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Research Article

Effects of Personalized Precise Exercise Training with Holistic Integrative Protocol on Cardiac Rehabilitation in Patients with Chronic Heart Failure: A Pilot Clinic Investigation

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Abstract

Background: Reports on the effects of an exercise training - based holistic management program among patients with chronic heart failure are limited.

Objective: To explore the effects of individualized exercise-based holistic management on cardiopulmonary function, management of co-morbidities, and prognosis on CHF patients.

Design: A pilot clinic investigation.

Setting: Beijing Rehabilitation Hospital.

Participants: 30 clinically stable patients (NYHA class □-□) with left ventricular ejection fraction <45%.

Intervention: All patients were randomly divided into Control group (n = 15) and Exercise group (n = 15).

Main Outcome Measures: Before and after a 12-week intervention, general evaluations of all patients, including cardiopulmonary function, exercise tolerance, and quality of life, were recorded. The dosage adjustments of drugs to treat co-morbidities (hypertension, diabetes, and hyperlipidaemia) were analyzed. Following the 12-week treatment, all patients were followed-up for one year to assess the average rehospitalization rate of heart failure-related events.

Results: After 12-week holistic management, the cardiopulmonary function, exercise tolerance, and quality of life of patients in the Exercise group improved significantly. The levels of blood pressure, glucose, and lipids of patients in the Exercise group remained stable after the drug dosages for treating co-morbidities were decreased. Surprisingly, a few patients completely stopped taking their prescribed drugs for co-morbidities. The average rehospitalization rate of heart failure-related events in the Exercise group decreased greater than that in the Control group.

Conclusion: Personalized exercise training with holistic integrative protocol could improve patients' holistic function, facilitate the management of co-morbidities, and aid in reducing the average rehospitalization rate of heart failure events, thus is suggested for application in treatment of patients with chronic heart failure.

Keywords: Heart failure; Personalized; Holistic management; Rehabilitation; Exercise training

Introduction

Chronic heart failure is a complex clinical syndrome characterized by symptoms, such as breathlessness and fatigue, resulting in marked reductions in patients' exercise capacity and health-related quality of life. Exercise training, recommended by guidelines [1,2]. Is an important component of cardiac rehabilitation offered to patients with chronic heart failure? Many trials have confirmed that exercise training can improve exercise capacity and quality of life of patients [3-7]. Exercise training should be implemented under the guide of exercise prescriptions to achieve effective functional improvement, and assure safety. Symptom-limited Cardiopulmonary Exercise Testing (CPET) is now considered the gold standard method for exercise capacity assessment and has been used to formulate precise individual exercise prescriptions [8-10]. Our previous study [11-13]. Explored the effects of exercise training on cardiac rehabilitation in patients, and verified the efficacy and safety of exercise training in stable patients with chronic heart failure.

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The holistic management program includes, in addition to exercise, lifestyle adjustment, drug therapy, control of risk factors, and so on [14,15]. In our study, we found that blood pressure and/or blood glucose of patients with hypertension and/or diabetes decreased significantly during exercise rehabilitation, and the dosage of prescribed drugs had to be adjusted to maintain blood pressure and glucose stability, respectively. In another study [16]. 5 medical workers with hypertension without other co-morbidities completely stopped taking their anti-hypertensive drugs after a 12-week exercise program with holistic rehabilitation. Although the above findings indicate that personalized exercise integrative program could facilitate the dosage reduction of some drugs, even eliminating drug administration in some cases, no guidelines have been proposed to implement such changes. Moreover, the effects of personalized exercise training with holistic integrative protocol on cardiac rehabilitation, including management of co-morbidities and drug therapy, in patients remain unclear. Thus, the presented study aimed to explore the impacts of personalized exercise training with holistic integrative protocol on holistic function and the control of co-morbidities (hypertension, diabetes, and hyperlipidaemia) in patients with chronic heart failure.

Methods

Design and participants

This study was a randomized controlled investigation with the Control group and Exercise group. A total of 37 clinically stable patients (NYHA class -) with left ventricular ejection fraction <45% in Beijing Rehabilitation Hospital of Capital Medical University from January 2015 to January 2018 were recruited. All patients' statuses remained stable for at least one month without any clinical symptoms or physical signs. We excluded patients with acute coronary syndrome, acute heart failure, active myocarditis, acute pericarditis, malignant arrhythmia, severe valvular heart disease, uncontrolled hypertension, and non-cardiovascular causes of exercise limitation. 30 participants were eligible for the study (Figure 1). All patients in the Exercise group were managed for 12 weeks in hospital followed by one year of home-based training. This study was approved by the Beijing Rehabilitation Hospital Ethics Committee. All participants provided written informed consent.

