


Comparison of cardiac rehabilitation (exercise + education), exercise only, and usual care for patients with coronary artery disease: A non-randomized retrospective analysis

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Abstract

Cardiac rehabilitation program is well-established but the Rehabilitation After Myocardial Infarction Trial (RAMIT) is reported that it does not affect mortality and morbidity of patients after myocardial infarction during follow-up period. The objectives of the study were to compare functional walking capacity, risk factor control, and morbidities in follow-up for cardiac rehabilitation (exercise + education), exercise only, and usual care among patients with coronary artery disease. A total of 492 male and female patients (age range: 45–73 years) with coronary artery disease after myocardial infarction or underwent percutaneous coronary intervention or coronary artery bypass grafting surgeries referred to cardiac rehabilitation were included in the study. Patients were participating in a cardiac rehabilitation program (exercise + education, CRP cohort, $n = 125$), exercise only (USC cohort, $n = 182$), or usual care (NCR cohort, $n = 185$). Data regarding incremental shuttle walk test, lipid profile, the Patient Health Questionnaire 9, and morbidities in follow-up of patients were retrospectively collected and analyzed. After completion of 1 year, cardiac rehabilitation program ($p < 0.0001$, $q = 20.939$) and exercise ($p < 0.0001$, $q = 6.059$) were successfully increased incremental shuttle walk test. After completion of 1 year, cardiac rehabilitation program reduced low-density lipoprotein ($p = 0.007$, $q = 3.349$) and depressive symptoms ($p < 0.0001$, $q = 5.649$). Morbidities were reported fewer in the patients of CRP cohort than those of USC ($p = 0.003$, $q = 3.427$) and NCR ($p = 0.003$, $q = 4.822$) cohorts after completion of 1 year of program. Cardiac rehabilitation program (exercise + education) improved functional walking capacity, controlled risk factors, and reduced morbidities of patients with coronary artery disease than exercise only and usual care (Level of evidence: III).

Abbreviations: ANOVA, Analysis of variance; BL, Before program; CADEQ-II, Coronary Artery Disease Education Questionnaire-II (version, Chinese); CRP Cohort, Cardiac rehabilitation program cohort; EL, After completion of 1 year of program; EUROASPIRE IV, European Action on Secondary and Primary Prevention by Intervention to Reduce Events IV; NCR Cohort, no cardiac rehabilitation program or exercise or education cohort; OMEGA study, A randomized, placebo-controlled trial to test the effect of highly purified omega-3 fatty acids; q , Critical value for *post hoc* analysis; RAMIT, The Rehabilitation After Myocardial Infarction Trial; USC Cohort, Exercise only no education cohort.

Yanqun Hu and Li Li contributed equally.

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KEYWORDS

cardiac rehabilitation program, coronary artery disease, coronary artery disease education questionnaire, myocardial infarction, patient health questionnaire 9, pedometer

1 | INTRODUCTION

Cardiovascular diseases are the leading cause of morbidity and mortality and are the leading burdens of diseases.¹ Dyslipidemia, high blood pressure, obesity, diabetes, smoking, psychosocial stress, less fruit and vegetable intake, alcohol consumption, and less physical activity are the main risk factors for myocardial infarction in Chinese men and women.² Therefore, efforts, for example, as early revascularization therapies and secondary prevention are made to improve the quality of life of patients after acute myocardial infarction³ but outcomes of these efforts are not satisfactory⁴ and do not have large impact on success of cure of patients.⁵ Cardiac rehabilitation is an outpatient model of secondary prevention and is designed to reduce the burdens of cardiovascular diseases.⁶ Cardiac rehabilitation includes the education of patients and exercises.^{1,6} Cardiac rehabilitation plays an important role in the management of the risk factors and prognosis for patients after acute myocardial infarction.^{7,8} Usual care after acute myocardial infarction could include standard medical care, for example, pharmacological treatment, but do not include any type of advice or structured exercise training, for example, *Tai Chi*, aerobic exercises.⁹ Maintaining heart-health behavior changes initiated through the cardiac rehabilitation program likely to reduce mortality and morbidity in the long term.¹ The review of randomized controlled trials of exercise-based interventions with at least six months' follow-up on lower-risk myocardial infarction individuals reported that cardiac rehabilitation programs reduced the risk of hospitalization but not the risk of further myocardial infarction or revascularization.⁹ However, a crossover trial on heterogeneous myocardial infarction individuals reported that cardiac rehabilitation program reduced mortality and maintained risk factors compared to usual care.¹ Also, in China² and outside of China,¹⁰ the benefits of the cardiac rehabilitation program have been supported by large numbers of evidence-based randomized trials. However, the Rehabilitation After Myocardial Infarction Trial (RAMIT) reported that cardiac rehabilitation program does not affect mortality, risk factors control, and morbidity of patients after myocardial infarction.¹¹ Therefore, there is a need for further retrospective study before designing clinical trials to evaluate the effects of a cardiac rehabilitation program in patients with coronary artery disease.

The objectives of a non-randomized retrospective analysis were to compare functional walking capacity, risk factor control, cardiovascular disease knowledge of patients, heart-health behaviors, mortality, and morbidities in a year for cardiac rehabilitation (exercise + education), exercise only, and usual care in patients with coronary artery disease.

2 | MATERIALS AND METHODS

2.1 | Ethics Approval and consent to participate

The designed protocol of the established study (Reg. No.: HPPH151420 dated June 15, 2020) was approved by the Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University) review board and the Chinese Society of Cardiology. Informed consent was signed by all participants regarding the program and publication of the study in the form of article(s) with anonymized information of patients before the start of the study. Being a retrospective study, registration of the Chinese clinical registry was waived by the Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University) review board.

2.2 | Study population

Patients (aged ≥ 18 years) with coronary artery disease after myocardial infarction or underwent percutaneous coronary intervention or coronary artery bypass grafting surgeries referred to a cardiac rehabilitation program were included in the analysis. Patients who were unable to take part in program, physical comorbidity, and serious mental illness were excluded from the analysis.

