Clinical Significance of Stress-induced ST Segment Elevation in Patients with Previous Anterior Myocardial Infarction

Analysis of Lactate Metabolism with Atrial Pacing

Kohji HIYAMUTA, M.D.

SUMMARY

To clarify the mechanism of stress-induced ST segment elevation in patients with previous anterior myocardial infarction, we examined myocardial lactate metabolism during atrial pacing in 32 patients with previous anterior myocardial infarction (MI group) and 11 control subjects (control group). In the MI group, atrial pacing resulted in new or additional ST segment elevation in leads with Q waves in 15 patients (ST elevation group), ST segment depression in 7 (ST depression group), but induced no appreciable ST segment changes in the remaining 10 patients (ST unchanged group). In all patients, the ST segment changes were identical to the results of exercise stress testing which was carried out prior to the atrial pacing. Lactate extraction ratio increased moderately during the atrial pacing in the control group ($p < 0.01$). Although marked reduction of the myocardial lactate extraction ratio was noted in the ST depression group ($p < 0.05$), no significant change in the ratio was evoked in the ST elevation group or the ST unchanged group during atrial pacing. Left ventricular end-diastolic pressure (LVEDP) increased markedly in the ST depression group during atrial pacing, but the elevation was less evident in the other groups. The ST elevation group demonstrated the lowest left ventricular ejection fraction and the severest degree of left ventricular asynergy. Thus, the present study indicates that aggravated left ventricular asynergy in the infarcted area and associated left ventricular dysfunction, rather than peri-infarction zone ischemia is a possible mechanism of stress-induced ST segment elevation in leads with Q waves following previous anterior myocardial infarction.

Additional Indexing Words:

Stress-induced ST segment elevation	Previous anterior myocardial infarction
Atrial pacing stress test	Lactate extraction ratio
Left ventricular asynergy	Peri-infarction zone ischemia

From the Third Department of Internal Medicine, Kurume University School of Medicine, Kurume.

Address for reprint: Kohji Hiyamuta, M.D., Third Department of Internal Medicine, Kurume University School of Medicine, 67 Asahi-machi, Kurume 830, Japan.

Received for publication January 26, 1988.

Accepted March 14, 1988.

PATIENTS with previous anterior myocardial infarction (MI) often show persistent ST segment elevation in precordial leads with Q waves. The sign is generally considered to be a specific indicator of left ventricular asynergy, but unlikely to indicate residual myocardial ischemia.¹⁾ Exercise stress also induces new or additional ST segment elevation in leads with Q waves in patients with previous anterior MI. Many investigators state that the aggravation of the mechanical wall motion abnormalities of the left ventricle during exercise accounts for the exercise-induced ST segment elevation in leads with Q waves,²⁾⁻⁹⁾ but several reports still suggest that myocardial ischemia is the cause for this phenomenon.¹⁰⁾⁻¹³⁾ Thus, the exact mechanism of the exercise-induced ST segment elevation in leads with Q waves is still controversial.

In the present study, therefore, we investigated myocardial lactate metabolism during atrial pacing stress testing and attempted to elucidate the role of myocardial ischemia in exercise-induced ST segment elevation in leads with Q waves in patients with previous anterior MI.

METHODS

Patient population: The study population consisted of 32 consecutive patients with previous anterior MI, 30 men and 2 women, aged from 33 to 67 years (mean 56 years). The control group included 11 subjects, 7 men and 4 women, aged from 42 to 65 years (mean 51 years), who were referred for the evaluation of chest pain and who showed no abnormalities in intracardiac pressures, coronary arteriograms and left ventriculograms. The diagnosis of previous anterior MI was confirmed by reviewing medical records for a history of typical chest pain, serial electrocardiographic changes and enzymatic changes.

Exercise stress test: Prior to the cardiac catheterization, all study patients underwent symptom-limited maximal exercise stress testing on a treadmill or bicycle ergometer. End points were additional ST segment elevation ≥ 2 mm or ST segment depression ≥ 2 mm, blood pressure fall of 10 mmHg or more, frequent ventricular arrhythmias, progressive chest pain, dyspnea, intolerable leg fatigue or target heart rate. The time interval between the exercise stress test and the cardiac catheterization was within 6 days on average.

Atrial pacing protocol: The cardiac catheterization was performed at 114 days, on average (ranging from 38 to 234 days) after the onset of MI. All medications were discontinued at least 12 hours before the catheterization. Under local anesthesia, the brachial artery and vein were isolated in the right antecubital fossa. After routine right and left heart catheterization, a No. 6

NIH catheter was introduced into the coronary sinus for blood sampling. The catheter was positioned in the great cardiac vein close to its junction with the anterior interventricular vein. A No. 6 pacing catheter was advanced into the right atrium. A No. 8 Sones' catheter or microtip pressure transducer (Millar's mikro-tip®) was introduced into the left ventricle.

