

Efficacy of an early home-based cardiac rehabilitation program for patients after acute myocardial infarction

A three-dimensional speckle tracking echocardiography randomized trial

Lin Xu, PhD^a, Zekun Cai, MD^{a,b}, Meihua Xiong, MD^a, Yekuo Li, PhD^c, Guoying Li, MD^c, Yu Deng^a, William Kongto Hau, PhD^d, Shuo Li, PhD^e, Wenhua Huang^{f,*}, Jian Qiu, MD^{a,*}

Abstract

Background: The effect of an early short-term home-based cardiac rehabilitation (CR) program on ventricular function in acute myocardial infarction (AMI) patients is not yet clear. The purpose of this study was to evaluate the efficacy of our CR program on the improvement of myocardial function using three-dimensional speckle tracking echocardiography (3D-STE) in AMI patients.

Methods: Fifty-two AMI patients were randomly assigned to 2 groups after discharge: the rehabilitation group, which participated in an early, home-based CR program, and the control group, which received only usual care. All subjects in both groups underwent 3D-STE examinations of the left ventricle within 48 hours of percutaneous coronary intervention and again 4 weeks after discharge. Global longitudinal strain (GLS), global radial strain (GRS), global area strain (GAS), global circumferential strain (GCS), left ventricular ejection fraction (LVEF), and segmental strains were computed. The CR program was initially conducted with supervised inpatient training, followed by an unsupervised home-based training program during a 4-week follow-up.

Results: We obtained segmental strains from 832 segments, of which 319 were defined as interventional segments, 179 as ischemic segments, and the remaining segments as normal segments. At the 4-week follow-up, when controlling for baseline values, the rehabilitation group showed significant improvements in GLS, GRS, GCS, GAS, LVEF, and in all of the segmental strains of the 3 subgroups compared with the control group ($P < 0.05$).

Conclusion: Our study suggests that an early, home-based CR program can greatly improve the ventricular function of AMI patients in a short period of time.

Abbreviations: 2D-STE = two-dimensional speckle tracking echocardiography, 3D-STE = three-dimensional speckle tracking echocardiography, AMI = acute myocardial infarction, BMI = body mass index, CAG = coronary angiography, CO = cardiac output, CR = cardiac rehabilitation, DBP = diastolic blood pressure, GAS = global area strain, GCS = global circumferential strain, GLS = global longitudinal strain, GRS = global radial strain, HR = heart rate, HRmax = maximum heart rate, LV = left ventricular, LVEDM = left-ventricular end-diastolic mass, LVEDV = left ventricular end-diastolic volume, LVEF = left ventricular ejection fraction, LVESM = left-ventricular end-systolic mass, LVESV = left ventricular end-systolic volume, METs = metabolic equivalents, PCI = percutaneous coronary intervention, PEB = perceived exertion Borg, SBP = systolic blood pressure, SV = stroke volume.

Keywords: cardiac rehabilitation, home-based, strain, ventricular function

Editor: Massimo Sacchetti.

Clinical Trial Registration: NCT 02584192.

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and the interpretations discussed.

LX, ZC and MX have contributed equally to this work.

This research was supported by the Science and Technology Planning Project of Guangdong Province (grant numbers 2013A022100036, 2014A020212257), the Shenzhen Innovation Funding (grant numbers JCYJ20140901003939025, CXZZ20140901004122087), and Guangdong Image-guided Therapy Innovation Team (grant number 2011S013).

The authors have no conflicts of interest to disclose.

^a Department of Cardiology, Guangzhou General Hospital of Guangzhou Military Region, PLA, ^b The Second Affiliated Hospital of Shantou University Medical College, Shantou, China, ^c Department of Ultrasound, Guangzhou General Hospital of Guangzhou Military Region, PLA, Guangzhou, ^d LiKaShing Faculty of Medicine, Institute of Cardiovascular Medicine and Research, University of Hong Kong, Hong Kong, China, ^e Department of Medical Imaging, Department of Medical Biophysics, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON, Canada, ^f School of Basic Medical Science, Southern Medical University, Guangzhou, China.

* Correspondence: Wenhua Huang, School of Basic Medical Science, Southern Medical University, Guangzhou, China (e-mail: hwh@fimmu.com); Jian Qiu, Guangzhou General Hospital of Guangzhou Military Region, PLA, Guangzhou, 510010, China (e-mail: xxgnkj@yaeh.net).

Copyright © 2016 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0, which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author.

Medicine (2016) 95:52(e5638)

Received: 5 April 2016 / Received in final form: 14 August 2016 / Accepted: 21 November 2016

<http://dx.doi.org/10.1097/MD.0000000000005638>

1. Introduction

Significant efforts, such as early revascularization therapy and secondary prevention after acute myocardial infarction (AMI), have been made to improve the quality of life of AMI patients. However, the outcomes of these efforts are still unsatisfactory.^[1] The importance of cardiac rehabilitation (CR) has gradually been recognized as part of secondary prevention for AMI patients who have undergone percutaneous coronary intervention (PCI). CR is defined as a way “to help patients regain a place in society as near normal as possible following a cardiac event.”^[2] CR programs for AMI patients have evolved into comprehensive, professional programs that include advice and support for lifestyle changes to control cardiovascular risk factors. Currently, it is widely accepted that a CR program plays an important role in improving the risk factor management and prognosis of AMI patients.^[3,4] However, in routine clinical practice, the conventional left ventricular ejection fraction measurement always failed to precisely assess the improvement of segmental cardiac function.

Echocardiography is a powerful, real-time imaging tool used to evaluate left ventricular (LV) function. Recently, speckle-tracking echocardiography (STE) has been used to quantitatively evaluate the LV global and segmental myocardial function. Previous studies have shown the value of longitudinal, circumferential, and radial strains derived from 2D-STE for the identification of reversible myocardial function.^[5,6] Other studies have shown that strain and strain rate in the assessment of myocardial systolic dysfunction were superior to conventional wall motion analysis and LVEF.^[7,8] The recently developed real-time, three-dimensional (3D) STE imaging can analyze the entire left ventricle spatially and temporally.^[9]

However, few studies to date have used 3D-STE to assess the segmental and global LV function of AMI patients in an early, short-term, home-based CR program. Furthermore, we speculate that the 3D-STE can be more valuable and sensitive to evaluate the segmental cardiac function for a short-term CR program. The purpose of our study, therefore, was to assess the efficacy of an early, short-term CR program to improve the global and segmental myocardial function of AMI patients after PCI.