2.3 | Sample size calculation

The sample size was calculated according to the 80% ($\beta = 0.1$) power calculation and a 5% significance level ($\alpha = 0.05$). The minimum patient required in each cohort was 120.

2.4 | Cohorts

The participants in each cohort allocated themselves. A total of 125 patients did participate in the cardiac rehabilitation program (completed a minimum of 30 exercise sessions and a minimum of 15 education sessions) at the Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University), Hainan, China, and the referring hospitals. They were included in the CRP cohort. A total of 182 patients did not participate in a cardiac rehabilitation program or education but received exercise only (no education but completed a minimum of 30 exercise sessions) at the Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University), Hainan, China, and the referring hospitals. They were included in the USC cohort. A total of 185 patients did

not participate in a cardiac rehabilitation program or exercise or education. They were included in the NCR cohort.

2.5 | Exercise

It was for 1 year. This included 48 sessions (once in a week). Each session included warm-up exercise (10 minutes), training phase (aerobic exercise, impedance exercise, and flexible exercise; 70 minutes), and relaxation of the exercise (10 minutes).² Physiotherapists (a minimum of 3 years of experiences) of institutes were involved in the exercise.

2.6 | Education

It is based on information of patients in different topics. The patients' education was about how to deal with sudden heart problems, for example, the symptoms and signs of a heart attack like chest pain or discomfort; if any events for heart attack occurred, then how to deal with the event(s),² and also, to educate about the Chinese smoking cessation program. A total of 24 sessions of 30 minutes (twice in a month) each were taken by the trained instructors of institutes.

2.7 | Sociodemographic and clinical measures

Sociodemographic (gender, age, educational status, marital status, and working status) and clinical conditions (indications for cardiac rehabilitation program and comorbidities) of patients were collected through medical records of patients.

2.8 | Functional walking capacity

For evaluation of functional walking capacity, an incremental shuttle walk test was performed. Patients were walked with an indoor flat 10 m course. The test was performed externally, with signal beeps at regular intervals to indicate when the patients have rotated around the cone and to start the next shuttle. The test began with a walking speed of 0.5 m/s, with an increase in the speed of 0.17 m/s each min for a maximum of 12 minutes.¹² The test was performed at the start of the program and after 1 year of completion of the program by a trained instructor of institutes.

2.9 | Risk factor control

Blood pressure in resting stage (less than 140 mmHg systolic and less than 90 mmHg diastolic blood pressure considered as normal),¹³ lipid profile (total cholesterol (<170 mg/dl considered normal), low-density lipoprotein (< 100 mg/dl considered normal),

high-density lipoprotein (> 45 mg/dl considered normal), triglycerides (<200 mg/dl considered normal)), fasting glucose (< 100 mg/dl considered normal), body mass index (less than 30 kg/ m² considered as normal), waist circumference (less than 100 cm for men and less than 85 cm for women considered normal),¹⁴ and depressive symptoms (Chinese version of Patient Health Questionnaire 2¹⁵; scores <9 considered normal) were evaluated at the start of program and at the end of 1 year of completion of program. These parameters were measured by physicians (a minimum of 3 years of experiences) of institutes and pathologist (a minimum of 3 years of experiences) of institutes.

2.10 | Cardiovascular disease knowledge of patients

At the start and the end of 1 year of program, Coronary Artery Disease Education Questionnaire-II (version: Chinese) was administered by trained instructors of institutes. The score ranges from 0 to 84. The higher scores indicated better knowledge.¹⁶

2.11 | Heart-health behaviors

Exercise, diet (food frequency questionnaires, the range from -36 to +47, the higher scores indicated better diet),¹⁷ and self-reported smoking parameters were included in heart-health behaviors. Exercise was assessed through the International Physical Activity Questionnaire (version: Chinese) for a week at each assessment point. Mean steps per week were evaluated. A total of 7,500 steps/day or more were considered appropriate.¹⁸ The electronic motion sensors pedometers (OMRON HJ-328, Omron, Kyoto, Japan) were used. Trained instructors of institutes evaluated these parameters at the start of the program and after 1 year of completion of the program.

Data regarding morbidity according to normal pathological and the other tests value (emergency department hospitalization, re-admission, non-fatal myocardial infarction, angina, percutaneous coronary intervention, and coronary artery bypass grafting surgeries) and mortality due to cardiac causes during 1 year were collected from medical records of patients.

2.12 | Statistical analysis

SPSS v25.0 (IBM Corporation, Armonk, New York, USA) was used for statistical analyses purpose. Descriptive data are presented as number (frequency) and continuous and ordinal data are presented as mean \pm SD. Fisher exact test was used for descriptive data and one-way analysis of variance (ANOVA) following Tukey's Honest Significant Difference test (considering critical value (q) >3.315 as significant) were performed for continuous and ordinal data.¹ 'q-value' is threshold for *post hoc* test and 3.315 is threshold for 95%

