Assessment of Coronary Artery Calcification in Elderly Adults

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Abstract:

Background: Early identification of atherosclerosis in older adults is paramount due to high cardiovascular morbidity and mortality. Our aim was to investigate CAC in a population of adults ≥55 years without previous history of cardiovascular heart disease (CHD) and its association with cardiovascular risk factors.

Methods: This was a retrospective analysis of 6,573 individuals with a mean age of 61.8 years (range 55-85; 68.2% males) who underwent Electron Beam Computed Tomography for CAC score (CACS) assessment.

Results: CAC was present in 70.5% of the overall cohort (78.8% of males and 52.7% of females). Twenty six per cent (26%) of those with CAC did not have any CHD risk factors. CACS ranged from 0 to 7,908 (mean 223.3±512.9); males presented a higher mean CACS (284.57 ± 571.1), compared to females (mean CACS 92.2 ± 324.8), $p<0.0001$. The mean CACS in males increased from 154.2 for ages 55-59 years to 760.2 in those aged 80 to 84 whilst in females mean CACS increased from 39.5 to 224.4, for corresponding age groups. The mean CACS appears to increase with age irrespective of gender.

In each gender, age and hypercholesterolemia were associated with higher CACS. Furthermore, in males family history and DM were positively associated with CACS while in females, smoking status and hypertension were positively associated with CACS.

Conclusion: A broad distribution of CACS was seen in older subjects. Assessment of CACS may place patients into a higher risk group for future events, and lead to more aggressive treatment with preventative therapies.

Keywords: Coronary calcium, Risk factors, Elderly, Electron beam computed tomography, Coronary artery calcification.

INTRODUCTION

Atherosclerosis and coronary heart disease (CHD) are leading causes of death and disability in both genders [1]. Coronary artery calcification (CAC) is the radiologic surrogate marker of atherosclerosis, as it is present only in atherosclerotic arteries [2, 3]. CAC is assessed non-invasively with electron-beam computed tomography (EBCT). In asymptomatic adults, "traditional" cardiovascular risk factors have been strongly associated with the degree of CAC [4-7]. Furthermore, CAC score (CACS) predicts CHD events independently of "traditional" risk factors [8-10].

Although CAC reflects the extent of atherosclerosis, it is unclear if it has the same predictive value for different age groups. CACS has a strong and graded association with age, therefore the utility of CAC assessment in older adults (≥ 55 years old) has been questioned [11]. Due to a rise in life expectancy, the population of older adults has increased; hence further studies of risk stratification are required. In older individuals CHD is more severe, diffuse and associated with left main coronary artery disease than that of younger populations. [12]. Until now, only one population-based study has been performed in older adults [13].

The aim of the present study is to assess CAC in a population of older individuals without previous history of CHD and/or any associations of CAC with "traditional" cardiovascular risk factors.

METHODS

Data Collection

Between January 2002 and December 2009, 16,247 asymptomatic men and women aged 22-85 years underwent Electron Beam Computed Tomography (EBCT), at European Scanning Centre (London, UK) as part of a preventive health examination or because of physician referral. Using this database, we selected 6,573 consecutive adults aged 55 to 85 years. Demographic information and the presence of risk factors were abstracted from referral

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letters and questionnaires completed by the patients prior to their test. Individuals with previously documented coronary CHD or chronic kidney disease were excluded from this study.

Computed Tomography Scanning

All EBCT CAC studies were performed using the same scanner (Imatron C300 Ultrafast computed tomography scanner, **GE** Healthcare) and the same scan protocol. Forty contiguous, 3-mm-thick slices were obtained during a single breath hold, beginning at the lower edge of the carina. The field of view was 26cm, and the scan time was 100 ms per slice, with synchronized electrocardiographic triggering at 80% of the RR interval. At least two adjacent pixels (i.e. area ≥0.93mm^2) with a density >130 Hounsfield units were required to define a lesion. Coronary artery calcium scores were calculated according to the method proposed by Agaston *et al.* [14].

All patients had given a written consent for the test and for the use of anonymised clinical data for research purposes. The study did not require specific ethics approval since it was based on clinically obtained information.

Risk Factors

For the purpose of the present study, hypertension (HTN) was defined as the use of antihypertensive medications or known but untreated hypertension. Dyslipidaemia was defined as the use of cholesterol-lowering medications or having known but untreated total serum cholesterol >240mg/dl (6.2 mmol/l). Diabetes mellitus (DM) was defined as a fasting plasma glucose level of at least 126 mg/dl (7.0 mmol/l), use of hypoglycaemic medications or self-reported previous physician diagnosis. The body-mass index (BMI) was calculated as the weight (in kilograms) divided by the square of the height (in meters). Obesity was defined as BMI ≥30. Family history (FHx) of coronary artery disease was obtained by asking the participants whether any first-degree relative (men <55 years and women <65 years) had had a fatal or non-fatal myocardial infarction, coronary angioplasty, or coronary-artery bypass surgery. Current smokers and those who stopped smoking fewer than 30 days prior to the CT scan were included in the smoking category, whereas the remainder were characterised as non-smokers.

