Detection of Coronary Artery Disease with Exercise Two-dimensional Echocardiography

Description of a Clinically Applicable Method and Comparison with Radionuclide Ventriculography


SUMMARY Two-dimensional echocardiography (2-D echo) was performed in 73 patients evaluated for coronary artery disease (CAD) and in four normal volunteers before and immediately after a maximal treadmill exercise test. Diagnostic images were obtained from the apical and parasternal windows. In 17 patients with normal coronary arteriograms, ejection fraction (EF) increased from 66 ± 9% (± SD) at rest to 73 ± 8% after exercise (p < 0.001), while in 56 patients with proved CAD, EF fell from 56 ± 13% at rest to 53 ± 16% after exercise (p < 0.01). The sensitivity of postexercise 2-D echo for detecting CAD (based on abnormal EF response and/or regional dyskinesia) was 91% (51 of 56 patients) and the specificity was 88% (15 of 17). Sensitivity for one-, two- and three-vessel disease was 64% (seven of 11), 95% (20 of 21) and 100%, respectively. Patients with multivessel disease showed a significant fall in wall motion score index, from 0.79 ± 0.25 to 0.63 ± 0.26. Exercise radionuclide ventriculography (RNV) was also performed in 41 of the subjects (17 normals and 24 CAD patients) on a bicycle ergometer. The overall sensitivity of 2-D echo in this subgroup was 92%, compared with 71% for RNV. The sensitivity of 2-D echo for one-vessel disease (n = 4) was 50%, that for two-vessel disease (n = 12) was 100% and that for three-vessel disease (n = 12) was 100%. The specific values for RNV were 0%, 80% and 90%. The specificity of 2-D echo was 88% and that of RNV was 82%. A significantly higher peak heart rate response was observed on the treadmill than on the bicycle ergometer in both CAD patients and normal subjects. We conclude that postexercise 2-D echo is a clinically applicable technique for the diagnosis and evaluation of CAD patients and compares favorably with exercise RNV.

ADVANCES in two-dimensional echocardiography (2-D echo) have made 2-D echo stress testing feasible for assessing cardiac function. Most groups have attempted continuous 2-D echo imaging during upright or supine bicycle ergometry. However, considerable movement artifact at high work loads has rendered the success rate of this approach unsatisfactory. We have postulated, as did Maurer and Nanda, that obtaining a 2-D echo immediately after maximal symptom-limited treadmill exercise may improve the quality of images without significantly altering the effects of ischemia on regional wall motion or ejection fraction (EF). We therefore undertook a prospective study to test the applicability of postexercise 2-D echo in the detection of coronary artery disease (CAD). We compared the results of 2-D echo with those of exercise radionuclide ventriculography (RNV), which is the standard technique of assessing cardiac function during exercise.

Methods

The study population consisted of 73 patients (63 males and 10 females, mean age 54 years, range 28–75 years) with suspected CAD and four normal volunteers (two males and two females, mean age 46 years, range 34–54 years). Sixty-nine patients were evaluated for chest pain, two for dyspnea and two for ventricular arrhythmias. Patients with unstable angina, recent myocardial infarction or valvular heart disease were excluded. Cardiac medications were not discontinued before exercise. Twenty-five patients were taking propranolol and five digoxin at the time of study. All 73 patients underwent coronary angiography within 1 week of the exercise study.

Echocardiographic Method

The 2-D echoes were obtained in all 77 subjects before exercise without previous echo screening. The studies were performed using a commercially available 90° mechanical sector scanner (Advanced Technology Laboratories Mark III). With the patient in the supine left lateral position, the transducer was hand-held on the patient’s chest and multiple views were obtained through the left parasternal and apical windows. The acoustic windows providing the best images were marked on the patient’s chest using a washable felt-tip marker for reference during the postexercise study. Twelve-lead ECG recordings were obtained at rest and at each 3-minute level of exercise with leads V1-V6 monitored continuously during exercise. The chest electrodes were positioned so as not to
overlie the marked site for the echo acoustic window. Patients performed maximal symptom-limited exercise on a motor-driven treadmill using a standard Bruce or multistage branching protocol. Immediately after exercise, patients resumed the supine left lateral position and the 2-D echo was repeated within 30–60 seconds and recorded continuously for 6 minutes after exercise. The transducer was first placed in the apical window and continuously manipulated through the apical four-chamber and two-chamber view, followed by the parasternal long-axis view. Patients were not required to hold their breath. All echoes were videotaped on a 3/4-in U-matic videocassette recorder equipped with frame-by-frame bidirectional playback capability.

