Journal of Vessels and Circulation
Qom University of Medical Sciences
Winter 2023. Volume 4. Number 1

Research Paper

Investigating the Outcome of Cardiac Rehabilitation Program on Plasma Adiponectin Levels and Lipid Profile in Patients With Coronary Heart Disease

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Please cite this article as Kargarfard M, Soltani MM, Soltani M, Hojjat Sh, Seyedebrahimi R, Ababzadeh Sh, et al. Investigating the Outcome of Cardiac Rehabilitation Program on Plasma Adiponectin Levels and Lipid Profile in Patients With Coronary Heart Disease. J Vessel Circ. 2023; 4(1):29-36. http://dx.doi.org/10.32598/JVC.4.1.138.1

doi: http://dx.doi.org/10.32598/JVC.4.1.138.1

Article info:
Received: 10 Aug 2022
Accepted: 25 Sep 2022
Publish: 01 Jan 2023

Keywords:
Coronary heart disease, Cardiac rehabilitation program, Adiponectin, Lipid profile

ABSTRACT

Background and Aim: A cardiac rehabilitation program (CRP) is a non-pharmacological treatment for patients with coronary heart disease (CHD). The present study investigates the effects of CRP on adiponectin and lipid profiles in CHD patients for 8 weeks.

Materials and Methods: A total of 60 patients with CHD were divided into 2 groups: the exercise group (EG), who completed a series of CRP (3 times a week, in the morning at 60%-85% of maximum heart rate, lasted 45-60 min for 8 weeks), and a control group who did not exercise during 8 weeks. In each group, 16 patients were female and 14 patients were male (n=30). The body mass index, waist-to-hip ratio, and cardiorespiratory variables were determined at baseline after the 8 weeks. Medication and diet remained unchanged in both groups during this period. The data were evaluated by the independent t-tests via the SPSS software, version 26. The significant level was considered $P<0.05$.

Results: The results showed a significant difference in anthropometric and cardiorespiratory variables, except in resting diastolic blood pressure between the two groups after CRP. Also, a significant decrease was observed in the exercise group for serum total cholesterol, low-density lipoprotein, and triglycerides levels, resting diastolic blood pressure, body weight, body mass index, waist-to-hip ratio, and a significant increase for functional capacity, high-density lipoprotein, and adiponectin levels compared to baseline ($P<0.05$). The high-density lipoprotein-cholesterol level in the exercise group was higher than the control group after CRP ($P<0.05$).

Conclusion: Cardiac rehabilitation based on aerobic exercise training may improve plasma lipid profile and adiponectin level in CHD patients, in the absence of changes in diet or medication.

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Introduction

Coronary heart disease (CHD) is one of the world's top 10 causes of mortality. The prevalence of CHD has increased markedly in Iran in recent years [1]. It can result in myocardial infarction [2]. CHD has a considerable relationship with various factors in the body.

Adiponectin is a 244-amino acid protein, and its high levels can reduce CHD [3]. This protein has anti-atherosclerotic and anti-inflammatory properties that may play an important role in preventing the progression of CHD. Therefore, low adiponectin levels are a good biomarker for the diagnosis of early-stage atherosclerosis and coronary artery disease (CAD) [4]. Adiponectin is produced almost exclusively in adipose tissue in healthy people while it is paradoxically downregulated in obese people [5].

Current guidelines recommend that cardiac rehabilitation programs (CRP) may improve the functional status of CHD patients [6]. Physical activity has considerable benefits in patients with myocardial infarction and may reduce the risk of mortality following a heart attack [7]. Physical activity impacted the risk factors of CHD as follows: Reducing resting blood pressure, management of body weight, improving lipid profile, increasing insulin sensitivity, decreasing blood clotting, and increasing fibrinolytic activity [8].

Some studies found that plasma adiponectin concentrations increased with a fixed period or frequency of exercise [9, 10]; however, others found that adiponectin decreased or remained unchanged with physical activity [11, 12]. These results are controversial. The present study evaluates the changes in circulating adiponectin and plasma lipids parameters in CHD patients with a comprehensive CRP compared to those who have not had any physical exercise training after 8-weeks of CRP.

