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A head-to-head comparison of the coronary calcium score by computed tomography with myocardial perfusion imaging in predicting coronary artery disease

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Abstract

Objectives   The coronary artery calcium (CAC) score has been shown to predict future cardiac events. However the extent to which the added value of a CAC score to the diagnostic performance of myocardial perfusion imaging (MPI) by single photon emission computed tomography (SPECT) is unclear. The purpose of this study is to investigate the correlation between CAC score and SPECT in patients with suspected coronary artery disease. **Methods**   A retrospective review of the CAC scores by use of the Agatston calcium scoring method and cardiac SPECT diagnostic reports was conducted in 48 patients, who underwent both coronary computed tomography (CT) and SPECT examinations due to suspected coronary artery disease. A Pearson correlation test was used to determine the relation between CAC scores and MPI-SPECT assessments with regard to the evaluation of the extent of disease. **Results**   Forty-seven percent of the patients had CAC scores more than 100, while 42% of these patients demonstrated abnormal, or probably abnormal, MPI-SPECT. Of the 23% of patients with a zero CAC score, only 7% had normal MPI-SPECT findings. No significant correlation was found between the CAC scores and MPI-SPECT assessments (r value ranged from 0.012 to 0.080), regardless of the degree of coronary calcification. **Conclusions**   There is a lack of correlation between the CAC scores and the MPI-SPECT findings in the assessment of the extent of coronary artery disease. CAC scores and MPI-SPECT should be considered complementary approaches in the evaluation of patients with suspected coronary artery disease.

1   Introduction

Multi-slice computed tomography (CT) has been increasingly used to detect coronary artery calcium and diagnose coronary artery stenosis. Quantifying the amount of coronary artery calcium (CAC) with non-enhanced CT scans has been widely accepted as a reliable non-invasive technique for screening patients with a potential risk of developing major cardiac events, and is usually quantified using the Agatston score.[1–4] The clinical application of CAC scoring has been supported by evidence showing that the absence of calcium reliably excludes obstructive coronary artery stenosis,[5] and that the amount of CAC is a strong predictor for risk assessment of myocardial infarction and sudden cardiac death, independent of conventional coronary risk factors.[6,7] However, its predictive value is, in the end, determined by the patients' symptoms. In symptomatic patients, CAC scoring is considered as being only marginally related to the degree of coronary stenosis, and it is well known that both obstructive and non-obstructive coronary artery disease (CAD) can occur in the absence of calcification.[8,9] According to these reports, low CAC scores are less valuable in the prediction of the prevalence, or severity, of coronary artery disease caused by the non-calcified coronary plaques.

Myocardial perfusion imaging (MPI) with gated single photon emission computed tomography (SPECT) has been widely used in the diagnosis of CAD and risk stratification with high diagnostic accuracy[10,11] when compared to CT angiography. The presence of ischemia could be used to classify the patients as having CAD and candidates for receiving aggressive medical therapy and management. However, a normal MPI does not necessarily exclude significant coronary stenosis, while high CAC scores sometimes do not result in abnormal perfusion on MPI.[12–14] Thus, the exact relationship between CAD and MPI is not very clear. The purpose of this study is to correlate CAC scores with MPI by SPECT in a group of patients with suspected CAD. An

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important strength of this study is that simultaneous assessment of MPI and CAC scores was performed on all consecutive patients with suspected CAD, thus, the results could be applicable to similar populations of patients undergoing MPI examination.

2 Methods

2.1 Patient data collection

This retrospective study consisted of 48 patients (33 men and 15 women; mean age 61.7 years; range 44–81 years) with suspected coronary artery disease who underwent both multi-slice CT and MPI-SPECT examinations within two weeks. Patients who were referred first by general practitioners for coronary CT scans, and then, for MPI-SPECT by nuclear physicians, met the following inclusion criteria: no previous history of CAD; typical or atypical chest pain, dyspnea or signs of myocardial perfusion on a resting or stress ECG test. Medical history, including cardiovascular risk factors, blood pressure, lipid profile, electrocardiography (ECG) and 10-year CAD risk, predicted on the basis of the Framingham risk score, was obtained for all patients (pretest probability: low to moderate). Patients were excluded if they had a previous history of myocardial infarction, unstable angina, percutaneous coronary intervention (angioplasty) or coronary bypass surgery; allergy to contrast medium and renal insufficiency (serum creatinine > 1.5 mg/dL). All patients were in a stable condition at the time of the study. The study was approved by the local ethics research committee and written informed consent was obtained from all patients. The characteristics of the study population are summarised in Table 1.

