Significance of Downsloping ST-Segment Depression
Induced by Low-level Exercise in Severe
Coronary Artery Disease
Assessment with Myocardial Ischemia
and Collateral Perfusion

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SUMMARY

Exercise-induced downsloping ST-segment depression is a common manifestation of severe myocardial ischemia. Although greater downsloping ST-segment depression is suspected to indicate more severe ischemia, its exact relationship to regional myocardial blood flow (RMBF) has not yet been clarified. We investigated the relationship between the magnitude of downsloping ST-segment depression and exercise-induced changes in RMBF and collateral perfusion. Nitrogen-13 ammonia positron emission tomography was performed in 6 healthy volunteers and 72 patients with angiographically proven coronary artery disease. The left ventricle was divided into 11 regions of interest, and RMBF in each region was measured at rest and during low-level supine bicycle exercise. Downsloping ST-segment depression of 0.1 mV or more at 80 milliseconds after the J point was accepted as significant. Low-level exercise induced downsloping depression of 0.1 to 0.2 mV in 10 patients (group D1) and downsloping depression of 0.2 mV or more in 8 patients (group D2). Multivessel disease was common in both group D1 (80% of patients) and group D2 (88% of patients). Collateral circulation was significantly more frequent in group D1 (90%) than in group D2 (13%, p < 0.01). Ischemic areas were larger and cardiac function was worse in group D2 than in group D1. The RMBF increased sufficiently in all regions (56 ± 30%) with exercise in the healthy group. In group D1, RMBF was unchanged or decreased in ischemic areas (10 ± 23%) but increased sufficiently in surrounding areas (50 ± 32%). In group D2, RMBF was unchanged in ischemic areas (17 ± 24%) and increased insufficiently in surrounding areas (41 ± 21%). Therefore, exercise-induced downsloping ST-segment depression of 0.1 to 0.2 mV may reflect an underly-
ing change in blood flow in viable myocardium with collateral perfusion, and downsloping depression of 0.2 mV or more may reflect more severely impaired myocardium without collateral perfusion. (Jpn Heart J 1997; 38: 207-218)

**Key words:** Downsloping ST-segment depression, Regional myocardial blood flow, Collateral perfusion, Cardiac function, Positron emission tomography

**Electrocardiographic (ECG) stress testing** has been widely performed to detect coronary artery disease (CAD). The relationships between the morphology and magnitude of exercise-induced ST-segment depression and the severity of CAD have been investigated.1-3) Downsloping ST-segment depression indicates increased severity of CAD better than do other types of ST-segment depression.4) Although greater downsloping ST-segment depression is suspected to indicate more severe myocardial ischemia, its exact relationship to myocardial blood flow has not yet been clarified. Recently, nuclear cardiology has continued to develop. The combination of exercise testing and myocardial perfusion imaging might allow more accurate assessment of exercise-induced myocardial ischemia.5)

In this study, we used nitrogen-13 (N-13) ammonia positron emission tomography (PET) with low-level exercise to investigate the relationship between the magnitude of downsloping ST-segment depression and exercise-induced changes in collateral perfusion and myocardial ischemia as indicated by myocardial blood flow.

**Methods**

**Subjects:** The subjects were 6 healthy male volunteers (mean age, 34.3 ± 5.2 years) and 72 patients (54 men and 18 women; mean age, 62.0 ± 8.0 years) with angiographically proven CAD (34 with angina pectoris and 38 with previous myocardial infarction) who had not undergone coronary revascularization. Patients who had ST-segment depression due to bundle branch block or showed the effects of digitalis or antiarrhythmic drugs on resting ECG were excluded from the study. Informed consent was obtained from all subjects.

**Coronary angiography:** The site of coronary artery stenosis was designated according to the classification of the American Heart Association.6) The extent of coronary artery stenosis was expressed as 100%, 99%, 90%, 75%, and 50%. Coronary artery stenosis of 75% or greater was defined as significant. The presence of collateral circulation that was supplied by the contralateral artery was noted. According to the classification of Cohen and Rentrop,7) grading of collateral filling was as follows: 0 = none, 1 = filling of side branches only, 2 = partial
filling of the epicardial segment, 3 = complete filling of the epicardial segment. Collateral circulation was considered positive when filling was grade 2 or 3 and was considered negative when filling was grade 0 or 1.8)