Table 1: Characteristics of the Study Population at the Time of EBCT Scanning

	Overall (n=6573)	Men (n=4483)	Women (n =2090)
Age, years	61.8 ± 5.6	61.6 ± 5.5	62.3 ± 5.7
Age groups, n (%)			
55-59	2751 (41.8%)	1956 (43.6%)	795 (38%)
60-64	2038 (31%)	1372 (30.6%)	666 (31.8%)
65-69	1104 (16.8%)	712 (15.8%)	392 (18.7%)
70-74	462 (7%)	304 (6.8%)	158 (7.5%)
75-79	173 (2.6%)	111 (2.5%)	62 (2.9%)
80-84	45 (0.7%)	28 (0.6%)	17 (0.8%)
Race, n (%)			
Caucasian	5714 (86.9%)	3926 (87.5%)	1788 (85.5%)
South Asian	319(4.8%)	226 (5%)	93 (4.4%)
Black	131(1.9%)	84(1.8%)	47(2.2%)
Chinese	19 (0.3%)	7(0.1%)	12 (0.6%)
Other	390 (5.9%)	240(5.3%)	150 (7.1%)
CAD risk factors			
Family history for CAD, n (%)	1004 (15.2%)	575(12.8%)	429 (20.5%)
Hypertension, n (%)	2340 (35.6%)	1621 (36.1%)	719 (34.4%)
Hypercholesterolemia, n (%)	1691 (25.7%)	1225 (27.3%)	466 (22.2%)
DM, n (%)	555 (8.4%)	439 (9.8%)	116 (5.5%)
BMI (mean ± SD)	26.4 ± 3.9	26.9 ± 3.5	25.5 ± 4.5
Smoking			
Current smoker, n (%)	670 (10.2%)	517 (11.5%)	153 (7.3%)
Ever smoked, n (%)	2276 (34.6%)	1643 (36.6%)	633 (30.2%)

Statistical Analysis

Results are presented as mean ± standard deviations (SD). Continuous variables were compared using Student's t test and categorical variables were compared using Pearson's x^2 test. Associations between risk factors and CAC score were examined using logistic regression analysis. In a multivariable model we entered calcium score and cardiovascular risk factors and computed regression coefficients for calcium score and all entered cardiovascular risk factors. All tests were two tailed, and a *p* value <0.05 was considered statistically significant.

RESULTS

The study population consists of 6,573 individuals with mean age 61.8 ±5.6 years; 4,483 (68.2%) were males and 2,090 (31.8 %) females (Table **1**). The male subgroup was younger to its female counterpart (*p* <0.001); males were more likely to be smokers (*p* <0.0001) and presented higher incidence of hypercholesterolemia (*p* <0.0001) and DM (*p* <0.0001) (Table **1**). Furthermore, they had higher BMI (*p* <0.0001) and were more likely to be Caucasians (*p* <0.02). Conversely, FHx of CHD was more common in female subgroup (*p* <0.0001). Finally, there was no difference in the prevalence of HTN between the two genders (*p* <0.1).

Overall, CAC was present in 70.5% of the cohort (78.8% of males and 52.7% of females). Twenty six per cent of those presented with CAC did not have any CHD risk factors. CACS ranged from 0 to 7,908 with mean 223.3 ±512.9 and median 31.4; males had higher mean CACS (284.57 ± 571.1, median CACS 64.6), compared to females (mean CACS 92.2 ± 324.8, median CACS 1), *p* <0.0001. The mean CACS in males increased from 154.2 for ages 55-59 years to 760.2 in those aged 80 to 84. In the female subgroup, mean CACS increased from 39.5 to 224.4 for the two age groups, respectively. The progress of mean and median CACS with age is demonstrated in Figure **1**. The mean CACS appears to increase with age irrespectively of the gender, but in females CACS was lower with a "time-lag" of about 10 years after the age of 60 (Figure **2**). For both males and females aged more than 80 years, the mean CACS presented a slight reduction.

The prevalence of CACS of 0, 1-100, 101-400, 401-1000, >1000 were 30.2%, 35%, 19.8%, 9.2% and 5.6% respectively, in overall population. The prevalence and distribution of CAC among various age group, for males and females are shown in Table **2**.

