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Original Research Article

Study of coronary artery calcium by multi-slice spiral CT as a tool for high risk cardiovascular screening

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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. We explored utility of multi-slice spiral CT scan for detection of CAC as a tool for screening in asymptomatic high-risk cases above 40 years of age.
Methods: Fifty-eight asymptomatic cardiovascular high-risk cases were included as per 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 calculated. An ECG was also recorded. Coronary artery calcium was estimated in each patient by multi -slice spiral CT scan. Fifty age and gender matched consenting participants were enrolled as controls and comparisons drawn.
Results: Out of 58 cases scanned, 41 had no detectable CAC by multi-slice CT scan whereas in 17 cases (29.2%), calcium was detected. Mean CAC score was observed to increase as number of risk factors increased.
Conclusions: Multi-slice CT scan is a useful tool for detection of coronary artery calcium (CAC) when utilised for high risk screening in older adults having one or more known cardiovascular risk factors.

Keywords: CAC, Cardiovascular risk, Screening

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. 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) quantifies the relative burden of CAC deposits as a marker of atherosclerosis.

Early diagnosis and modification of various risk factors appropriate to the individual patient is one essential element to future limitation of mortality and morbidity from coronary disease.

With this goal in mind, present study attempted to explore utility of estimation of CAC by multi-slice spiral CT scan as a tool for screening in asymptomatic high-risk cases above 40 years of age.

METHODS

The present study was a hospital based prevalence study carried out in the Department of Medicine and Department of Radiology, tertiary care centre in central India. The study duration was two years.

Inclusion criteria

- Asymptomatic individuals >40 years old
- Presence of any of the following 6 risk factors:

a) Systemic Hypertension
b) Diabetes Mellitus
c) Dyslipidemia
d) Smoking
e) Family history of CAD
f) Obesity.

Exclusion criteria

- Symptomatic or individuals suspected for CAD, History of previous MI, ECG suggestive of changes of IHD
- Presence of medical illness (endocrinopathies except diabetes mellitus, liver diseases, kidney diseases, valvular heart diseases)
- Pregnancy
- Refusal to give written consent.

Operational Definitions

Hypertension

Systolic BP >140 mmHg and diastolic BP >90 mmHg on the average of >2 readings taken on each of two or more visits after initial screening or one who was a known case of hypertension or was on antihypertensive medications.[7]

Diabetes

- Symptoms of diabetes plus random blood glucose concentration >200 mg/dl
- Fasting (8 hour) plasma glucose >126 mg/dl.
- Two-hour plasma glucose > 200 mg/dl during an oral glucose tolerance test
- Patients currently receiving insulin or oral hypoglycemic agents.[8]

Dyslipidemia

- Total Cholesterol > 200 mg/dl
- LDL Cholesterol > 130 mg/dl
- Triglycerides- > 150 mg/dl
- HDL Cholesterol < 40 mg/dl
- Patients on hypolidemic drugs.[9]

Smoking

By asking the subject if they ever had >10 cigarettes/day for at-least 1 year.

Family history of CAD

If a first-degree relative of subject had suffered MI or had died suddenly, or had undergone revascularization before the age of 65 years.

Obesity

Body Mass Index >30.

Fifty-eight asymptomatic cardiovascular high-risk cases were included as per 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 calculated. An ECG was also recorded. Coronary artery calcium was estimated in each patient by multi-slice spiral CT scan. Coronary calcifications were quantified using the Agatston score.[10] Four absolute coronary score (CS) were considered: zero, mild score (1-100), moderate score (101-400) and severe score (>400).

Fifty age and gender matched consenting participants were enrolled as controls. The work up for all the controls was exactly similar to the cases, as mentioned above.

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 & Chi-square tests.

RESULTS

In the present study, 58 cases at high risk of developing coronary events were evaluated, along with equal number of age and sex matched controls. The study sample consisted of 35 (60.3%) males and 23 (39.7%) females. Out of 58 cases, majority 48 (82.7%) were between 41-60 years. The mean age of male participants (53.71±9.33 years) was higher than females (50.17±10.07 years).

Dyslipidemia (65.5%), hypertension (51.7%) and diabetes mellitus (51.7%) were the most frequently observed risk factors; followed by smoking (34.4%), family history of IHD (22.4%) and obesity (12%). Majority of cases had two risk factors (37.9%), followed by one risk factor (32.8%) and >3 risk factors (29.3%).