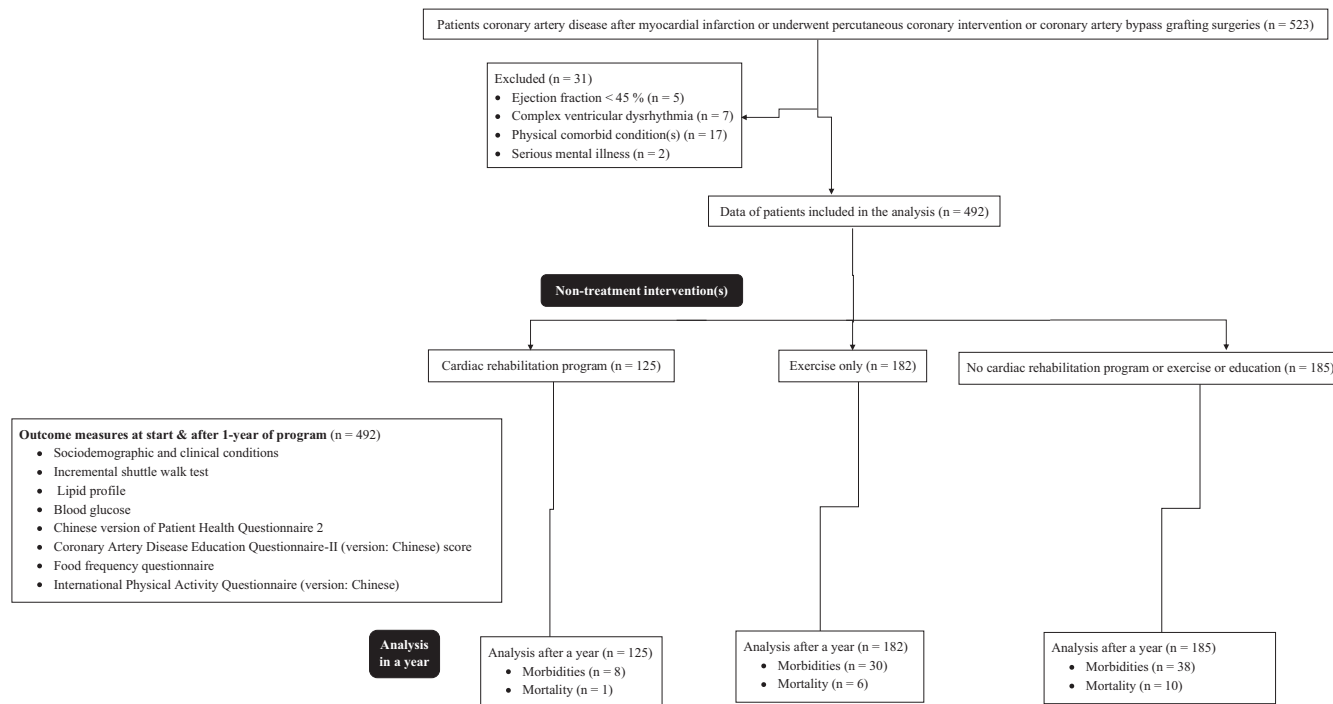


FIGURE 1 Flow diagram of the study

TABLE 1 Sociodemographic conditions of patients at the start of the cardiac rehabilitation program or exercise or education sessions

Characters		Cohorts			Comparisons between cohorts
		CRP	USC	NCR	
Non-treatment intervention(s)		Cardiac rehabilitation program	Exercise only	No cardiac rehabilitation program or exercise or education	
Numbers of patients enrolled		125	182	185	p-value
Gender	Male	94 (75)	154 (85)	148 (80)	.121
	Female	31 (25)	28 (15)	37 (20)	
Age (years)	Minimum	45	46	47	.069
	Maximum	75	74	73	
	Mean \pm SD	52.15 \pm 9.18	53.41 \pm 8.45	54.56 \pm 9.45	
Educational status	Primitive	26 (21)	39 (21)	41 (22)	.691
	Completed high school but not a bachelor degree	74 (59)	95 (52)	97 (52)	
	Bachelor or higher degree	25 (20)	48 (27)	47 (26)	
Ethnicity	Han Chinese	115 (92)	167 (92)	167 (90)	.928
	Mongolian	9 (7)	13 (7)	15 (8)	
	Tibetan	1 (1)	2 (1)	2 (1)	
	Uighur Muslims	0 (0)	0 (0)	1 (1)	
Marital status	Married	89 (71)	133 (73)	132 (71)	.913
	Unmarried/ single	36 (29)	49 (27)	53 (29)	
Working status	Employed	84 (67)	107 (59)	121 (65)	0.251
	Unemployed	41 (33)	75 (41)	64 (35)	

Descriptive data are presented as number (frequency) and continuous and ordinal data are presented as mean \pm SD.

Fisher exact test was used for descriptive data and one-way ANOVA was performed for continuous data.

Results were considered significant if $p < 0.05$.

significance. Univariate following multivariate analysis was performed for an association between morbidity of patients and sociodemographic and clinical conditions of patients.⁷ Results were considered significant if *p*-values reported less than 0.05.

3 | RESULTS

3.1 | Study population

From 13 January 2018 to 1 December 2018, a total of 523 patients (aged ≥ 18 years) with coronary artery disease after myocardial infarction or underwent percutaneous coronary intervention or coronary artery bypass grafting surgeries were referred to a cardiac rehabilitation program at the Hainan General Hospital (Hainan Affiliated Hospital of Hainan Medical University), Hainan, China and the referring hospitals. Among them, five patients had ejection fraction $< 45\%$, and seven patients had complex ventricular dysrhythmia (unable to

take part in program). Therefore, these patients were not subjected to exercise. A total of 17 patients had physical comorbid condition(s) (e.g., leg amputation, Parkinson's disease, disabling stroke, advanced cancer) and two patients had a serious mental illness. Therefore, data of these patients ($n = 31$) were excluded from the analysis. Data regarding functional walking capacity, risk factor control, patients' knowledge for cardiovascular disease, heart-health behaviors, mortality, and morbidity in a year for the cardiac rehabilitation program and usual care of total of 492 patients were retrospective collected after written approval from consent authorities and analyzed (Figure 1).

3.2 | Sociodemographic and clinical conditions of patients

From 45 to 73 years male and female patients with coronary artery disease after myocardial infarction or underwent percutaneous

TABLE 2 Clinical conditions of patients at the start of the cardiac rehabilitation program or exercise or education sessions.

