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**effect of exercise training on left ventricular remodeling in patients with myocardial infarction and possible mechanisms**

Cai M *et al*. ET on LVRM in myocardial infarctions

Meng Cai, Lei Wang, Yan-Long Ren

**Meng Cai, Lei Wang,** Department of Geriatrics, Beijing Jishuitan Hospital, Beijing 100000, China

**Yan-Long Ren,** Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China

**Author contributions:** Wang L and Ren YL conceived of the Study; Cai M, Wang L and Ren YL participated in the study and collected the clinical date; Cai M and Wang L performed the statistical analysis and drafted the manuscript; Ren YL revised the manuscript; all authors read and approved the final manuscript.

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**Corresponding author: Yan-Long Ren, MD, Professor,** Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, No. 2 Anzhen Road, Beijing 100029, China. renyanlong@yeah.net

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**Abstract**

BACKGROUND

A growing amount of evidence provides support for the hypothesis that acute myocardial infarction (AMI) patients should go through cardiopulmonary exercise testing (CPET) about 3-5 d after AMI is diagnosed, make reasonable exercising prescription, and conduct exercise training with guide.

AIM

To investigate the effect of exercise training (ET) on left ventricular systolic function and left ventricular remodeling (LVRM) and to study the possible mechanisms of LVRM by the changes of matrix metallopeptidase 9 (MMP-9) and tissue inhibitor of metalloproteinases 1 (TIMP-1) in patients with acute ST-segment elevation myocardial infarction (STEMI).

METHODS

Sixty patients with first STEMI undergoing direct peripheral component interconnect from February 2008 to [October](http://dict.cnki.net/dict_result.aspx?searchword=%e5%8d%81%e6%9c%88&tjType=sentence&style=&t=october) 2008 were randomly assigned to exercise group (*n* = 30) and control group (*n* = 30). The levels of MMP-9 and TIMP-1 were measured in all patients at 1 d, 10-14 d, 30 d and 6 mo after admission. Two-dimensional echocardiography and cardiopulmonary exercise testing were done in patients at 10-14 d and 6 mo after admission.

RESULTS

There was no significant difference in CPET at baseline between the exercise group and the control group. At 6 mo, the time of exercise, peak and anaerobic threshold values of O2 uptake and metabolic equivalents increased in both groups, but markedly increased in exercise group. At baseline, there were no significant differences in left ventricular ejection fraction (LVEF) between exercise group and control group. At 6 mo, LVEF increased in exercise group, but not in control group. At 6 mo, the percentage of positive result of LVRM was respectively 26.6% in exercise group and 52.6% in control group (*P* < 0.05). The levels of plasma MMP-9 and TIMP-1 and the ratio of MMP-9 to TIMP-1 in both groups had no significant difference at 1 d and 10-14 d after AMI, but at 30 d and 6 mo, the levels of plasma MMP-9 and TIMP-1 in the exercise group was significantly lower than those in the control group; The ratio of MMP-9 to TIMP-1 in the exercise group was significantly higher than that in the control group.

CONCLUSION

ET under supervision based on home condition in early and recovery stage of AMI can improve exercise cardiopulmonary function and prevent the LVRM. Therefore, it may reduce unfavorable remodeling response by decreasing the levels of plasma MMP-9 and TIMP-1 and adjusting the ratio of MMP-9 to TIMP-1 hereafter.

**Key Words:** Myocardial infarction; Rehabilitation; Exercise training; Ventricular remodeling; Matrix metallopeptidase 9; Tissue inhibitor of metalloproteinases 1

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**Core Tip:** Exercise training (ET) under supervision based on home condition in early and recovery stage of acute myocardial infarction can improve exercise cardiopulmonary function and prevent the left ventricular remodeling. And there was no negative effect on left ventricular ejection fraction. Therefore, it may reduce unfavorable remodeling response by decreasing the levels of plasma matrix metallopeptidase 9 (MMP-9) and tissue inhibitor of metalloproteinases 1 (TIMP-1) and adjusting the ratio of MMP-9 to TIMP-1 hereafter.

