Value of calcium scoring in addition to myocardial perfusion imaging in patients with coronary artery disease

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Abstract:

Background: coronary artery disease possible to have existed with little or no signs, or it may quickly develop to an abrupt arterial closure of the artery with catastrophic outcomes and possibly resulting in sudden death as initial presentation.

Death rates due to coronary artery disease (CAD) have fallen dramatically over the last 20 years, mostly due to improved diagnosis and treatment of people with known or suspected CAD. Improvements in the assessment of known or suspected CAD individuals beside safe guidance for treatment choices have been made possible by the increasing use of noninvasive imaging methods. And thus, there is a continuous searching for new noninvasive techniques for early detection of CAD.

Aim of work: This study aimed to determine the correlation between MPI and CAC scoring in individuals with various CAD risk factors, as well as the diagnostic role for CAC scoring in CAD diagnosis.

Patients and Methods: the present study included fifty individuals who were recruited from Nuclear Medicine unit at Kasr Al-Aini Hospital (NEMROK), Cairo University during the period of October 2017 to February 2018. SPECT Tc-99m SestaMIBI myocardial perfusion imaging was performed over the course of two days using the technique ECG-gated SPECT. Bull's-eye display with 17 segments reflecting the whole myocardium was generated. Additional gated high dose CT images were obtained for the estimation of CAC score, the readings of the CAC score were then compared to those of MPI study.

Results: The study showed that both MPI defect size and severity are strongly correlated with CAC score with mean CAC score in case of normal MPI 155.6+/-152 and in case of abnormal MPI 1096+/-570.9 and p-value <0.0001. We also found that the more the clinical risk the more the CAC score reading and the more the cases with +ve MPI study, that's why we recommended that in low clinical risk score we shall start with CAC scoring if it's found to be discrete or low risk we shouldn't proceed with MPI study instead we go on with CAC score screening, while if the patient initially is intermediate or high risk we shouldn't go for CAC scoring instead MPS is the study of choice.

Conclusions: There is strong correlation between total CACs and MPI defect size and severity. So at the end of our study we highlighted the following: Total CACs can be used as initial imaging procedure in clinically low risk patients with CAD. MPI study should be the first imaging choice in clinically intermediate or high risk patients with CAD.

Keywords: Value – Calcium Scoring – Myocardial – Perfusion Imaging – coronary artery disease

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Introduction:

Among the biggest causes of mortality globally is coronary artery disease (CAD). In the United States, CAD is responsible for almost a third of all deaths among those 35 and older [1,2]. In 18 percent of advanced CAD patients, a sudden arterial closure leading to sudden death, however CAD may present itself with little or no symptoms at all [3].

Over the last two decades, CAD mortality has dropped significantly, in light of more accurate diagnosis and treatment of patients with established or suspected CAD. Noninvasive imaging methods have

improved the assessment of individuals with established or suspected CAD and provided a safe guidance for treatment choices [4].

It is widely accepted that single photon computed tomography myocardial perfusion imaging (SPECT) gives additional advantage above clinical risk factors in the detection of CAD [5]. Electron-beam computed tomography (EBCT) and multi-detector computed tomography (MDCT) seem to be the two most often used fast CT modalities for assessing coronary artery calcium (CAC). Both systems use thin slice CT imaging to eliminate motion artefacts. Usually, 30-40 axial scans are acquired. The calcium scoring method uses the X-ray attenuation coefficient, or CT number, and the area of calcium deposits [6].

Cardiac computed tomography has grown increasingly frequent in the US and other countries in the past 15 years, mostly to identify individuals at risk of obstructive coronary artery disease based on calcium levels in the coronaries [4]. But even though rapid CT has been implemented for two reasons in the previous five to ten years:

(1) to help estimate asymptomatic individuals' risk of coronary heart disease
(2) to evaluate CHD risk in patients presenting with unusual symptoms associated with myocardial ischemia.

Aim of Work:

- Examine the correlation between myocardial perfusion imaging (MPI) and calcium score in individuals with various coronary heart disease risk factors.
- Assess the role of calcium score in CAD diagnosis, in addition to MPI.

Patients and Methods:

The current study was prospective one that implemented over a period from October 2017 till February 2018, on 50 patients [34 males (68%) & 16 females (32%) with mean age 55.8 years]. The study was performed in Nuclear Medicine Unit (NEMROCK center), Cairo University.