Table 1 Patient demographics

Males	33/ (69%)
Females	15/ (31%)
Age (years, mean ± SD)	61.7 (9.8)
Cardiovascular risk factors	
Smoking	13 (27%)
Hypertension	41 (83%)
Diabetes	8 (17%)
Dyslipidemia	13 (27%)
Angina pectoris	
Atypical	7 (14.6)
Typical	41 (85.4%)

2.2 Coronary CT scanning protocol

All patients were scanned on a dual-source CT scanner (Somatom Definition, Siemens Medical Solutions, Forchheim, Germany). A non-enhanced scan was performed for CAC scoring. Scanning parameters were as follows: detector collimation 2 × 32 × 0.6 mm, slice collimation 2 × 64 × 0.6 mm by means of a z-flying focal spot, gantry rotation time 330 ms, pitch of 0.2–0.5 depending on the heart rate, tube current time product 350 mAs and tube potential 120 kV. CT scans were performed from the level of the tracheal bifurcation to the diaphragm. Non-enhanced CT scans were performed with prospective ECG-triggering with images acquired at three mm slice thickness.

2.3 Coronary artery calcium scoring

Coronary artery calcifications were quantified using calcium scoring software (Syngo CaScore, Siemens) and measurments were performed by a qualified CT technologist using the standard Agatston calcium scoring algorithm.[4] The extent of CAD was determined according to the recommended CT calcium score guidelines using five CAC score categories: none (0), minimal or low (1–10), mild (11–100), moderate (101–400) and extensive or high (401 or greater).

2.4 MPI-SPECT imaging protocol

Rest and stress ECG-gated MPI protocols were performed in all patients using technetium (^{99m}Tc)-tetrofosmin (500 MBq). The stress test was performed on an exercise-modified Bruce treadmill and associated (such as adenosine infusion) protocol. Images were acquired on a triple-head SPECT camera (ADAC Vertex with VXGP collimators) using a low-energy, high-resolution, parallel-hole collimator with a 360 rotation in a continuous mode. All projection images were stored in a 64 × 64 × 16 acquisition and processing frame matrix size.

2.5 MPI-SPECT image analysis

The myocardial perfusion assessment was performed by a nuclear physician with more than 10 years of experience in nuclear cardiology using a 20-segment model, and myocardial perfusion for each segment was evaluated using a five-point continuous scoring system as recommended by Xu et al.[15] (0: normal; 1: mildly abnormal; 2: moderately abnormal; 3: severely abnormal; 4: absence of segmental uptake). The observer was blinded to any clinical information and CAC scores. The segmental perfusion scores during rest and stress were added to calculate the summed rest score (SRS) and the summed stress score (SSS). The summed difference score (SDS) was calculated by subtracting the SRS from the SSS.

2.6 Statistical analysis

Data were entered into SPSS V 19.0 for analysis (SPSS, Chicago, Illinois). All continuous variables were expressed as mean ± SD. A one way analysis of variance (ANOVA)

was used for analysis of continuous variables and a Pearson test was used to demonstrate the correlation between CAC and MPI scores. A P value of less than 0.05 indicated statistically significant difference.

3 Results

Table 2 lists the CAC and MPI-SPECT scores as assessed in these patients. There are variable degrees of differences between the CAC and corresponding MPI-SPECT scores. Figure 1 shows the distribution of CAC and MPI scores among these 48 patients. Forty-seven percent of the patients

Table 2. Percentages of coronary artery calcium score and MPI-SPECT results.

CAC 0	23%
CAC 1–10	9%
CAC 11–100	21%
CAC 101–400	21%
CAC > 400	26%
Mean summed stress score	6 (2–10)
Mean summed rest score	2 (0–6)
Summed difference score	4 (0–8)
MPI normal	7%
MPI mildly abnormal	17%
MPI moderately abnormal	34%
MPI severe abnormal	15%
MPI absence of segmental uptake	27%

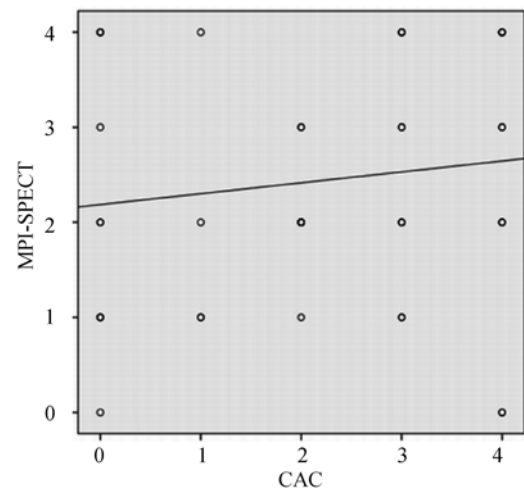CAC: coronary artery calcium; MPI: myocardial perfusion imaging.

had moderate and extensive calcifications with CAC scores more than 100, while 42% of these patients demonstrated abnormal, or probably abnormal, MPI assessments. Analysis of the relationship between overall CAC scores and MPI assessments indicated no correlation with a Pearson correlation factor r of 0.019 (Figure 2).

