Association between heart rate at rest and myocardial perfusion in patients with acute myocardial infarction undergoing cardiac rehabilitation – a pilot study

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Abstract

Introduction: This study was conducted to determine if there was a link among heart rate at rest (rHR), muscle volume changes, and single photon emission computed tomography (SPECT) parameters after 6-month cardiac rehabilitation in patients with acute myocardial infarction (AMI).
Material and methods: Twenty-nine consecutive AMI patients (mean age: 63.0 ±9.1 years) who received appropriate percutaneous coronary intervention on admission were enrolled. ^{99m}Tc-Sestamibi myocardial SPECT images were obtained at the early (30 min) and delayed (4 h) phases after tracer injection at 2 weeks (0M) and 6 months (6M) after the onset of AMI. Within a few days of SPECT, all patients underwent cardiopulmonary exercise test for evaluation of cardiac rehabilitation effects. Before the initiation of exercise test, leg muscle volume was measured. All patients were stratified into the ≥ 70 beats per minute (bpm) (n = 15) or < 70 bpm (n = 14) group based on rHR at 6M.
Results: There were no significant differences in the recanalization time, peak cardiac enzyme, or initial left ventricular ejection fraction between the two groups. After the 6-month training, the muscle volume changes in the lower limbs (< 70 bpm, 0.23 ±0.22; ≥ 70 bpm, –0.07 ±0.26, p < 0.05) were significantly greater in the < 70 bpm group than the ≥ 70 bpm group. The decreased rate of rHR had a significant correlation with the improved global severity (r = 0.62, p = 0.001) and extent (r = 0.48, p = 0.017) of left ventricle evaluated by ^{99m}Tc-Sestamibi myocardial SPECT delayed phase.
Conclusions: The result of this preliminary study demonstrated that improved myocardial perfusion was closely related to decreased rHR after cardiac rehabilitation.

Key words: cardiac rehabilitation, exercise capacity, myocardial infarction, skeletal muscle, single photon emission computed tomography.

Introduction

Since 1990, single-photon emission computed tomography (SPECT) with technetium-99m hexakis 2-methoxy-isobutyl-isonitrile (^{99m}Tc-sestamibi) has been used to assess the extent of myocardial damage at rest in patients with acute myocardial infarction (AMI) [1, 2]. ^{99m}Tc-sestamibi SPECT, which measures the extent and severity of ischemia, is commonly used for risk stratification of patients with coronary artery disease (CAD)

[3]. Repeated myocardial imaging with ^{99m}Tc-sestamibi performed in the acute phase and days after primary reperfusion treatment allows reliable assessment of the area at risk, the final infarct size, and the volume of salvaged myocardium by reperfusion therapy [4-6]. In addition, the infarct size (i.e., the number of residual cardiac segments with perfusion defects), as measured with SPECT, is strongly associated with the mortality risk [7].

Most AMI patients receive cardiac rehabilitation, as well as statin administration, for improvement of their prognoses [8-11]. Since the close association between the heart rate at rest (rHR) and coronary mortality was first described by Dyer *et al*. [12], rHR has gained broad attention among physicians [13, 14]. VanHees *et al*. [15] reported that physical training after AMI decreased the rHR. To date, only a handful of studies have reported the association between the findings on myocardial nuclear imaging and the effects of cardiac rehabilitation [16], and no studies have demonstrated an association between the findings of myocardial SPECT and the rHR after cardiac rehabilitation in AMI patients. The present study was aimed at clarifying the aforementioned association in AMI patients after successful percutaneous coronary intervention (PCI) and cardiac rehabilitation.

