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Agreement Determination between Coronary Calcium-Scoring and Coronary Stenosis Significance on CT-Angiography

Background/Objective: The most important lesions in coronary artery disease (CAD) are coronary artery plaques, many of which are calcified. Multi-slice spiral CT (MSCT) scanners can concurrently perform coronary calcium scoring (Ca-Score) as a predictor of CAD and coronary CT-angiography (CCTA) as the determining factor in therapeutic decision-making. We aimed to determine the agreement of a Ca-Score more than 100 (based on Agatston technique) with coronary artery stenosis significance on CCTA.

Patients and Methods: Using ECG-gated MSCT, 65 patients who were referred for CCTA were assessed both for their Ca-Score and a significant ($\geq 50\%$ diameter reduction) coronary stenosis, simultaneously. Their total Ca-Score were classified in three groups (a-0, b-less than 100, and c- ≥ 100). The severity of coronary stenosis was categorized to further three groups (1-lack of stenotic lesion, 2- presence of non-significant stenosis, and 3-presence of significant stenosis).

Results: Of 65 patients referred for CCTA, 42 (64.61%) had no CAD, 8 (12.3%) had non-significant lesions, and 15 (23.09%) had significant stenoses. Forty-three (66.2%) out of 65 subjects had a zero, 14 (21.5%) had scores <100 , and 8 (12.3%) had ≥ 100 Ca-Score. In the first group (Ca-score = 0), only one had significant stenosis; while 50% of the patients in the second group (Ca-score < 100) and 87.5% from the third group (Ca-score of ≥ 100) had significant stenosis. Significant coronary stenosis has a moderate-to-good agreement with a Ca-Score of 100 or higher, compared to those with a Ca-Score of less than 100, and this was statistically significant ($P < 0.0001$).

Conclusion: In patients with a calcium score of 100 or more, performing CCTA may be advisable to assess the likelihood of significant CAD.

Keywords: Computed Tomography (CT), angiography, calcium-scoring, coronary artery stenosis

Introduction

Coronary artery disease (CAD) is the leading cause of death in adults in many western countries, and nowadays, both the prevalence and the incidence are increasing in urban regions of Iran, as well. ¹⁻⁴ Atherosclerotic coronary artery calcifications are most frequently found as calcium (Ca) lumps in advanced atherosclerotic lesions (AHA: American Heart Association) plaque type Vb), but may occur as small deposits of calcium in earlier lesions. ⁵

Until recently, cardiac Computed Tomography (CT) applications were almost exclusively directed at detection and quantification of coronary calcium deposits, mainly using Electron Beam CT (EBCT). ⁶ Nevertheless, with development of multi-slice spiral CT (MSCT) scanners, using multiple detector rows (so far, up to 64) and even more recently, dual-source CT scanners, coronary CT angiography (CTA) is now a feasible and minimally invasive technique for detecting and characterizing asymptomatic coronary plaques at a high sensitivity, specificity, and accuracy, and has been suggested as an effective filter before catheter

angiography.^{7,8}

Cross-sectional CTA may visualize the presence and composition of these plaques and quantify the plaque burden better than conventional angiography, which only visualizes the vascular lumen. However, it is not yet well-established how this information would be used to guide patient management.⁹⁻¹¹ Simultaneous performance of Ca-scoring and CTA has resulted in feasibility of comparison of both data to determine agreement between their findings.^{12, 13}

Our study was designed to evaluate the level of agreement between severity of stenosis on CTA and calcium burden, as measured in dedicated CT protocols for Ca-scoring, comparing their results.

Patients and Methods

A population of 65 patients (47 males and 18 females) with clinical indication for non-invasive CT angiographic study of coronary arteries was enrolled in our study during September 2004 through July 2005. The most frequent indications for coronary CTA in our patients were atypical chest pain and equivocal findings in exercise test and/or radionuclide scan. Patients' age range was 26 to 77 years (mean: 52.4 ± 11.8 years). The exclusion criteria were a history of coronary artery bypass graft and/or prior stent placement, as well as lack of sinus rhythm or history of any allergic reaction to contrast agent.

The study was performed using a 4-channel MSCT scanner (SOMATOM Sensation 4, Siemens Medical Solutions, Forchheim, Germany).