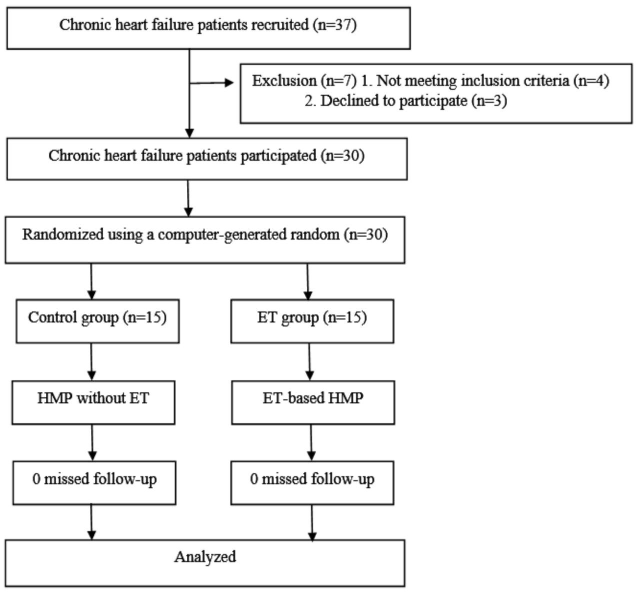

Figure 1: Flow diagram of the study design.
ET: Exercise Training; HMP: Holistic Management Program.

Intervention

After acquiring basic clinical data, the patients were randomly divided into two groups: the Control group (n = 15) was treated with conventional therapy without exercise; and the Exercise group (n = 15) participated in the exercise program according to the individualized exercise prescription by CPET. Before and after a 12-week intervention, general evaluations of all patients, including CPET, resting lung function, echocardiogram, 6-min walking distance, and quality of life score, were recorded. The dosage adjustments of drugs to treat co-morbidities (hypertension, diabetes, and hyperlipidaemia) during the 12-week intervention were analyzed.

Exercise-based holistic management protocol

The holistic management of patients contained exercise, medication, nutrition, psychology, no smoking, and so on [1,17,18]. Patients were provided with individualized information of lifestyle adjustment and self-care to support self-management. Patients in the Control group were treated with the above rehabilitation program, excluding exercise, while patients in the Exercise group were treated with all the above treatments, including exercise training. Precise and personalized exercise intensity prescriptions were tailored according to the function evaluation by CPET. Patients in the Exercise group exercised using an ergometer at an intensity of Δ50% power above anaerobic threshold [11,12]. Where Δ50%power (W) = [(power at anaerobic threshold - incremental rate × 0.75) + (power at peak work - incremental rate × 0.75)]/2. They underwent five training sessions per week for 12 weeks under the multi-parameter detection. After 5-min of warm-up, patients had to exercise on a cycle ergometer (Custo-med, Germany) for 30 min at permanent individualized power, which was followed by a 5-min cool-down period. Besides the personalized exercise with the ergometer, patients in the Exercise group were encouraged to add one or two types of resistance exercises, such as an elastic belt, yoga, baduanjin, or tai chi training, for 0.5 -1 h per day.

Dosage adjustments of drugs treated co-morbidities

The dosage adjustments of drugs to treat co-morbidities, such as hypertension, diabetes, and hyperlipidaemia, were performed during the 12-week intervention according to each patient's status and / or detection results. The blood pressure and peripheral blood glucose of patients were detected every day, and the blood lipids of patients were detected every month. The dosages of anti-hypertension drugs were reduced if the patients showed hypotension-related symptoms, resting systolic blood pressure less than 90 mmHg, and/or poor blood pressure response during exercise in patients with hypertension. The dosages of anti-diabetes drugs of patients with diabetes were decreased if hypoglycemia - related symptoms appeared and / or if blood glucose was less than 3.9 mmol/L. oppositely, the dosages of the drugs to treat co-morbidities were increased if the levels of blood pressure, glucose, and lipids did not reach target levels according to related guidelines.

Long-term management after 12-week intervention

A follow-up with all patients was performed by telephone,

Table 1: Characteristics of patients with chronic heart failure in the Control and Exercise groups.

