Exercise at ventilatory threshold aggravates left ventricular remodeling in patients with extensive anterior acute myocardial infarction

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Background The effects of physical training on ventricular remodeling after extensive anterior acute myocardial infarction (AMI) have not yet been defined. This randomized controlled study examines whether exercise aggravates left ventricular (LV) remodeling in patients with extensive anterior AMI.

Methods Forty-eight consecutive patients with a first extensive anterior AMI and an LV ejection fraction (EF) of <45% assessed with left ventriculography (LVG) within 3 days of onset were randomly allocated to a training group (n = 24) or a control group (n = 24). Exercise intensity was determined by the heart rate of each patient at ventilatory threshold (VT). Three weeks after onset, a second LVG was performed, followed by a supervised exercise program at VT for 12 weeks. The LVG was reassessed after the exercise program. We then calculated the global LV volume (end-diastolic volume index [EDVI], end-systolic volume index [ESVI]) and systolic expansion volume index (SEVI), a new parameter for measuring the infarction site expansion at the end-systolic phase.

Results Both EDVI and ESVI significantly decreased in the control group from 1 to 4 months after onset (91.2 ± 26.1 to 83.3 ± 24.0 mL/m^2, $P < .05$; 52.4 ± 22.5 to 45.7 ± 18.8mL/m^2, $P < .01$, respectively), but not in the exercise group. The SEVI also significantly decreased in the control group from 1 to 4 months (33.1 ± 16.9 to 25.7 ± 13.9 mL/m^2, $P < .05$), but not in the training group (34.2 ± 12.9 to 36.5 ± 15.5 mL/m^2, P = not significant).

Conclusion Exercise while healing in patients with extensive anterior AMI, even at the VT level, induces LV enlargement and thus might aggravate LV remodeling. Therefore, in these patients, clinicians should consider withholding exercise training for at least 8 weeks, versus the 3-week period used in this trial. (Am Heart J 2004;147:113–20.)

The left ventricle progressively enlarges in some patients with acute myocardial infarction (AMI) during the healing period, and this process is referred to as left ventricular (LV) remodeling.[1–3] The LV volume is the most powerful predictor of survival after AMI.[4] Several factors influence remodeling, such as infarction size,[5] reperfusion therapy and vessel patency,[6] anterior wall involvement, medications including angiotensin-converting enzyme (ACE) inhibitors,[7] and loading conditions.[8] However, some factors that influence the remodeling process remain undefined or controversial.

Physical training after AMI improves exercise performance, autonomic function, peripheral metabolism, and oxygen consumption.[9] Exercise programs at ventilatory threshold (VT) determined with exercise testing are considered to be beneficial and safe for patients with AMI.[10,11] However, previous reports about their effects on LV remodeling after anterior AMI with LV dysfunction have demonstrated contradictory results.[12–16] Jugdutt el al suggested that exercise training in patients with reduced LV function after AMI leads to further myocardial damage.[12] However, Giannuzzi et al reported that training did not worsen the spontaneous deterioration of LV function after anterior AMI.[13,14] Jette et al[15] and Dubach et al[16] have also reported that training has no deleterious effects on LV volume in patients with AMI. In all of these trials, LV volume and function were determined with echocardiography. However, because the LV apex is one of the least reliably visualized regions, especially in the anterior AMI, the LV volume of the anterior AMI is difficult to evaluate with 2-dimensional-echocardiography. This study examines in a randomized fashion whether exercise at VT accelerates LV remodeling in patients with extensive anterior AMI who have not yet healed com-

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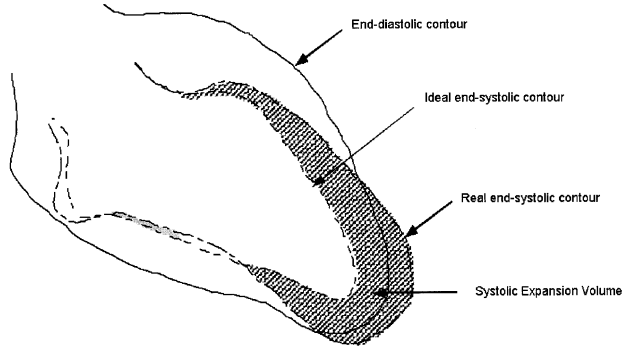
Table I. Clinical characteristics of patients in training and control groups