Atrial pacing was initiated at a rate of 90 beats per minute and was increased by 20 beats per minute every 3 min until the pacing rate of 150 beats per minute was attained, unless (1) the patient complained of intolerable chest pain and/or revealed more than 1 mm of additional ST segment deviation or (2) second degree atrioventricular block impeded achieving the optimal pacing rate. Electrocardiograms in leads I, II, III, V₁, V₃ and V₅ were recorded before, during and after the cessation of the pacing. Left ventricular peak systolic pressure (LVSP) and left ventricular end-diastolic pressure (LVEDP) were measured simultaneously. Post-pacing LVEDP was determined by averaging 10 successive beats immediately after the termination of the pacing. Post-pacing ST segment changes were measured on the 10th beat after the cessation of pacing to avoid the influence of pacing-induced tachycardia. The degree of ST segment depression was determined at a point 0.08 sec after the J point and that of ST segment elevation was measured at a point 0.06 sec after the bottom of the Q wave in the lead in which it was most prominent. More than 1 mm of new or additional ST segment deviation was taken as significant. Blood samples were withdrawn simultaneously from the great cardiac vein and left ventricle for determination of the lactate level at each stage.

Lactate analysis: Lactate level was measured in whole blood by the electrochemical and enzymatic method using a Lactate Analyzer 640® (Kontron-Roche).^{14),15)} The determination of the lactate level was performed in duplicate. The coefficient of variance of the method in whole blood samples was 5.4% in our laboratory.

The myocardial lactate extraction ratio was calculated by the following formula;

$$R = (A - V) / A \times 100 (\%)$$

where R is the myocardial lactate extraction ratio, A is the lactate level in the left ventricle and V is the lactate level in the great cardiac vein.

Coronary arteriography and left ventriculography: After completion of the metabolic and hemodynamic studies, selective coronary arteriography was carried out in multiple view using Sones' technique. Intraluminal narrowing of more than 75% according to the criteria of the American Heart Association¹⁶⁾ was considered to be significant. The left ventriculograms were obtained in the right anterior oblique and left anterior oblique views. End-systolic vol-

Fig. 1. Method of evaluating % regional area change (floating axis method).

ume index (ESVI), end-diastolic volume index (EDVI), stroke index (SI) and left ventricular ejection fraction (LVEF) were measured according to the method of Kennedy,¹⁷⁾ using the correction equation; Volume (true) = $0.81 \times \text{Volume (measured)} + 1.9 \text{ (ml)}$. To assess the size of the infarcted area, percent abnormally contracting area (ACA) was calculated as a percentage of the akinetic length for the total end-diastolic circumference of the left ventricle in the right anterior oblique view.¹⁸⁾ Percent regional area change was determined by the floating axis method¹⁹⁾ dividing the left ventricle into 18 segments excluding the aortic and mitral valve areas (Fig. 1). The number of segments which showed lower regional area change below -1.7 standard deviations was calculated as the number of asynergies (No. of AS), and the integration of the degree of asynergy was scored as the asynergy score (AS score). LVEF, ACA, No. of AS and AS score were independently calculated by 3 cardiologists and the average values were used in the further analyses. Informed consent was obtained from all subjects before the procedure.

Statistical analysis: All values are expressed as mean $\pm$ standard deviation. Unpaired Student's *t*-test or Chi-square test was employed for comparison between groups, and paired *t*-test for comparison of values at rest and peak pacing or exercise, respectively. A *p* value of less than 0.05 was considered to be statistically significant.

RESULTS

The control group manifested no significant ST segment shifts during the atrial pacing. According to the electrocardiographic responses to the atrial pacing, 32 patients with previous anterior MI were divided into 3 groups. (1) Fifteen patients developed new or additional ST segment elevation ≥ 1.0 mm in leads with Q waves (ST elevation group; Fig. 2). (2) Ten

Fig. 2. A patient in the ST elevation group. He revealed additional ST segment elevation of 2.5 mm in V_6 with pacing. LVEDP rose from 26 mmHg (at rest) to 29 mmHg (with pacing). Lactate extraction ratio did not change significantly (10.1% at rest, 11.3% at peak pacing).