	Control group (n=15)	Exercise group (n=15)	*P*
Age (y), mean (SD)	67.2(7.7)	65.1(8.1)	0.467
Gender, n, male (%)	12(80)	14(93)	0.283
Body mass index, Kg/m^2, mean (SD)	25.2(3.9)	25.7(2.3)	0.661
Smoking history, n (%)	9(60)	10(67)	0.705
Ischemic cardiac disease, n (%)	13(87)	14(93)	0.543
Hypertension, n (%)	8(53)	10(67)	0.456
Diabetes, n (%)	5(33)	4(27)	0.69
Hyperlipidemia, n (%)	11(73)	9(60)	0.439
ACEI/ARB, n (%)	12(80)	13(87)	0.624
Beta-blocker, n (%)	11(73)	12(80)	0.666
Diuretic, n (%)	8(53)	9(60)	0.713
Digoxin, n (%)	3(20)	1(7)	0.598

ACEI: Angiotensin-Converting Enzyme Inhibitors; ARB: Angiotensin - Receptor Blockers.

network, or interview after 12-week intervention. Patients in the Exercise group were encouraged to continue exercising according to individual status or habits, such as jogging, walking, swimming, elastic belt, baduanjin, and tai chi, and were provided continuously with individualized information for lifestyle adjustment and self-care. Patients in the Control group were treated with conventional therapy without exercise. Home blood pressure and peripheral blood glucose readings for all patients were self-monitored, and the blood lipid test was performed in the hospital every 3 or 6 months. Drugs and/or exercise of all patients were adjusted according to the patient's holistic status or detection results.

Average rehospitalization rate within one year after 12-week intervention

After the 12-week intervention, all patients were followed up for one year by either contacting the patient or family, and the average rehospitalization rate of heart failure-related events was assessed. Rehospitalization due to heart failure-related events was defined as the occurrence of typical symptoms and signs of heart failure exhibited by patients, who thus at least a 24-h hospital needed stay.

Outcome Measures

The primary end point was peak oxygen uptake (VO_2, mL/min) which were measured by symptom-limited CPET and expressed as a value adjusted to body weight (mL/kg/min). All CPET values were reported in absolute terms and normalized to percentage of predicted (%pred). Secondary end points included CPET values except peak VO_2, rest lung function, echocardiography, BNP, QoL score and 6 Min Walking Distance (6 MWD). Both Left Ventricular End-Diastolic Diameter (LVEDD) and LVEF of all patients were evaluated separately by Doppler echocardiography in ultrasound department, Plasma BNP concentrations were detected by human BNP ELISA kit (Huanzhong Bioengineering Institute Shijiazhuang, China) according to the manufacturer's instructions. Health-related QoL was measured by the Minnesota Living with Heart Failure (MLWHF) questionnaire. 6 min walking tests were conducted in a standardized format as previously reported [19,20].

All the above parameters were estimated at the base and at the end of 12-week rehabilitation program.

Data Analysis

SPSS 26.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Kolmogorov-Smirnov test was used to test normality and normal distribution of continuous variables. Continuous variables were presented as mean ± Standard Deviation (SD). All analyses were performed using commercial software. Paired-sample *t-test* was used to analyze the difference before and after intervention, and independent-sample *t-test* was used to analyze the difference between the Control and Exercise groups. The Fisher exact probability test was performed for categorical variables. *P* values of <0.05 were considered statistically significant.

Results

Flow of participants through the study

Figure 1 shows the design of the study and flow of participants through the investigation. All 30 patients completed the intervention and follow-up. The mean age of all patients was 66 ± 8 years; and 87% were male. The etiology of chronic heart failure was ischemic in 90% of the patients. Most of the patients received angiotensin-converting enzyme inhibitors or angiotensin - receptor blockers, and beta-blockers. There was no statistical difference in sex, age, body mass index, etiology, smoking, co-morbidities, and drugs between the Control and Exercise groups. Characteristics of patients in both groups are detailed in Table 1.

Impacts of personalized exercise training on holistic function

All patients finished the symptom-limited CPET, and patients in the Exercise group completed the 12-week Exercise program safely, without any serious cardiac event occurring during either program. As shown in Table 2, peak VO_2 of patients elevated obviously after training. In the Exercise group, peak VO_2 significantly improved in patients after the 12-week exercise program (compared with pro-exercise, $P < 0.05$). After 12-week exercise, peak VO_2 in patients in Exercise group were significantly higher than that of patients in Control group ($P < 0.05$). The other CPET parameters (anaerobic threshold, peak O_2 pulse, and peak workload) in Exercise group were significantly higher than those of patients in Control group ($P < 0.05$).