A zero CAC score was found in 23% of the patients; however, only 7% of these were noted to demonstrate the normal MPI-SPECT results. Of 10 patients with a zero CAC score,
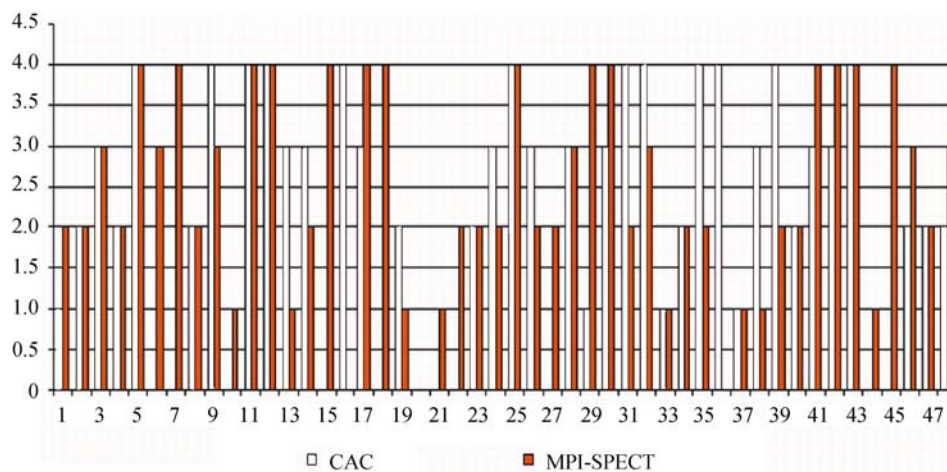
Figure 2. Graph shows that there is a lack of correlation between coronary artery calcium scores and the corresponding myocardial perfusion SPECT assessments, with r value of 0.019. CAC: coronary artery calcium; MPI-SPECT: myocardial perfusion imaging with gated single photon emission computed tomography (SPECT).

Figure 1. Distribution of the CAC scores with myocardial perfusion imaging among the 48 patients with suspected coronary artery disease. As shown in the figure, there is a significant discordance between the CAC and MPI-SPECT score, with abnormal SPECT scores (range from 1 to 4) noticed in 10 patients with a zero CAC. CAC: coronary artery calcium; MPI-SPECT: myocardial perfusion imaging with gated single photon emission computed tomography.

abnormal MPI-SPECT scores were found to range from 1 to 4 (mean score 2.6). In contrast, normal MPI- SPECT scores were found in two patients with a CAC score of four. A CAC score of 1–10 was identified in 9% of the patients with probably normal MPI-SPECT findings in 17% of the patients. A CAC score of 11–100 was found in 21% of patients with equivocal MPI-SPECT findings in 34% of the patients. A CAC score of the 101–400 was reported in 21% of the patients with probably abnormal MPI-SPECT findings in 15% of these patients. Similarly, there was no correlation between the CAC scores and MPI assessments in the group of patients with low to moderate calcification, with a Pearson correlation factor *r* of 0.012.

Extensive calcifications (CAC score > 400) were noticed in 26% patients, while 27% of patients were found to have abnormal MPI. Again, there was no correlation between the CAC scores and MPI assessments in the group of patients with extensive calcification, with a Pearson correlation factor *r* of 0.080.

4   Discussion

Although based on a relatively small sample size, this study presents important findings which are considered valuable for the clinical diagnosis of patients with suspected coronary artery disease. There is a lack of correlation between the CAC scores and MPI-SPECT assessments, with a significant difference observed between these scoring techniques, especially in the patients with zero or mild calcification (CAC scores 0–100). Thus, CAC scores cannot be reliably used as single parameters to predict the disease prognosis in this group of patients.

