Exercise Myocardial Perfusion Imaging

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The role of physical exercise in myocardial perfusion imaging is critical for two reasons: (1) stress is essential to create heterogeneity of blood flow in myocardial regions supplied by normal versus stenosed coronary arteries and (2) exercise data provide invaluable information that can influence the interpretation of perfusion images. Image interpretation and correlation with exercise data provide important prognostic information on a patient's risk for subsequent cardiac events.

Key Words: myocardial perfusion imaging; coronary artery disease; risk stratification

J Nucl Med 1994; 35:726–729

The mechanistic principle of radionuclide myocardial perfusion imaging for the detection of coronary artery disease (CAD) depends on stressing the metabolic demands of the heart and creating heterogeneity of myocardial blood flow between regions supplied by normal and significantly stenosed coronary arteries.

At rest, most patients with CAD are asymptomatic. Even when a critical coronary artery lesion is present, resting myocardial blood flow may be equal in both normal and stenosed arteries (Fig. 1). Moreover, resting myocardial blood flow is sufficient to sustain normal myocardial metabolism. In this baseline condition, the distribution of myocardial blood flow is homogeneous, and if a myocardial perfusion radiotracer is injected at rest, the uptake throughout the myocardium is homogeneous, resulting in a normal image.

If the patient exercises, however, myocardial blood flow increases markedly in regions supplied by normal arteries, whereas no such increase occurs in regions supplied by coronary arteries with significant stenoses. This heterogeneity in distribution of myocardial blood flow, caused by hemodynamically significant coronary artery stenosis, can be visualized by the injection of a myocardial perfusion radiotracer (Fig. 1). It is important to realize that *heterogeneity* of regional myocardial blood flow will cause myocardial perfusion defects on images, and it is not necessary to induce myocardial ischemia.

Received Dec. 10, 1993; revision accepted Dec. 28, 1993.
This paper was presented in part at the Annual Meeting of the Society of the Nuclear Medicine on June 9, 1993, as part of a Continuing Medical Education Seminar organized by the Cardiovascular Council.
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DETECTION OF CAD

Numerous studies in the literature have documented the value of planar and SPECT exercise myocardial perfusion imaging for detection of CAD (*1–12*). Over the last 15 yr, this procedure has consistently identified CAD in millions of patients. Several reviews of the literature indicate a sensitivity and specificity of approximately 80% to 90% using quantitative interpretation (*13*). Depending on how patients are selected, the reported specificity may be lower, which can be explained by referral bias (*14*). Since patients with abnormal myocardial perfusion images are more likely to be referred for coronary angiography than patients with normal studies, patients with angiographically normal coronary arteries are likely to have abnormal stress perfusion images. Quantitative and objective display, with reference to a normal database, is important for reproducible and consistent interpretation.

RISK STRATIFICATION

Although exercise myocardial perfusion imaging is extremely useful to identify CAD, an equally relevant clinical application of this procedure is the determination of long-term outcome and prognosis. A large body of data supports the premise that radionuclide myocardial perfusion images are useful to risk-stratify patients for future cardiac events (*15–21*). According to data collected by Kaul et al., redistribution of exercise-induced ^{201}Tl defects (i.e., evidence of the potential for ischemia) is associated with a significantly increased rate of subsequent cardiac events (*22*). In a more recent study by Hendel et al., using dipyridamole-thallium imaging, patients with fixed defects had an adverse long-term prognosis (*23*).

The extent of abnormalities on myocardial perfusion images has a significant prognostic value. Ladenheim et al. analyzed the cardiac event rate as a function of the number of reversible defects (*24*). There was a significant relation between the extent and severity of myocardial perfusion defects and patient outcome.

