Exercise Echocardiography Versus 201TI Single-Photon Emission Computed Tomography in Evaluation of Coronary Artery Disease

Analysis of 292 Patients

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Background. Exercise echocardiography (digital cine-loop technique) and 201TI single-photon emission computed tomography (SPECT) were performed simultaneously in 292 patients being evaluated for coronary artery disease.

Methods and Results. Pretreadmill and posttreadmill echocardiographic images of diagnostic quality were obtained in 289 patients, and the left ventricle was divided into anterior, inferior, and lateral regions. Any wall motion or perfusion abnormality observed within each region was classified as totally reversible, fixed, or partially reversible. Exercise echocardiography and SPECT were normal in 137 patients and abnormal in 118 (88% agreement). Equal numbers of regional abnormalities were detected by one test when missed by the other. The two tests had an 82% agreement in detecting the same type of finding within the regions analyzed. SPECT detected more reversible abnormalities than echocardiography, whereas echocardiography detected more fixed abnormalities than SPECT. Regions with a fixed abnormality by echocardiography frequently showed partial reversibility of a perfusion defect by SPECT. Nearly one third of regions with fixed perfusion defects by SPECT demonstrated normal resting function or reversible abnormalities by echocardiography. Sensitivity for coronary artery disease by angiography (≥50% diameter stenosis) in 112 patients was similar for the two tests, ranging from 58% and 61% (echocardiography and SPECT, respectively) for one-vessel disease to 94% for three-vessel disease. The specificities for echocardiography and SPECT were 88% and 81%, respectively.

Conclusions. Exercise echocardiography had a diagnostic accuracy comparable to that of SPECT for the detection of regional abnormalities produced by significant coronary artery disease. A greater number of abnormal regions were detected with the combined use of both tests. (Circulation 1992;85:1026–1031)

Key Words • echocardiography • exercise • testing • 201TI • computed tomography, single-photon emission • coronary artery disease

The application of exercise echocardiography to the detection and assessment of coronary artery disease (CAD) was facilitated initially by the development of the postexercise technique where images of the left ventricle were obtained before and immediately after treadmill exercise.1,2 The increase in popularity of exercise echocardiography, however, occurred with the development of digital image acquisition and cine-loop playback that provided side-by-side comparisons of rest and exercise images.3–6 The ranges of sensitivity and specificity reported for exercise echocardiography have been comparable to those of 201TI single-photon emission computed tomography (SPECT).1–4,7–10 Although one technique evaluates myocardial perfusion and the other ventricular function, both exercise 201TI SPECT and exercise echocardiography can detect reversible ischemia, distinguish ischemia from fixed resting abnormalities, and identify regions supplied by specific coronary vessels. Importantly, both techniques have been shown to have diagnostic accuracy superior to that of exercise ECG2,4,10 and may therefore have similar applications in the evaluation of patients with CAD. The present study was designed to prospectively compare the results of exercise echocardiography with those of 201TI SPECT in a large patient population studied in a laboratory where the two techniques have been properly validated.2,10

Methods

The study population comprised 292 patients (195 men and 97 women; mean age, 57±8 years) referred for exercise 201TI SPECT for the evaluation of known or suspected CAD. Fifty-two percent of the patients were receiving cardiac medication, with 90% of these consisting of β-blockers, coronary vasodilators, or both. As a
rule, medications were not discontinued before the test. The patients underwent symptom-limited maximal treadmill exercise using the Bruce protocol with continuous 12-lead ECG monitoring. Mean exercise duration was 7.5±3.2 minutes. Peak exercise heart rate was 148±23 beats per minute with maximal systolic and diastolic blood pressures of 162±24 and 84±14 mm Hg, respectively. Two thirds of the patients achieved a peak exercise heart rate of ≥140 beats per minute.

Exercise Echocardiography

Two-dimensional echocardiography was performed before exercise with the patient lying on the left lateral recumbent position and with the use of a phased-array sector scanner (model 77020A, Hewlett-Packard) and a 2.25-MHz transducer. Images of the left ventricle were obtained in the standard parasternal and apical views as previously described and recorded continuously on videotape. Immediately after termination of exercise, the patient resumed the left lateral recumbent position. Whenever possible, echocardiographic images of the left ventricle were obtained first from the apical window, rotating from the four-chamber to the two-chamber view, and then in the parasternal long-axis and short-axis views at the midpapillary muscle level. In patients with technically difficult apical views at rest, the parasternal images were recorded first. The first view was always obtained within 30 seconds after termination of exercise. The entire sequence of views was continuously repeated for 3 minutes and recorded on videotape.

