Coronary artery calcium (CAC) score – a prognostic tool in coronary artery disease?

Original Article

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(Received 19 December 2011, Revised 24 December 2011, Accepted 25 December 2011)

ABSTRACT

Introduction: The aim of this study was to evaluate the impact of measurement of coronary artery calcification score (CAC) in patients with suspected coronary artery disease (CAD) and a normal myocardial perfusion scan.

Methods: In a prospective study we measured the calcium score of 74 patients (29 m, 45 f, mean age 58.7 (m) and 64.4 (f)) with suspicion of CAD and a normal perfusion scan. In all patients a pharmacological stress myocardial perfusion imaging (MPI) with dipyridamole was performed. Both the myocardial perfusion scintigraphy and calcium scoring were performed on a T6 Symbia gamma camera (Siemens, Knoxville, USA). Attenuation correction was performed using a low dose CT.

Results: The mean total CAC score was 182.6±435.7 and ranged from 0 -2309. 21/29 of the male patients (72%) and 17/45 of the female patients (38%) had an Agatston score of > 10. There were 9 cases (5m, 4f) with a calcium score of > 400 and 3 cases (2m, 1f) with a calcium score > 1000. No cardiac event was noted in these patients during a mean follow up time of 10.3 months (range 7-13 months, median 11 months) except one cardiac death of a patient with total Agatston score of 278. Seven patients also underwent angiography because of their clinical symptoms, 4 of which (57%) had an elevated Agatston score.

Conclusion: Our study showed that calcium score measurement accompanied with SPECT imaging is feasible in routine myocardial perfusion imaging with SPECT/CT machines. Calcium score measurement in patients with normal stress myocardial perfusion scintigraphy, may be useful in risk stratification of the patients. Further prospective studies with larger patient numbers and longer follow-up time are needed to find out the impact of this advantage by hybrid imaging.

Keywords: Coronary artery disease, Myocardial perfusion imaging, Coronary artery calcification score.

Iran J Nucl Med 2011;19(2):46-51

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INTRODUCTION

Coronary artery disease (CAD) is still one of the leading causes of mortality. Stress myocardial perfusion imaging (MPI) is the standard non-invasive method to detect and determine myocardial ischemia in both symptomatic and selected asymptomatic patients (1). Combined with a patient's medical history, co-morbidities like hypertension, diabetes, hyperlipidemia MPI is one of many steps in assessing CAD and planning further medical management of patients.

A positive MPI for ischemia would lead to a more aggressive lipid management, antithrombotic agents, optimized diabetes and hypertension therapy and if needed coronary revascularisation.

If the MPI shows no signs of haemodynamically significant CAD, the risk of significant cardiac events is low and well defined as <1% per year in the absence of co-morbidities, about 1% per year in the presence of angiographically documented CAD and between 1 and 2% per year in the presence of significant co-morbidities (2-4).

However MPI sensitivity remains limited in ruling out CAD stenosis under 50% of diameter of coronary artery. Thus, individuals with normal test results might still have substantial CAD (5) that would otherwise remain undetected and therefore untreated.

Several studies showed that adding coronary CT-angiography into the diagnostic process, and therefore having a visual assessment of the coronary anatomy helps identify individuals with substantial luminal stenosis/CAD who might benefit from more aggressive therapy.

The correlation between computed tomography angiography (CTA) and coronary angiography findings was previously reported as excellent and is well established nowadays (5).

The coronary artery calcium score (CAC) is a relatively new modality for cardiac risk estimation and stratification (1,6). In the last decade, several studies showed that CAC is a valuable risk marker as it is directly related to atherosclerotic plaque burden and independently predicts severe cardiac events in patients with known CAD (7) or all cause mortality (8).

The Agatston score has been defined by Agatston and Janowitz and dates back into the 1980s. The original work was based on Electron Beam computed tomography (also known as Ultrafast CT or EBCT). For quantification of coronary calcium, the Agatston Score is calculated as the product of the lesion's surface area and a weighting factor ranging from one to four, which was assigned according to the peak attenuation of the lesion (9). Territories with stents are expectedly excluded from quantifications (7).

Budoff et al. reported that the 10 year survival in asymptomatic patients with CAD was 99.4% in patients with a CAC score (Agatston Score) of 0 but was only 87.8% in those with an Agatston Score greater than 1000 (8).