The 2-D echoes were analyzed at rest and after exercise for the presence of regional wall motion abnormalities. Regional wall motion at the basilar, middle and distal third of the septum, lateral, anterior and inferoposterior walls and at the apex was classified as normal, hypokinetic, akinetic or dyskinetic, based on the subjective impression of inward motion of the endocardial echo toward the center of the left ventricular (LV) cavity and the degree of thickening of the myocardium (fig. 1). The assessment of wall motion was aided by the use of slow-motion, bidirectional and stop-frame video playback. A wall motion score index (WMSI) was derived by assigning a numerical value of −1 for dyskinetic, zero for akinetic, +1 for hypokinetic, +2 for mild hypokinesis and +3 for normal to the wall motion of each visualized segment (fig. 1). The score was computed as the sum of all the regional scores divided by the number of segments visualized times three. A normally contracting ventricle would therefore have a score index of 1.00, while a ventricle with an abnormally contracting segment would have a score less than 1.00. LVEF was measured at rest and immediately after exercise by a method previously validated in this laboratory using the average of LV diameters at the basal, middle and apical third of the cavity and an assessment of apical contraction. All 2-D echo measurements and interpretations were done by an experienced observer independently and without knowledge of the results of the stress ECG, coronary angiography or radionuclide studies.

The rest and stress ECGs were interpreted by an experienced, independent observer and read as positive for ischemia if there was at least 1 mm of ST-segment depression beyond resting baseline at 80 msec after the J point.

**Scintigraphic Method**

Exercise RNV was performed within 24 hours of the postexercise 2-D echo in 37 of the 73 patients and in the four normal subjects using the multigated blood pool imaging technique. After in vivo labeling of the patient’s own red blood cells with 30 mCi of technetium pertechnetate,13 multigated imaging was performed in the anterior, shallow left anterior oblique (LAO) and steep (70%) LAO projection at rest and in a shallow LAO projection during low, intermediate and peak levels of supine bicycle exercise.14 Three-minute exercise stages were carried out on a calibrated supine bicycle ergometer (Quinton) to maximal effort (range 300–1400 kpm). Exercise was terminated with the development of symptoms or significant ECG abnormalities.

Data were collected with a standard small-field-of-view gamma camera (Ohio Nuclear) interfaced with a dedicated on-line computer system (Technicare Corp.). The shallow LAO projection (approximately 35°) with 15° of caudal tilt was used to optimally separate the ventricles and visualize the septum. Data at rest were accumulated to a preset density of 250 counts per pixel, and during exercise, data were acquired during the last 2 minutes of each 3-minute exercise stage. EF was calculated from the shallow LAO projection using a separate region of interest for end-diastole and end-systole according to the formula: 

\[
EF = \frac{[\text{end-diastolic counts} - \text{end-systolic counts}] \times 100}{\text{end-diastolic counts}}
\]

Regional wall motion was assessed in each view as normal, hypokinetic, akinetic or dyskinetic.

The analysis of EF and wall motion at rest and after exercise was performed with a dedicated computer system (Technicare Corp.). The shallow LAO projection (approximately 35°) with 15° of caudal tilt was used to optimally separate the ventricles and visualize the septum. Data at rest were accumulated to a preset density of 250 counts per pixel, and during exercise, data were acquired during the last 2 minutes of each 3-minute exercise stage.

**FIGURE 1**. The views obtained with two-dimensional echocardiography: parasternal long-axis (left), apical four-chamber (middle) and apical two-chamber (right). Each wall was divided into basilar, middle and distal segments, and the motion in each segment assigned a numerical wall motion score (WMS), ranging from +3 for normal to −1 for dyskinesis. A WMS index (WMSI) was calculated as the sum of the WMS for each segment visualized, divided by three times the number of segments seen. S1–S3 = proximal to distal septum; P1–P2 = proximal and mid-posterior wall; L1–L2 = proximal to distal lateral wall; A1–A3 = proximal to distal anterior wall; I1–I3 = proximal to distal inferior wall; Apx = apex.
during exercise was made by an experienced observer blinded to the results of angiography and postexercise 2-D echo.