**Cardiac PET study:** Exercise PET studies were performed with a previously described method9) within 1 week after coronary angiography. The regional myocardial blood flow (RMBF) was measured with a PET scanner (Headtome IV, Shimadzu, Kyoto, Japan) and a perfusion tracer, N-13 ammonia (half-life, 10 minutes) labeled with positrons produced by a compact cyclotron (Japan Steel Works, Tokyo, Japan) at Nakano National Chest Hospital. The spatial resolution of static images at the center of the field of view was adjusted to 6 mm with a Butterfield filter. Exercise testing was performed on a supine bicycle ergometer (Monark, Varberg, Sweden) at a fixed workload of 25 watts for a total of 6.5 minutes. The RMBF was measured at both rest and 5 minutes after the start of exercise. During the resting scan, the subject lay on a couch in the PET gantry tunnel, and the transmission scan was taken with 2 mCi of a germanium-68 external source for 5 minutes. The transmission scan data were used to correct the radiation attenuation in the emission scan data and also to confirm the position of the subject’s heart. Next, 10 to 20 mCi of N-13 ammonia was administered by intravenous injection while the subject was in the supine position. Immediately after injection of the tracer, blood was sampled from the radial artery at a constant rate of 10 mL/min for 2 minutes. After the blood sample was thoroughly mixed, 1 mL was used to measure radioactivity with a decay correction. Five minutes after injection of the tracer, the emission scan was started and continued for 10 minutes. After about 20 minutes, three points on the subject’s skin were marked to allow accurate repositioning, after which the subject and the couch were moved from the scanning position to the exercise position. The bicycle ergometer was placed on the couch and the subject was instructed to exercise with the bicycle ergometer in the supine position. Five minutes after the start of exercise, 10 to 20 mCi of N-13 ammonia was administered intravenously, after which the subject continued to exercise for a further 1.5 minutes. Arterial blood was again sampled at the same rate (10 mL/min) for 2 minutes after injection of the tracer. The subject and couch were repositioned within the PET scanner with reference to the three landmarks for the next emission scan, which was performed for 10 minutes.

**Myocardial perfusion imaging:** Myocardial images were obtained by synchronizing the R wave on ECG with the opening of the gate. The average R R interval was divided into five time frames. Data were collected from the first four time frames. Myocardial images of five slices were taken in 13-mm increments from the base to the apex of the left ventricle. Twenty images were obtained from four time frames of five slices each. Images of the first time frame, which repre-
sented the end-diastolic phase of the left ventricle, were chosen for quantitative analysis of RMBF. The left ventricle was divided into 11 regions of interest, which included 3 regions in the anterior wall, 2 regions in the septum, 1 region in the apex, 3 regions in the lateral wall, and 2 regions in the inferoposterior wall.\(^{10}\)

**Quantitative measurement of RMBF:** The RMBF of each region was calculated with the formula of Hara et al.\(^ {10}\): 

\[
\text{RMBF} = \left\{ \frac{Q}{E \cdot \int_0^2 \overline{C_a(t)} \, dt} \right\} \times 100
\]

where \(Q\) (cps/cm\(^3\)) is the radioactivity of each region, \(\int_0^2 \overline{C_a(t)} \, dt\) (cps·min/mL) is the integration of radioactivity in the arterial blood withdrawn at a constant rate for 2 minutes, and \(E\) is the extraction fraction, for which 0.82 was used in our study. The calculated value corresponds to the RMBF (mL/min/100 cm\(^3\)) in 100 cm\(^3\) of myocardium. According to Schelbert et al.,\(^ {11}\) 82% of arterial N-13 ammonia is trapped in the myocardium. In each patient, the mean RMBF was calculated from the RMBF of the 11 regions. Ischemic areas were defined in both patients with angina pectoris and patients with previous myocardial infarction as regions that showed an increase in RMBF of 10% or less with exercise in the territory of stenotic coronary arteries and regions shown by ECG abnormal Q waves to be infarcted.\(^ {12,13}\)

**Measurement of cardiac function:** Cardiac output was measured with the N-13 ammonia dilution method at both rest and 5 minutes after the start of exercise during the PET study, as previously reported.\(^ {14}\) The cardiac output was calculated according to the formula: 

\[
\text{cardiac output (L/min)} = \frac{I (\text{N-13 ammonia})}{\int_0^2 \overline{C_a(t)} \, dt}
\]

where \(I (\text{N-13 ammonia})\) represents the total injected dose of N-13 ammonia decay-corrected to time zero. The value of \(I (\text{N-13 ammonia})\) was calculated from the radioactivity with decay correlation of noninjected N-13 ammonia at 10 minutes (half-life) after injection of the tracer. The cardiac index was calculated from cardiac output and body surface area, and the stroke index was calculated from the cardiac index.