	Control group (n = 24)	Training group (n = 24)	P
Male	17 (71)	21 (88)	ns
Age (y)	61.8 ± 12.2	59.1 ± 11.6	ns
History			
Diabetes	8 (33)	6 (25)	ns
Hypercholesterolemia	10 (42)	11 (46)	ns
Hypertension	9 (38)	16 (67)	ns
Smoking	16 (67)	17 (71)	ns
Killip class I	15 (63)	19 (79)	ns
Peak creatine kinase (IU/L)	3992 ± 1800	3555 ± 2602	ns
Single vessel disease	19 (79)	22 (92)	ns
Reperfusion therapy success	19 (79)	17 (71)	ns
EF at 1 month (%)	45.8 ± 11.6	43.1 ± 8.4	ns
Medications			
ACE inhibitors	12 (50)	12 (50)	ns
Nitrates	22 (92)	22 (92)	ns
Calcium-channel antagonists	9 (38)	6 (25)	ns
β-Blockades	3 (13)	1 (4)	ns
Diuretics	5 (21)	9 (38)	ns

Data are expressed as means ± SD or number (%) of patients. *EF,* Ejection fraction; *ACE,* angiotensin-converting enzyme; *ns,* not significant.

Figure 1



Schema of systolic expansion volume index. 1) End-diastolic contour of right anterior oblique view was traced. 2) Ideal end-systolic contour, namely, assumed curve acquired as though systolic function was normal, and computed with reversed centerline method. 3) Ideal ESV was calculated with the Simpson rule. 4) Real ESV was also calculated with the Simpson rule. 5) SEVI was calculated as: SEVI = (Real ESV [mL] − Ideal ESV [mL])/Body surface area (m^2)

pletely. To evaluate the hypothesis that exercise at VT aggravates LV remodeling soon after extensive anterior AMI, we enrolled only patients with LV dysfunction after anterior AMI. We performed biplanar left ventriculography (LVG) on all patients, because this is the most reliable means of measuring LV volume in patients with this condition. Exercise intensity was determined according to the heart rate at VT of each patient, and the training program was supervised at our hospital.

Methods

Patients

Our single-center, randomized protocol was approved by the ethical committee of Jichi Medical School. The inclusion criteria were: 1) first extensive anterior Q wave AMI (extensive anterior AMI means anterior infarction with LV dysfunction defined as a LV ejection fraction [EF] <45% in this study); 2) LVEF <45%, assessed with LVG performed within 72 hours after onset; 3) no contraindications for physical training and no difficulty in participating in the supervised training program; and 4) repeated LVG could be obtained. The exclusion criteria were: 1) cardiogenic shock; 2) overt congestive heart failure uncontrolled by conventional therapy; 3) ongoing myocardial ischemia necessitating coronary artery bypass grafting; 4) ventricular tachyarrhythmias requiring treatment; 5) age > 80 years; and 6) chronic respiratory insufficiency, renal impairment, or other serious concomitant diseases. During the period of June 1994 through May 1996, 238 patients were admitted to our coronary care unit because of AMI, and 48 of these patients were eligible for participation in the study. All enrolled patients underwent coronary angiography (CAG) with multiple views and biplanar LVG within 72 hours after onset and, when indicated, reperfusion therapy; direct percutaneous transluminal coronary angioplasty (PTCA) was performed in all instances immediately after admission. All patients provided informed written consent to participate in the study and were randomly allocated to an exercise training or control group.

Three weeks after the onset of AMI, all study patients underwent pre-discharge assessment including: 1) repeat CAG and LVG; and 2) symptom-limited cardiopulmonary exercise testing with a bicycle ergometer in which the load was increased by a ramp system (10 watts/min), with simultaneous sampling and analysis of the expiratory gas (RM-300i by Minato, Osaka, Japan, or WSMR-1400 by Westron, Kashiwa, Japan). The VT was determined with the V-slope method.[17]

After discharge from hospital approximately 4 weeks after onset, patients in the exercise group started a training program that consisted of a supervised session of 20 minutes of bicycle ergometry or walking on a treadmill twice a day, 3 times a week, for 12 weeks. The intensity of the exercise program was determined by the heart rate of each patient at VT. During training sessions, the heart rates of the patients were monitored with continuous electrocardiography. Patients in the control group were counseled not to overexert themselves during everyday activities after discharge throughout the study period. The number of steps taken each day by all patients in both groups was recorded with a pedometer. After the 12-week training program was completed (about 4 months after onset), all study patients were readmitted and assessed with the same examinations as were applied before their discharge.

