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EFFECTS OF PHASE II CARDIAC REHABILITATION ON INSULIN RESISTANCE AND MYOCARDIAL REMODELING IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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A b s t r a c t

We have designed a new 2-week hospitalized phase II Cardiac Rehabilitation (CR) program in Japan. The purpose of the present study is to determine long-term effects on physical parameters, especially insulin resistance and myocardial remodeling in patients with acute myocardial infarction. Twenty-five patients (20 men, 5 women, mean age: 52±11years, peak CK 2378±1881 IU/l, mean EF 60±18%) with AMI were enrolled in this program. Plasma propeptide of type I procollagen (PICP), HOMA-R and proinsulin were evaluated. The physical status was assessed by the exercise tolerance (AT and peak VO_2), exercise frequency, serum lipid profiles and BMI. All the parameters were evaluated before, 1, 6 and 12 months after the participation in the program. Serum lipid profiles (HDL cholesterol, triglyceride), BMI, peak VO_2 and AT were improved significantly, PICP was stable at the 1, 6 and 12 months follow-up. Eighty percent of patients had regular exercise activity (REA). There was no significant difference in PICP between REA and the sedentary subjects. Proinsulin and HOMA-R were stable at the 1, 6 and 12 months follow-up. The change in HOMA-R was not related to exercise tolerance; it strongly correlated with the change in BMI (r=0.61). These results suggest that Phase II CR program does not accelerate myocardial remodeling and our 2-week hospitalized Phase II CR program contributes to not only maintain insulin sensitivity but also to improve the management of other cardiac risk factors.

K e y w o r d s

Diabetes, Rehabilitation, Cardiovascular risk, Myocardial infarction, Exercise

INTRODUCTION

While the mortality from acute myocardial infarction (AMI) has fallen, it remains a leading cause of mortality and morbidity in the Western world.

Approximately 50% of deaths from AMI occur in the first hour prior to admission to hospital, which emphasizes the importance of primary and secondary prevention. In the past decade several studies suggested that there are some ways to go in this regard, especially the lifestyle changes and risk factor modification in the post-AMI patients. Cardiovascular diseases are the leading cause of death in people with type 2 diabetes (non-insulin dependent – NIDDM). Compared to people without diabetes, people with diabetes have a strongly increased risk of coronary heart disease (*1, 2*). People with type 2 diabetes without prior myocardial infarction have as high a risk of death from coronary heart disease as non-diabetic patients with a previous history of myocardial infarction (*3, 4*). Effective management of patients after AMI through lifestyle modification can delay the onset of complications, including cardiovascular and metabolic disorders. However, there are several problems which are not completely solved. First of all, the period of hospitalization during Phase I cardiovascular rehabilitation (CR) has been becoming shorter as a result of recent advances in medical interventions (stent, PTCA), and also for economic reasons. The lifestyle modification, particularly in terms of daily exercise, cessation of smoking and a balanced food intake, should be acquired during Phase II CR (or so-called recovery stage, since discharge from hospital until return to work) and maintained thereafter. However, according to numerous recent reports the participation in the Phase II CR remains still very low – only 9–15% in the U.S.A., 14–23% in U.K. and 5–12% in Japan of all the patients after AIM participate in Phase II CR. The main reasons of why the participation ratio in Phase II CR is low are lack of the primary physician's recommendation for participation, long commute time (frequent visit rate and long distance to visit local hospitals, so that the patients have a hard time to modify their lifestyle), patient "denial" of severity of illness, and a history of depression (*5*). A new 2-week hospitalized phase II cardiac rehabilitation program (2-WCR) has been designed and administered by a multidisciplinary team. The objective of this pilot study was to evaluate the effectiveness of 2-WCRP on insulin resistance and cardiac remodeling in non-insulin dependent (NIDDM) patients and to clarify whether the physical and psychological status of these patients improved after participation in the program.