**INTRODUCTION**

Cardiac pulmonary function recovery after acute myocardial infraction (AMI) for a long time has been taking the attention of the vast numbers of medical professionals and patients[1], and now that the occurrence and development of left ventricular remodeling (LVRM) in patients is vital to AMI prognosis. A growing amount of evidence provides support for the hypothesis that AMI patients should go through cardiopulmonary exercise testing (CPET) about 3-5 d after AMI is diagnosed, make reasonable exercising prescription, and conduct exercise training (ET) with guide[2,3]. Moreover, it can improve left ventricular systolic function, exercise tolerance and quality of life, with no adverse impact on cardiac structure[4,5]. Furthermore, previously study indicated[6,7]that ET can also help slow down the development of LVRM.

Many experiments support that matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinases-1 (TIMP-1) play an important role in LVRM[8,9]. However, so far, no study has been done on relationship between rehabilitation exercise and changes of MMP-9 and TIMP-1 plasma level in AMI.

In our study, effects of ET on LVRM in patients with acute ST segment elevation myocardial infarction (STEMI) were studied and the possible mechanisms were investigated by detecting variations of MMP-9 and TIMP-1.

**MATERIALS AND METHODS**

***Participant***

Sixty patients were recruited who experienced the first occurrence of STEMI within the period from February to October 2008 in our hospital. All patients had Killip grade I-II cardiac function and received direct percutaneous coronary intervention (PCI) in the Emergency Department.

**Inclusion criteria:** AMI diagnostic criteria: Diagnostic criteria for STEMI complied with ACC/AHA Guidelines for the Management of Patients with ST Elevation Myocardial Infarction[10]. Inclusion criteria: (1) First occurrence of acute STEMI; (2) Age 35-74 years;

(3) Grade I-II (Killip’s) cardiac function: LVEF > 40%; (4) Absence of serious cardiac arrhythmia; (5) Absence of serious post-AMI complications; and (6) Willingness to receive CEPT and ET treatment and sign informed consent.

**Exclusion criteria:** (1) Suspected diagnosis of AMI, however, nonconformity to the above diagnostic criteria; (2) History of AMI and heart valve diseases and pulmonary embolisms; (3) Serious complications of acute AMI (pulmonary edema, serious cardiac arrhythmia and cardiac shock); (4) Concomitant atrial fibrillation or paced rhythm or preexcitation syndrome; (5) Concomitant serious diseases of other systems (*e.g.*, human immunodeficiency virus infection, malignant tumor, serious primary hepatic or renal diseases and chronic lung diseases); (6) Inability to exercise and unwillingness to cooperate; (7) Unwillingness or inability to accept PCI; and (8) Unwillingness to sign informed consent.

Standard secondary prevention and treatment of coronary heart disease were administered in all patients according to Guidelines for the Management of Acute Coronary Syndrome.

***Study methods***

**Randomization:** Sixty patients were randomized in a 1:1 ratio to either rehabilitation exercise group (rehabilitation exercise guidance was provided) (*n* = 30) or control group (no rehabilitation exercise guidance was provided) (*n* = 30). Routine post-AMI secondary prevention medications were given regularly to patients in both rehabilitation exercise group and control group.

**Study protocol:** (1) Emergency PCI was performed after admission; (2) Blood samples were drawn immediately, on day 10-14, day 30 and in 6 mo after admission; plasma was separated and stored in a -80 oC freezer for plasma MMP-9 and TIMP-1 tests; (3) Echocardiography was performed on day 10-14 and in 6 mo after AMI; (4) CPET was performed on day 10-14 after AMI and again in 6 mo; and (5) After discharge, the patients routinely took secondary prevention medications of coronary heart disease. Patients in the rehabilitation exercise group took regular walking exercise. Exercise time, intensity and frequency depend on the exercise prescription. Family guidance was provided to patients in this group and the exercise prescription was adjusted in week 1. Patients in the control group were not given any exercise prescription and their exercise were not intervened. For patients in both groups, telephone follow-up was performed every two weeks and outpatient follow-up monthly until the end of 6 mo. See the protocol operation flowsheet (Figure 1) and the follow-up observation schedule (Table 1) for details.

***MMP-9 and TIMP-1 assay***

Three mL of fasting venous blood was drawn in the morning and added into a vacuum blood collection tube containing 10% EDTA, mixed well and centrifugated at 3000 rpm at 4 °C for 10 min. Twenty μL of the supernatant was retained and preserved in a -80 °C freezer. ELISA was carried out by special personnel blinded using kits manufactured by BIOSAURCE.