Patients were instructed to abstain for 12 hours from all products containing caffeine. If there was an average heart rate higher than 70 beats per minute (bpm), they would receive an oral β -blocker (50-100 milligrams of Metoprolol [Alborztab, Tehran, Iran]), to obtain rates of 60 bpm or less. We first ensured that the patient had no contraindications to beta blockade, such as asthma, atrioventricular block, obstructive airway disease, low cardiac output states, or severe left ventricular dysfunction. A history of contrast agent allergy resulted in deferring performance of CTA, as mentioned above.

Images were obtained with synchronously Electrocardiography (ECG)-gated spiral scanning. Scanning was performed from tracheal carina down to the apex

of the heart, using retrospective ECG-gated reconstruction temporal window settings at 40% to 70% of the ECG peak of consecutive R waves (R-R interval). Scanning parameters for calcium-scoring series were 120 kV and 133 mAs, 500-milliseconds (ms) rotation time, 4×2.5 -mm collimation, and 3.75-mm table feed per rotation; and for the contrast enhanced series (CTA) were as follows: 120 kV and 400 mAs, 500-ms rotation time, 4×1 -mm slice collimation, and 1.5-mm table feed per rotation. A bolus of 120-140 milliliter of a non-ionic contrast medium (Ultravist 320 mgI/ml, Schering, Berlin, Germany) was administered via an 18-gauge cannula through an antecubital vein at a rate of 4 ml/s. Bolus-tracking (CARE Bolus) with continuous aortic monitoring was used to determine scanning start time. Scan data for continuous volume images of the entire heart, based on 1.25-mm slice-width and strongly overlapping increment could be acquired within 30-40 seconds. Three-dimensional reconstructions with about 1-mm slice width and submillimeter increment provided data of adequate quality for visualization of the coronary arteries.

Calcium-score was calculated by Syngo software, on a Wizard workstation (Siemens Medical Solutions, Erlangen, Germany) for the total coronary artery territory and for right coronary artery (RCA), left circumflex artery (LCx), left anterior descending artery (LAD) and left main coronary artery (LMCA), individually. We used Agatston calcium-scoring method for the aforementioned major coronary arteries, both integrally and independently.¹⁴ Coronary artery calcification was defined as the presence of at least two adjacent pixels with a CT-number of at least 130 Hounsfield Units (HU). In each slice, all calcifications along a coronary artery were manually confined as a region of interest and the volume of calcium deposit and the number of all marked calcified lesions were then automatically measured and recorded by the Ca-Score module of Syngo software. Patients' Ca-score category was classified according to Agatston score as follows: (1) Zero Ca-Score; (2) Ca-score more than zero and less than 100; (3) Ca-score equal to or greater than 100. CTA images were reconstructed in the 3D and Vessel View modules of the Syngo software and evaluated with multiplanar reconstruction (MPR), curved-MPR, thin maximum intensity projection (MIP), and volume rendering technique

(VRT) reformats (Figures 1 and 2).

Three radiologists interpreted the images together and a general consensus was achieved in all cases. Patients' coronary CTA category was determined as follows: (1) Coronary artery stenosis of less than 50% diameter narrowing was defined as non-significant CAD; (2) Diameter reduction of 50% or more was defined as significant CAD; (3) If no stenosis or coronary intimal irregularities were detected, coronary artery disease was excluded.

Statistical analysis was carried out using 11.5 version of SPSS software (SPSS Inc.; Chicago, IL; USA).

Results

Among the 65 subjects in this study, 42 (64.6%) had no CT-angiographically detectable coronary artery lesion, 8 patients (12.3%) had non-significant lesions, and 15 (23.1%) had significant stenosis. Of the 15 patients with significant coronary artery disease, CTA showed a single-vessel disease in 12 patients (18.5%), a two-vessel disease in 2 patients (3.1%), and a three-vessel disease in 1 patient (1.6%). The coronary calcification was quantified using: (a) Equivalent Agatston score, of which the threshold was 130 HU; (b) Calcified volume (mm^3); (c) Number of calcified lesions; and (d) Equivalent calcium mass (mg of calcium hydroxy apatite).

