

Original paper

Correlation between Coronary Calcium Score and Severity of Coronary Artery Disease in Coronary CT-Angiography

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Abstract

Background: The presence of calcification in the epicardial coronary arteries indicates that the patient has coronary atherosclerosis, CT scan is a reliable noninvasive investigation to detect the degree of coronary calcification.

Aim: to study correlation between the degree of coronary calcification and severity of coronary artery stenosis by CT-angiography

Patient and method: one hundred and seventy-five patient ,119(68%) are male and56 (32%) are females. mean age is 55.52for males &55.30 for females, who was referred to the Iraqi Medical center in Karbala for CCTA between october2009- Nov.2013. They have either clinical diagnosis of CAD or chest pain suggestive of CAD. They were studied using CT-64 slices, initially by smart score to assess their calcium level using Agatston score, then contrast given to complete the examination, all coronary arteries were studied for any stenosis. The result was analyzed using SPSS 19.

Results & Discussion: There is statistically significant positive correlation (P value less than 0.005) between the degree of CAC score and the degree of vascular obstruction, also with the number of diseased vessel. It also revealed that 12.9%. of symptomatic patients with negative calcium score may have obstructive lesion although of fewer vessel & of mild obstructive lesion

Conclusion: in symptomatic patient CAC score reflect the severity of CAD especially if it is of high degree but in the absence of calcification it does not exclude presence of diseased vessel.

Keyword: coronary artery disease, coronary calcium, coronary CT-Angiography

Abbreviations: CAD: coronary artery disease. CAC: coronary artery calcium, CCTA: Coronary Computed Tomography Angiography

Introduction

Atherosclerosis is a diffuse disease that affects many arteries of the body not just the coronary arteries. In the early stages, it causes changes in the walls of the arteries with increases in cholesterol content and scar tissue. In later stages, it causes plaques that thicken the wall of the artery and in some cases it cause narrowing of the center of the artery so that the flow of blood is gradually reduced. At this stage, calcium is generally present in the plaques⁽¹⁾. Coronary artery calcium is typically present in direct proportion to the overall

extent of atherosclerosis, although typically only a minority (approximately 20%) of plaque is calcified.⁽²⁾

Coronary artery calcification is an independent risk factor for coronary heart disease, with even low coronary calcium scores doubling the risk of coronary events⁽³⁾. The relative risk associated with coronary calcification is greater than that associated with established factors, such as smoking, hypertension and diabetes mellitus. The progression of coronary artery calcification is associated with a higher incidence of coronary events, even in those people who are asymptomatic at

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the time of initial scanning ⁽⁴⁾. Thus, the presence of coronary artery calcification is not only indicative of atheromatous plaque disease, but its progression may correspond with cardiovascular event rates.

The availability of a noninvasive technique to detect coronary calcification makes it possible to obtain direct information on the presence of atherosclerosis in the coronary arteries. The sum of the area and density weightings across the coronary arteries is the unit less calcium score originally defined by Agatston and colleagues. Other quantification methods are available, including a calcium volume determination and mass score ⁽²⁾. As a non-invasive measure of overall coronary artery disease burden CAC testing is a clinically useful screening test for coronary atherosclerosis. It is currently recommended by ACCF/AHA guidelines in select asymptomatic patients ^(5&19)

The detection and quantification of coronary artery calcification (CAC) significantly improves cardiovascular risk prediction in asymptomatic patients. Many have advocated for expanded CAC testing in symptomatic patients based on data demonstrating that the absence of quantifiable CAC in patients with possible angina makes obstructive coronary artery disease (CAD) and subsequent adverse events highly unlikely. However, the widespread use of CAC testing in symptomatic patients may be limited by the high background prevalence of CAC and its low specificity for obstructive CAD ⁽⁷⁾

Some studies shows that modern coronary CTA has proven to be the most sensitive noninvasive modality to evaluate suspected coronary artery disease in patients with stable or acute chest pain syndromes ^(8&9)

It is well established that the detection of coronary calcium indicates an increased risk of incident CAD above that predicted by standard risk factors, from 2-fold for scores of up to 100 and increasing to 11-

fold for scores above 1000. Similar findings are shown for gender and ethnicity from the Multi-Ethnic Study of Atherosclerosis ^(2&19). Also other study shows CAC volume was positively and independently associated with CAD and CVD risk at any level of CAC volume.