***Evaluation of ventricular remodeling***

Evaluation of ventricular remodeling was performed by experienced and professional echocardiography physicians on day 10-14 and in month 6 after the AMI onset.

Routine ultrasound and Doppler tissue images were collected in the long and short axis views of left ventricle, apical four-chamber view, left ventricular two-chamber view and the apical long axis view using a VIVID-I echocardiography system manufactured by GE (United States).

LVEF was evaluated using Biplane Simpson’s method as follows:

LVEF = (LVEDD - LVESD)/LVEDV × 100% (Left ventricular end-diastolic dimension as LVEDD, left ventricular end-systolic dimension as LVESD, left ventricular end-diastolic volume as LVEDV).

Biplane Simpson method was performed to measure LVESV and LVEDV. LVESV and LVEDV were measured on day 10-14 (LVESV1 and LVEDV1) and in 6 mo (LVESV2 and LVEDV2) after AMI. If both LVESV2/LVESV1 and LVEDV2/LVEDV1 were higher than 1.1 or either one was higher than 1.2 (*i.e.* increased by 10%-20% as compared to the baseline value), left ventricular dilation would be considered.

***Preparation of CPET and exercise prescription***

The measurement was performed by professional rehabilitation physicians.

CPET was performed using a MAX-II cardiopulmonary exercise device manufactured by PHYSIO DYNE (United States).

Graded treadmill exercise test, 3 min per grade, was carried out using the modified Bruce protocol. The patient’s movement electrocardiogram, gaseous metabolism changes and vital signs were monitored, and the spontaneous symptoms were inquired about any time.

The patient’s exercise time, peak oxygen uptake, peak metabolic equivalent, anaerobic threshold and metabolic equivalent at anaerobic threshold were measured.

The evaluation was terminated in any of the following circumstances: (1) The patient developed instability of gait, weakness of bilateral lower limbs, dizziness, pale complexion, fatigue, short breath and asthma or the patient asked for rest; (2) The systolic pressure increased by less than 10 mmHg or decreased as compared to the level at rest; the blood pressure increased abnormally, and the systolic pressure was higher than 230 mmHg; (3) Higher than grade II angina (Canadian angina grading); (4) Malignant arrhythmia occurred, including ventricular tachycardia, multifocal premature ventricular contraction or higher than second-degree type II atrioventricular block, sinus arrest, *etc*; (5) Myocardial ischemic changes, *i.e.* transient ST-segment depression ≥ 0.5mm in 2 continuous limb leads or chest leads; or transient ST segment elevation ≥ 1mm in 2 continuous leads (NIZ) (or ST segment descent of V1 or V2 ≥ 1 mm); (6) Achievement of the target heart rate, *i.e.* 70%-80% of the maximum heart rate (maximum heart rate = 220 - age); and (7) Respiration exchange rate ≥ 1.1.

***Preparation of the exercise prescription***

Individualized exercise prescriptions were prepared for patients in the rehabilitation exercise group by rehabilitation physicians according to CPET results before discharge. The exercise method was walking, and the exercise time, intensity and frequency were implemented per the exercise prescription. In addition to walking rate prepared by the rehabilitation physician, patient’s self-felt fatigue was considered for controlling the exercise intensity. Patient was asked to exercise at the anaerobic threshold level or a slightly lower level. Patients in the control group were not given the exercise prescription or any exercise guidance and were allowed to arrange their daily activities themselves.

***Statistical analysis***

Statistical analysis was performed using SPSS13.0 software. Measurement data were presented as mean ± SD. For comparison of continuous variables between two groups, *t* test was carried out. *P* values < 0.05 were considered to be statistically significant.

**RESULTS**

***Clinical data***

A total of 60 male patients (mean age, 56 ± 8 years) were enrolled in this study, 30 in each group.

Tables 2 presents the patients’ characteristics at baseline. Patients in the two groups were not statistically different in age, myocardial infarction area, history of smoking, concomitant diseases (*P* > 0.05). All patients accepted standard secondary prevention and treatment of coronary heart disease using aspirin, clopidogrel, statins, angiotensin-converting enzyme inhibitor(ACEI)/angiotensinreceptorblocker(ARB), b-receptor blocker, *etc.*, with no statistical difference between the two groups (*P* > 0.05). Data of the two groups were comparable (Table 2).

