Exercise-induced Silent Myocardial Ischemia in Single Vessel Coronary Artery Disease Associated with Q Wave Infarction*

Assessment by Thallium 201 Single-Photon Emission Computed Tomography

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Purpose: To examine the relationship between the symptom of ischemia and the amount of abnormally perfused myocardium, coronary arteriography and exercise and redistribution thallium 201 single-photon emission computed tomography (SPECT) were analyzed.

Materials and methods: The study group consisted of 153 patients with single-vessel coronary artery disease; 53 patients had no pathologic Q waves (group 1) and 100 patients had pathologic Q waves consistent with the area supplied by the diseased vessel (group 2). Twenty normal subjects were used as control subjects. The apical, mid, and basal left ventricular levels of the short-axis view and apical portion of the long-axis view were divided into 20 segments, and segmental images were scored blindly on a 0 (normal) to 4 (severely reduced uptake) scale. The redistribution score was defined as the thallium 201 defect score of exercise subtracted from that of the redistribution image and was used as a measure of the amount of ischemic myocardium.

Results: The redistribution score in 20 control subjects was 0.20±0.06, and the upper limit of normal redistribution score was defined as mean±2×SD (4.32). In group 1, 40 of 53 patients had a redistribution score above the normal range. In group 2, 34 of 100 patients had a redistribution score above the normal range. Of 40 patients in group 1, angina during exercise was observed in 22 patients (55 percent). Twenty-two patients who had angina had a redistribution score of 15.2±6.7, while those who did not have angina had a score of 13.7±5.2 (p = NS). Of 34 patients in group 2, angina was observed in 10 patients (29 percent) during exercise. Ten patients with angina had a redistribution score of 10.1±4.4, and those without angina had a score of 9.9±3.4 (p = NS).

Conclusion: Thus, the incidence of silent ischemia without the Q wave infarct zone was found to be higher than that within the ischemic zone without Q wave. Patients with silent and symptomatic ischemia during exercise have similar amounts of ischemic myocardium demonstrated by tomographic thallium 201 imaging; this was found in patients who had Q wave infarction and in those who did not.

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In patients with coronary artery disease, painful and asymptomatic ischemic episodes occur in various clinical settings. Cohn1 classified patients with silent ischemia as totally asymptomatic, symptomatic following myocardial infarction, or asymptomatic with some episodes of myocardial ischemia and asymptomatic at other times. Silent ischemia following myocardial infarction was classified as one type of clinical presentation, and could be a different entity from that without myocardial infarction. The relationship between the symptom of angina pectoris and the amount of ischemic myocardium has been reported previously in patients who had myocardial infarction and in those who did not, but not conclusively. The results of some earlier studies indicate no significant relationship between silent myocardial ischemia and prior myocardial infarction, but others show that silent ischemia is frequent in patients with prior myocardial infarction.

In the present study, we investigated the relationship between the symptom of angina pectoris and the amount of ischemic myocardium. Studies were performed on coronary artery disease patients who had Q wave myocardial infarction and in those who did not. Testing was done with thallium 201 single-photon emission computed tomography (SPECT).

Methods

Study Patients

The study group was comprised of 153 consecutive patients referred to our institution for SPECT. These patients had single-vessel disease, as evidenced by results of preceding coronary arteriography. Patients were divided into two groups: those who had pathologic Q waves on the ECG and those who did not. The pathologic Q waves were consistent with the area supplied by the diseased vessel. Patients with multi-vessel diseases thus were not

LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; SPECT = single-photon emission computed tomography

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included in this study to avoid the occurrence of ischemia outside the infarct zone. Patients with prior coronary angioplasty or coronary artery bypass graft surgery also were excluded. Thallium 201 exercise and redistribution scintigraphy and cardiac catheterization were performed at least one month after acute myocardial infarction. All patients were clinically stable at the time of this study. Twenty control subjects underwent cardiac catheterization for evaluation of atypical chest pain and had normal left ventriculograms, coronary arteriograms, and hemodynamic variables.

**Exercise Protocol and Imaging Procedure**

All cardiac medications were discontinued at least 48 h before the procedure, except for sublingual nitroglycerin, which was allowed for anginal attacks. In a fasting state, the patient bicycled in the supine position, with an initial work load of 25 or 50 W and subsequent increments of 25 W every 3 min. The presence of an ischemic symptom was defined as having chest pain during exercise. Standard 12-lead ECGs and blood pressure determinations using a cuff sphygmomanometer were obtained at rest and throughout the exercise test and recovery period. Electrocardiographic findings were considered positive if there was greater than or equal to 1 mm of horizontal or downsloping ST segment depression for 0.08 s or more after the J point.