2. Methods

2.1. Study population

Fifty-two AMI patients (mean age 55.6 ± 9.2 years, 84.6% men) admitted to the General Hospital of Guangzhou Military Command of People's Liberation Army between November 2014 and January 2015 were enrolled in our study. The participants in this study met the following inclusion criteria: between 18 and 65 years of age with a confirmed ST-elevation AMI diagnosis,^[10] suitable for the CR program, and undergoing PCI at admission to the hospital. However, participants with known ischemic heart disease, recurrent angina, valvular heart disease, intraventricular conduction disturbances, malignant arrhythmia, cardiac shock, or poor echocardiographic conditions that would preclude an STE examination were excluded. Participants with a neuromuscular disease diagnosis, or hemodynamic instability; those with an inability to perform exercise training or poor medication adherence or nonperformance of the CR program were excluded. Patients with chronic lung disease or other physical disease were also excluded. Two cardiovascular specialists, Dr JQ and Dr JM, with more than 20 years of clinical experience were responsible for the selection of suitable patients.

Informed consent was obtained from each patient. The study protocol conforms to the ethical guidelines of Helsinki Declaration as reflected in a priori approval by the institution's human research committee of the General Hospital of Guangzhou Military Command of People's Liberation Army.

2.2. Study design

After admission, participants were randomized into 1 of 2 groups: the rehabilitation group (RG) ($n=26$), who were instructed to participate in an early, home-based CR program, and the control group (CG) ($n=26$), who received only usual care. A random sequence using random number tables was generated by a cardiologist who was blinded to the study. The allocations were prepared by numbered, opaque, sealed envelopes before the trial. Figure 1 shows the flow chart of the study design.

2.3. Clinical information

The clinical information about the participants was recorded within the first 12 hours of admission and included age; gender; and cardiovascular risk factors, such as smoking, hypertension, diabetes, hyperlipidemia, and chronic renal failure. Clinical data, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), time from onset to admission (hour), and door-to-balloon time (minute), were then collected. After 4-week CR program, HR, SBP, DBP, and BMI were measured again.

2.4. Angiographic assessment

All participants underwent coronary angiography (CAG) and received dual-antiplatelet therapy (aspirin and clopidogrel) before PCI. The coronary angiogram was performed with a digital subtraction angiography machine (Allura Xper FD20, Philips Medical Systems Nederland B.V., Best, The Netherlands). The interventions were independently carried out by 10 years of experienced interventional cardiologists who were blinded to the study protocol and patient characteristics. The SYNTAX scores were calculated after the angiographic procedure using the online calculator, version 2.11. For segmental strain assessment, the myocardium was divided into several segments based on the results of the CAG. The perfusion region of the PCI location and the distal part from stented segments was defined as the interventional segment; the perfusion region of coronary artery stenosis $\geq 50\%$ in diameter without intervention and its distal part was defined as the ischemic segments, and the remaining segments were defined as normal segments (Fig. 2).

2.5. Echocardiographic image acquisition and analyses

All of the echocardiographic image acquisitions were performed in all participants at baseline, within 48 hours after PCI and at a 4-week follow-up. The examinations were carried out independently by two 8 years of experienced examiners who were blinded to the study protocol and patient characteristics. Echocardiographic data were acquired with an ultrasound Vivid E9 system (GE Vingmed Ultrasound AS, Horten, Norway), which was equipped with one 2D 3.5-MHz transducer (M5S-D), one 3D 3.5-MHz transducer (4C-D), off-line speckle-tracking analysis software, and 1 background processing workstation (EchPAC BT 11.1.0, GE Medical System, Horten, Norway). All subjects were connected to the ECG and were maintained in the left lateral

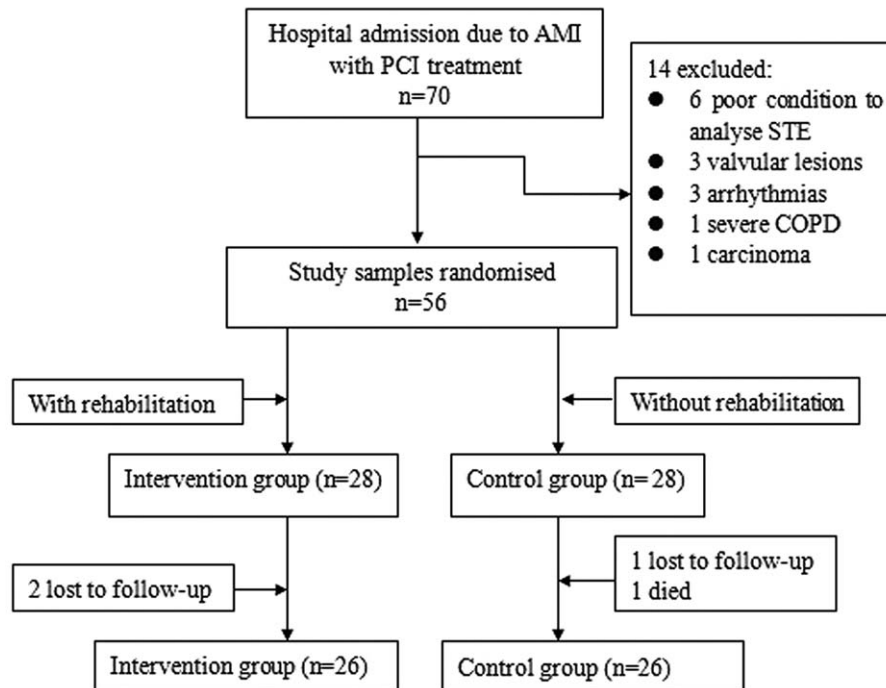


Figure 1. Flow chart of patient enrolment.

decubitus position. Resting conventional echocardiography was first performed to observe the cardiac structure with parasternal long axis, short axis, and apical 4-chamber views. The peak early and late diastolic flow velocities (E-wave and A-wave respectively) were measured, and then the E/A ratio was calculated. The 3D volumetric transducer was then used to obtain a clear image of the LV endocardium with an apical 4-chamber view in the 4D mode. The patients were asked to hold their breath at the end of expiration. The imaging allows a sector with a depth of 30° and a width of 100° in real time. The 3D dynamic images of the LV in full-volume acquisition were collected and stored. The frame rate of the volumetric image was 25 to 35 frames/s.