Effects of exercise on resting lung function were shown in Table 3, after 12-week exercise, the variables of patients, such as forced vital capacity, forced expiratory volume at first second and were significant higher in patients of the Exercise group than those in the Control group ($P < 0.05$). Effects of exercise on echocardiography, 6-min walking distance and quality of life were shown in Table 4, after the exercise program, left ventricular ejection fraction and 6-min walking distance increased, while the quality of life score decreased significantly in patients of the Exercise group compared with patients before exercise and control group ($P < 0.05$). But exercise training had no obvious effect on left ventricular end-diastolic diameter in patients.

Effects of personalized exercise integrative program on management of co-morbidities

As shown in Table 5. After 12-week intervention, the levels

Table 2: Changes of cardiopulmonary exercise testing parameters among patients with chronic heart failure in the Control and Exercise groups before and after 12-week intervention (mean (SD)).

Parameters	Control group (n=15)			Exercise group (n=15)			P_1	P_2
	Baseline	After 12 weeks	*P*	Baseline	After 12 weeks	*P*		
Resting HR (beats/min)	73.0(10.4)	71.9(14.3)	0.583	76.6(11.4)	74.0(12.7)	0.325	0.508	0.675
Peak HR (beats/min)	120.4(23.1)	113.7(21.9)	0.163	125.3(26.3)	128.2(20.2)	0.559	0.589	0.076
Resting SBP (mmHg)	112.8(18.3)	117.7(19.2)	0.15	116.0(11.8)	119.2(15.0)	0.547	0.574	0.821
Peak SBP (mmHg)	158.6(29.8)	151.8(31.1)	0.394	165.9(23.1)	173.7(16.0)	0.175	0.458	0.026
Resting DBP (mmHg)	66.9(7.5)	65.9(8.6)	0.763	69.7(6.2)	70.7(5.8)	0.561	0.264	0.09
Peak DBP (mmHg)	76.3(9.5)	74.3(8.1)	0.613	78.4(11.6)	77.7(5.2)	0.815	0.586	0.243
Anaerobic threshold								
(L/min)	634.5(149.1)	693.7(159.6)	0.143	721.6(181.8)	1032.2(285.4)	0.002	0.163	<0.001
(mL/min/kg)	9.6(1.8)	9.8(2.1)	0.679	9.8(1.9)	13.8(3.7)	0.001	0.683	0.001
(% predicted)	61.3(17.6)	64.4(17.2)	0.535	62.8(17.3)	82.7(14.0)	0.001	0.82	0.004
Peak O_2 uptake								
(L/min)	918.5(277.7)	895.5(200.6)	0.61	1026.3(262.3)	1561.2(437.3)	0.001	0.284	<0.001
(mL/min/kg)	13.6(2.8)	13.1(2.4)	0.379	14.0(2.5)	20.3(4.1)	<0.001	0.722	<0.001
(% predicted)	59.3(18.4)	58.6(16.4)	0.86	60.3(19.0)	80.2(13.9)	0.001	0.885	0.001
Peak O_2 pulse								
(mL/beat)	8.5(2.4)	8.9(2.2)	0.22	9.2(2.4)	12.5(2.3)	0.001	0.423	<0.001
(% predicted)	79.3(31.0)	87.7(28.7)	0.162	80.9(18.9)	99.3(12.0)	0.002	0.864	0.172
Peak Workload								
(W)	78.3(22.1)	76.6(22.3)	0.713	81.1(19.6)	123.1(26.9)	<0.001	0.722	<0.001
(% predicted)	73.1(19.5)	72.3(20.1)	0.913	76.9(17.8)	92.4(23.9)	0.005	0.581	0.019

HR: Heart Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.
P1: P Value between Control Group and Exercise Group at Baseline. P2: P Value between Control Group and Exercise Group after 12 Weeks.

Table 3: Changes of resting lung function among patients with chronic heart failure in the Control and Exercise groups before and after 12-week intervention (mean (SD)).

