Study Protocol Clinical Trial

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Study on the clinical assessment of integrated rehabilitation of Traditional Chinese Medicine and western medication for acute myocardial infarction

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Abstract

Objective: This trial aims to evaluate the efficacy and safety of the Baduanjin exercise in patients with acute myocardial infarction (AMI).

Methods: A single-center, open, randomized controlled clinical trial will be conducted to evaluate the effectiveness of the Baduanjin exercise on the rehabilitation of AMI patients. It plans to enroll 64 patients. Patients will be divided evenly into 2 groups using a random number table method. There will be 32 cases in each group. Patients in the experimental group will be treated with standardized drug therapy combined with Baduanjin exercise, while patients in the control group will be treated with standardized drug therapy combined with routine exercise. The primary outcome is the peak oxygen consumption (Peak VO_2) during cardiopulmonary exercise test (CPET). The secondary outcomes include CPET, echocardiography, Seattle angina pectoris scale, hospital depression and anxiety scale, Pittsburgh Sleep Quality Index scale, scores of 4 examinations, and diagnostic methods of traditional Chinese medicine and composite endpoint events, etc.

Discussion: This study will be the first to evaluate the effect of the Baduanjin exercise on the Peak VO_2 in patients with AMI.

Study registration: This study has been registered on the Chinese Clinical Trial Registry (No: ChiCTR1800016209, protocol version 1.2).

Abbreviations: AMI = acute myocardial infarction, BNP = B-type natriuretic peptide, CPET = cardiopulmonary exercise test, hs-CRP = hypersensitive C-reactive protein, Peak VO_2 = peak oxygen consumption, PSQI = Pittsburgh Sleep Quality Index scale, TnT = 2, 4, 6-trinitrotolurene, V0 = enrollment, V1 = discharged, V2 = discharged from hospital for 1 month (28 ± 7) days, V3 = discharged from hospital for 3 months (84 ± 7) days, V4 = discharged from hospital for 6 months (168 ± 7) days.

Keywords: Baduanjin, myocardial infarction, peak oxygen consumption, protocol, randomized controlled trial, rehabilitation

ZZ and XW contributed equally to this work and should be considered co-first authors.

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The study will be conducted according to the principles of the Helsinki Declaration. The Research Ethics Committee of the First Teaching Hospital of Tianjin University of Traditional Chinese Medicine has approved the study. If there is any modification of the protocol and informed consent or changes of the principal investigator during the study, it will be submitted to the ethics committee for re-reviewing. All participants will be informed about the details of the trial, including the purpose, arrangement, and probable risks and benefits. And signed informed consent will be obtained from all participants before enrolment.

The results will be published in a peer-reviewed journal and disseminated at relevant conferences.

The related documentation during the current study will be available from the corresponding author or chief investigator on reasonable request.

This trial is currently recruiting participants. The study will run from May 1, 2018 to June 30, 2021.

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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1. Introduction

The incidence of acute myocardial infarction (AMI) is increasing year by year in China.[1] Revascularization and drug therapy could improve the symptoms and reduce the mortality rate of AMI patients.[2,3] However, survivors following reperfusion therapy still have some problems, such as reduced exercise tolerance, poor quality of life, anxiety, depression, etc. The mortality rate, the risk of incident stroke, or rehospitalization rate within the first 6 months after discharge from the hospital is about 25%.[4] Some studies have shown that aerobic exercise in cardiac rehabilitation can improve exercise ability, reduce the all-cause mortality, cardiovascular mortality, and rehospitalization rate of AMI patients.[5–7] However, only 38.8% of countries in the world have a cardiac rehabilitation program.[8] Participating in the cardiac rehabilitation program may be restricted due to aging, solitude, absence of awareness, no medical insurance, etc.[9] Alternative simple and feasible exercise-based rehabilitation for AMI will still be needed.