Cardiac Catheterization

Left-heart catheterization was performed in the 73 patients within 1 week of postexercise 2-D echo using either the Sones or Judkins technique. The coronary arteriograms were filmed in multiple projections, including the angulated hemi axial views. Left ventriculography was performed in the 30° right anterior oblique (RAO) projection. Significant CAD was defined as a greater than 50% luminal diameter narrowing in one or more vessels.

Analysis of Data

An abnormal (positive) test by 2-D echo or RNV was defined as one showing abnormal regional wall motion at rest or with exercise and/or an abnormal EF response. In a previous study from this laboratory, the method of determining EF was found to be reproducible when the tests were repeated a second time with r value, standard error and difference between mean values of 0.98, ± 3.2% and 1.6%, respectively (n = 15). Thus, an abnormal EF response by 2-D echo was defined in this study as a less than 4% increase in EF with exercise. An abnormal EF response by RNV was defined as a less than 5% increase in EF with exercise, following the results of previous reproducibility studies with this technique. In patients with hyperdynamic states at rest (EF > 70%), a flat response (0–4% increase) by either test was accepted as normal.

The results of the 2-D echo and the RNV exercise tests were compared to angiography. Sensitivity (%) was calculated as (true positives/[true positives + false negatives]) × 100 and specificity (%) as (true negatives/[true negatives + false positives]) × 100. Comparisons of changes in EF and WMSI from rest to exercise and of the peak heart rates and blood pressures recorded during treadmill and bicycle testing were made with the t test for paired variables. Significance was established at p < 0.05.

Results

Success of 2-D Echo

All 77 patients had at least two views at rest, one of which was in every case the apical four-chamber. The apical two-chamber and the parasternal long-axis views were obtained in 76 (99%) and 66 patients (86%), respectively. All but one patient had at least two views of diagnostic quality immediately after exercise; the remaining patient had only an apical four-chamber view. In 66 patients (86%), apical two-chamber and four-chamber views were obtained after exercise. Parasternal long-axis views were of diagnostic quality after exercise in 64 patients (83%). Examples of the images are shown in figures 2 and 3.

Detecting CAD by 2-D Echo

Of the 73 patients who underwent coronary angiography, 17 were found to have no significant CAD. Of the 56 patients with significant CAD, 11 had one-, 21 two- and 24 three-vessel disease (table 1). The mean EF in the patients without CAD was 66 ± 9.4% at rest and 73 ± 8.4% after exercise (p < 0.001). In the CAD patients, the mean EF was 56 ± 13.3% at rest and 53 ± 16.4% after exercise (p < 0.01) (fig. 4). In figure 5, the EF responses of CAD patients are separated according to the number of vessels involved. Seventeen patients with CAD (seven with one-, five with two- and five with three-vessel disease) had an increase of greater than 4% and were false negatives by EF response. The overall decrease in postexercise EF in the patients with CAD was due primarily to the substantial decrease in EF in the patients with three-vessel disease (from 55 ± 14% to 47 ± 13%, p < 0.001).

Two of the 17 normal subjects and 48 of the 56 CAD patients had postexercise wall motion abnormalities (table 1). Of these, one of the two normal subjects and 32 of the 48 CAD patients had resting abnormalities as well. The WMSI did not change significantly from rest.
to immediately after exercise in patients with one-vessel disease (fig. 6), but fell from $0.81 \pm 0.25$ to $0.69 \pm 0.25$ ($p < 0.01$) in patients with two-vessel disease and from $0.78 \pm 0.26$ to $0.58 \pm 0.26$ ($p = 0.001$) in those with three-vessel disease, suggesting a greater magnitude of exercise-induced ischemia in the three-vessel disease group.

