

Effects of a home based exercise intervention on cardiac biomarkers, liver enzymes, and cardiometabolic outcomes in CABG and PCI patients

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Background: We investigated the impact of a home-based exercise intervention (HBEI) on cardiac biomarkers, liver enzymes, cardiometabolic outcomes, and health-related quality of life (HRQL) in clinically stable patients after coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI). **Materials and Methods:** The study was a nonrandomized clinical trial conducted in Tehran, Iran, from July 2019 to January 2020. Forty cardiac patients (after the cardiac intervention, CABG, $n = 32$; PCI, $n = 8$) were recruited based on the study inclusion criteria and were allocated consecutively to one of two groups: (1) HBEI ($n = 18$) and (2) conventional center-based exercise program (CBEP, $n = 22$). The CBEP group performed the routine exercise program of Sadr Heart Clinic, and the HBEI group performed a home-based remotely monitored exercise protocol, both three times per week, for 8 weeks. The following variables were assessed before and after the intervention: anthropometric measures; blood pressure; lipid profile; cardiac biomarkers including cardiac troponin I, creatine kinase, and total and Mb isozyme; liver enzymes including aspartate aminotransferase and alanine aminotransferase; creatinine; urea; exercise capacity; and HRQL. **Results:** In comparison with pretest in both CBEP and HBEI groups, a significant improvement in all of the measured variables ($P < 0.05$), but not in ejection fraction was observed ($P > 0.05$). Moreover, in the CBEP group, a more significant decline in troponin I levels ($P = 0.03$), and in the HBEI group, a greater reduction in weight ($P = 0.01$) and body mass index ($P = 0.04$) occurred. **Conclusion:** The findings suggest that a properly designed and monitored HBEI may be as effective as conventional center-based cardiac rehabilitation (CR) exercise programs and should be encouraged in those cardiac patients who are unable or uninterested in conventional center-based CR exercise programs.

Keywords: Biomarkers, cardiac patients, functional capacity, health-related quality of life, rehabilitation

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INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of death worldwide: more people die annually from CVDs than from any other cause.^[1,2] An estimated 17.9 million people died from CVDs in 2016, representing 31% of all global deaths, and out of whom 7.4 million were because of coronary artery disease (CAD). Moreover, the mortality rate in low-and middle-income countries is estimated to be higher.^[1-3] Coronary artery bypass grafting (CABG) and percutaneous coronary

intervention (PCI) are effective and established treatments for CAD. Still, these interventions are associated with depressed cardiac functions and other limitations,^[4] which makes cardiac rehabilitation (CR) inevitable. CR is a Class I recommended intervention in patients with CAD and believed to have a beneficial impact on the quality of life, cardiovascular risk factors, and clinical outcomes, including mortality.^[5]

Exercise training is one of the five core components of comprehensive CR (including patient assessment, exercise training, dietary counseling, risk factor

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management, and psychosocial intervention). It has been shown to improve secondary prevention outcomes in patients with CVDs.^[6] Supervised exercise-based CR has been shown to reduce cardiovascular risk factors (e.g., obesity and sedentary behavior), improve exercise capacity, and lower body mass. Moreover, it has been reported to improve peripheral vascular and muscle function, restore cardiac function, limit health deterioration related to CVD, and improve health-related quality of life (HRQL).^[6,7] Therefore, participation in exercise-based CR is essential for CAD patients to improve their health and safety during activities of daily living.^[7]

Despite this, however, CR is significantly underused among eligible patients. Thomas *et al.*, 2019, reported that although referral to CR is generally improving, patient participation remains alarmingly low across most demographic groups.^[8] Participation is especially low in some individuals such as women, older adults, individuals with lower socioeconomic status, and those who are uninsured or underinsured.^[9] Hence, it has been declared that new CR strategies are crucial for nearly 80% of eligible patients who do not attend hospital-based CR programs.^[10,11]

Home-based or alternative center- and home-based CR programs have been introduced as a potential approach to overcome the barriers of participation, increase the adherence rate, and widen patient access.^[8,11-13] Moreover, scientific evidence supports the notion of exercise-based CR in a home setting, and studies have reported little or no difference in outcomes after exercise-based CR between the center and home-based groups.^[11-13] Even in one study, it has been concluded that low-risk CABG surgery patients may acquire more significant benefits with a monitored, home-based exercise program than a center-based program.^[6] Despite that, the strength of evidence reported to be low-to-moderate, and in comparison with center-based exercise training, “stand-alone” home-based CR programs are still in their infancy.^[8] Hence, further research is required to determine the optimal exercise protocols and provide standards for home-based CR exercise programs, yet.