Material and methods

Subjects

The study subjects were 29 consecutive patients (mean age: 63.0 ±9.1 years) with *de novo* AMI due to single coronary arterial disease diagnosed between October 2009 and June 2011. On arrival at the emergency department, venous blood samples were collected from the cubital vein. The diagnosis of AMI was made by cardiologists, based on electrocardiographic changes, echocardiographic findings, presence of human heart fatty acid binding protein in the serum as detected by immunochromatography, and hematological findings, including the blood levels of MB isoenzyme of creatinine kinase (CK-MB). In order to determine the actual onset time of the AMI, the patients and their family members were interviewed. In primary PCI, a thrombus aspiration catheter was employed to negotiate the occluded lesions; coronary angiography was performed during the PCI. The PCI procedure was considered successful when the residual stenosis was less than 25%, in the absence of dissection, as previously described [17]. Blood samples were collected every 3 h after the PCI to determine the peak levels of the cardiac enzymes. All patients were treated with conventional medications after PCI, and none showed exacerbation of the symptoms or needed hospitalization for AMI-related complications before or after the scintigraphic examinations. Patients with previous myocardial infarction, left main trunk lesion, cardiogenic shock, cardiomyopathies, atrial fibrillation, active infectious disease, hematological disease, end-stage renal and hepatic disease, and patients who were not able to undergo the cardiac rehabilitation program, were completely excluded from the study subjects.

The study protocol included blood tests, PCI, ^{99m}Tc-sestamibi radionuclide examination, and cardiac rehabilitation. This study was performed in accordance with the ethical principles set forth in the Declaration of Helsinki, and was approved by the Human Investigation Committee of St. Marianna University School of Medicine (study protocol No. 1604). The nature and purpose of this study were thoroughly explained to all patients prior to their enrollment in this study, and written informed consent was obtained from each of the patients.

Radionuclide studies

All study patients underwent myocardial SPECT 2 weeks (0M) and 6 months (6M) after the onset of AMI. ^{99m}Tc-sestamibi (740 MBq; Fuji Film RI Pharma Co. Ltd., Tokyo, Japan) was injected into the left antecubital vein, followed by acquisition of SPECT images in two phases: initially at 30 min after the radionuclide injection (early ^{99m}Tc-sestamibi uptake), and subsequently, at 4 h after the radionuclide injection (delayed uptake) as previously reported [18].

Before performing the SPECT, anterior and lateral planar images were acquired for 300 s using a gamma camera equipped with a low-/medium-energy general-purpose collimator and a 512 × 512 matrix. ^{99m}Tc-sestamibi images were obtained using a double-headed gamma camera (Symbia E; Siemens-Asahi Medical Technologies Ltd., Tokyo, Japan) equipped with a low-/medium-energy general-purpose collimator. Two detectors (2 × 180°) were used to acquire 64 views for 25 s in 5.6° steps using a 64 × 64 matrix. The energy window of ^{99m}Tc was centered at 140 keV ± 15%.

Raw imaging data were reconstructed using Butterworth-filtered back-projection (order, 8; cutoff frequency, 0.37 cycles/cm). Transaxial slices were reconstructed and reoriented to represent coronal slices, and then horizontal long- and short-axis slices were acquired by axis shift.

Standard electrocardiographically gated images were acquired in 64 steps at 19 s per step, using the step acquisition mode in the time duration between two consecutive R waves of the electrocardiogram (RR) interval, and divided into 16 frames. Tracer uptake was assessed by non-gated early images created from the sums of all of the gated images obtained in the standard acquisition mode.

Data analysis

Regions of interest (ROIs) were drawn over the entire heart and upper mediastinum depicted in the planar images. The heart-to-mediastinum (H/M) ratio and global washout rate (WR) of ^{99m}Tc-sestamibi were calculated from the pixel counts in the ROIs using the following equations: H/M = mean pixel count of the cardiac ROIs/mean pixel count of the mediastinal ROIs; WR (%) = [(mean early cardiac pixel count mean delayed cardiac pixel count)/mean early cardiac pixel count] × 100. Backgrounds or time-decay corrections were not applied to the calculation of the WR.

Once the SPECT images were acquired and reconstructed from the early images, quantitative gated SPECT (QGS) software (Cedars-Sinai Medical Center, Los Angeles, CA) was used to evaluate the ventricular edges and calculate the left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and left ventricular ejection fraction (LVEF) [19].