Tai Chi and Yoga exercise is economical and time-saving. However, they include some complex actions and irregular practices can cause sports injuries.[10] The use of these exercises is restricted in the early stage of AMI. Baduanjin exercise is a low-intensity aerobic exercise with simple actions and easy to learn.[11,12] Some studies have shown that Baduanjin exercise can improve lung function, exercise ability, control blood pressure, blood lipid, quality of life, quality of sleep, relieve depression, and other adverse emotions.[13–16] There is no clinical study on the effect of the Baduanjin exercise on exercise tolerance in patients with AMI.

2. Methods

2.1. Study design

It is a single-center, open, randomized controlled clinical trial. We will enroll 64 patients with AMI in the Cardiovascular Department of the First Teaching Hospital of Tianjin University of Traditional Chinese Medicine. The informed consent was approved by the Ethics Committee of First Teaching Hospital of Tianjin University of Traditional Chinese Medicine (TYLL2018 [K]012). It was registered in the Chinese clinical trial registry (ChiCTR1800016209). The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist is provided as Supplemental Digital Content (Additional file 1, http://links.lww.com/MD/E710).

2.2. Inclusion criteria

1. Patients were ST-elevation myocardial infarction or non-ST-elevation myocardial infarction confirmed by coronary angiography and treated with reperfusion therapy, whose condition became relatively stable after treatment.
2. Aged more than 30 years old;
3. Willing to participate in cardiac rehabilitation;
4. Sign up the informed consent.

2.3. Exclusion criteria

1. Patients with severe cardiovascular diseases such as unstable angina, uncontrolled heart failure, malignant arrhythmia, cardiac shock, uncontrolled hypertension (systolic pressure more than 160 mm Hg, diastolic pressure more than 100 mm Hg), severe ventricular/supraventricular arrhythmia, uncontrolled tachycardia (heart rate >120 bpm in a resting state), and severe valvular heart valve disease that requires surgical intervention, hypertrophic obstructive cardiomyopathy, acute pericarditis, congenital heart disease, etc.
2. Patients with severe pulmonary disease, uncontrolled diabetes, severe hepatic and renal insufficiency (creatinine < 30 mL/min), malignant tumor, and other diseases;
3. Severe conditions as severe myocardial ischemia or hypoglycemia occurred during the exercise;
4. Patients with neurological or orthopedics diseases, or with dementia/cognitive impairment and other related diseases, who cannot carry out rehabilitation exercise training;
5. Patients with poor compliance or who refuse to sign up the informed contest;
6. Patients who have practiced Baduanjin or Taichi in the past;
7. Other situations that are not suitable for participation in trials.

2.4. Interventions

The standardized drug therapy is recommended by Guidelines for Diagnosis and Treatment of Acute ST-elevation Myocardial Infarction[17] and Guidelines for Diagnosis and Treatment of Non-ST-elevation Acute Coronary Syndrome (2016).[18]

During hospitalization, experimental group patients change from sitting Baduanjin exercise to vertical Baduanjin exercise gradually under guardianship according to their condition.

When they were discharged from the hospital, they exercised 3 to 5 times a week, including 5 minutes of warm-up exercise (such as stretching and joint activity, etc), 10 to 15 minutes of Baduanjin exercise, and 5 minutes finishing exercise after Baduanjin exercise. The intervention measures of patients in the control group were standardized drug therapy combined with routine exercise (except traditional sports such as Baduanjin, Tai Chi Chuan, Yoga, etc). During hospitalization, the patients in the control group exercised under guardianship according to their condition. After discharge, the exercise prescription was made according to the results of peak oxygen consumption (CPET): self-feeling tired degree from easy to hard, 3 to 5 times every week, 30 minutes every time.

Patients in the 2 groups need to come to the hospital for outpatient follow-up and exercise and medication guidance every 2 weeks within 3 months after discharge. During 3 to 6 months after discharge, the researcher will encourage the patients to independently adhere to Baduanjin exercise or routine exercise by telephone/WeChat. The observation notes include the time of inclusion, enrollment (V0), discharged (V1), discharged from hospital for 1 month (28 ± 7) days (V2), discharged from hospital for 3 months (84 ± 7) days (V3), discharged from hospital for 6 months (168 ± 7) days (V4).