All participants included in the present study had the standard ECG-gated single-photon emission computed tomography (SPECT) Technetium-99m SestaMIBI myocardial perfusion imaging (99mTc SestaMIBI). Then additional CT images of the heart were obtained for calcium scoring.

Adult males or females with either symptomatic or asymptomatic CAD were included in the current study, while patients with LBBB, valvular heart disease, acute MI, cardiomyopathy (proved to be non-ischemic), children or pregnant females were excluded.

Methodology and data collection: The data collection sheet included:

- Medical history:

 Personal history: age, sex & habits of medical importance.

 History of present illness:

o Risk factors: diabetes, hypertension, hyperlipidaemia, smoking, history of ischemic heart disease or ICU admission and positive family history for ischemic heart disease.

o Chest pain (onset, course, duration, relation to exertion, sites of radiation, relieving factor).

o History of cardiac investigation (stress ECG, echocardiography, cardiac catheterization) if done.

- General Examination: (pulse rate, blood pressure, height, body weight and body mass index were measured).

- Myocardial perfusion scan (MPS):

 All patients had two-day myocardial perfusion SPECT (rest & exercise stress).

 All cardiac medications were ceased 48-72 hours before the study.

 Fasting for 4–6 hours before the test was advised.

 Fifteen minutes after the 99mTc-Sestamibi injection, fatty meals (egg, milk, chocolate) were given to help the liver and biliary system clearance.

- Stress protocol:

 The standard 12-lead baseline ECG was applied with an intravenous line was kept open. Patients were monitored, throughout the study.

 A modified Bruce approach was used for graded treadmill exercise (Table 1). Following maximal exertion or patient tolerance, the radiopharmaceutical was administered one minute later to maximise tracer extraction.

Table (1): Treadmill Graded modified Bruce protocol [7]

Stage (min)		Total time (min)	Speed (mile/h)	Grade (%)
Standard Bruce protocol	1 (3)	3	1.7	10
	2 (3)	6	2.5	12
	3 (3)	9	3.4	14
	4 (3)	12	4.2	16
	5 (3)	15	5.0	18
	6 (3)	18	6.0	20
Modified Bruce protocol	1 (3)	3	1.7	0
	2 (3)	6	1.7	5
	3 (3)	9	1.7	10
	4 (3)	12	2.5	12
	5 (3)	15	3.4	14
	6 (3)	18	4.2	16
	7 (3)	21	5.0	18

There is no slope in the modified Bruce's starting speed, unlike the standard Bruce, then the speed slightly increased. Older patients and those with physical restrictions may benefit more from this technique.

- *Technology & Processing Radiopharmaceutical:*

Each trial received 15 to 25 mCi (555 to 925 MBq) of 99mTc SestaMIBI according to body weight.

Imaging protocol: Cameras with dual heads and integrated x-ray transmission were used to capture rest/stress gated images (Seimens). utilizing parallel hole low-energy high-resolution collimators, emission data were gathered from the patient in a supine position. The acquisition orbits were body contour across a 180° arc, with 30 pauses and 30 seconds each stop. The image acquisition matrix was 128×128. Images were taken at 140 keV using a 20% symmetric window. Resting SPECT images were taken 45-60 minutes following radiopharmaceutical administration. Stress SPECT images were collected 30–45 minutes after exercise and radiopharmaceutical administration. The RR time acceptability window was 20% for both resting and stress SPECT images that gated via 8 frames per cycle. The attenuation of the stress and supine SPECT pictures was rectified using a low-dose CT based transmission scan as explained subsequently.

- SPECT acquisition parameters:
  - 90° dual-head gamma camera
  - Collimator with low energy consumption and good resolution is used. Photon peak energy is 140 keV, with a 20% energy window.
  - A magnification (Zoom) factor of 1.
  - Matrix: 128×128.
  - Orbit: Non-circular.
  - Patient position: supine with raised left arm.
  - Rotation for Supine SPECT: counterclockwise; 180° from right anterior oblique 45° to left posterior oblique position 135°.
- The CT part:
  - It was acquired at a slice step 1mm. a current of 80 mA, and voltage of 130 KV.
  - The total SPECT/CT time was approximately 25 minutes.
- Gated parameter:
  - Electrocardiogram synchronized data with R wave trigger, 8 frames/cardiac cycle to generate a total of 32 projections (40 s per projection).
- SPECT reconstruction parameters:
  - Filter: Butterworth.
  - Reconstruction: iterative (3D Flash).
  - Images: Short-axis, vertical long-axis, and horizontal long-axis.