**ECG exercise testing with PET study:** Exercise testing was performed with low-level supine bicycle ergometer exercise of 25 watts for 6.5 minutes (3 to 4 metabolic equivalents [METS]). Exercise was discontinued when severe chest pain (class 3/4 according to the Kattus criteria\(^ {15}\)), severe dyspnea (7/10 on the new Borg scale\(^ {16}\)), marked change in blood pressure, or serious arrhythmia was observed or when the target heart rate (85% of age-predicted maximal heart rate) was attained.

Standard 12-lead ECG (Siemens, Erlangen, Germany) and blood pressure (Colin, Tokyo, Japan) were continuously recorded throughout the study, and the rate-pressure product (heart rate [HR] · systolic blood pressure [SBP]): beats per minute [bpm] · mmHg) was calculated as an index of myocardial oxygen consumption.
ST-segment changes were assessed in the 12-lead ECG with maximal ST-segment depression at 5 minutes after the start of low-level exercise. Leads that showed negative T waves on resting ECG were excluded. ST-segment depression was measured from the isoelectric PR segment at 80 milliseconds after the J point.17) Downsloping ST-segment depression of 0.1 mV or more lasting 80 milliseconds was accepted in this study to investigate our objective. Patients with downsloping ST-segment depression were divided into two groups on the basis of the magnitude of ST-segment displacement: group D1 patients had a depression of 0.1 to 0.2 mV, while group D2 patients had a depression of 0.2 mV or more.

**Statistical analysis:** Continuous variables are expressed as mean value ± SD and were compared by an unpaired Student’s t-test or Mann-Whitney U-test between two groups and by a one-way analysis of variance (ANOVA) among more than two groups. Categorical data are expressed as proportions and were compared by a chi-square test. A p-value <0.05 was considered statistically significant.

**Results**

**Patient characteristics:** No patients had to stop exercising during the PET study for the reasons stated above. Of the 72 patients with angiographically proven CAD, low-level exercise induced downsloping ST-segment depression of 0.1 to 0.2 mV in 10 patients (group D1), downsloping ST-segment depression of 0.2 mV or more in 8 patients (group D2), and other types of ST-segment depression of 0.05 to 0.2 mV in the remaining 54 patients (group O). Other types of ST-segment depression included junctional, slowly upsloping, and horizontal depression.

Age was 61.1 ± 8.2 years in group O, 65.0 ± 6.9 years in group D1, and 61.1 ± 8.2 years in group D2 and did not differ significantly among the three groups (Table I). The proportion of patients with previous myocardial infarction was 26 of the 54 patients (48%) in group O, 7 of the 10 (70%) in group D1, and 5 of the 8 (63%) in group D2 and did not differ significantly among the three groups. The peak rate-pressure product during low-level exercise was 14,572 ± 3756 bpm·mmHg (HR: 84.5 ± 13.3 bpm, SBP: 160.1 ± 29.4 mmHg) in group O, 15,780 ± 3978 bpm·mmHg (HR: 90.9 ± 12.5 bpm, SBP: 174.8 ± 41.8 mmHg) in group D1, and 15,975 ± 2862 bpm·mmHg (HR: 94.1 ± 10.2 bpm, SBP: 169.5 ± 27.8 mmHg) in group D2 and did not differ significantly among the three groups.