Characters		Cohorts			Comparisons between cohorts
		CRP	USC	NCR	
Non-treatment intervention(s)		Cardiac rehabilitation program	Exercise only	No cardiac rehabilitation program or exercise or education	
Numbers of patients enrolled		125	182	185	<i>p</i> -value
Indications for a cardiac rehabilitation program	Myocardial infarction	99 (79)	151 (83)	157 (85)	.548
	Percutaneous coronary intervention	18 (14)	17 (9)	17 (9)	
	Coronary artery bypass grafting surgeries	8 (7)	14 (8)	11 (6)	
Comorbidities	Depression	21 (17)	43 (24)	49 (26)	.984
	Kidney disease(s)	4 (3)	5 (3)	6 (3)	
	Liver diseases	3 (2)	2 (1)	2 (1)	
	Rheumatic disease(s)	7 (6)	12 (7)	18 (10)	
	Cerebrovascular disease(s)	1 (1)	2 (1)	2 (1)	
	Cancer	1 (1)	2 (1)	2 (1)	
	Pulmonary disease(s)	3 (2)	5 (3)	9 (5)	
Medications	Aspirin	74 (59)	112 (62)	115 (62)	.155
	Statins	8 (6)	15 (8)	17 (9)	
	β -Blockers	17 (14)	31 (17)	35 (19)	
	Angiotensin-converting enzyme inhibitor	7 (6)	9 (5)	11 (6)	
	Antiplatelets	5 (4)	4 (2)	3 (2)	
	Angiotensin receptor blocker	14 (11)	11 (6)	4 (2)	
Incremental shuttle walk test (m)		335.15 \pm 25.47	341.42 \pm 27.85	339.52 \pm 32.45	.175

Descriptive data are presented as number (frequency) and continuous data are presented as mean \pm SD.

Fisher exact test was used for descriptive data and one-way ANOVA was performed for continuous and ordinal data.

Results were considered significant if $p < 0.05$.

TABLE 3 Fewer successful or unsuccessful outcome measures

Characters	Cohorts			USC			NCR			Comparisons between cohorts							
	CRP			Exercise only			No cardiac rehabilitation program or exercise or education			p-value at BL		p-value at EL		CRP vs USC		CRP vs NCR	
Non-treatment intervention(s)		Cardiac rehabilitation program		Exercise only			No cardiac rehabilitation program or exercise or education			p-value at BL		p-value at EL		CRP vs USC		CRP vs NCR	
Level	BL	EL		BL	EL		BL	EL									
Numbers of patients enrolled	125	125		182	182		185	185									
Systolic blood pressure (mmHg)	120.12 ± 21.12	118.11 ± 15.22		122.15 ± 20.15	120.15 ± 18.35		123.45 ± 22.45	120.22 ± 20.12		.389	.323	.143	.401	.549	N/A	N/A	N/A
Diastolic blood pressure (mmHg)	81.12 ± 15.85	78.23 ± 11.72		82.45 ± 16.45	81.23 ± 15.32		83.11 ± 14.15	82.12 ± 13.14		.103	.465	.143	0.537	.043	2.637	3.478	0.882
Waist circumference (cm)																	
Male	91.12 ± 10.11	90.10 ± 9.15		92.82 ± 9.15	91.45 ± 9.14		93.01 ± 10.11	92.85 ± 9.85		.469	.189	.891	0.053	.083	N/A	N/A	N/A
Female	78.15 ± 8.11	75.34 ± 7.45		79.11 ± 7.15	78.12 ± 6.25		79.51 ± 8.45	79.23 ± 7.85		.161	.584	.883	0.774	.089	N/A	N/A	N/A
Total cholesterol (mg/dl)	142.22 ± 29.15	138.18 ± 28.52		145.25 ± 26.15	141.25 ± 26.22		144.22 ± 26.44	143.24 ± 27.11		.269	.146	.725	0.626	.275	N/A	N/A	N/A
Triglycerides (mg/dl)	179.12 ± 27.18	175.23 ± 25.31 ^a		182.23 ± 24.14	180.20 ± 20.11		183.45 ± 23.41	182.41 ± 21.32		.243	.384	.655	.309	.018	2.753	3.989	1.632
Sleep apnea present	15 (12)	8 (6)		27 (15)	21 (12)		25 (14)	24 (13)		.075	.354	0.319	.776	.172	N/A	N/A	N/A
Smoking	7 (6)	3 (2)		12 (7)	10 (5)		15 (8)	14 (8)		0.249	.661	.319	.679	.103	N/A	N/A	N/A

Descriptive data are presented as number (frequency) and continuous and ordinal data are presented as mean ± SD.

Fisher exact test was used for descriptive data and one-way ANOVA following Tukey's Honest Significant Difference test was performed for continuous data.

Results were considered significant if p less than 0.05 and q greater than 3.315.

N/A: Not applicable.

BL: Before the start of the program, EL: After completion of 1 year of program.

^aSignificantly lower than NCR cohort.

coronary intervention or coronary artery bypass grafting surgeries referred to a cardiac rehabilitation program were included in the study. At the start of the cardiac rehabilitation program or exercise or education sessions, the included patients had no differences

($p > 0.05$ for all characters) for sociodemographic and clinical conditions among cohorts. The detailed sociodemographic and clinical conditions of patients are reported in Tables 1 and 2.