The Best CTA reconstructions were utilized to differentiate between the absence of CAD, non-significant stenoses, and significant stenoses. Figure 3 shows the calcified plaques volume in each one of the coronary vessels and figure 4 displays distribution of significant coronary artery stenosis as detected in CT angiography. None of our study subjects had a significant stenosis in the left main coronary artery. Forty-three (66.2%) of our patients out of 65 had zero Ca-scoring, 14 (21.5%) had <100 Ca-scores, and 8 (12.3%) had ≥ 100 Ca-scores. In the first group (Ca-score=0), only one had significant stenosis, while patients in the second (Ca-score <100) and third (Ca-score ≥ 100) groups had 50% and 87.5% significant coronary artery stenosis, respectively ($P < 0.0001$) (Figure 5).

Since CTA cannot be regarded as a standard of reference modality in determining the significance of coronary stenoses, and coronary fluoroscopic an-

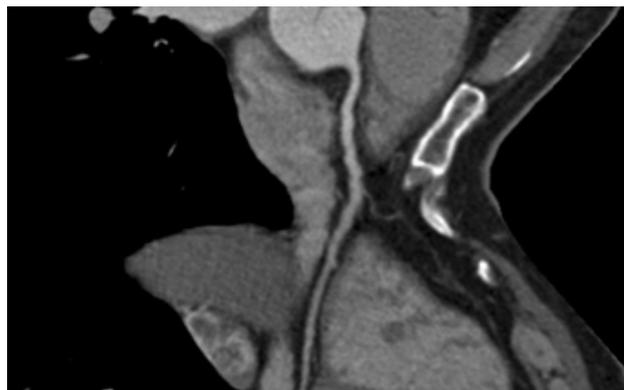


Fig 1. A curved multiplanar reconstruction (MPR) view of right coronary artery of one of the patients, normally seen along its entire length, lacking any stenosis



Fig 2. A volume rendering perspective of the proximal portion of all major coronary arteries, illustrating their normal appearance in one of the patients

giography is still the modality of choice in this regard, we measured the agreement between Ca-score and a relatively accurate modality, namely CTA. The agreement coefficient of κ between calcium scores (in 3 classes of 0, <100 and ≥ 100) and CT angiography findings (in 3 classes of normal, $<50\%$ and $\geq 50\%$ stenosis) were 0.54, 0.50 and 0.48 for LAD, LCx and RCA, respectively. When considered for entire coronary arterial circulation, this agreement was measured to be 0.553 (all of these measurements had a P value of less than 0.0001). Measured κ for the presence of any calcified plaque, resulting in more than 0 Agatston calcium score and the presence of any coronary artery lesion (irrespective of its severity) was 0.762 for the entire coronary arteries and were 0.744,

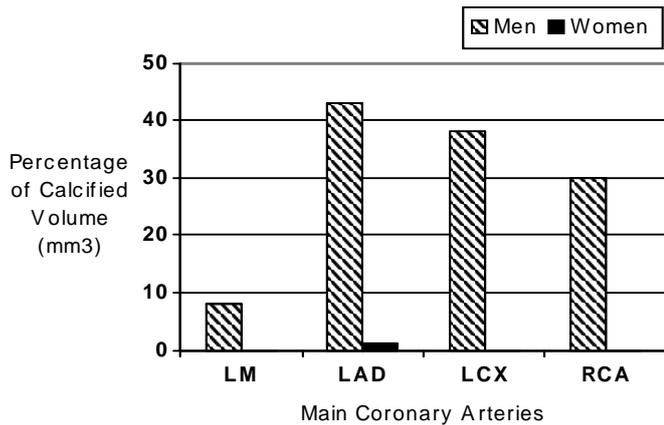


Fig 3. Graph showing percentage of presence of calcified volume in different parts of the coronary arterial system of patients, classified by gender .

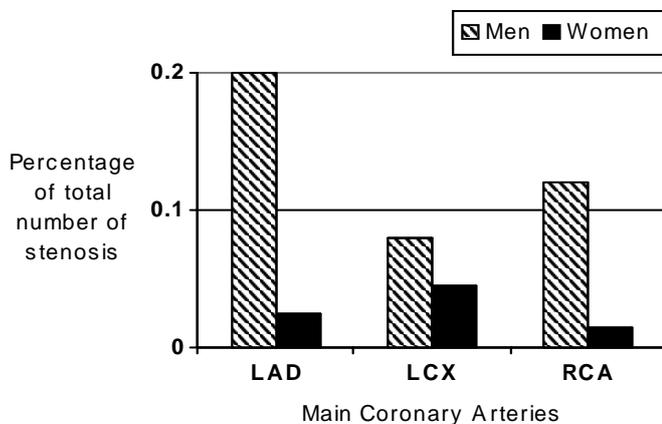


Fig 4. Graph showing percentage of total number and distribution of significant coronary stenosis depicted in CT-angiography in 65 patients. LAD: left anterior descending artery; LCx: left circumflex artery; RCA: right coronary artery; none of our patients had significant stenosis in left main coronary artery.

