) and severe score (>400).

Angiography was done in 18 cases that had given separate consent for the same. Co-relation of coronary calcium with different age groups, sex, risk factors, electrocardiography and angiography was drawn.

Approval from Institutional Ethics Committee was obtained before start of the study. Informed written consent was obtained from each patient before participation in the study.

The data was analysed using SPSS (version 20); by applying paired t-test, ANOVA and odd's ratio wherever applicable.

RESULTS

Out of total 51 participants studied, 42 (82.4%) were males and 9 (17.6%) females. Mean age of males was 46.0±9.0 years whereas of female cases was 47.1±10.2 years; with the overall range being 3-62 years. Maximum number of cases were in the age group of 40-59 years (n=31, 60.8%).

Hypertension (56.9%) and dyslipidemia (47.0%) were the most frequently observed risk factors in the study population followed by smoking (41.2%), obesity (23.5%) and diabetes mellitus (17.6%). Majority of cases had three or more risk factors (31.4%) followed by two (29.4%) and one risk factor (27.4%), while no risk factor was observed in 6 cases (11.8%).

In the present study, out of 51 cases scanned, 40 cases (78.4%) had detectable CAC by multi-slice CT scan; where as in 11cases (21.6%) no calcium was detected. In majority, i.e. in 30 cases (58.8%), CAC score ranged from 1 to 100 (mild score); 6 cases (11.8%) had score between 101-400 (moderate score) while in 4 cases (7.8%) CAC score was more than 400 (severe score) (Table 1).

Table 1: Grading of coronary artery calcium (CAC) score.

CAC score *	Males (N=42)	Females (N=9)	Total (n=51)
Normal (0)	8 (15.7%)	3 (5.9%)	11 (21.6%)
Mild (1 - 100)	25 (49%)	5 (9.8%)	30 (58.8%)
Moderate (101 - 400)	6 (11.8%)	0	6 (11.8%)
Severe (> 400)	3 (5.9%)	1 (1.9%)	4 (7.8%)

*Agatston calcium scoring guidelines.

There was a progressive increase in the mean total coronary artery calcium score with the increasing age i.e. from 30 to 62 years. However, the CAC score was

significantly increased only in cases of 60-62 years of age group as compared to other age groups (p=0.004). While correlating mean CAC with sex of the participants, Mean CAC in male cases was observed to be 129.7±357.2 (range 0 - 868.7) where as it was 113.4±284.5 (range 0 - 2069.0) in females. However, this difference was statistically not significant (p>0.05).

Table 2: Correlation of mean total CAC score with risk factors.

Risk factor	Present/Absent	Mean CAC±SD	P value
Hypertension	Present (n=29)	165.8±409.9	NS
	Absent (n=22)	75.5±226.6	
Dyslipidemia	Present (n=24)	151.3±284.3	NS
	Absent (n=27)	108.2±395.9	
Smoking	Present (n=21)	202.5±457.6	NS
	Absent (n=30)	78.3±243.0	
Obesity	Present (n=12)	456.6±613.0	<0.05
	Absent (n=39)	24.2±31.9	
Diabetes Mellitus	Present (n=9)	342.9±668.6	NS
	Absent (n=42)	80.6±209.3	
Family H/o CAD	Present (n=8)	86.6±173.9	NS
	Absent (n=43)	132.7±371.2	

When individual risk factors were considered, the mean total CAC score was higher in cases having risk factor as compared to cases not having it. However, their differences were statistically not significant, except in the cases of Obesity (p<0.05) (Table 2).

All cases without risk factor and with only one risk factor had CAC score in range of 0 - 100. Whereas 9 out of 16 cases with presence of three or more risk factors had moderate to severe CAC score; the difference was statistically insignificant.

Table 3: Correlation of ECG diagnosis of MI with Mean total CAC score.