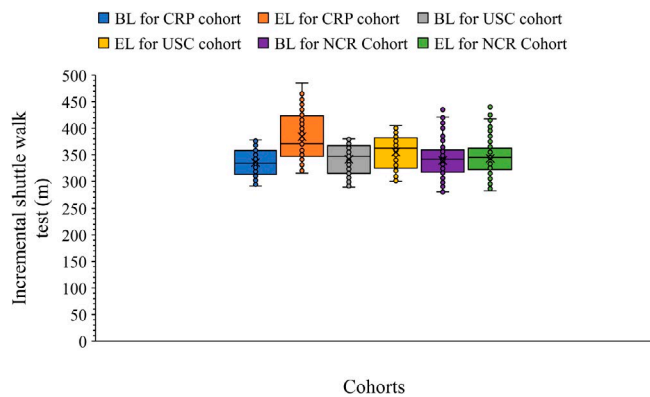


FIGURE 2 Incremental shuttle walk test analysis. BL: Before program, EL: After completion of 1 year of program

3.3 | Outcome measures

There was no significant improvement in systolic and diastolic blood pressure, waist circumference, total cholesterol, triglycerides, sleep apnea, and smoking habit after 1 year of program. After 1 year of program, the triglycerides level was significantly lower for patients of CRP cohort than those for NCR cohort (175.23 ± 25.31 mg/dl/patient vs 182.41 ± 21.32 mg/dl/patient, Table 3).

3.3.1 | Incremental shuttle walk test

After completion of 1 year, cardiac rehabilitation program (335.15 ± 25.47 m vs 384.24 ± 41.12 m, $p < 0.0001$, $q = 20.939$)

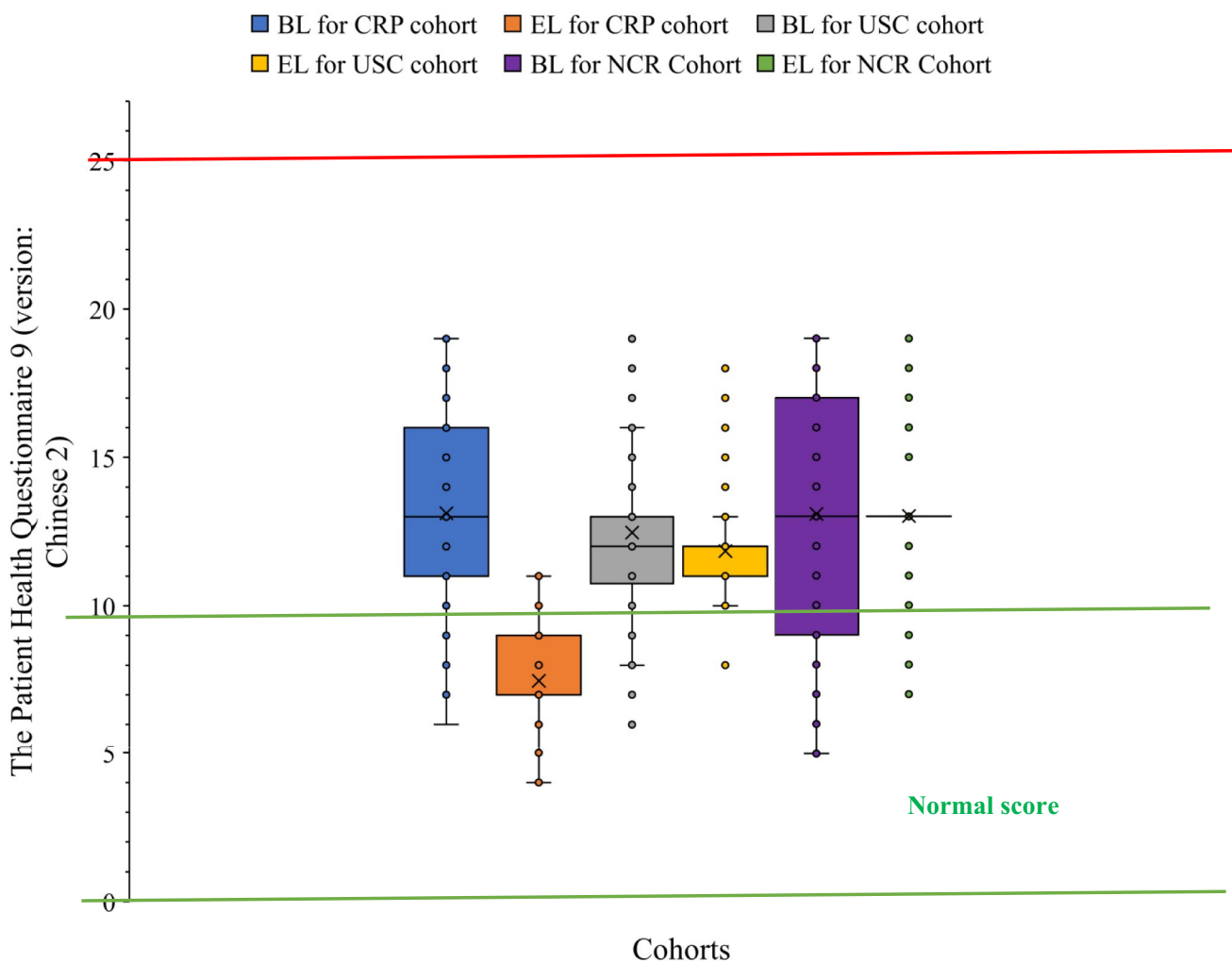


FIGURE 3 The Patient Health Questionnaire 9 (version: Chinese 2) evaluation. Range: 0–27. The higher scores indicated more depression. Scores <9 were considered normal. BL, Before program; EL, After completion of 1 year of program

and exercise (341.42 ± 27.85 m vs 355.19 ± 31.45 m, $p < 0.0001$, $q = 6.059$) increased incremental shuttle walk test value but there was no increase in incremental shuttle walk test value in the patients of NCR cohort (339.52 ± 32.45 m vs 343.18 ± 33.14 m, $p = 0.284$) after 1 year. Also, patients of CRP cohort had significant improvement in incremental shuttle walk test value than those of USC cohort ($p < 0.0001$, $q = 10.175$) and NCR cohort ($p < 0.0001$, $q = 14.429$) after 1 year. Patients of USC cohort had significantly improved incremental shuttle walk test value than those of NCR cohort ($p < 0.0001$, $q = 4.679$) after completion of 1 year (Figure 2).