Cardiac rehabilitation, exercise test, and skeletal muscle volume

All patients received inpatient cardiac rehabilitation for 2-3 weeks, underwent the first cardiopulmonary exercise testing (CPX), and then exercise-based cardiac rehabilitation on an outpatient basis. Symptom-limited CPX was performed at 1 and 6 months after the onset of AMI using an MAT-2500 treadmill (Fukuda Denshi Co., Tokyo, Japan). After the initial 3-minute rest on the treadmill and 3-minute warm-up (speed 1.6 km/h; grade 0%), the CPX was performed with a gradual increase in the exercise intensity at 1-minute intervals. The 12-lead ECG was monitored continuously; heart rate (HR) was measured by the R-R interval on the electrocardiogram (ECG; ML-9000, Fukuda Denshi Co., Tokyo, Japan). Systolic blood pressure was measured with a cuff via an automatic blood pressure monitor (FB-300, Fukuda Denshi Co., Tokyo, Japan) at 1-minute intervals. Oxygen uptake (VO_2), carbon dioxide output (VCO_2), and the rate of respiratory airflow were measured during the test using an AE-300 cart (Minato Medical Science, Osaka, Japan). Anaerobic threshold (AT), peak VO_2 and the minute ventilation/VCO_2 (VE/VCO_2) slope were calculated based on the CPX results. AT was determined by the original V-slope method [20]. An apparent leveling off of the VO_2 (VO_2 plateau in spite of increasing exercise intensity) was used as a sign for terminating the exercise. The appropriate intensities of the outpatient rehabilitation exercise in each patient were determined using the HR measured at the AT in the CPX conducted at 1M.

Before the start of the CPX, the skeletal muscle volume was measured using a single-cycle bioelectrical impedance data acquisition system (Muscle-α, Art Haven 9 Co., Kyoto, Japan), as previously described [21].

Statistical analysis

The results are expressed as means ± SD. The significances of differences between the ≥ 70 beats per minute (bpm) and < 70 bpm groups were assessed using an unpaired *t* test. A paired *t* test was used to compare the parameters in each patient obtained in the early and delayed phases. A linear regression analysis was conducted to evaluate the significance of the changes in the rHR and the ^{99m}Tc-sestamibi myocardial scintigraphic parameters. Values of *p* of less than 0.05 were considered to indicate statistical significance.

Results

Patient characteristics and laboratory findings

Table I shows the characteristics of the patients enrolled in this study. All patients were stratified into the ≥ 70 bpm (n = 15) or < 70 bpm (n = 14) group according to the rHR at 6M. Data obtained were analyzed and compared between the two groups.

In the < 70 bpm group, the culprit lesion was in the left anterior descending coronary artery (LAD) in 5 patients, and in the non-LAD vessels in 9 patients. In the ≥ 70 bpm group, the culprit lesion was in the LAD in 5 patients, and in the non-LAD vessels in 10 patients. All patients received appropriate primary PCI. Thrombolysis in Myocardial Infarction (TIMI) [22] grade 3 flow was obtained in all patients after the PCI.

No significant differences in the age, gender ratio, body mass index, medical history, cardiac enzyme level on admission, time from onset to revascularization, or peak cardiac enzyme level were found between the two groups (Table I). In all patients, loading doses of 200 mg of acetylsalicylic acid and 300 mg of clopidogrel sulfate were administered after the PCI, followed by maintenance doses of 100 mg of acetylsalicylic acid and 75 mg of clopidogrel sulfate. Most of the patients received an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, β-blocker, and/or some type of statin as prophylaxis against secondary cardiac events and deterioration of cardiac function. There were no significant differences in the medications administered between the two groups (Table I).