CAC was also shown to be even a stronger predictor of outcome than diabetes mellitus (10).

With the introduction of hybrid devices, single photon emission computed tomography (SPECT-CT), in nuclear medicine it is possible to perform MPI and measurement of coronary artery calcification (CAC) score on the same day if necessary.

We investigated the value of adding CAC in patients with suspected coronary artery disease (CAD) who had a negative MPI for stratifying the risk of future cardiac events.

METHODS

74 patients (29 M, 45 F, age range 49-85 yrs, mean age 58.7 (M) and 64.4 (F)) with

suspected CAD who were sent for MPI and showed a normal perfusion pattern in stress MPI were included into the study. The patients were selected consequently in a time period of 13 months.

A pharmaceutical stress protocol using dipyridamole (0.5 mg/ kg) was used. Sixty minutes after intravenous injection of 370 MBq ^{99m}Tc-Sestamibi, a 180° SPECT acquisition was performed using a dual head SPECT-CT system (Symbia T6, Siemens). The acquisition parameters chosen were 6°/step and 25 sec. per frame and a LEHR (low energy high resolution) collimator. Afterwards a low-dose CT scan (130 kV, 20 mAs) was done for attenuation correction of the emission data. The emission raw data were reconstructed using an advanced iterative reconstruction method that incorporates system resolution in 3D dimensions (Flash3D, Siemens). The reconstruction parameters chosen were 12 subsets and 4 iterations. After SPECT acquisitions an electrocardiogram triggered CT scan (using 130kV, 30 Ref. mAs, 0,42 sec. rotation time, 3 mm slice thickness, 60% phase optimization) was performed and used for CAC measurement.

The scintigraphic images were analyzed by two experienced nuclear medicine physicians and CAC was calculated by an experienced cardiologist. The patients were followed every 6 months and any soft cardiac event (unstable angina or CCU admission) and hard cardiac event (myocardial infarction or cardiac death) were recorded.

Data were analyzed using SPSS software (Version 16). Descriptive analysis was done using univariate analysis. Independent t-test was used for comparison of quantitative variables between the groups. Chi-Square test was used for comparison of qualitative variables. P<0.05 was considered significant in all comparisons.

RESULTS

From traditional risk factors 72.3% of the patients had hypertension (HTN), 40.6% had hyperlipidemia and 21.5% had a family history of CAD. Also smoking was noted in 24.6% and diabetes mellitus in 18.5% of the patients. 4.6% of the patients had previous history of coronary artery bypass grafting (CABG) and 6.2% had previous history of stroke.

The mean total CAC score was 182.6±435.7 and ranged from 0 -2309. The mean CAC score in the left main artery (LMA) was 15.7(±56.4). The CAC score was 86.2±193 in the left anterior descending artery (LAD), 29.9±90.5 in the left circumflex artery (LCX) and 47.2±160.1 in the right coronary artery (RCA) (Figure1).

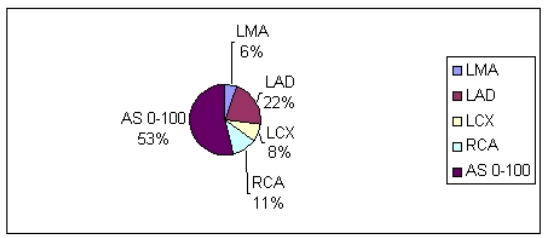

Figure 1. Agatston Score over 100 in territories of the coronary arteries (LMA, LAD, LCX, RCA)

AS: Agatston Score

LMA: Left Main Artery

LAD: Left Anterior Descendant Artery

LCX: Left Circumflex Artery

RCA: Right Coronary Artery

38/74 (51%) of patients including 21/29 of the male patients (72%) and 17/45 of the female patients (38%) had an Agatston score of > 10. Only 5.5% of the patients had a CAC score>100 in LMA, while it was 21.6%, 8.1% and 10.8% for LAD, LCX and RCA respectively.

Also CAC score>400 was noted in 0%, 5.4%, 2.7% and 2.7% of LMA, LAD, LCX and RCA territories respectively. Total Agatston score was ≥100 in 29.7% and >400 in 12.2% (5m, 4f) of patients.

There were 9 cases (5m, 4f) with a CAC score of > 400, 3 of which (2m, 1f) with a CAC score > 1000.

