Exercise-Induced ST-Segment Elevation — Role of Left Ventricular Wall Motion Abnormalities and Coronary Artery Narrowing —

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We studied the causes of exercise-induced ST-segment elevation. Group I consisted of 15 patients with anterior myocardial infarction in the absence of a coronary artery luminal narrowing of 75% or more. Group II consisted of 36 patients with predominantly exertional angina and a luminal narrowing of 90% or more in the left anterior descending coronary artery in the absence of previous myocardial infarction. In group I, exercise-induced ST-segment elevation occurred frequently during treadmill exercise (15/15, 100%). None of the patients showed ^{201}Tl redistribution. The standard deviation of the phase in radionuclide ventriculography increased during bicycle exercise. Of group II patients, only those with 99% narrowing and poor collaterals showed exercise-induced ST-segment elevation (13/14, 93%), whereas none of those with complete occlusion or 99% narrowing and good collaterals, or 90% narrowing showed ST-segment elevation. In group II, patients with exercise-induced ST-segment elevation showed lower ^{201}Tl uptake during exercise and washout in the territory of the diseased vessel than those without exercise-induced ST-segment elevation. In conclusion, wall motion abnormalities may cause exercise-induced ST-segment elevation independently of myocardial ischemia. In patients with predominantly exertional angina, exercise-induced ST-segment elevation may be a marker for 99% narrowing with poor collaterals and severe myocardial ischemia.
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ST-segment elevation is relatively rare in exercise-stress testing for the detection of coronary artery disease!^{1–5} Left ventricular wall motion abnormalities and/or myocardial ischemia due to severe coronary artery disease or coronary artery spasm have been suggested as possible causes of exercise-induced ST-segment elevation. However, wall motion abnormalities and severe coro-

nary artery disease often coexist. It is not yet clear whether or not wall motion abnormalities can cause exercise-induced ST-segment elevation independently of myocardial ischemia in patients with myocardial infarction. The precise prevalence of exercise-induced ST-segment elevation in patients without previous myocardial infarction is also not yet known. In addition, the details of the relation between exercise-induced ST-segment elevation and the severity of coronary artery disease in patients with predominantly exertional angina have not been

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studied. To address these issues, we reviewed treadmill exercise electrocardiograms in two patient groups: group I=patients with myocardial infarction in the absence of coronary artery narrowing, and group II=patients with predominantly exertional angina and one-vessel disease in the absence of previous myocardial infarction. In addition, we analyzed data from exercise-stress tomographic ^{201}Tl myocardial imaging and exercise-stress radionuclide ventriculography.

METHODS

Patients

The study patients were retrospectively selected from subjects who underwent treadmill exercise testing and subsequent coronary arteriography and left ventriculography within the past 5 years. The results of coronary arteriography and left ventriculography were assessed according to the criteria of the AHA.⁶ Group I consisted of 15 patients (13 men and 2 women, a mean age 57 years, range 35 to 78) who had had an episode of acute anterior myocardial infarction more than 8 weeks before testing and abnormal contractility (none, dyskinetic or aneurysmal) in the left ventriculogram in the absence of postinfarct angina, together with coronary artery luminal narrowing of 75% or more. Ten of the 15 patients had intracoronary thrombolysis and/or angioplasty of the left anterior descending coronary artery. Group II consisted of 36 patients (23 men and 13 women, a mean age 63 years, range 28 to 74) who had predominantly exertional angina and one-vessel disease of the left anterior descending coronary artery with luminal narrowing of 90% or more in the absence of pathological Q waves and abnormal contractility (none, dyskinetic or aneurysmal) in the left ventriculogram. Patients with resting angina in the middle of the night or in the early morning were excluded. Patients with intraventricular conduction abnormality or atrial fibrillation were also excluded.