Fig. 3. A patient in the ST unchanged group. He is 1 of the 3 exceptional patients showing lactate production with pacing. The ST segment did not shift significantly, but the peaking of T waves was noted with pacing. LVEDP rose from 13 mmHg to 21 mmHg. He complained of chest discomfort at peak pacing. Lactate extraction ratio fell to a negative value (from 10.3% at rest to -2.9% at peak pacing).

Fig. 4. A patient in the ST depression group. He is a patient with a nontransmural anterior myocardial infarction (inverted T waves in V_2 - V_4). He manifested chest pain and ST segment depression in V_3 at a rate of 130 beats/min. LVEDP rose from 13 mmHg to 21 mmHg. Lactate extraction ratio fell from 27.3% at rest to -56.7% at peak pacing.

patients showed no appreciable ST segment deviation (ST unchanged group; Fig. 3). (3) The remaining 7 patients revealed ST segment depression ≥ 1.0 mm in precordial leads (ST depression group; Fig. 4). In all patients, the ST segment changes were identical to the results of exercise stress testing which was carried out prior to the atrial pacing.

Pacing-induced metabolic changes: In the control group, the majority of patients showed a moderate increase in the lactate extraction ratio at peak pacing (from 18.0% to 23.3%; $p < 0.01$) (Fig. 5 and Table I). In the ST elevation group, the lactate extraction ratio did not change significantly, except in 1 patient who showed lactate production at peak pacing. The exceptional patient had one vessel disease of the left anterior descending artery without any collaterals and developed 2 mm of additional ST segment elevation with mild chest discomfort during the pacing. However, the other 14 patients in the ST elevation group showed neither lactate production nor cardiac symptoms. In the ST unchanged group, the lactate extraction ratio did not change significantly although 3 patients showed lactate production at peak pacing associated with anginal symptoms. Two of these patients demonstrated peaking of T waves in precordial leads. In the ST depression group, 3 patients had already shown lactate production at rest. All patients in this group developed appreciable reduction in lactate extraction at peak pacing (from 8.4% to -21.7%; $p < 0.05$) and 5 of them demonstrated lactate production at peak pacing. Six patients in this group complained of anginal

Fig. 5. The control group (C) showed an increase in lactate extraction ratio ($p < 0.01$). In the ST elevation group ($ST\uparrow$), the lactate extraction ratio did not change significantly except in 1 patient. In the ST unchanged group ($ST\rightarrow$), the lactate extraction ratio did not change significantly, although 3 of 10 patients showed lactate production and some of them revealed the peaking in the T waves with pacing. In the ST depression group ($ST\downarrow$), a marked reduction in the lactate extraction ratio was noted ($p < 0.05$). * $p < 0.05$, ** $p < 0.01$, NS = not significant.

Table I. Pacing-induced Metabolic Changes

	control group (n = 11)	ST elevation group (n = 15)	ST unchanged group (n = 10)	ST depression group (n = 7)
Lactate at rest				
Left ventricle (mmol/L)	0.76 ± 0.24	0.77 ± 0.30	0.63 ± 0.20	0.61 ± 0.29
Great cardiac vein (mmol/L)	0.63 ± 0.25	0.63 ± 0.21	0.56 ± 0.19	0.55 ± 0.24
Extraction ratio (%)	18.0 ± 14.3	16.6 ± 12.5	12.6 ± 8.6	8.4 ± 25.2
Lactate at peak pacing				
Left ventricle (mmol/L)	0.78 ± 0.21	0.77 ± 0.28	0.61 ± 0.16	0.64 ± 0.32
Great cardiac vein (mmol/L)	0.61 ± 0.24	0.65 ± 0.20	0.57 ± 0.17	$0.72 \pm 0.21^{**}$
Extraction ratio (%)	$23.3 \pm 15.7^{**}$	13.9 ± 11.3	6.9 ± 8.9	$-21.7 \pm 28.5^{*}$

* $p < 0.05$ versus at rest, ** $p < 0.01$ versus at rest.

chest discomfort during the atrial pacing.

Pacing-induced hemodynamic changes: Among the 3 groups with MI, heart rate (HR), LVSP and rate pressure product (RPP) at both the resting state and peak pacing state did not differ (Table II). LVEDP at rest was highest in the ST elevation group. In each group, it increased significantly from the resting state to immediately after the termination of pacing, but the degree of elevation was greatest in the ST depression group.

