Editorial Comment

Exercise Thallium-201 Single Photon Emission Computed Tomography for the Diagnosis of Coronary Artery Disease: What Should We Expect From SPECT?*

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Since its introduction for medical use in 1975 by Lebowitz et al. (1), thallium-201 myocardial perfusion scintigraphy has become the most widely used noninvasive imaging technique for the detection of exercise-induced myocardial ischemia. In comparison with electrocardiography, thallium-201 imaging improves the sensitivity and specificity of exercise testing for ischemic heart disease (2). In the past decade, visual interpretation of the widely utilized planar thallium-201 imaging method has been improved by computer techniques that allow spatial and temporal quantitation of regional myocardial thallium-201 uptake (3–9). More recently, three-dimensional imaging of thallium-201 using rotational single photon emission computed tomography (SPECT) has become a routine clinical procedure. Advantages of this technique over planar imaging include enhancement of the contrast between perfusion defects and adjacent normal tissue and the elimination of myocardial segmental overlap. Direct comparisons have demonstrated superiority of SPECT over planar thallium-201 myocardial perfusion imaging for many clinical uses. These include improved diagnosis of myocardial infarction (10–14), enhancement of overall detection of exercise-induced ischemia (15–18), especially in the circumflex artery distribution (13,16), better prediction of the extent of disease (15,16) and more accurate localization of the stenosed branches of coronary vessels responsible for a given perfusion defect (19). For detection or exclusion of ischemic heart disease, receiver operating characteristic (ROC) analysis has demonstrated that SPECT imaging is superior to planar imaging at each level of interpretive certainty (20).

Quantitation of SPECT thallium-201 images improves interpretation. An important advance in the clinical utility of SPECT thallium-201 has been the recent development of quantitative analysis for image interpretation, which significantly improves on visual analysis of the tomographic slices (17,18,21–23). Display of the SPECT data in the form of a polar map or “bull’s-eye” plot (18,21,22) simplifies the interpretation of tomographic slices. This approach utilizes the circumferential maximal count (or maximal average count) profiles of the short-axis slices of the left ventricle and converts them into polar coordinate profiles. These profiles are displayed as a “bull’s-eye” plot or polar map that consists of a series of concentric circles with the apex at the center and the base at the outer edge. The result is a two-dimensional representation of three-dimensional tomographic perfusion data. This technique allows comparison of patients with varied heart sizes and shapes with a normal database obtained by averaging the plots of patients with very low likelihood (<5%) of coronary artery disease. The quantitation of SPECT images reduces intra- and interobserver variability by objectifying and simplifying the process of image interpretation, thereby benefiting both the experienced and the inexperienced observer.

The present study. In this issue of the Journal, Mahmarian et al. (21) report the largest comprehensive comparison of quantitative and visual analysis of SPECT thallium-201 images to date. They examined the exercise and redistribution thallium-201 SPECT studies of 360 consecutive patients who had also undergone coronary arteriography using visual analysis and computer-quantified polar maps. For defining the presence or absence of coronary artery disease, the two methods showed similar sensitivities (both 87%) but a trend toward higher specificity with quantitation (87% versus 76%). Additionally, they report excellent intra- and interobserver agreement for sizing of perfusion defects.

With respect to detection of disease in individual coronary vessels, Mahmarian et al. (21) found that the quantitative approach had higher sensitivity than that of the planar approach for disease of the left anterior descending and circumflex coronary arteries, but not for the right coronary artery. The improved sensitivity was not burdened by a significant decrease in specificity for these vascular territories. These results are in general agreement with previously published, but smaller, direct comparisons of quantitative and qualitative analysis (17,18), except that detection of

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disease in the right coronary artery distribution was maintained or improved by quantitation in those studies. In the subgroup of patients without previous myocardial infarction, the investigators found less overall sensitivity for detection of coronary disease with both quantitative and visual assessment (79% and 78%, respectively). This finding is also in agreement with results of other investigators (17) who were careful to analyze these patients separately. This distinction is important in the evaluation of any diagnostic technique, because the diagnosis of coronary artery disease is far less certain in patients with prior infarction and this group tends to have more severe and more easily discerned perfusion abnormalities. Inclusion of patients with prior myocardial infarction will tend to inflate the sensitivity calculation.