Three millicuries (111 MBq) of thallium 201 was injected intravenously when the patient had angina, ECG change, or submaximal heart rate, and exercise was continued for another 60 s. The SPECT images were obtained 5 min after isotope injection and 4 h later using a conventional gamma camera (Toshiba, GCA-601E) equipped with a low-energy general-purpose parallel-hole collimator (Toshiba RDC-63A). A 20 percent energy window was positioned on the 80 keV photopeak of thallium 201. Thirty-six equidistant projections were obtained for 30 s each over a 180-degree rotation from the 45-degree right anterior oblique to the 45-degree left posterior oblique projection and were stored on a magnetic disk having a 64 x 64 matrix. The raw data were smoothed by a five-point weighted averaging system. Filtered back projection was performed using a Shepp and Logan filter. Tomograms were reoriented in the short-axis and vertical long-axis planes and reconstructed at 1 pixel per slice, representing a 5.3-mm thickness. The short-axis and long-axis slices were analyzed from the apex to the base and from the septum to the lateral wall of the heart. Short-axis slices were divided into six equal segments (anterior, anterosepal, inferoseptal, inferior, inferolateral, and anterolateral) at apical, mid, and basal ventricular levels. The apical portion of the short-axis images was divided into anterior and inferior segments, so that there was a total of 20 segments per patient (18 from the short-axis and 2 from the vertical long-axis views) without duplication of the same anatomic area on different projections (Fig. 1). Semiquantitative analysis of each segment of the exercise and redistribution views was performed on a 0 to 4 scale (0 = normal, 1 = equivocally reduced thallium uptake, 2 = mildly reduced uptake, 3 = moderately reduced uptake, 4 = severely reduced uptake) and was used for confirmation of the visual analysis. The score reflecting the amount of thallium defect was generated for the entire left ventricle by summing individual scores of a total of 20 segments for each of the exercise and redistribution images. A higher total score was considered to indicate a larger extent of thallium defect. The thallium defect score immediately after exercise was subtracted from that of the redistribution image, and the score thus obtained was defined as the redistribution score and was used as an amount of ischemic myocardium. For each patient, a redistribution score greater than 2 SDs above the mean from a series of 20 normal subjects was considered as abnormal. Radionuclide measurements were made by two investigators blinded to all clinical or catheterization variables. Interobserver variability of radionuclide analysis was determined, and the mean interobserver variability was 7 percent for the thallium redistribution score and differences of opinion were resolved by consensus.

**Cardiac Catheterization**

All patients underwent left ventriculography and selective coronary arteriography within 7 days of the exercise and redistribution SPECT imaging. Selected coronary segments were assessed quantitatively by means of a caliper. Significant stenosis of the coronary artery was defined as 75 percent or more luminal diameter stenosis.

**Analysis**

Data were expressed as mean ± SD. Statistical analyses were performed with the Student's t test and χ² analysis. The data were analyzed retrospectively. A probability value of less than 0.05 was considered significant.

**RESULTS**

**Exercise and Redistribution Single-Photon Emission Computed Tomography Imaging of Control Subjects**

The control group consisted of 20 subjects (7 men and 13 women), aged 56.1 ± 8.3 years. Mean exercise

![Diagram](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21669/)
duration was 7.8 ± 2.8 min. Maximal heart rate was 138 ± 20 beats per minute, maximal blood pressure was 178 ± 24/101 ± 15 mm Hg, and the rate-pressure product was 25,449 ± 5,069 beat·mm Hg/min. The redistribution score derived from exercise and redistribution SPECT images was 0.20 ± 2.06. The upper limit of the normal redistribution score was defined as the mean + 2 × SD and was 4.32. The redistribution scores of all 20 control subjects fell into this normal range. Patients with coronary artery disease were divided either below this upper limit of redistribution score as the absence of redistribution or above this upper limit as the presence of redistribution.

Exercise and Redistribution Single-Photon Emission Computed Tomography Imaging of Patients With Coronary Artery Disease

Patient characteristics, exercise scintigraphic results, and coronary pathoanatomy for a total of 153 patients with single-vessel coronary artery disease of more than 75 percent stenosis are shown in Table 1. There were 53 patients without pathologic Q waves (group 1) and 100 with pathologic Q waves (group 2). In group 1, six patients had non-Q wave myocardial infarction. There were no significant differences in age, distribution of gender, and determinations of diabetes between the two patient groups. No differences were observed in exercise duration, peak heart rate, peak systolic and diastolic blood pressure levels, and rate-pressure product. The pathoanatomy of coronary artery disease showed no differences.

The redistribution scores above the upper limit of the normal range were observed in 40 of 53 patients in group 1 and 34 of 100 patients in group 2. Figure 2 shows the presence or absence of ischemic symptoms during exercise.