Moreover, despite their increasing use as clinical tools for disease management, cardiac biomarkers (i.e., proteins released into the bloodstream from damaged heart muscle reflecting the molecular processes involved in the progression or regression of the myocardial disease) and the effect of exercise based CR programs (center based or home based) on them has been poorly investigated.^[14,15] Besides that, less is known about the effect of exercise-based CR on liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are elevated in cardiac patients and are related to increased risk of overall

and CVD mortality.^[16-18] Hence, the present study aimed to investigate the effect of 8 weeks remotely monitored home-based exercise intervention (HBEI) versus a conventional center-based CR exercise program in patients after CABG surgery and PCI to determine the efficacy of a HBEI in terms of cardiac biomarkers, liver enzymes, cardiometabolic outcomes, and HRQL in these patients.

MATERIALS AND METHODS

Study design

This was a nonrandomized clinical trial (IRCT20200408046997N1) performed in Shahid Lavasani Hospital and Sadr Heart Clinic of Tehran, Iran, from July 2019 to January 2020. The study was approved by the National Committee for Ethics in Biomedical Research (protocol code: IR. SSRC. REC.1398.041), and written informed consent was obtained, and the study was conducted in accordance with the principles expressed in the Declaration of Helsinki. Forty clinically stable patients, out of 159 patients who had undergone CABG surgery or PCI (50–60 years, six women), were enrolled consecutively. Then, using consecutive assignment method, they were assigned to an 8-week HBEI ($n = 18$) or center-based exercise program (CBEP, $n = 22$) groups.

Patients were considered eligible if they were between 50 and 60-year-old, 6–8 weeks post-CABG surgery and PCI, clinically stable, able to move freely, and achieved between 50% and 80% of gender and age-predicted maximum metabolic equivalent (MET) level on a progressive exercise test at baseline. Patients were excluded if they were clinically unstable, had recurrent angina, had uncontrolled high blood pressure, had respiratory or musculoskeletal conditions, and were unable to exercise. There were no important changes to methods after trial commencement. Missing data were omitted by the listwise deletion method, and the final analysis was performed on 11 subjects in the HBEI group and 12 subjects in the CBEP group [Figure 1].

Exercise-based cardiac rehabilitation

Patients assigned to the HBEI group attended individual exercise consultation and instruction on how to do HBEI and were provided with an exercise log at baseline. They also received regular two to three times per week telephone-assisted exercise counseling during the study. Patients were advised to exercise at least three times per week. Each exercise session included a 10–15 min warm-up, followed by 25–35 min of combined aerobic (predominantly self-paced walking and running), resistance (with light weights and their body weights), breathing exercise (pursed-lip breathing), and a final 10 min of stretching and cool down. The exercise intensity was monitored using the Borg 6–20 scale of perceived exertion,