Treadmill Exercise Testing

Each patient in group I was taking a calcium antagonist and a long-acting nitrate, and all drugs were administered before this testing to prevent coronary artery spasm. In group II, testing was performed before

treatment or 48 h after the withdrawal of antianginal drugs. Among patients with exercise-induced ST-segment elevation in group II, follow-up testing was performed to assess the effect of medical therapy with coronary artery dilators.

A computerized treadmill system (Marquette, CASE 2 or 12) was used. Each patient underwent multistage exercise according to a modified Bruce protocol in which a stage at 3.8 miles/h and 14% was added between stages III and IV.⁷ A modified 12-lead electrocardiogram (according to the Mason and Likar method⁸) was recorded at rest in the supine and standing positions every minute during exercise, and after 1, 2, 3 and 5 min of recovery in the supine position. Leads II, V_1 and V_5 were monitored continuously during testing. In group I, the end point of exercise was the achievement of 85% of the age-adjusted predicted maximum heart rate (target heart rate). In group II, the end point was the development of moderate anginal chest pain, new or additional ST-segment depression (0.2 mV or more at 80 msec from the J point) or ST-segment elevation (0.1 mV or more at 40 msec from the J point) in at least one lead, except aVR, aVL and V_1 , compared with the level at rest in the standing position, or the achievement of the target heart rate. A significant change in the level of the ST-segment was defined as new or additional horizontal or down-sloping depression (0.1 mV or more) or elevation (0.05 mV or more) at 1 min of recovery compared with the level at rest in the supine position in at least one lead. Exercise-induced U-wave inversion was defined as new discrete negative deflection (0.05 mV or more) in the TP-segment.

Cardiac Catheterization

Cardiac catheterization was performed within 4 weeks after treadmill exercise testing. Selective coronary arteriography was performed in multiprojections using the Judkins technique. Luminal narrowing was measured using calipers on the arteriograms after the administration of nitrate. Left ventriculography was performed in the 30-degree right anterior oblique and 60-degree left anterior oblique projections. Patients in group I had abnormal contractility (none, dyskinetic or aneurysmal) in the anterolateral

ral, apical or septal segment and no luminal narrowing of 75% or more in major coronary artery branches. Those with abnormal contractility in the diaphragmatic, posterobasal or posterolateral segment were excluded. Patients in group II had luminal narrowing of 90% or more in the proximal or mid portion of the left anterior descending coronary artery (segment 6 or 7) in the absence of luminal narrowing of 75% or more in any other major coronary artery branch and abnormal contractility (none, dyskinetic or aneurysmal) in the left ventriculogram. Luminal narrowing in the left anterior descending coronary artery was graded as complete occlusion, 99% narrowing with severe delayed filling, 99% narrowing with mild or moderate delayed filling, or 90% narrowing. Collateral filling was classified according to the criteria proposed by Cohen and Rentrop⁹ as follows: grade 0=no visible filling, grade 1=filling of side branches of the artery by collateral circulation, grade 2=partial filling of the epicardial segment by collateral circulation, and grade 3=complete filling of the epicardial segment by collateral circulation.

Exercise-Stress Tomographic ²⁰¹Tl Myocardial Imaging

Exercise-stress ²⁰¹Tl imaging was performed after treadmill exercise testing in 14 patients in group I and 20 patients in group II. Supine bicycle exercise was begun at 25W, and work rate was increased by 25W every 3 min. Thallium-201 chloride (111 MBq) was injected intravenously at peak exercise, and patients continued to exercise for an additional minute. A modified 12-lead electrocardiogram was recorded at rest, every minute during exercise, and after 1, 2 and 3 min of recovery. The end points of exercise were similar to those in the treadmill exercise testing. A gamma camera (Hitachi, GAMMA-VIEW) equipped with a high-resolution, low-energy, parallel-hole collimator was used. The image data were acquired with a minicomputer used for nuclear medicine (Hitachi, HARP). Initial imaging was begun 10 min after the termination of exercise and delayed imaging was performed 4 h later. Thirty-two projections at 5.6-degree intervals over a 180-degree arc from the 45-degree right anterior oblique to