A revolving cine monitor was used to check for patient movements in all raw data sets. It was way of preserving the linearity between projected photon counts and pixel values by using the 3D ordered subsets expectation maximisation (OSEM) algorithm and built-in processing to sum the projection data from the ECG-gated SPECT scan, and then reconstruct perfusion images from those results. Cross-sectional cardiac images: Transaxial. coronal and sagittal (short, horizontal long, and vertical long axes), were created using cardiac SPECT software.

Quantitative evaluations

For further analysis, 3D sampling of the entire myocardium was used to convert perfusion images into 2D polar maps or bull's-eye displays generated with circumferential slice count profiles obtained from short-axis SPECT slices, with the apex at the centre and the base of the ventricle at the periphery, which in turn split into 17 segments, each representing a coronary artery, allowing visual evaluation of the degree and extent of perfusion abnormalities for each vascular area8. (Fig. 1).

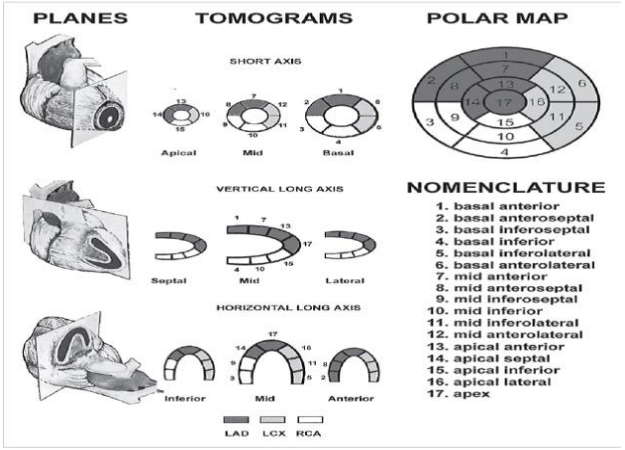

Fig. (1): Cardiac plane definition, including tomograms and polar maps of the standardised 17 left ventricular myocardial segments, as well as their nomenclature and association with coronary vasculature; the LAD, LCX, and RCA8

Perfusion defect measurement and calculation:

- Depending on tracer uptake, each segment was visually rated as: 0, normal; 1, mildly reduced; 2, moderately reduced; 3, severely reduced; and 4, rest and stress images with no tracer absorption.
- Summed rest score (SRS) was calculated by added scores of the 17 segments of the rest images, summed rest score (SSS) was calculated by added scores of the 17 segments of the stress images and summed difference score (SDS) was calculated by subtracting SRS from the SSS scores [8].
- According to the SSS score, patients were classified into normal group (score<4) and abnormal group (score≥4).

Calculation of gated quantitative indices

- Tomographic pictures were utilized to quantify functional properties such as end systolic (ESV) volume, diastolic volume (EDV) and myocardial motion, followed by a calculation of the left ventricle's ejection fraction [9].

$$EF = \frac{EDV - ESV}{EDV} \times 100.$$

Calcium Scoring Imaging protocol:

- Gated CT images were collected using PET/CT scanner (Ingenuity TF 64) from (Philips Healthcare,

Cleveland, OH, USA) combining a modular, LYSO-based PET component with a 64-channel CT component.

Coronary Artery Calcification Detection:

 CACs are identified by analyzing the cardiac detector's zone of interest. Calcification candidates are paired components with HUs more than 130 and a diameter of more than 3mm. The heart valves, the major veins, and the coronary arteries are all potential locations for calcifications. Because of this, additional structures like as pacemakers and other devices with high HU units are also easy to mistake with calcium deposits. CAC is distinguished from other calcifications or artefacts by a series of heuristics. It's based on four observations:

- A lot of muscle around CACs, Blood and cardiac muscle surround calcifications on the major veins or on the cardiac valves. Blood has a standard HU range of [0, 130], while muscle is in the range [−500, 0].
- HU of CACs are much lower than those of metallic implants.
- CACs are surrounded by cardiac muscle, not immediately next to the lungs.
- CACs are smaller than calcifications in the cardiac major vessels.