Type of MI (ECG diagnosis)	Range of CAC	Mean CAC±SD
AWMI (n=33)	0 - 2069.0	109.8±365.1
IWMI (n=14)	0 - 287.9	56.2±87.4
Both AWMI and IWMI (n=4)	0 - 1060.0	514.5±527.0

While correlating CAC score with MI (as diagnosed by ECG); mean total CAC score was found to be higher in cases having both anterior wall myocardial infarction (AWMI) and inferior wall myocardial infarction (IWMI) (514.5±527.0) as compared to isolated anterior wall myocardial infarction (109.8±365.1) or inferior wall myocardial infarction (56.2±87.4). However, these differences were not statistically significant (Table 3).

Further, CAC was detected in all the branches of coronary arteries irrespective of the region of myocardial infarction. No correlation was observed between presences of CAC in any particular branch of coronary artery and region of myocardial infarction (Table 4).

Table 4: Distribution of mean CAC score in branches of coronary arteries in different regions of myocardial infarction.

Region of MI	LM*	LAD*	Cx*	RCA*
AWMI (n=33)	4.1±10.5 (n=8)	70.6±251.9 (n=14)	5.8±21.3 (n=9)	31.6±119.7 (n=12)
IWMI (n=14)	5.0±14.0 (n=4)	13.1±27.9 (n=7)	10.9±28.6 (n=5)	29.8±71.3 (n=7)
AWMI and IWMI (n=4)	3.7±7.4 (n=1)	363.6±384.4 (n=3)	38.2±76.4 (n=1)	101.1±138.7 (n=3)

*LM- Left Marginal Artery, LAD- Left Anterior Descending Artery, Cx- Circumflex Artery, RCA- Right Coronary Artery.

Table 5: Comparison of findings of cardiac CT and angiography.

CT Findings	Angiographic findings	
	Negative for coronary artery disease (n=6)	Positive for coronary artery disease (n=12)
Negative for calcification (n=2)	2	0
Positive for calcification (N=16)	4	12

Coronary angiography could be done in 18 out of total 51cases. Out of 18 patients, 6 had no angiographically demonstrable abnormality. Mean CAC score in-group with abnormal angiography (n=12) (217.9±302.8) was significantly higher than that in the group with normal angiography (n=6) (8.5±18.3) (p<0.05). Out of the total 18 angiograms; no abnormality was detected in 6 cases, single vessel disease in 3 cases, double vessel disease in 3 cases and triple vessel disease in 6 cases. CAC was found to be insignificantly higher in cases having double vessel disease (218.6±256.1) and triple vessel disease (295.2±391.5) as compared to single vessel disease (62.9±37.5) and normal angiogram (8.5±18.3). Distribution of calcification showed that 3 cases had

calcification in one vessel, 4 cases had calcification in two vessels and 5 cases had calcification in three vessels.

Angiographically detectable coronary artery disease was present in 12 out of 18 cases (66.6%). Coronary calcification was detected in 16 cases out of 18 (88.9%). For detection of angiographically detectable disease, the sensitivity of multi-slice CT was 100% and the specificity was 33.3%. When testing for presence of angiographically detectable disease, the positive predictive value of multi-slice CT demonstrating calcification was 75%. The negative predictive value of multi-slice CT scan demonstrating no calcification was 100% (Table 5).

DISCUSSION

The amount of coronary calcification detected by cardiac CT scan has been identified as a strong predictor of cardiovascular morbidity and mortality. More and more credible data are showing association between the presence and amount of coronary calcification and the cardiovascular event rate.[8] With this study, we explored utility of multi-slice spiral CT scan for detection of CAC in post myocardial infarction cases in our set up and also studied CAC score correlation with various risk factors, region of myocardial infarction by ECG diagnosis and with coronary angiography.

Quantification of calcium in coronary arteries has been shown to reflect the total atherosclerotic plaque burden. This quantification can be determined in straightforward manner by using advanced high-speed CT scans including spiral CT scan.[3] With similar approach and the mentioned objective in mind, 51 post-myocardial infarction cases fulfilling selection criteria were studied.