**CAD and collateral circulation:** Of the 54 patients in group O, 11 (21%) had single-vessel disease with stenosis of 50%, 19 (35%) had single-vessel disease with stenosis of 75% or greater, 24 (44%) had multivessel disease with stenosis of 75%
Table I. Baseline Characteristics of 72 Patients with Coronary Artery Disease

<table>
<thead>
<tr>
<th></th>
<th>Group O (n = 54)</th>
<th>Group D1 (n = 10)</th>
<th>Group D2 (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>61.1 ± 8.2</td>
<td>65.0 ± 6.9</td>
<td>61.1 ± 8.2</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>40 (74%)</td>
<td>7 (70%)</td>
<td>7 (88%)</td>
</tr>
<tr>
<td>female</td>
<td>14 (26%)</td>
<td>3 (30%)</td>
<td>1 (12%)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>angina pectoris</td>
<td>28 (52%)</td>
<td>3 (30%)</td>
<td>3 (37%)</td>
</tr>
<tr>
<td>previous MI</td>
<td>26 (48%)</td>
<td>7 (70%)</td>
<td>5 (63%)</td>
</tr>
<tr>
<td>Low-level exercise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>peak RPP (bpm · mmHg)</td>
<td>14572 ± 3756</td>
<td>15780 ± 3978</td>
<td>15975 ± 2862</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>84.5 ± 13.3</td>
<td>90.9 ± 12.5</td>
<td>94.1 ± 10.2</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>160.1 ± 29.4</td>
<td>174.8 ± 41.8</td>
<td>169.5 ± 27.8</td>
</tr>
</tbody>
</table>

MI = myocardial infarction; RPP = rate-pressure product; HR = heart rate; SBP = systolic blood pressure; bpm = beats per minute.

Figure 1. Exercise-induced ST-segment depression and CAD and collateral circulation. Multivessel disease (bold borderline) was significantly more frequent in groups D1 and D2 than in group O (both *p < 0.05). Collateral circulation was significantly more frequent in group D1 than in groups D2 (†p < 0.01) and O (‡p < 0.001).

or greater, and only 1 (2%) had collateral circulation (grade 2) (Figure 1). Of the 10 patients in group D1, 2 (20%) had single-vessel disease with stenosis of 75% or greater, 8 (80%) had multivessel disease with stenosis of 75% or greater, and 9 (90%) had collateral circulation (grade 2 to 3). Of the 8 patients in group D2, only 1 (12%) had single-vessel disease with stenosis of 75% or greater, 7 (88%) had multivessel disease with stenosis of 75% or greater, and only 1 (13%) had collat-
Figure 2. Changes in RMBF with low-level exercise. Mean size of ischemic areas was significantly larger in groups D1 (*p<0.05) and D2 (†p<0.01) than in group O. Changes in RMBF in both ischemic areas and healthy (surrounding) areas with low-level exercise differed among the four groups.

Table II. Changes in Regional Myocardial Blood Flow and Cardiac Function with Low-Level Exercise

<table>
<thead>
<tr>
<th></th>
<th>Healthy group (n = 6)</th>
<th>Group O (n = 54)</th>
<th>Group D1 (n = 10)</th>
<th>Group D2 (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMBF (mL/min/100cm³)</td>
<td>Rest: 81.8 ± 12.4</td>
<td>73.9 ± 15.7</td>
<td>72.1 ± 16.6</td>
<td>69.6 ± 10.5*</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>Rest: 6.20 ± 0.83</td>
<td>5.66 ± 0.58*</td>
<td>4.78 ± 0.99#</td>
<td>4.42 ± 0.69c</td>
</tr>
<tr>
<td>Cardiac index (L/min/m²)</td>
<td>Exercise: 9.59 ± 1.61</td>
<td>7.98 ± 0.89*</td>
<td>6.31 ± 1.30</td>
<td>5.74 ± 0.88b</td>
</tr>
<tr>
<td>Stroke index (mL/beat/m²)</td>
<td>Rest: 51.7 ± 7.80</td>
<td>44.6 ± 5.28*</td>
<td>39.9 ± 6.36*</td>
<td>40.8 ± 9.62*</td>
</tr>
</tbody>
</table>

*p<0.05, †p<0.02, #p<0.01, #p<0.001 versus the healthy group.

Multivessel disease was present significantly more frequently in groups D1 and D2 than in group O (both p<0.05) but did not differ significantly between groups D1 and D2 (Figure 1). Collateral circulation was observed significantly more frequently in group D1 than in groups D2 (p<0.01) and O (p<0.001).

