Clinical Investigations

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Association of Coronary Artery Calcium With Severity of Myocardial Ischemia in Left Anterior Descending, Left Circumflex, and Right Coronary Artery Territories

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ABSTRACT

Background: An increasing coronary artery calcium score is associated with a higher likelihood of myocardial ischemia.

Hypothesis: The association of the coronary calcium score with myocardial ischemia in different coronary arteries needed to be investigated.

Methods: We correlated the coronary artery calcium (CAC) score with the severity of myocardial ischemia diagnosed by myocardial perfusion imaging in the left anterior descending (LAD), left circumflex (LCX), and right coronary artery (RCA) territories in 206 patients, mean age 66 years, without cardiac stents or coronary artery surgery.

Results: The mean CAC score in the LAD coronary artery was 160 ± 218 in patients with no or mild ischemia and 336 ± 379 in patients with moderate or severe ischemia ($P = 0.039$). The mean CAC score in the LCX coronary artery was 57 ± 117 in patients with no or mild ischemia and 161 ± 191 in patients with moderate or severe ischemia ($P = 0.018$). The mean CAC score in the RCA was 114 ± 237 in patients with no or mild ischemia and 261 ± 321 in patients with moderate or severe ischemia ($P = 0.045$). Stepwise linear regression analysis showed that male gender ($P < 0.0001$), age ($P < 0.0001$), and moderate or severe ischemia ($P = 0.023$) were significantly associated with high LAD coronary artery CAC scores. Male gender ($P < 0.0001$), age ($P = 0.0002$), and moderate or severe ischemia ($P = 0.006$) were significantly associated with high LCX coronary artery CAC scores. Male gender ($P < 0.0001$) and age ($P < 0.0001$) were significantly associated with high RCA CAC scores.

Conclusions: Higher CAC scores are significantly associated with moderate or severe ischemia in the LAD and LCX coronary arteries.

Introduction

An increasing coronary artery calcium (CAC) score is associated with a higher likelihood of myocardial ischemia[1–4] and is useful in the diagnosis and prognosis of coronary artery disease (CAD)[5–8] and in CAD risk-factor control.[9] To the best of our knowledge, data on the association of the CAC score with moderate or severe myocardial ischemia determined by myocardial perfusion imaging (MPI) in the left anterior descending (LAD), left circumflex (LCX), and right coronary artery (RCA) territories are limited. This article reports the association of the CAC score with moderate or severe myocardial ischemia in the LAD, LCX, and RCA territories in 206 patients.

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Methods

The study population included 206 patients (113 men and 93 women), mean age 66 ± 11 years, who were seen in a private cardiology practice at New York Medical College. None of the patients had a cardiac stent or prior coronary artery surgery.

Scans for CAC scoring were obtained using a Siemens Somatom Sensation cardiac computed tomography system (Siemens AG, Munich, Germany). Calcium scoring was performed as a component of a complete cardiac computed tomography study that included 64-multislice coronary computed tomography angiography (CTA), or as a stand-alone procedure in patients referred for calcium scoring alone. Calcium scans were performed using a spiral scanning protocol (rotation time 0.33 ms, slice collimation 0.6 mm, slice width 3.0 mm, pitch factor 0.2, increment of 1.5 mm, kernel B35) or using a sequential scanning protocol

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with electrocardiogram triggering (rotation time 0.33 ms, slice collimation 0.6 mm, slice width 3.0 mm, pitch factor 0.2, increment of 1.5 mm, kernel B35). Calcium scoring was performed by 1 of 2 cardiologists experienced in cardiac computed tomography using a TeraRecon Aquarius workstation (TeraRecon Inc., Foster City, CA). CAC scores were calculated for the LAD coronary artery, for the LCX coronary artery, and for the RCA.

Stress testing was performed using a sestamibi exercise stress test in 146 patients, a thallium exercise stress test in 1 patient, an adenosine sestamibi stress test in 56 patients, a dobutamine stress test in 2 patients, and a dipyridamole stress test in 1 patient as previously described.[8] A single isotope was used. There was attenuation correction. Ischemia was graded as none, mild, moderate, or severe in the territories of the LAD, LCX, and RCA by a cardiologist experienced in stress testing and in nuclear cardiology.