Table 1: Correlation of mean total coronary artery calcium (CAC) score with age and gender in cases and controls.

	Cases		Controls	
	Range	**Mean CAC±SD**	**Range**	**Mean CAC±SD**
Age group (years)				
41-50 (n=31)	0-239	34.44±73.34	0-0.9	0.09±0.25
51-60 (n=17)	0-548	79.42±147.51	0-9.6	0.6±2.4
> 61 (n=10)	0-579.6	90.68±196.22	0-0.6	0.06±0.18
41-75 (n=58)	0-579.6	57.32±125.08	0-9.6	0.22±1.26
Gender				
Male (n=35)	0-579.6	69.31±146.81	0-9.6	0.33±1.62
Female (n=23)	0-251.6	39.07±81.53	0-0.8	0.06±0.21

Table 2: Grading of coronary artery calcium (CAC) score in cases and controls.

	Cases			Controls		
CAC score	**Males (n=35)**	**Females (n=23)**	**Total (n=58)**	**Males (n=35)**	**Females (n=23)**	**Total (n=58)**
Normal (0)	23 (65.7%)	18 (78.3%)	41 (70.8%)	31 (88.6%)	21 (91.3%)	52 (89.7%)
Mild (1-100)	4 (11.4%)	1 (4.3%)	5 (8.6%)	4 (11.4%)	2 (8.7%)	6 (10.3%)
Moderate (101-400)	6 (17.1%)	4 (17.4%)	10 (17.2%)	0	0	0
Severe (> 400)	2 (5.8%)	0	2 (3.4%)	0	0	0

Table 3: Comparison of coronary artery calcium (CAC) scores of cases having risk factors with that of controls.

Risk Factor	Mean CAC score±SD in cases with risk factor	Mean CAC score±SD in controls without risk factor	P-value
Hypertension (n=30)	78.86±129.74	0.22±1.26	<0.001
Diabetes Mellitus (n=30)	41.6±112.56	0.22±1.26	0.003
Dyslipidemia (n=38)	49.13±111.11	0.22±1.26	0.006
Smoking (n=20)	119.29±179.78	0.22±1.26	<0.001
Family history of CAD (n=13)	151.24±173.47	0.22±1.26	<0.001
Obesity (n=7)	52.44±97.8	0.22±1.26	<0.001

Mean coronary artery calcium (CAC) scores of cases in different age groups were found to be significantly higher in cases than controls ($p<0.05$). Further, a progressive increase was observed in the mean CAC score with increasing age, but it was statistically insignificant ($p>0.05$). As for gender, mean CAC score was found significantly higher in cases than in controls. In both cases and controls, males showed higher CAC scores than females; but the differences were not statistically significant (Table 1).

Out of 58 cases scanned, 41 had no detectable CAC by multi-slice CT scan whereas in 17 cases (29.2%), calcium was detected. Among these 29.2%, CAC ranged from 101-400 (moderate score) in majority of the cases. Amongst controls, 52 (89.7%) were having normal CAC scores; whereas 6 (10.3%) were having detectable coronary calcium and all the 6 had mild (1-100) scores only. Number of participants having detectable CAC score were significantly more in cases as compared to controls ($p<0.05$) (Table 2).

Mean CAC score was observed to increase as number of risk factors increased. It was 6.74±29.38 in cases with one risk factor and 44.93±133.03 in those with two risk factors; the difference being statistically insignificant ($p<0.05$). But it was significantly higher in those with 3 or more risk factors (129±150.63) than the rest ($p<0.05$). We also compared the risk factors independently with controls for the CAC score. All the risk factors showed significantly higher CAC scores (Table 3).

When cases were studied for presence of individual risk factor against all other remaining risk factors, mean CAC score was found to be higher in cases with hypertension, smoking or family history of CAD.

But statistically significance was observed in case of smoking ($p=0.002$) and family history of CAD ($p=0.008$) (Table 4).

Table 4: Correlation of mean total CAC score of individual risk factor with other risk factors.