Comparing the regions of abnormal wall motion with the coronary anatomy in the CAD patients, 90% of patients with anterior, septal or apical wall motion abnormalities had significant disease of the left anterior or descending coronary artery. Likewise, 94% of patients with inferior, 96% with posterior and 96% with lateral wall motion abnormalities had critical lesions in the right coronary artery, circumflex artery or both.

The combination of regional wall motion abnormalities and abnormal EF response resulted in two positive tests in the 17 normal subjects (88% specificity) and 51 positive tests in the 56 CAD patients (91% sensitivity). The sensitivity of postexercise 2-D echo for one-, two- and three-vessel disease was 64%, 95% and 100%, respectively.

Comparison with Stress ECG

Table 1 lists the results of the ECG analysis at rest and after exercise. Twenty-nine of 56 patients with CAD had ECG evidence of prior myocardial infarction, i.e., Q waves. Forty patients had ST depression $\geq 1$ mm with exercise, including 21 of the 29 patients with resting Q waves. The overall sensitivity for the stress ECG (combining Q waves and ST shift) was 86%. Table 2 is a list of the 2-D echo and the stress ECG results in the 40 patients without evidence of previous MI. Both tests were positive in one of the 16 patients with normal coronary arteries, while the postexercise 2-D echo was positive in 19 of 24 and the stress ECG in 17 of 24 CAD patients. Postexercise 2-D echo detected abnormalities in 16 of 17 patients with multivessel disease, while the stress ECG was positive in only 13.

Effects of Medications

All five patients taking digoxin had multivessel disease and ECG evidence of previous infarction. Exercise-induced ischemia was evident by 2-D echo (abnormal EF response and/or a fall in WMSI) in all five and by ECG (ST depression) in three patients. Twenty-three of the 25 patients taking propranolol had documented CAD (six one-, six two- and 11 three-vessel disease); 12 had ECG evidence of previous infarction (Q waves) and abnormal resting wall motion by 2-D echo. Exercise-induced ischemia was evident by 2-D echo in 21 of the 23 CAD patients and by ECG in 19. One-vessel disease was present in both patients with false-negative 2-D echoes and in two of the four false-negative stress ECGs. The two patients with normal coronary arteries taking propranolol were true negative by both 2-D echo and stress ECG.
Comparison with RNV

The results of postexercise 2-D echo and RNV are summarized in table 3. The four normal volunteers are included in the group of 17 normals. The 2-D echo was positive in two of the 17 normal subjects and RNV was positive in three, yielding a specificity of 88% and 82%, respectively. Both tests were normal in all four normal volunteers. The false-positive studies for the two techniques did not overlap; the two patients incorrectly classified by 2-D echo were different from the three patients incorrectly diagnosed by RNV. Postexercise 2-D echo was positive in 22 of 24 patients with CAD (92% sensitivity). Both false negatives were patients with one-vessel disease. RNV was positive in 17 of the 24 patients with CAD (71% sensitivity). The sensitivity of RNV for one-, two-, and three-vessel disease was 0 (none of four), 80% (eight of 10) and 90% (nine of 10), respectively.

The peak heart rate and systolic blood pressure during treadmill exercise were compared with those during supine bicycle exercise in order to assess the cardiac work load produced by the two exercise modalities (table 4). Both the normal group and the CAD patients achieved a significantly higher heart rate on the treadmill. The peak systolic blood pressure during supine bicycle exercise was higher than that during treadmill in the normal group but was statistically similar in the CAD patients.

Discussion

Exercise echocardiography has not gained widespread acceptance as a clinical tool, primarily because

Table 1. Results of Two-dimensional Echocardiography and Stress Electrocardiography

<table>
<thead>
<tr>
<th>2-D echo</th>
<th>Stress ECG</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Abn RWM</td>
</tr>
<tr>
<td>Normal</td>
<td>17</td>
</tr>
<tr>
<td>CAD</td>
<td>56</td>
</tr>
<tr>
<td>One-vessel</td>
<td>11</td>
</tr>
<tr>
<td>LAD</td>
<td>6</td>
</tr>
<tr>
<td>RCA</td>
<td>3</td>
</tr>
<tr>
<td>Cx</td>
<td>2</td>
</tr>
<tr>
<td>Two-vessel</td>
<td>21</td>
</tr>
<tr>
<td>LAD-RCA</td>
<td>10</td>
</tr>
<tr>
<td>LAD-Cx</td>
<td>5</td>
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<tr>
<td>Cx-RCA</td>
<td>6</td>
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<tr>
<td>Three-vessel</td>
<td>24</td>
</tr>
</tbody>
</table>