RMBF: The mean RMBF increased significantly with low-level exercise from 81.8 ± 12.4 to 126.9 ± 16.6 mL/min/100 cm³ (p<0.001) in the healthy group, from 73.9 ± 15.7 to 101.7 ± 25.8 mL (p<0.001) in group O, from 72.1 ± 16.6 to 95.4 ± 17.8 mL (p<0.01) in group D1, and from 69.6 ± 10.5 to 90.5 ± 13.9 mL (p<0.01) in group D2 (Table II). The mean RMBF at rest was significantly lower only in group D2 than in the healthy group but did not differ significantly among groups D1 and O and the healthy group. However, the mean RMBF at 5 minutes of low-level exercise was lowest in group D2 (p<0.001 vs. the healthy group), followed by group D1 (p<0.01 vs. the healthy group), group O (p<0.02 vs. the
Figure 3. Differences in increased rates of RMBF with low-level exercise. The difference between maximal and minimal increased rates of RMBF with exercise was significantly greater in group D1 than in other groups (*p < 0.001).

healthy group), and the healthy group and differed significantly among the four groups (p < 0.05 by the ANOVA). As shown in Figure 2, the mean size of ischemic areas was significantly larger in groups D2 (3.63 ± 1.41, p < 0.01, Mann-Whitney U-test) and D1 (2.30 ± 1.16, p < 0.05, Mann-Whitney U-test) than in group O (1.46 ± 1.73). The RMBF increased with exercise in all regions (56 ± 30%) in the healthy group. In group O, RMBF increased in both ischemic areas (30 ± 38%) and surrounding areas (43 ± 16%) with exercise. In group D1, RMBF was unchanged or decreased in ischemic areas (10 ± 23%) but increased in surrounding areas (50 ± 32%) with exercise. In group D2, RMBF was unchanged in ischemic areas (17 ± 24%) and increased in surrounding areas (41 ± 21%) with exercise. As shown in Figure 3, the difference between maximal and minimal increased rates of RMBF during exercise was significantly greater in group D1 (94 ± 51%, p < 0.001 vs. other groups) than in the healthy group (35 ± 4%), group O (50 ± 24%), or group D2 (60 ± 20%).

Cardiac function: Cardiac index at rest was lowest in group D2 (p < 0.01 vs. the healthy group), followed by group D1 (p < 0.01 vs. the healthy group), group O (p < 0.05 vs. the healthy group), and the healthy group and differed significantly among the four groups (p < 0.05 by the ANOVA) (Table II). The cardiac index at 5 minutes of exercise was lowest in group D2 (p < 0.001 vs. the healthy group), followed by group D1 (p < 0.001 vs. the healthy group), group O (p < 0.02 vs. the healthy group), and the healthy group and differed significantly among the four groups (p < 0.05 by the ANOVA).
DISCUSSION

ST-segment depression and severity of CAD: The relationship between the morphology and magnitude of exercise-induced ST-segment depression and the severity of CAD has been noted.\textsuperscript{1-3} Goldschlager et al.\textsuperscript{4} reported that downsloping ST-segment depression indicates multivessel or left main coronary artery disease. Stuart et al.\textsuperscript{18} reported that downsloping ST-segment depression is a better indicator of future coronary events than is horizontal or upsloping depression. Downsloping ST-segment depression of 0.1 mV or more is generally thought to indicate severe myocardial ischemia.

We have previously reported that exercise-induced downsloping changes in ST-segment morphology may be associated with the underlying changes of the RMBF, particularly in areas with collateral circulation.\textsuperscript{19} In this study, we investigated the relationship between the magnitude of downsloping ST-segment depression and changes in collateral perfusion and RMBF with low-level exercise. Downsloping ST-segment depression of 0.1 mV or more induced by low-level exercise indicated significantly more severe CAD and significantly larger areas of exercise-induced ischemia than did other types of ST-segment depression. Patients with downsloping ST-segment depression were pathophysiologically classified into two groups on the basis of the magnitude of ST-segment depression: group D\textsubscript{1} patients had a depression of 0.1 to 0.2 mV and group D\textsubscript{2} patients had a depression of 0.2 mV or more. Group D\textsubscript{1} patients had collateral circulation significantly more frequently than did group D\textsubscript{2} patients.