2.5. Outcomes

Primary outcome: peak oxygen consumption (Peak VO_2) was the main outcome measure. Patients underwent a CPET at V1, V2, and V3.

Secondary outcomes: The power and other indicators of CPET will be recorded at V1, V2, and V3. The ultrasound testers investigate echocardiography for patients at V0, V1, V2, and V3.

Seattle angina pectoris scale, Hospital Depression Anxiety Scale, Pittsburgh Sleep Quality Index scale (PSQI), Scores from the 4 examinations, and diagnostic methods of traditional Chinese medicine will be completed by the same trained physician. The composite endpoint is an aggregative indicator including all-cause death, AMI, revascularization, heart failure, malignant arrhythmias, cardiogenic shock, stroke, and pulmonary embolism. Statistical indicators include B-type natriuretic peptide (BNP), 2, 4, 6-trinitrotolurene (TnT); hypersensitive C-reactive protein (hs-CRP), 4 items of blood lipid, urinary albumin clearance rate, intravenous glucose, outpatient or hospitalization expenses, number of hospitalization, etc.

Safety outcomes: The safety outcomes include blood pressure, heart rate, 12-point resting electrocardiogram, blood routine, serum potassium, serum creatinine, urea nitrogen, and adverse events.

2.6. Follow-up time and measurement indexes

Baseline data includes the patient's current vital signs, medications taken, and coronary artery revascularization. Laboratory tests include blood pressure, BNP, TnT, hs-CRP, serum potassium, creatinine, urea nitrogen, intravenous glucose, 4 items of blood lipid, urinary albumin excretion rate.

After enrollment, patients are followed up in the hospital at V1, V2, and V3, and telephone follow-up at V4. Details are given in Table 1. The implementation process is shown in Figure 1.

2.7. Sample size

According to a previous trial,[19] Peak VO_2 at the end of the twelfth week of the treatment was 24.6 ± 5.2 mL/kg/min in the experimental group and 19.4 ± 4.4 mL/kg/min in the control group. The experimental group and the control group are grouped in a 1: 1 ratio. The significance level α is 0.05, and the power $(1 - \beta)$ is 0.80. Considering an unfinished rate of no more than 20%, the number of cases in each group is at least 32. The calculation formula is listed as follows:

$$n = \left[\frac{(u_{1-\alpha} + u_{1-\beta}) * \sigma}{\delta}\right]^2 \times 2$$

2.8. Randomization method and blinding

After the patient signs the informed consent, they will be assigned into the experimental group or control group by stratified

Table 1

Summary table of research procedures.

	Enrollment V0	Discharged V1	Discharged from hospital for (28±7) d V2	Discharged from hospital for (84±7) d V3	Discharged from hospital for (168±7) d V4
Determine inclusion or exclusion	√				
Sign the informed consent	√				
Basic medical history					
Filling in general information	√				
Medical history	√				
Physical examination	√	√	√	√	
Medications taken	√	√	√	√	√
Compliance judgment		√	√	√	
Evaluation of therapeutic efficiency					
Cardiopulmonary exercise test		√	√	√	
Echocardiography	√	√	√	√	
Seattle angina pectoris scale		√	√	√	
Hospital Depression Anxiety Scale	√	√	√	√	
Pittsburgh sleep quality index		√	√	√	
Four examinations and diagnostic methods of Traditional Chinese Medicine	√	√	√	√	
Outpatient or hospitalization expenses and hospital admissions		√	√	√	√
End event and certification		√	√	√	√
BNP, hs-CRP	√	√	√	√	
TnT	√	√	√		
Four items of blood lipid and intravenous glucose	√	√	√	√	
Safety observation					
Adverse even	√	√	√	√	√
BP, HR	√	√	√	√	
ECG	√	√	√	√	
Serum potassium, creatinin, etc	√	√	√	√	
Make an appointment for the next visit		√	√	√	
Study completion		√	√	√	√
Case report form review		√	√	√	√

BNP = B-type natriuretic peptide, BP = blood pressure, ECG = electrocardiogram, HR = heart rate, hs-CRP = hypersensitive C-reactive protein, TnT = 2, 4, 6-trinitrotolurene.