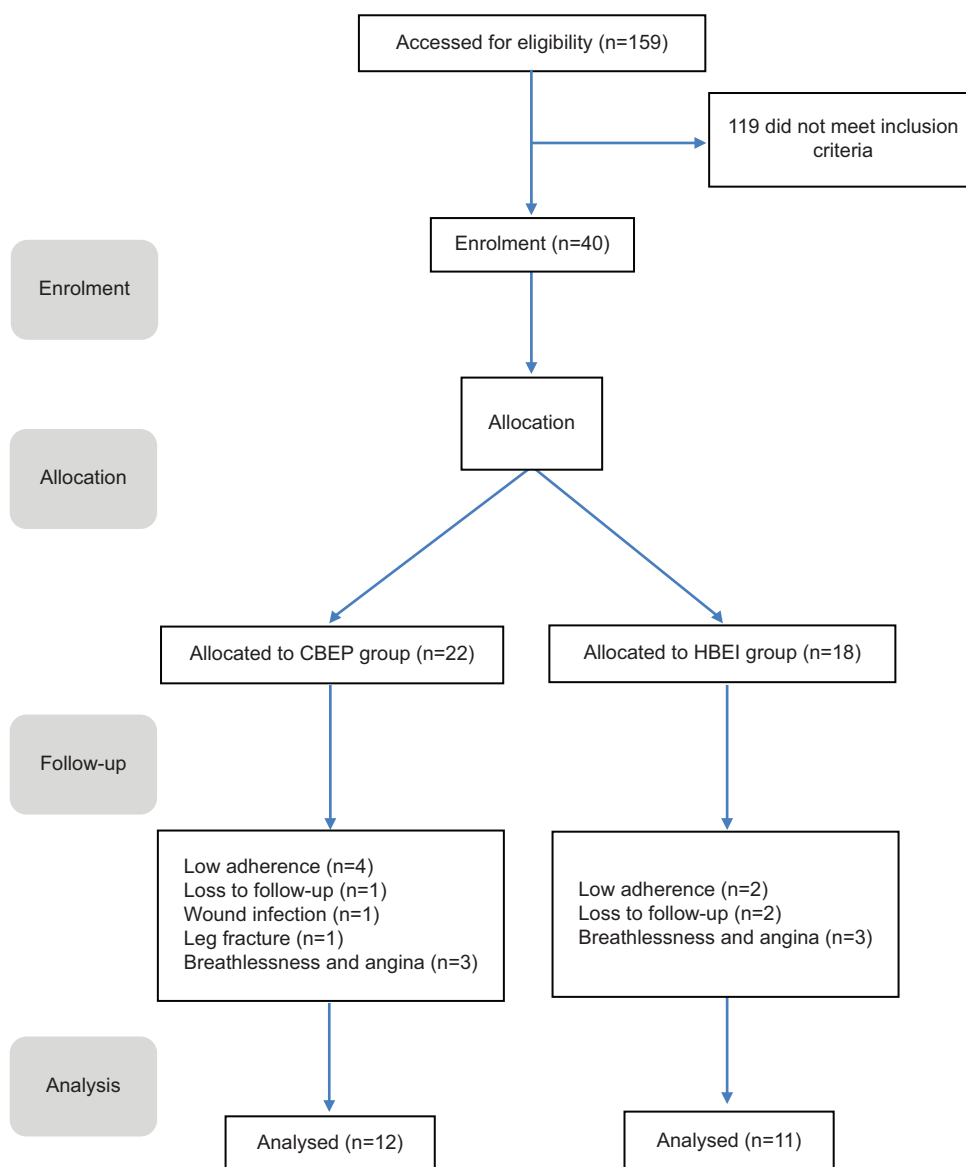


Figure 1: Flowchart of the study. CBEP = Centre-based exercise program; HBEI = Home-based exercise intervention

with light intensity as up to 11, and moderate intensity as 12–14 on the scale.^[4]

In the CBEP group, patients completed a conventional three times per week, an 8-week center-based CR exercise program at Sadr Heart Clinic, which can be regarded as usual care for CABG and PCI patients. Briefly, it included 10–15 min of warm-up followed by 40–60 min of aerobic exercise corresponding to 50%–80% of their peak heart rate (10–20 min of leg cycling on lower body ergometer, 20 min of walking on a treadmill, and 10 min of arm cycling on upper body ergometer) and a final 10 min of cooling down.

Anthropometric measurements

Height and weight were measured using a stadiometer and mechanical column scale (SECA 755) and recorded to the closest 0.01 m and 0.1 kg, respectively. Body mass

index (BMI) was calculated using the patient’s weight in kg divided by the square of height in m².

Exercise capacity

The exercise capacity test consisted of an exercise stress test performed on a treadmill at the beginning and the end of exercise on a treadmill (Ergotop Medical Treadmill) using a ramp protocol. After a 10-min warm-up on the treadmill, the workload (speed or slope) was increased progressively every 2 min, according to the modified Naughton protocol.^[19] Blood pressure and heart rate were measured manually, and 12-lead electrocardiogram (ECG), using the ECG management system of Mortara (X-Scribe), was measured continuously throughout the test. The criteria used to terminate the test included any abnormality in blood pressure, heart rate, and ECG records, dyspnea, angina, dizziness, or leg fatigue/pain.