3.3.2 | Body mass index

After completion of 1 year, patients who received cardiac rehabilitation program, USC cohort's patients, and NCR cohort's patients were significantly decreased body mass index. Among the patients of CRP cohort, body mass index was significantly decreased than those of USC and NCR cohort. Also, the patients of USC cohorts reported decrease in body mass index than those of NCR cohort.

3.3.3 | Low-density lipoprotein

After completion of 1 year, low-density lipoproteins were reduced for patients of CRP cohort, whereas patients of USC and NCR cohort did not report reduction in low-density lipoprotein.

3.3.4 | High-density lipoprotein

After completion of 1 year, patients of CRP and USC cohort reported higher high-density lipoprotein but those of NCR cohort did not report higher high-density lipoprotein. The increase in the high-density lipoprotein after 1 year in patients of CRP cohort was not significantly higher than those of USC cohort but significantly higher than those of NCR cohort. Also, patients of USC cohort reported higher high-density lipoprotein after 1 year than those of NCR cohort.

3.3.5 | Fasting glucose level

After completion of 1 year, patients of CRP cohort and USC cohort reported significant decrease in fasting glucose level but the same was not decreased in patients of NCR cohort. Patients of CRP cohort had significantly decreased fasting glucose level than those of USC and NCR cohorts after 1 year of program. Patients of USC cohort had significantly decreased fasting glucose level than those of NCR cohort after 1 year of program.

3.3.6 | Coronary Artery Disease Education Questionnaire-II (version: Chinese) score

After 1 year of detection of coronary artery disease, the patients of CRP, USC, and NCR reported significantly higher score

TABLE 4 Successful outcome measures

Outcome measures	Cohorts							
	CRP				USC			
	Cardiac rehabilitation program				Exercise only			
Level	BL	EL			BL	EL		
Numbers of patients enrolled	125	125	p-value	q-value	182	182	p-value	q-value
Body mass index (kg/m ²)	28.12 ± 2.73	26.15 ± 2.11	<.001	8.918	29.12 ± 2.51	27.85 ± 2.14	<.001	7.603
^d Depressive symptoms	13.12 ± 3.45	7.47 ± 1.52	<.0001	5.649	12.47 ± 2.98	11.85 ± 1.45	.012	2.829
Low-density lipoprotein (mg/dl)	90.12 ± 15.14	85.18 ± 13.23	.007	3.349	85.45 ± 19.18	82.35 ± 17.21	.106	N/A
High-density lipoprotein (mg/dl)	36.63 ± 7.15	41.52 ± 6.52	<.0001	8.959	38.21 ± 4.91	40.21 ± 4.21	<.0001	5.218
Fasting glucose (mg/dl)	99.45 ± 9.48	92.32 ± 7.55	<.0001	9.311	97.47 ± 8.41	95.11 ± 4.35	.0009	4.123
^a CADEQ-II score	22.12 ± 7.15	46.25 ± 8.25	<.0001	34.132	23.15 ± 8.15	31.27 ± 7.99	<.0001	12.969
^b Diet	8.21 ± 4.12	13.22 ± 3.13	<.0001	16.239	9.13 ± 3.14	10.11 ± 3.22	.004	3.358
^c Pedometer (steps/ day)	5,152 ± 505	7,515 ± 509	<.0001	51.762	5,238 ± 515	6,524 ± 628	<.0001	30.869

Continuous and ordinal data are presented as mean ± SD.

Fisher exact test was used for descriptive data and one-way ANOVA following Tukey's Honest Significant Difference test was performed for continuous and ordinal data.

Results were considered significant if p less than 0.05 and q greater than 3.315.

N/A: Not applicable, BL: Before start of program, EL: After completion of 1 year of program.

^aCoronary Artery Disease Education Questionnaire-II (version: Chinese) score: Range: 0–84. The higher scores indicated better knowledge.

^bRange: –36 to +47, the higher scores indicated better diet.

^cThe International Physical Activity Questionnaire (version: Chinese).

^dThe Patient Health Questionnaire 9 (version: Chinese 2). Range: 0–27. The higher scores indicated more depression.

of Coronary Artery Disease Education Questionnaire-II (version: Chinese). Patients of CRP cohort reported higher amount of increase in such score than those of USC and NCR cohorts after 1 year of program. Also, Patients of USC cohort reported significantly higher score than those of NCR cohort after 1 year of program.

3.3.7 | Diet score

After 1 year of coronary artery disease detection and completion of program, patients of CRP and USC cohorts reported higher score for diet but those of NCR cohort did not report higher score for diet. Patients of CRP cohort reported higher score of diet than those of USC and NCR cohorts after 1 year of program.

3.3.8 | Pedometer

The International Physical Activity Questionnaire (version: Chinese) for Pedometer reported that after 1 year of coronary artery disease detection, patients of CRP, USC, and NCR cohort had higher steps per day. Patients of CRP cohort reported higher steps per day than those of USC cohort and NCR cohort after 1 year of program. Also, patients of USC cohort reported higher steps per day than NCR cohort after 1 year of program.

3.3.9 | Depressive symptoms

After 1 year only, patients of CRP cohort had decreased depressive symptoms (Figure 3).

The results of the successful outcome measures are reported in Table 4.

3.4 | Morbidity and mortality

There was no significant difference between mortality due to cardiac causes among cohorts ($p = 0.145$). Morbidity was fewer in the patients of CRP cohort than those of USC ($p = 0.003$, $q = 3.427$) and NCR cohort ($p = 0.003$, $q = 4.822$) during 1 year of follow-up. The details of mortality due to cardiac causes and morbidities during 1 year of follow-up among the patients are reported in Table 5.