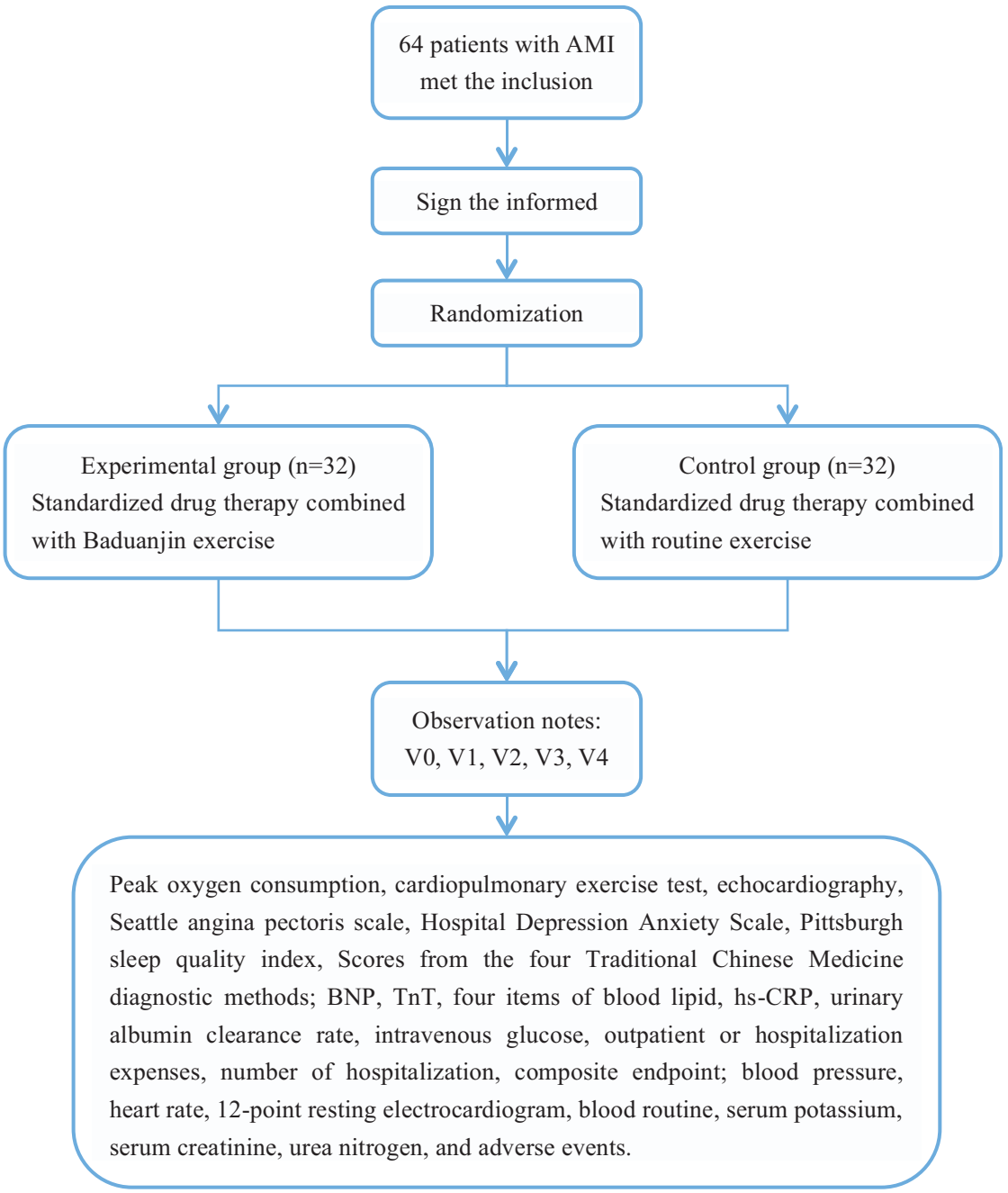

Figure 1. Flow chart of research implementation. Notes: AMI = acute myocardial infarction, V0 = enrollment, V1 = discharged, V2 = discharged from hospital for 1 month (28 ± 7) days, V3 = discharged from hospital for 3 months (84 ± 7) days, V4 = discharged from hospital for 6 months (168 ± 7) days, BNP = B-type natriuretic peptide, TnT = 2, 4, 6-trinitrotolurene, hs-CRP = hypersensitive C-reactive protein.

randomization (1:1) according to whether the ST segment elevates or not. The random number table will be saved by a special person who will not participate in the assignment, specific implementation, data management, and statistical analysis. Laboratory personnel, ultrasound testers, CPET operators, and statistical analysts are unaware of patients' grouping and interventions. And there is no blinding in the outcome assessment.

2.9. Data monitoring

A supervisor will be set up to monitor and evaluate the safety of patients. The supervisor uses this data to guide the implementation of the study, monitor clinical evaluations, conduct standardized guidance, and determine whether the trial should be terminated.

2.10. Data management and statistical analysis

An Excel data-sheet is created. An independent researcher will check the data and lock the database before statistical analysis. Statistical analysis is performed using SPSS 19.0. For counting data, frequency and percentage are used for data description, and the χ^2 test is used for data comparison. For measurement data,

the *t* test is used for normal distribution data. Interval data are presented with means and 95% confidence intervals. The rank-sum test is used for non-normal distribution data. $P < .05$ indicates that the difference is statistically significant. Participants who have received treatment but there is no valid evaluation data will be considered as missing and will be included in the effectiveness analysis.

3. Discussion

This trial aims to evaluate whether standardized drug therapy combined with Baduanjin exercise can improve exercise tolerance in patients with AMI.