PATIENTS AND METHODS

Twenty-five patients with AMI and NIDDM (age 52.2 ± 11 years, 20 men, 5 women, mean EF 60 ± 18%, peak creatine kinase 2378 ± 1881 IU/l) referred from primary care were enrolled in the 2 weeks lasting rehabilitation program. This program consisted of exercise training, education and counseling, and another 34 patients with AMI who did not participate in the program served as the control group. The physical status was assessed by symptom-limited spiroergometry and determination of exercise tolerance (AT and peak VO_2). Spiroergometry was performed by all patients according to a standardized protocol by *Wasserman et al.* (*6*). The test was done at a progressively increasing working rate (10 W/min) up to the maximal tolerance level on an electromagnetically braked bicycle ergometer. Heart rate was monitored continuously using a 12-lead electrocardiograph and blood pressure was measured noninvasively every 2 min. The peak workload was recorded; oxygen uptake and carbon dioxide production were calculated breath by breath (CPX/D system, Medical Graphics Corporation, St. Paul, Minneapolis), interpolated, and averaged over 10s periods. Peak oxygen uptake (VO_{2peak}) and oxygen uptake at anaerobic threshold (VO_{2AT}) were determined according to the method by *Wasserman et al.* (*6*). Individual Body Mass Index was calculated according to the formula BMI = weight (kg) / height^2 (m^2).

REHABILITATION PROTOCOL

The two-week non-pharmacological rehabilitation program in hospital was performed as a group based exercise and group (individual) education training. The exercise training consisted of bicycle ergometry (for 2 x 30 min/day at 80–100% of heart rate at the level of individually determined anaerobic threshold), walking (1–2 km/day) and stretching performed every day in group classes supervised by a physiotherapist. The education program was done in group classes taught by a nurse, a physiotherapist and a dietitian, and consisted of a group lecture (30–60 min/day), individual nutrition counseling (60 min/day), and individual discharge instruction (60 min/day).

BIOCHEMICAL PARAMETERS

HOMA-R. The HOmeostasis Model Assessment (HOMA) Ratio is a mathematical model which can estimate an individual's degree of insulin sensitivity and the level of beta cell function from simultaneous measurements of fasting plasma glucose and fasting plasma insulin concentrations. HOMA-R models the physiologic glucose-insulin feedback system and estimates an individual's insulin sensitivity based on the assumption that any one combination of glucose and insulin is associated with a given insulin sensitivity, or, conversely, their insulin resistance. HOMA-R has become a much used method for estimating insulin sensitivity and beta cell function in people with non-insulin treated type 2 diabetes.

PICP (carboxyterminal propeptide of type I procollagen). Collagen types I and III are the major fibrillar collagen in the myocardium. PICP is cleaved from the procollagen molecule during collagen synthesis and released into the bloodstream. Some studies demonstrated that the plasma PICP levels in 2–3 weeks after AIM were significantly higher in the group with dilation of myocardium than in the group with no dilation (*8*).

Proinsulin. Proinsulin is a predictor of insulin that is enzymatically cleaved from insulin. Several studies have suggested that proinsulin concentrations are more strongly related to cardiovascular risk factors and carotid wall thickness than are insulin concentrations. Increased proinsulin concentrations predict death and morbidity caused by CHD over a period of 27 years, independent of other major cardiovascular risk factors (*9*).

The changes in exercise performance, BMI and selected biochemical parameters were evaluated after 1, 6 and 12 months after discharge home. The physical activity lasting over 20 min and realized more than 2 times per week was considered as home-based regular physical activity.

ETHICS

Before inclusion in the study all the subjects provided informed consent. The study was approved by the local Ethics Committee, and conformed with the principles outlined in the Declaration of Helsinki and with the GCP guidelines of the European Community.

STATISTICS

All data are presented as mean ± SD. Statistical analysis was performed using the McNemar test of symmetry and the Wilcoxon paired test. The P value < 0.05 was considered as significant.