***Cardiopulmonary exercise function***

No significant difference was found between the two groups with respect to baseline exercise time, anaerobic threshold, metabolic equivalent at anaerobic threshold, peak oxygen uptake and peak metabolic equivalent on day 10-14 after admission (*P* > 0.05). the above exercise indicators significantly increased at the follow-up visit in month 6 as compared to baseline values (*P* < 0.05-0.01) (Table 3), the increased being more pronounced in the rehabilitation group (*P* < 0.05-0.01) (Table 4) and the differences being statistically significant.

***Echocardiography results***

LVRM positive indicators: LVRM was considered positive when both LVEDV2/LVEDV1 and LVESV2/LVESV1 were higher than 1.1 or either one was higher than 1.2[4]. The positive rate in the control group was significantly higher than that in the rehabilitation exercise group (52.6% *vs* 26.6%, P<0.01).

LVEF: Baseline values of LVEF of the two groups were not significantly different. LVEF of the rehabilitation exercise group at the follow-up visit in month 6 was higher than but not statistically significantly different from the baseline values (58.4% ± 8.6% *vs* 57.73% ± 7.89%, *P* > 0.05), and LVEF of the control group at the follow-up visit in month 6 was lower than but not statistically significantly different from the baseline values (53% ± 8.86% *vs* 56.1% ± 7.98%, *P* > 0.05). LVEF of the rehabilitation exercise group in month 6 was significantly higher than that of the control group (58.4% ± 8.6% *vs* 53% ± 8.86%, *P* < 0.01) (Table 5).

***MMP-9 and TIMP-1***

Plasma MMP-9 Level of patients in the two groups was not significantly different immediately after AMI and on day 10-14 (*P* > 0.05). It decreased in both groups on day 30 and at month 6, with the decreased being more pronounced in the rehabilitation exercise group (*P* < 0.05).

Plasma TIMP-1 Level of patients in the two groups was not significantly different immediately after AMI and on day 10-14 (*P* > 0.05). It increased in both groups on day 30 and at month 6, with the increased being less pronounced in the rehabilitation exercise group (*P* < 0.05).

MMP-9/TIMP-1 ratio of patients in the two groups was not significantly different immediately after AMI and on day 10-14 (*P* > 0.05). The MMP-9/TIMP-1 ratio of the rehabilitation exercise group was higher than that of the control group on day 30 and at month 6 (*P* < 0.05), the difference being statistically significant (Table 6).

**DISCUSSION**

***Effects of ET on post-AMI LVRM***

This study examines the effect of exercise training on LVRM in patients with STEMI. Ultrasonic cardiogram (UCG) shows that LVEF of the ET group was significantly higher than that of the control group, indicating that guided rehabilitation exercise in early stage of AMI could maintain patient’s left ventricular systolic function, which is consistent with findings in previous studies[11,12]. In contrast with decreasing of cardiac function in control group, slightly increasing was observed in ET group, possibly for the following reasons. (1) The patients’ LVRM was mild; (2) Exercise increased myocardial elastic recoil, decreased resting heart rate and prolonged left ventricular filling time in AMI patients, thereby enlarged cardiac output; and (3) Exercise reduced poor wall motion and increased left ventricular systolic synchrony.

Consistent with previous reports[13-19], ET resulted in significantly lower LVRM positive rate (26.6% in ET group *vs* 52.6% in control group) using LVEDV2/LVEDV1 and LVESV2/LVESV1 ratio as LVRM positive indicators, suggesting that LVRM was more apparent in the control group than in the ET group and ET may, to a certain extent, limit LVRM.

***Effects of ET on plasma MMP-9 and TIMP-1 of patients with AMI***

The study results showed that plasma MMP-9, TIMP-1 and MMP-9/TIMP-1 Levels of patients in the ET group and the control group were not significantly different immediately after AMI and on day 10-14. On day 30 and at month 6, Compared with control group, plasma MMP-9 and TIMP-1 Levels were significantly lower and MMP-9/TIMP-1 ratio was significantly higher at 30 d and 6 mo in ET group, in which positive LVRM rate was high, indicating that high plasma MMP-9 and TIMP-1 Levels and low MMP-9/TIMP-1 ratio in post-AMI recovery period all had adverse effects on LVRM.