CAC score using multi-slice CT has been validated as a useful imaging tool for risk stratification and reclassification of risk of coronary artery disease.[16] The CAC score is a highly sensitive marker with increased prognostic value for determining the atherosclerotic disease compared with conventional cardiovascular risk factors. However, issues have been raised as to whether using only a CAC score is a reliable tool of determining the extent of CAD, since non-calcified coronary artery plaque may not be detected. There is growing evidence to show the discrepancy between low CAC and corresponding myocardial perfusion findings.[8,17,18] This is confirmed by the results in this analysis as there is no correlation between the CAC scores and MPI assessments, whether the analysis is based on a comparison of overall CAC scores and MPI assessments, or on low or high CAC scores with corresponding MPI assessments.

Several studies have reported the presence of obstructive non-calcified plaque in 8.7% of symptomatic patients with zero or low calcium scores.[8,17] Cheng *et al.*[17] reported that low, but detectable, CAC scores were less reliable in predicting the plaque burden due to their association with high overall non-calcified coronary artery plaque. Similarly, Greenland, *et al.*[18] demonstrated a CAC of zero did not usually eliminate the risk of future CAD events. Our results are in line with those findings. Twenty-three percent patients had a zero CAC score with only 7% of these patients verified by the myocardial perfusion SPECT to be normal. It could be concluded that low CAC scores are significantly less predictive of the prevalence, or severity, of underlying non-calcified coronary plaque,[19] although further studies based on a larger cohort of patients should be conducted.

It has been reported that the MPI-SPECT in cardiac imaging is a widely accepted test for the diagnostic and prognostic evaluation of patients with known, or suspected, CAD.[10,20] This study indicates that MPI-SPECT may provide more accurate assessments of the extent of CAD, or the prediction of disease outcomes, than CAC alone, given that, in patients with zero CAC, some could demonstrate abnormal myocardial perfusion. Schaap, *et al.*[21] in their recent study concluded that a CAC score did not significantly improve the diagnostic performance of SPECT in patients with significant CAD. The association between CAC and MPI-SPECT demonstrates that as the CAC score increases, so does the occurrence and severity of myocardial perfusion abnormalities.[22,23] High values of CAC often indicate the presence of stenotic lesions and are associated with an increased risk of adverse cardiovascular events.[16,24,25] Similarly, our study shows that patients with a high calcium score had abnormal, or probably abnormal, MPI-SPECT results, although the correlation between these imaging modalities was not significant. However, studies have been reported that patients with a high CAC score did not demonstrate a significantly different percentage of abnormal MPI findings than in patients with a low CAC score.[12,14] A high CAC in patients with normal MPI-SPECT reflects non-obstructive atherosclerosis, which is regarded as a preclinical state with strong predictive value for the development of CAD, thus, aggressive risk factor modification should be recommended according to the guidelines.[26] A CAC score and MPI should be considered complementary approaches rather than individual parameters in the assessment of patients with suspected CAD.

Several limitations in this study should, however, be acknowledged. Firstly, only a limited number of patients were included in this study and further studies based on a larger cohort are needed. Secondly, this study is only a

retrospective analysis of the diagnostic reports without the inclusion of follow-up details on patients, thus, there is no information available about the disease outcomes, such as major cardiac events relative to the CAC or MPI scores. Thirdly, the cut off value for CAC at 401 or greater in this study is much lower than the suggested value in the literature (> 700),[27,28] thus, this could affect the diagnostic specificity in detecting significant CAD. Lastly, the diagnostic accuracy of coronary CT angiography was not assessed with regard to the evaluation of the degree of coronary stenosis, with no correlation to subsequent myocardial perfusion analysis, thus, no information is available about the diagnostic value in terms of sensitivity and specificity. This could be explained by the fact that the current study only focused on the correlation between CAC and MPI-SPECT. Recent evidence shows that coronary calcium scores assessed with non-enhanced CT might be supported by coronary CT angiography or coronary CT angiography might be performed alone with the aim of acquiring more diagnostic information.[29,30] Further studies are required to investigate the potential value of coronary CT angiography for both calcium scoring and assessment of coronary stenosis.

In conclusion, this study demonstrates the lack of direct correlation between the CAC score and the corresponding myocardial perfusion assessed by SPECT in patients with suspected coronary artery disease. In particular, in patients with a zero or low CAC scores, myocardial perfusion imaging shows potential abnormalities in some patients which indicates significant lack of agreement between these two methods. This highlights the limitations in using CAC scores alone as a predictor of coronary disease outcomes. Coronary calcium score should be combined with myocardial perfusion imaging in low-to-intermediate risk patients to improve the diagnostic performance.

Acknowledgements

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