the 45-degree left posterior oblique position were obtained for 30 sec each with a 64×64 matrix. Short-axis, vertical long-axis and horizontal long-axis tomograms were reconstructed at a thickness of 1 pixel (5.6 mm) per slice. In both groups, the initial and delayed images were interpreted by 3 observers. A defect was classified as reversible (partial or complete redistribution) or nonreversible (no redistribution or equivocal). A consensus of the opinions of the three observers was taken. In group II, the territory of the left anterior descending coronary artery was assessed according to the results of coronary arteriography in each patient. A circumferential profile of ²⁰¹Tl uptake was obtained for a vertical long-axis slice including the apex of the heart in the initial and delayed imaging. Sixty radii spaced at 6-degree intervals were constructed from the visually located center of the left ventricle. Each point in the profile represented the maximum counts per pixel along a radius. The circumferential profile of the initial percent uptake was generated by normalizing the number of counts in each point to create a percentage of the maximum counts. The circumferential profile of the washout rate was generated by dividing the difference between the initial and delayed counts by the initial counts for each point along the profile. The minimum value of the initial percent uptake and that of the washout rate were used as indexes of the severity of exercise-induced myocardial ischemia.

Exercise-Stress Radionuclide Ventriculography

Exercise-stress radionuclide ventriculography was performed in 7 patients in group I within 4 weeks after cardiac catheterization. Each patient was positioned on the supine bicycle ergometer. Red blood cells were labeled in vivo using an intravenous injection of technetium-99m pertechnetate (740 MBq) after intravenous injection of stannous pyrophosphate (5 mg). A gamma camera was placed in the left anterior oblique projection. The degree of obliquity was determined by the position which provided separation of both ventricles. Bicycle exercise was begun at 25W, and the work rate was increased by 25W every 4 min. A modified 12-lead electrocardiogram was

TABLE I ELECTROCARDIOGRAPHIC FINDINGS IN PATIENTS WITH ANTERIOR MYOCARDIAL INFARCTION IN THE ABSENCE OF CORONARY ARTERY NARROWING (n=15)

	Number of patients								
	I	II	III	aVF	V ₂	V ₃	V ₄	V ₅	V ₆
Pathological Q wave	2	0	0	0	13	14	10	1	0
Maximum exercise-induced ST-segment elevation	0	0	0	0	1	6	8	0	0

TABLE II ELECTROCARDIOGRAPHIC FINDINGS IN PATIENTS WITH ONE-VESSEL DISEASE OF THE LEFT ANTERIOR DESCENDING CORONARY ARTERY AND EXERCISE-INDUCED ST-SEGMENT ELEVATION IN THE ABSENCE OF PREVIOUS MYOCARDIAL INFARCTION (n=13)

	Number of patients								
	I	II	III	aVF	V ₂	V ₃	V ₄	V ₅	V ₆
Exercise-induced ST-segment elevation	1	0	0	0	10	13	9	1	1
Maximum change	0	0	0	0	3	7	3	0	0

TABLE III INCIDENCE OF EXERCISE-INDUCED ST-SEGMENT ELEVATION IN PATIENTS WITH ONE-VESSEL DISEASE OF THE LEFT ANTERIOR DESCENDING CORONARY ARTERY (LAD) IN THE ABSENCE OF PREVIOUS MYOCARDIAL INFARCTION (n=36)

LAD lesion	Exercise-induced ST-segment elevation
Complete occlusion with grade 3 collaterals	0/4 (0%)
99% narrowing with high grade 2 collaterals	0/4 (0%)
99% narrowing with 0 to low grade 2 collaterals	13/14 (93%)
90% narrowing	0/14 (0%)

Collateral filling is classified according to the criteria by Cohen and Rentrop⁹

recorded at rest, every minute during exercise and after 1, 2 and 3 min of recovery. The end point of exercise was similar to that in the treadmill exercise testing. Multigated acquisition in which an R-R interval was divided into 20 frames was performed for the last 3 min of each 4-min period using a

Fig.1. Electrocardiograms at rest and after 1 min of recovery in a patient in group I with abnormal contractility (none or dyskinetic) in the anterolateral, apical and septal segments. Exercise-induced ST-segment elevation is shown in leads V₂ to V₅ (maximum change, 0.25 mV in lead V₃). The images show no significant exercise-induced ST-segment depression.