RESULTS

The evaluation of exercise habits revealed that 17 patients (70%) maintained regular exercise activity (REA group) during a long-term follow-up (> 2 times per week), while 8 patients (30%) had a lower level of exercise activity (LEA group; < 2 times per week). After participation in the 2-WCRP, the exercise tolerance (VO_{2peak}) increased significantly (*Fig.1*).

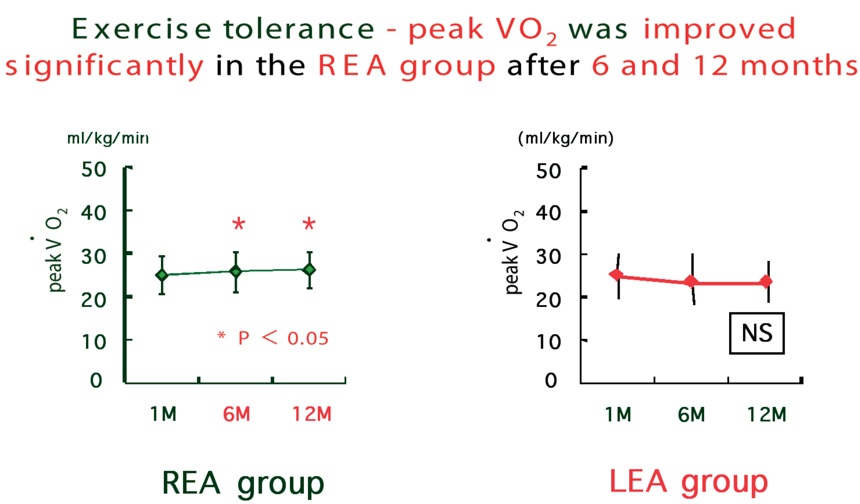

Fig. 1

The BMI and serum lipid profiles of the patients in the REA group were also significantly improved (*Figs. 2 and 3*).