Echocardiography

The echocardiographic evaluation was performed in accordance with the recommendations of the American Society of Echocardiography. Images were obtained with a 3.5-MHz transducer using a GE Vivid ultrasound system (Philips Healthcare). Left ventricle systolic function was estimated by the ejection fraction (EF), using the following equation: $EF (\%) = ([\text{End diastolic volume} - \text{end systolic volume}] / \text{end diastolic volume}) \times 100$.

Biochemical analysis

For biochemical parameter assessments, venous blood samples were taken in the morning after 12 h of fasting at baseline and 48 h after the last exercise session. Serum Creatine kinase Mb isozyme (CK)-Mb, total CK, AST, and ALT concentrations were determined photometrically using special kits (Pars Azmon Inc). Cardiac troponin I levels were assessed by the enzyme-linked fluorescent assay technique using VIDAS® highly sensitive cardiac troponin I kit (BioMerieux). Moreover, total cholesterol (TC), total triacylglycerol (TAG), and high-density lipoprotein cholesterol (HDL-C) concentrations were measured by commercially available kits (Pars Azmon Inc). Serum creatinine and urea levels were assessed by Biorexfars kits using an enzymatic photometric method (BS-380 mindray Blood Chemistry Analyzer). The low-density lipoprotein cholesterol (LDL-C) level was calculated using directly measured values and the following equation: $LDL-C (mg/dL) = TC - HDL-C - (TAG/5)$.

Quality of life assessment

The short-form health survey (SF-36) was used to assess HRQL in patients. This questionnaire consists of 36 items, which are used to calculate eight subscales, including physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. The first four scores and the last four scores were used to compute the physical composite score and the mental composite score (MCS), respectively.^[6]

Statistical analysis

The data were presented as mean \pm standard deviation. The Kolmogorov–Smirnov test was applied for assessing normality. Pre- to postchanges of variables were tested using a paired-sample *t*-test. Analysis of covariance (posttest as the dependent variable and pretest as a covariate) was used for between-group comparisons. Statistical analysis was conducted using IBM SPSS Statistics 20 (IBM, New York, NY, USA). The level of statistical significance was set at $\alpha = 0.05$.

RESULTS

Baseline characteristics

There were no significant differences in baseline clinical and demographic characteristics between two groups [Table 1],

and they attended the program about 6–8 weeks after CABG surgery or PCI.

Biochemical markers

As presented in Table 2, levels of troponin I, CK-Mb, and total CK in both HBEI and CBEP groups decreased significantly at the end of the study ($P < 0.05$). Furthermore, between-group comparisons revealed that there were no statistically significant differences between groups at CK-Mb and total CK levels at posttest ($P = 0.46$ and $P = 0.84$, respectively). Still, levels of troponin I was significantly lower at the CBEP group ($P = 0.032$). In both groups, a significant reduction in AST and ALT had occurred in comparison with pretest ($P < 0.05$), but no significant difference was observed between groups at posttest ($P = 0.85$ and $P = 0.14$, respectively). Moreover, in both groups, serum levels of creatinine and urea decreased significantly comparing to pretest ($P < 0.05$), but again between group comparisons revealed that there was not any significant difference between groups at posttest ($P = 0.11$ and $P = 0.08$, respectively). A significant within-group improvement was found concerning lipid profile (LDL-C, HDL-C, TAG, and TC) in both groups ($P < 0.05$); however, no statistically significant difference between HBEI and CBEP groups was found in lipid profile changes.

Blood pressure and ejection fraction

Both groups showed significant reductions in systolic blood pressure, diastolic blood pressure, and MAP after 8 weeks of exercise comparing to baseline ($P < 0.0001$), but there were no statistically significant changes in EF ($P > 0.05$). Moreover, between-group comparisons revealed that the difference between HBEI and CBEP groups was not statistically significant ($P = 0.99$) [Table 2].

Exercise capacity

There was a significant increase in MET peak after 8 weeks of exercise in both groups in comparison with pretest ($P < 0.0001$). However, the finding showed that the difference between HBEI and CBEP groups in the amount of changes was not statistically significant ($P = 0.07$) [Table 2].

Weight and body mass index

Weight and BMI in both HBEI and CBEP groups were decreased significantly in comparison with baseline ($P < 0.0001$). Moreover, HBEI group had significantly lower weight and BMI than CBEP at posttest (weight: -2.1 vs. -1.4 kg, respectively; $P = 0.01$; BMI: -0.08 vs. -0.5 kg/m², respectively; $P = 0.04$) [Table 2].