After the software identified the endocardial and epicardial borders for the entire 3D dataset, a left ventricular 3D model was generated, and left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), cardiac output (CO), stroke volume (SV), left-ventricular end-diastolic mass (LVEDM), left-ventricular end-systolic mass (LVESM), and left ventricular ejection fraction (LVEF) were measured. Myocardial deformation was analyzed by speckle tracking within the 3D region of interest. The 3D peak systolic LV global longitudinal strain (GLS), global radial strain (GRS), global circumferential strain (GCS), and global area strain (GAS) were automatically obtained by the dedicated software (EchoPAC, Version 112; GE Healthcare). The system divided the left ventricular wall into 16 segments.^[9] Meanwhile, each segmental strain was shown in the bull’s eye plot (Fig. 2). Five patients with poor visualization (more than 2 segments that could not be analyzed) were excluded from further investigation.

2.6. The procedure of CR program

We designed a CR program for the participants in this study (Table 1). It consisted of 2 stages: an inpatient phase for 1 week, followed by an early outpatient phase for 4 weeks. In the RG, the

participants in the inpatient phase were scheduled to do casual limb movements while in bed and simple walk training (e.g., walking around the house or the ward corridor) to get out of bed as soon as possible. The exercise training was conducted with supervision according to the American Heart Association recommendations.^[11] The energy expenditure during exercise training was estimated to be 2 to 4 metabolic equivalents (METs). Exercise training during the inpatient phase could help prepare patients for the early outpatient phase. During the training time, exercises were designed so that participants would maintain a perceived exertion Borg (PEB) scale rating between 4 and 5 (scale 0–10) or reach approximately 60% maximum heart rate (HRmax), which corresponds to mild-moderate exercise intensity.^[11,12]

The participants in the RG would then enter the early outpatient phase of the CR program. The progressive exercise training in this phase was conducted without supervision after discharge. The exercise program has been previously similarly described.^[11,12] The exercise program consisted of a 5-minute warm-up period (stretching), 20 minutes of aerobic exercise (i.e., walking or jogging, gymnastics), and a 5-minute cool-down period (stretching).

The participants in the CG were instructed to follow the usual care program, including continuing the physical activity that began during inpatient care.

All participants were taught to use the PEB scale when they performed physical activity. They were instructed to stop exercising if their PEB scale rating was over 6. The participants were also cautioned not to run during exercise.

2.7. Follow-up

At discharge, all participants received a health education brochure that included information about cardiac disease, risk factor management, the importance of continuing to exercise training, dietary advice, psychological support, and compliance

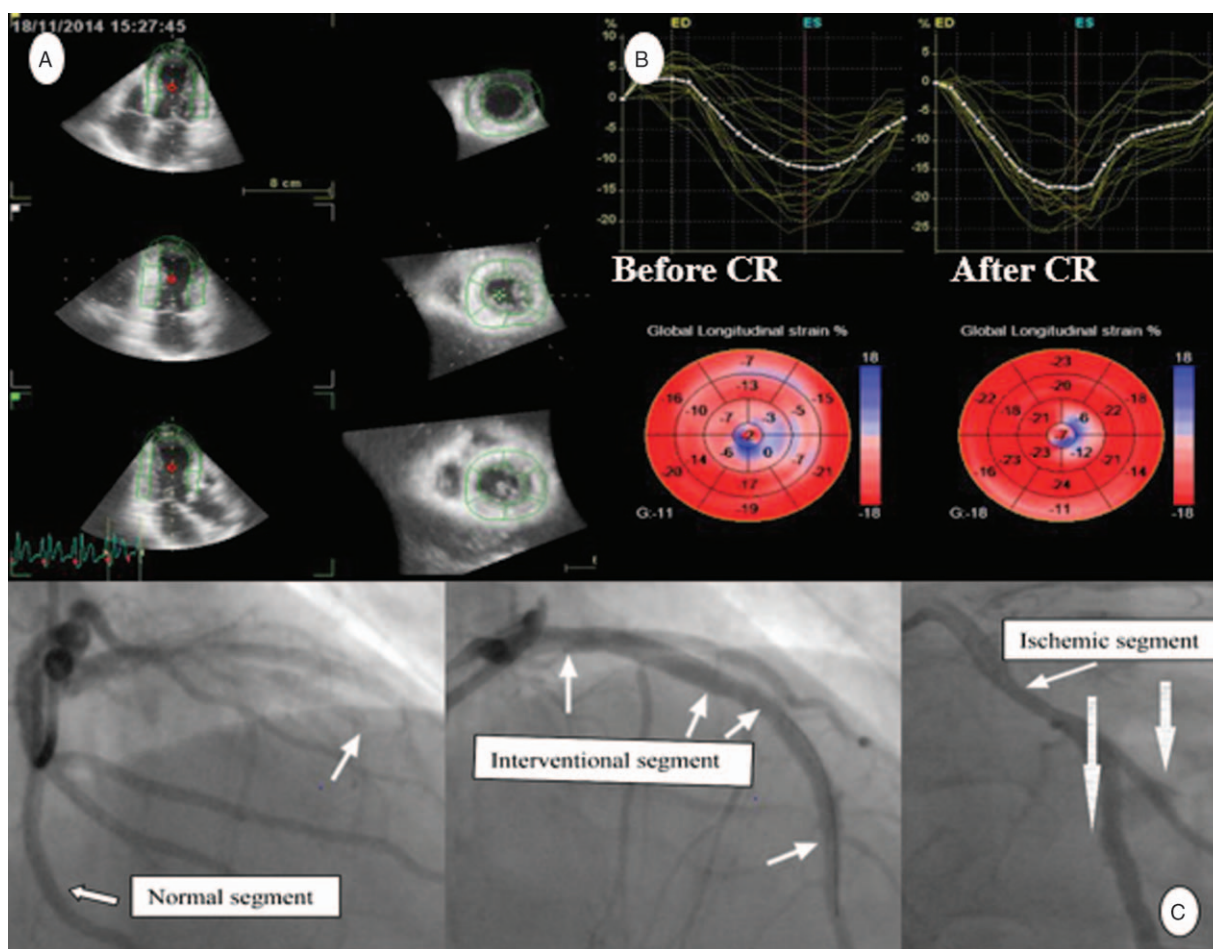


Figure 2. Three-dimensional speckle tracking echocardiography (3D-STE) and the result of coronary angiography (CAG). A, The software identified the endocardial and epicardial borders in each frame for the entire 3D dataset; myocardial deformation was therefore analyzed by the software. B, Global and segmental left ventricular longitudinal strains are shown as a bull's eye plot at baseline, 48 hours after PCI and at a 4-week follow-up. C, CAG showed that the middle part of the left anterior descending coronary was occluded, and stent implantation was subsequently performed. PCI = percutaneous coronary intervention.

with their pharmacologic regimen. We conducted a phone interview to the patients participated into CR program once a week. During the phone interview, we checked the compliance of the patients to the exercise program, and encouraged them to keep doing the exercises, whereas in the CG, participants were encouraged to maintain physical activity. All patients were instructed to return 4 weeks after discharge for reevaluation.