Functional benefits of collateral circulation: Despite numerous studies,\textsuperscript{8,20,21} the functional role of collateral circulation in the prevention of ischemic myocardium remains controversial. Collateral circulation provides perfusion to the starved myocardium at rest, which at best supplies about 40% of the normal coronary flow.\textsuperscript{29} Because the flow is never enough, ischemia almost always occurs when myocardial oxygen consumption increases with exercise.\textsuperscript{23} Thus, cardiac function is reduced to some degree with exercise.\textsuperscript{24}

In this study, we assessed the effects of collateral circulation on ECG downsloping ST-segment depression and changes in RMBF and cardiac function induced by low-level exercise in patients with severe CAD. Ninety percent of patients in group D\textsubscript{1} but only 13% of patients in group D\textsubscript{2} had collateral circulation. It is possible that group D\textsubscript{1} patients who had triple-vessel disease tended to have had undergone more ischemic preconditioning and thus received greater stimulation for collateral formation than did group D\textsubscript{2} patients. Ischemic areas were smaller and the difference between the maximal and minimal increased rates of RMBF with low-level exercise was significantly greater in group D\textsubscript{1} than in group D\textsubscript{2}. In group D\textsubscript{1}, RMBF was unchanged or decreased in ischemic areas.
but increased sufficiently in surrounding areas with low-level exercise. The peculiar change in RMBF was not related to the presence or amount of infarcted myocardium but might be related to collateral perfusion during low-level exercise. Collateral circulation with exercise might play a beneficial role in two factors: confining the ischemic myocardium to a focal but viable area and increasing blood flow in the surrounding myocardium to preserve cardiac function in the whole heart. In group D2, exercise-induced ischemic areas were extensive and cardiac dysfunction was more severe. Weiner et al.25) reported that downsloping ST-segment depression of 0.2 mV or more indicates a worse cardiac prognosis than does downsloping depression of 0.1 to 0.2 mV. This study supports our results. Most patients in each group underwent coronary revascularization, percutaneous transluminal coronary angioplasty, or coronary artery bypass graft surgery after this study.

**Low-level exercise:** Ischemic ST-segment depression of 0.1 mV or more induced by low-level exercise of less than 4 METS or Bruce stage 1 or less indicates severe myocardial ischemia.26) Weiner et al.25) reported that patients in whom ST-segment depression developed at Bruce stage 1 of low-level exercise had a worse cardiac prognosis. Low-level exercise of less than 4 METS may be appropriate to assess the severity and prognosis of CAD. In addition, we used low-level exercise in the present study for two main reasons. One was the safety of patients, as in the study of Gibson et al.27) The objective of the study was to assess the clinical significance of downsloping ST-segment depression in patients with angiographically proven CAD, not to detect CAD on the basis of the presence of ischemic ST-segment depression, as in ordinary exercise-tolerance testing. No patients had to discontinue testing owing to severe chest pain or serious arrhythmia during exercise. The other reason low-level exercise was used was to determine RMBF quantitatively. The extraction fraction was almost constant, regardless of increases in coronary blood flow within the physiologic range of 44 to 200 mL/min/100 g.28) The mean RMBF increased significantly from 81.8 ± 12.4 to 126.9 ± 16.6 mL/min/100 cm³ (p < 0.001) in the healthy group and from 69.6 ± 10.5 to 90.5 ± 13.9 mL (p < 0.01) in group D2 with low-level exercise. In this range of myocardial blood flow, the extraction fraction remained the same. These results suggest that our method of quantitative assessment of RMBF was valid. Laarman et al.29) determined the extent and location of CAD with quantitative analysis of thallium-201 imaging with low-level bicycle exercise of 30 watts for 3 minutes. Although higher-level exercise stress may be provided to obtain more information, we believe that low-level exercise used in the study can provide meaningful results.

**Partial-volume effect:** In the quantitative measurement of RMBF, myocardial perfusion imaging with PET is subject to the partial-volume effect.30) However,
according to our previous reports, our method might be improved to minimize the partial-volume effect and not to impose a serious problem clinically.

**Conclusions:** In conclusion, low-level exercise-induced downsloping ST-segment depression indicates more severe CAD and more severe myocardial ischemia than do other types of ST-segment depression. The magnitude of downsloping ST-segment depression induced by low-level exercise might be related in part to collateral perfusion and myocardial viability in patients with severe CAD. Downsloping depression of 0.1 to 0.2 mV may reflect an underlying change in blood flow, particularly in viable myocardium with collateral perfusion. Downsloping depression of 0.2 mV or more may reflect more severely impaired myocardium without collateral perfusion. Analysis of ST-T changes on low-level exercise ECG with simultaneous PET may provide more precise information on coronary impairment.

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