This type of qualitative analysis suggests that computer

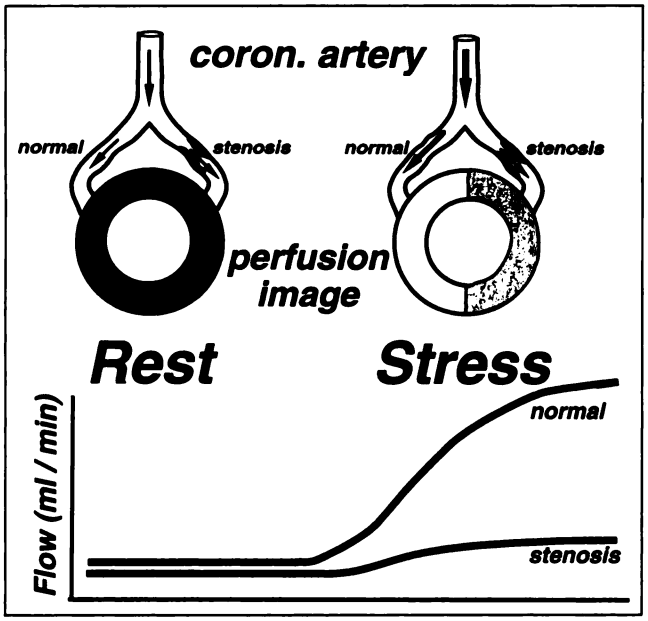

FIGURE 1. Schematic representation of the principle of rest/stress myocardial perfusion imaging. (Top) Two branches of a coronary artery are shown; one is normal (left) and one has a significant stenosis (right). (Middle) Myocardial perfusion images of the territories supplied by the two branches. (Bottom) Schematic representation of coronary blood flow in the branches at rest and during stress. At rest, myocardial blood flow is equal in both coronary artery branches. When a myocardial radiotracer is injected at rest, uptake is homogenous (normal image). During stress, coronary blood flow increases 2.0 to 2.5 times in the normal branch, but not to the same extent in the stenosed branch, resulting in heterogenous distribution of blood flow. This heterogeneity of blood flow can be visualized with ^{201}Tl of ^{201}Tl-sestamibi as an area with relatively decreased uptake (abnormal image with a myocardial perfusion defect).

quantification of defects is essential. Figure 2 shows quantitative analysis of a planar image with a lower septal defect. A circumferential profile display shows that the defect is below the lower limit of normal. The defect improves quantitatively on the delayed images, a graphic display of defect reversibility. Similar quantitative interpretation techniques are used for SPECT images (Fig. 3). Using either a circumferential count profile or a bull's-eye display, defect reversibility can be displayed quantitatively.

Beyond quantitative analysis of defect reversibility, there are other patterns important to recognize on myocardial perfusion images that indicate high risk for subsequent cardiac events. Figure 4 shows planar ^{201}Tl images of a large heart with multiple perfusion defects involving the septum, apex and anterior wall. These defects are only partially reversible. The most striking feature on this image is the increased uptake of ^{201}Tl in the lungs, which reflects ischemic left ventricular dysfunction during exercise. The presence of both fixed and transient defects, as well as increased lung uptake, indicates very high risk of a subsequent cardiac event.

Several investigators have shown that stress myocardial perfusion imaging provides better prognostic information than stress electrocardiography (ECG) or coronary angiography. High-risk patients are characterized by multiple defects, increased lung uptake and transient left-ventricular dilatation on ^{201}Tl stress images (*26*).

IMPORTANCE OF EXERCISE AND ECG DATA

In addition to image interpretation, the exercise test itself provides important prognostic information in such variables as duration of exercise, achieved workload, change in heart rate and ECG changes. Nuclear physicians and cardiologists should be aware that these exercise parameters may be of tremendous help to provide more complete and clinically relevant interpretation of images, even though each parameter in itself may be less sensitive or specific than the perfusion images.