Both groups were encouraged to adhere to their prescribed medications.

2.8. Statistical analysis

All continuous variables were presented as the mean ± standard deviation or median (25th and 75th percentiles) depending on

Table 1

The cardiac rehabilitation (CR) program for the rehabilitation group.

The inpatient phase of the CR program	
The first 12 h	Stay in bed, turn over in bed, casually move limbs, gradually sit up, eat, brush teeth, defecate
The first 1 to 2 d	Try to get out of bed, sit on a chair 3 times/d for not more than 30 min at a time
The first 3 to 4 d	Slowly walk indoors with help 3 times/d for 10 min at a time
The first 5 d	Walk around ward corridor 3 to 4 times/d for 10 to 20 min at a time, use the toilet, shower without help
The first 6 d	Walk slowly in the hospital 2 times/d for 10 to 20 min at a time
7 to 10 d	Basic life self-care; slow walks 3 times/d for 15 min at a time
The early outpatient phase of the CR program	
The first week	Outdoor walking (near normal pace), 3 times/d for 15 to 20 min at a time
The second week	Outdoor walking, 3 times/d for 20 min at a time
The third week	Outdoor walking, 3 times/d for 20 to 30 min at a time
The fourth week	Outdoor walking or jogging, 3 times/d for 20 to 30 min at a time
1 to 3 mo	Gradually participate in social activities, work

whether the data were normally distributed. The normally distributed data were assessed with the Kolmogorov–Smirnov test. Categorical data were presented as frequencies and percentages (%). With a detection of at least 10% difference in the GLS between the baseline and 4-week follow-up values, 25 patients per group were required to achieve 80% power and 5% alpha risk. Thus, to allow for a 20% dropout rate, we enrolled 70 patients in our study. Comparisons of parametric values among groups were performed with Student *t* test and the χ^2 test when appropriate. Comparisons of intragroup values were performed with the paired Student *t* test. Differences in week-4 global and segmental strains between the groups were calculated by analysis of covariance using the baseline values as the covariate. A 2-tailed *P* value <0.05 was considered to indicate statistical significance. All statistical analyses were carried out using SPSS software (IBM Company, New York).

3. Results

3.1. Subject characteristics

Fifty-two patients were enrolled in our study, including 44 males (84.6%) and 8 females (15.4%). The mean age was 55.6±9.2 years old (35–73 years old). Table 2 shows the demographic and clinical characteristics of the patients according to age, gender, systolic blood pressure, diastolic blood pressure, body mass index, heart rate, cardiovascular risk factors, SYNTAX score, PCI location, and medication. The analysis indicated no significant differences between groups (*P*>0.05).

Table 2
Demographic and clinical characteristics of patients with and without cardiac rehabilitation at baseline.

	Rehabilitation group (n=26)	Control group (n=26)	<i>P</i> value
Age, y	55.8±9.7	55.5±8.9	0.917
Male gender, %	22 (84.6%)	22 (84.6%)	1.000
Heart rate	81.3±15.0	85.2±14.6	0.343
Body mass index, kg/m ²	24.2±2.5	25.2±3.5	0.700
Time from onset to admission, h	5.4±2.7	5.3±2.6	0.890
Door-to-balloon time, min	79±45	78±56	0.750
Smoking, %	22 (84.6%)	21 (80.8%)	0.717
Hypertension, %	9 (34.6%)	10 (38.5%)	0.775
Hyperlipidemia, %	15 (57.7%)	18 (69.2%)	0.392
SBP, mm Hg	127.7±15.0	122.1±17.1	0.217
DBP, mm Hg	77.7±10.2	74.3±12.1	0.272
Diabetes mellitus, %	5 (19.2%)	8 (30.8%)	0.341
Chronic renal failure, %	0 (0.0%)	0 (0.0%)	1.000
ST-elevation acute myocardial infarction	26 (100%)	26 (100%)	1.000
Coronary artery disease			
LAD coronary artery PCI, %	18 (69.2%)	16 (61.5%)	0.564
Non-LAD coronary artery PCI %	8 (30.8%)	10 (38.5%)	0.564
SYNTAX score	16.6±6.7	15.3±7.2	0.527
Medication, %			
ASA and Clopidogrel	26 (100%)	26 (100%)	1.000
ARB and/or ACE inhibitor	24 (92.3%)	21 (80.8%)	0.227
β-blocker	23 (96.2%)	22 (100%)	0.687
Nitrate agent	13 (57.7%)	10 (69.2%)	0.407
Statins	26 (100%)	26 (100%)	1.000

ACE inhibitor=angiotensin converting enzyme inhibitor, ASA=acetylsalicylic acid, Chronic renal failure=creatinine >2.0 mg/dL; >176.8 μmol/L, DBP=diastolic blood pressure (mm Hg), LAD=left anterior descending artery, PCI=percutaneous coronary intervention, SBP=systolic blood pressure (mm Hg).

Table 3
Global and segmental strains of all participants at baseline and at the end of trial (week 4).

