

Assessment of left ventricular function during exercise; the use of radionuclide cineangiography

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In patients with many forms of heart disease, left ventricular function is normal or nearly normal when the patient is at rest, even when disease clinically is moderately severe. However, the interposition of stress, such as that produced by physical exercise, causes demand for left ventricular work to exceed functional reserve capacity, with functional abnormality then becoming apparent. Until recently, assessment of left ventricular function during exercise has required invasive techniques, and thus has been impractical in many clinical situations. However, with the development of radionuclide cineangiography, a computer-based method for making movies of the beating heart in less than 2 minutes of imaging, it has become possible to assess regional and global left ventricular function, not only at rest but during intense exercise. We have now employed radionuclide cineangiography during exercise in the study of more than 2000 patients with various forms of heart disease. The following data will illustrate the variety of situations in which the technique can be usefully employed clinically.

In evaluating the efficacy of the method in detecting coronary artery disease, we found that in 35 normal subjects, no regional dysfunction was present at rest or during exercise; left ventricular ejec-

tion fraction invariably rose during exercise (mean ejection fraction 57% at rest, 71% with exercise, $p < 0.001$). However, in 59 of 63 (93%) patients with coronary artery disease, whether or not regional dysfunction was present at rest, at least one region of dysfunction was noted during exercise, invariably corresponding to the area of distribution of a coronary artery with $\geq 50\%$ stenosis by coronary arteriography. In contrast, only 310 (51%) patients had positive exercise electrocardiograms ($p < 0.01$ compared with radionuclide results). In addition, ejection fraction almost invariably decreased to subnormal levels during exercise (mean ejection fraction 46% at rest, 34% during exercise, $p < 0.001$), though it had been normal at rest in 35 of the 63 patients. These abnormalities in global and regional function were present even in the 16 asymptomatic patients studied. Moreover, in 21 of 21 patients with chest pain, but normal coronary arteries, ejection fraction and regional function were normal during exercise. In 27 of 28 patients with coronary artery disease studied after nitroglycerin, regions of dysfunction previously provoked by exercise were absent or markedly diminished, and ejection fraction during exercise improved (ejection fraction, 36% before and 48% after nitroglycerin, $p < 0.001$). Similarly, in 23 patients studied before and 6 months after coronary artery bypass grafting, though no change was present at rest, during exercise after operation regional function was improved in 19 patients (all with patent grafts), and ejection was increased (37% before, 51% after operation, $p < 0.001$). These data indicate that radionuclide cineangiography during exercise is highly sensitive and specific in the diagnosis of coronary artery disease, and can accurately assess the

functional severity of disease and the efficacy of therapy.

The technique also can be used to assess patients with other forms of heart disease. In patients with aortic regurgitation, left ventricular dysfunction at rest, which is associated with poor long-term prognosis after aortic valve replacement, often develops before symptoms. To determine whether evidence of left ventricular dysfunction could be detected before it appeared at rest, we studied 43 patients with severe aortic regurgitation. Though normal at rest in 14 of 21 symptomatic patients (average, 47%), ejection fraction was normal during exercise only in one (average, 38%, $p < 0.001$). Ejection fraction was normal at rest in 21 of 22 asymptomatic patients (average, 62%), but was normal during exercise only in 13 (average, 57%, $p < 0.001$). Thus, exercise-induced left ventricular dysfunction can precede symptoms and dysfunction at rest. Radionuclide assessment of left ventricular function during exercise may prove valuable in sequentially following the state of left ventricular function in patients before the onset of symptoms and irreversible left ventricular failure. The technique, therefore, may be of value in determining prognosis and appropriate timing of surgical intervention.

The findings in asymptomatic patients take on added importance when viewed in the light of our findings that aortic valve replacement in symptomatic patients often does not lead to restitution of normal left ventricular function. In our symptomatic patients with aortic regurgitation, ejection fraction rose to normal (average, 57%) at rest after operation; however, ejection fraction during exercise after operation, though significantly improved compared with the preoperative value, was

still significantly depressed (average, 52%).

In contrast, in symptomatic patients with severe aortic stenosis, ejection fraction at rest before operation generally was above normal (average, 68%), though it fell during exercise (average, 56%). After operation, though there was no change in ejection fraction at rest, ejection fraction during exercise returned to normal (average, 72%). These findings suggest that chronic volume loading, as seen in patients with aortic regurgitation, may be associated with more severe intrinsic myocardial damage than is chronic pressure-loading, as seen in patients with severe aortic stenosis.

In patients with asymmetric septal hypertrophy, ejection fraction often is supernormal at rest, irrespective of the presence or absence of left ventricular outflow tract obstruction. However, during exercise, most patients with obstruction maintain normal ejection fractions, whereas most patients without ob-

struction have depressed left ventricular ejection fraction. These findings are consistent with the results of morphological studies, which indicate that the cardiomyopathic process in patients with asymmetric septal hypertrophy is more widespread in those patients without obstruction. Moreover, the findings raise the possibility that in patients without obstruction, the addition of inotropic support may be of clinical value, despite evidence of supernormal left ventricular function when the patient is at rest.

Data such as these illustrate the potential value of noninvasive radionuclide cineangiography in the evaluation of patients with heart disease. The technique is of value in the diagnosis of coronary artery disease, in the evaluation of the functional severity and effects of therapy of many forms of heart disease, and appears to be of potential value in determining prognosis and in timing therapy.