In a study of patients with confirmed CAD by McNeer et al., the ability to exercise longer than Stage IV of the Bruce protocol (at least 12 min) is associated with a far better prognosis compared with the inability to reach Stage III (*27*). Similarly, patients who achieve a heart rate >160

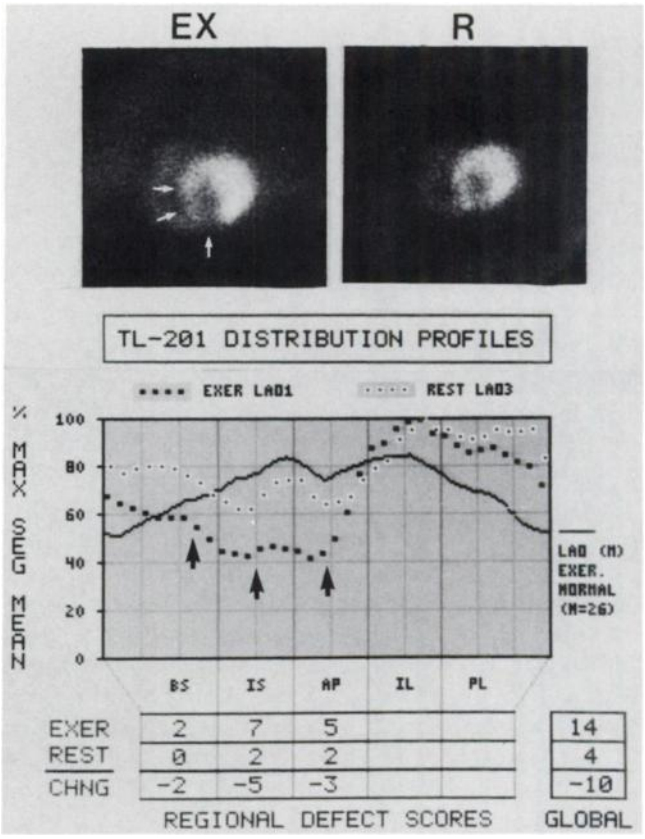

FIGURE 2. Quantitative analysis of planar LAO ^{201}Tl exercise (EX) and redistribution (R) images using circumferential count profiles. Images in the top panel show a partially reversible inferoseptal defect (arrow). The bottom panel shows distribution profiles (EX, R), normalized to the area with the highest counts in the inferolateral (IL) wall. The continuous black curve indicates the lower limit (mean – 2 s.d.) of normal ^{201}Tl distribution. The exercise profile is below the lower limit of normal in the basal septal (BS), inferoseptal (IS) and apical (AP) segments in concordance with the visual impression. The redistribution profiles show significant improvement toward normal. The exercise defect in quantified as the integral below normal: 14, redistribution defect is small; 4, reversibility of the defect is 71%.