0.737 and 0.564, for LAD, LCx and RCA respectively ($P < 0.0001$ for all measured quantities).

Compared with other coronary arteries, the most extensively calcified volume was found in the LAD. (The mean volume in LAD, LCx, RCA and LMCA were 28.9 ± 99.9 , 24.3 ± 115.5 , 19.4 ± 90.2 and 5.1 ± 35.5 respectively) ($P < 0.0001$). Significant coronary stenosis in CT-angiography was most frequently detected in the proximal and middle portions of the LAD, as well. Figure 6 demonstrates the mean volume of coronary calcification in patients with CAD, which was closely related to the patient's age; in patients younger than 40 years, the mean calcified volume was 0.00 mm^3 and it increased from $4.6 \pm 11.7 \text{ mm}^3$ in the 41–50 years age group to $28.2 \pm 44.5 \text{ mm}^3$ in the 51–60 years age group. It was approximately $261.0 \pm 478.3 \text{ mm}^3$ in patients older than 60 years ($P < 0.0001$).

Furthermore, there was a difference ($P < 0.05$) be-

tween male and female patients with CAD concerning the calcified volume; in the corresponding age groups, the calcified area in female CAD patients was significantly lower than that of the same age male patients (Figure 6).

Discussion

Unenhanced cardiac CT scan clearly displays calcifications of the coronary artery tree.^{1,5} Quantification of atherosclerotic plaque burden by MSCT may be useful to individualize global risk of myocardial infarction, as shown by Fayad et al , and more recently by Leber and his colleagues.^{5,15}

It seemed that the calcified area tends to be more extensive with increasing number of diseased vessels or increasing degree of stenosis.¹⁰ In many patients, however, coronary calcium is found in the absence of any clinical coronary symptoms. Therefore, it has been suggested that coronary calcium may represent a preclinical stage of CAD.¹

Since the histologic composition of coronary plaques may predict eventual outcomes of CAD, screening studies that can identify plaque morphology may best provide a risk assessment of the coronary heart disease. According to Thompson and Stanford, in patients experiencing acute and severe cardiac events, coronary calcium is almost always present in amounts that exceed that found in asymptomatic individuals.¹⁰

Based on the expert consensus document of the American College of Cardiology/American Heart Association, the absence of detectable coronary artery calcified plaques in EBCT, portends a low likelihood of a major cardiac event within the next 2–5 years (5–10% overall risk).¹⁶ This can probably be likely applied to MSCT calcium score measurements, as well: albeit it seems to be challengeable.

The CTA served to assess the degree and localization of stenosis. Early indications in the literature, which our personal experience has corroborated, is that coronary CTA is considerably accurate in detecting stenoses of more than 50% diameter reduction in coronary vessels of more than 1.5–2 mm caliber.^{5,7,9} CTA of the coronary arteries often detects the presence of coronary atherosclerosis, characterized by plaques of varying densities. Low-density atheroscle-

Significant Stenosis According to Ca Score (CS) Group

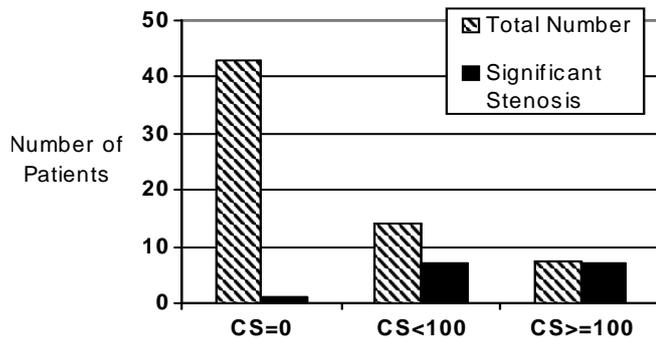


Fig 5. Graph showing classification of the patients according to calcium score groups (ratio of patients with coronary stenosis to total number of patients in each calcium score group).