Fig.2. Electrocardiograms at rest and after 1 min of recovery in a patient in group II with luminal narrowing of 99% in the mid portion of the left anterior descending coronary artery and low grade 2 collaterals. Exercise-induced ST-segment elevation is shown in leads V_2 – V_6 (maximum change, 0.30 mV in lead V_3), significant exercise-induced ST-segment depression is shown in leads II, III, aVF and V_1 , and U-wave inversion is shown in leads V_3 to V_5 .

Fig.3. Electrocardiograms at rest in the supine and standing positions, during exercise and in the recovery period in a patient in group II with luminal narrowing of 99% in the proximal portion of the left anterior descending coronary artery and grade 0 collaterals. Exercise-induced ST-segment depression is shown in leads V_5 and V_6 , and subsequent ST-segment elevation is shown in leads V_1 to V_6 (maximum change, 0.38 mV in lead V_4).

64×64 matrix. Regional wall motion in both ventricles was evaluated. Phase analysis¹⁰ was performed using the first harmonic of the Fourier transform of the time-activity curve of each pixel (32×32 format) in both ventricles. The phase scale from –180 to +180 degrees represented the point of initial decline from the fitted curve maximum in relation to the R-wave. The mean and standard deviation of the phase were measured. The standard deviation of the phase was used as an index of the synchronicity of ventricular contraction.

Statistical Analysis

Data are shown as the mean±standard deviation or as a percentage. Data were analyzed using the paired or unpaired t test.

RESULTS

Cardiac Catheterization

Group I: Abnormal contractility (none, dyskinetic or aneurysmal) was seen in the anterolateral segment in 10 (67%) of the 15 patients, in the apical segment in 15 (100%) patients, and in the septal segment in 10 (67%) patients.

Group II: Luminal narrowing of 90% or more was observed in the proximal portion of the left anterior descending coronary artery (segment 6) in 24 of the 36 patients, and in the mid portion of the left anterior descending coronary artery (segment 7) in the remaining 12 patients. Four patients had complete occlusion with grade 3 collaterals, 4 had 99% narrowing with severe delayed filling and high grade 2 collaterals, 14 had

TABLE IV QUANTITATIVE ANALYSIS OF EXERCISE-STRESS TOMOGRAPHIC THALLIUM-201 MYOCARDIAL IMAGES IN PATIENTS WITH ONE-VESSEL DISEASE OF THE LEFT ANTERIOR DESCENDING CORONARY ARTERY (LAD) IN THE ABSENCE OF PREVIOUS MYOCARDIAL INFARCTION (n=20)

	n	Territory of LAD		
		Minimum initial percent uptake (%)	Minimum washout rate (%)	Maximum washout rate (%)
ST $\uparrow$	8	39.9 $\pm$ 15.0*	-10.3 $\pm$ 25.8*	47.5 $\pm$ 7.7
ST $\downarrow$ or angina in the absence of ST $\uparrow$	12	61.1 $\pm$ 8.6	22.4 $\pm$ 17.8	47.7 $\pm$ 9.9

ST $\uparrow$, exercise-induced ST-segment elevation; ST $\downarrow$, exercise-induced ST-segment depression.

*p<0.01

Fig.4. Tomographic ^{201}Tl myocardial images and the initial percent uptake and washout rate profiles in a patient in group II with luminal narrowing of 99% in the proximal portion of the left anterior descending coronary artery with grade I collaterals and exercise-induced ST-segment elevation. A severe decrease in ^{201}Tl uptake in the initial image and its redistribution in the delayed image are shown in the anterolateral and apical segments perfused by the left anterior descending coronary artery. A regional decrease in both the initial percent uptake (minimum value, 25%) and the washout rate (minimum value, -10%) is shown in the territory of the left anterior descending coronary artery.