Of the 48 patients who gave consent and were eligible for the study, 2 in the control group were withdrawn from the study, because of bleeding from a duodenal ulcer in 1 and non-compliance by the other. The LVG in 2 patients in the control group could not be followed up because of non-compliance by 1 and allergy to the contrast medium in the other. Therefore, 44 patients completed the study, 24 of whom were in the training group and 20 of whom were in the control group. The clinical characteristics of the 2 groups were comparable at the baseline evaluation (Table I).

Of the 24 patients assigned to the training group, 1 patient could participate in the supervised training program for only 1 day because of his job, and another patient could participate for only 5 days because of bronchial asthma. The other 22 patients fully complied with the program, so the overall participation rate was 80% (692/864; patient × day), 2.4 days/week/patient. Data from all 24 patients in the training group were analyzed according to the intention-to-treat method. The mean number of steps taken per day was 4537 ± 1786 in the control group and 9779 ± 2354 in the training group, according to recordings on a non-training day ($P < .01$). Therefore, the control group was considered to have followed the instruction not to exceed everyday activities.

Prescription of ACE inhibitors was encouraged. Other prescriptions, including diuretics, β-blockades, nitrates, and calcium channel antagonists, were left to the discretion of the attending physicians. However, once medications had been prescribed, changes in the prescription after hospital discharge were discouraged.

Biplanar LVG

Biplanar LVG was performed in 30° right anterior oblique and 60° left anterior oblique projections at a rate of 30 frames/second per view. All biplanar ventriculograms were simultaneously acquired and recorded on cine film. Magnification and pincushion distortion were corrected with calibrated grids individualized for each image intensifier. A normal, non-post-premature sinus beat was selected, and the endocardial contours at end-diastole and end-systole were traced and entered into a Cardio 500 computer system (Kontron, Munich, Germany). End-diastolic volume (mL), end-systolic volume (mL), and EF (%) were then calculated by using the Simpson rule. Measurements were corrected for body surface area and are expressed as volume indexes (mL/m^2).

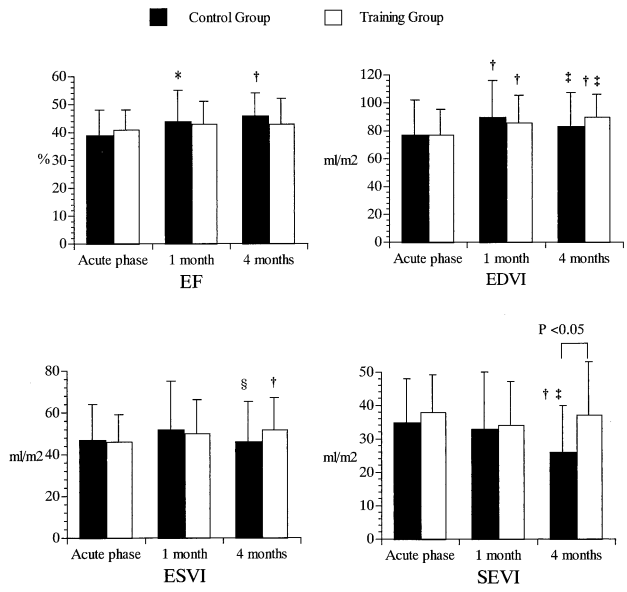
The modified centerline method described by Sheehan et al[18] quantified the regional LV function. The SD/chord and regional wall motion scores were then computed with these formulas:

SD/chord = sum of chords in hypokinetic region /region width

Regional wall motion score = region width*100/80

Systolic expansion volume (mL) is defined in this study as 1 index of infarction site expansion and is computed with the reversed centerline method (Figure 1). The procedure consisted of tracing the end-diastolic contour of the right anterior oblique view. Thereafter, we computed the ideal end-systolic contour (ie, the assumed curve acquired as though the systolic function was normal) using the reversed centerline method from the end-diastolic contour. The ideal end-systolic volume was calculated with the Simpson rule, and the real end-systolic volume was also calculated. The systolic expansion volume was defined as the difference between real end-systolic volume and ideal end-systolic volume. Because end-diastolic phase and contour is simple to identify with LVG, interobserver and intraobserver variabilities for this method in our laboratory were sufficiently small (3.5% ± 1.9% and 2.9% ± 1.5%, respectively). Values were corrected for body surface area and are expressed as the volume index (systolic expansion volume index, mL/m^2). One investigator who was blinded to the treatment group to which the patient had been assigned, analyzed all data.

Figure 2



Serial changes in EF, EDVI, ESVI, and SEVI. Both EDVI and ESVI significantly decreased from 1 to 4 months in the control group (*closed bars*) and increased in the training group (*open bars*). SEVI did not significantly or serially change in the training group, but significantly decreased in the control group. Serial changes between groups significantly differed. *$P < .05$ vs acute phase; †$P < .01$ vs acute phase; ‡$P < .05$ vs 1 month; §$P < .01$ vs 1 month.

Statistical analyses

Baseline characteristics of the 2 groups were compared with the χ^2 test for categorical variables and with the unpaired t test for continuous variables. Serial changes within each group in quantitative ventriculographic variables were analyzed with the paired t test. Differences in serial changes between the 2 groups were assessed with multivariate repeated measures analysis of variance. Values are expressed as means plus or minus SD, and differences were considered significant when a 2-tailed test resulted in a P value $< .05$. The term "acute phase" represents the period within 72 hours from onset (12.2 ± 10.3 hours from onset); "1 month" represents the period before discharge (28 ± 5 days from

Table II. Serial changes in left ventricular volume and function in training and control groups

		Control group (n = 20)	Training group (n = 24)	*P* (ANOVA)
EF (%)	Acute phase	39 ± 9	41 ± 7	ns
	1 Month	44 ± 11*	43 ± 8	
	4 Months	46 ± 8†	43 ± 9	
EDVI (mL/m^2)	Acute phase	77 ± 25	77 ± 18	<.05
	1 Month	90 ± 26†	86 ± 19†	
	4 Months	83 ± 24‡	90 ± 16†‡	
ESVI (mL/m^2)	Acute phase	47 ± 17	46 ± 13	<.01
	1 Month	52 ± 23	50 ± 16	
	4 Months	46 ± 19§	52 ± 15†	
SEVI (mL/m^2)	Acute phase	35 ± 13	38 ± 11	<.05
	1 Month	33 ± 17	34 ± 13	
	4 Months	26 ± 14†‡‖	37 ± 16‖	

Data are expressed as means ± SD of patients. *P* values were assessed by repeated measures analysis of variance (ANOVA). *EDVI,* End-diastolic volume index; *ESVI,* end-systolic volume index; *SEVI,* systolic expansion volume index.
*$P < .05$ vs acute phase.
†$P < .01$ vs acute phase.
‡$P < .05$ vs 1 month.
§$P < .01$ vs 1 month.
‖$P < 0.05$ between 2 groups.

Table III. Serial changes in regional left ventricular function in training and control groups

		Control group (n = 20)	Training group (n = 24)	*P* (ANOVA)
SD/chord	Acute phase	3.6 ± 0.6	3.7 ± 0.6	ns
	1 Month	3.3 ± 0.5†	3.1 ± 0.8†	
	4 Months	3.0 ± 1.0‡	3.0 ± 0.8†	
RWM score	Acute phase	64 ± 14	64 ± 14	ns
	1 Month	61 ± 22	53 ± 23*	
	4 Months	46 ± 27†§	49 ± 22†	

Data are expressed as means ± SD of patients. *P* values were assessed by repeated measures analysis of variance (ANOVA). *RWM,* Regional wall motion.
*$P < .05$ vs acute phase.
†$P < .01$ vs acute phase.
‡$P < .05$ vs 1 month.
§$P < .01$ vs 1 month.

onset), and "4 months" represents the period 12 weeks after discharge (115 ± 10 days from onset).