Material and Methods

Study participants

A total of 60 patients with CHD (aged 51-75 years) were referred to Isfahan Cardiovascular Research Centre between February 2011 to December 2012. The participants were randomly divided into 2 groups: The exercise group and the control group. The exercise group (mean age=64.17±5.58 years) received a CRP (3 times a week, in the morning, at 60%-85% of maximum heart rate [MHR], lasted 45-60 min for 8 weeks). The control group received no exercise program (mean age=63.73±6.04 years). In each group, 16 patients were female and 14 patients were male (n=30).

Following informed consent, all patients were followed up regularly at the CRP center. The participants received psychological and nutritional counseling. During the eight weeks, there were also weekly educational sessions about cardiovascular diseases, which introduced risk factors, diagnoses and treatment approaches, medications and their complications, stress reduction methods, and a healthy lifestyle.

Study criteria

The inclusion criteria were as follows: a) Being approved in the physical, physiological, and psychological test; b) Residing and working in Isfahan City, Iran; c) Not having participated in regular physical activities; and d) Having a stable heart failure for at least 3 months. Meanwhile, the exclusion criteria were as follows: a) History of surgery within the previous 4 months; b) Existence of unstable angina, acute phase of myocardial infarction or unstable arrhythmia; c) Having of obstructive cardiomyopathy, exercise-induced ischemia, arrhythmias, hypertension, resting blood pressure more than 200/120 mmHg, aortic stenosis; d) Exercise limitation due to neuromuscular and or musculoskeletal diseases; e) Uncontrolled systemic disease, such as diabetes mellitus, migraine; f) Being older than 75 years; h) The neurological disorders, such as depression and anxiety. A checklist was completed for the patients at the time of admission according to medical history and physical examination.

Physical and physiological measurements

One week before the initiation of the rehabilitation program, the subjects visited in the morning after a 12-h fast in the laboratory, having refrained from physical activity for 24 h. The weight and height of all participants were measured. Then, the body mass index (BMI) was calculated as weight/height^2 (kg/m^2). After a 5-min rest, the blood pressure (BP) was measured with a standard sphygmomanometer from the right arm in a sitting position.

The patients were evaluated in the body mass, BMI, waist to hip (WHR), and cardiorespiratory variables, including functional capacity (FC), resting heart rate (RHR), resting systolic blood pressure (RSBP), and resting diastolic blood pressure (RDBP) on 1 week before training and 1 day following the CRP. They performed no exercise a day before the test and consumed their last meal at least 3 h before CRP.

Exercise training program

The exercise training was performed 3 times per week for eight weeks based on a previous study with a slight modification [13]. Each exercise session, includes 10 min of warm-up, 40 min of aerobic exercise, stretching, balance, treadmill walking, bicycle exercises, and 10 min of cool-down. The average exercise intensity for each individual was calculated from the heart rate maximum (HRmax) achieved during the exercise test based on a modified version of the Bruce treadmill protocol [14]. The exercise training intensity started at a level between 60% and 65% of the HRmax and gradually increased so that the patients were exercising at 75%–80% HRmax in the eighth week. Finally, intensity, duration, resting and HR, and blood pressure were recorded for each session.

Blood sampling

Blood samples were obtained from all subjects 48 h before and after the CRP. After the centrifugation of blood, serum and plasma were immediately frozen at -80°C. Serum levels of adiponectin and lipid profile including total cholesterol (TC), low-density lipoproteins (LDL), triglyceride (TG), and high-density lipoproteins (HDL) levels were assayed using an ELISA kit (Biovendor, Germany).

Statistical analysis

The data were reported as Mean±SD and analyzed using the SPSS software, version 26 (SPSS Inc., Chicago, IL, USA). Data normality was evaluated using the Kolmogorov-Smirnov test. The data were evaluated by the independent t-tests. $P<0.05$ was considered statistically significant.

Results

There was no significant difference in all cardiorespiratory and hemodynamics parameters between exercise and control groups at baseline ($P>0.05$). Also, no significant difference was observed in lipid profiles between the two groups (Table 1).

Table 1. Comparison of anthropometric variables, cardiorespiratory, and blood markers at baseline

Characteristics	Exercise	Control	P
Age (y)	64.17±5.58	63.73±6.04	0.77
Height (m)	165.48±7.58	165.39±8.07	0.96
Weight (kg)	83.27±6.99	84.67±9.15	0.19
BMI (kg/m^2)	31.45±1.73	31.44±1.42	0.08
WHR (cm)	1.00±0.02	0.99±0.03	0.65
FC (MET)	7.26±1.76	7.52±1.76	0.57
RHR (beat/min)	77.70±5.03	78.03±7.38	0.84
RSBP (mm/Hg)	131.60±9.01	130.20±6.52	0.49
RDBP (mm/Hg)	85.23±6.33	84.00±5.13	0.41
TC (mg/dL)	271.83±61.61	275.87±55.10	0.79
HDL (mg/dL)	36.37±6.05	37.37±5.16	0.49
LDL (mg/dL)	135.37±24.92	132.10±22.52	0.60
TG (mg/dL)	186.67±75.24	188.00±58.89	0.94

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Note: P, derived from independent student t-tests for significant differences between groups in the baseline.