Abbreviations: Abn = abnormal; RWM = regional wall motion; R = rest; Ex = exercise; EF = ejection fraction; Q = Q waves on resting ECG; ST ↓ = ischemic ST depression with exercise; CAD = coronary artery disease; LAD = left anterior descending coronary artery; RCA = right coronary artery; Cx = circumflex coronary artery.
of the difficulty in obtaining adequate images during vigorous exercise. Exaggerated chest and lung movement during exercise obscures the echo window in some subjects. This problem limited early studies using M-mode echo. Depending on the amount of stabilization of the patient or transducer, 20–83% of subjects could be imaged successfully during exercise. Studies applying 2-D echo to supine bicycle exercise have reported a 71–78% success rate. Despite the difficulty of the technique, Wann et al. observed that wall motion abnormalities persisted after the termination of exercise and that they were more easily imaged without the movement artifacts of peak exercise. Taking advantage of that observation, Mauer and Nanda designed a protocol of postexercise echo. They studied 48 patients immediately after maximal treadmill exercise and obtained adequate 2-D echoes in 41 (85%). They also demonstrated a good correlation between exercise-induced asynergy detected by echo and areas of decreased thallium perfusion, verifying the reliability of 2-D echo.

The echo protocol used in the present study was similar to that used by Mauer and Nanda. Images were obtained within 30 seconds in most cases, and the wall motion abnormalities produced by exercise were readily apparent for at least 90 seconds before gradually resolving. Although the supine position eliminated chest wall movement as a source of imaging artifact, lung movement remained vigorous for several minutes after exercise. The heart was frequently visible for only one or two beats at end-expiration and the use of a slow-motion, bidirectional video playback unit became essential for the analysis of wall motion. As other investigators have reported, the apical views appear to be enhanced after exercise, often producing a better image after exercise than at rest. With the emphasis on the apical views immediately after exercise and the use of a bidirectional playback system, we obtained interpretable images in all 77 patients studied, and at least two postexercise views in 76.

Our results indicate that postexercise 2-D echo can be highly sensitive (91%) and specific (88%) in detecting CAD. EF was substantially higher after exercise in normal subjects (66% at rest vs 73% with exercise), in contrast to a significant decrease in patients with CAD (56% vs 53%). A decrease in postexercise WMSI similarly identified patients with CAD. Forty-eight patients had postexercise wall motion abnormalities. One patient with one-vessel disease had a regional wall motion abnormality at rest compatible with CAD, but it normalized with exercise. Altogether, 49 of the 51 positive studies in the CAD patients demonstrated regional wall motion abnormalities, with only two patients showing a decrease in EF without detectable regional wall motion changes. In addition, a marked decrease in WMSI was frequently associated with the presence of multivessel CAD. Therefore, in most patients, the assessment of regional wall motion before and after exercise without the more tedious measurement of EF may be sufficient for detecting significant CAD.

The sensitivity of 2-D echo for CAD in our clinical population may have been favored by the large proportion of patients with resting wall motion abnormalities (32 of 56) and pathologic Q waves (29 of 56). However, the results in the 24 CAD patients with normal resting wall motion were similar to those in the overall population: 94% sensitivity for multivessel disease and 43% for one-vessel disease. In addition, in patients with resting wall motion abnormalities secondary to
previous infarction, detection of exercise-induced ischemia may be an important clinical indicator of viable myocardium at jeopardy. Worsening of wall motion occurred in 17 of the 32 patients with resting abnormalities; 16 of 17 had significant multivessel disease.

Our results could have been influenced by the relatively high prevalence (73%) of CAD in our study population. This is a limitation of any study performed in a hospital-based population. The prevalence of CAD with and without previous infarctions in our study population was no different from that in several of the studies used to validate exercise RNV for detecting CAD. The results of studies of this kind, however, should be extrapolated with caution to the asymptomatic population with a low prevalence of disease, in which a test would be used for screening.