Relationship between Patients' Age and Calcium-Score (Volume)

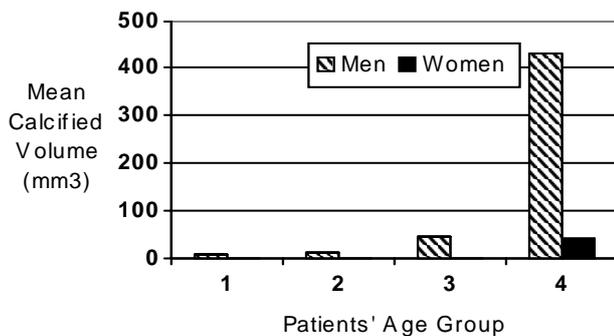


Fig 6. Graph showing difference in mean calcified volume of men and women with coronary artery disease regarding their age group (1= younger than 40 years-old, 2= 41-50 years-old, 3= 51-60 years old, 4= older than 60 years-old)

rotic plaques can be categorized by an enhancement of up to 50 HU; intermediate-density plaques by an enhancement of 50 to 100 HU; calcified, high-density plaques by an enhancement of more than 350 HU. Atheromatous plaques are typically in the 50 HU reading, while fibrotic plaques are in the 80 to 90 HU range, and calcium range is more than 400 HU.¹⁷⁻¹⁹

Some investigations have confirmed the accuracy of CTA in determination of calcified plaques and their resultant stenosis measurements in other non-coronary arteries, such as that performed by McKinney et al., on carotid arteries.²⁰ Our study shows that there is an overall moderate-to-good agreement between the presence of stenosis on CTA (either significant or non-significant in flow limitation) and the presence of calcified plaque, on CT. However, this agreement was less (0.45-0.55) for calcium scores of

more than 100 and significant coronary stenosis, in comparison with concurrence of non-significant stenosis and calcium scores of less than 100 (by Agatston technique).

Comparing the distribution of calcified areas and that of the coronary artery stenosis, we found that for both parameters the distribution pattern in the proximal segments is nearly identical and more consistent in LAD. A relatively lower measured κ between RCA calcified plaques and significant stenosis may be attributed to RCAs higher amplitude of motion during cardiac cycle, resulting in its more difficult assessment of RCA.

A high coronary Ca-score seems to be a sensitive but not specific marker for obstructive CAD. Previous studies have shown that calcification in the coronary arteries well correlated with significant vessel stenosis (mostly defined as equal to and/or greater than 50% diameter reduction).^{8,9,15,16} Nevertheless, in most of them no cut-off value for calcium score has been determined. A recently published article by Lau and coworkers, comparing the results of coronary Ca-scoring and CTA with those of conventional catheter angiography, as a standard of reference in determining stenosis severity, showed that CTA is more accurate than Ca-scoring in demonstrating coronary stenoses.²¹ They concluded that a calcium-score of greater than or equal to 400 could be used to potentially identify patients with significant coronary stenoses not detected at CT-angiography. Nonetheless, our study showed that a Ca-score of equal to or greater than 100 (Agatston measurement method) may be considered as a value for a relatively high concordance with significant coronary artery stenosis (approximately 87.5% of this group revealed significant CAD). This difference might be attributed to a lack of comparing our study results with those of an invasive quantitative coronary angiography.

Furthermore, in comparison with other similar studies, different MSCT scanners are used for evaluation. A Ca-score of more than 100 seemed to represent a valuable criterion in predicting coronary artery stenosis. A considerable number of these patients had critical stenosis in at least one of the coronary vessels. So we can recommend that if a coronary Agatston calcium-score of more than 100 is found, coronary CTA have to be considered mandatory to exclude

significant stenosis.

The most important drawback of our study was its lack of correlation with fluoroscopic invasive quantitative coronary angiography as the gold standard. This was mainly relevant to that most of our patients had normal findings, resulting in their exclusion from an invasive catheter coronary angiography.

Furthermore, since our center is the first coronary CTA center in Iran, many of our patients are referred from different provinces and cities, all over the country; hence, some of them were unable to be adequately followed up.

Another limitation of our investigation was radiologists' awareness of Ca-scores while interpreting the CTA of the same patient. This was due to the immediate consecution of these sessions in a prospective assessment, resulting in an inability to preserve the blindness of the interpreters to Ca-scoring results.

We suggest further studies on comparing the results of both Ca-score and coronary CTA with those of the fluoroscopic catheter angiography to determine significance of their relationship.

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