Traditional exercises such as Tai Chi[19,20] and yoga[21,22] are beneficial for patients with cardiovascular disease. These exercises have no special requirements on the field and are therefore easily accepted by patients. Patients with AMI usually exercise Taijiquan 14 to 21 days after discharge.[19] However, irregular exercises and insufficient leg strength are likely to cause knee joint pain, which often occurs in the initial learning stage.[23] Some antijoint activities of yoga are beyond the range of normal joints, which can cause sports injuries,[10] and then affect compliance. Baduanjin exercise is moderate in intensity and short in duration (a set of Baduanjin takes about 12 min). Compared to Tai Chi and Yoga, the Baduanjin is easier to learn. The vertical Baduanjin will help enhance the stability of the lower limbs.[24–26] The exercise intensity of Baduanjin can be adjusted according to the patient's condition, which has certain advantages for cardiac rehabilitation of AMI.

Exercise capacity is an independent predictor of all-cause mortality and cardiovascular mortality in patients with AMI.[27,28] CPET is used to test the exercise capacity of patients with AMI.[29,30] Studies[31] have shown that early exercise rehabilitation after AMI is beneficial, but 3 to 5 days after AMI is an absolute contraindication to CPET.[32] Therefore, CPET is selected at the time of discharge in this study. As the primary outcome, Peak VO_2 can reflect exercise capacity and predict long-term prognosis.[33] Left ventricular function measured by echocardiography can predict cardiovascular events[34] and cardiac workload[35] in patients with AMI. BNP is an important indicator for predicting heart failure in patients with AMI.[36] TnT and hs-CRP can reflect the severity of myocardial necrosis and are related to the prognosis.[37] Seattle angina pectoris scale is used to evaluate the clinical symptoms and quality of life, Hospital Depression Anxiety Scale, and PSQI are used to reflect the internal mental state of patients. The composite endpoint was evaluated in 6 months after discharge. Currently, there is no randomized controlled trial about the effect of the Baduanjin exercise on exercise tolerance for patients with AMI. This study is expected to prove that Baduanjin exercise is a potentially valuable exercise rehabilitation method for patients with AMI.