Extracellular collagen matrix (ECM) remodeling was found in recent studies to lead to myocardial fibrosis and progressive ventricular dilatation and to result in heart failure[20-22]. It is currently believed that ECM plays a very important role in LVRM and that ECM synthesis-degradation imbalance is associated with development and progression of LVRM. Among ECM secreted by fibroblasts, collagen, mainly type I and type III collagen, accounts for the major part. About 85% of the collagen is type I, which is responsible for myocardial strength and endurance, and about 11% is type III, which is responsible for myocardial elastic recoil. MMP-9 is a gelatinase, which mainly degrades type I and type III collagen. TIMP-1 is a natural inhibitor of MMP-9 and promotes synthesis and deposition of collagen. MMP-9/TIMP-1 imbalance is thought to be able to further enhance remodeling progression[23]. Kelly *et al*[24] studied variation of post-AMI MMP-9 Levels and found that increased in MMP-9 Level at early stage of AMI was positively correlated with leukocyte and neutrophil levels, suggesting that plaque rupture and increased in inflammatory factors promoted release of MMP-9, which intensified collagen degradation and contributed to development and progression of early-phase LVRM. At the subsequent 90-d follow-up, MMP-9 curve turned from a high peak in the acute phase into a flat top, which had protective effect on left ventricular function. According to the analysis, excessively high MMP-9 Levels enhanced collagen degradation whereas excessively high TIMP-1 Level led to excessive decomposition of collagen. Only when an appropriate ratio is maintained can the normal shape and function of cardiac ventricles be kept.

***Plasma MMP-9 and TIMP-1 level***

Significantly more deceased in plasma MMP-9 Level and less increased in plasma TIMP-1 Level were observed in ET patients on day 30 and at month 6, as compared to control patients, indicating that although collagen synthesis and deposition were inevitable in late stage of AMI, rehabilitation exercise might delay LVRM occurrence and lower positive LVRM rate by inhibiting excessive degradation and reducing excessive synthesis and deposition of collagen.

***MMP-9/TIMP-1***

Although the mechanism of LVRM is still not completely known, MMP-9/TIMP-1 imbalance is suggested as an important reason for ECM remodeling, as also shown in the present study[25]. MMP-9/TIMP-1 ratio of the ET group was significantly higher than control group; namely, the proportion of TIMP-1 in plasma of patients in the ET group was lower. Evidence is available that high concentration of TIMP-1 in plasma may be increased the activity of fibroblasts and enhance collagen synthesis and deposition[26]. It is thus deduced that ET has decreased the concentration of TIMP-1 in plasma, adjusted the proportions of MMP-9 and TIMP-1 and reduced excessive collagen synthesis and deposition in late stage of AMI. The effect of ET on post-AMI LVRM of patients is possibly related to its action in adjusting the MMP-9/TIMP-1 ratio.

However, this study has the following limitations: (1) Although the principle of randomization was followed as far as possible in design and implementation of the trial, given the relatively small sample size, some artificial factors such as patients’ individual exercise habits, working time, *etc.* could not be excluded, leading to randomness reduction and selection bias; (2) Rehabilitation exercise was home based. Although telephone follow-up was performed once every two weeks and outpatient follow-up once per month, the problem of unfixed exercise intensity of the ET group still could not be avoided, leading to errors in study results; (3) The exercise intensity administered in the study was low and the follow-up duration was short. Therefore, individual exercise habits count for an important part of exercise intensity, which might lead to errors in study results; (4) Regarding exercise indicators, the first UCG examination was performed on day 10-14 after AMI and the result was used as the baseline UCG value. The effect of post-AMI early-stage LVRM on ventricular structure and function was neglected, which may have certain influence on the study results; and (5) Due to limited fund and patients’ reasons, cardiac structure and function were not evaluated using heart MRI or ventriculography. UCG evaluation is subject to subjective influence.

**CONCLUSION**

This study draws a conclusion that early rehabilitation exercise after AMI can, to some extent, inhibit progression of LVRM and maintain left ventricular function. Moreover, the post-AMI LVRM limitation by ET is likely due to its action in lowering MMP-9 and TIMP-1 Levels and adjusting MMP-9/TIMP-1 ratio.