Left ventricular volumes and asynergy: ESVI and EDVI were the largest,

Table II. Pacing-induced Hemodynamic Changes

	control group	ST elevation group	ST unchanged group	ST depression group
HR (beats/min)				
at rest	74.7±15.9	76.1±13.3	71.0±13.1	62.7±7.8*
at peak pacing	133.8±19.9	138.0±12.6	137.0±17.0	130.0±16.3
LVSP (mmHg)				
at rest	135.4±21.1	133.1±18.8	139.0±7.0	131.9±19.9
at peak pacing	123.8±9.7	123.7±16.6	128.4±7.5	137.6±21.7
RPP (×1000)				
at rest	10.3±2.6	10.2±2.3	9.9±1.9	8.4±2.0
at peak pacing	16.5±2.7	17.1±3.1	17.6±2.1	17.6±1.8
LVEDP (mmHg)				
at rest	9.3±4.3	17.9±5.8**	14.1±3.1*	13.0±4.9
just after pacing	13.7±4.8	21.8±7.4**	18.2±3.3*	23.9±7.6**
ΔLVEDP (mmHg)	4.5±2.7	3.9±2.6	4.1±3.1	10.9±4.3**

HR=heart rate; LVSP=left ventricular systolic pressure; LVEDP=left ventricular end-diastolic pressure; RPP=rate-pressure product (LVSP×HR).

ΔLVEDP=LVEDP (just after pacing)–LVEDP (at rest).

* p<0.05 versus control group, ** p<0.01 versus control group.

Table III. Left Ventricular Volumes and Asynergy

	control group	ST elevation group	ST unchanged group	ST depression group
ESVI (ml/m ²)	24.6±9.0***	82.8±46.8	37.2±14.4**	38.7±24.6*
EDVI (ml/m ²)	91.1±17.3***	123.8±43.5	88.6±16.8**	97.6±34.0
SI (ml/m ²)	66.1±12.8***	41.0±8.1	49.5±10.5*	58.9±14.1**
LVEF	0.73±0.07***	0.37±0.14	0.58±0.10**	0.63±0.12**
ACA (%)	—	34.4±10.5	6.7±6.9**	4.2±9.1**
No. of AS	—	14.3±4.3	6.7±3.5**	5.7±4.5**
AS score	—	−16.1±25.6	−7.8±7.7*	−8.1±7.0*

ESVI=end-systolic volume index; EDVI=end-diastolic volume index; SI=stroke index; LVEF=left ventricular ejection fraction; ACA=abnormally contracting area; No. of AS=number of asynergy; AS score=asynergy score.

* p<0.05 versus ST elevation group, ** p<0.01 versus ST elevation group, *** p<0.001 versus ST elevation group.

and SI was the smallest in the ST elevation group (Table III). Consequently, LVEF was significantly lower in the ST elevation group than in the other groups with MI (p<0.01). The ST elevation group also showed higher values of ACA (both p<0.01) and No. of AS (both p<0.01), and a lower AS score (both p<0.05) as compared with the ST unchanged group and the ST depression group.

Table IV. Clinical Characteristics

	control group	ST elevation group	ST unchanged group	ST depression group
Age (years)	51.1±7.5	55.7±9.0	54.4±7.7	60.9±4.8
Sex (M/F)	6/5	15/0	9/1	6/1
Resting electrocardiogram				
No. of Q waves	—	4.0±1.3	1.7±1.6**	0.9±1.9**
Coronary arteriogram				
No. of diseased vessels	—	1.7±0.8	1.6±0.9	2.0±0.8
Pts. with collateral vessels				
well-developed	—	1	0	5
poorly-developed	—	4	1	0
none	—	9	9	2

** p<0.01 versus ST elevation group.

Table V. Exercise Stress Data

	ST elevation group	ST unchanged group	ST depression group
Values at rest			
HR (beats/min)	77.1±11.3	78.5±19.0	67.4±7.2
SBP (mmHg)	131.1±22.1	130.2±15.6	125.1±6.8
RPP (×1000)	10.1±2.5	9.8±2.2	8.4±0.9
Values at peak exercise			
HR (beats/min)	126.7±17.6	135.1±18.4	114.0±23.8
SBP (mmHg)	163.7±25.5	181.4±24.1	162.3±11.7
RPP (×1000)	20.9±4.7	24.4±4.2	18.6±4.7**
Mets	5.2±1.1	6.6±1.9*	6.1±0.9

HR=heart rate (beats/min); SBP=systolic blood pressure; RPP=rate pressure product (SBP × heart rate); Mets=metabolic equivalents.

* p<0.05 versus ST elevation group, ** p<0.01 versus ST unchanged group.