**Table 1—Patient Characteristics, Exercise Scintigraphic Results, and Coronary Pathoanatomy in 153 Patients With Single-Vessel Coronary Artery Disease**

<table>
<thead>
<tr>
<th>Clinical Data</th>
<th>Pathologic Q Waves</th>
<th>p Value*</th>
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<tbody>
<tr>
<td></td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>No. of patients</td>
<td>53</td>
<td>100</td>
</tr>
<tr>
<td>Age, yr</td>
<td>59.7 ± 9.7</td>
<td>58.6 ± 8.4</td>
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<tr>
<td>Males/females</td>
<td>41/12</td>
<td>76/24</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (6%)</td>
<td>10 (10%)</td>
</tr>
<tr>
<td>Exercise duration, min</td>
<td>6.8 ± 2.4</td>
<td>6.9 ± 1.9</td>
</tr>
<tr>
<td>Peak heart rate, beats per minute</td>
<td>124 ± 22</td>
<td>124 ± 22</td>
</tr>
<tr>
<td>Peak systolic pressure, mm Hg</td>
<td>172 ± 29</td>
<td>171 ± 31</td>
</tr>
<tr>
<td>Peak diastolic pressure, mm Hg</td>
<td>90 ± 19</td>
<td>91 ± 16</td>
</tr>
<tr>
<td>Rate-pressure product, beat·mm Hg/min</td>
<td>21720 ± 6103</td>
<td>21021 ± 5295</td>
</tr>
<tr>
<td>Coronary artery involved</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>34 (64%)</td>
<td>50 (50%)</td>
</tr>
<tr>
<td>RCA</td>
<td>8 (15%)</td>
<td>20 (20%)</td>
</tr>
<tr>
<td>LCX</td>
<td>11 (21%)</td>
<td>30 (30%)</td>
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</table>

*NS = not significant.
in 40 patients in group 1 and 34 patients in group 2. In group 1, 22 (55 percent) had ischemic symptoms and 18 (45 percent) did not. In group 2, 10 (29 percent) had ischemic symptoms and 24 (71 percent) did not (p<0.05). The ECG changes during exercise were present in 28 patients (70 percent) of group 1 and 19 patients (56 percent) of group 2 (Fig 3). No significant differences were observed between groups 1 and 2.

Figure 4 shows the redistribution scores of patients with and without ischemic symptoms in each group. Of 40 patients in group 1, 22 who had ischemic symptoms had a redistribution score of 15.2±6.7, while 18 who did not have ischemic symptoms had a redistribution score of 13.7±5.2. There were no significant differences between patients who had ischemic symptoms and those who did not. Of 34 patients in group 2, 10 who had ischemic symptoms had a redistribution score of 10.1±4.4 and 24 who did not have ischemic symptoms had a redistribution score of 9.9±3.4. No significant differences were observed between patients who had ischemic symptoms and those who did not. The redistribution scores in group 1 were significantly higher than those in group 2 in both groups of patients who had ischemic symptoms and those who did not (p<0.05). Table 2 shows the redistribution scores of the left anterior descending coronary artery (LAD), the right coronary artery (RCA), and the circumflex coronary artery (LCX) of patients who had ischemic symptoms and those who did not in each group. In each vascular territory, no significant differences were observed between patients who had ischemic symptoms and those who did not.

The redistribution scores were within the normal range in 13 of 53 patients in group 1 and in 66 of 100 patients in group 2. None of 13 patients in group 1 had ischemic symptoms during exercise, and 4 of 66 patients in group 2 did. The ECG changes during exercise were observed in 1 of 13 patients in group 1 who did not have ischemic symptoms. The ECG changes were observed in 12 of 66 patients in group 2, none of whom had ischemic symptoms.

**Discussion**

**Silent Ischemia in Patients Who Had Myocardial Infarction**

The frequency of silent myocardial ischemia could vary with characteristics of patient populations and methods for detecting ischemia. Results of some earlier studies have suggested that silent myocardial ischemia is frequent in patients with prior myocardial infarction, but other reports have shown no significant relationship between silent myocardial ischemia and prior infarction. In 473 patients with ischemic ECG response and angiographically documented coronary artery disease, Falcone et al reported that 269 patients (118 who had prior myocardial infarction) had chest pain during exercise testing and 204 patients (77 who had prior myocardial infarction) developed exercise-induced silent myocardial ischemia. In patients from the Coronary Artery Surgery Study with ischemic ST-segment depression and angiographically proved coronary artery disease, 424 patients (242 who had prior myocardial infarction) had angina during exercise testing and 456 patients (244 with prior myocardial infarction) did not. In the 219 patients with significant coronary artery disease, Mahmarian et al reported that silent myocardial ischemia was fivefold more common than symptomatic ischemia (83 vs 17 percent). Ozawa et al observed differences of exercise-induced silent myocardial ischemia in patients who had pathologic Q waves and in those who did not. Of 152 patients with ischemic ST-segment depression during exercise tests and angiographically proved coronary artery disease, 48 of 104 patients

