# EDITORIAL

# Complementary roles of coronary calcium scanning and myocardial perfusion SPECT

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The assessment of coronary artery calcium (CAC) by electron beam tomography (EBT) or multidetector spiral computed tomography (CT) and the evaluation of myocardial perfusion and function by use of myocardial perfusion single photon emission computed tomography (SPECT) (MPS) are both valuable in the noninvasive assessment of patients with suspected coronary artery disease (CAD). CAC provides unique anatomic information regarding coronary atherosclerotic burden,[1] whereas MPS assesses the physiologic significance of coronary stenosis and provides information regarding stress-induced ischemia. These fundamental differences in the measurements result in the techniques being highly complementary. Many reports have demonstrated that EBT testing can be of clinical value by providing a marker of atherosclerotic burden in patients with risk factors for CAD but not yet clearly needing aggressive medical therapy.[1-6] Frequently, this occurs at a stage of atherosclerosis before there is a stenosis, a time at which the results of stress testing would usually be negative. MPS has proved useful in risk stratification and in identifying patients who require coronary angiography for purposes of possible coronary revascularization.[7-11] Although several reports have shown that CAC is also useful in risk stratification, ischemia determined by MPS provides unique information regarding the likelihood of benefit from a revascularization procedure.[11] The wide use of MPS, coupled with the increasingly recognized utility and growing availability of CAC scanning, raises a new clinical problem for clinicians as to how to integrate CAC scanning with conventional stress imaging tests in the clinical assessment of patients with suspected and known CAD.

In this issue of the *Journal of Nuclear Cardiology*, Anand et al[12] assess the prevalence of abnormal stress-rest MPS results in a study of a group of asymptomatic patients without a history of CAD undergoing CAC testing by EBT. On the basis of prior studies showing a low prevalence of abnormal MPS results in patients with an Agatston CAC score lower than 100,[13] the authors prospectively recruited 220 patients with a CAC score of 100 or greater from a group of 864 patients with risk factors for CAD who were referred for CAC testing to undergo MPS by use of a 2-day sestamibi stress-rest protocol. When classified by the conventional system described by Rumberger et al,[14] 119 patients had moderate atherosclerosis (CAC score of 100-399) and 101 had severe atherosclerosis (CAC score ≥400). Abnormal MPS results were present in 18% of the moderate and 45% of the severe CAC groups. In a multivariable analysis, CAC was the only predictor of abnormal MPS results, which in this group of asymptomatic patients was considered "silent ischemia."

Despite the overlap by noninvasive stress tests[7-11] and CAC scanning[1-6] for assessing outcomes, only two published reports have previously investigated the relationship between the results of stress MPS and the presence and magnitude of CAC abnormality. In the first study, He et al[13] noted a threshold phenomenon with a very low frequency of abnormal MPS studies in patients with a CAC score lower than 100 (2.6% of 76 patients) and a clear increase in the frequency of abnormal MPS studies in patients with high CAC values. They reported abnormal MPS studies in 11.3% of 142 patients with a CAC score of 101 to 399 and in 46% of 137 patients with a CAC score of 400 or greater. This observation formed the basis for the referral to MPS of only patients with a CAC score of 100 or greater used by Anand et al[12] in the current issue. In the second study, Moser et al[15] used multidetector spiral CT for the CAC assessment of 794 asymptomatic patients and reported on 102 who were also assessed by MPS. Concordant with the results of He et al, these investigators found rates of ischemic MPS of 5%, 24%, and 53% in patients with CAC scores of 100 or lower, 101 to 400, and 400 or greater, respectively. In a work currently in press, our group has evaluated over 1000 patients undergoing both CAC testing and MPS. In

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patients with a CAC score lower than 100, we found trends similar to all of the other studies, with a very low frequency of MPS ischemia; however, in our study, the frequency of ischemia by MPS in the higher calcium score groups was substantially lower than in the other studies.[16] These differences are most likely explained by either differences in the interpretative criteria used to assess the MPS results or differences in the risk factors other than coronary calcium of the populations (or both). In this regard, it may be of note that the MPS studies in the report of Anand et al[12] were assessed by one observer only. Whether the observer knew that the patients were part of the investigation (and thus that they had coronary calcium scores >100) was not described.