Myocardial scintigraphic study

The results of LVEDV, LVESV, and LVEF calculated from the imaging are presented in Table II. No significant differences in the regional WR, global WR,

Table I. Patients' characteristics

Variable	rHR < 70 bpm (n = 14)	rHR ≥ 70 bpm (n = 15)	Value of p
Age [years]	64.3 ±8.4	61.9 ±9.9	NS
M/F (n)	14/0	13/2	NS
Body mass index [kg/m^2]	24.4 ±1.6	22.6 ±3.0	NS
Diabetes mellitus [%]	13	47	NS
Hypertension [%]	43	60	NS
Hyperlipidemia [%]	50	60	NS
Smoking [%]	64	40	NS
Time to revasc from the onset [h]	8.7 ±9.6	13.4 ±20.9	NS
Culprit:			
LAD, LCx, RCA (%)	36, 43, 21	34, 13, 53	NS
Laboratory findings:			
BNP [pg/ml]	136 ±143	128 ±169	NS
Peak CK [IU/l]	3306 ±2336	2516 ±1488	NS
(Sampling time [h])	(17.7 ±14.1)	(18.1 ±19.6)	
Peak CK-MB [IU/l]	292.0 ±162.8	262.0 ±199.3	NS
(Sampling time [h])	(13.3 ±7.7)	(17.5 ±19.8)	
Medications:			
ACE-I, ARB [%]	92.9	100	NS
β-Blocker [%]	85.7	66.7	NS
Aspirin [%]	100	100	–
Dihydropyridine [%]	85.7	80	NS
Statin [%]	78.6	93.3	NS
Loop diuretics [%]	0	0	–
Antialdosterone [%]	0	20	NS
Calcium blocker [%]	14.3	6.7	NS
Nicorandil [%]	42.9	40	NS
Insulin [%]	0	6.7	NS
Warfarin [%]	14.3	0	NS

Some values are expressed as mean ± SD; rHR – resting heart rate, M/F – male/female, LAD – left anterior descending coronary artery, LCx – left circumflex coronary artery, RCA – right coronary artery, BNP – brain natriuretic peptide, CK – creatinine kinase, CK-MB – MB isoenzyme of CK, ACE-I – angiotensin angiotensin-converting enzyme inhibitor, ARB – angiotensin receptor blocker

early/delayed global extent scores, or early/delayed severity scores either at 0M or at 6M were observed between the < 70 bpm and ≥ 70 bpm groups. Comparison of the parameters at 0M and 6M revealed no significant improvement of the cardiac imaging parameters in either the < 70 bpm group or the ≥ 70 bpm group (Table III).

Cardiopulmonary exercise test and muscle volume

At 6M, the mean rHR was 61.4 ±7.3 bpm in the < 70 bpm group and 77.9 ±9.0 bpm in the ≥ 70 bpm group ($p < 0.001$). At 0M, the rHR and peak rHR were higher in the 70 bpm group (76.9 ±8.9 bpm and 148.9 ±19.5 bpm) than those in the < 70 bpm group (67.4 ±7.4 bpm, $p < 0.01$ and 136.4 ±16.5 bpm, $p < 0.05$). Peak HR at 6M was also higher in the ≥ 70 bpm group (154.7 ±21.8 bpm) than that in the < 70 bpm group (138.5 ±22.1 bpm, $p < 0.001$) (Table IV).

No significant differences in the changes of the CPX parameters were observed after 6 months of rehabilitation in either group. On the other hand, significant differences in the changes of the whole-body muscle volume (1.7 ±2.0 kg vs. –1.1 ±2.9 kg,

Table II. The results from the radionuclide study

Variable	rHR < 70 bpm (n = 14)		rHR ≥ 70 bpm (n = 15)		Value of p
	0M	6M	0M	6M	
LVEDV [ml]	102.1 ±21.4	107.8 ±20.3	108.9 ±34.3	101.9 ±41.1	NS
LVESV [ml]	49.4 ±17.8	48.5 ±16.6	62.7 ±30.4	51.0 ±36.8	NS
LVEF [%]	52.1 ±9.1	55.6 ±10.6	44.9 ±10.9	55.3 ±14.4	NS
Regional washout rate [%]	33.7 ±7.0	30.5 ±7.2	36.4 ±11.6	31.5 ±14.3	NS
Global washout rate [%]	28.1 ±7.0	26.8 ±5.3	32.2 ±10.3	28.6 ±11.7	NS
Early global extent [%]	40.0 ±18.2	44.8 ±19.1	42.1 ±20.6	43.8 ±24.5	NS
Early global severity [%]	6.3 ±5.9	6.2 ±4.9	7.5 ±7.4	7.3 ±8.9	NS
Delay global extent [%]	44.6 ±18.2	42.6 ±14.4	42.8 ±18.9	38.9 ±20.3	NS
Delay global severity [%]	10.3 ±8.6	7.4 ±6.0	10.2 ±9.3	7.9 ±9.7	NS