Comparison with Stress ECG

Detection of abnormal regional wall motion by 2-D echo appeared to improve the sensitivity of the stress ECG for two- and three-vessel disease (from 90% to 95% and from 92% to 100%, respectively). This improvement was more apparent in the patients with normal wall motion and no Q waves at rest, in whom 16 of the 17 with multivessel disease had positive postexercise 2-D echoes while only 13 had positive stress ECGs. Thus, 2-D echo provided additional information regarding the development of new ischemic areas in patients with resting abnormalities and appeared more sensitive in detecting ischemia in patients with multivessel disease and no previous infarction. In addition, worsening of wall motion after exercise confirmed the presence of ischemia suggested by ST depression in the patients receiving digoxin. Overall, 2-D echo was positive for ischemia in 26 of the 28 CAD patients receiving digoxin or propranolol, while the stress ECG was positive in 22.

Comparison with RNV

Our findings suggested a slightly better sensitivity and specificity of 2-D echo over RNV in the 41 patients who underwent both tests. The sensitivity and specificity of RNV in this study were comparable to those in a previous report. The work load achieved by treadmill in terms of heart rate was greater than that with bicycle exercise and may have contributed to the better 2-D echo results. In addition, 2-D echo had the advantage of providing multiple views of the myocardium immediately after exercise, while the RNV technique was limited to the LAO view during exercise. Furthermore, the inferior wall is frequently difficult to evaluate by gated RNV unless specifically examined by an RAO or steep LAO projection. Therefore, 2-D echo may be better suited for a complete assessment of regional wall motion immediately after exercise, and this may improve the sensitivity for detecting exercise-induced regional ischemia.

Table 3. Results of Postexercise Two-dimensional Echocardiography and Exercise Radionuclide Ventriculography

<table>
<thead>
<tr>
<th></th>
<th>Abn RWM Rest</th>
<th>2-D echo</th>
<th>RNV</th>
<th>2-D echo</th>
<th>RNV</th>
<th>Abn EF response</th>
<th>Positive test</th>
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<tbody>
<tr>
<td>Normal</td>
<td></td>
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<td>n</td>
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<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-vessel</td>
<td>24</td>
<td>15</td>
<td>15</td>
<td>21</td>
<td>16</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>LAD</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>RCA</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Two-vessel</td>
<td>7</td>
<td>7</td>
<td>8</td>
<td>10</td>
<td>7</td>
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<tr>
<td>LAD-RCA</td>
<td>5</td>
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<td>3</td>
<td>5</td>
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<tr>
<td>LAD-Cx</td>
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<td>2</td>
<td>3</td>
<td>3</td>
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<tr>
<td>Three-vessel</td>
<td>10</td>
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<td>7</td>
<td>10</td>
<td>9</td>
<td>8</td>
<td>7</td>
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</table>

*Four patients did not have angiography (normal subjects).
Abbreviations: RNV = radionuclide ventriculography. See table 1 for other abbreviations.

Table 4. Peak Heart Rate and Peak Systolic Blood Pressure Achieved by Treadmill and Bicycle Exercise

<table>
<thead>
<tr>
<th></th>
<th>Peak HR (beats/min)</th>
<th>Peak SBP (mm Hg)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>TM</td>
<td>Bike</td>
</tr>
<tr>
<td>Normals</td>
<td>160 ± 20 p &lt; 0.001</td>
<td>138 ± 24</td>
</tr>
<tr>
<td>n = 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td>135 ± 25 p &lt; 0.001</td>
<td>113 ± 34</td>
</tr>
<tr>
<td>n = 24</td>
<td></td>
<td></td>
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</table>

Abbreviations: HR = heart rate; SBP = systolic blood pressure; CAD = coronary artery disease; TM = treadmill; Bike = bicycle.
In conclusion, postexercise 2-D echo is clinically applicable, sensitive and specific in the detection of CAD. Postexercise 2-D echo compares favorably with exercise RNV in detecting changes in EF and wall motion indicative of ischemia.

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