Clinical characteristics: In the resting electrocardiogram, the number of abnormal Q waves in the precordial leads was 4.0 ± 1.3 in the ST elevation group which was significantly greater than those of the ST unchanged group (1.7 ± 1.6 ; $p < 0.01$) and the ST depression group (0.9 ± 1.9 ; $p < 0.01$), respectively (Table IV). Four of 7 patients in the ST depression group had non-transmural anterior MI. All patients with MI had significant narrowing of the proximal portion of the left anterior descending artery. Average value of the number of diseased vessels was 1.7 ± 0.8 in the ST elevation group, 1.6 ± 0.9 in the ST unchanged group and 2.0 ± 0.8 in the ST depression group, respectively (not significant). The distal portion of the left anterior descending artery had well-developed collateral vessels only in 1 patient in the ST

elevation group and none in the ST unchanged group, while 5 of 7 patients in the ST depression group had well-developed collaterals. On exercise stress testing, HR, systolic blood pressure (SBP) and RPP at rest were not different among the 3 groups with MI (Table V). At peak exercise, the ST depression group showed lower HR, SBP and RPP than did the other groups. Exercise capacity was 6.6 ± 1.9 Mets in the ST unchanged group, 6.1 ± 0.9 Mets in the ST depression group and 5.2 ± 1.1 Mets in the ST elevation group. Chest pain developed during exercise in 4 of 7 patients in the ST depression group, but in none in the other groups.

DISCUSSION

Possible mechanism of stress-induced ST segment elevation

In the present study, we attempted to determine the relation between peri-infarction zone ischemia and stress-induced ST segment elevation in leads with Q waves in patients with previous MI. We then analyzed myocardial lactate metabolism during atrial pacing by collecting blood samples from the great cardiac vein and by selecting patients with previous anterior MI.

In 7 patients manifesting ST segment depression during atrial pacing, 5 developed lactate production associated with a marked elevation of LVEDP and well-developed collaterals to the left anterior descending artery on coronary angiogram. These patients showed smaller infarct size on the left ventriculogram and 4 of them were diagnosed as nontransmural MI. These patients, hence, could be considered to have salvaged and viable myocardium in the peri-infarction zone, which is susceptible to the development of ischemia during stress. Therefore, the mechanism of ST segment depression in these patients would be the development of peri-infarction zone ischemia. The 2 patients who did not show lactate production despite ST segment depression had significant narrowing in the left circumflex coronary artery in addition to the left anterior descending artery. Myocardial ischemia remote from the infarcted area might have possibly induced ST segment depression in these patients, although we collected samples only from the great cardiac vein and could not determine the lactate level in the blood drained from the circumflex-perfused area in the present study.

In 10 patients who did not present any significant ST segment change, 7 patients did not develop significant changes in lactate metabolism during the atrial pacing. The majority of these patients had larger infarct sizes with poorly or nondeveloped collaterals to the infarction-related artery and had no significant narrowing in other major branches of the coronary arteries. The other 3 patients who produced lactate during atrial pacing but no ST

segment deviation developed anginal pain, and in 2 of these 3 patients it was associated with peaking of the T wave. These observations were coincident with the previous reports that ST segment depression or peaking of the T wave might be a sign of myocardial ischemia.^{20),21)}

On the other hand, no lactate production was observed in 14 of 15 patients who manifested ST segment elevation in leads with Q waves. LVEDP which showed the highest value at rest increased significantly after pacing. However, the degree of the increase was significantly smaller than that in the ST depression group and was comparable with those in the control and ST unchanged groups. The larger infarct sizes and no or poorly developed collaterals might indicate negligible or no salvaged viable myocardium in the peri-infarction zone in these patients. These findings imply that myocardial ischemia in the peri-infarction zone is unlikely to be the primary cause of ST segment elevation in leads with Q waves in patients with old MI. The present result was therefore contrary to several previous observations,¹⁰⁾⁻¹³⁾ which suggested that peri-infarction zone ischemia might be involved in exercise-induced ST segment elevation in leads with Q waves. However, in the study by Dunn et al,¹⁰⁾ 48% of the patients with ST segment elevation during exercise never showed reversible perfusion defects on exercise thallium-201 myocardial scanning, and in the report by Fox,¹³⁾ 42% of the patients with exercise-induced ST segment elevation failed to have abolition of the ST change after coronary bypass surgery. Therefore, it is plausible that myocardial ischemia is not sufficient by itself to cause ST segment elevation in patients with previous MI.

In the present study, only one patient in the ST elevation group developed lactate production during atrial pacing. Although there remains a possibility that some of the remaining patients could show lactate production during more strenuous stress such as exercise, it is of note that these patients developed apparent ST segment elevation without any evidence of metabolic signs of myocardial ischemia. The present study, thus, clearly indicates that ST segment elevation could occur in the absence of any evidence of peri-infarction zone ischemia, while the sign might be observed incidentally with myocardial ischemia.