![Figure 4: Redistribution score (RDS) and presence of symptom (Sx) in patients with and without pathologic Q waves. NS = not significant.](image-url)

**Table 2—Redistribution Score by Vessel in Patients Who Had Ischemia and Those Who Did Not**

<table>
<thead>
<tr>
<th>Symptom ( + )</th>
<th>Pathologic Q Waves</th>
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<tbody>
<tr>
<td>LAD</td>
<td>15.6±6.1 (14)</td>
<td>11.2±5.1 (6)</td>
<td></td>
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<tr>
<td>RCA</td>
<td>16.8±9.0 (4)</td>
<td>12.0 (1)</td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td>12.0±4.6 (4)</td>
<td>7.3±0.9 (3)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15.2±6.7 (22)</td>
<td>10.1±4.4 (10)</td>
<td></td>
</tr>
<tr>
<td>Symptom ( - )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>15.5±4.9 (11)</td>
<td>10.3±3.5 (12)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>13.5±3.8 (4)</td>
<td>8.7±3.3 (9)</td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td>7.3±1.3 (3)</td>
<td>9.9±3.4 (24)</td>
<td></td>
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</tbody>
</table>

*Numbers of patients are enclosed within parentheses.
who did not have abnormal Q waves were asymptomatic, while 24 of 48 patients who did have abnormal Q waves were asymptomatic. Kurata et al reported that chest pain during exercise testing was seen in 16 of 51 patients with peri-infarction ischemia. The present study showed that the frequency of silent ischemia was significantly higher in patients who had transmural infarction than in those who did not have transmural infarction.

**Presence of Angina and Amount of Myocardial Ischemia**

A considerable body of evidence supports the theory that myocardial ischemia resulting in angina is greater than that associated with silent ischemia. In contrast, when groups of silent ischemia patients were compared with angiographically and clinically matched groups of symptomatic patients, the degree of ST-segment depression, hemodynamic change, and exercise-induced reduction in ventricular function were similar. Tomographic thallium imaging has demonstrated that patients with silent or painful ischemia during exercise have similar amounts of ischemic myocardium, including patients who had a prior history of myocardial infarction and those who did not. Ozawa et al observed that symptomatic patients who did not have pathologic Q waves had more severe and extensive ischemia than asymptomatic patients; in patients who had pathologic Q waves, the severity of myocardial ischemia in asymptomatic patients might be equal to that in symptomatic patients as assessed by the number of leads showing ST-segment depression and maximum voltage of ST depression. In patients with prior myocardial infarction, Kurata et al found that the uptake scores of thallium 201 in patients with a transient defect within the prior infarct zone was not significantly different from that of patients with transient defect outside the prior infarct zone.

In the present study, 100 of 153 patients had a prior myocardial infarction. The number of fixed defects might be enhanced in detriment to transient defects. The amount of ischemia in the Q wave infarct zone was similar in patients who had symptoms and in those who did not. In patients who did not have Q wave infarction, the amount of ischemia tended to be larger in patients who had angina than in those who did not; however, the differences were not significant.

**Clinical Techniques and Study Limitations in Detection of Silent Ischemia and Amount of Ischemic Myocardium**

In the present study, the maximal heart rate achieved was not sufficiently high that might be due to supine exercise. However, the results on comparison of redistribution scores between patients who had symptoms and those who did not would not be different even with the higher maximal heart rate. Pohost recommended that silent ischemia should be defined by at least two of the noninvasive variables of myocardial ischemia (eg, significant ST-segment depression, "redistribution" by thallium scintigraphy, or exercise-induced regional wall motion abnormality) or by angiographically documented coronary artery disease with at least one of the noninvasive variables of myocardial ischemia. HEcht et al suggested a greater role of SPECT imaging in evaluating myocardial ischemia and the amount of jeopardized myocardium in the study of silent ischemia.

An important advance in the clinical utility of SPECT imaging has been a recent development of quantitative analysis for image interpretation, which significantly improves on the visual analysis of tomographic sections. This technique allows comparison of patients with varied heart sizes and shapes with a normal database obtained by averaging the plots of patients with very low likelihood of coronary artery disease. The quantitation of SPECT images reduces intra- and inter-observer variability by objectifying and simplifying the process of image interpretation. In order to allow more time for thallium 201 redistribution and, thus, to improve the predictive accuracy of thallium 201 redistribution scintigraphy, some investigators recommended performing repeated imaging in patients with fixed defects at 4 h as late as 16 to 72 h after tracer injection. In the present study, late imaging was not performed. Although a late image may have yielded additional patients with redistribution, this was not part of the study protocol. There is no a priori reason to assume that such late redistribution would occur with a different frequency in symptomatic and asymptomatic patients. Patients in the present study had single-vessel disease and the influence of ischemia in other coronary arteries would not disturb the interpretation of thallium 201 scintigraphy.

**References**

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