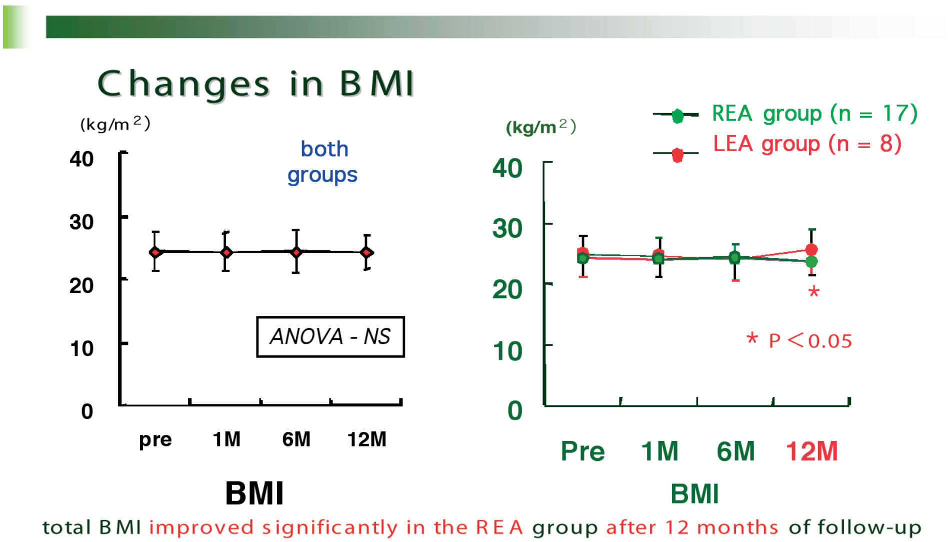

Fig. 2

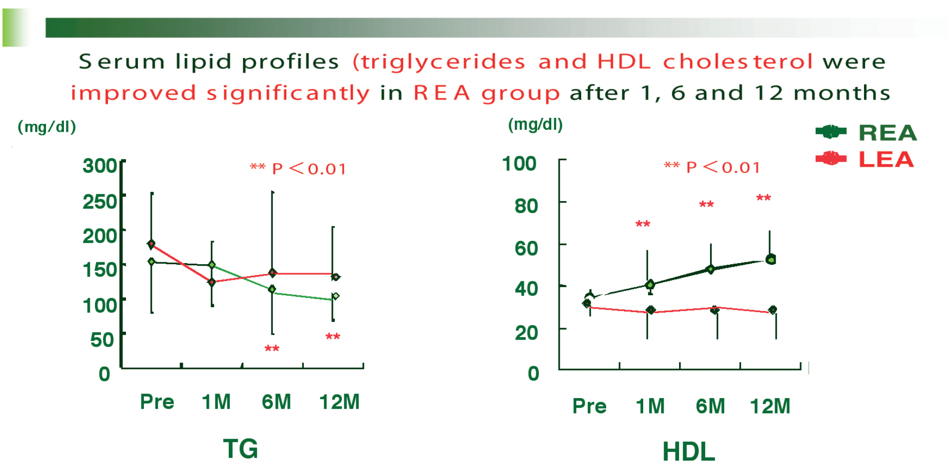

Fig. 3

At a 6-month follow-up these parameters remained improved and regular physical activity was maintained. Even at a 12-month follow-up, the lipid profiles remained improved and also the intensity and frequency of regular physical activity was kept. PICP and proinsulin remained stable at 1, 6 and 12 months' follow-up, and these changes were without statistical significance (*Figs. 4 and 5*). The parameter HOMA-R improved significantly at the long-term follow-up (*Fig. 4*).