There is concordance in all reports to date that the frequency of ischemia by MPS in asymptomatic patients with a CAC score lower than 100 is very low, supporting the patient selection in the study of Anand et al.[12] Consequently, there is widespread agreement that, in general, such asymptomatic patients do not require further testing for ischemia. Exceptions to this might occur in the presence of symptoms or other compelling information such as marked ST depression on a prior stress electrocardiogram or a prominent family history of premature CAD. On the other hand, the data are less clear regarding which asymptomatic patients do require further testing. In their initial formulations, Rumberger et al[14] suggested that patients in the CAC category from 100 to 400 might have exercise electrocardiographic testing alone, with consideration of an imaging test if the CAC score was greater than the 75th percentile for age and sex. The data of He et al,[13] Moser et al,[15] and now Anand et al suggest that stress MPS might be appropriate in this group, whereas our data in press would suggest that the cutoff level might be 400 or greater in most patients.[16]

Anand et al[12] note in the "Discussion" section that the optimum CAC threshold for an individual would depend on the prevalence of obstructive CAD, which might be estimated on the basis of risk factors. With this approach, the threshold for selecting patients for MPS would be higher for a given patient if there is a low likelihood based on all available information that obstructive CAD is present; conversely, when the clinical suspicion of obstructive CAD is higher, the threshold used to guide the referral for MPS would be reduced. Because the CAC measurement is an imperfect marker of atherosclerosis, being negative when only soft plaque is present, some patients merit direct testing for ischemia.[4] In support of this concept, it is noteworthy that 4% of patients with unheralded acute myocardial infarction have been found to have no coronary calcium at the time of myocardial infarction[17] and that the sensitivity of a CAC score greater than 0 for angiographically significant CAD is generally considered to be 90% to 95%.[18,19] Thus, none of the articles regarding CAC scanning and MPS have suggested that the CAC test should replace the MPS study in patients with a relatively high clinical suspicion for the presence of obstructive CAD.

Another aspect of the possible need for both tests emerges when consideration is given as to which patients may merit CAC testing after having undergone MPS. Our preliminary results have indicated that a large proportion of patients referred for MPS have no evidence of ischemia but have a CAC score in a range that places them at high long-term risk (CAC score of 100-400).[16] It is also of note that in the studies published to date in which patients have had both CAC and MPS testing, half or more of the patients with a CAC score of 400 or greater have had no evidence of ischemia; in these patients it would not appear to be appropriate to rely on the MPS results to determine the need for aggressive medical management.

With the rapid developments of faster and higher-resolution CT scanners, noninvasive CT coronary angiography is becoming more commonly used for clinical purposes. The availability of this powerful new modality will add further complexity to the concepts regarding appropriate selection of tests. It may be that the natural evolution of technology will help solve much of this dilemma. With the further development of cardiac dedicated CT/positron emission tomography and CT/SPECT systems, it may be that a large body of data will be available in the future that will allow patients to have information regarding coronary calcium, coronary stenoses, and stress-induced ischemia, potentially providing large databases that can be a source of evidence regarding which test or combination of tests is most appropriate in a given setting.