Abbreviations: BMI: Body mass index; WHR: Waist-to-hip ratio; FC: Functional capacity; RHR: Resting heart rate; RSBP: Resting systolic blood pressure; RDBP: Resting diastolic blood pressure; TC: Total cholesterol; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TG: Triglyceride.

Table 2. Comparison of anthropometric and cardiorespiratory variables in exercise and control groups before and after cardiac rehabilitation program

Characteristics	Exercise			Control			P[2]
	Before	After	P[1]	Before	After	P[1]	
Weight (kg)	83.27±6.99	77.90±8.12	0.001*	84.67±9.15	88.20±9.13	0.31	0.001#
BMI (kg/m^2)	31.45±1.73	29.44±2.63	0.001*	31.44±1.42	31.71±1.57	0.2	0.02##
WHR (m)	1.00±0.02	0.93±0.05	0.001*	0.99±0.03	1.03±0.04	0.001*	0.001#
FC (MET)	7.26±1.76	9.45±1.46	0.001*	7.52±1.76	7.23±1.60	0.006**	0.02##
RHR (beat/min)	77.70±5.03	73.33±4.08	0.001*	78.03±7.38	80.37±7.12	0.001*	0.02##
RSBP (mm/Hg)	131.60±9.01	124.77±7.29	0.001*	130.20±6.52	134.53±6.50	0.002**	0.02##
RDBP (mm/Hg)	85.23±6.33	84.07±4.32	0.15	84.00±5.13	84.53±4.56	0.30	0.76

[1]Significant difference between before and after the study in each group, [2]Significant differences between exercise and control groups after 8 weeks of CRP, *P≤0.001, **P≤0.01 comparison before and after CRP in each group, #P≤0.001, ##P≤0.05 between exercise and control groups after CRP.

Abbreviations: BMI: Body mass index; WHR: Waist-to-hip ratio; FC: Functional capacity; RHR: Resting heart rate; RSBP: Resting systolic blood pressure; RDBP: Resting diastolic blood pressure.

Cardiorespiratory fitness and hemodynamics parameters in each group before and after the eighth session are shown in Table 2. It shows the differences in all parameters, except for RDBP between the exercise and control groups (P<0.05). Also, body weight, BMI, WHR, RHR RSBP, and FC significantly improved in patients after exercise. The FC was significantly decreased after 8 weeks in the control group (P<0.05).

Table 3 shows the serum levels of lipid profiles and adiponectin in two groups before and after the 8 weeks of the study. There was no significant difference in the lipid profiles, including TC, LDL-cholesterol, triglycerides, and plasma adiponectin levels between the two groups (P>0.05), while the level of HDL-cholesterol in the exercise group was higher than the control group after CRP (P<0.05). Also, in comparison with the baseline data, the exercise group showed significantly lower scores on the blood markers, including triglycerides, LDL-cholesterol,

Table 3. Comparison of plasma adiponectin levels and lipid profile in exercise and control groups before and after cardiac rehabilitation program

Characteristics	Exercise			Control			P[2]
	Before	After	P[1]	Before	After	P[1]	
Total cholesterol (mg/dL)	271.83±61.61	246.27±57.80	0.001*	275.87±55.10	268.57±5.97	0.19	0.36
HDL-cholesterol (mg/dL)	36.37±6.05	41.40±5.98	0.001*	37.37±5.16	36.60±4.77	0.06	0.03#
LDL-cholesterol (mg/dL)	135.37±24.92	124.43±19.36	0.001*	137.53±19.68	135.43±16.89	0.11	0.21
Triglyceride (mg/dL)	186.67±75.24	176.97±69.97	0.001*	188.00±58.89	183.07±50.80	0.32	0.82
Adiponectin (µg/mL)	5.08±0.96	6.82±1.19	0.002**	5.66±1.07	5.61±1.20	0.82	0.14

[1]Significant difference between before and after the study in each group, [2]Significant differences between exercise and control groups after 8 weeks of CRP, *P≤0.001, **P≤0.01 comparison before and after CRP in each group, #P≤0.05 between exercise and control groups.

HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

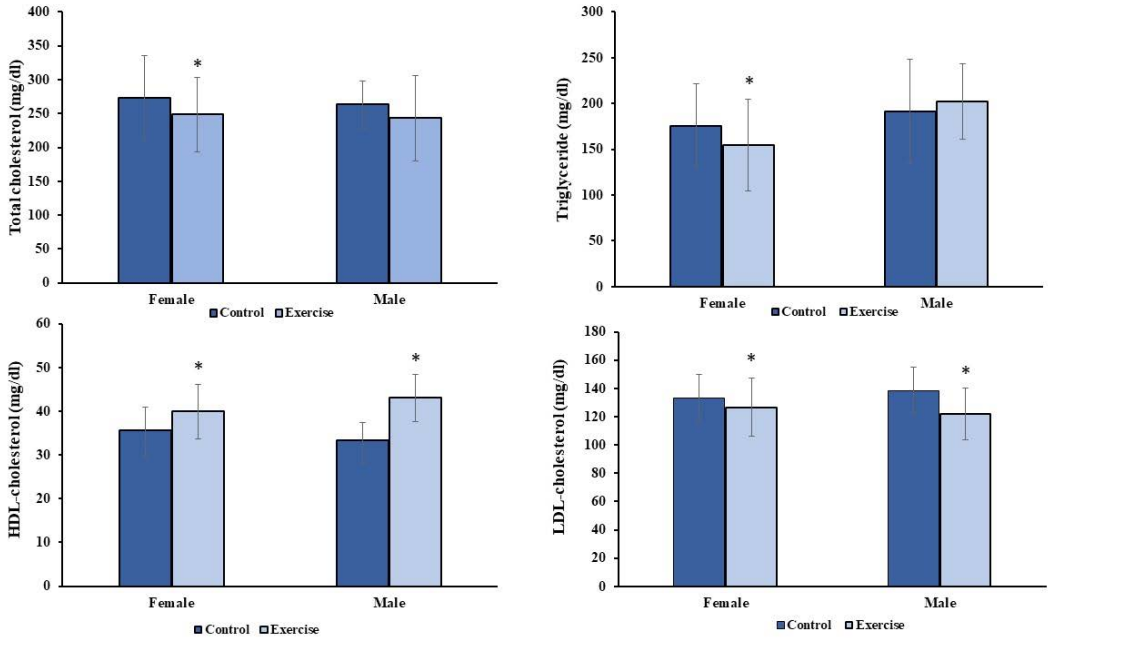

Figure 1. Associations between sex and levels of lipid profiles in exercise and control groups after cardiac rehabilitation program

*P<0.05

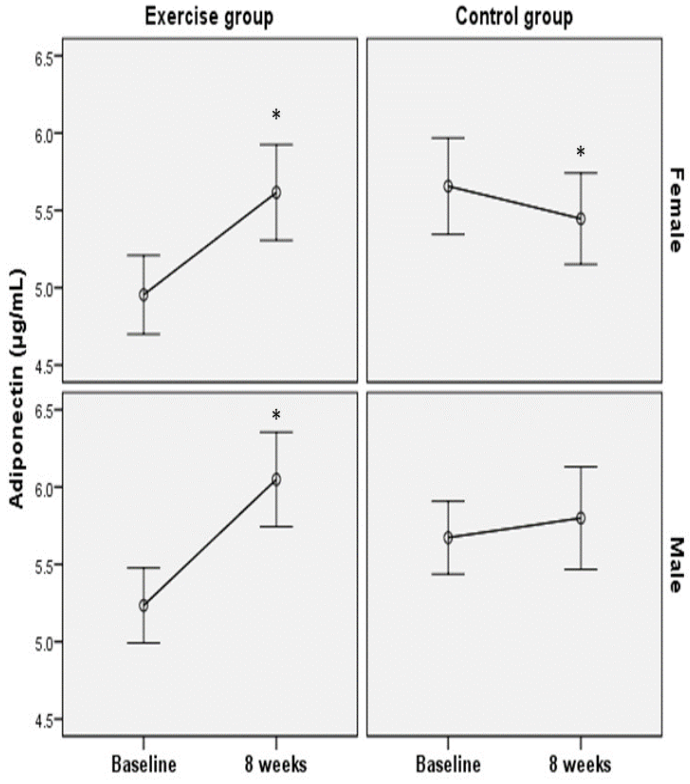

Figure 2. Associations between sex and adiponectin level in exercise and control groups at baseline and after CRP

*P<0.05

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and TC after CRP. However, the levels of HDL-cholesterol and adiponectin increased following the 8-week exercise-training program (P≤0.01). In contrast, there was no significant difference in lipid profiles (triglycerides, LDL- LDL-cholesterol, TC, HDL-cholesterol) and adiponectin levels before and after the 8-week in the control group (P>0.05).