Risk factor		Mean CAC±SD	P-value
Hypertension	Present (n=30)	78.86±129.74	
	Absent (n=28)	34.24±117.81	0.08
Diabetes mellitus	Present (n=30)	41.60±112.56	
	Absent (n=28)	74.16±137.29	0.83
Dyslipidemia	Present (n=38)	49.13±111.11	
	Absent (n=20)	72.88±150.01	0.75
Smoking	Present (n=20)	119.29±179.78	
	Absent (n=38)	24.70±65.55	0.002
Family history of CAD	Present (n=13)	151.24±173.47	
	Absent (n=45)	30.19±93.27	0.008
Obesity	Present (n=7)	52.44±97.8	
	Absent (n=51)	57.99±129.16	0.54

DISCUSSION

With the objective of exploration of utility of estimation of CAC by multi-slice spiral CT scan as a direct tool for screening in asymptomatic high-risk cases above 40 years of age, in the present study, 58 cases at high risk of developing coronary events were evaluated and findings compared with those in age and sex matched controls.

Goel et al observed no coronary calcium in almost 90% patients <40 years of age.[11] According to Haberl et al, 55% asymptomatic men and women <40 years of age had no coronary calcium.[12] Therefore, chances of detecting significant calcium in cases below 40 years were less. Hence, in the present study, cases above 40 years of age were included. Mean age of participants in the present study was 52.31 years, which is similar to that observed by previous researchers.[6,7,10,11] Maximum cases were in the age group 41-50 years, which is consistent with the study of Agatston et al, while Goel et al and Haberl et al reported maximum cases in comparatively older age groups.[10-12]

We observed most dylipidemia (65.5%), hypertension (51.7%), diabetes (51.7%) and smoking (34.4%) to be more frequently observed risk factors, while family history of CAD (22.4%) and obesity (12.06%). Wong et al, observed diabetes in only 8% cases, in comparison to 51.7% observed in the present study.[13] Schmermund et al and Raggi et al observed family history of CAD as the most common risk factor, with significantly lesser cases of dyslipidemia.[2,14] In the present study the number of cases having 1, 2 and >3 risk factors were 32.8%, 37.9% and 29.3% respectively; which is in agreement with observations of Arad et al, who reported 7%, 23%, 36%, 26%, 6% and 2% cases having 0, 1, 2, 3, 4 and 5 risk factors.[15] However Shrivastava et al reported the increase to be statistically insignificant.[3]

Many workers like Janowitz et al, Wong et al, Arad et al, Raggi et al, and others, observed that CAC increases as age advances.[13-16] It was found statistically insignificant increase in mean CAC score with increasing age among cases, which was not there in controls. Same set of workers also reported males to be having significantly higher CAC scores than their female counterparts. We found the difference to be insignificant. Small sample size in the present study might have led to results being insignificant; since previous studies were conducted with relatively higher sample sizes.

In the present study, 29.2% cases and 10.3% controls had detectable coronary calcium on CT scan. Mean CAC was significantly higher in cases than controls. Few of the previous studies (Shrivastava et al, Raggi et al, Eggen et al) had observed very high prevalence of detectable calcium on CT scan.[3,14,17] This was seemingly because these studies had included symptomatic cases of CAD. The controls having detectable coronary calcium in 10.3% subjects may be attributed to presence of coronary risk factor(s) other than the six we included in analysis.

The presence of calcium in coronary arteries is invariably an indicator of intimal atherosclerosis and thus its detection may have diagnostic significance.

When individual risk factors were compared with controls, all the 6 risk factors studied showed significantly higher CAC scores. Thus, all the analysed risk factors were reported to be of significance even individually, as far as prevalence of CAD goes. Mean total CAC scores were higher in cases with smoking, family history of CAD and hypertension. But the differences were statistically significant only for smoking and family history of CAD. The insignificant difference in groups of other risk factors may be due to wide dispersion of CAC score and small sample size. Previous studies mostly reported significance for the correlations with individual risk factors.[13-17]

CONCLUSION

In conclusion, the present study demonstrates that multi-slice CT scan is a useful tool for detection of coronary artery calcium (CAC) when utilized for high risk screening in older adults having one or more known cardiovascular risk factors. The relatively small sample size was a major limitation and led to results at times being insignificant. Plus, the fact that present study sample was mostly from lower socioeconomic strata, who mostly don't have sedentary lifestyle. Thus, the sample was not truly representative of the society and hinders external validity of the results. We recommend studies with larger and more representative samples for corroboration. It may also prove prudent to conduct prospective study with prolonged follow-up with incidence of actual coronary events as outcome.

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