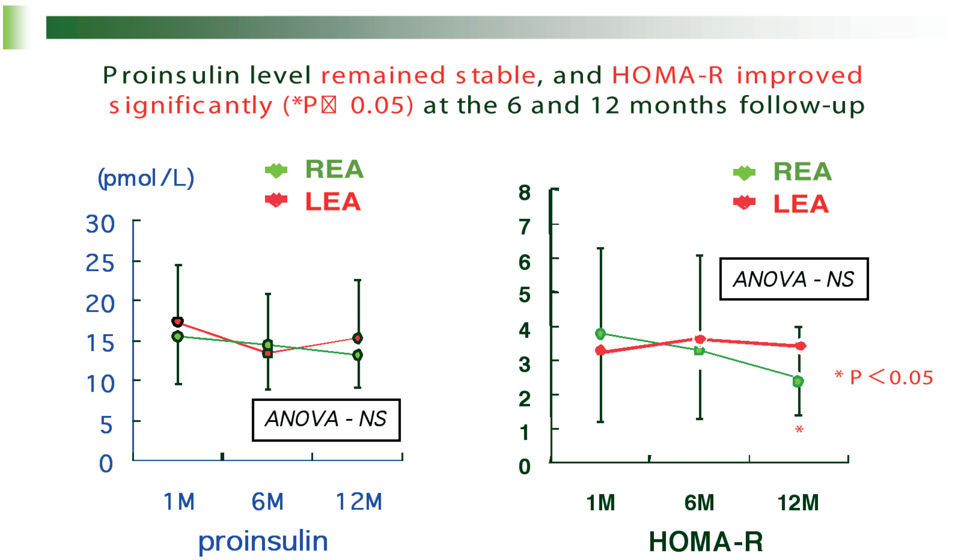

Fig. 4

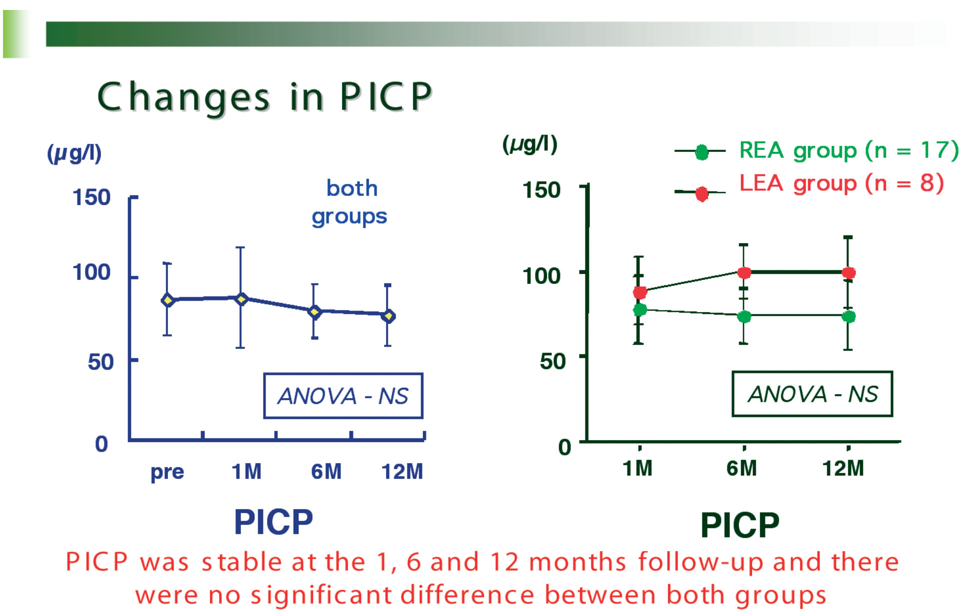

Fig. 5

The changes in HOMA-R were not related to exercise tolerance but strongly correlated with the change in BMI (*Fig. 6*).