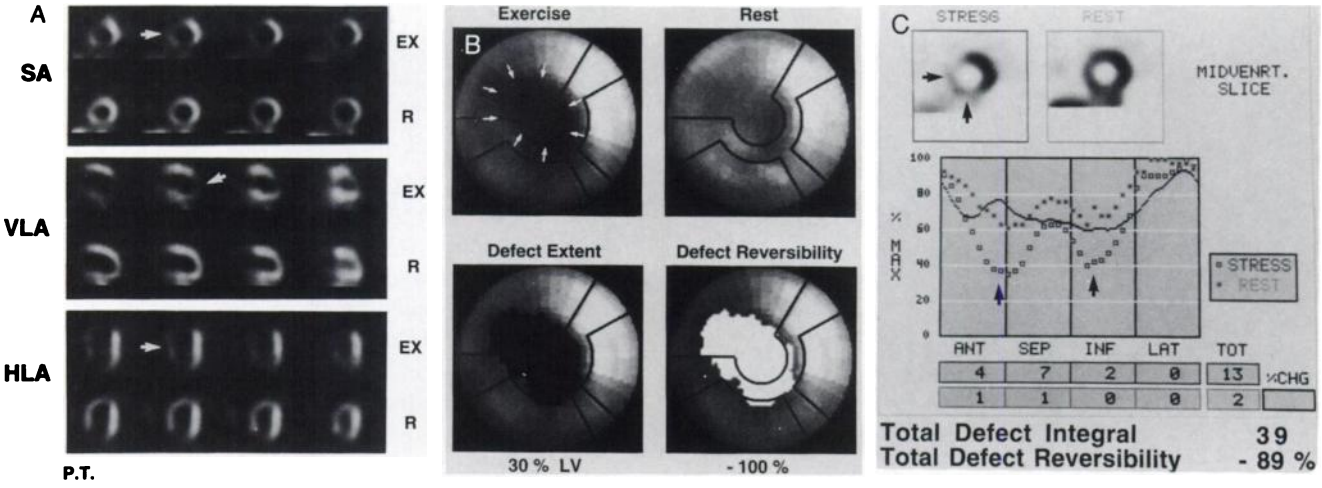

FIGURE 3. (A) Exercise (EX) and rest (R) SPECT ^{99m}Tc-sestamibi images. Reversible anteroapical and septal perfusion defects (arrows) are present. (B) Polar map, or bull's-eye display, of the relative distribution of ^{99m}Tc-sestamibi image (A). The exercise polar map shows the defect as a dark area (arrows) in the apical and anteroseptal area. The defect extent is compared to the normal database and displayed as a "black-out area." The defect extent is 30% of the left ventricle (LV). On the rest polar map, the distribution of ^{99m}Tc-sestamibi is within the normal range. Defect reversibility is displayed as a "white-out area," and is quantified here as 100%. (C) Circumferential count distribution profile of a representative midventricular slice (similar to Fig. 4). The stress defect is in the anteroseptal and inferior area. In the midventricular slices, the total stress defect integral is 13 and the rest defect integral is 2. Applying the same quantification to all short-axis slices, the total exercise defect integral is quantified as 39. The total defect reversibility is quantified as 89% of the stress defect.

bpm at peak exercise have a greater survival rate than patients who achieve <120 bpm. Finally, patients with no ST-segment depression on the exercise ECG have better survival rates than patients with positive exercise ECGs.

By combining data from exercise tolerance, peak exercise heart rate and ECG response, the prediction of high-risk patients becomes even more accurate. Patients with negative ECGs who can exercise longer and achieve higher heart rates have significantly better chances of survival, even with confirmed CAD, than patients with positive ECGs who cannot exercise for longer time periods and who cannot achieve higher heart rates (Fig. 5). Other high-risk indicators include a failure to increase blood pressure by >20 mmHg and a decrease in blood pressure.

Exercise data are extremely valuable in evaluating patients with known or suspected CAD, particularly when myocardial perfusion images are equivocal. In patients with equivocal perfusion studies (e.g., small defect) and low-risk exercise data, the image may be interpreted as normal. On the other hand, the same myocardial perfusion image in a high-risk patient can be interpreted as showing "some" ischemia.