Maximum Patients in present study were between 50-59 years of age, which is consistent with previous similar studies. However, when younger patients in age group of 30-39 years were compared, we observed higher incidence as compared to other studies. These may be due to the fact that in the Indian population CAD has been reported to appear a decade earlier compared with the age incidence in developed countries.[9]

In the present study, most frequently observed risk factors were hypertension (56.9%) and dyslipidemia (47%). Whereas less frequently observed risk factors were family history of CAD (15.6%) and diabetes mellitus (17.6%). Our findings are similar with the incidence of risk factors reported by other workers.[10,11]

In the present study, out of 51 post myocardial infarction cases that underwent multi-slice CT scan, 40 (78.4%) had detectable CAC. This is in agreement with findings from previous researchers, only they had higher prevalence/odds ratios to report. E.g. In 1242 consecutive necropsies conducted by Eggen DA et al way back in 1960s, they had observed 93% prevalence of calcium in cases dying of atherosclerotic CAD while only 49% in the case of natural deaths.[12] Tanenbaum SR et al observed 88% prevalence of CAC in angiographically significant CAD, while in cases with normal angiography no calcium was detected.[13] Agatston AS et al observed 96% prevalence of CAC in cases with established CAD and only 39% in cases without CAD.[7] The presence of calcium in the coronary arteries is invariably an indication of intimal atherosclerosis and thus its detection may have diagnostic significance.[14] Eleven cases with myocardial infarction were negative for CAC. This may be due to plaque erosion as plaque erosions are associated with lesser calcium and therefore coronary artery calcium may be less or zero.[15,16]

In the present study, when CAC score was classified for grading of calcium density more than half cases had mild score and around one fifth had no detectable calcium. In the present study, when CAC score was classified for grading of calcium density 58.8% cases had mild score. Raggi P et al and Shrivastava S et al, observed maximum cases having moderate and severe score in their study of post MI cases, which is not consistent with our observations.[3,17] This inconsistency may be because of higher mean ages of cases in studies of Raggi P et al (53 years) and Shrivastava S et al (52.3 years) as compared to 46.2 years in present study.[3,17] Moreover, different techniques were used to estimate CAC score in these studies, which would have contributed to the disagreement in findings.

In the present study, progressive increase in the mean total CAC score was observed with increasing age. However, the CAC score was significantly increased ($p<0.05$) only in the cases of 60-62 years of age group as compared to others.

Our findings are similar to that of Goel M et al and Haberl R et al, who also observed higher mean total CAC scores with increasing age.[17,18] Janowitz WR et al observed that incidence of CAC increased from a few percent in the second decade to nearly 100% by the 8th decade of life in men and women.[19] This is due to increased incidence of coronary atherosclerosis with advancing age.

In the present study, conventional risk factors for CAD studied were hypertension, dyslipidemia, smoking, obesity, diabetes and family history of coronary artery disease. Mean total CAC score was higher in cases having risk factors as compared to cases not having risk factors. However, difference was statistically not significant except in cases of obesity. This insignificant difference may probably due to wide dispersion of CAC score values and no comparison was made with normal controls. Similar findings were reported by Shrivastava et al.[3] On the contrary, Goel M et al, reported significantly higher prevalence of detectable calcium in cases with diabetes mellitus, hypertension and smoking.[17] Mean total CAC score in patients with three or more risk factors

was high as compared to cases with less than 3 risk factors, though this difference was statistically not significant. Similar findings were reported by Shrivastava et al in an Indian study. However, Lee DJ et al and Goel M et al reported significant, continuous, graded relation of mean total calcium score with an increasing number of risk factors.[3,17,20] So, the correlation of CAC score and cardiac risk factors need further studies with larger sample size in similar settings to comment any further.