Clinical consent for performing CAC scores and stress testing was obtained from all 206 patients.

Student *t* tests were used to examine whether there were significant differences in the LAD, LCX, and RCA CAC scores and continuous baseline characteristics between patients with no or mild ischemia vs moderate or severe ischemia. χ^2 or Fisher exact tests were used to investigate whether there were significant differences in dichotomous baseline characteristics between patients with no or mild ischemia vs moderate or severe ischemia. Stepwise linear regression analysis was performed using the variables in the Table 1 to identify significant risk factors for LAD, LCX, and RCA CAC scores.

Results

Table 1 shows the baseline characteristics of patients with no or mild myocardial ischemia vs moderate or severe myocardial ischemia. The Table 1 also lists levels of statistical significance. Stepwise linear regression analysis showed that male gender ($P < 0.0001$), age ($P < 0.0001$), and moderate or severe ischemia ($P = 0.023$) were significantly associated with high LAD coronary artery CAC scores. Stepwise linear regression analysis showed that male gender ($P < 0.0001$), age ($P = 0.0002$), and moderate or severe ischemia ($P = 0.006$) were significantly associated with high LCX coronary artery CAC scores. Stepwise linear regression analysis showed that male gender ($P < 0.0001$) and age ($P < 0.0001$) were significantly associated with high RCA CAC scores.

Table 1. Baseline Characteristics of Patients With No or Mild Myocardial Ischemia vs Moderate or Severe Myocardial Ischemia

Variable	No or Mild Ischemia, n = 183	Moderate or Severe Ischemia, n = 23	*P* Value
Age, y	65 ± 12	69 ± 8	0.032
Men, n (%)	96 (52)	17 (74)	NS
Women, n (%)	87 (48)	6 (26)	NS
Current smoking, n (%)	12 (7)	2 (9)	NS
Systemic hypertension, n (%)	152 (83)	20 (87)	NS
Hypercholesterolemia, n (%)	147 (80)	20 (87)	NS
Diabetes mellitus, n (%)	38 (21)	7 (30)	NS
LAD CAC score	160 ± 218	336 ± 379	0.039
Left circumflex CAC score	57 ± 117	161 ± 191	0.018
Right coronary CAC score	114 ± 237	261 ± 321	0.045

Abbreviations: CAC, coronary artery calcium; LAD, left anterior descending coronary artery; NS, not significant.

Discussion

For noninvasive evaluation of patients with known or suspected CAD, calcium scoring and MPI are 2 important modalities that evaluate different pathological processes. MPI examines for possible ischemia, and calcium scoring correlates closely with atherosclerotic burden. The algorithm to determine the appropriate test for every patient is not fully elucidated. One approach to analyze these 2 modalities is to evaluate their diagnostic and prognostic capacity.

A meta-analysis of 8 studies involving 916 patients was performed comparing CAC scores >0 to 10 with MPI in predicting obstructive CAD.[5] The results showed that CAC scoring has similar accuracy (75% vs 76%), higher sensitivity (91% vs 82%), lower specificity (52% vs 67%), lower positive predictive value (75% vs 81%), and higher negative predictive value (80% vs 67%).

Several studies have evaluated the prognostication of CAD in these 2 tests. Ramakrishna et al showed in a study of 835 patients that having a CAC score >400 had a similar 10-year mortality as a high-risk summed stress score on MPI (27% vs 31%, respectively).[6] Rozanski et al showed in a study of 1153 patients that having a CAC score of 400 to 999 had similar rates of death and myocardial infarction as those with ischemic MPI (2.6% vs 3.1%, respectively) at 32-month follow-up.[7] Uebleis et al showed in a study of 260 patients that a CAC score >400, perfusion abnormalities at rest (summed rest score of 2 or greater), or severe perfusion abnormalities under stress (summed stress score of 13 or greater) are independent risk factors of subsequent severe cardiac events at 5.4-year follow-up ($P = 0.0095$, 0.023, and 0.007, respectively).[8] These 3 studies suggest that a CAC score of 400 has a similar prognostic value as an abnormal MPI.