3.5 | Risk factor evaluation for morbidity

Univariate analysis reported that male patients ($p = 0.041$), older age (>50 years, $p = 0.042$), myocardial infarction than percutaneous coronary intervention or coronary artery bypass grafting surgeries ($p = 0.034$), one or more comorbidity ($p = 0.025$), high body mass index ($p = 0.022$), unhealthy diet ($p = 0.042$), and absence of cardiac rehabilitation program ($p = 0.021$) were associated with morbidity during 1 year of follow-up of enrolled patients. A multivariate analysis

NCR		Comparisons between cohorts						
No cardiac rehabilitation program or exercise or education		q-value at EL						
BL	EL	p-value	q-value	p-value at BL	p-value at EL	CRP vs USC	CRP vs NCR	USC vs NCR
185	185							
29.42 ± 2.09	28.41 ± 2.01	<.001	6.129	.055	<.0001	9.929	13.244	3.639
13.08 ± 3.89	13.01 ± 2.15	.831	N/A	.154	<.0001	20.071	25.793	6.271
87.45 ± 20.22	86.21 ± 19.31	.547	N/A	.098	.089	N/A	N/A	N/A
37.15 ± 6.18	38.01 ± 6.22	.183	N/A	0.061	<.0001	2.824	7.591	5.276
99.44 ± 9.42	97.31 ± 8.35	.022	3.201	.067	<.0001	4.922	8.833	4.319
24.16 ± 9.14	26.32 ± 8.35	.018	3.506	.103	<.0001	22.259	29.713	8.184
9.37 ± 5.11	10.27 ± 4.15	.064	N/A	.051	<.0001	10.582	10.069	.606
5,285 ± 537	5,451 ± 542	.003	4.252	.088	<.0001	21.254	44.413	25.605

TABLE 5 Mortality due to cardiac causes and morbidities during 1 year of follow-up after coronary artery disease detection

Parameters	Cohorts			Comparisons between cohorts			
	CRP	USC	NCR	p-value	q-value		
Non-treatment intervention(s)	Cardiac rehabilitation program	Exercise only	No cardiac rehabilitation program or exercise or education		CRP vs USC	CRP vs NCR	USC vs NCR
Numbers of patients enrolled	125	182	185				
Mortality	1 (1)	6 (3)	10 (5)	0.145	N/A	N/A	N/A
Morbidity							
Emergency department hospitalization	2 (2)	9 (5)	9 (5)	.003	3.427 ^a	4.822 ^a	1.534
Re-admission	2 (2)	7 (4)	11 (6)				
Non-fatal myocardial infarction	1 (1)	5 (3)	5 (3)				
Angina	1 (1)	2 (1)	3 (2)				
Percutaneous coronary intervention	1 (1)	5 (3)	7 (4)				
Coronary artery bypass grafting surgeries	1 (1)	2 (1)	3 (2)				
Total	8 (8)	30 (17)	38 (22)				

Data are presented as number (frequency).

One-way ANOVA following Tukey's Honest Significant Difference test was performed for comparisons of data.

Results were considered significant if $p < 0.05$ and $q > 3.315$.

N/A: Not applicable.

^aSignificant value.

Parameters	76		
	Odds ratio	Confidence interval	p-value
Gender (male vs female)	0.851	0.452–0.856	.052
Age (>50 years vs ≤50 years)	0.892	0.652–0.896	.053
Indications for cardiac rehabilitation program (Myocardial infarction ^a vs percutaneous coronary intervention or coronary artery bypass grafting surgeries)	1.023	0.521–0.953	.048
Comorbidity (presence of ≥comorbidity ^a vs absence of comorbidity)	1.58	0.536–0.985	.041
Body mass index (>30 kg/m ² vs ≤30 kg/m ²)	0.852	0.652–0.853	.053
Diet (unhealthy vs healthy)	0.953	0.523–0.856	.055
Exercise only or no exercise or no education ^a vs cardiac rehabilitation program	1.853	0.456–0.953	.039

Multivariate analysis.

An odds ratio of more than 1 and a p-value less than 0.05 were considered significant.

Patients without morbidity (n = 416) were considered as the reference standard.

^aSignificant parameter responsible for the morbidity of enrolled patients.

reported that myocardial infarction than percutaneous coronary intervention or coronary artery bypass grafting surgeries ($p = 0.048$), one or more comorbidity ($p = 0.041$), and absence of cardiac rehabilitation program ($p = 0.039$) were associated with morbidity during 1 year of follow-up of enrolled patients (Table 6).

During 1 year of follow-up, no adverse effects due to exercise or cardiac rehabilitation program or education were reported in any of the patient.

TABLE 6 Association of parameters for risk of morbidity during 1 year of follow-up of the patients

4 | DISCUSSION

The study reported that patients who received cardiac rehabilitation programs had high incremental shuttle walk test value and significantly decreased body mass index and depressive symptoms than those who received exercise only or did not receive exercise and education. The results of the functional walking capacity, body weight,

and the Patient Health Questionnaire 9 (version: Chinese 2) of the current study were agreed with randomized trials on Brazilian^{1,8,19} and Chinese^{3,20} patients with coronary artery disease. The study concluded that cardiac rehabilitation program improves the functional and mental capacity of patients with coronary artery disease.

The study showed that Coronary Artery Disease Education Questionnaire-II (version: Chinese) score, diet score, lipid profile, blood glucose level, and pedometer were superior in patients who received cardiac rehabilitation program than those who received exercise only or did not receive exercise and education after 1 year. The results of the Cardiovascular disease knowledge of patients, diet, the risk factor control, and the International Physical Activity Questionnaire (version: Chinese) of the current study were agreed with randomized trials on Brazilian patients.¹ The current study concluded that the cardiac rehabilitation program improves cardiovascular knowledge, lipid profile, and diet and exercise behavior of patients with coronary artery disease.

The study did not report significant improvement in systolic and diastolic blood pressure, waist circumference, and presence of sleep apnea in patients after 1 year among patients who received a cardiac rehabilitation program. The results of the hemodynamic parameters, waist circumference, and presence of sleep apnea of the current study agreed with the results of the RAMIT trial.¹¹ However, randomized trials on Brazilian population^{1,19} reported such improvement. The small sample size was the reason for such failure of results.¹⁹ Further research is required with a focus on these risk factors management.