The trial has some limitations. A single-center design may lead to selective bias in patient inclusion. Owing to the small sample size and many exclusion conditions, some high-risk patients who have not undergone revascularization or incomplete revascularization may be excluded, which may limit the extrapolation of conclusions. Nonmedical supervised training may affect patient compliance, making trial results subject to confounding factors. In conclusion, the trial aims to prove that combined with the Baduanjin exercise based on standardized drug treatment can improve exercise tolerance and long-term prognosis of patients with AMI after revascularization.

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References

[1] China cardiovascular disease report writing groupSummary of China cardiovascular disease report 2016. China Circ J 2017;521–30.
[2] Yeh RW, Sidney S, Chandra M, et al. Population trends in the incidence and outcomes of acute myocardial infarction. N Engl J Med 2010; 362:2155–65.
[3] Furman MI, Dauerman HL, Goldberg RJ, et al. Twenty-two years (1975 to 1997) trends in the incidence, in-hospital and long-term case-fatality rates from initial Q-wave and non-Q-wave myocardial infarction: a multi-hospital, community-wide perspective. J Am Coll Cardiol 2001; 37:1571–80.
[4] Fox KA, Dabbous OH, Goldberg RJ, et al. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). BMJ 2000;333:1091.
[5] O'Connor GT, Buring JE, Yusuf S, et al. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. Circulation 1989;80:234–44.
[6] Oldridge NB, Guyatt GH, Fischer ME, et al. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. JAMA 1988;260:945–50.
[7] Suaya JA, Stason WB, Ades PA, et al. Cardiac rehabilitation and survival in older coronary patients. J Am Coll Cardiol 2009;54:25–33.
[8] Turk-Adawi K, Sarrafzadegan N, Grace SL. Global availability of cardiac rehabilitation. Nat Rev Cardiol 2014;11:586–96.
[9] Jackson L, Leclerc J, Erskine Y, et al. Getting the most out of cardiac rehabilitation: a review of referral and adherence predictors. Heart 2005;91:10–4.
[10] Kwong JS, Lau HL, Yeung F, et al. Yoga for secondary prevention of coronary heart disease. Cochrane Database Syst Rev 2015;2015: CD009506.
[11] Jin L, Xue qinbQBo, Li R, et al. Comparative study on energy consumption characteristics of Baduanjin and the ninth set of radio gymnastics. Chin J Sports Med 2015;34:588–91.
[12] Koh TC. Baduanjin—an ancient Chinese exercise. Am J Chin Med 1982;10:14–21.
[13] Du WY, Su SZ, Zhao YB, et al. Clinical observation of Baduanjin on improving balance function and gait in the elderly. Hebei Traditional Chin Med 2018;987–90.
[14] Wang JY, Ding Y, Li YQ. Meta-analysis of the effect of Baduanjin on physiological function of middle-aged and elderly people. J Jishou Univ (Nat Sci) 2016;2:73–7.
[15] Zhou XQ, Zeng YG, Yang BL. Effects of fitness Qigong Baduanjin on blood lipid in middle-aged and elderly people. J Beijing Sport Univ 2007;6:795–7.
[16] Chen YQ, Liu RZ, He R. Effects of Baduanjin on sleep quality of elderly hypertension patients. Hunan J Traditional Chin Med 2015;4:52–3.
[17] Journal of cardiology, Chinese medical association, editorial board of the Chinese journal of cardiovascular diseasesGuidelines for diagnosis and treatment of acute ST-elevation myocardial infarction. Chin J Cardiovasc Dis 2015;5:380–93.
[18] Chinese society of cardiology, editorial board of the Chinese journal of cardiovascular diseasesGuidelines for diagnosis and treatment of non-ST-elevation acute coronary syndrome (2016). Chin J Cardiovasc Dis 2017;5:359–76.