Parameters	Control group (n=15)			Exercise group (n=15)			P_1	P_2
	Baseline	After 12 weeks	*P*	Baseline	After 12 weeks	*P*		
Tidal volume (L)	0.6 (0.1)	0.7 (0.1)	0.298	0.7 (0.2)	0.7 (0.3)	0.101	0.591	0.407
Tidal volume (%pred)	136.8 (34.0)	127.2 (17.6)	0.297	123.4 (25.2)	131.1 (20.8)	0.197	0.228	0.585
MV (L/min)	13.0 (3.8)	13.4 (3.1)	0.709	13.3(3.3)	14.6 (3.4)	0.174	0.828	0.337
FVC(L)	3.0 (0.7)	3.1 (0.8)	0.449	3.1 (0.6)	3.7 (0.6)	0.005	0.484	0.028
FVC(%pred)	88.6 (13.7)	88.8(12.4)	0.978	91.5 (11.0)	100.2 (11.3)	0.029	0.531	0.013
FEV1 (L)	2.3 (0.7)	2.4 (0.6)	0.457	2.4 (0.5)	2.9 (0.5)	0.002	0.696	0.038
FEV1 (%pred)	88.1 (15.1)	85.9 (13.2)	0.641	90.9(14.2)	99.0 (10.6)	0.029	0.612	0.006
FEV1 / FVC	78.9 (7.6)	76.9 (5.8)	0.283	75.4 (5.5)	76.9 (5.5)	0.385	0.161	0.98
MVV (L)	82.8(17.6)	83.3 (24.0)	0.912	80.8 (21.7)	100.1 (30.1)	0.029	0.782	0.103
MVV (%pred)	79.2 (14.9)	76.9 (15.3)	0.659	77.5 (18.7)	90.0 (20.2)	0.049	0.786	0.056
DLCO-SB (mmol/min/kpa)	6.3 (2.0)	5.8 (1.7)	0.52	6.0 (1.1)	6.5 (1.1)	0.072	0.628	0.209
DLCO-SB (%pred)	79.2 (21.2)	69.1 (13.2)	0.179	73.3 (16.3)	76.3 (13.5)	0.368	0.400	0.152

MV: Minute Ventilation; FVC: Forced Vital Capacity; FEV: Forced Expiratory Volume; MVV: Maximum Voluntary Ventilation; DLCO-SB: Diffusing Capacity of The Lung for Carbon Monoxide Determined in Single Breath.
P1: P Value between Control Group and Exercise Group at Baseline. P2: P Value between Control Group and Exercise Group after 12 Weeks.

of glycosylated hemoglobin, total cholesterol, and low-density lipoprotein cholesterol in the Exercise group decreased significantly compared with pre-exercise training ($P < 0.05$). Between the groups, the blood pressure, glycosylated hemoglobin, or blood lipid levels obviously decreased in the Exercise group (compared with Control group, $P < 0.05$). The number of patients whose drug dosages were adjusted during the 12-week intervention is provided in Table 6. We found that no patient in the Exercise group required increased

Table 4: Changes of plasma BNP, echocardiogram, 6MWD and quality of life score among CHF patients in the Control and Exercise groups before and after 12-week intervention (mean (SD)).

Parameters	Control group (n=15)			Exercise group (n=15)			P_1	P_2
	Baseline	After 12 weeks	*P*	Baseline	After 12 weeks	*P*		
LVEF (%)	38.3(4.8)	38.7(4.5)	0.697	39.1(5.7)	47.4(8.0)	<0.001	0.705	0.001
LVEDD (mm)	58.7(5.9)	58.0(5.9)	0.24	58.9(5.7)	56.8(5.8)	0.052	0.925	0.58
6MWD (m)	383.3(62.8)	394.0(74.1)	0.378	393.1(55.8)	508.9(57.0)	<0.001	0.657	<0.001
quality of life	38.7(11.6)	40.7(12.3)	0.318	42.3(9.3)	11.5(6.4)	<0.001	0.357	<0.001

BNP: B-Type Natriuretic Peptide; 6MWD: 6-Minute Walking Distance; CHF: Chronic Heart Failure; LVEF: Left Ventricular Ejection Fraction; LVEDD: Left Ventricular End-Diastolic Diameter.
P1: P value between Control group and Exercise group at baseline. P2: P value between Control group and Exercise group after 12 weeks.

Table 5: Changes of resting blood pressure, glycosylated hemoglobin, and lipid profiles among patients with chronic heart failure in the Control and Exercise groups before and after 12 weeks intervention (mean (SD)).