Results

LV volume and regional function

Serial changes in EF, end-diastolic volume index (EDVI), end-systolic volume index (ESVI), and systolic expansion volume index (SEVI) are shown in Figure 2 and Table II. The EDVI significantly increased from the acute phase to 1 month in both groups ($P < .01$), but significantly decreased from 1 to 4 months in the control group and significantly increased in the training group. Serial changes between the 2 groups differed significantly ($P < .05$). The ESVI significantly decreased from 1 to 4 months in the control group and increased by 5% in the training group. These serial changes between the groups differed significantly ($P < .01$). EF significantly increased from the acute phase to 1 month ($P < .05$) and from the acute phase to 4 months ($P < .01$) in the control group, but did not serially change significantly in the training group. However, the differences between the groups were not significant. The SEVI did not change significantly and serially in the training group, although it decreased significantly in the control group. Serial changes between the groups differed significantly ($P < .05$).

Table IV. Clinical characteristics of patients treated with or without ACE inhibitors

	Control group		Training group		
ACE inhibitors	**+ (n = 10)**	**− (n = 10)**	**+ (n = 12)**	**− (n = 12)**	***P***
Male	7 (70)	6 (60)	10 (83)	11 (92)	ns
Age	59.7 ± 12.1	65.7 ± 7.7	55.4 ± 8.2	62.8 ± 13.6	ns
History					
Diabetes	4 (40)	4 (40)	4 (33)	2 (17)	ns
Hypercholesterolemia	5 (50)	4 (40)	6 (50)	5 (42)	ns
Hypertension	3 (30)	5 (50)	8 (67)	8 (67)	ns
Smoking	6 (60)	7 (70)	8 (67)	9 (75)	ns
Killip class I	7 (70)	6 (60)	9 (75)	10 (83)	
Peak creatine kinase (IU/L)	3,657 ± 1,661	4,364 ± 2,148	3,995 ± 3,414	3,028 ± 1,319	ns
Single vessel disease	8 (80)	8 (80)	11 (92)	11 (92)	ns
Reperfusion success	9 (90)	8 (80)	8 (67)	9 (75)	ns

Data are expressed as means ± SD or number and ratio (%) of patients. *ACE,* Angiotensin-converting enzyme.

Table V. Serial changes in left ventricular volume and function in patients treated with or without ACE inhibitors

		Control group		Training group	
ACE inhibitors		**+ (n = 10)**	**− (n = 10)**	**+ (n = 12)**	**− (n = 12)**
EF (%)	Acute phase	42 ± 7	36 ± 9	41 ± 6	40 ± 8
	1 Month	45 ± 10	43 ± 12	44 ± 9	43 ± 8
	4 Months	48 ± 7†	45 ± 8	44 ± 9	41 ± 10
EDVI (mL/m^2)	Acute phase	80 ± 25	74 ± 26	79 ± 16	75 ± 20
	1 Month	94 ± 22	87 ± 30	89 ± 19	84 ± 18
	4 Months	82 ± 24‡	84 ± 25	93 ± 15*	88 ± 17†
ESVI (mL/m^2)	Acute phase	47 ± 17	47 ± 18	47 ± 13	45 ± 13
	1 Month	53 ± 20	51 ± 25	51 ± 17	48 ± 14
	4 Months	44 ± 18§	48 ± 20	53 ± 16	52 ± 15*
SEVI (mL/m^2)	Acute phase	32 ± 15	38 ± 10	37 ± 12	38 ± 10
	1 Month	33 ± 17	33 ± 18	34 ± 15	35 ± 11
	4 Months	27 ± 17	25 ± 11†	37 ± 18	36 ± 13

Data are expressed as means ± SD of number of patients.
*$P < .05$ vs acute phase.
†$P < .01$ vs acute phase.
‡$P < .05$ vs 1 month.
§$P < .01$ vs 1 month.

Sequential transitions of SD/chord and regional wall motion score are described in Table III. Both parameters significantly decreased within both study groups, but the deviation between the 2 was not significantly different.