**ARTICLE HIGHLIGHTS**

***Research background***

A growing amount of evidence provides support for the hypothesis that acute myocardial infarction (AMI) patients should go through cardiopulmonary exercise testing about 3-5 d after AMI is diagnosed, make reasonable exercising prescription, and conduct exercise training with guide.

***Research motivation***

To investigate the effect of exercise training on left ventricular systolic function and left ventricular remodeling and to study the possible mechanisms of left ventricular remodeling (LVRM) by the changes of matrix metallopeptidase 9 (MMP-9) and tissue inhibitor of metalloproteinases 1 (TIMP-1) in patients with acute ST-segment elevation myocardial infarction (STEMI).

***Research objectives***

60 patients with first STEMI undergoing direct percutaneous coronary intervention from February 2008 to [October](http://dict.cnki.net/dict_result.aspx?searchword=%e5%8d%81%e6%9c%88&tjType=sentence&style=&t=october) 2008 were randomly assigned to exercise group (*n* = 30) and control group (*n* = 30).

***Research methods***

The levels of MMP-9 and TIMP-1 were measured in all patients at 1 d, 10-14 d, 30 d and 6 mo after admission. Two-dimensional echocardiography and cardiopulmonary exercise testing were done in patients at 10-14 d and 6 mo after admission.

***Research results***

In cardiopulmonary exercise testing of the two group, at 6 mo, the time of exercise, peak and anaerobic threshold values of O2 uptake and metabolic equivalents increased in both groups, but markedly increased in exercise group than those in control one. There was no significant differences in LVESV, LVEDV and left ventricular ejection fraction (LVEF) between the two group, at 6 mo, LVEF increased in exercise group, but not in control group. Change in LVEF in exercise group [is significantly](http://dict.cnki.net/dict_result.aspx?searchword=%e6%9b%b4%e6%98%be%e8%91%97&tjType=sentence&style=&t=more+significantly) higher than in control group. At 6 mo, the percentage of positive result of LVRM was respectively 26.6% in exercise group and 52.6% in control group (*P* < 0.05). The levels of plasma MMP-9 and TIMP-1 and the ratio of MMP-9 to TIMP-1 in both groups had no significant difference at 1day and 10-14 days after AMI, but at 30 days and 6 mo, the levels of plasma MMP-9 and TIMP-1 in the exercise group was significantly lower than those in the control group; The ratio of MMP-9 to TIMP-1 in the exercise group was significantly higher than that in the control group.

***Research conclusions***

exercise training under supervision based on home condition in early and recovery stage of AMI can improve exercise cardiopulmonary function and prevent the LVRM. Therefore, it may reduce unfavorable remodeling response by decreasing the levels of plasma MMP-9 and TIMP-1 and adjusting the ratio of MMP-9 to TIMP-1 hereafter.

***Research perspectives***

Randomized controlled trial design for investigate the effect of exercise training on left ventricular systolic function and left ventricular remodeling and to study the possible mechanisms of LVRM in patients with acute STEMI.