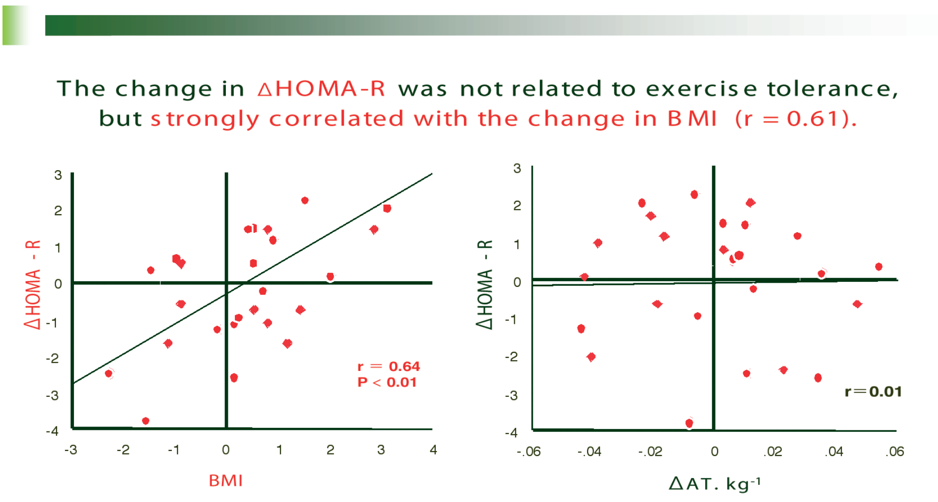

Fig. 6

DISCUSSION

One of the primary aims of cardiovascular rehabilitation is the secondary prevention of risk factors. Modified diets and routine exercise programs effectively lower the levels of LDL-C and elevate the levels of HDL-C. Exercise substantially reduces systolic and diastolic blood pressures during and after the exercise period. Exercise also contributes to weight loss and improves regulation of capillary blood glucose concentrations in patients with DM. Exercise training programs result in physiologic changes, such as improved peripheral utilization of oxygen and glycolytic-oxidative metabolic capacity, which improve the functional capacity to decrease cardiac effort. Blood flow increases during and after active exercise. Physical training elevates muscular metabolic demand, and increased collateral circulation is the presumed mechanism of symptomatic improvement. Coexisting cardiac limitations should be considered when an exercise program is planned. Gradual improvement should be seen within 3–6 months of exercise, which is a noninvasive and inexpensive activity with minimal complications and is an invaluable first-line treatment for patients with AIM. Most patients with AIM, including those with concomitant diabetes, can undertake exercise with a high level of safety. However, exercise is not without risk, and the recommendation that people with diabetes participate in physical activity is made on the basis that the benefits outweigh the risks. The American Diabetes Association developed a position statement on exercise in the management of type 1 and type 2 diabetes (*9*). These guidelines aim to minimize the possible risks of exercise for people with diabetes and recommend that particular attention be paid to appropriate screening, program design, monitoring and patient education when developing an exercise program. Nevertheless, people with AIM complicated with diabetes have a poorer short- and long-term prognosis than people without diabetes (*10*). Diabetic patients after AIM have 2x higher mortality than non-diabetics and cardiovascular death accounts for 80% of the mortality in diabetics (*11*). If no contraindications to exercise exist, the type of exercise that a person with diabetes performs is generally a matter of personal preference. Most research documenting the benefits of physical activity for people with diabetes incorporates aerobic activity such as walking, cycling, rowing, or swimming and circuit-type resistance exercise (*12, 13, 14, 15*). An area of ongoing concern is represented by the possible adverse effect of physical activity on existing complications of diabetes. It has been suggested that people with complications of diabetes are often told to refrain from exercise for fear of deterioration of the condition and development of further complications (*16*). This leads to further compromise of physical and cardiovascular conditioning. It is important to develop exercise prescriptions for individuals with diabetes complications that will result in improved participation in normal activities and psychosocial well-being while minimizing the risk of further deterioration. In addition to giving consideration to the varied physical characteristics related to exercise prescription for people with AIM and diabetes, attention should also be paid to the different psychological characteristics associated with exercise adherence. People with NIDDM report on a higher frequency of relapse from physical activity programs than the general population (*17*). They often have a low self-efficacy for changing the physical activity behavior and have little belief in the beneficial effects of physical activity (*18*). Furthermore, the most frequently cited barriers to physical activity generally relate to AIM and include physical discomfort from exercise, being too overweight to exercise and having little or no support (*19, 20*). These factors, which may reduce exercise adherence, need to be given due consideration when integrating such patients into cardiac rehabilitation. The 2-WCR program is a new multidisciplinary program involving doctors, nurses, cardiac technicians, dietitians, pharmacists and psychologists. As well as a structured exercise program with cardiac monitoring aimed at optimizing exercise capability, this approach enables the patient's concerns to be dealt with and educated by the appropriate people in the early postinfarction period.

CONCLUSION

The management of post-AMI patients presents many challenges and also many opportunities to improve prognosis. The benefits of cardiovascular rehabilitation involve the physical, emotional, and psychosocial aspects of the patient's life. With persistence, patients achieve improvements in exercise tolerance and functional capacity. A reduction in cardiac symptoms, as well as perceived stress and anxiety, occurs and leads to improved productivity and psychological well-being. Patients learn to adapt and become self-reliant as they realize that they can influence their hypertension, DM, weight, and smoking activity by means of behavioral and lifestyle modifications. With comprehensive rehabilitation, the patient's QOL improves, they return to work faster than they otherwise might, and their rates of hospital readmission are reduced. It is vital to assess risk factors such as NIDDM and to deal with them appropriately. The 2-week hospitalized phase II cardiac rehabilitation program represents a new approach in standard rehabilitation programs and patients can derive physical and psychological benefits from it. This study suggests that the 2-WCR program does not accelerate myocardial remodeling, could provide beneficial effects on the patient's physical recovery phase, and may also contribute to the prevention of the onset of other cardiac risk factors.

A c k n o w l e d g e m e n t

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