Values are expressed as mean ± SD; 0M – 0 months, 6M – 6 months, LVEDV – left ventricular end-diastolic volume, LVESV – left ventricular end-systolic volume, LVEF – left ventricular ejection fraction. Other abbreviations were are the same as in Table I

Table III. The changes of radionuclide parameters after 6 months of treatment

Radionuclide study	rHR < 70 bpm (n = 14)	rHR ≥ 70 bpm (n = 15)	Value of p
LVEDV [ml]	5.7 ±23.2	–2.0 ±25.5	NS
LVESV [ml]	–0.93 ±20.3	–7.79 ±19.1	NS
LVEF [%]	3.5 ±12.7	9.6 ±9.1	NS
Regional washout [%]	–3.5 ±6.8	–5.5 ±12.8	NS
Global washout [%]	–1.2 ±7.9	–4.1 ±10.2	NS
Early global extent [%]	3.3 ±20.0	1.9 ±15.6	NS
Early global severity [%]	–0.5 ±3.8	0.07 ±4.1	NS
Delay global extent [%]	–5.1 ±17.0	–3.1 ±19.2	NS
Delay global severity [%]	–3.6 ±4.6	–1.7 ±3.3	NS

Values are expressed as mean ± SD. Abbreviations were are the same as in Tables I and II

$p < 0.05$), lower limb muscle volume (0.23 ±0.22 vs. –0.13 ±0.45, $p < 0.05$) and thigh muscle volume (0.19 ±0.22 vs. –0.13 ±0.45, $p < 0.05$) were found between the < 70 bpm group and the ≥70 bpm group (Table V).

Associations between the improvements of ^{99m}Tc-sestamibi global extent and severity scores versus decrease in the rHR after cardiac rehabilitation

Figure 1 shows the association between the ^{99m}Tc-sestamibi SPECT parameters and the rHR after 6 months of cardiac rehabilitation. The changes in the global severity score calculated from the ^{99m}Tc-sestamibi early SPECT images were significantly correlated with those of the rHR after rehabilitation ($r = 0.48$, $p = 0.016$). A significant correlation was also observed between the changes in the global severity score calculated from the ^{99m}Tc-sestamibi delayed SPECT images and those of the rHR ($r = 0.62$, $p = 0.0013$). No correlation was found between the changes in the global extent score calculated from the ^{99m}Tc-sestamibi early SPECT images and those of the rHR; however, a significant correlation was observed between the changes in the global extent score calculated from the ^{99m}Tc-sestamibi delayed SPECT images and those of the rHR ($r = 0.48$, $p = 0.017$).

Discussion

Cardiac rehabilitation for patients with acute myocardial infarction is well recognized to contribute to improvement of exercise tolerance [9, 23]. In the present study, however, cardiac rehabilitation improved neither the cardiac contractility nor the exercise tolerance. This result could be explained by: (1) the patients already having had favorable heart function prior to the rehabilitation; (2) maintenance of the heart function by successful reperfusion, etc. Some previous reports have also reported that while 2 months of physical training improved the exercise tolerance, it did not improve

Table IV. The results from cardiopulmonary exercise test and muscle volume before and after rehabilitation