Health-related quality of life

Changes in HRQL are shown in Figure 2. Findings showed that there were statistically significant improvements from baseline in the physical and MCSs of the SF-36 in both

Table 1: Patient's characteristics at baseline

	Home-based exercise intervention (n=11)	Center-based exercise program (n=12)	P
Age (years)*	55.4 (3.9)	54.8 (2.7)	NS
Male, n (%)	8 (73)	9 (75)	NS
Female, n (%)	3 (27)	3 (25)	NS
Employed full/part-time, n (%)	7 (63.7)	7 (58.4)	NS
Completed secondary school diploma, n (%)	2 (18.2)	3 (25)	NS
CABG, n (%)	7 (63.6)	8 (72.7)	NS
PCI, n (%)	4 (36.4)	4 (27.3)	NS

*Mean (standard deviation). CABG=Coronary artery bypass grafting; PCI=Percutaneous coronary intervention; NS=Not significant

Table 2: Mean values (standard deviation) and changes from baseline (%) for measured variables

	Home-based exercise intervention				Center-based exercise program				Between-group (P)
	Baseline	8 weeks	Percentage change	P	Baseline	8 weeks	Percentage change	P	
Troponin I (ng/L)	6.2 (2.1)	3.01 (1.3)	-51.4	0.0001*	7.4 (1.7)	2.4 (1.1)	-67.5	0.0001*	0.032#
CK-Mb (IU/L)	22.5 (6.1)	16.6 (6.5)	-26.2	0.01*	21.3 (5.8)	14.8 (2.4)	-30.5	0.002*	0.46
CK total (IU/L)	128.3 (34.9)	61.5 (17.8)	-51.8	0.001*	97.1 (27.4)	57.2 (16.3)	-41.09	0.0001*	0.84
AST (U/L)	32.2 (5.2)	23.6 (5.5)	-26.7	0.0001*	32.7 (9.9)	23.6 (7.4)	-27.8	0.001*	0.85
ALT (U/L)	27.1 (4.8)	20.6 (4.8)	-23.9	0.0001*	35.1 (13.4)	22.5 (6.3)	-35.8	0.0001*	0.14
Creatinine (mg/dl)	1.0 (0.23)	0.82 (0.21)	-18	0.0001*	0.96 (0.26)	0.83 (0.2)	-13.5	0.0001*	0.11
Urea (mg/dl)	41.7 (8.1)	34.3 (8.1)	-17.7	0.0001*	38.9 (13.5)	29.1 (7.6)	-25.1	0.004*	0.08
LDL-C (mg/dl)	78 (13.3)	65.8 (14.3)	-15.6	0.0001*	83.7 (8)	67.9 (9.02)	-18.8	0.0001*	0.31
HDL-C (mg/dl)	29.7 (5.8)	41.2 (6.1)	38.7	0.0001*	33.6 (7.3)	45.2 (7.9)	34.5	0.0001*	0.83
TAG (mg/dl)	217.3 (47.4)	160.9 (32.6)	-25.9	0.0001*	242 (62)	190.7 (34.5)	-21.1	0.002*	0.07
TC (mg/dl)	196.9 (10.9)	171.2 (16.7)	-13.5	0.0001*	197.7 (19.5)	163.4 (24.3)	-17.3	0.0001*	0.15
SBP (mmHg)	132 (10.4)	123.9 (10.7)	-6.1	0.0001*	133.5 (8.7)	124.9 (7.2)	-6.4	0.0001*	0.84
DBP (mmHg)	81 (8)	75 (7.2)	-7.4	0.0001*	79.5 (7.2)	73.6 (4.4)	7.4	0.001*	0.76
MAP (mm Hg)	98 (7.5)	91.3 (7.2)	-6.8	0.0001*	97.5 (6.8)	90.7 (4.4)	-6.9	0.0001*	0.84
EF (%)	49.5 (4.1)	49.6 (4.2)	0	0.99	51.5 (3.2)	51.6 (3.2)	0	0.99	0.99
EC (MET)	5.64 (0.55)	6.88 (0.51)	21.9	0.0001*	5.54 (0.62)	7.22 (0.43)	30.3	0.0001*	0.07
Weight (kg)	78.6 (5)	76.5 (4.8)	-2.6	0.0001*	80.8 (6.2)	79.4 (5.8)	-1.7	0.0001*	0.01#
BMI (kg/m ²)	28.6 (2.2)	27.8 (2.2)	-2.8	0.0001*	30.2 (3.2)	29.7 (3.1)	-1.6	0.0001*	0.04#