While observing correlation of ECG diagnosis of myocardial Infarction with mean total CAC score; it was found that out of 51 cases studied 33 cases had AWMI, 14 cases had IWMI and 4 cases had both. Mean total CAC score was found maximum in cases having both AWMI and IWMI (514.5±527.0). Cases having isolated AWMI had insignificantly higher mean total CAC score (109.8±365.1) as compared to those with isolated IWMI (56.2±87.4). The higher calcium score observed in the group of anterior wall MI as well as having both anterior wall and inferior wall MI cases may be due to involvement of left anterior descending (LAD) coronary artery, which is generally the most severely affected vessel. In the autopsy study, Mautner et al reported the calcific deposits to be most frequently present in the territory of Left anterior descending (LAD) artery.[21] In vivo investigations were also consistent with these findings. So, our finding sits well with available literature. But no correlation was observed regarding quantity of CAC in particular branch of coronary artery with region of myocardial infarction. The culprit vessel was not calcified in all cases, and the mean calcium score of the culprit vessel was only slightly above that of the remaining arteries. These findings are consistent with findings of previous investigations that have shown a similar extent of calcification in stable coronary plaques and in those prone to rupture.[22] Thus coronary calcification detected by cardiac CT scan seem to be a measure of the coronary atherosclerotic plaque burden but may not assist to locate the culprit vessel.

Study found high CAC score to be associated with increased presence and severity of angiographically proven CAD. This finding corroborates what was observed previously by Shrivastava et al, Breen JF et al and Kaufmann RB et al.[3,23,24]

Coronary artery angiography was done in 18 cases. Out of which no abnormality was detected in six cases, single vessel disease in three cases, double vessels in three cases and triple vessel disease in six cases. CAC was found to be higher in cases having double vessel (218.6±256.1) and triple vessel disease (295.2±391.5) as compared to single vessel disease (62.9±37.5) and normal angiogram (8.5±18.3) Differences were statistically not significant. Agatston AS et al observed continuous and statistically significant increase in calcium score as the angiographic disease increased from normal coronaries to 1-, 2- and 3-vessel disease.[7] Schmermund A et al and Janowitz WR et al observed similarly, that coronary calcium score increases with number of vessels involved and their values were statistically significant.[2,19] Our study with its limitation of small number of cases and wide dispersion of CAC score has not provided statistical significance.

Angiographically significant CAD was present was present in 12 out of 18 cases (66.6%). Coronary calcification was detected in 16 patients out of 18 cases (88.9). For detection of angiographically detectable disease the sensitivity of multi-slice CT scan was 100% and the specificity was 33.3%. When testing the presence of angiographically detectable disease the positive predictive value of multi-slice CT scan demonstrating calcification was 75%. The negative predictive value of multislice CT scan demonstrating no calcification was 100%. In a large study conducted by Budoff MJ et al in 710 symptomatic subjects comparing EBCT scan with coronary angiography; the sensitivity, specificity and negative predictive value (NPV) were quite close to what we reported. Fallavollita JA et al compared the EBCT detection of calcium with coronary angiography in 106 patients and found an 85% sensitivity and 45% specificity in detecting significant stenos.[25,26] Four patients who had calcification detected at CT scan did not have angiographically detectable disease and were classified as false positive cases while determining test performances. It is highly probable that these individuals had atherosclerosis that was not detected on the angiography either because of compensatory enlargement of the arteries or because diffuse atherosclerosis causing narrowing of the entire lumen so that no focal stenosis was visible on angiography. Thus, the apparent lower specificity of coronary calcium score (CCS) may in fact be due to the inability of angiographies to detect extra luminal plaque.

CONCLUSION

Study report CAC to be a measure of atherosclerotic plaque burden and may be recommended as a screening test for demonstrating significant atherosclerosis in susceptible subjects. Small sample size was the major limitation of our study, along with inability to enroll controls for validation. Further research with larger sample size and including participants with lower CAD risk is recommended.

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