Variable	rHR < 70 bpm (n = 14)		rHR ≥ 70 bpm (n = 15)	
	0M	6M	0M	6M
Cardiopulmonary Exercise Test:				
Rest HR [bpm]	67.4 ±7.4	61.4 ±7.3	76.9 ±8.9*	77.9 ±9.0†
Rest SBP [mm Hg]	111.9 ±15.2	118.8 ±19.3	118.5 ±28.0	127.9 ±22.5
Peak HR [bpm]	136.4 ±16.5	138.5 ±21.1	148.9 ±19.5**	154.7 ±21.8††
Peak SBP [mm Hg]	187.6 ±30.1	189.4 ±21.6	169.9 ±32.9	183.1 ±27.7
Peak DBP [mm Hg]	83.4 ±19.2	88.7 ±18.7	86.0 ±16.5	85.6 ±14.0
AT [ml/kg/min]	19.2 ±2.7	23.0 ±3.3	21.1 ±3.2	21.8 ±5.3
Peak VO_2 [ml/kg/min]	25.8 ±3.4	28.7 ±4.6	27.1±5.6	28.1 ±7.2
VE/VCO_2	28.4 ±3.8	27.0 ±3.1	29.3 ±5.4	28.2 ±6.2
Muscle volume:				
Whole body [kg]	33.5 ±1.8	35.3 ±2.7	33.5 ±1.8	33.4 ±3.4
Upper limbs [kg]	1.3 ±0.2	1.3 ±0.2	1.3 ±0.3	1.2 ±0.2
Humerus [kg]	0.7 ±0.2	0.8 ±0.1	0.7 ±0.2	0.7 ±0.2
Antebrachium [kg]	0.6 ±0.08	0.6 ±0.08	0.6 ±0.2	0.5 ±0.09
Lower limbs [kg]	4.9 ±0.8	5.2 ±0.8	5.1 ±0.8	4.7 ±0.9
Femurs [kg]	2.9 ±0.5	3.2 ±0.6	3.1 ±0.6	2.8 ±0.6
Crus [kg]	2.0 ±0.4	2.0 ±0.3	2.0 ±0.4	1.9 ±0.4

*Values are expressed as mean ± SD; HR – heart rate, SBP – systolic blood pressure, DBP – diastolic blood pressure, AT – anaerobic threshold, VO_2 – oxygen uptake, VE – respiratory minute volume, VCO_2 – carbon dioxide output. Other abbreviations were are the same as in Table I; *p < 0.01 vs. 0M rHR < 70 bpm, **p < 0.05 vs. 0M rHR < 70 bpm, †p < 0.001 vs. 6M rHR < 70 bpm, ††p < 0.001 vs. 6M rHR < 70 bpm*

Table V. Changes of parameters obtained from cardiopulmonary exercise test after 6 months of rehabilitation

Variable	rHR < 70 bpm (n = 14)	rHR ≥ 70 bpm (n = 15)	Value of p
Cardiopulmonary Exercise Test:			
Rest HR [bpm]	–7.1 ±7.1	0.1 ±8.3	NS
Rest SBP [mm Hg]	9.2 ±16.2	14.5 ±22.3	NS
Rest DBP [mm Hg]	3.6 ±10.5	8.8 ±14.5	NS
Peak HR [bpm]	–0.08 ±19.3	7.3 ±21.6	NS
Peak SBP [mm Hg]	2.3 ±37.6	13.2 ±29.2	NS
Peak DBP [mm Hg]	8.1 ±30.6	1.3 ±12.8	NS
AT [ml/kg/min]	3.2 ±3.3	0.9 ±4.1	NS
Peak VO_2 [ml/kg/min]	2.4 ±3.6	1.2 ±4.1	NS
VE/VCO_2	–1.3 ±2.5	–1.2 ±4.2	NS
Muscle volume:			
Whole body [kg]	1.7 ±2.0	–1.1 ±2.9	< 0.05
Upper limbs [kg]	0.03 ±0.11	–0.06 ±0.18	NS
Humerus [kg]	0.02 ±0.09	–0.01 ±0.16	NS
Antebrachium [kg]	0.01 ±0.04	–0.05 ±0.20	NS
Lower limbs [kg]	0.23 ±0.22	–0.07 ±0.26	< 0.05
Femurs [kg]	0.19 ±0.22	–0.13 ±0.45	< 0.05
Crus [kg]	0.04 ±0.16	0.06 ±0.27	NS