An alternative explanation for this electrocardiographic sign proposed in previous studies²⁾⁻⁹⁾ is that stress-induced ST segment elevation may be related to abnormal left ventricular wall motion, including left ventricular aneurysm. It is well known that body surface potentials are increased by expansion of left ventricular volume (Brody effect).^{22),23)} Lab²⁴⁾ demonstrated that mechanical stress or strain affects the repolarization phase of the action potential. Thus, it is plausible that a stress-induced increase in left ventric-

ular volumes could produce ST segment elevation. In the present study, patients with pacing-induced ST segment elevation presented larger asynergy scores and the number of asynergies, lower left ventricular ejection fraction and higher LVEDP. The present observation is thus compatible with previous reports that patients with stress-induced ST segment elevation have larger infarct sizes and more advanced left ventricular dysfunction. Although we could not determine left ventricular volumes during atrial pacing, Bekki²⁵⁾ reported a greater increase in end-systolic volume in patients with exercise-induced ST segment elevation as compared with those without ST segment elevation. Thus, the patients with larger infarct sizes and more advanced left ventricular dysfunction are more likely to develop further increases in left ventricular volumes during exercise or pacing stress and to produce ST segment elevation in leads with Q waves. However, further studies are required to confirm the hypothesis.

Technical considerations

We analyzed myocardial lactate metabolism during atrial pacing to evaluate myocardial metabolism in patients with previous MI. The reason we employed atrial pacing testing was that exercise induces increased metabolic changes in general skeletal muscle, especially in the lower limbs, and the release of lactate from this musculature leads to a rise in arterial lactate level, which often compromises the evaluation of myocardial lactate metabolism.^{26),27)} However, we recognize that atrial pacing testing and exercise testing are different from each other in several aspects. Therefore, in the present study, we selected those patients who showed the same pattern of ST segment deviation during exercise and atrial pacing, so the ST segment deviations during atrial pacing could be considered to have been evoked by mechanisms similar to those during exercise.

Various metabolic markers of myocardial ischemia have been proposed, including lactate extraction, pH,^{28),35)} phosphate,^{29),35)} potassium ions,^{28),29),33)} lactate/pyruvate ratio^{29),31),35)} and beta-hydroxybutyrate/acetoacetate ratio.^{30),35)} However, there was no significant difference in diagnostic value of myocardial ischemia among lactate extraction ratio, coronary venous lactate/pyruvate ratio or excess lactate.³¹⁾ Thus, the lactate extraction ratio has been most widely employed as a metabolic indicator of myocardial ischemia in clinical studies,^{32),34),36)–38)} and we used the technique in the present study. Cohen et al³⁸⁾ who first applied the myocardial lactate extraction ratio in assessing myocardial metabolism in coronary artery disease, proposed that a ratio of less than 10% was a sign of myocardial ischemia, there has been no consistent agreement concerning the

ratio below which abnormal lactate metabolism is indicated. Gertz³⁹⁾ recently investigated the correlation of myocardial lactate extraction with other metabolic parameters (glucose and free fatty acids) and hemodynamic changes, and pointed out that a lactate extraction ratio of less than 10% might not be an indicator of abnormal physiology which depended on other metabolic parameters. He then concluded that only overt production of lactate should be used as a marker of myocardial ischemia. We therefore used a negative lactate extraction ratio as evidence of myocardial ischemia in the present study.

As we did not measure coronary blood flow, the net lactate release from myocardium could not be determined in the present study. Although net lactate release could indicate the severity and amount of ischemic myocardium, no significant difference in sensitivity in detecting myocardial ischemia in coronary artery disease was demonstrated between lactate extraction and the measurement of net lactate release.³¹⁾

Clinical implications

Since we selected those patients with previous anterior MI who showed identical ST segment deviations during exercise and atrial pacing stress, the results of myocardial lactate metabolism during atrial pacing could be applied to explain the mechanism of these electrocardiographic signs during exercise. Thus, the study indicates that the exercise-induced ST segment elevation may be the manifestation of deterioration of left ventricular asynergy or dysfunction rather than peri-infarction zone ischemia.