*Paired samples t-test; #ANCOVA=Analysis of covariance. CK=Creatine kinase; CK-Mb=Creatine kinase Mb isozyme; AST=Aspartate aminotransferase; ALT=Alanine aminotransferase; LDL-C=Low-density lipoprotein cholesterol; HDL-C=High-density lipoprotein cholesterol; TAG=Triacylglycerol; TC=Total cholesterol; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; MAP=Mean arterial pressure; EF=Ejection fraction; EC=Exercise capacity; BMI=Body mass index, MET=Metabolic equivalent; CK=Creatine kinase

groups ($P < 0.0001$). However, no significant difference was observed between HBEI and CBEP groups (physical composite: 8.7 vs. 9.5 scores, respectively; $P = 0.73$; mental composite: 2.8 vs. 3.8 scores, respectively; $P = 0.30$).

DISCUSSION

Our main finding was that the CBEP led to a significantly greater improvement in serum cardiac troponin I levels and a relatively higher increase in EC, and on the other hand, HBEI resulted in slightly higher reductions in weight and BMI. Few studies investigated the effect of exercise training on cardiac biomarkers in cardiac patients. To our knowledge, this is the first study investigating the impact of exercise-based CR (at home and center) on cardiac troponin I and CK-Mb in patients after CABG and PCI. Recently, it has been reported that cardiac troponin levels of more than 5.5 ng/L in men and more than 4.2 ng/L in women were associated with increased risk of subsequent coronary heart

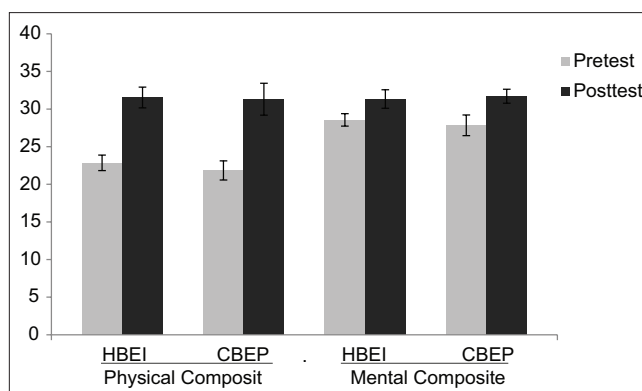


Figure 2: Changes in health-related quality of life

disease (CHD) in comparison with the lowest quartile (1.55–3.93). The relationship remained true even after adjusting for age, sex, race, ethnicity, education level, diabetes, C-reactive protein, and renal function Framingham risk score.^[20] In the present study, serum levels of troponin I were higher than the upper limit at baseline. However, it reduced to

the lowest quartile in both HBEI and CBEP groups after 8 weeks of intervention (6.2-3.01 and 7.4-2.4, respectively). This reduction shows that both HBEI and CBEP are effective in improving cardiomyocyte damage and reducing the risk of subsequent CHD.

Still, the more significant reductions in the CBEP group suggest that institutional supervised exercise may have a superior effect. Contrary to our findings, Ahmad *et al.* reported that exercise training did not lead to significant changes in cardiac biomarkers in patients with chronic heart failure.^[15] Different findings may be attributed to differences in the types of subjects.

