

## ROLE OF CORONARY CALCIUM SCORE AS A SCREENING TOOL FOR EXCLUDING SIGNIFICANT CORONARY ARTERY DISEASE IN HIGH RISK ASYMPTOMATIC PATIENTS

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### **ABSTRACT:**

#### **OBJECTIVES:**

To determine correlation of zero coronary artery calcium score (CACs) with non-significant coronary artery stenosis by using computed tomography coronary angiography (CTCA).

#### **METHODOLOGY:**

62 patients with suspected coronary artery disease (CAD) underwent CACS test and CTCA from April 2018 to November 2020. Patients were examined with 160 slice multidetector CT and grouped according to their age, gender, CACS, and maximum coronary luminal stenosis. CACS was assessed using Agatston scoring and degree of stenosis was assessed by automatic software and severity was scored according to CAD-RADS. The correlation between these two main variables was calculated using Spearman rank correlation.

#### **RESULTS:**

The 62 patients were divided into four groups according to CACS, using the Agatston Unit (AU). Group 1; 0 AU (41 patients, 66.13%), Group 2; 1-100 AU (13 patients, 20.97%) Group 3; 101-400 AU (4 patients, 6.45%), Group 4; 401-1000 AU (4 patients, 6.45%). In 41 patients with zero calcium score (32 males and 9 females), 38 patients (92.68%) were found to have no coronary artery stenosis, 2 patients (4.87%) had mild coronary artery stenosis and 1 patient (2.43%) had moderate coronary artery stenosis. Total 35 patients presented for screening purpose out of which 25 (71%) had zero calcium score and no significant coronary artery disease.

#### **CONCLUSION:**

In high risk patients, zero calcium score excludes significant coronary artery stenosis (50%), hence coronary calcium score is a good screening tool before subjecting patients to coronary angiography.

**KEYWORDS:** Coronary Calcium Score, Coronary Artery Disease, Agatston Score, Framingham Risk Score

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#### **INTRODUCTION:**

Cardiovascular disease is one of the leading causes of death worldwide and coronary artery disease (CAD) accounts for half of all such deaths<sup>1,2</sup>. According to the 2017 National Health Interview Survey in USA, the age-adjusted prevalence of all types of heart disease was 10.6%; the corresponding age-adjusted prevalence of heart disease among whites, blacks, Hispanics, and Asians was 11.0%,

9.7%, 7.4%, and 6.1%, respectively<sup>3</sup>. A study conducted in Pakistan, comprising 2000 subjects showed 125 subjects (6.25%) with documented ischemic heart disease (IHD). The disease burden of IHD was therefore estimated as 5.09375 million with this prevalence<sup>4</sup>. Coronary artery calcification is a direct result of atherosclerosis. Non-invasive coronary artery imaging with computed tomography coronary angiography (CTCA) is a highly evolved method for the management of patients suspected of having coronary artery disease (CAD)<sup>5</sup>. Agatston et al developed the "Agatston score" which is currently the standard for measuring CACS<sup>6</sup>. The Agatston score has been shown to be related to the number of stenosed vessels determined by coronary angiography<sup>7</sup>. Coronary calcium is the result of mural atheromatous plaque except for patients with renal failure, who may also have medial calcification. Japanese researchers confirmed that an elevated CACS determined by using CTCA is an independent predictor of mid-to long-term cardiovascular mortality and morbidity in patients that are suspected of having CAD<sup>8</sup>. The recommendation of CACS by unenhanced CT as an initial diagnostic test, in a rapid access chest pain clinic (RACPC), for patients with stable chest pain has been tested prospectively by Yerramasu et al In the patients with zero CACS only 1.5% had obstructive CAD and only 0.8% underwent revascularization. It was concluded that in patients with stable chest pain symptoms and low likelihood of CAD the absence of obstructive CAD can be safely predicted by the absence of detectable coronary calcification in an unenhanced CT. Patients with CACS of >400 AU were found to have a high prevalence of obstructive CAD and further investigation in the form of invasive coronary angiography or functional imaging were considered to be more suitable rather than CTA. These results are in line with the NICE guidelines for the investigation of stable chest pain<sup>9</sup>. CACS has been found to help in risk classification in patients with chest pain, even in the absence of prior risk factor screening<sup>10</sup>. Additionally CACS can identify patients in whom interventional angiography might be a better option, as the final decision regarding CAD management cannot be made on CTA<sup>11</sup>. The aim of this study was to determine whether zero calcium score could exclude significant plaque disease and to determine the correlation between coronary calcium score and maximum coronary luminal stenosis in the evaluation of CAD and obviate unnecessary CTCA or more invasive angiography.