All studies were analyzed on an off-line computer-assisted station equipped with digital processing (model CAD 886, Microsonics). The physicians interpreting the echocardiograms were blinded to the SPECT, ECG, and clinical findings. Representative cycles of rest and postexercise images at comparable views were digitized at a frame rate of 33 frames per second for 16 frames and positioned side-by-side on a quadscreen format. The computer corrected the differences in heart rate so that when played continuously, the rest and postexercise cycles appeared to be at comparable rates.

The left ventricle was divided into anterior and inferior septum and anterior, lateral, and inferoposterior walls. Each wall was subdivided into a basilar, mid, and apical segment. For comparison with SPECT and angiography, segments were grouped into regions according to a specific coronary artery distribution. The anterior region consisted of the anterior wall and septum. The inferior region consisted of the inferior septum and inferoposterior wall, and the lateral region comprised the posterolateral and lateral walls.

Wall motion at rest was classified in each segment as normal, hypokinetic, akinetic, or dyskinetic using well-established and previously validated criteria that make use of both endocardial motion and wall thickening. A similar classification was used after exercise with the addition of hyperdynamic motion. A de novo exercise-induced segmental wall motion abnormality was defined as a change from normal at rest to hypokinesis or akinesis after exercise (or relative hypokinesis when adjacent segments were clearly hyperdynamic). Worsening of a resting segmental wall motion abnormality was defined as a change from hypokinesis to akinesis or dyskinesis or spreading of a resting abnormality to a contiguous segment within the distribution of the same coronary artery territory.

201TI SPECT

At peak exercise, 3 mCi 201TI was injected intravenously and flushed with a saline solution. The patient was asked to exercise for an additional 30 seconds. After completion of the echocardiographic recording, SPECT was performed using a large-field-of-view, single-crystal, rotating gamma camera (ARC 3000-3300, ADAC) equipped with a high-resolution, parallel-hole collimator with a septal length and thickness of 33 and 0.15 mm, respectively. Image acquisition was performed over a 180° arc from the 45° left posterior oblique to the 45° right anterior oblique position, at 6° intervals, and for 40 seconds per image. Images were stored on a 2-gigabyte laser disc for analysis. Redistribution images were obtained 4 hours after exercise.

Transaxial reconstruction used a back-projection technique with a Butterworth (order: 5) high-pass filter with a low-pass window at a 50% cutoff. Reconstructed tomographic slices of 6-mm thickness were reoriented in the short, horizontal long, and vertical long axes and displayed sequentially to assess perfusion defects in the different walls of the left ventricle. Analysis of the scintigraphic images was performed by experienced observers unaware of the results of the echocardiographic study. As with the echocardiogram, the walls were grouped into vascular regions as follows: The anteroseptal, anterior, and anterolateral walls comprised the anterior region; the inferior, inferior, and posteroseptal walls comprised the inferior region; and the posterolateral and lateral walls comprised the lateral region. Perfusion defects were visually analyzed for the presence of complete, partial, or no redistribution 4 hours after 201TI injection.

Definition of Abnormalities for Comparison Between the Two Techniques

For the purpose of determining the concordance between the two techniques in the detection of ischemia (i.e., reversible abnormality) versus a fixed segmental abnormality (scar) within the same regions, ischemia was defined by echocardiography as an exercise-induced wall motion abnormality or worsening of a resting abnormality and by SPECT as a complete or partially reversible perfusion defect. A fixed abnormality was defined by echocardiography as a resting wall motion abnormality that remained unchanged with exercise and by SPECT as a perfusion defect that did not change with redistribution. Because one test considers regional function and the other considers relative perfusion, factors other than ischemia or infarction can induce wall motion or perfusion abnormalities, thus limiting the above classifications. These classifications are often used in clinical practice, yet not much knowledge is available as to how often the two techniques agree in their detection.