Parameters	Control group (n=15)			Exercise group (n=15)			P_1	P_2
	Baseline	After 12 weeks	*P*	Baseline	After 12 weeks	*P*		
SBP (mmHg)	115.7(11.4)	118.0(10.4)	0.351	117.6(12.3)	120.3(11.4)	0.132	0.659	0.574
DBP (mmHg)	67.8(7.4)	66.6(4.5)	0.207	68.9(8.7)	69.5(8.2)	0.494	0.719	0.236
Glycosylated hemoglobin (%)	6.1(0.7)	6.0(0.5)	0.119	6.0(0.7)	5.8(0.6)	0.024	0.703	0.452
triglyceride (mmol/L)	1.7(0.5)	1.6(0.4)	0.201	1.7(0.5)	1.5(0.5)	0.097	0.973	0.811
Total cholesterol (mmol/L)	4.2(0.9)	4.2(0.7)	0.446	4.3(0.8)	3.8(0.7)	<0.001	0.880	0.166
LDL-C(mmol/L)	2.4(0.5)	2.5(0.7)	0.844	2.5(0.7)	2.0(0.5)	0.001	0.686	0.038
HDL-C(mmol/L)	1.1(0.3)	1.1(0.4)	0.587	1.1(0.3)	1.2(0.3)	0.068	0.910	0.528

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LDL-C: Low-Density Lipoprotein Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol.
P1: P Value between Control Group and Exercise Group at Baseline. P2: P Value between Control Group and Exercise Group after 12 Weeks.

Table 6: The number of patients with co-morbidities (hypertension, diabetes, and hyperlipidemia) whose drug dosages were adjusted in the Control and Exercise groups.

	Control group				Exercise group			
	Reduced	Unchanged	Increased	Total	Reduced	Unchanged	Increased	Total
Anti-Hypertension drugs	1	6	1	8	4	6	0	10
Anti-Diabetes drugs	1	3	1	5	3	1	0	4
Anti-Hyperlipidemia drugs	0	9	2	11	1	8	0	9

drug dosage to treat co-morbidities during the 12-week treatment. For patients with reduced drug dosage, their resting blood pressure, blood glucose, and lipid profiles maintained stable levels without aggravation. Surprisingly, one patient stopped taking his anti-diabetes drugs completely, and two patients stopped taking their anti-hypertension drugs, excluding angiotensin-converting enzyme inhibitors/angiotensin - receptor blockers and beta-receptor blockers, which are recommended for secondary prevention in patients.

Effects of exercise on average rehospitalization rate

No patient died during the 12-week intervention or during the 1-year follow-up. After the 12-week exercise program, average rehospitalization rate after 1-year follow-up was significantly lower in patients of the Exercise group than the Control group (6.67% in Exercise group *vs.* 46.67% in Control group, $P = 0.035$).

Discussion

Chronic heart failure, the terminal stage of various heart diseases, seriously affects the quality of life of patients. The prevalence of heart failure in the Chinese population was 0.9% in 2000 [21]. And the in-hospital mortality was 4.1% in 2014 [22]. In the United States, the lifetime risk of developing heart failure is 20% for Americans ≥40 years of age [2]. Thus, chronic heart failure is a major public health problem with high morbidity and mortality. Exercise training, which can improve exercise capacity and quality of life, is now widely used as an important therapy for stable patients based on recommendation guidelines [1,2,23]. Consistent with previous reports [3,6]. This study determined that an exercise program with holistic management could effectively improve the cardiopulmonary function and exercise capacity of patients, as indicated by improvement in forced vital capacity, forced expiratory volume at first second, peak oxygen uptake, peak workload, left ventricular ejection fraction, and 6-min walking distance.