Values are expressed as mean ± SD. Other abbreviations were are the same as in Tables I and III

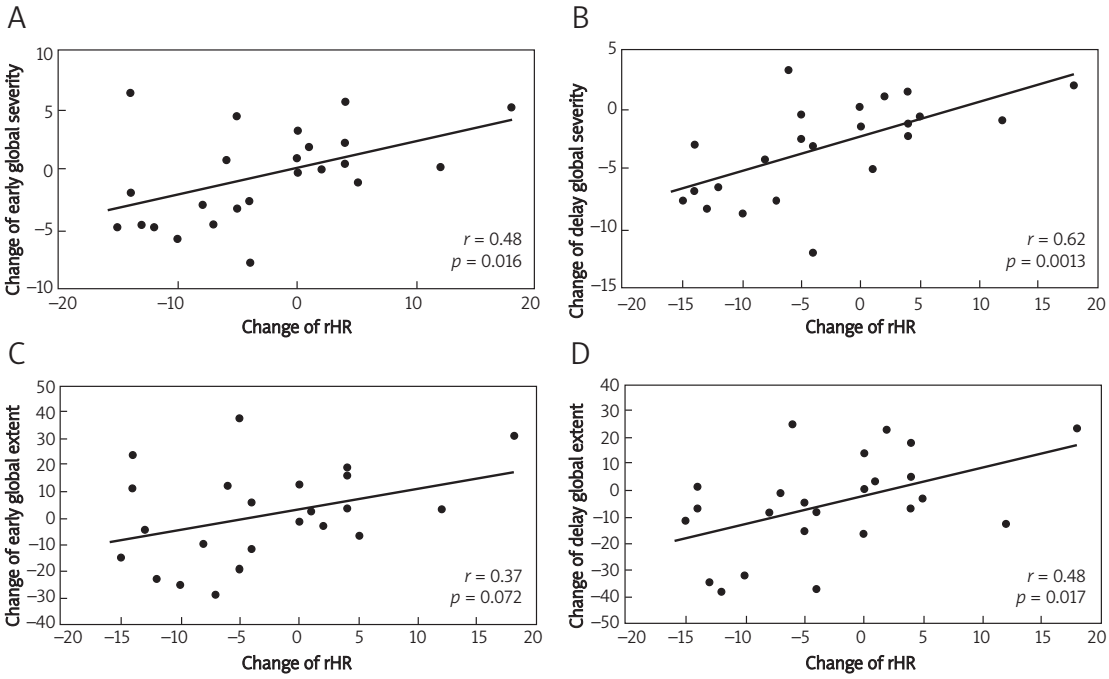

Figure 1. Associations between the changes in the extent of the 99mTc-sestamibi extent and severity scores and the changes of the rHR after cardiac rehabilitation: **A** – early global severity, **B** – delay global severity, **C** – early global extent, **D** – delay global extent

There was a significant correlation between the changes of the global severity score obtained from ^{99}mTc-sestamibi early SPECT images and the changes of the rHR after the rehabilitation (r = 0.48, p = 0.016). A significant correlation was also observed between the changes of the global severity score obtained from ^{99}mTc-sestamibi delayed SPECT images and the changes of the rHR (r = 0.62, p = 0.0013). In regard to the global extent score, a significant correlation was observed between the changes of the global extent score obtained from ^{99}mTc-sestamibi delayed SPECT images and the changes of the rHR (r = 0.48, p = 0.017).

the LVEF [24, 25]. In the above-mentioned report on the effects of exercise, the patients performing regular exercises showed steady improvement of the exercise tolerance for one year, without developing left ventricular remodeling [26]. In the present study also, no changes potentially leading to left ventricular remodeling were noted during the first half-year period. The effects of rehabilitation in patients with myocardial infarction are probably unlikely to appear within a short period of time (e.g., 6 months), thus necessitating long-term follow-up to verify the effects. The prognosis of the patients may be improved after cardiac rehabilitation because of the efforts to improve the lifestyle and to prevent relapse of infarction through continuation of habitual exercises, etc.