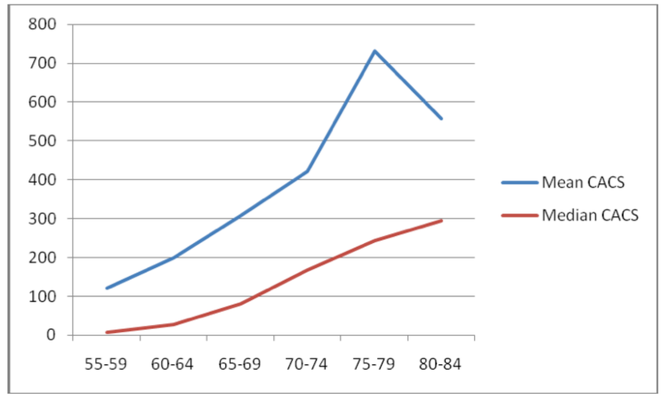

Figure 1: The progress of mean and median CACS with age. (CACS: Coronary Artery Calcium Score).

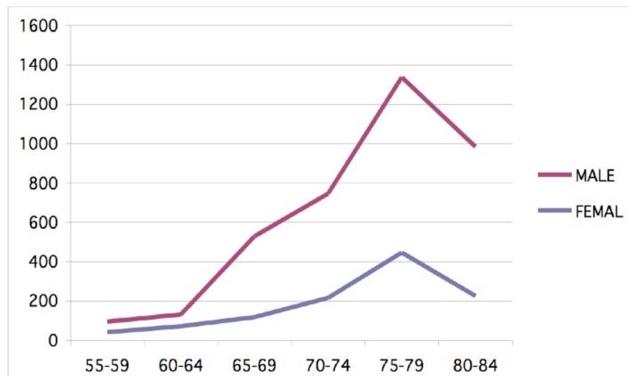

Figure 2: The progress of mean CACS in males and females. (CACS: Coronary Artery Calcium Score).

CACS 0 was reported in 30.2% of the cohort (61.9 ± 5.6 years, 7.4% smokers, 26.6% with HTN, 10% with FHx, 5% with DM, 12% obese, 9.6% with hypercholesterolemia and 2.9% with >3 CHD risk factors); but the prevalence of CACS 0 was higher in females 49.6% (62.4± 5.7 years) than in males 21.2%, *p* < 0.0001. Severe CAC (CACS: 400-1000) was noted in 9.2% (61.6 ± 5.5 years) of the cohort (11.8% smokers, 12.3% diabetics, 41.1% with HTN, 17.4% with FHx, 7.7% obese, 37.8% with hypercholesterolemia, 9.8% with >3 CHD risk factors) with male predominance (12% *vs* 3% in females, *p* <0.0001). Similarly, extensive CAC (CACS ≥ 1000) was reported in 8.6% of the total population (9.8% smokers, 34.5% with HTN, 28.2% with FH, 12.3% diabetics, 5.5% obese, 31.4% with hypercholesterolemia and finally 8.2% with > 3 CHD risk factors), with higher prevalence in males (7.3%) than in females (1.8%), *p* <0.0001.

The associations between CHD risk factors and the CACS were analyzed separately for males and females

Table 2: Prevalence and Distribution of CAC in Male and Female Among the Various Age Groups

CAC groups	55-59		60-64		Age groups (years) 65-69		70-74		75-79		80-84	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
	n=1956	n=795	n=1372	n= 666	n= 712	n=392	n=304	n=158	n= 111	n= 111	n=28	n=17
0, (%)	28.8%	62.7%	19.8%	54.5%	12.8%	31.3%	4.6%	26.5%	6.3%	14.5%	7.1%	5.8%
1-100, (%)	42.8%	27.1%	35.5%	31.2%	27.6%	43.4%	26.3%	36.7%	16.2%	35.8%	14.2%	47%
101-400, (%)	16.9%	7.9%	26.6%	10.6%	30.3%	18.4%	28.9%	22.8%	30.6%	25.8%	28.5%	29.4%
401-1000, (%)	8.6%	1.8%	10.9%	1.9%	17.5%	5.1%	23.0%	8.2%	16.2%	12.9%	21.4%	11.7%
>1000, (%)	2.8%	0.4%	7.1%	1.6%	11.6%	1.8%	17.1%	5.7%	30.6%	11.9%	28.5%	5.8%

in Table **3**. In both genders age and hypercholesterolemia were associated with higher CACS. Additionally in males, family history and DM were positively associated with CACS while in females it was the smoking status and hypertension that were positively associated with CACS.

DISCUSSION

Significant changes noted in the cardiovascular system in older people are considered to be the results of aging. Older adults have more severe atherosclerosis and a higher prevalence of multi-vessel coronary artery disease, frequent silent myocardial ischemia, and myocardial infarction with a higher cardiac event rate compared with younger age groups [15-18]. Therefore, early detection of atherosclerosis in the elderly is critical. The presence of CAC is closely associated with the presence of atherosclerotic lesions in the coronary arteries. Detection of coronary calcium by imaging techniques has evolved and become more sophisticated with advanced imaging technology.