Mortality due to cardiac causes was fewer for patients who received cardiac rehabilitation program but no significant difference among cohorts ($p = 0.145$). Improvement of the functional capacity of patients reduces mortality.^{21,22} The results of the mortality of the current study agreed with randomized trials on Brazilian patients^{1,19} and the RAMIT trial¹¹ but did not agree with a randomized, placebo-controlled trial to test the effect of highly purified omega-3 fatty acids (the OMEGA study).⁷ The insufficient follow-up period (1 year) is responsible for such decremental results.¹ The study is required to perform with a large sample size. Possibly a longer follow-up period is required to evaluate the effect of cardiac rehabilitation program among patients with coronary artery disease.

Patients who received cardiac rehabilitation program had less morbidity after 1 year of cardiac rehabilitation program than those who received exercise only or did not receive exercise and education. The results of the morbidity of the current study were agreed with randomized trials on Brazilian patients^{1,19} and the OMEGA study⁷ but did not agree with the RAMIT trial.¹¹ However, the RAMIT trial is the only one among large studies that did not demonstrate any beneficial effect of cardiac rehabilitation program. Moreover, the RAMIT trial has limitations of underpowering and selection bias on enrollment and randomization of participants.²³ Also, in the RAMIT trial,¹¹ rehabilitation sessions averaged to 20 hours over 6–8 weeks. However, current study had a minimum of 30 exercise sessions (90 min/week) and a minimum of 15 education sessions (30 minutes,

twice in a month). Also, the model of the cardiac rehabilitation program delivery in the current study was different compared with the "classical" model (residential or ambulatory patients) used in Western Europe and USA. The current study concluded that cardiac rehabilitation program reduces morbidity due to cardiac causes and ultimately reduces the mortality of patients with coronary artery disease.

The study reported that myocardial infarction, one or more comorbidity, and the absence of a cardiac rehabilitation program were associated with morbidity of enrolled patients. The results of the association of parameters for risk of morbidity of patients of the current study agreed with the OMEGA study,⁷ European Action on Secondary and Primary Prevention by Intervention to Reduce Events IV (EUROASPIRE IV),⁴ and a nationwide cross-sectional study.²⁴ Cardiac rehabilitation program would be an advisable task to adopt after myocardial infarction or percutaneous coronary intervention or coronary artery bypass grafting surgeries.

The study has several limitations, for example, the non-randomized retrospective study and lack of randomized retrospective study. The randomized retrospective study is not possible in the Chinese population because patients have legal rights for the selection of cardiac rehabilitation programs. The sample size was small. The mortality and morbidity were reported outside hospitals. Data regarding dyslipidemia and hypoglycemia were not collected and analyzed. Incremental shuttle walk test cannot be used instead of a symptom-limited exercise test with accuracy,⁷ but an incremental shuttle walk test was performed during the cardiac rehabilitation program instead of a treadmill test or 6-minute walk test.⁸ A cardiac rehabilitation program, exercise, and educations were performed at institutes. The home-based model for the cardiac rehabilitation program was not applied. The quality of the evidence for outcome measures in the study was reported by their Chinese versions and in the grade systems. The outcome measures are not generalized to the other population. Additionally, the potential treatment variation was due to multiple healthcare facilities, trainers, and assessors. This may have impacted the results obtained. Which components of education and exercises have substantial effects on betterment of patients are not discussed. Patients with ejection fraction <45% ($n = 5$) as result of sequela of the myocardial infarction were excluded but the International guidelines recommended the cardiac rehabilitation program with Class I level recommendation among them. The mixed population of coronary artery disease (after myocardial infarction or percutaneous coronary intervention or coronary artery bypass grafting surgeries) was included in the current study, but obviously these three index events are not comparable in terms of exercise capacity and recovery. The protocol of exercise training included only one session per week for 1 year. Therefore, it cannot be presumed for the other physical activities performed by the patients, and represent a bias. The reason(s) for a very low rate of prescription of all of recommended drugs in the study population is not discussed. The modifications, adaptation, and/or optimization of treatment(s) during the long term (1 year) are not discussed.

5 | CONCLUSIONS

The cardiac rehabilitation program is associated with a decrease in body mass index and depressive symptoms and improvement in incremental shuttle walk test value, cardiovascular knowledge, and diet and exercise behavior of patients with coronary artery disease after myocardial infarction or percutaneous coronary intervention or coronary artery bypass grafting surgeries. Also, cardiac rehabilitation program reduces morbidity of patients. A further non-randomized study should be done for long follow up to evaluate effects of cardiac rehabilitation program on the mortality in Chinese population. However, for future studies, the therapeutic algorithm will be prospective to meet the social need, for example, distributing cohort as per risk stratification, in a high-, moderate-, and low-risk population and cut off at maximum heart rate or maximum oxygen uptake or metabolic equivalent if possible.

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CONFLICT OF INTEREST

The authors declared that they have no conflict of interest or any other competing interest regarding results and/or discussion reported in the research.

AUTHORS' CONTRIBUTIONS

The authors read and approved the manuscript for publication. YH and LL contributed equally to data curation, formal analysis, the literature review, resources, and visualization of the study. TW contributed to conceptualization, software, validation, resources, and the literature review of the study. YL contributed to the investigation, resources, literature review, data curation, and formal analysis of the study. XZ contributed to the methodology, resources, literature review, supervision, and validation of the study. SH contributed to formal analysis, data curation, resources, the literature review, and supervision of the study. LH contributed to software, formal analysis, resources, and literature review of the study, draft, review, and edited the manuscript for intellectual content. The authors agree to be accountable for all aspects of work ensuring integrity and accuracy.

DATA AVAILABILITY STATEMENT

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

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