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Editorial Comment

A New, Highly Specific Thallium-201 Marker for Severe and Extensive Coronary Artery Disease

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Thallium scintigraphy for assessment of regional myocardial perfusion. Although definition of coronary artery narrowing by coronary arteriography provides anatomic information, it does not answer the question of whether a given lesion significantly affects myocardial blood flow and function, particularly under conditions of increased demand (1,2). Thallium scintigraphy is the most widely utilized technique for determination of regional myocardial blood flow (3), although several newer techniques are available such as positron emission tomography (4,5), digital subtraction angiography (6), Doppler flow probe (7), dynamic computed tomography (8) and scintigraphy with technetium-labeled tracers of blood flow (9).

Accurate assessment of significant coronary artery disease using thallium-201 is affected by limitations of thallium scintigraphy. These limitations include Compton scatter and attenuation of the low energy photon (69 to 83 keV) used for imaging and the measurement of relative, not absolute, differences in tracer concentration. Planar imaging has the additional problem of presenting three-dimensional data in two dimensions, which is less accurate than tomographic imaging for detecting the site of coronary artery disease, especially in the distribution of the circumflex coronary artery (10,11). These factors make detection of multivessel disease difficult. Therefore, in addition to evaluation of images for reversible perfusion defects, certain scintigraphic findings have been reported which suggest significant multivessel or left main coronary disease (12–14). These include visual assessment of left ventricular dilation (14) and quantitative methods to evaluate myocardial and pulmonary thallium uptake and washout (15–19). In an attempt not only to detect multivessel disease, but also to evaluate the extent and severity of disease (that is, the amount of myocardium "at risk"), Weiss and colleagues (20) in this issue of the Journal elaborate on the finding of transient left ventricular dilation.

Proposed mechanism of transient left ventricular dilation. In normal subjects, the increased stroke volume during exercise is achieved by a combination of increased heart rate and a change in the relation of end-diastolic and end-systolic volumes. The relative importance of these two mechanisms may differ during supine and upright exercise, and during different levels of exercise (21,22). During upright exercise the end-diastolic volume tends to increase (although at maximal exercise it may decrease slightly) whereas end-systolic volume decreases by an average of one-third the rest value (21–23). However, in patients with significant coronary artery disease changes in end-diastolic and end-systolic volumes are variable (24–26). End-diastolic volume may increase to a greater extent than in normal subjects, and end-systolic volume can average a twofold increase from rest values during both upright (23) and supine (27) exercise. How changes in left ventricular volumes are related to changes in left ventricular size measured by thallium imaging has not been verified.

Left ventricular size on thallium images as a marker of severe and extensive coronary artery disease. Weiss and colleagues (20) propose that persistence of increased left ventricular size on thallium images during immediate acquisition (from 6 to 16 minutes after stopping exercise) may be related to the amount of ischemic myocardium. Factors other than ischemia that alter preload and afterload, such as increased mitral regurgitation, assumption of the supine position and elevated blood pressure, also affect exercise left ventricular volumes. Whereas age did not affect the response of end-diastolic volume to exercise, exercise ejection fraction declined with age, implying that end-systolic volume increased (28). The sex of the patient appears to influence exercise left ventricular volume; end-diastolic counts increased 20 to 30% in women and only 10% in men (29). The rest end-diastolic volume may affect the magnitude of change in end-diastolic volume during exercise (26).

Technical aspects of thallium imaging. Quantitative measurement of left ventricular size is affected by technical factors. The most obvious is the lack of a well defined epicardial border in patients with prior myocardial infarction. In addition, the heart may assume a slightly different orientation with respect to the anterior projection on the immediate and delayed images. These factors could affect the number of pixels measured by the epicardial contour. Finally, the maximal heart rate achieved during exercise may exert some influence not only on detection of the epi-

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cardial edge because of blurring due to cardiac motion but also on left ventricular size because ungated thallium images represent a summed cardiac cycle (30).

Utility of the markers of severe and extensive coronary artery disease. The utility of a given marker for disease detection is dependent on several factors including reproducibility of the measurement and the ability to obtain similar information using different techniques. For example, in the article by Weiss and colleagues (20), do the different results for visual and quantitative assessment of left ventricular dilation represent technical differences between the methods or a problem with reproducibility? For detection of severe and extensive coronary artery disease, quantitative assessment of transient left ventricular dilation was less sensitive than, and visual assessment equally as sensitive as, thallium defects or washout abnormalities, or both. For detection of patients without significant coronary artery disease (less than 50% stenosis), quantitative transient left ventricular dilation, exercise time and electrocardiographic criteria were all similarly specific. The latter two criteria were only slightly less specific when evaluating a mixed group of patients, some with severe but none with both severe and extensive disease (Groups I to III). Transient left ventricular dilation was slightly less sensitive than thallium defects or washout abnormalities, or both. From the data presented by Weiss and colleagues, it is difficult to evaluate whether the abnormal transient dilation ratio identified additional patients not identified by other markers because five of the seven patients had prior myocardial infarction, which identified at least severe one-vessel disease.

Conclusions. Thallium scintigraphy can provide useful information about physiologically significant coronary artery lesions. However, several limitations exist. 1) Thallium-201 images currently yield qualitative, not quantitative, information about blood flow; 2) planar images yield two-dimensional, not three-dimensional, information; and 3) the low energy photon used for thallium-201 imaging is readily attenuated, resulting in poor spatial resolution. Tomographic imaging and the possibility of using technetium-labeled blood flow tracers may ameliorate these problems. For interpretation of planar thallium images, ancillary signs have been identified that may help identify patients with a significant amount of myocardium at risk. Before accepting new diagnostic criteria, confirmation must be obtained by reproducing the results in other laboratories using an appropriate study design (31).

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JACC Vol. 9, No. 4
April 1987:760-2

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