99% narrowing with mild or moderate delayed filling and grade 0 to low grade 2 collaterals, and 14 had 90% narrowing.

Treadmill Exercise Testing (Tables I to III)

Group I: Exercise duration was 8.8 ± 3.9 min. Heart rate at peak exercise was 143 ± 18 beats/min. The end point of exercise was the achievement of the target heart rate in all 15 patients.

At rest, pathological Q wave (0.04 sec or more in duration and 25% or more of the R-wave amplitude in depth) was seen in lead V_3 in 14 (93%) of the 15 patients, in V_2 in 13 (87%) patients, in V_4 in 10 (67%) patients, in I in 2 (13%) patients, and in V_6 in 1 (7%) patient. All 15 patients had significant exercise-induced ST-segment elevation (0.21 ± 0.10 mV). The maximum change was in lead V_4 in 8 (53%) patients, in V_3 in 6 (40%) patients, and in V_2 in 1 (7%) patient (Table I). None of the patients had significant exercise-induced ST-segment depression or U-wave inversion. A typical case is shown in Fig. 1.

Group II: Exercise duration was 6.5 ± 3.3 min. Heart rate at peak exercise was 129 ± 17 beats/min. The end point of exercise was the development of moderate anginal chest pain and/or ST-segment depression or elevation in 33 patients, and achievement of the target heart rate in the remaining 3 patients.

Thirteen patients had significant exercise-induced ST-segment elevation (0.20 ± 0.12 mV). Significant exercise-induced ST-elevation was seen in lead V_3 in all 13 patients, in V_2 in 10 (77%) patients, in V_4 in 9 (69%) patients, and in V_5 , V_6 and I in 1 (8%) patient. The maximum change was in lead V_3 in 7 (54%) of the 13 patients, in V_4 in 3 (23%) patients, and in V_2 in 3 (23%) patients (Table II). Thirteen (93%) of the 14

TABLE V PHASE ANALYSIS OF EXERCISE-STRESS RADIONUCLIDE VENTRICULOGRAMS IN PATIENTS WITH ANTERIOR MYOCARDIAL INFARCTION IN THE ABSENCE OF CORONARY ARTERY NARROWING (n=7)

	Rest	Peak exercise	P value
Phase of both ventricles (degrees)			
Mean	-15.4 ± 14.4	-0.7 ± 11.9	<0.01
Standard deviation	25.4 ± 13.3	30.1 ± 11.8	<0.05

Fig. 5. Radionuclide ventriculograms and phase histograms of both ventricles at rest and at peak exercise in a patient in group I with abnormal contractility (none or dysknetic) in the anterolateral, apical and septal segments. Wall motion abnormalities and phase delay are shown in the anteroapical and apicoinferior regions at rest and at peak exercise (arrows). The mean phase of both ventricles is -19 degrees at rest and 4 degrees at peak exercise. The standard deviation of the phase of both ventricles is 19.3 degrees at rest and 20.8 degrees at peak exercise. LV, left ventricle; RV, right ventricle.

patients with 99% narrowing and grade 0 to low grade 2 collaterals had significant exercise-induced ST-segment elevation. None of

the patients with complete occlusion and grade 3 collaterals, 99% narrowing and high grade 2 collaterals or 90% narrowing had significant exercise-induced ST-segment elevation (Table III). Four (31%) of the 13 patients had exercise-induced horizontal or down-sloping ST-segment depression of 0.1 mV or more in leads II, III, aVF, V_4 , V_5 or V_6 before ST-segment elevation, 9 (69%) had ST-segment depression with ST-segment elevation and 8 (62%) had exercise-induced U-wave inversion in lead V_3 , V_4 , V_5 or V_6 . Two cases are shown in Figs 2 and 3.