In the CORE 64 prospective multicenter trial of patients with suspected symptomatic CAD referred for conventional coronary angiography, 64-slice CCTA had a patient-based sensitivity of 85% and specificity of 90% (excluding patients with a calcium score greater than 600) for detecting stenosis 50% or greater. However, the NPV of 83% in this study was lower than in other studies ⁽¹⁹⁾

Patients with ischemic heart disease have been found to have a very high incidence of coronary artery calcification at autopsy ⁽¹¹⁾

Patient & Method

CT data of one hundred seventy-five patients, One hundred & nineteen (68%) are males, 56 (32%) are females mean age is 55.52 for males & 55.30 for females were studied between October 2009 to Nov. 2013.

They were referred as symptomatic patient, either they are diagnosed to have CAD to assess the extent of their disease or they have chest pain suggestive of CAD but not confirmed. Eleven case have stent but they got recurrent complaint of chest pain.

All underwent 64-slice coronary CTA in our institution the data were retrospectively reviewed to identify their calcium score using Agatston scoring system by studying the smart score. A test is considered to be positive if calcification is detected within the coronary arteries. Absolute Agatston scores of less than 10 is grade 1, 11 to 99 is grade 2, 100 to 400 is grade 3, and above 400 is grade 4. Then accordingly it is proposed to categorize individuals into groups having non , minimal, moderate, or extensive amounts

of calcification, respectively. These calcium score result is correlated with the result of their CTA. The results of the CTA study were for the degree of obstruction & the number of blood vessel affected.

The data were analyzed using SPSS program using Pearson Chi-Square coefficient correlation factor to study the correlation between the variable of CAC score, number of vessel affected & degree of stenosis. T-test is used to show the statistical significance.

The protocol used for doing the CTA

The institutional review board approved the study, the patients are well informed about the procedure & their consent is taken.

All CT examinations were performed by a 64-slice CT scanner (light speed VCT 64, GE Medical Systems, France) with retrospective ECG gating, the examination consist from two steps: Patients with a heart rate greater than 75 beats/min were pre medicated with an oral dose of 40 mg propranolol for three days before the scan. Sublingual nitroglycerine was delivered to the patient just before the procedure. For venous access, an upper extremity vein (antecubital vein of the right arm) and a 20-gauge IV cannula was used.

In the first step is the calcium score assessment, scan protocol “non- contrast Smart Score cine, 120kv / 430mA / 0.625mm/ 0.35sec “, (latter on the data reviewed on GE advantage work station version 4.4 using the Smart score 4 software)

The second step of examination is coronary angiography & the scan protocol is given in Table 1. A total of 80–85 mL of contrast media with high iodine concentration (≥ 350 mg/mL) was injected with a flow rate of 5 mL/s, followed by a 20 mL saline wash out. The scan timing was determined with smart preparation technique by placing the region of interest over the proximal ascending aorta and start exam after getting the best contrast concentration on monitor phase images.

Raw spiral CT data were reconstructed in various phases of the cardiac cycle to obtain images with the highest quality (without motion artifact). Reconstruction performed at 75% of R-R interval was found to be optimal for image analysis in most patients & 40%- 80% of the R-R interval in some patients.

Image analysis

Images reconstructed at the optimal phase were transferred to another workstation (advantage work station 4.4 by GE) where image analysis was performed. All images were reviewed first in axial projection, then with post processing tools such as multiplanar reconstructions (MPR), curved planar reformat (CPR), thin-slab maximum intensity projection (thin MIP), and volume-rendering technique (VRT) with transparent background display.

All CT examinations were reviewed by a radiologists experienced in cardiovascular radiology & cardiovascular physician

Table 1. Scan protocol of 64-slice coronary CT angiography Scan protocol (GE light speed VCT 64)

Tube current	automatically modified
Tube voltage	120 kV
Tube rotation time	350 ms
Section thickness	0.6
Increment	0.22
Field of view	10.8 cm
ECG gating	Retrospective

Results

The study result is that there is a positive correlation between the degree of calcification and the severity of the coronary artery stenosis on one hand and the number of the diseased vessel in the other hand as it will be presented below in Table 2&3.

Sixty-two out of 175 patients (35.4%) of who has no calcification (grade 0) fifty-four of them (87.1%) have normal coronaries, eight (12.9%) have coronary artery disease, five of them 8% have one vessel disease (one less than 70%, four more than 70%) & three 4.9% have two

vessel disease(one have two vessel less than70% &two have two vessel disease more than70%).