SPECT thallium-201: can its diagnostic accuracy be improved? In this age of technologic advances and the emergence of new and potentially competing techniques for myocardial perfusion imaging, the diagnostic accuracy reported in this and other reports of the SPECT thallium-201 technique is in need of some improvement, especially in the subcategory of patients without prior infarction. One potentially correctable source of error is attenuation of tracer activity due to body tissues (18,24–26). Thallium-201 is a low energy tracer (68 to 83 keV photons). The images obtained with thallium-201 represent both the myocardial uptake of tracer and the fraction of photons that are able to penetrate body tissues. Artifactual perfusion defects due to the left breast, chest wall, right ventricle and diaphragm are often easy to recognize on planar imaging, but may appear only as decreased segmental tracer content on SPECT. One practical approach to the problem of attenuation has been the development of gender-specific normal data bases (18,26). Studies of men tend to show more inferior wall or diaphragmatic attenuation with anterior to inferior wall ratios >1.0, whereas women have more anterior wall (breast) attenuation. Thus, it could be argued that the use of a mixed gender normal data base for comparison in the study by Mahmarian et al. (21) resulted in reduced sensitivity (81%) to left anterior descending coronary artery disease because their study included predominantly men, whereas their normal data base had more women. The specificity for left anterior descending artery disease in women and for posterior descending artery disease in men might similarly be reduced by a single normal data base comparison.

Recent studies (27,28) have also shown that attenuation of the inferior wall can be minimized by acquisition of thallium-201 tomograms in the prone rather than the commonly employed supine position. This requires the generation of separate normal data bases for prone studies (27), but significantly improves the specificity of detection of posterior descending coronary artery disease (28).

The principle of compensating for attenuation differences related to gender could be extended to the development of many normal files for the varied body sizes and shapes as well as gender. However, a better approach may be to correct, rather than compensate for, the nonuniform attenuation using newly developed computer techniques. Attenuation distribution can be determined from back projection of a rotationally acquired transmission tomogram. In one report (29), attenuation correction significantly improved image quality, uniformity and quantitative information in a study of phantoms and patients. This approach deserves further research.

As emphasized in the discussion section of the article by Mahmarian et al. (21), studies comparing noninvasive detection of coronary artery disease with the visually analyzed coronary arteriogram will be flawed by underestimation of diagnostic accuracy. Coronary anatomy imaged by "lumenography" and visually assessed is at best an imprecise standard for comparison with a physiologic assessment of coronary flow and the development of myocardial ischemia (30). The accuracy of the many noninvasive imaging techniques for the diagnosis of ischemic heart disease should now be reassessed using coronary flow reserve measurements or videodensitometric analysis of coronary arteriographic data (31,32). By using a physiologic reference standard, it may be possible to assess the true diagnostic accuracy of quantitative SPECT perfusion studies. Also, because the test result influences selection of patients for coronary arteriography, the well described phenomenon of post-test referral bias (33,34) tends to improve apparent sensitivity and lower apparent specificity of noninvasive diagnostic tests.

The future of myocardial perfusion imaging. In the near future, the SPECT techniques described by Mahmarian et al. (21) will be routinely applied to new perfusion tracers, such as the technetium-99m–labeled isonitrile complexes (35). These compounds have better imaging characteristics and less radiation burden than thallium-201 (36), allowing higher dose administration and improved perfusion image contrast (37). Electrocardiographic gating of the SPECT acquisition, as has recently been performed with blood pool imaging (38), will allow the simultaneous assessment of myocardial regional perfusion, systolic excursion and wall thickening. The assessment of exercise ventricular performance and regional wall motion with first pass radionuclide angiography can also be obtained with a bolus injection of technetium-99m isonitrile administered before SPECT perfusion data acquisition (39).

There have been many recent advances in the development of other noninvasive techniques for the assessment of myocardial perfusion. The use of paramagnetic agents such as gadolinium-diethylenetriamine-pentaacetic acid (40) or manganese gluconate combined with calcium gluconate (41) for the assessment of myocardial perfusion and infarction with nuclear magnetic resonance (NMR) imaging may rival SPECT in the future, but needs much further development.
Contrast echocardiography can delineate myocardial perfusion (42,43), but intravenous (rather than intracoronary) contrast agents and better image characteristics need to be developed.

Ultrafast computed tomography has proved valuable in the evaluation of large vessel myocardial blood flow (44,45). Experimental quantitation of tissue level perfusion has also been reported (46–49). This approach offers promise for the quantitation of regional myocardial perfusion and coronary flow reserve in patients.

Positron emission tomography (PET) is an elegant and well validated technique for assessing myocardial perfusion, noninvasive flow reserve with dipyridamole and myocardial viability (31,32,50–53). It provides the opportunity to obtain truly quantitative measurements of absolute myocardial blood flow (50). The diagnosis of coronary artery disease and definition of areas at risk have been obtained with unsurpassed accuracy using PET (32,51). The financial expense of PET has been prohibitive, but the technique may rapidly become cost-competitive with SPECT imaging (52).

Conclusions. Along with the advent of technetium-99m-labeled perfusion compounds and attenuation correction or compensation, or both, the increasing use of quantitative analysis, as described by Mahmarian et al. (21), will improve the diagnostic accuracy of SPECT perfusion imaging. Despite the rapid advances in the other technologies noted, SPECT perfusion imaging will remain the most cost-effective noninvasive method for assessing the physiologic impact of ischemic heart disease for years to come. As with all sophisticated techniques, the reliability and accuracy of the results greatly depend on the experience and expertise of those performing and interpreting these procedures.

References