When the patients were divided into the high heart rate at rest (≥ 70 bpm) group and low heart rate at rest (< 70 bpm) group, an inter-group difference was found in the lower limb muscle volume, particularly the thigh muscle volume after cardiac rehabilitation. In the low heart rate at rest group, the muscle volume was maintained in many patients during the first half-year period. In the high heart rate at rest group, on the other hand, reduced muscle volume was noted in many patients during the same period. Lower limb muscles serve as an important factor regulating the exercise tolerance in patients with heart diseases, and may serve as a factor determining exercise [27, 28]. One possible reason for the failure to maintain muscle volume in some patients despite continued rehabilitation was inadequate lower limb muscle training (advised before discharge from the hospital) under a non-supervised training program in these patients. The inadequate lower limb muscle training probably delayed the development of the peripheral skeletal muscles, leading to delay in peripheral artery/vein development. In these cases, it is estimated that although the effects of rehabilitation did not become obviously evident, the heart rate increased and the cardiac output was maintained, leading to maintained peripheral arterial/venous return and maintained exercise tolerance. In the > 70 bpm group, the LVEF in the acute stage after the onset of AMI was lower (although the difference was not statistically significant), suggesting the possibility that the compromised heart function affected the appearance of the effects of rehabilitation. However, considering that the LVEF became close to normal by 6 months after the onset of AMI, it seems unlikely that the baseline heart function affected the effects of rehabilitation in these cases. The results of the present study do not fully answer the question which of acute-stage angioplasty or rehabilitation con-

tributed more to the heart rate in these patients. However, the finding of the differences in the systemic muscle volume and lower limb muscle volume between the ≥ 70 bpm group and < 70 bpm group despite the absence of significant differences in the 6-month SPECT data between the two groups suggests a greater impact of the changes of the systemic skeletal muscle volume than of the changes in the heart.

High rHR is consistently associated with an increased risk of in-hospital events and the long-term mortality in patients with AMI [29]. The recently conducted Beautiful Study has revealed that HR ≥ 70 bpm or < 70 bpm in patients with compromised heart function is a determinant of prognosis [30]. The Systolic Heart Failure Treatment with the If Inhibitor Ivabradine (SHIFT) study has also demonstrated that, among patients with compromised heart function, the prognosis is favorable in the subset of patients with low HR [31]. It is well known that 5 bpm reductions in HR with β-blockers lead to a decrease in the mortality by 18%. The recognition of this relationship has attracted close attention to HR [32]. In the present study, no significant reduction in rHR was observed, although the newly identified correlation indicated that post-reperfusion myocardial injury (as assessed with SPECT) was less severe in patients with lower HR. Since they were treated with β-blockers without any changes in the dosage regimen during the study period, the change over time rather than the influence of medication was closely associated with our study result.

The small number of subjects in the present study may mask a significant result. However, as Figure 1 shows, the patients who had successful reperfusion and a larger salvaged myocardium tended to have lower rHR, which is closely associated with the newly identified correlation. If this correlation can be observed in a larger study population, changes in rHR in AMI patients probably indicate the effect of PCI on the myocardium as well as that of cardiac rehabilitation on the whole body. Hence, the evaluation of diagnostic imaging and physical findings seems essential when the course of treatment for myocardial infarction is considered. These are the clinical implications of this study.

The main limitation of the study was connected with the small number of subjects included. Furthermore, it was not a controlled trial. Acute myocardial infarction patients not receiving PCI should be included as controls in future studies. The prognostic SPECT values in patients with ischemic cardiac disease remain unknown in this study. Further investigations on larger numbers of patients should be conducted to elucidate the potential usefulness of ^{99m}Tc-sestamibi parameters as a prognostic incremental indicator.

In conclusion, AMI patients showing a decrease of the rHR after 6 months of cardiac rehabilitation also showed a significant increase of the leg muscle volumes. The results of this preliminary study demonstrated that improved myocardial perfusion was closely associated with the decrease of the rHR after cardiac rehabilitation.

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