[19] Nery RM, Zanini M, de Lima JB, et al. Tai Chi Chuan improves functional capacity after myocardial infarction: a randomized clinical trial. Am Heart J 2015;169:854–60.
[20] Salmoirago-Blotcher E, Wayne PM, Dunsiger S, et al. Tai Chi is a promising exercise option for patients with coronary heart disease declining cardiac rehabilitation. J Am Heart Assoc 2017;6:e006603.
[21] Qiu FB. On yoga and its psychophysiological function. J Shandong Univ Phys Educ 2004;5:60–1.
[22] Chen SQ. Research progress on physiological and psychological effects of yoga. Chin J Sports Med 2012;8:740–5.
[23] Zhu D, Li L, Qiu PX, et al. Investigation and analysis of knee pain among tai chi practitioners in Shanghai. Chin J Sports Med 2011;9: 820–4.
[24] Xie QX. Comparative study on fitness function between Taijiquan and Qigong Baduanjin. J Changchun Normal Univ 2015;34:78–81.
[25] Jin L, Li R, Chen J, et al. Surface Electromyography analysis of the lower extremities of subjects participating in Baduanjin exercises. Evid Based Complement Alternat Med 2017;2017:1304190.
[26] Li M, Fang Q, Li J, et al. The effect of Chinese traditional exercise-Baduanjin on physical and psychological well-being of college students: a randomized controlled trial. PLoS One 2015;10:e130544.
[27] Vanhees L, Fagard R, Thijs L, et al. Prognostic significance of peak exercise capacity in patients with coronary artery disease. J Am Coll Cardiol 1994;23:358–63.
[28] Dominguez H, Torp-Pedersen C, Koeber L, et al. Prognostic value of exercise testing in a cohort of patients followed for 15 years after acute myocardial infarction. Eur Heart J 2001;22:300–6.
[29] Zhao W, Bai J, Zhang FC, et al. Safety of early cardiopulmonary exercise test in myocardial infarction patients with acute ST-elevation. J Peking Univ Health Sci 2011;43:608–11.
[30] Jain A, Myers GH, Sapin PM, et al. Comparison of symptom-limited and low level exercise tolerance tests early after myocardial infarction. J Am Coll Cardiol 1993;22:1816–20.
[31] Zhang YM, Lu Y, Tang Y, et al. The effects of different initiation time of exercise training on left ventricular remodeling and cardiopulmonary rehabilitation in patients with left ventricular dysfunction after myocardial infarction. Disabil Rehabil 2016;38:268–76.
[32] Ross RM. ATS/ACCP statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med 2003;167:1451.
[33] Krone RJ, Gillespie JA, Weld FM, et al. Low-level exercise testing after myocardial infarction: usefulness in enhancing clinical risk stratification. Circulation 1985;71:80–9.
[34] Dei CL, Metra M, Cuccia C, et al. Prognostic significance of clinical, ergometric and coronarographic data in patients soon after myocardial infarction. Cardiologia 1989;34:317–25.
[35] Brzostek T, Van de Werf F, Mortelmans L, et al. Early and late exercise capacity after acute myocardial infarction treated with recombinant tissue-plasminogen activator. Eur Heart J 1994;15:641–7.
[36] Yokoyama Y, Tanabe K, Yamada S, et al. Changes in plasma level of brain natriuretic peptide during exercise in recovery phase of myocardial infarction and the clinical significance. J Cardiol 1996;27:121–31.
[37] Vogiatzis I, Dapcevic I, Datsios A, et al. A comparison of prognostic value of the levels of proBNP and troponin T in patients with acute coronary syndrome (ACS). Med Arch 2016;70:269–73.