Regarding traditional risk factors the mean summed CAC score was 220.7±519.0 in patients with hypertension and 91.9±157.9 in patients without hypertension (P=0.13). Subgroup analysis showed that only the mean CAC score on LCX was significantly higher in patients with hypertension compared to patients without hypertension (40.2±110.7 Vs 5.4±19.6 , P=0.04).

The mean summed CAC score was 254.1±561 in patients with hyperlipidemia and 139.3±365.3 in patients without hyperlipidemia (P=0.3). No statistically significant difference was noted in all coronary arteries as well (P>0.3).

The mean summed CAC score was 208.4±494.3 in patients with diabetes mellitus and 81.8±123.5 in patients without diabetes mellitus (P=0.1). The mean summed CAC score was 117.5±283.5 in smokers and 392±742.3 in non-smokers (P=0.1).The mean CAC score was 187.6±473.5 in patients with normal coronary arteries and 163.6±202 in patients with abnormal coronary angiography (P=0.8).

No soft or hard cardiac event was noted in these patients during a mean follow up time of 10.3 months (range 7-13 months, median 11 months) except one cardiac death which is seen in a patient with total Agatston score of 278.

Seven Patients underwent coronary angiography because of their clinical symptoms, 4 of which (57%) had an elevated Agatston score. Two patients underwent Coronary angiography in another clinic where we could not obtain data regarding the degree of coronary stenosis.

In the present study the angiographic results showed coronary artery disease in 3 cases despite a negative MPI and Agatston score of 0.

DISCUSSION

When MPI shows presence of ischemia suggesting of CAD, it is not surprising that those patients are more likely to have a higher CAC than patients with normal MPI, as coronary calcification is related to the overall atherosclerotic burden.

However patients with clinically suspected CAD and normal MPI are still at risk of suffering cardiac events, even when the risk is comparatively small. The small rate of 1/74 cardiac event (1.35%) in our patients after a median time of 11 months is in accordance with other reports in patients with a normal MPI pattern (10). CAC in 51% of the patients was greater than 10 and in 12% greater than 400, indicating an intermediate risk for this group of patients who would benefit from a more aggressive treatment (10).

Chang et al. showed that CAC and SPECT findings are independent and complementary predictors of short- and long-term cardiac event. Also a high CAC score, even when SPECT results are normal, identifies patient at risk to develop cardiac events. Their study also showed that CAC was a stronger predictor of cardiac event than diabetes mellitus. In that study cardiac event rates increased significantly three years after a normal MPI, thus suggesting that MPI is better short term risk assessor and CAC score might be better in estimating long-term prognosis as CAC shows calcification before SPECT abnormalities (10).

In an even larger population study of 25.253 asymptomatic patients, CAC provided an independent estimator of all-cause mortality and highly correlated with mortality risk.

Those findings showed a linear relationship between CAC and all-cause mortality (8).

Furthermore in the findings of Arad et al. CAC was shown to be even more accurate in predicting CAD than the Framingham Risk Score (11).

Greenland and colleagues state that CAC should primarily be used as a screening method in patients considered being at intermediate risk as they may be reclassified in a higher risk group and might benefit from more aggressive therapeutic measures (6). Furthermore they did not recommend to use CAC in patient with low CHD risk (below 10% 10-year risk of CAD-events) neither performing CAC measurement in asymptomatic patients with high CAD risk as they have already been appraised as needing intensive risk reducing therapy (6).

CAC is measured with SPECT-CT on a one-day basis, thus providing immediate information for the clinician regarding possible risk of CAD. Another advantage of using SPECT-CT compared to CTA is the lower amount of radiation to which the patient is exposed. Hausleitner et al. investigated median doses of CTA in different sites and found them to differ quite significantly between sites and CT-systems, which in their published results varies between 9-19mSv (Protection 1-Study) (12). CTA also includes risk of allergy to contrast dye. (5) Renal insufficiency, autonomy of the thyroid gland or hyperthyroidism is contraindications for iodine contrast dye which is not the case when using isotopes for MPI and SPECT-CT.

CONCLUSION

Increased calcium score is a known predictor of worse clinical outcome; calcium scoring in addition to a normal stress perfusion scintigraphy on a SPECT-CT device might improve risk stratification of the patients on the same day and depict those in need of more aggressive treatment. This may lead to a faster patient management and more convenience for the patient. Further prospective studies with larger patient numbers and longer follow-up time are needed to find out the impact of this advantage by hybrid imaging.

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