	Baseline	Week 4	<i>P</i> value
Global strains (n=52)			
GLS	-12.3±3.7	-13.8±3.2	0.001
GRS	34.6±9.9	36.1±9.6	0.201
GCS	-13.4±3.3	-13.7±3.6	0.542
GAS	-23.2±5.4	-24.3±5.3	0.094
LVEF	52.9±9.3	54.1±9.2	0.315
Segmental strains of interventional segments (n=319)			
SLS	-11.6±6.3	-13.1±6.2	0.003
SRS	28.8±19.2	32.3±18.0	0.004
SCS	-11.1±8.4	-12.5±7.5	0.014
SAS	-20.1±11.0	-22.4±9.9	0.001
Segmental strains of ischemic segments (n=179)			
SLS	-14.6±9.9	-14.2±6.3	0.603
SRS	37.1±19.4	38.8±17.9	0.994
SCS	-14.7±8.7	-14.7±7.5	0.314
SAS	-25.0±10.4	-26.0±9.6	0.359
Segmental strains of normal segments (n=334)			
SLS	-13.2±6.3	-14.5±5.9	0.003
SRS	36.5±16.9	37.5±16.3	0.612
SCS	-14.6±8.0	-14.3±7.2	0.394
SAS	-25.6±10.4	-25.6±9.0	0.997

GAS=segmental area strain, GCS=global circumferential strain, GLS=global longitudinal strain, GRS=global radial strain, LVEF=left ventricular ejection fraction, SAS=segmental area strain, SCS=segmental circumferential strain, SLS=segmental longitudinal strain, SRS=segmental radial strain.

3.2. Global and segmental strains of all the participants

Table 3 shows the changes in global and segmental strains between the baseline and the 4-week follow-up. At the global level, the GLS was significantly higher at the end of the trial than at the baseline (*P*<0.05), while no significant improvements in the GRS, GCS, GAS, and LVEF were observed between the baseline and 4-week follow-up (*P*>0.05).

From the 52 participants, we obtained segmental strains from 832 segments, of which 319 were defined as intervention segments, 179 as ischemic segments, and the remainder as normal segments. Segmental strains of intervention segments were all significantly higher at the end of the trial than at baseline (*P*<0.05), while no statistically significant change was observed for the segmental strains of the ischemic segments (*P*>0.05). The SLS of the normal segments increased from the baseline to the 4-week follow-up (*P*<0.05), while no significant changes were observed for the SRS, SCS, or SAS (*P*>0.05).

3.3. Global changes between groups at week 4

The groups had no significant differences in any parameters at baseline (all *P*>0.05). At the 4-week follow-up, when controlling for baseline values, the RG showed significant improvements in the SV, GLS, GRS, GCS, GAS, and LVEF compared with the CG (*P*<0.05), while no significant changes were observed for the HR, SBP, DBP, BMI, E/A Ratio, LVEDV, LVESV, CO, EDM, or ESM (*P*>0.05) (Table 4).

3.4. Segmental changes between groups at week 4

The 3 subgroups had no significant differences in any parameters at baseline (*P*>0.05) except the segmental LS of the ischemic segments. At the 4-week follow-up, when controlling for baseline values, the RG showed significant improvement in all segmental strains of the 3 subgroups compared with the CG (*P*<0.05) (Table 5).

Table 4

Global changes between groups at baseline and at the end of trial (week 4).

	Baseline (n=26)			Week 4 (n=26)		
	RG	CG	P value	RG	CG	P value
HR	81.7 ± 14.9	84.7 ± 15.8	0.473	66.0 ± 11.1	70.1 ± 11.5	0.159
SBP	127.7 ± 15.0	122.1 ± 17.1	0.217	117.8 ± 11.3	111.7 ± 11.1	0.107
DBP	77.7 ± 10.2	74.3 ± 12.1	0.272	73.5 ± 6.4	70.8 ± 8.5	0.471
BMI	24.17 ± 2.5	23.84 ± 3.5	0.700	23.03 ± 2.7	22.54 ± 3.2	0.390
E/A ratio	1.0 ± 0.2	1.0 ± 0.2	1.000	1.1 ± 0.2	1.0 ± 0.5	0.052
LVEDV	98.2 ± 17.6	102.2 ± 33.3	0.586	105.1 ± 25.4	104.1 ± 32.3	0.186
LVESV	46.8 ± 12.2	49.7 ± 26.7	0.623	46.3 ± 17.7	51.9 ± 23.5	0.302
CO	3.9 ± 1.3	3.8 ± 0.9	0.785	3.9 ± 0.9	3.5 ± 0.7	0.123
SV	51.4 ± 11.4	52.5 ± 13.1	0.752	58.8 ± 14.4	52.2 ± 13.3	0.012
EDM	148.4 ± 16.6	144.6 ± 15.1	0.392	148.81 ± 13.6	143.38 ± 15.3	0.313
ESM	148.1 ± 16.1	144.7 ± 15.1	0.434	149.5 ± 13.6	144.2 ± 14.8	0.30
GLS	-12.1 ± 3.3	-12.5 ± 4.1	0.712	-15.0 ± 2.3	-12.5 ± 3.6	<0.001
GRS	34.5 ± 9.0	34.6 ± 10.8	0.973	40.1 ± 8.5	32.1 ± 9.0	<0.001
GCS	-13.5 ± 3.1	-13.4 ± 3.5	0.901	-15.1 ± 3.7	-12.3 ± 3.0	0.001
GAS	-23.3 ± 5.0	-23.2 ± 5.9	0.964	-26.6 ± 4.5	-22.0 ± 5.2	<0.001
LVEF	52.5 ± 7.7	53.3 ± 10.9	0.752	56.6 ± 9.2	51.6 ± 8.6	0.008

BMI = body mass index, CO=cardiac output, DBP = diastolic blood pressure, EDM=end-diastolic left-ventricular mass, ESM=end-systolic left-ventricular mass, GAS=global area strain, GCS=global circumferential strain, GLS=global longitudinal strain, GRS=global radial strain, HR=heart rate, LVEDV=left ventricular end-diastolic volume, LVEF=left ventricular ejection fraction, LVESV=left ventricular end-systolic volume, SBP = systolic blood pressure, SV=stroke volume.

Table 5

Segmental changes between groups at baseline and at the end of trial (week 4).