We can apply the results first to the treatment of patients with previous anterior MI. Those patients with exercise-induced ST segment elevation in leads with O waves should be carefully examined for whether or not they have left ventricular dysfunction. Medications for treating left ventricular dysfunction, such as diuretics and vasodilators, could be the first choice of therapy for these patients, while negative inotropic agents like beta-blockers or calcium antagonists should be administered with caution. Secondly, the exercise stress tests give us important clues in predicting long term prognosis after MI that has been said to be related to the severity of the impairment of left ventricular function in addition to the number of diseased coronary arteries. In this study, patients with exercise-induced ST segment elevation showed severely impaired left ventricular function, so they should be closely followed up for the development of congestive heart failure even if they did not exhibit it at the time of discharge.

On the other hand, relief of residual myocardial ischemia by aorto-coronary bypass surgery or coronary angioplasty should be the primary modality

of therapy for patients with exercise-induced ST segment depression. Absence of these electrocardiographic changes may suggest no serious complications and possibly a favorable prognosis after myocardial infarction.

CONCLUSION

Stress-induced ST segment elevation in previous anterior myocardial infarction indicates an extensive area of infarction and severe left ventricular dysfunction. Although myocardial ischemia in the peri-infarction zone may be accompanied by this phenomenon, it does not play a main role and the aggravated left ventricular asynergy in the infarcted area and associated left ventricular dysfunction are the primary causes of the stress-induced ST segment elevation in patients with previous myocardial infarction.

REFERENCES

1. Gewirtz H, Horacek BM, Wolf HK, Rautaharju PM, Smith ER: Mechanism of persistent S-T segment elevation after anterior myocardial infarction. *Am J Cardiol* **44**: 1269, 1979
2. Gewirtz H, Sullivan M, O'Reilly G, Winter S, Most AS: Role of myocardial ischemia in the genesis of stress-induced S-T segment elevation in previous anterior myocardial infarction. *Am J Cardiol* **51**: 1289, 1983
3. Gorlin R, Klein MD, Sullivan JM: Prospective correlative study of ventricular aneurysm. Mechanistic concept and clinical recognition. *Am J Med* **42**: 512, 1967
4. Manvi KN, Ellestad MH: Elevated ST segments with exercise in ventricular aneurysm. *J Electrocardiol* **5**: 317, 1972
5. Weiner DA, McCabe C, Klein MD, Ryan TJ: ST segment changes post-infarction: Predictive value for multivessel coronary disease and left ventricular aneurysm. *Circulation* **58**: 887, 1978
6. Chahine RA, Raizner AE, Ishimori T: The clinical significance of exercise-induced ST-segment elevation. *Circulation* **54**: 209, 1976
7. Lahari A, Raftery EB, Wilkins R, Craig MM: Correlation of coronary angiography, left ventricular angiography and graded treadmill exercise testing in the diagnosis of left ventricular aneurysm. *Ann Radiol* **22**: 261, 1979
8. Waters DD, Chaitman BR, Bourassa MG, Tubau JF: Clinical and angiographic correlates of exercise-induced ST-segment elevation. Increased detection with multiple ECG leads. *Circulation* **61**: 286, 1980
9. Paine TD, Dye LE, Roitman DI, Sheffield LT, Rackley CE, Russel RO, Rogers WJ: Relation of graded exercise test findings after myocardial infarction to extent of coronary artery disease and left ventricular dysfunction. *Am J Cardiol* **42**: 716, 1978
10. Dunn RE, Bailey IK, Uren R, Kelly DT: Exercise-induced ST-segment elevation. Correlation of thallium-201 myocardial perfusion scanning and coronary arteriography. *Circulation* **61**: 989, 1980
11. Fortuin NJ, Friesinger GC: Exercise-induced S-T segment elevation. Clinical, electrocardiographic and arteriographic studies in twelve patients. *Am J Med* **49**: 459, 1970
12. Atterhoeg JH, Ekelund JG, Kaijser L: Electrocardiographic abnormalities during exercise 3 weeks to 18 months after anterior myocardial infarction. *Br Heart J* **33**: 871, 1971
13. Fox KM, Jonathan A, Selwyn AP: Significance of exercise induced ST segment elevation in