Exercise training, a key component for secondary prevention of chronic heart failure, should be implemented as a guided exercise prescription to assure safety and efficiency for patients. Symptom-limited cardiopulmonary exercise testing has been used to evaluate exercise capacity objectively and quantitatively and to formulate precise individualized exercise prescriptions; thus, it is considered the gold standard method for exercise capacity assessment [8-10]. Thus, a scientific statement by the AMA recommends implementing cardiopulmonary exercise testing routinely before exercise [24]. Our previous study [13]. Investigated the safety and efficiency of exercise at different levels of intensity and found that high intensity (Δ50% power above anaerobic threshold) exercise had better effects on exercise capacity than moderate intensity (80% anaerobic threshold power) exercise and was considered safe. Therefore, in this study, we explored the effects of high intensity exercise program on cardiac rehabilitation in stable patients, which revealed improvements in exercise capacity and quality of life of patients in the Exercise group. Moreover, average rehospitalization rate after a 1-year follow-up was decreased significantly, and no serious cardiac event occurred during the 12-week exercise program. Additionally, the results show that peak systolic blood pressure during cardiopulmonary exercise testing of patients in the Exercise group increased significantly after the 12-week exercise, which, together with the increase of left ventricular ejection fraction, indicates that cardiac function was improved markedly by exercise training. Although the precise mechanism by which exercise-based rehabilitation programs benefit patients remains unclear, it has been reported that exercise improves myocardial perfusion by alleviating endothelial dysfunction and dilating coronary vessels [25,26], attenuates ventricular remodeling [27,28]. And improves myocardial contractility and diastolic filling [25,29]. In addition, exercise training can improve skeletal muscle O_2 transport and utilization [30]. Modify autonomic nervous system function [31]. And attenuate the production of pro-inflammatory cytokines and natriuretic peptides [32,33].

Co-morbidities, such as hypertension, diabetes, and hyperlipidaemia, may aggravate heart failure symptoms and further impair quality of life, contributing to the rehospitalization and mortality of patients [1,34]. Thus, it is pertinent to monitor and manage co-morbidities in these patients as a key component of the holistic care. Until now, there was no systematic study on the management of blood pressure, glucose, and lipid levels as well as dosage adjustment of drugs for treating co-morbidities in patients during the exercise program. In this present study, we explored the effects of personalized exercise integrative program on resting blood pressure, glucose, and lipid levels in patients. Results revealed that no patients required an increased drug dosage to treat co-morbidities, and the dosages were reduced in many patients, especially with diabetes and hypertension, during 12-week intervention in the Exercise group. Moreover, the levels of blood pressure, glucose, and lipids remained stable without aggravation. The above findings suggest that exercise training could improve blood pressure regulation and glucose and lipid metabolism. Collectively, the blood pressure, glucose, and lipid levels of all patients were stable before intervention, while the dosage of related drugs was adjusted timely during the 12-week intervention, and hypertension and/or diabetes of patients remained at safe levels. Therefore, after the 12-week intervention, there was no difference in blood pressure, glycosylated hemoglobin, and lipid levels between the Control group and Exercise group, except low-density lipoprotein cholesterol, which was lower in the Exercise group. In addition, the adjustment of drugs over time proved to be an important factor of cardiac rehabilitation by helping to maintain stable blood pressure, glucose, and lipid levels, decrease adverse reaction to exercise, and increase the safety and efficiency of exercise in patients.

Considering that cardiac rehabilitation of chronic heart failure is a long-term holistic management, its benefits may dissipate if the exercise program stops. Therefore, after the 12-week intervention, follow-up with all patients was conducted by telephone, network, or interview, and the patients in the Exercise group were encouraged to continue exercising and maintain a healthy lifestyle. We found that the levels of blood pressure, glucose, and lipids of patients in the Exercise group did not change. Moreover, the average rehospitalization rate of heart failure-related events within 1 year decreased significantly more in the Exercise group than in the Control group, indicating improved prognosis by personalized exercise integrative program.

The above data verify that personalized exercise training with holistic integrative protocol could improve cardiopulmonary function and excise capacity, promote the effective management of chronic heart failure co-morbidities, improve the holistic status, and reduce average rehospitalization rate of heart failure-related events in patients. Based on stable blood pressure, glucose, and lipid levels in patients, the dosage reduction resulted in higher efficacy, better safety, and reduction of side effects of drugs used to treat co-morbidities, additionally decreasing the economic burden on patients.

Limitations

This study is attributed to it being conducted at a single center; thus, data were collected for a smaller sample size and lower ratio of female patients (13%). We included only the patients who were able to complete the 12-week exercise program and excluded patients whose statuses were not stable for 1 month after the last cardiovascular acute event.

Conclusion

In stable patients with chronic heart failure, personalized precise exercise training with holistic integrative protocol resulted in clinically significant improvements in cardiopulmonary function, exercise capacity, and quality of life, facilitated the management of co-morbidities, and reduced the average rehospitalization rate of heart failure-related events. These results may help to provide suggestions for the effective development of clinical cardiac rehabilitation for patients.

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