Tabl 2. Calcification * diseased vessels Cross-tabulation

Calcification		diseased vessels							Total	
		normal	one vessel less than70%	one vessel more than70%	two vessels than70%	two vessel more than70%	three vessel less than 70%	three vessel two of them more than 70%		three vessel more than 70%
Non	Count	54	1	4	1	2	0	0	0	62
	% within Calcification	87.1%	1.6%	6.5%	1.6%	3.2%	.0%	.0%	.0%	100.0%
	% within diseased vessels	70.1%	10.0%	20.0%	11.1%	8.3%	.0%	.0%	.0%	35.4%
grade1	Count	20	5	5	3	4	0	0	1	38
	% within Calcification	52.6%	13.2%	13.2%	7.9%	10.5%	.0%	.0%	2.6%	100.0%
	% within diseased vessels	26.0%	50.0%	25.0%	33.3%	16.7%	.0%	.0%	5.3%	21.7%
grade2	Count	3	3	6	4	5	2	4	2	29
	% within Calcification	10.3%	10.3%	20.7%	13.8%	17.2%	6.9%	13.8%	6.9%	100.0%
	% within diseased vessels	3.9%	30.0%	30.0%	44.4%	20.8%	33.3%	40.0%	10.5%	16.6%
grade3	Count	0	1	1	1	9	3	1	5	21
	% within Calcification	.0%	4.8%	4.8%	4.8%	42.9%	14.3%	4.8%	23.8%	100.0%
	% within diseased vessels	.0%	10.0%	5.0%	11.1%	37.5%	50.0%	10.0%	26.3%	12.0%
grade4	Count	0	0	4	0	4	1	5	11	25
	% within Calcification	.0%	.0%	16.0%	.0%	16.0%	4.0%	20.0%	44.0%	100.0%
	% within diseased vessels	.0%	.0%	20.0%	.0%	16.7%	16.7%	50.0%	57.9%	14.3%
Total	Count	77	10	20	9	24	6	10	19	175
	% within Calcification	44.0%	5.7%	11.4%	5.1%	13.7%	3.4%	5.7%	10.9%	100.0%
	% within diseased vessels	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

When we proceed to grade one of calcification which is 0-10 on Agatston grading we have 38 patient (21.7%) out of 175 patient within this grade, 20 (52.6) have normal coronaries, 18 (47.4%) have

coronary stenosis of variable severity & number of diseased vessel as follow: ten (26.4%) have one vessel disease, {five (13.2%) less than 70%stenosis, other five (13.2%) more than7 0% }. Seven (18.4%)

have two vessel disease {four of them (10.5%) the stenosis is less than 70%, three (7.9%) have stenosis more than 70 %}.One (2.6) have three vessel disease over 70%.

Patient who have grade two of calcification which is 10-100 on Agatston the followings results: the number of the patient in this category is 29 patient (16.6%) of the total sample, only three (10.3% of those 29 patients) has normal coronary study while the remaining 26 (89.7%) has diseased coronary arteries.

The 3rd group who have calcification score over 100- 400 according to Agatston scoring system involve 21 patient(12%) of the total sample.no one have normal

Table-3 Chi-square Tests

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	161.399 ^a	28	.000
Likelihood Ratio	175.115	28	.000
Linear-by-Linear Association	106.054	1	.000
N of Valid Cases	175		

coronary artery all have some variable of number of diseased vessel with variable severity of stenosis Table 2

The 4th grade of calcification which is over 400 there is 25 patient (14.4%) of the total sample all have diseased coronaries as in grade 3 but the coronary lesion is more severe & the number of diseased coronaries is more.

When the result analyzed by SPSS version 19 & studding the chi square using Pearson correlation coefficient it reveals a positive statistically significant results between the CAC score and CAD with P value of less than 0.005 as seen in tables 3&4.

Table 4. Calcification degree & diseased vessels Cross-tabulation (summary)

Count

	diseased vessels								Total
	normal	one vessel less than70%	one vessel more than70%	two vessel less than70%	two vessel more than70%	three vessel less than 70%	three vessel two of them more than 70%	three vessel more than 70%	
Calcification Non	54	1	4	1	2	0	0	0	62
grade1	20	5	5	3	4	0	0	1	38
grade2	3	3	6	4	5	2	4	2	29
grade3	0	1	1	1	9	3	1	5	21
grade4	0	0	4	0	4	1	5	11	25
Total	77	10	20	9	24	6	10	19	175

Discussion

The detection and quantification of coronary artery calcification (CAC)

significantly improves cardiovascular risk prediction in asymptomatic patients. The use of CAC testing in symptomatic patients has traditionally been limited due

to fundamental concerns thought to limit its accuracy and/or diagnostic efficiency ⁽⁷⁾