We aimed to investigate the prevalence and distribution of CAC in a large number of asymptomatic British individuals ≥ 55 years of age. Our results show that the presence and extent of CAC is strongly associated with increased age and male gender. Furthermore, the associations between CHD risk factors and CAC were different between males and females. Overall, no calcification was detected in 30.2% of the cohort, 21.2% were males and 49.6% females. It is noteworthy to mention that males had higher CACS than females in all age categories; furthermore, the coronary arteries in females are 10 years “younger” than in males of the same age group. Interestingly, in the subgroup 80-84 years, a decreased in the mean CACS was noted (for both genders). This is probably due to the relative small number of individuals in this subgroup (*n*= 45, 0.7% of the total cohort). In our study, 19.3% of males had CACS >400 and 5.1% of females; Furthermore, 1.6% of females and 13.2% of males without CHD risk factors had CACS>400.

Age and gender are strongly associated with degree of coronary calcification. In our cohort, cardiovascular risk factors had a positive association with CACS, but there were differences between the two genders. In males FH, DM and hypercholesterolemia were associated with CACS; while in females smoking status, hypercholesterolemia and hypertension were associated with CACS.

Table 3: Multivariable-Adjusted Regression Coefficients Between CAD Risk Factors and Male and Female ≥ 55 Years

Clinical Characteristics	Regression coefficients (95% CI) Male	*p*-Value	Regression coefficients (95% CI) Female	*p*-Value
Age	28.1 (24.9-31.2)	<0.0001	12.9 (9.4-16.5)	<0.0001
Family history of CAD	99.1 (46-152.2)	0.0003	21.5 (-9.16-52.2)	0.16
Hypertension	35.7 (-1.7-73.3)	0.06	40.6 (12.1-69.2)	0.005
Hypercholesterolemia	139.8 (99.2-180.4)	<0.0001	51.1 (17.9-84.2)	0.002
DM	157.1 (96.1-218.1)	<0.0001	1.9 (-58.9-62.7)	0.9
Smoking	53.3 (-3.03-109.6)	0.06	90.8 (41.5-140.2)	0.0003
Obesity	-0.0003(-0.5-0.5)	0.9	0.02 (-0.11-0.15)	0.7

To the best of our knowledge, only one more population-based study has been performed in older individuals. Newman *et al.* examined CAC in 614 older adults with an age range 67 to 99 years [13]. CACS increased with age and was lower in blacks as compared to the whites. Age, male gender, white race, CHD, years of smoking and cholesterol level was independently associated with CACS.

In the same study [13], 9.3% of the participants had CACS of 0, 21.7% had CACS 1-100, 23.7% had 101-400, 23.6% 400-1,000 and finally 21.5% had CACS>1,000. Conversely, in our age matched sub-cohort the prevalence of CACS 0, 1-100, 101-400, 401-1000 and >1000 was 16.2%, 31.2%, 26.6%, 14.7% and 11.2%, respectively. The difference in the prevalence of zero, low and very high CAC is due to the difference in the demographic characteristics of the cohorts in two studies**.** In our study the majority of individuals were males, whilst in Newman *et al.* study there was a clear female preponderance. Furthermore, 86.9% of our cohort was Caucasians and 1.9% Blacks, whilst Newman *et al.* cohort comprised 76.7% Caucasians and 23.3% Blacks; it is well-known that despite a worse cardiovascular risk profile, black Americans have significantly less CAC than white Americans [19, 20]. Lastly, in Newman's study 33.2% of the cohort had clinical cardiovascular disease, 33.4% subclinical cardiovascular disease and 33.45%- no history, while in our study we excluded individuals with previous history of CAD.

Whereas the status of coronary artery calcium as a marker of increased cardiovascular risk is well established, the indication for testing continues to be a topic of debate. The use of CAC is considered to be an age-dependent phenomenon and most studies on CAC have not included older people. Elias-Smale *et al.* show that CAC is a strong and independent predictor of CHD in the older also and improves cardiovascular risk prediction [21]. Also, Raggi *et al.* show that elderly without CAC have a good outcome compared with high CAC [22].

In contrast with some physicians believes that CAC in older adults is universal and so the estimation of CACS is under question, in our study we reported that several individuals had no CAC, especially females. In this study, we defined the levels of CAC in asymptomatic older individuals with no previous history of CHD and we found that the range of calcification is broad, while male gender and age are strongly associated with the amount of CAC. In females the CACS reached the levels of males CACS with a delay of 10 years. The assessment of CACS is a useful tool in older individuals, as it can confirm the presence of CAC. In this way the abnormal levels of calcium may place patients into a higher risk group in terms of future events, and lead to more aggressive treatment with preventative therapies.

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DECLARATION OF CONFLICTING INTERESTS

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