Segmental LS	Interventional segments	Ischemic segments	Normal segments
RG			
Baseline	-11.2 ± 5.8	-13.1 ± 6.2	-13.9 ± 6.3
Week 4	-14.0 ± 6.0	-15.2 ± 6.4	-15.5 ± 5.5
CG			
Baseline	-11.9 ± 6.8*	-13.0 ± 12.1*	-13.5 ± 6.4*
Week 4	-12.2 ± 6.2	-13.3 ± 6.1	-13.4 ± 6.1
RG-CG†			
P value	0.008	0.037	0.001
Segmental CS	Interventional segments	Ischemic segments	Normal segments
RG			
Baseline	-11.2 ± 8.2	-14.9 ± 8.4	-15.1 ± 8.4
Week 4	-13.4 ± 7.7	-16.4 ± 7.0	-15.5 ± 7.3
CG			
Baseline	-10.9 ± 8.6*	-14.6 ± 9.0*	-14.9 ± 7.6*
Week 4	-11.6 ± 7.2	-13.3 ± 7.7	-12.9 ± 6.8
RG-CG†			
P value	0.034	0.006	0.001
Segmental RS	Interventional segments	Ischemic segments	Normal segments
RG			
Baseline	28.1 ± 18.0	37.4 ± 18.7	37.9 ± 17.2
Week 4	35.5 ± 18.1	43.1 ± 18.0	41.2 ± 15.7
CG			
Baseline	29.4 ± 20.3*	36.8 ± 20.2*	37.2 ± 16.6*
Week 4	29.4 ± 17.5	35.0 ± 17.0	33.1 ± 16.0
RG-CG†			
P value	0.001	0.002	<0.001
Segmental AS	Interventional segments	Ischemic segments	Normal segments
RG			
Baseline	-20.1 ± 10.3	-25.3 ± 10.2	-26.1 ± 11.6
Week 4	-24.2 ± 10.2	-28.0 ± 10.0	-27.4 ± 8.3
CG			
Baseline	-20.2 ± 11.5*	-24.8 ± 10.7*	-25.0 ± 8.8*
Week 4	-20.7 ± 9.5	-24.3 ± 9.2	-23.4 ± 9.3
RG-CG†			
P value	0.001	0.01	<0.001

AS=area strain, CG=control group, CS=circumferential strain, LS=longitudinal strain, RS=radial strain.

*Refers to the P>0.05, compared with baseline values in RG between 3 subgroups.

† Comparison in week 4 between RG and CG, adjusted for baseline values, calculated by analysis of covariance (ANCOVA).

Table 6
Inter-observer and intra-observer ICCs of 3D-STE strain parameters and LVEF.

	Inter-observer	Intra-observer
GLS	0.82 (0.68–0.96)	0.95 (0.81–0.98)
GRS	0.98 (0.92–0.99)	0.99 (0.98–0.99)
GCS	0.88 (0.52–0.97)	0.92 (0.69–0.98)
GAS	0.88 (0.52–0.97)	0.99 (0.93–0.99)
LVEF	0.98 (0.93–0.99)	0.98 (0.93–0.99)

Abbreviations as in Table 3.

3.5. Reproducibility

Ten patients were randomly chosen for interobserver and intraobserver variability analyses. The data were obtained by 2 experienced examiners with more than 10 years' experience using 3D-STE. Five days later, the original examiner rechecked the previous 3D-STE images. The interobserver and intra-observer intraclass correlation coefficient (ICC) between the 2 examiners was calculated and is showed in Table 6.

4. Discussion

The main finding of this study was that an early home-based CR program was useful for the improvement in the global and segmental LV function in AMI patients treated with PCI. This CR program consists of exercise intervention carried out in the inpatient setting, and an unsupervised home-based training after discharge.

4.1. Myocardial strain assessment

3D-STE is becoming a convenient technique for efficiently determining myocardial function.^[13,14] The potential superiority of 3D-STE over 2D-STE imaging has recently been verified using cardiac magnetic resonance as a reference, in which 3D strain parameters provided higher diagnostic accuracy in reflecting the dysfunctional myocardium in an AMI animal model.^[15] Cardiac dysfunction is related to myocardial fiber injury in certain directions; meanwhile, the evaluation of cardiac systolic function is the mainstay of risk assessment and management of cardiac diseases. 3D-STE has been verified to be superior to the conventional LVEF measurement.^[7,8] Therefore, the measurements of the 3D longitudinal, radial, and circumferential strains should be able to reflect the LV global and segmental recovery of myocardial fiber directly after CR program.

Based on the cardiac anatomy, the motions along the longitudinal axis play an important role in maintaining the LV systolic function. The longitudinally orientated myocardial fibers are located in the subendocardial myocardium, which is most susceptible to myocardial ischemia or transmural infarct. Thus, 3D-LS was shown to be an accurate predictor of segmental and global LV functional improvement in AMI patients.^[16] At the global level, we found that all patients had improvement in LV function at the 4-week follow-up according to the GLS, whereas there was no significant difference in the LVEF. This also indicated that the GLS could be superior to the conventional LVEF measurement in the evaluation of myocardial function. Furthermore, Kalam et al^[17] conducted a meta-analysis to compare LVEF and GLS in the prediction of cardiovascular outcomes. They found that GLS had superior prognostic value to LVEF for predicting major adverse cardiac events.

In contrast, we did not find statistically significant changes in the GRS, GCS, or GAS among all the participants at the 4-week follow-up. However, significant changes in the segmental strain values of the PCI interventional segments were found in our study, as shown in Table 3. This finding might indicate that the recovery of myocardial function starts from the segment of myocardium first. However, in our analysis, both the global and segmental strains had statistically improvement in the RG than in the CG, as shown in Tables 4 and 5. Such different results might be attributed to the fact that radial and circumferential strain does not represent a specific set of muscle fibers.^[18] GRS was estimated by both endocardial and epicardial speckle tracking data, which mainly reflected the thickening of the ventricular wall during the systolic phase. Zhu et al^[19] observed that the reduced RS may be multiply affected by the presence of injuries of 3 myocardial layers. Due to Kai O.H' findings, it is therefore important to compare various segments in the resting state, whereas the measurement of a single segment seems to be sufficient during exercise testing.^[20]

In addition, GCS was incomplete in the assessment of LV function because it consists of simultaneous LV shortening, thickening, and twisting.^[21] Area strain is the sum of longitudinal and circumferential strain vectors, which are uniquely provided by 3D-STE. GAS reflects the global function assessment of the endocardial myocardium.^[22] Wang et al^[14] demonstrated that 3D-GAS could gauge the value of myocardial infarction size, but its diagnostic value was not better than 3D-GLS.