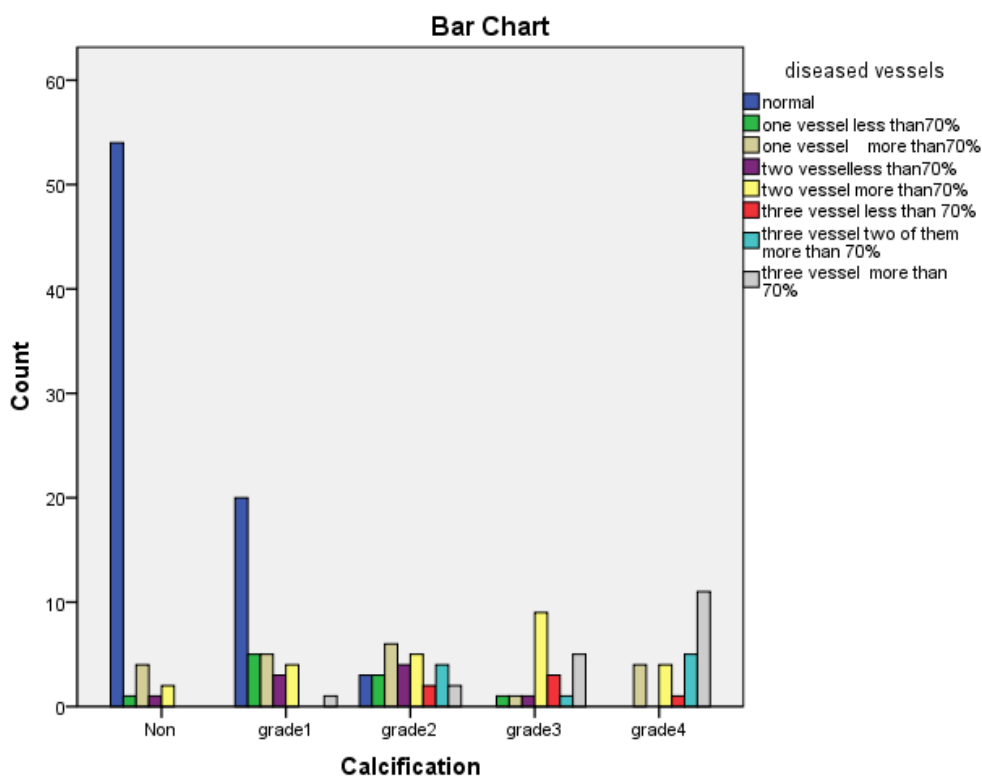
The CAC score has been proposed as an alternate approach for stratification of global cardiac risk, evaluation of chest pain patients and prediction of future cardiac events ⁽¹²⁾

The result of this study which was done on symptomatic patients to study the

diagnostic value of CAC for CAD In general it shows positive correlation between the degree of calcification of the coronary artery disease and to both severity of the stenosis &the number of diseased vessel.as seen in tables number 3&4, this increment is of statistical significance with P value less than 0.005

Table 5. percentage of patient number in each calcium grade to the total patient &percentage of patient among each calcification grade having coronary disease

Calcification Grade	Percentage of patient in each grade of calcification	Percentage of patient have CAD
0	35.4%	12.9%
1	21.7%	47.4%
2	16.6%	89.7%
3	12.0%	100.0%
4	14.3%	100.0%



Graph 1. Correlation between degree of calcification ,number diseased coronary artery its severity

In patients where there is no calcification only 12.9% have coronary artery disease of mild severity mostly one to two vessel disease & less than 70%. with more increment of degree of coronary calcification to grade 2 (10-100 on

Agatston scale) the degree of coronary disease jump to (47.3%) with increase in the severity of coronary stenosis & number of diseased vessel This increment in both the degree of obstruction & number of diseased artery reach 100% in patients

who have grade 4 calcification as seen in in table-2

In comparative with other studies, one done in Netherland by van Werkhoven Et al ⁽¹³⁾, on symptomatic patient where study include 576 patients with suspected coronary artery disease (CAD), CAC score and CTA were performed , CAC score was categorized into three grades as 0, 1 to 400, and >400 the result of the study shows CAC score In patients with CAC score 0, prevalence of significant CAD increased from 3.9% to 4.1% and 14.3% . In grade 2 of CCS 36.2, & in grade 3 (81.1%). The result also shows escalating association of CAC score & CAD which is compatible with the result of this study as seen in the comparative table –6 between our results & Werkhoven result They conclude that non-enhanced computed tomography for calcium detection is a reliable means to exclude obstructive CAD in stable, symptomatic patients ⁽¹³⁾