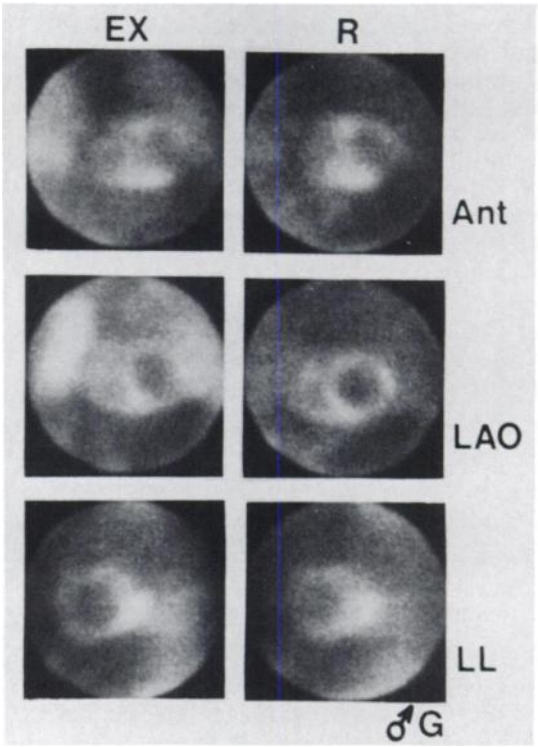

FIGURE 4. A typical example of high-risk ^{201}Tl stress images. On the postexercise images (EX), increased pulmonary uptake can be observed on all three views, particularly on the LAO, which was the first view acquired after discontinuation of exercise. Furthermore, the heart is enlarged and shows a large anteroseptal myocardial perfusion defect. In addition, there is an abnormal area in the inferolateral wall. The patient had triple-vessel CAD on coronary angiography. The images indicate multiple areas of exercise-induced myocardial ischemia and evidence of exercise-induced left-ventricular dysfunction. Ant = anterior; LL = left lateral. Reprinted with permission from the American Heart Association (*Circulation*, 1978;57:64).

CONCLUSION

Exercise myocardial perfusion imaging is an invaluable diagnostic test to evaluate patients with CAD. More important than merely detecting the presence of CAD, perfusion images may provide prognostic information on the risk of future cardiac events. Parameters of exercise testing performance and ECG changes should be correlated with radionuclide imaging data for a more comprehensive evaluation of a patient with known or suspected CAD.

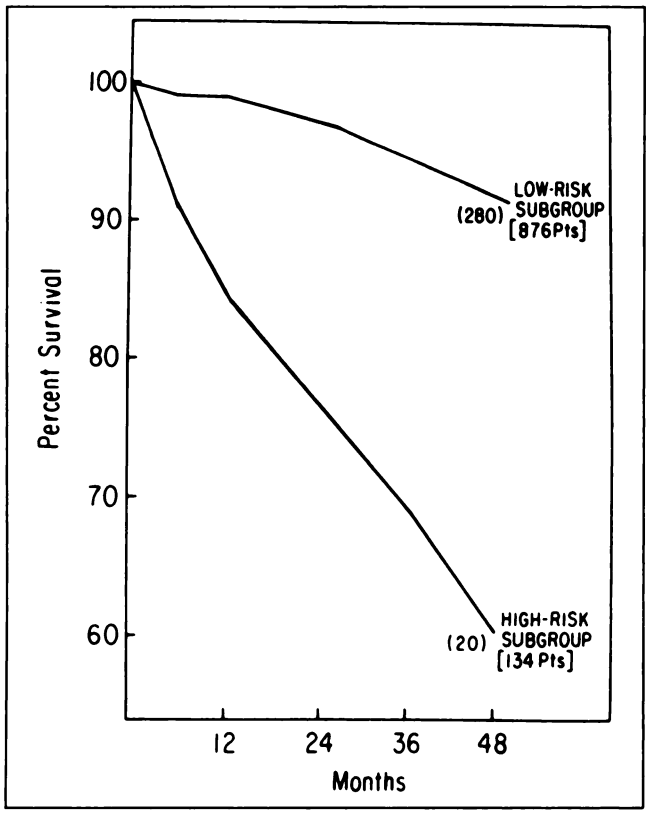

FIGURE 5. Cumulative life table survival rates in low- and high-risk subgroups on the basis of stress ECG results and exercise parameters. Numbers in parentheses represent the number of patients followed for 48 mo. Numbers in brackets represent the number of patients in each subgroup. The low-risk subgroup includes patients with a negative exercise ECCG or exercise duration ≥Stage IV and/or a maximum heart rate ≥160. The high-risk subgroup includes patients with a positive exercise ECG and exercise duration <Stage III. Reprinted with permission from the American Heart Association (*Circulation* 1978;57:64).

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