4.2. The problem of reproducibility

For left ventricular strain measurements performed in each of the 3 views, intraobserver ICCs were ≥ 0.92 among time points spanning a total 24-week period, while the interobserver ICCs were ≥ 0.82 for all global strain measurements. Interobserver and intraobserver reproducibility findings were similar in analyses adjusting for frame rate. Excellent reproducibility of global radial strain measurements and very good reproducibility of global longitudinal, circumferential, and area strain measurements were observed. It may be related to the fact that the feature of our tracking software we used is based mainly on integrated endocardial and epicardial tracking as well as Lagrangian algorithm-based estimates.^[23]

4.3. Participation in and benefit of CR

Currently, comprehensive CR programs are recognized as a key component of the management of patients with recent myocardial infarction or acute coronary syndrome. Exercise-based CR remains a class I indication in most clinical practice guidelines. Despite these guidelines, participation in inpatient and outpatient CR programs varies largely among the countries, and most of the outcomes are often poor. Two main reasons why patients do not participate in CR have been proposed: after PCI, AMI patients often do not have a physician's recommendation to participate in the CR program; some physicians refuse to advise patients to participate in the CR program for safety. However, a recent study conducted by Rauch et al^[3] has shown that the early-supervised CR programs could decrease 1-year mortality greatly. It is encouraging that post-AMI patients could be suitable for a CR program, and these AMI patients may benefit from this intervention, although these patients had a variety of comorbidities. But it is still challenging to apply the CR program to the AMI patients. First, the cardiac rehabilitation is not covered by

medical insurance in China yet. Patients in China have to bear the additional costs for participating in the supervised CR program themselves. Furthermore, patients might consider the rehabilitation is lack of value, or it is inconvenient for the patients living in remote area to participate in the CR program.^[24] Therefore, it is of great demand to design 1 unsupervised home-based CR program for the AMI patients in China. This CR program should be easily conducted in the home environment with very lost cost.

To the best of our knowledge, we first applied the 3D-STE to evaluate the global and segmental LV function recovery in a short-term CR program with exercise intervention. In our study, the global strain parameters (GLS, GRS, GCS, GAS) and 3D-LVEF in the RG showed significant improvement compared with the CG. Moreover, the segmental strains of the intervention segments showed significant improvement in the RG compared with the CG. Improvements in LV function after AMI were mainly related to recovery from myocardial stunning, defined as the dysfunctional but viable myocardial regions. Exercise intervention could accelerate this recovery process. Finally, this study verified the performance of our short-term home-based CR program, which was reacted on the 3D-STE.

When 1 AMI patient was enrolled in our study, we conducted risk stratification and determined whether this patient was suitable for the CR program according to the guideline from the AHA exercise, cardiac rehabilitation, and prevention committee.^[11,12] In our study, both the RG and CG, all participants received PCI and standard medical treatment. The differences of treatments before the CR program between 2 groups were not statistically significant, as shown in Table 1. For the patients in the RG, we educated them how to carry out a home-based CR program after their discharge, and thus, they did not need to go back to the CR center. This free-form CR program could solve the above-mentioned challenges. Wang et al.^[25] conducted a randomized controlled trial to evaluate the effectiveness of a home-based self-management CR program for community-dwelling patients with AMI in Singapore. Inspired by the work of Wang et al, we first educated all the AMI participants about risk factor management, and added the exercise training into our CR program that was not included in the work of Wang et al.^[26,27] We conducted a phone interview weekly to check the compliance of the patients to the exercise program, and to encourage them to keep doing the exercises and prescribed medication schedule. Telephone interview with discharged patients is an effective intervention to improve compliance with the treatment plan, improve communication between doctors and patients, perfect rehabilitation treatment, and decrease cost savings resulting from this intervention.^[28] Previous studies have reported that patients who participated in a supervised exercise-based CR program or a comprehensive multilayer program could achieve improvement in their physical functions.^[29,30] Therefore, exercise training in an early short-term home-based CR program could improve the left ventricular function efficiently.

4.4. Clinical implications

Assessment of the LV global and segmental strain using 3D-STE can be easily conducted in about 10 minutes for 1 experienced ultrasound physician. We believe that 3D-STE can be 1 powerful tool to provide valuable information for the AMI patients in the unsupervised CR programs. The information provided by the 3D-STE can be also used by the clinical doctors to suggest suitable CR program for the AMI patients.

4.5. Limitation of our study

Several limitations of our study should be highlighted in the end of this paper. First, this study had a small number of participants at a single center. The CR program is short-term (4 weeks) intervention in the outpatient phase. Further studies with a larger sample size and a longer CR intervention phase are warranted to validate the impact of our CR program on the improvement of LV function. Another limitation of the study was the reference method to evaluate the myocardial ischemia using the results of the CAG. Because it is affected by the self-adjustment mechanism of the coronary circulatory system and dependent on the type of dominant coronary artery, the supply of myocardial perfusion and the degree of coronary artery stenosis were not the same. The metabolic energy of cardiac muscle cells in the coronary system is demonstration by the microcirculation, which involves the micro artery and the small vein. Therefore, the segment with impaired function was not always aligned with the anatomy of the coronary arteries and may occur in patients without angiographically significant stenosis, which might lead to the inaccurate grouping of ischemic or normal segments. Our early, home-based CR program was lack of the information regarding functional capacity to modify the intensity or progression of the exercise training. This may limit the ability to adjust the rehabilitation as needed. The exercise test was not performed in our study because our study is a short-term rehabilitation study after AMI. There is certainly a risk to perform intense exercise test for these patients in the treadmill at the early stage after PCI treatment. The exercise intensity of our CR program was designed to reach approximately 60% HRmax. The intensity of the exercise treadmill test in our hospital using a Bruce treadmill protocol reached approximately 85% HRmax. Furthermore, myocardial function recovery was proven to start earlier than skeletal muscle recovery for our CR program.^[31] Therefore, it is better to evaluate the cardiac function directly than the skeletal function. After careful consideration, we thus did not carry out the exercise test.

5. Conclusion

An early, home-based CR program can clearly improve the left ventricular function of AMI patients within short period of time. Our study suggests that a simple, early, home-based CR program is an excellent and convenient self-rehabilitation program and appears to be the preferred choice for most patients. Moreover, 3D-STE is a reproducible and efficient tool to evaluate myocardial function.

Acknowledgments

The authors gratefully acknowledge the volunteers who participated in our study.

References

- [1] Kotseva K, Wood D, De Backer G, et al. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. *Eur J Cardiovasc Prev Rehabil* 2009;16:121–37.
- [2] Brown RA. Rehabilitation of patients with cardiovascular diseases: report of a WHO Expert Committee [meeting held in Geneva from 23 to 29 July 1963]. *World Health Organ Tech Rep Ser* 1964;270:3–46.
- [3] Rauch B, Riemer T, Schwaab B, et al. Short-term comprehensive cardiac rehabilitation after AMI is associated with reduced 1-year mortality: results from the OMEGA study. *Eur J Prev cardiol* 2014;21:1060–9.
- [4] Peixoto TC, Begot I, Bolzan DW, et al. Early exercise-based rehabilitation improves health-related quality of life and functional capacity after acute myocardial infarction: a randomized controlled trial. *Can J Cardiol* 2015;31:308–13.