In summary, the work of Anand et al[12] combined with the prior literature implies the following regarding the need for MPS in asymptomatic patients who have had CAC testing: MPS is generally not needed when the CAC score is lower than 100. When the CAC score exceeds 400, stress imaging would appear to be beneficial, because the frequency of inducible ischemia is substantial within this CAC range. Some patients with CAC scores in the range of 100 to 400 may require stress test referral after CAC imaging, and the study of Anand et al[12] as well as work in press suggest that the need for further testing in this CAC category may depend on the degree of clinical risk.[16] Future study involving a large number of patients with CAC scores in the range of 100 to 400 is needed to define the best combination of clinical predictors for predicting an ischemic MPS study in this CAC score range. Finally, patients with normal MPS studies frequently have high CAC scores, indicat-

ing the presence of extensive coronary atherosclerosis. This observation suggests the need to consider CAC or other testing for atherosclerosis in patients with normal MPS studies in order to identify a subgroup of patients who would then receive more aggressive anti-atherosclerotic intervention that might not have been indicated based on the results of risk factors and MPS testing alone.

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## References

1. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area. A histopathologic correlative study. Circulation 1995;92:2157-62.
2. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 2004;291: 210-5.
3. O'Malley PG, Taylor AJ, Jackson JL, Doherty TM, Detrano RC. Prognostic value of coronary electron-beam computed tomography for coronary heart disease events in asymptomatic populations. Am J Cardiol 2000;85:945-8.
4. Berman DS, Schisterman EF, Miranda R, et al. Nuclear cardiology and electron-beam computed tomography: competitive or complementary? Am J Cardiol 2001;88:51E-55E.
5. Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. Radiology 2003;228: 826-33.
6. Kondos GT, Hoff JA, Sevrukov A, et al. Electron-beam tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5635 initially asymptomatic low- to intermediate-risk adults. Circulation 2003;107:2571-6.
7. Ladenheim ML, Pollock BH, Rozanski A, et al. Extent and severity of myocardial hypoperfusion as predictors of prognosis in patients with suspected coronary artery disease. J Am Coll Cardiol 1986; 7:464-71.
8. Iskandrian AS, Chae SC, Heo J, et al. Independent and incremental prognostic value of exercise single-photon emission computed tomographic (SPECT) thallium imaging in coronary artery disease. J Am Coll Cardiol 1993;22:665-70.
9. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Stress myocardial perfusion SPECT is clinically effective and cost-effective in risk-stratification of patients with a high likelihood of CAD but no known CAD. J Am Coll Cardiol 2004;43: 200-8.
10. Poornima IG, Miller TD, Christian TF, et al. Utility of myocardial perfusion imaging in patients with low-risk treadmill scores. J Am Coll Cardiol 2004;43:194-9.
11. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation 2003;107:2900-7.
12. Anand DV, Lim E, Raval U, Lipkin D, Lahiri A. Prevalence of silent myocardial ischemia in asymptomatic individuals with subclinical atherosclerosis detected by electron beam tomography. J Nucl Cardiol 2004;11:449-56.
13. He ZX, Hedrick TD, Pratt CM, et al. Severity of coronary artery calcification by electron beam computed tomography predicts silent myocardial ischemia. Circulation 2000;101:244-51.
14. Rumberger JA, Brundage BH, Rader DJ, Kondos G. Electron beam computed tomographic coronary calcium scanning: a review and guidelines for use in asymptomatic persons. Mayo Clin Proc 1999;74:243-52.
15. Moser KW, O'Keefe JH, Bateman TM, McGhie IA. Coronary calcium screening in asymptomatic patients as a guide to risk factor modification and stress myocardial perfusion imaging. J Nucl Cardiol 2003;10:590-8.
16. 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. In press 2004.
17. Raggi P, Callister TQ, Cooil B, et al. Identification of patients at increased risk of first unheralded acute myocardial infarction by electron-beam computed tomography. Circulation 2000;101: 850-5.
18. O'Rourke RA, Brundage BH, Froelicher VF, et al. American College of Cardiology/American Heart Association Expert Consensus Document on electron-beam computed tomography for the diagnosis and prognosis of coronary artery disease. J Am Coll Cardiol 2000;36:326-40.
19. Haberl R, Becker A, Leber A, et al. Correlation of coronary calcification and angiographically documented stenoses in patients with suspected coronary artery disease: results of 1,764 patients. J Am Coll Cardiol 2001;37:451-7.