Subgroup analysis of patients treated with or without ACE inhibitors

Half the patients could not tolerate ACE inhibitors because of adverse effects. Clinical characteristics of the patients were comparable in the 4 groups (Table IV). The EDVI and ESVI values significantly decreased in patients in the control group who were treated with ACE inhibitors from 1 to 4 months, but increased regardless of ACE inhibitor use in the training group (P = not significant, Table V).

Effects on hemodynamic factors and exercise capacity

Serial changes in hemodynamic factors and exercise capacity during cardiopulmonary exercise testing are shown in Table VI. The intensity of the training program was maintained at approximately 70% of the maximal heart rate (110 ± 10 beats/min). Resting systolic blood pressure increased significantly in both study groups. Peak exercise capacity and oxygen consumption significantly increased in the training group, but not in the control group. Although the heart rate

Table VI. Cardiopulmonary exercise test

	Control group (n = 20)		Training group (n = 24)	
Training program	**Before**	**After**	**Before**	**After**
Rest				
HR (beats/min)	66 ± 9	71 ± 14	68 ± 9	70 ± 6
SBP (mm Hg)	112 ± 9	118 ± 12‡	119 ± 12	126 ± 12§
RPP	74 ± 14	81 ± 15	81 ± 12	88 ± 14
Peak				
Load (Watts)	88 ± 34	89 ± 34	107 ± 32	143 ± 49§†
HR (beats/min)	145 ± 16	132 ± 21§	152 ± 19	161 ± 18†‡
SBP (mm Hg)	175 ± 24	172 ± 25	183 ± 25	193 ± 18†
RPP	255 ± 56	229 ± 58‡	280 ± 56	311 ± 49†‡
V O_2 (mL/kg/min)	16.8 ± 3.0	16.5 ± 3.7	18.7 ± 5.3	21.6 ± 5.6§†
VT				
Load (Watts)	46 ± 19	51 ± 18	54 ± 17	73 ± 27§†
HR (beats/min)	108 ± 18	103 ± 15	110 ± 13	112 ± 14
SBP (mm Hg)	144 ± 23	145 ± 23	145 ± 21	157 ± 16§*
RPP	157 ± 42	151 ± 36	161 ± 37	177 ± 33*
V O_2 (mL/kg/min)	11.0 ± 1.5	11.7 ± 2.3	12.4 ± 4.0	14.3 ± 3.9‡*
VT HR/peak HR (%)	75 ± 12	77 ± 10	73 ± 8	70 ± 6†

Data are presented as mean value ± SD. *Before,* Before exercise (1 month). *After,* after exercise (4 months); *HR,* Heart rate; *SBP,* systolic blood pressure; *RPP,* rate-pressure product (mmHg × bpm × 10^{-3}); *V O_2,* oxygen consumption; *VT,* ventilatory threshold.
*$P < .05$ interaction.
†$P < .01$ interaction.
‡$P < .05$ within groups.
§$P < .01$ within groups.

at VT did not serially change in the training group, the workload and systolic blood pressure at VT increased significantly.

Complications and cardiac events

Major complications including ventricular tachyarrythmia, which could interrupt the training program, did not develop during the study period. Mild angina developed in 4 patients 10 weeks after discharge (2 in each group), without the need for a dose increase. Modest congestive heart failure in 3 patients required an increased dose of furosemide (1 patient in the training group and 2 patients in the control group) after discharge. However, hospitalization was not required, and the training program was maintained. No other serious events occurred throughout the study period in any of the patients.

Discussion

This study is a prospective, randomized trial that was designed to address whether exercise training at VT aggravates LV remodeling in patients with extensive anterior AMI. Both EDVI and ESVI significantly decreased from 1 to 4 months in the control group, but significantly increased from the acute phase to 4 months in the training group. These data suggest that training at VT could induce LV enlargement.