Six of the 13 patients with exercise-induced ST-segment elevation in group II underwent follow-up treadmill exercise testing after medical treatment with calcium antagonists and long-acting nitrates. None of the 6 patients had an increase in exercise duration of 1 min or more or a change in heart rate at peak exercise of 10 beats/min or more. They also had significant exercise-induced ST-segment elevation after treatment.

Exercise-stress Tomographic ^{201}Tl Myocardial Imaging (Table IV)

Group I: Heart rate at peak exercise was 129 ± 16 beats/min. All 14 patients had significant exercise-induced ST-segment elevation. All of the patients had a nonreversible defect in anterior and/or apical segments.

Group II: All 20 patients had a reversible defect in anterior and/or apical segments. The data were compared between two subgroups as follows: 8 patients who had significant ST-segment elevation in this testing (8 with 99% narrowing and grade 0 to low grade 2 collaterals) and 12 patients who had significant ST-segment depression or angina in the absence of ST-segment elevation in this testing (3 with complete occlusion and grade 3 collaterals, 1 with 99% narrowing and high grade 2 collaterals, 1 with 99%

narrowing and grade 1 collaterals, and 7 with 90% narrowing). There was no significant difference in heart rate at peak exercise between the two groups (113 ± 14 vs 115 ± 16 beats/min, $p = \text{NS}$). The minimum initial percent uptake in the territory of the left anterior descending coronary artery was significantly lower in patients with ST-segment elevation than in those without ST-segment elevation ($39.9 \pm 15.0\%$ vs $61.1 \pm 8.6\%$, $p < 0.01$). There was no significant difference in the maximum washout rate in the territory of the right coronary artery and left circumflex coronary artery between the two groups ($47.5 \pm 7.7\%$ vs $47.7 \pm 9.9\%$, $p = \text{NS}$). The minimum washout rate in the territory of the left anterior descending coronary artery was significantly lower in patients with ST-segment elevation than in those without ST-segment elevation ($-10.3 \pm 25.8\%$ vs $22.4 \pm 17.8\%$, $p < 0.01$). A typical case is shown in Fig. 4.

Exercise-stress Radionuclide Ventriculography (Table V)

Exercise-stress radionuclide ventriculography was performed in 7 patients in group I. Heart rate at peak exercise was 131 ± 23 beats/min. All 7 patients had significant exercise-induced ST-segment elevation, as well as wall motion abnormalities and phase delay in the anteroseptal and apicoinferior regions both at rest and during exercise. Wall motion in the right ventricle and lateral region was increased in all 7 patients. A significant delay of the mean phase of both ventricles was found from rest (-15.4 ± 14.4 degrees) to peak exercise (-0.7 ± 11.9 degrees, $p < 0.01$). The standard deviation of the phase of both ventricles significantly increased from rest (25.4 ± 13.3 degrees) to peak exercise (30.1 ± 11.8 degrees, $p < 0.05$). A typical case is shown in Fig. 5.

DISCUSSION

This study demonstrates a high incidence of exercise-induced ST-segment elevation in patients with myocardial infarction in the absence of coronary artery narrowing, and in patients with predominantly exertional angina and 99% narrowing with poor collaterals in the absence of previous myocardial infarction. Exercise-induced ST-segment elevation

involved the aggravation of wall motion abnormalities in the former and severe myocardial ischemia in the latter.

The prevalence of exercise-induced ST-segment elevation has ranged from 4 to 8% in previous studies with large patient populations.¹⁻⁵ The incidence of previous myocardial infarction in patients with exercise-induced ST-segment elevation has ranged from 47 to 88%. Bruce et al⁵ analyzed the data of 3,050 patients enrolled in the Coronary Artery Surgery Study. Patients with exercise-induced ST-segment elevation during exercise and recovery ($n = 68$) had a frequent history of myocardial infarction (88%) and left ventricular enlargement and dysfunction.