- patients with previous myocardial infarction. *Br Heart J* **49**: 15, 1983
14. Racine P, Klenk HO, Kochsiek K: Rapid lactate determination with an electrochemical enzymatic sensor: Clinical usability and comparative measurements. *Z Klin Chem Klin Biochem* **13**: 533, 1975
15. Soutter WP, Sharp F, Clark DM: Bedside estimation of whole blood lactate. *Br J Anaesth* **50**: 445, 1978
16. Austen WG, Edwards JE, Frye RL, Gensini GG, Gott VL, Griffith LSC, McGoon DC, Murphy ML, Roe BB: AHA Committee Report: A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. *Circulation* **51**: News from AHA, 1975
17. Kennedy JW, Trenholme SE, Kasser IS: Left ventricular volume and mass from single-plane cineangiogram. A comparison of anteroposterior and right anterior oblique methods. *Am Heart J* **80**: 343, 1970
18. Feild BJ, Russell RO Jr, Dowling JT, Rackley CE: Regional left ventricular performance in the year following myocardial infarction. *Circulation* **46**: 679, 1972
19. Moynihan PF, Parisi AF, Feldman CL: Quantitative detection of regional left ventricular contraction abnormalities by two-dimensional echocardiography. I. Analysis of methods. *Circulation* **63**: 752, 1981
20. Master AM: Exercise testing for evaluation of cardiac performance. *Am J Cardiol* **30**: 718, 1972
21. Lepeschkin E, Surawicz B: Characteristics of true-positive and false-positive results of electrocardiographic Master two-step exercise tests. *New Engl J Med* **256**: 511, 1958
22. Brody DA: Theoretical analysis of intracoronary blood mass influence on the heart-lead relationship. *Circ Res* **4**: 731, 1956
23. Nelson CV, Rand RW, Angelakos ET, Hugenholtz PG: Effect of intracardiac blood on the spatial vectorcardiogram. I. Results in the dog. *Circ Res* **31**: 95, 1972
24. Lab MJ: Mechanically dependent changes in action potentials recorded from the intact frog ventricle. *Circ Res* **42**: 519, 1978
25. Bekki H: Hemodynamic evaluation of exercise-induced ST-segment depression and elevation in ischemic heart disease. Left ventricular cineangiography during exercise. *Jpn Heart J* **24**: 669, 1983
26. Bourassa MG, Campeau L, Rois MA, Rico O: Myocardial lactate metabolism at rest and during exercise in ischemic heart disease. *Am J Cardiol* **23**: 771, 1969
27. Parker JO, West RO, Case RB, Chiong MA: Temporal relationships of myocardial lactate metabolism, left ventricular function, and S-T segment depression during angina precipitated by exercise. *Circulation* **40**: 97, 1969
28. Obeid A, Smulyan H, Gilbert R, Eich RH: Regional metabolic changes in the myocardium following coronary artery ligation in dogs. *Am Heart J* **83**: 189, 1972
29. Owen P, Thomas M, Young V, Opie L: Comparison between metabolic changes in local venous and coronary sinus blood after acute experimental coronary arterial occlusion. *Am J Cardiol* **25**: 562, 1970
30. Whereat AF, Chan A: Effects of hypoxemia and acute coronary occlusion on myocardial metabolism in dogs. *Am J Physiol* **223**: 1398, 1972
31. Neill WA, Kremkau EL: Criteria for detecting ischemic myocardial hypoxia from lactate and pyruvate data during atrial pacing in humans. *J Lab Clin Med* **83**: 428, 1974
32. Herman MV, Elliot WC, Gorlin R: An electrocardiographic, anatomic, and metabolic study of zonal myocardial ischemia in coronary heart disease. *Circulation* **35**: 834, 1967
33. Case RB, Nasser MG, Crampton RS: Biochemical aspects of early myocardial ischemia. *Am J Cardiol* **24**: 766, 1969
34. Gorlin R: Assessment of hypoxia in the human heart. *Cardiology* **57**: 24, 1972
35. Opie LH, Owen P, Thomas M, Samson R: Coronary sinus lactate measurements in assess-

- ment of myocardial ischemia. Comparison with changes in lactate/pyruvate and beta-hydroxybutyrate/acetoacetate ratios and with release of hydrogen, phosphate and potassium ions from the heart. *Am J Cardiol* **32**: 295, 1973
36. Brachfeld N: Characterization of the ischemic process by regional metabolism. *Am J Cardiol* **37**: 467, 1976
37. Hattori R, Takatsu Y, Yui Y, Sakaguchi K, Susawa T, Murakami T, Tamaki S, Kawai C: Lactate metabolism in acute myocardial infarction and its relation to regional ventricular performance. *J Am Coll Cardiol* **5**: 1283, 1985
38. Cohen LS, Elliot WC, Klein MD, Gorlin R: Coronary heart disease. Clinical, cinearteriographic and metabolic correlations. *Am J Cardiol* **17**: 153, 1966
39. Gertz EW, Wisneski JA, Neese R, Houser A, Korte R, Bristow JD: Myocardial lactate extraction: Multi-determined metabolic function. *Circulation* **61**: 256, 1980