Several reports have described the influence of training on LV remodeling after AMI.[12–16] Many of them have demonstrated that training influences LV remodeling little. Jette et al reported that exercise training had a minimal effect on LV size and function in patients with anterior AMI.[15] Their patients started training comparatively later after onset (approximately 2 months). Dubach et al reported that training had no deleterious effects on LV volume and function in patients with AMI.[16] Their patients started training approximately 5 weeks after onset and maintained it for 2 months, at an intensity of 60% to 70% of the maximal heart rate. However, only half their patients (13/25, 52%) had anterior AMI. Giannuzzi et al reported that training induced no additional negative effect on ventricular size and topography in patients with anterior AMI.[13] Their patients started training 4 to 8 weeks after onset and continued for 6 months. However, relatively few patients with LV dysfunction were involved. Giannuzzi et al also reported that training might attenuate LV remodeling in selected patients with LV dysfunction after AMI.[14] Like the patients in our study, their patients started training approximately 3 to 5 weeks after onset and continued for 6 months, at an intensity of 80% of the maximal heart rate. The conflicting may be because they measured LV volume and function with echocardiography. However, the LV apex is 1 of the most difficult areas to visualize with

echocardiography. In addition, the effect of the reperfusion therapy and the patency of the infarction-related coronary artery throughout the experimental period are not clearly defined in their study. In contrast, we determined the LV volume and function with biplanar LVG, and each patient underwent CAG 3 times to define the patency of the infarction-related coronary artery, and it was kept patent when possible.

Serial changes of LV volume

The EDVI in our control group significantly increased from the acute phase to 1 month, but significantly decreased from 1 to 4 months. Several reports have referred to serial changes in LV volume after AMI,[3,6,19] but none have suggested such spontaneous regression of the LV volume. Many of these studies exclude patients who received PTCA or in whom vessel patency was not clearly defined. Our study included 15 of 20 patients (75%) in the control group who had a patent infarction-related coronary artery throughout the study period. This may have contributed to the regression of LV enlargement. Eighteen of the 24 patients in the training group (75%) had a patent coronary artery related to the infarction throughout the study period, like those in the control group. However, the EDVI in the training group significantly increased from 1 to 4 months, and the tendency of the ESVI was the same. Our data indicated that even exercise at VT could induce LV enlargement in patients with extensive anterior AMI.

Serial changes of systolic expansion volume

We defined SEVI, a new parameter quantifying infarction site expansion at the end-systolic phase. Both SEVI and ESVI decreased significantly from 1 to 4 months in the control group, which indicates that ESVI is reduced from 1 to 4 months after infarction expansion regresses. However, serial changes in SEVI were not significant in the training group, which indicates that exercise at VT inhibits the spontaneous regression of infarction expansion during the healing period. Other reports indicate that lengthening or hypertrophy of non-infarcted contractile segments is the structural change that results in late ventricular remodeling after AMI.[2,3] However, our study found no evidence that non-infarcted segments deteriorated. Therefore, we cannot conclude that exercise-induced LV enlargement is LV remodeling. However, because ESVI is the most powerful predictor of survival after AMI,[4] this inhibition of volume reduction might lead to further deterioration of the non-infarcted segments after a longer follow-up period.

Effects on exercise capacity

This study found that peak oxygen consumption significantly increased in the training group after 12 weeks of training, whereas in the control group it did not significantly improve. These data demonstrated that training at VT improves the exercise capacity of the patients.

Study limitations

This study is not a multicenter study, and we examined a relatively small number of patients during a short period. Although LVG is the most reliable method for measuring LV volume, SEVI is a invalidated method for evaluating infarction site expansion. A further study is required to confirm that exercise at VT inhibits the spontaneous regression of infarction expansion during the healing period after AMI.

Although the use of ACE inhibitors was encouraged, half the study patients could not tolerate these agents. However, the effects of ACE inhibitors on LV remodeling seemed favorable in the control group but not in the training group. These data indicated that the favorable effects of ACE inhibitors were abrogated by exercise training. β-blockers were also prescribed for a few of the patients. This is probably because the incidence of vasospastic angina in the Japanese population is high even after episodes of AMI.[20,21]

Clinical implications

Our results suggest that exercise programs should be postponed in patients with extensive anterior AMI. Because of the results from previous studies, the start of an exercise program at 2 to 3 months versus 3 weeks after the onset of AMI might be safer and more beneficial. Early exercise appears to enlarge LV volume, which is the major determinant of survival in patients with extensive anterior AMI, and exercise training is beneficial even when it is initiated late after onset.

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