To understand how these 2 modalities relate to each other, a regional analysis based on vessel distribution territory should be explored. Uebleis et al studied 158 patients with CAD and found that global and regional CAC do not correlate with the presence of myocardial perfusion defects and significant coronary artery stenoses, respectively.[10] This study did not evaluate the relationship between regional CAC and regional ischemia. Schuif et al performed a comparative regional analysis of coronary atherosclerosis and CAC scores on multislice CT vs MPI in 140 patients.[11] The average calcium score in coronary arteries with normal myocardial perfusion on MPI was 69 ± 167, and a higher calcium score of 272 ± 646 was noted in coronary arteries with abnormal perfusion on MPI ($P < 0.001$). Abnormal perfusion was seen in 13% of patients with CAC scores

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<10, and increased to 46% in patients with CAC scores >400. The relationship between CAC and MPI per coronary artery/vascular territory was not analyzed. However, vessel analysis between CTA and MPI showed that significant stenoses in RCA result in more frequent abnormal MPI than significant stenoses of the LAD and LCX. The authors suggested that there might be a higher frequency of severe total or subtotal occlusions in the RCA than in the LAD and LCX.

In our study, a stepwise linear regression analysis showed an association between moderate/severe ischemia with high CAC in the LAD and LCX, but not the RCA. Although the lack of association between CAC and RCA ischemia could be due to low sample size, another possibility is that ischemia in the RCA might be overestimated (ie, due to diaphragmatic attenuation).

Conclusion

Our data suggest a moderate agreement between atherosclerosis diagnosed by CAC scoring and ischemia diagnosed by MPI at the vessel level. Further studies should be done to explore areas of overlap and clinical scenarios where a certain test is superior to further stratify our treatment options.

References

1. He Z-X, Hedrick TD, Pratt CM, et al. Severity of coronary artery calcification by electron beam computed tomography predicts silent myocardial ischemia. *Circulation.* 2000;101:244–251.
2. Berman DS, Wong ND, Gransar H, et al. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. *J Am Coll Cardiol.* 2004;44:923–930.
3. Rozanski A, Gransar H, Wong ND, et al. Use of coronary calcium scanning for predicting inducible myocardial ischemia: influence of patients' clinical presentation. *J Nucl Cardiol.* 2007;14:669–679.
4. Schenker MP, Dorbala S, Hong ECT, et al. Interrelation of coronary calcification, myocardial ischemia, and outcomes in patients with intermediate likelihood of coronary artery disease. A combined positron emission tomography/computed tomography study. *Circulation.* 2008;117:1693–1700.
5. Hacioglu Y, Gupta M, Budoff MJ. Noninvasive anatomical coronary artery imaging versus myocardial perfusion imaging: which confers superior diagnostic and prognostic information? *J Comput Assist Tomogr.* 2010;34:637–644.
6. Ramakrishna G, Miller TD, Breen JF, et al. Relationship and prognostic value of coronary artery calcification by electron beam computed tomography to stress-induced ischemia by single photon emission computed tomography. *Am Heart J.* 2007;153:807–814.
7. Rozanski A, Gransar H, Wong ND, et al. Clinical outcomes after both coronary calcium scanning and exercise myocardial perfusion scintigraphy. *J Am Coll Cardiol.* 2007;49:1352–1361.
8. Uebleis C, Becker A, Griesshammer I, et al. Stable coronary artery disease: prognostic value of myocardial perfusion SPECT in relation to coronary calcium scoring—long-term follow-up. *Radiology.* 2009;252:682–690.
9. Rozanski A, Gransar H, Shaw LJ, et al. Impact of coronary artery scanning on coronary risk factors and downstream testing (early identification of subclinical atherosclerosis by noninvasive imaging research) prospective randomized trial. *J Am Coll Cardiol.* 2011;57:1622–1632.
10. Ubleis C, Rist C, Griesshammer I, et al. Cardiac SPECT/CT: correlation between atherosclerosis, significant coronary artery stenoses and myocardial perfusion parameters in patients with known coronary artery disease [in German]. *Radiologe.* 2010;50:366–371.
11. Schuif JD, Wijns W, Jukema W, et al. A comparative regional analysis of coronary atherosclerosis and calcium score on multisclice CT versus myocardial perfusion on SPECT. *J Nucl Med.* 2006;47:1749–1755.

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