## METHODOLOGY:

This was a cross-sectional descriptive study carried out from April 2018 to November 2020, in Lady Reading Hospital Peshawar. All the Subjects were referred for CTA by their physicians from hospital OPD and from the private sector. The sampling technique was non-probability consecutive sampling. All the included patients were asymptomatic and sent for screening purposes as per inclusion criteria. Patients were evaluated by their physician regarding high risk for CVD according to Framingham risk score which included age, gender, systolic BP, high cholesterol, smoking and the presence of diabetes. Patients who had undergone percutaneous or surgical myocardial revascularization, patients with history of acute coronary syndrome or cardiomyopathy of ischemic cause and heart rate >70 with optimal beta blocker were excluded. The study was approved by the research and ethical committee of the hospital. CCTA of coronary arteries were performed using a 160-slice multi-slice CT scanner (Toshiba model cxxg-012a, prime Aquilion Japan Aquilion 64™-Toshiba™ Medical Systems). An oral beta blocker, metoprolol 50 mg, was administered 30 minutes before the test in patients with sinus rhythm and heart rate (HR) >70 bpm to bring it down to less than 70 bpm. The study was conducted in two phases: in the first phase, CS was determined by the Agatston score with non-contrast computed tomography using longitudinal scan coverage from the level of the tracheal bifurcation to the lower border of cardiac silhouette, including the diaphragm for evaluation of the whole cardiac area. A field of view (FOV) of 200 mm, slice thickness of 2.5-3 mm and interval 1.25-1.5 mm, 2x32x0.6 mm collimation, rotation time of 350 msec and tube current up to 350-450 mAs was used. Calcification was defined as the presence of a lesion with an area greater than 1 mm, and peak intensity equal to or greater than 130 Hounsfield Units (HU), which was automatically identified and marked with color by the software. In the second phase, CCTA was performed using the same CACS parameters for FOV construction, voltage 120 kVp, and 400 mAs. Up to 1.5mL/kg iopamidol, which is a nonionic and iodinated contrast, was administered intravenously to patients at concentrations of 350-370 mg/mL and rate of 4.5-5.5 mL/s (Ultravist® 370, Bayer Health Care and Pharmaceuticals). Images were initially reconstructed at the mid-diastolic phase (70% of R-R interval) of the cardiac cycle. Additional reconstruction windows were constructed after examination by using maximum intensity projection

and volume rendering technique. Images were sent to the workstation for analysis of coronary arteries by radiologists having level 1 and level 2 UK accreditation. The degree of coronary luminal narrowing was measured both by automatic (software) and manual method by calculating the area of the narrowest part of the lumen in relation to the area of the lumen immediately distal to the same segment. Coronary stenosis severity was scored qualitatively according to CAD-RADS™ i.e. minimal <25%, mild 25-49%, moderate 50-69%, severe 70-99%, and occluded 100%. Significant stenosis was defined as  $\geq 50\%$  of the luminal narrowing<sup>12</sup>. All the patients' information including name, age, gender, chief complaints (chest pain, dyspnea) were recorded. Data was entered and analyzed in statistical software SPSS (version 23). Mean and standard deviation was calculated for continuous variables i.e., age, and frequencies and percentages were calculated for categorical variables i.e., gender, coronary calcium score and coronary artery stenosis. Correlation between calcium score and coronary artery stenosis was calculated using Spearman rank correlation and p-value of less than 0.01 was considered significant.

## RESULTS :

Table 1: Calcium Score Vs. Luminal Stenosis

Coronary Calcium Score	Coronary Luminal Stenosis					
	Normal	Minimal	Mild	Moderate	Severe	Total
0	38	0	2	1	0	41
1-100	0	4	3	4	2	13
101-400	0	0	4	0	0	4
401-1000	0	0	0	2	2	4
Total	38	4	9	7	4	62

## DISCUSSION :

The use of CAC score in asymptomatic subjects at intermediate risk is considered appropriate and is recommended as evidenced by international consensus statements like 2010 ACCF/SCCT/ACR, 2014 ACR. The risk assessment was done using traditional clinical stratification methods, such as the Framingham risk score<sup>1</sup>. CTCA has proven to have a higher negative predictive value for CAD than stress echocardiography. However, a normal SE and CAC score of zero excludes obstructive CAD (NPV 100%) and any CAD in 92% of the patients. CT calcium scoring adds incremental risk stratification, especially in patients with low Framingham score<sup>13</sup>. A meta-analysis done by Sarwar et al published in 2009,<sup>14</sup> which included 13 studies with a collective