Coronary Angiography

A subgroup of 112 patients without previous coronary bypass surgery or angioplasty underwent coronary angiography within 1 month of the exercise test. The angiographic results were reviewed, and signifi-
cant coronary stenosis was defined as ≥50% luminal diameter narrowing.

Results

The echocardiographic images were of adequate quality for analysis in 289 patients (99%). All patients had adequate SPECT images. Both tests were normal in 137 patients and abnormal in 118, resulting in an 88% agreement between the two. The 34 patients with discordant results are described in Table 1. Seventeen patients had normal SPECT with abnormal echocardiography; 16 of the 17 had evidence of CAD by either angiography (n=5) or a previously documented myocardial infarction. One patient had false-positive exercise echocardiography. Seventeen patients had normal echocardiography with abnormal SPECT; 11 had evidence of CAD by either angiography (n=6) or a previously documented myocardial infarction. Four patients had false-negative SPECT, and two patients did not have independent confirmation of CAD. Abnormalities seen only by echocardiography were localized to the inferior region in 13 of the 17 patients. In contrast, the abnormalities seen only by SPECT were distributed evenly among the three coronary regions.

Analysis of Agreement by Regional Abnormalities

A total of 867 regions were analyzed in the 289 patients (Table 2). Partial agreement (i.e., normal versus abnormal findings) was observed in 763 (88%), and complete agreement (i.e., exact findings) was observed in 711 (82%). When both tests were abnormal (118 patients), they frequently (97%) shared at least one abnormal coronary artery region. Of 255 regions that were classified as abnormal by either of the two tests, 151 (65%) were abnormal by both. Fifty-three regions (21%) were abnormal only by SPECT, with reversible perfusion defects in 27, partially reversible defects in five, and fixed defects in 21. Similarly, 51 regions (20%) were abnormal only by echocardiography, with exercise-induced wall motion abnormalities in 17, worsening of resting abnormalities in six, and fixed abnormalities in 28.

More ischemic abnormalities were observed by SPECT than by echocardiography (120 versus 74). The increased detection of ischemia by SPECT occurred primarily in 32 regions with partially reversible perfusion defects and a fixed wall motion abnormality by echocardiography. Of 711 regions with normal wall motion at rest, 46 (6.5%) had evidence of exercise-induced ischemia by echocardiography versus 58 (8.2%) by SPECT (50 with a reversible perfusion defect and eight with a partially reversible defect).

Exercise echocardiography detected more fixed abnormalities than SPECT (128 versus 84). Of 28 regions with a fixed wall motion abnormality and normal SPECT, 25 were inferior in location (24 of 25 had a significant lesion in the right coronary artery and/or ECG evidence of an inferior myocardial infarction). This contrasts with the other discrepancies between SPECT and echocardiography, which were evenly distributed among the three coronary regions. Of the 84 regions that demonstrated a fixed perfusion defect by SPECT, 26 (30%) had either normal resting wall motion (n=24) by echocardiography or resting hypokinesia that worsened with exercise.

Analysis of Agreement by Overall Interpretation

The agreement between echocardiography and SPECT in the overall interpretation of test results is shown in Table 3. Complete agreement was observed in 222 of the 289 patients (77%). Detection of an ischemic exercise response was greater by SPECT than by echocardiography (87 versus 54 patients). Most of the improved detection of ischemia by SPECT consisted of a partially reversible perfusion defect occurring within the same region of a fixed wall motion abnormality by echocardiography.
Table 4. Comparison of Exercise Echocardiography and 201Tl SPECT With Coronary Angiography in 112 Patients

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Echocardiography</th>
<th>SPECT</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>One vessel</td>
<td>58% (24/41)</td>
<td>61% (25/41)</td>
<td>63% (26/41)</td>
</tr>
<tr>
<td>Stenosis</td>
<td>85% (22/26)</td>
<td>85% (22/26)</td>
<td>96% (25/26)</td>
</tr>
<tr>
<td>Two vessels</td>
<td>86% (25/29)</td>
<td>86% (25/29)</td>
<td>90% (26/29)</td>
</tr>
<tr>
<td>Three vessels</td>
<td>94% (15/16)</td>
<td>94% (15/16)</td>
<td>94% (15/16)</td>
</tr>
<tr>
<td>Specificity</td>
<td>88% (23/26)</td>
<td>81% (21/26)</td>
<td>77% (20/26)</td>
</tr>
</tbody>
</table>

SPECT, single-photon emission computed tomography.
*Subgroup of patients with ≥70% luminal diameter stenosis involving only one coronary artery.

patients with normal resting wall motion, detection of ischemia was only slightly greater by SPECT than by echocardiography (17% versus 14%, respectively).