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**Footnotes**

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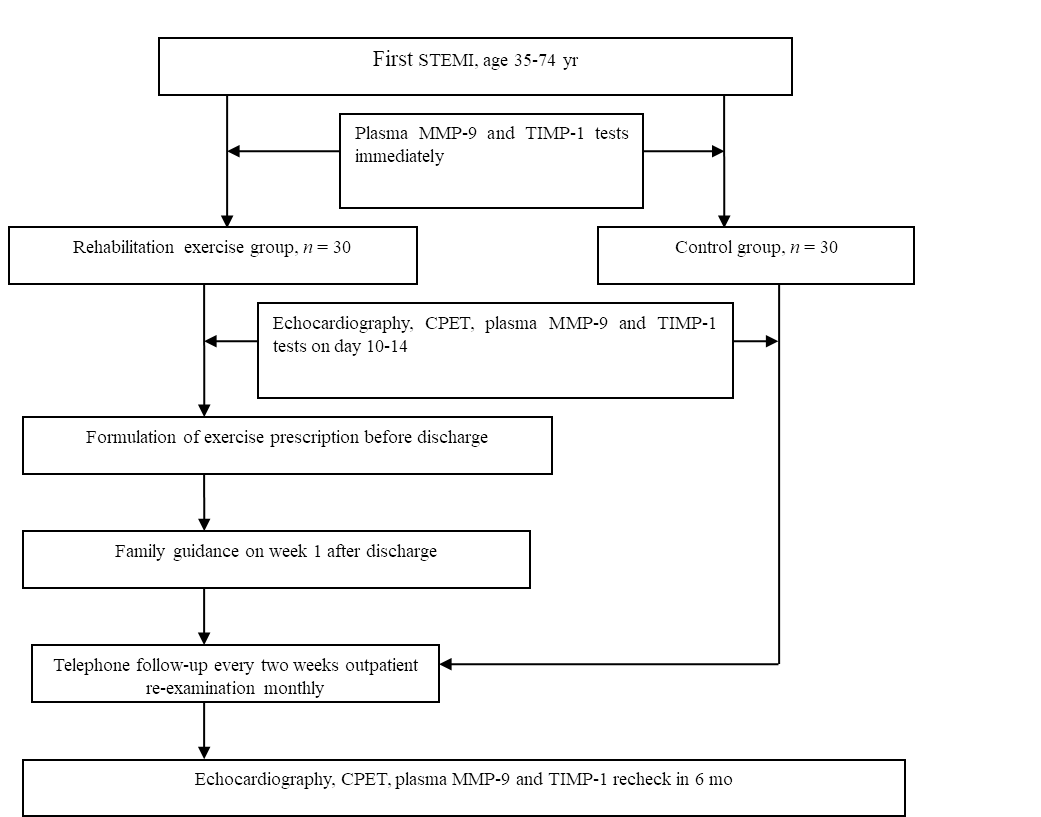
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**Figure Legends**



**Figure 1 Protocol operation flowsheet.** MMP-9: Matrix metallopeptidase 9; TIMP-1: Tissue inhibitor of metalloproteinases 1; CPET: Cardiopulmonary exercise testing;

**Table 1 Follow-up and examination schedule**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Items** | **Immediately** | **Day 10-14** | **Follow-up (mo)** | |
| **1** | **6** |
| Sign informed consent form | √ |  |  |  |
| Medical history | √ |  |  |  |
| Physical examination | √ |  | √ | √ |
| MMP-9 | √ | √ | √ | √ |
| TIMP-1 | √ | √ | √ | √ |
| Transthoracic echocardiography |  | √ |  | √ |
| CPET |  | √ |  | √ |
| Concomitant medication | √ | √ | √ | √ |

MMP-9: Matrix metalloproteinase-9; TIMP-1: Tissue inhibitor of metalloproteinases-1; CPET: Cardiopulmonary exercise testing.

**Table 2 Patients characteristics at randomization to intervention and control groups, *n* (%)**

|  |  |  |
| --- | --- | --- |
|  | **Rehabilitation exercise group** | **Control group** |
| ***n* = 30** | ***n* = 30** |
| Age (yr) | 55 ± 9 | 58 ± 8 |
| Infarction area, *n* (%) |  |  |
| Anterior AMI | 18 (60) | 15 (50) |
| Non-anterior AMI | 12 (40) | 15 (50) |
| History of smoking, *n* (%) | 28 (93.3) | 24 (80) |
| Concomitant diseases, *n* (%) |  |  |
| Diabetic mellitus | 2 (6.7) | 3 (10) |
| Hypertension | 5 (16.6) | 4 (13.3) |
| Hypercholesteremia | 3 (10) | 4 (13.3) |
| Drug therapy, *n* (%) |  |  |
| Aspirin | 30 (100) | 30 (100) |
| Clopidogrel | 29 (96.7) | 28 (93.3) |
| β-receptor blocker | 25 (83.3) | 28 (93.3) |
| ACEI/ARB | 29 (96.7) | 27 (90) |
| Statins | 28 (93.3) | 29 (96.7) |

AMI: Acute myocardial infraction; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensinreceptorblocker.