In the study period from April, 2018 to November 2020, a total of 62 patients with mean age of  $49 \pm 3$  years were subjected to CACS examination in Lady Reading Hospital Peshawar. Patients were divided into four groups according to CACS using the Agatston unit (AU). Group 1 included 41 patients (66.13%) with 0 calcium score, 13 patients (20.13%) in Group 2 with calcium score between 1-100 AU, 4 patients (6.45%) in Group 3 with CACS 101-400 AU and 4 patients (6.45%) in Group 4 with CACS 401-1000 AU. The associated degree of stenosis in the coronary bed is cross tabulated in Table 1. In 41 patients with zero calcium score (78% male, 22% female), 38 patients (92.68%) were found to have no coronary artery stenosis, 2 patients (4.87%) had mild coronary artery stenosis and 1 patient (2.43%) had moderate coronary artery stenosis. A total of 35 patients presented for screening purpose out of which 25 (71%) were having zero calcium score and no significant coronary artery disease. Result of Spearman's rank correlation indicated that there was a strong correlation between calcium score and coronary artery luminal stenosis (rs) [62]=0.872,  $p < 0.001$ .

total of 29,312 patients showed that a cardiovascular event occurred in 0.47% of the patients with a zero CACS and in those with a positive score 4.14% had such an event, this corresponds to a relative risk of 0.15 (95% CI: 0.11-0.21;  $p < 0.001$ ). Regarding significant stenosis on coronary angiography in patients with a CAC score of zero, the same meta-analysis included 10,355 symptomatic patients undergoing catheterization due to suspected CAD or acute coronary syndrome. A stenosis of  $>50\%$  was observed in 56% of the patients, of whom 98% had a positive CAC score i.e. 2% had zero calcium score. This data, taken together, shows that a positive CAC score, as a predictor of stenosis  $>50\%$ , has a sensitivity of 98%, a specificity of 40%, a negative predictive value (NPV) of 93%, and a positive predictive value (PPV) of 68%<sup>10</sup>. Based on

this high NPV, some authors suggest that patients with a CAC score of zero would not require further ancillary examinations<sup>1</sup>. In a study conducted by Moradi et al in Iran, out of the 385 patients with a zero calcium score, 4.2% had atherosclerotic plaques, and only 1.6% had significant (>50%) coronary stenosis, and 2.6% had no significant (<50%) coronary stenosis, with hyperlipidemia, diabetes and smoking as significant associations<sup>15</sup>.

There have been a few studies in which a higher percentage of patients with zero CS were found to have obstructive disease. In a study by Akram et al it was shown that symptomatic subjects and those >45 years of age had atherosclerotic plaque with zero CS (8.4%)<sup>16</sup>. In an original study done in Brazil, the main finding was that there was a considerable presence (9.3%) of obstructive ( $\geq$ 50%) coronary atherosclerotic plaques in patients with zero CS. However, there were clinical features found to be associated with this high percentage along with alcohol consumption and absence of obesity<sup>17</sup>. A study conducted in Peshawar showed about 9.3% of patients having significant coronary stenosis with zero calcium score in patients having atypical chest pain or equivocal result on ETT<sup>18</sup>, while our study showed 2.4% patients having significant stenosis with zero score. The difference in the results from our study and some of the studies might be due to the fact that the majority of our patients were asymptomatic and were sent for screening purposes. Our results are in accordance with international studies i.e. 2% in Neves et al<sup>1</sup>, 0.3% in Rosen et al<sup>19</sup> and 0.6% in Iwasaki et al<sup>20</sup>. Therefore, it can be safely concluded that zero calcium score obviates the need for more invasive methods in high-risk asymptomatic patients.

#### LIMITATIONS:

CACS as a screening tool for asymptomatic patients is very scarcely advised due to ionizing radiation and along with that, our study started in April 2018 and continued through the first year of COVID lockdown. Later it had to be terminated due to even lesser patient flow in the pandemic, so the number of patients was less than what we had initially anticipated.

#### CONCLUSION:

In high-risk asymptomatic patients, zero calcium score nearly excludes significant coronary artery (50% luminal stenosis), hence coronary calcium score is a good screening tool before subjecting patients to more invasive coronary angiography.

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