Although in other studies the use of CAC testing in symptomatic patients has traditionally been limited due to fundamental concerns thought to limit its accuracy and/or diagnostic efficiency as mentioned before ⁽⁷⁾

There are many Studies regarding the diagnostic accuracy of CAC testing in symptomatic patients have generally reported high sensitivity and negative predictive values (NPV) for obstructive CAD in the absence of coronary artery calcification ⁽⁸⁾

calcium scoring may miss non calcified plaques, which may have clinical

importance .In symptomatic patients with a CAC score of 0, obstructive CAD is possible and is associated with increased cardiovascular events ⁽¹²⁾ Sixty two patient of this study sample have normal calcium score 12.9% of them have diseased coronary artery although of mild severity, this finding is going with other studies done recently by investigators from the Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter registry (CONFIRM) evaluated 10,037 symptomatic low-intermediate risk patients undergoing ≥ 64 slice CCTA and found high sensitivity and NPV for the detection of any stenosis $\geq 50\%$ (sensitivity 89%, NPV 96%) and $\geq 70\%$ (sensitivity 92%, NPV 99%), respectively ⁽¹⁴⁾

Within this cohort more than 13% of patients with CAC = 0 had non-obstructive CAD (purely non-calcified plaque), and 3.5% and 1.4% had a stenosis $\geq 50\%$ and $\geq 70\%$, respectively i.e. totally 16% of the total patient they studied ,however other study done by a sub-study of the Coronary Evaluation Using Multi-Detector Spiral Computed Tomography Angiography Using 64 Detectors (CORE 64) multi-center trial demonstrated that among 291 high risk symptomatic patients with suspected ACS, 19% of those with CAC = 0 had at least one segment of $\geq 50\%$ stenosis on subsequent ICA , (13) also other study Of the 357 patients with a zero calcium score, 37 (10.36%) had atherosclerotic plaques; 9 patients (2.52%) had significant coronary stenosis ⁽¹⁶⁾

Table 6. comparative results of this study with variable studies for presence of CAD in patient with zero calcium score

Calcium score	This study	van Werkhoven Et al	CONFIRM	CORE 64	Oncel G, Oncel D
ZERO SCORE	12.9%	14.3	16%	19%	10.36
GRADE3	100%	N/AV	81.1%	N/AV	N/AV

So the result of this study is near to four studies .14.3 for 1st study, 16% for 2nd study, 12.9% for the underlying study &

19% for the 3rd study &10.36% for the last study

This confirm the previous studies that the value of CAC 0-1 in symptomatic patient carry high NPV, while it is valuable in asymptomatic & low to intermediate risk patients,

In patient with higher grade of calcification Agatston grade 2-4, this study reveal significant increment of degree of obstructive lesion & number of diseased blood vessel which is of high statistical significance with P value of less than 0.005, where there is 100% in grade 4 of CCA score have CAD in this study & 81.1% in the study by van Werkhoven Et al ⁽¹³⁾, (Table-5&6)

Although there is discrepancy among existing heterogeneous data regarding the accuracy of binary CAC testing suggests that there is a need for prospective studies assessing the clinical outcomes, cost and safety of this approach prior to widespread clinical adoption of early CAC score testing in symptomatic patients. in the 2012 ACCF/AHA guideline for the diagnosis of patients with potential stable ischemic heart disease, binary CAC score testing in symptomatic patients was given a class IIb recommendation (level of evidence 'C'): may be considered; so additional studies are needed; in this divergence of opinion ⁽¹⁷⁾

However some authors recommend direct invasive coronary angiography for those with high calcium scores (>400) despite atypical symptoms and a lack of any testing suggesting ischemia ⁽¹⁸⁾

Conclusion

1- Based on the data discussed above, when taken in aggregate, CAC testing in symptomatic patients performs reasonably well for excluding significant CAD based primarily on its high sensitivity and NPV. However, widespread endorsement of this approach should be cautioned for several reasons ,CAC scoring is a marker of CAD burden and not a direct anatomic or physiologic assessment of

stenosis or ischemia, respectively, the primary features that typically guide treatment in symptomatic patients.

2- Negative CAC does not exclude the presence of CAD but it makes it less likely & if present it will be of mild severity.

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