**Table 3 Cardiopulmonary exercise testing in rehabilitation exercise and control group**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Baseline** | | **6 mo after the onset of myocardial infarction** | |
| **Control group (*n* = 30)** | **Exercise group (*n* = 30)** | **Control group (*n* = 30)** | **Exercise group (*n* = 30)** |
| Exercise time (min) | 8.19 ± 2.55 | 8.11 ± 2.69 | 9.37 ± 2.48a | 11.89 ± 2.34b |
| Anaerobic threshold (mL/min) | 958.64 ± 298.65 | 977.23 ± 288.33 | 1235.88 ± 347.56b | 1388.07 ± 355.67b |
| Metabolic equivalent at anaerobic threshold | 3.76 ± 1.05 | 3.89 ± 1.01 | 4.58 ± 1.06b | 5.20 ± 1.19b |
| Peak oxygen uptake (mL/min) | 1272.37 ± 346.85 | 1267.35 ± 322.84 | 1507.88 ± 398.46b | 1664.67 ± 365.35b |
| Peak metabolic equivalent | 4.98 ± 1.03 | 4.87 ± 0.98 | 5.62 ± 1.01b | 6.38 ± 1.09b |

Comparison of the second cardiopulmonary exercise testing (CPET) and the first CPET of the same group, a*P* < 0.05，b*P* < 0.01. CPET: Cardiopulmonary exercise testing.

**Table 4 Differences of results of the two cardiopulmonary exercise testing of patients in the two groups**

|  |  |  |
| --- | --- | --- |
|  | **Changes of the two tests** | |
| **Control group (*n* = 30)** | **Exercise group (*n* = 30)** |
| Exercise time (min) | 1.13 ± 1.69 | 3.41 ± 2.88b |
| Anaerobic threshold (mL/min) | 252.13 ± 233.66 | 405.36 ± 207.89a |
| Metabolic equivalent at anaerobic threshold | 0.82 ± 0.71 | 1.46 ± 0.82b |
| Peak oxygen uptake (mL/min) | 232.73 ± 254.96 | 402.88 ± 258.35a |
| Peak metabolic equivalent | 0.77 ± 0.86 | 1.49 ± 0.93b |

Intergroup comparison, a*P* < 0.05, b*P* < 0.01. CPET: Cardiopulmonary exercise testing.

**Table 5 Echocardiography results in rehabilitation exercise and control group**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Baseline values** | | **6 mo** | |
|  | Control group (*n* = 30) | Rehabilitation exercise group (*n* = 30) | Control group (*n* = 30) | Rehabilitation exercise group (*n* = 30) |
| LVEF | 56.1% ± 7.98% | 57.73% ± 7.89% | 53% ± 8.86% | 58.4% ± 8.6%a |
| LVRM positive results | |  | 52.60% | 26.6%a |

Intergroup comparison, a*P* < 0.01. LVEF: Left ventricular ejection fraction; LVRM: Left ventricular remodeling.

**Table 6 Comparison of matrix metalloproteinase-9, tissue inhibitor of metalloproteinases-1 and matrix metalloproteinase-9/tissue inhibitor of metalloproteinases-1 in rehabilitation exercise and control group at different time points**

|  |  |  |  |
| --- | --- | --- | --- |
| **Items** | **Time** | **Rehabilitation exercise group (*n* = 30)** | **Control group (*n* = 30)** |
| MMP-9 (ng/mL) | Immediately | 6.7 ± 2.97 | 6.8 ± 3.12 |
|  | Day 10-14 | 8.2 ± 2.5 | 8.1 ± 2.55 |
|  | Day 30 | 4.2 ± 1.88 | 5.0 ± 1.98a |
|  | 6 mo | 4.0 ± 1.87 | 5.1 ± 2.02a |
| TIMP-1 (ng/mL) | Immediately | 2.1 ± 0.52 | 2.1 ± 0.51 |
|  | Day 10-14 | 2.4 ± 0.71 | 2.5 ± 0.65 |
|  | Day 30 | 2.8 ± 0.67 | 3.0 ± 0.55a |
|  | 6 mo | 2.7 ± 0.56 | 2.98 ± 0.51a |
| MMP-9/TIMP-1 | Immediately | 3.05 ± 1.05 | 2.98 ± 1.03 |
|  | Day 10-14 | 4.21 ± 1.58 | 4.11 ± 1.44 |
|  | Day 30 | 1.78 ± 0.88 | 1.25 ± 0.66a |
|  | 6 mo | 1.58 ± 0.67 | 1.22 ± 0.58a |

Intergroup comparison, a*P* < 0.05. MMP-9: Matrix metalloproteinase-9; TIMP-1: Tissue inhibitor of metalloproteinases-1.