Moreover, although both interventions were effective in improving EC, in the CBEP group, relatively higher increase was observed in METpeak comparing to the HBEI group. This finding is in line with the result of the most recent meta-analysis by Sud *et al.*, who concluded that center-based CR was associated with better short term exercise capacity.^[21] We speculate that a more considerable increase at METpeak in the CBEP group is probably due to both better implementation and monitoring of the intensity in the center-based CR program. The more significant decrease in troponin levels besides the greater improvement in exercise capacity observed in the CBEP group indicates that CBEP is probably a more effective strategy to improve cardiac function and EC. It also suggests a possible link between exercise-induced improvements in exercise capacity and serum troponin level changes after exercise-based CR in CABG and PCI patients. Hattori *et al.*, 2015, reported a negative correlation between cardiac troponin levels and walking distance in patients with stable chronic obstructive pulmonary disease.^[22] Both HBEI and CBEP groups showed similar improvement in serum CK-Mb levels. We speculate that this difference may be due to lower sensitivity and specificity of CK-Mb comparing to troponins. Still, findings showed that neither HBEI nor CBEP led to any improvement in EF, which suggests that observed increases in EC are probably because of exercise-induced peripheral adaptations rather than central adaptations (e.g., cardiac function). Both interventions resulted in a significant reduction in weight and BMI, but HBEI resulted in a more considerable decrease in weight and BMI. Contrary to our findings, previous studies have reported no differences in weight and BMI changes between home-based and center-based CR exercise programs.^[6,23-26] Arthur *et al.* noted that patients who participate in center-based programs might believe that the structured program schedule is sufficient for them or find it difficult to add additional physical activity to their lifestyle.^[6] On the other hand, we believe that in our study, learning to perform prescribed exercises in the home without direct supervision besides receiving regular phone calls from research staff may

have helped patients improve the confidence and sense of independence. Hence, they may have done some extra nonstructured exercise sessions during the week alongside their regular protocol; this, in turn, may have increased their calorie expenditure.

Furthermore, our results showed that HBEI led to the same reduction in serum levels of liver enzymes (AST and ALT) as CBEP did. Considering the relationship between liver enzymes and cardiovascular events, these exercise-induced reductions in liver enzymes may have clinical significance in this population. Recently, Moosavi-Sohroforouzani *et al.* reported that 8 weeks of center-based CR exercise program did not result in significant changes in serum ALT and AST levels in patients with CAD. Still, they reported that ALT reduced significantly in the home-based exercise group,^[17] which suggests the superior effect of HBEI. Considering the paucity of information, more research is needed to elucidate the impact of different CR exercise protocols on liver enzymes in cardiac patients.

Our findings showed that HBEI resulted in the same improvements in HRQL as those observed after CBEP. This finding is in line with most of the previous studies which surveyed the effect of both home-based CR and center-based CR on HRQL from baseline to posttest and different follow-up periods.^[6,11,27] Although the exact comparisons between studies are not actually possible because of the different follow up periods and various measurement instruments used,^[8] plausible reasons for improving HRQL after CR may be the improvements in exercise capacity, exercise related improvements in cardiac self efficacy, and general self efficacy and control. Since previous research has shown that exercise capacity, and cardiac and general self efficacy are important predictors of health status and quality of life.^[28-30]

Compliance to exercise is the main issue in both home-based and center-based CR programs, and studies have reported different program completion rates and adherence to the program. In the present study, in the HBEI group, 11 out of 18 patients and in the CBEP group, 12 out of 22 patients completed the program (a completion rate of 61.1% vs. 54.5%), which shows that completion rate has been slightly higher in HBEI group; interestingly, this result is consistent with the findings of previous studies. In a recent review, Thomas *et al.* noted that in general, adherence to home-based CR programs appears to be comparable to those observed in center-based CR programs.^[8] Moreover, Anderson *et al.* mentioned that there was evidence of marginally higher levels of program completion in home-based CR programs. Still, they were unable to pool adherence data results due to substantial variation in the way adherence was reported.^[11]

This study, however, is subject to some limitations. First, it was a nonrandomized single-center clinical trial in which the participants were predominantly men and relatively low-risk. As physical parameters and risk factors might be different in females,^[2] some adjustments may be needed to increase the clinical application of the exercise program. Second, daily physical activity was not measured in this study, and changes in the amount of physical activities might have affected the results. Third, the study was relatively short-term, and the number of patients was small, which reduces the generalizability of findings.

In summary, despite the limitations, we believe that this study makes a significant contribution to an accumulating pool of knowledge, demonstrating that in low-risk CABG and PCI patients, a HBEI may lead to similar improvements in cardiac biomarkers, liver enzymes, cardiometabolic outcomes, and quality of life as conventional center-based CR exercise programs. Hence, to improve clinical outcomes and HRQL, home-based exercise programs should be encouraged in CABG and PCI patients who are unable or uninterested in center-based CR exercise programs.

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Conflicts of interest

There are no conflicts of interest.

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