- [5] Mollema SA, Delgado V, Bertini M, et al. Viability assessment with global left ventricular longitudinal strain predicts recovery of left ventricular function after acute myocardial infarction. *Circ Cardiovasc Imaging* 2010;3:15–23.
- [6] Biering-Sørensen T, Hoffmann S, Mogelvang R, et al. Myocardial strain analysis by 2-dimensional speckle tracking echocardiography improves diagnostics of coronary artery stenosis in stable angina pectoris. *Circ Cardiovasc Imaging* 2014;7:58–65.
- [7] Hayat D, Kloeckner M, Nahum J, et al. Comparison of real-time three-dimensional speckle tracking to magnetic resonance imaging in patients with coronary heart disease. *Am J Cardiol* 2012;109:180–6.
- [8] Brown J, Jenkins C, Marwick TH. Use of myocardial strain to assess global left ventricular function: a comparison with cardiac magnetic resonance and 3-dimensional echocardiography. *Am Heart J* 2009;157:102.
- [9] Mor-Avi V, Lang RM, Badano LP, et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. *Eur J Echocardiogr* 2011;12:167–205.
- [10] White HD, Thygesen K, Alpert JS, et al. Clinical implications of the third universal definition of myocardial infarction. *Heart* 2014;100:424–32.
- [11] Balady GJ, Williams MA, Ades PA, et al. Core components of cardiac rehabilitation/secondary prevention programs: 2007 update: a scientific statement from the American heart association exercise, cardiac rehabilitation, and prevention committee, the council on clinical cardiology; the councils on cardiovascular nursing, epidemiology and prevention, and nutrition, physical activity, and metabolism; and the American association of cardiovascular and pulmonary rehabilitation. *Circulation* 2007;115:2675–82.
- [12] Ades PA. Cardiac rehabilitation and secondary prevention of coronary heart disease. *N Engl J Med* 2001;345:892–902.
- [13] Urbano-Moral JA, Patel AR, Maron MS, et al. Three-dimensional speckle-tracking echocardiography: methodological aspects and clinical potential. *Echocardiography* 2012;29:997–1010.
- [14] Wang Q, Zhang C, Huang D, et al. Evaluation of myocardial infarction size with three-dimensional speckle tracking echocardiography: a comparison with single photon emission computed tomography. *Int J Cardiovasc Imaging* 2015;31:1571–81.
- [15] Bhan A, Sirker A, Zhang J, et al. High-frequency speckle tracking echocardiography in the assessment of left ventricular function and remodeling after murine myocardial infarction. *Am J Physiol Heart Circ Physiol* 2014;306:H1371–83.
- [16] Abate E, Hoogslag GE, Antoni ML, et al. Value of three-dimensional speckle-tracking longitudinal strain for predicting improvement of left ventricular function after acute myocardial infarction. *Am J Cardiol* 2012;110:961–7.
- [17] Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. *Heart* 2014;100:1673–80.
- [18] Koopman LP, Slorach C, Hui W, et al. Comparison between different speckle tracking and color tissue Doppler techniques to measure global and regional myocardial deformation in children. *J Am Soc Echocardiogr* 2010;23:919–28.
- [19] Zhu W, Liu W, Tong Y, et al. Three-dimensional speckle tracking echocardiography for the evaluation of the infarct size and segmental transmural involvement in patients with acute myocardial infarction. *Echocardiography* 2014;31:58–66.
- [20] Hensel KO, Jenke A, Leischik R. Speckle-tracking and tissue-Doppler stress echocardiography in arterial hypertension: a sensitive tool for detection of subclinical LV impairment. *BioMed Res Int* 2014;2014:1–9.
- [21] Onishi T, Saha SK, Delgado-Montero A, et al. Global longitudinal strain and global circumferential strain by speckle-tracking echocardiography and feature-tracking cardiac magnetic resonance imaging: comparison with left ventricular ejection fraction. *J Am Soc Echocardiogr* 2015;28:587–96.
- [22] Ternacle J, Gallet R, Champagne S, et al. Changes in three-dimensional speckle-tracking-derived myocardial strain during percutaneous coronary intervention. *J Am Soc Echocardiogr* 2013;26:1444–9.
- [23] Henn MC, Cupps BP, Kar J, et al. Quantifying “normalized” regional left ventricular contractile function in ischemic coronary artery disease. *J Thorac Cardiovasc Surg* 2015;150:240–6.
- [24] Dunlay SM, Witt BJ, Allison TG, et al. Barriers to participation in cardiac rehabilitation. *Am Heart J* 2009;158:852–9.
- [25] Wang W, Jiang Y, He HG, et al. A randomised controlled trial on the effectiveness of a home-based self-management programme for community-dwelling patients with myocardial infarction. *Eur J Cardiovasc Nurs* 2016;15:398–408.
- [26] Wang W, Chair SY, Thompson DR, et al. Effects of home-based rehabilitation on health-related quality of life and psychological status in Chinese patients recovering from acute myocardial infarction. *Heart Lung* 2012;41:15–25.
- [27] Biese K, Lamantia M, Shofer F, et al. A randomized trial exploring the effect of a telephone call follow-up on care plan compliance among older adults discharged home from the emergency department. *Acad Emerg Med* 2014;21:188–95.
- [28] Lee HY, Kim JH, Kim BO, et al. Regular exercise training reduces coronary restenosis after percutaneous coronary intervention in patients with acute myocardial infarction. *Int J Cardiol* 2013;167:2617–22.
- [29] Lawler PR, Filion KB, Eisenberg MJ. Efficacy of exercise-based cardiac rehabilitation post-myocardial infarction: a systematic review and meta-analysis of randomized controlled trials. *Am Heart J* 2011;162:571–84.
- [30] Giannuzzi P, Temporelli PL, Marchioli R, et al. Global secondary prevention strategies to limit event recurrence after myocardial infarction results of the GOSPEL study, a multicenter, randomized controlled trial from the Italian Cardiac Rehabilitation Network. *Arch Intern Med* 2008;168:2194–204.
- [31] Imai S, Riley AL, Berne RM. Effect of ischemia on adenine nucleotides in cardiac and skeletal muscle. *Circ Res* 1964;15:443–50.