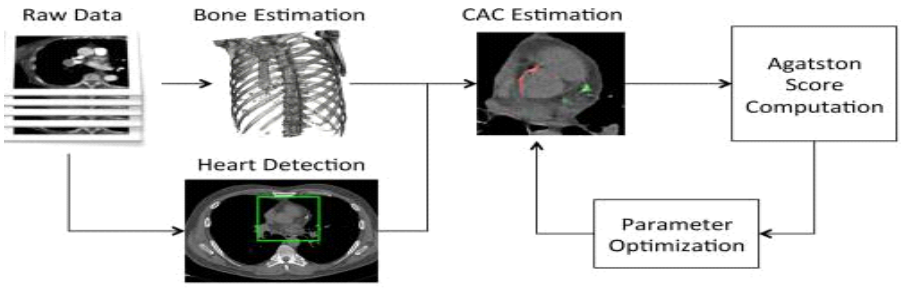

Fig (2): Method overview of CAC scoring

Area/Step method (Agatston):

 The area/step method – the most commonly used scoring method – is based on Agatston score, which takes into account the area of the calcified lesion and the average CT value within the lesion.

 The software used the area of each calcified focus and the peak CT number to compute lesion-specific scores (scored as 1 if 131 to 199 HU, 2 if 200 to 299 HU, 3 if 300 to 399 HU, and 4 if 400 HU or greater) accordance to Agatston's approach.

 Total CAC score was calculated by summing up all lesions in the coronary arteries, including those in the left main, left anterior descending, right coronary arteries, as well as in the left circumflex and right coronary arteries. The total CAC score was used as the principal EBCT/CT measurements in the current study.

Table (2): Area/Step method (Agatston)

Step/weight factor	Value when CT number is equal to or greater than	Value when CT number is less than value
1	Threshold	200 HU
2	200	300 HU
3	300	400 HU
4	400	-

Score for the ROI = (step/weight factor) x (the area of the lesion)
Slice thickness of 3mm is used to normalize the calculated score.

 Study acquisition parameters:

- Scan angle: 240 deg.
- Scan length: 150.0 mm
- Scan time: 0.28 sec
- Image type: axial
- Collimation: 40x0.625 mm
- Slice thickness: 2.50 mm
- Rotation time: 0.40 sec
- Cycle time: 0.5 sec
- Field of view: 220.0 mm
- Voltage: 120 KV
- mAs: 55 mAs

 CAC scoring is measured in each coronary artery separately and then their values are summed and total calcium score is evaluated.

 Results of CAC scoring are then compared to those of MPI study.

Methods of Statistical Data Analysis:

 In order to carry out the statistical analyses, we used SPSS 26 for Windows (SPSS Inc., Chicago, IL, USA).

 The results were expressed as the mean ±SD.

 The t test was used to compare numerical variables between the CAC and SSS scores. A ($p \leq 0.05$) was considered significant.

 Pearson linear correlation was used to examine the CAC score and MPI defect size and severity (SSS).

Results:

Demographic data: The study comprised 50 patients, with a mean age of 55.8 ±10.1 years (34 males, 16 females).

Risk factors of the patients: Regarding the prevalence of risk factors BMI, HTN, smoking, diabetes, dyslipidemia, family H/O, ICU admission and risk of stress condition were recorded within the study group by 64%, 40%, 38%, 34%, 34%, 32% ,26% and 20% respectively.

Clinical risk score analysis: In the current study, the Framingham risk score classified 20 individuals (40%) as low risk, 12 (24%) as intermediate risk, and 18 (36%) as high risk.

Myocardial perfusion SPECT analysis:

Table (3): Myocardial perfusion SPECT analysis in 50 patients of study population

Presentation		Number of cases	Percentage
MPI status	Absent	18	36%
	Present	32	64%
MPI pattern	Negative	18	36%
	Ischemia alone	24	48%
	Ischemia and infarct	5	10%
	Infarct alone	3	6%
Severity of ischemia	Absent	18	36%
	Mild	12	24%
	Moderate	13	26%
	Severe	7	14%
Defect size	Small	9	28%
	Medium	9	28%
	Large	14	44%
No. of segments	<4	12	37.5%
	4-8	14	43.75%
	>9	6	18.75%

Discussion:

Searching a non-invasive, accurate, and early detection of coronary artery disease (CAD) is an ongoing endeavor. The death rate from CAD has dropped dramatically over the last two decades due to earlier identification and improved treatment of individuals with confirmed or suspected CAD. Noninvasive cardiac imaging modalities have greatly improved the assessment of patients with established or suspected CAD4.