Dunn et al¹¹ demonstrated that exercise-induced ST-segment elevation is specific for the presence and site of the perfusion defect on planar ²⁰¹Tl images in patients with or without pathological Q waves. Dunn et al¹² subsequently studied 46 patients without pathological Q waves in anterior chest leads and noted an association between exercise-induced ST-segment elevation in leads V₁ and/or aVL, reversible anterior perfusion defects on ²⁰¹Tl images and left anterior descending coronary artery disease. However, in the Mason and Likar method, leads V₁ and aVL, like aVR, may face the interior of the left ventricle. Exercise-induced ST-segment elevation in these two leads may show subendocardial ischemia. Actually, only 14 (30%) of their 46 patients had exercise-induced ST-segment elevation in other anterior chest leads. In patients with left anterior descending coronary artery disease, the significance of exercise-induced ST-segment elevation in leads V₁ and/or aVL may be different from that in other anterior chest leads. Thus, we assessed exercise-induced ST-segment changes in 9 leads, excluding aVR, aVL and V₁.

It is well documented that in patients with myocardial infarction, exercise-induced ST-segment elevation frequently occurs in pathological Q waves or in leads adjacent to the Q waves. In previous reports, most patients with myocardial infarction have had severe coronary artery disease. It is still controversial whether wall motion abnormalities or myocardial ischemia is the major cause of exercise-induced ST-segment elevation. In

our study, there is little possibility that myocardial ischemia was induced in patients with myocardial infarction. Our findings show that in patients with myocardial infarction, exercise-induced ST-segment elevation occurs independently of clinical evidence of myocardial ischemia.

Phase analysis of the radionuclide ventriculogram is a means for evaluating the temporal sequence of ventricular contraction. The phase of the first harmonic of the Fourier transform indicates the onset of contraction in each pixel. The standard deviation of the phase is used as an index of the synchronicity of ventricular contraction. Changes in the phase from rest to exercise in patients with coronary artery disease have been studied previously. Ratib et al¹³ reported that in normal subjects, the standard deviation of the phase of both ventricles significantly narrowed from rest (16.5 ± 2.8 degrees) to peak exercise (13.2 ± 1 degrees), while that of the left ventricle did not change significantly (rest, 8.2 ± 1.7 ; peak exercise, 7.9 ± 0.8 degrees). In most of their patients with coronary artery disease, the standard deviation of the phase during exercise exceeded the normal upper limit (mean + 2 standard deviations). They concluded that phase analysis is a highly sensitive and specific indicator of exercise-induced myocardial ischemia. Furthermore, Norris et al¹⁴ demonstrated that the sensitivity for indicating coronary artery disease is improved when phase analysis is considered along with the global left ventricular ejection fraction responses. However, there is no data available regarding exercise-induced changes in the standard deviation of the phase among patients with myocardial infarction in the absence of coronary artery narrowing. In our patients with anterior myocardial infarction, the standard deviation of the phase of both ventricles was wide at rest, and significantly increased from rest to peak exercise. Our results suggest that the aggravation of wall motion abnormalities in the infarct area may be the major cause of exercise-induced ST-segment elevation in patients with myocardial infarction.

In prior studies, patients with exercise-induced ST-segment elevation in the absence of previous myocardial infarction varied with regard to the severity of coronary artery

disease, since they included patients with resting angina due to coronary artery spasm. We studied patients with predominantly exertional angina, and found that exercise-induced ST-segment elevation frequently occurred in patients with 99% narrowing. About one-third of the patients with exercise-induced ST-segment elevation showed ST-segment depression before ST-segment elevation during exercise. Furthermore, none of the patients with good collaterals had exercise-induced ST-segment elevation. In a previous study using exercise-stress tomographic ^{201}Tl imaging in patients with both complete occlusion in the right coronary artery or the left circumflex coronary artery and 90% narrowing in the left anterior descending coronary artery, we concluded that the perfusion reserve of collateral circulation is equal to or less than 90% narrowing!¹⁵ Gordon et al¹⁶ studied the vasomotion of epicardial coronary arteries during exercise. Exercise induced constriction in all atherosclerotic segments of coronary arteries (a change of $23 \pm 4\%$). The results of the present study suggest that in most patients with 99% narrowing, the diseased vessel may be completely occluded during exercise, and that good collaterals may prevent myocardial ischemia that shows ST-segment elevation.