Comparison With Coronary Angiography

CAD (≥50% diameter stenosis) was present in 86 of the 112 patients and involved one vessel in 41, two vessels in 29, and three vessels in 16 patients (Table 4). The sensitivity for detection of CAD was similar for both tests at all levels of disease, with a slight improvement when the results of the two tests were combined. Because of the large prevalence of one-vessel disease, one third of which consisted of lesions of only moderate (<70% stenosis) severity, the overall sensitivities for echocardiography and SPECT were 74% and 76%, respectively. However, single lesions of ≥70% stenosis were detected by either test with a sensitivity of 85%.

Furthermore, both tests were 86% and 94% sensitive in patients with two- and three-vessel disease, respectively. The specificities for exercise echocardiography and SPECT were 88% and 81%, respectively. Specificity dropped to 76% when the two tests were combined. The false-positive tests had either ischemia (two by echocardiography and three by SPECT) or fixed abnormality (one by echocardiography and two by SPECT).

Discussion

Both exercise echocardiography and 201Tl SPECT are excellent techniques for the evaluation of CAD. The diagnostic accuracy of SPECT depends on the computer algorithms used to reconstruct the tomographic planes, the resolution of the scintigraphic camera, and the experience of the interpreting physician. With current state-of-the-art ultrasound equipment and digital image acquisition techniques, exercise echocardiography depends for the most part on the technical expertise of the sonographer performing the examination and the experience of the interpreting physician. Similar to previous reports from this laboratory and others,1-3 the success rate of obtaining preexercise and postexercise echocardiographic images of diagnostic quality in this large nonselected population of patients was very high and should therefore not be considered a factor in selecting one test over the other.

When used simply to detect the presence of CAD (i.e., positive versus negative result), exercise echocardiography and SPECT agreed in 88% of the patients studied. Interestingly, the disagreements were evenly distributed between the two tests, suggesting that the two tests combined could improve the sensitivity for noninvasive evaluation of CAD. Although the primary objective of the present study was not to validate either test against angiography, the results obtained in the subgroup of patients who underwent coronary angiography were similar for the two tests and comparable to those previously reported by our laboratory and others.4-9 Sensitivity was improved slightly by the combined use of both tests at the expense of some decrease in specificity. It is possible that the sensitivity of SPECT may have been higher if quantitative techniques had been applied.10 However, these techniques were not available when the study was initiated.

In the patients in whom both tests were abnormal, analysis of the results demonstrated that the two tests almost always agreed as to the presence of an abnormality in one or more regions supplied by the same coronary artery. This finding corroborates the premise stated earlier that despite the fact that SPECT evaluates relative perfusion and echocardiographic wall motion, the two tests detect abnormalities produced by stenotic coronary artery lesions within similar regions of the left ventricle.

Furthermore, each test detected an equal number of abnormalities not detected by the other modality, suggesting that their combined use improves the evaluation of the extent of myocardial involvement by CAD.

Differentiation of Ischemia From Scar

In regions with normal wall motion at rest, detection of ischemia was slightly more frequent by SPECT than by echocardiography. On the other hand, in regions with resting wall motion abnormalities, ischemia was more apparent by SPECT, usually manifested as a partially reversible perfusion defect. Worsening of a resting wall motion abnormality with exercise has been shown to result from additional ischemia occurring in a region of a previous infarction12,13 or purely from resting ischemia (i.e., hibernating myocardium), as suggested by recovery of function in these segments after successful angioplasty of the corresponding coronary artery.14 However, a wall motion abnormality that remains fixed after exercise has been commonly interpreted as indicative of a scar from a previous myocardial infarction.7,12,13 The relatively frequent occurrence of partially reversible perfusion defects by SPECT in regions with fixed wall motion abnormalities by echocardiography (42 of 128, or 33%) accounted for the largest discrepancy between the two techniques in this study.