The aim of our study was to examine the correlation between myocardial perfusion imaging (MPI) and calcium scoring in individuals with various risk factors for coronary artery disease (CAD).

Our prospective study was done in nuclear medicine unit; NEMROCK center during the period of October 2017 to February 2018. It was carried upon 50 Egyptian referred for myocardial perfusion evaluation.

In our study among 50 patients, we found 32 patients (64%) had +ve MPS, while 18 patients had –ve MPS. Among the 32 patients with +ve MPS 20 patients (40%) were found to be of moderate and severe stress inducible ischemia while 12 patients (24%) were mild stress inducible ischemia according to our 17 segments SSS, SRS and SDS concerning both defect size as well as severity.

In correlation with CAC done by gated CT images we found that among the 20 patients (40%) of moderate to severe ischemia by MPI, only 2 patients (4%) were clinically low risk by Framingham clinical risk score (<10), having mean CAC 981.4+/- 48.

Tiziano Schepis et al. [10] investigated 77 individuals to see whether there was a link between myocardial perfusion abnormalities and CAC, and they found 0% of 12 patients with CAC less than or equal 10 had perfusion defect.

Compared to the previous study, our study revealed 15 patients among the whole 18 patients with normal MPI had mean CAC less than or equal 100 while the remaining three patients had mean CAC 201.5+/- 62.8 (101-400).

Matthew J. Budoff. [11] studied wide number of patients (1195 patients), showed that in patients with CAC< 100 the frequency of +ve MPS was very low <2%, compared to our study we found that in patients with CAC<100 no one (0%) was detected to have +ve MPS (100% -ve MPI).

Also they found on the other end of the spectrum that among the patients having CAC score >1000 only 20% had ischemic MPS in which less than half of them (8.6% of all the patients with CAC >1000) demonstrated moderate to severe ischemia in MPS. While in our study we found that among the whole studied patients 20 of them (40%) had mean CAC more than or equal to 981.14 +/- 48, 100% of the 20 patients showed +ve MPS and 100% of them were moderate to severe ischemia in MPS.

In our study among the 20 patients having moderate to severe ischemia in MPS two patients (4%) were low Framingham clinical risk score (>10) with mean CAC 981+/- 48, 7 patients (14%) were intermediate Framingham clinical risk score (10-20) with mean CAC 1080.9+/- 92 and 11 patients (22%) were high Framingham clinical risk score (>20) with mean CAC 1270.6+/- 180.6, denoting valuable relation between CAC score and MPI stress induced ischemia yet no observed correlation noticed between +ve Framingham clinical risk score and CAC as noticed in all categories of clinical risk as all of them had CAC >400.

Among the whole 50 patients 12 of them (24%) had mild ischemia (SSS <4) in MPS with mean CAC ranging between 339 and 810.8. Those with mild MPS and CAC less than 400 (yet more than 100) were found to be with low and intermediate Framingham clinical

risk score, while those with mild MPS and CAC more than 400 were found to be of high Framingham clinical risk score.

Mansour Almoudi and Zhong-Hua Sun [12], retrospectively studied 48 individuals with probable coronary artery disease who had both multi-slice CT and MPI-SPECT within two weeks.

In these 48 patients, 47% exhibited moderate to severe calcifications with CAC scores above 100, and 42% had abnormal or possibly abnormal MPI tests.

In our investigation, 20 patients (40%) exhibited moderate to severe calcifications with CAC >100, and 91.4% had abnormal or possibly abnormal MPI evaluations12.

Conclusion:

We would like to conclude that:

In 20 patients with low Framingham clinical risk score only two patients (10%) had CAC approaching 1000, and 18 patients (90%) had CAC <400 in which 15 patients (85%) had CAC <100. In 12 patients with intermediate Framingham clinical risk score, 7 patients (58%) had CAC >1000 and 5 patients (42%) had CAC <400. 75% of all patients with intermediate Framingham clinical risk score had +ve MPS out of them 60% showed CAC> 1000 while 15% showed CAC < 400 and the remaining 25% had –ve MPS with CAC < 400. In 18 patients with high Framingham clinical risk score all of them had +ve MPS and all of them had CAC approaching 1000 (more than or equal to 810.8). The above-mentioned data force us to start with CAC scoring in clinically low risk patients, while all the intermediate and high risk groups should be referred to MPS.

Limitations:

- Limited sample size.
- Absence of coronary angiography as a gold standard.
- Absence of follow up for our cases.

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