Gallik et al¹⁷ studied 12 patients who underwent exercise-stress tomographic ^{201}Tl myocardial imaging and showed exercise-induced ST-segment elevation in the absence of previous myocardial infarction. They demonstrated that exercise-induced ST-segment elevation indicates extensive and reversible hypoperfusion. A decrease in both the initial uptake of ^{201}Tl during exercise and its washout is regarded as a marker for myocardial ischemia!^{18,19} However, there has been no comparison of the initial uptake and washout between patients with and without exercise-induced ST-segment elevation. We found that both the initial percent uptake of ^{201}Tl and its washout rate in the territory of the diseased vessel were lower in patients with ST-segment elevation than in those with ST-segment depression or angina in the absence of ST-segment elevation. The washout rate of ^{201}Tl is affected by the heart rate at peak exercise. In our study, there was no significant difference in the heart rate at peak exercise between patient groups with

and without ST-segment elevation. Our results suggest that exercise-induced ST-segment elevation in the absence of previous myocardial infarction indicates severe myocardial ischemia. In addition, patients with ST-segment elevation showed a negative washout rate for ^{201}Tl . These patients received ^{201}Tl at peak exercise when the diseased vessel might be occluded. This negative washout rate can be attributed to both delayed accumulation of ^{201}Tl in the ischemic region and washout of ^{201}Tl in the non-ischemic region.

Yasue et al²⁰ evaluated the effects of anti-anginal drugs using treadmill exercise testing in patients with one-vessel disease, excluding those with luminal narrowing of 99% or more (n=47). Their study group included a high incidence of patients with both exertional and resting angina and those with exercise-induced ST-segment elevation. Diltiazem and nifedipine suppressed the attacks in 83% and 82% of these patients, respectively, whereas propranolol did not suppress the attacks in 87% of the patients. They concluded that anginal attacks are usually not caused by increased myocardial oxygen demand, but rather by dynamic coronary obstruction or a combination of both in most patients with one-vessel disease. On the other hand, in our study, coronary artery dilators did not suppress exercise-induced ST-segment elevation in patients who had predominantly exertional angina and 99% narrowing with poor collaterals. It may be difficult to prevent the exercise-induced occlusion of diseased vessels with 99% narrowing.

In this study, none of the patients with myocardial infarction had significant exercise-induced ST-segment depression or U-wave inversion. On the other hand, more than half of the patients with exercise-induced ST-segment elevation in the absence of previous myocardial infarction had significant exercise-induced ST-segment depression or U-wave inversion. There was no significant difference in the amplitude of exercise-induced ST-segment elevation between the two groups. These findings suggest that in patients with anterior myocardial infarction or left anterior descending coronary artery disease, exercise-induced ST-segment depression in limb or left-side chest leads

(which is reciprocal to ST-segment elevation in right-side chest leads) and U-wave inversion may be due to myocardial ischemia rather than to the aggravation of wall motion abnormalities.

This study was performed retrospectively. Another limitation is that ^{201}Tl myocardial imaging and radionuclide ventriculography were not performed in all patients. Future prospective studies with large patient populations are needed.

In conclusion, in patients with myocardial infarction, exercise-induced ST-segment elevation occurs independently of clinical evidence of myocardial ischemia and may be due to aggravation of wall motion abnormalities. In patients with predominantly exertional angina in the absence of previous myocardial infarction, exercise-induced ST-segment elevation, especially when it can not be suppressed by coronary artery dilators, may be a marker for 99% narrowing with poor collaterals and severe myocardial ischemia.

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