A partially reversible perfusion defect is often interpreted as a mixture of scar and ischemia.15-17 However, this finding may have other interpretations. It may be produced by slow delivery of thallium into abnormal regions due to low blood thallium levels or a high-grade coronary stenosis where flow is severely impaired and thus a marker of severe ischemia. On the other hand, a pure scar could show evidence of partial redistribution because of the computer processing used in creating a SPECT image. This processing uses relative rather than absolute thallium count density; that is, all of the pixels are normalized to the pixel with the highest radioactivity count. Therefore, partial redistribution could be induced by faster washout of thallium from adjacent normal regions and slower washout in an infarcted region with lower initial thallium uptake. In addition to
these mechanisms, the observed discrepancy between echocardiography and SPECT could be explained by the limitation of echocardiography in detecting residual function in regions of infarction because of the “threshold phenomenon”; that is, when half or more of the transmural thickness of a segment is infarcted, the segment becomes akinetic due to the tethering effect of the infarcted area on the noninfarcted myocardium.\textsuperscript{19-20} Although some viable myocardium may be present in these regions, accounting for the partial redistribution of the perfusion defect, the potential for functional improvement after revascularization might be limited. Future studies are needed to evaluate the significance of reversible perfusion defects in segments with fixed wall motion abnormalities.

The presence of a fixed perfusion defect by thallium was at one time thought to represent an area of scar. However, it has more recently been demonstrated that regions with severe ischemia may fail to improve by the 4-hour redistribution imaging.\textsuperscript{21-27} Our results suggest that combining echocardiography with SPECT may help further differentiate ischemia from scar in these regions. Interestingly, 30\% of regions with fixed perfusion defects by SPECT demonstrated evidence of viability by echocardiography; that is, normal wall motion at rest or resting hypokinesis that worsened with exercise. In a study by Brunken and associates,\textsuperscript{23} 58\% of segments with a fixed perfusion defect by stress planar \textsuperscript{201}TI scintigraphy demonstrated evidence of metabolic activity by positron emission tomography. The same investigators demonstrated earlier that segments with evidence by positron emission tomography of glucose utilization had an 85\% probability of improved wall motion after coronary revascularization.\textsuperscript{24}

With SPECT, Kiat and associates\textsuperscript{25} reported that as many as 64\% of segments with a fixed perfusion defect at 4 hours demonstrated reversibility by reimaging 18--72 hours after exercise. Furthermore, late reversibility of perfusion defect was found to be 95\% predictive of improved perfusion after coronary revascularization. More recently, reinjection of 1 mCi \textsuperscript{201}TI immediately after the 4-hour redistribution images has been suggested as an alternative to reimaging at 18--72 hours.\textsuperscript{25} Enhanced uptake of thallium by this technique was observed in almost 50\% of segments with fixed perfusion defects at 4 hours. This finding has correlated with redistribution at 24 hours and with evidence of glucose utilization by positron emission tomography.\textsuperscript{25,26} In a small group of patients, reversibility of perfusion defects by reinjection at 4 hours has also been predictive of improvement in perfusion and function after coronary angioplasty.\textsuperscript{27} To date, however, there are no studies relating the presence or absence of late reversibility of perfusion defects with the type of wall motion abnormality occurring with exercise.

An interesting observation in the present study was a greater detection of fixed resting abnormalities by exercise echocardiography than by SPECT. This increased sensitivity was more noticeable in the inferior wall and consisted primarily of a discrete wall motion abnormality in the basilar segment. This finding was highly specific for significant coronary artery stenosis in the corresponding vessel or for a previously documented inferior myocardial infarction.

In conclusion, exercise echocardiography and SPECT frequently agree in the detection of regional abnormalities indicative of CAD with comparable sensitivity. The choice of one test over the other may depend on availability, cost, level of expertise by the local laboratory, and, most important, the specific diagnostic information required. In selected patients, the combined use of exercise echocardiography and SPECT may enhance the assessment of the extent of myocardial involvement and assist in distinguishing viable from nonviable myocardium and thus help select patients who may benefit from coronary revascularization.

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