Figure 1 shows how the distributions of lipid biomarkers changed in control and exercise groups by sex. There was a significant reduction in triglycerides, TC, and LDL-cholesterol levels in exercised women compared to women without a training program (P≤0.01). Moreover, an increased level of HDL-cholesterol was observed in women and men after CRP (P≤0.01). However, there was no significant difference in triglycerides and TC levels in men's groups after exercise (P>0.05). Also, an exercise-training program could significantly increase the level of adiponectin in men and women patients compared to the baseline (P≤0.05) (Figure 2).

Discussion

We looked at how an 8-week cardiac rehabilitation program affected on lipid profiles and plasma adiponectin levels in CHD patients. According to the study's findings, patients who received CRP for 8 weeks had higher serum levels of adiponectin with significant reduction in body weight, BMI, and WHR. Weight loss and reduction of BMI can improve adiponectin levels in plasma [15].

Adiponectin synthesized by adipose tissue reduces blood glucose, inflammatory cytokines, and oxidative stress. It can lead to an improvement in insulin resistance. Also, adiponectin has anti-atherosclerotic and anti-inflammatory properties that may play an important role in preventing the progression of CAD [16]. In our study, the levels of LDL and TC decreased while an increase was observed in the level of adiponectin after an 8-week cardiac rehabilitation program. The low adiponectin expression in blood fluid is related to CAD [17]. Stojanovic et al. showed that low levels of adiponectin and insulin/adiponectin resistance were associated with CAD [18]. In addition, a low level of adiponectin may lead to the development of metabolic syndrome, insulin resistance, and hypertension in children which is related to a high prevalence of cardiovascular disorders [19]. Adiponectin includes 3 major forms: Low–molecular weight, middle–molecular weight, and high–molecular weight. Physical activity may impact different forms of adiponectin [20]. A study showed that adiponectin levels correlated directly with exercise training [21], while another study revealed no changes in adiponectin levels after exercise training [22]. Moreover, the adiponectin levels in different diseases, such as breast cancer, hypertension, and Type II diabetes mellitus may increase [23]. Yokoyama et al. confirmed that the use of diet and exercise provided no changes in adiponectin levels after 3 weeks [24]. The results of our findings are not consistent with this study. It may be because of the short time exercise (3 weeks). Becic et al. in 2018 showed that aerobic exercise can increase adiponectin levels in prediabetic and diabetic adults [25]. Another study evaluated the effect of 8 weeks of combined rehabilitation training on plasma levels of leptin and adiponectin in middle-aged men following coronary artery bypass surgery. The results showed that leptin plasma concentration had no change while adiponectin level significantly increased after the rehabilitation training [26]. Therefore, regular physical exercise can play a positive role in the reduction of cardiovascular disorders [27]. Mechanistically, exercise increases the production of endothelial nitric oxidase and Snitrosylation pathways in cardiac cells leading to a decrease the reactive oxygen species production. Thus, this mechanism provides a cardioprotection against heart injuries [28].

Total adiponectin has a reverse correlation with adiposity, triglycerides, and C-reactive protein the increase of adiponectin level and reduction of lipid profiles as one of the functional mechanisms of regular exercise can help to the prevention of CAD.

Conclusion

The results indicated that fairly low-intensity exercise can successfully contribute to plasma adiponectin secretion after 8 weeks of the cardiac rehabilitation program. Also, the levels of lipid profiles decreased following exercise training in patients with CHD. So, exercise activity can be used as an operative strategy for preventing and treatment of cardiovascular diseases.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Isfahan Cardiovascular Research Center Ethics Committee (Code: 0038).

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

All authors participated equally in the design, execution, and writing of all parts of this research.

Conflict of interest

All authors declared no conflict of interest.

Acknowledgments

The authors would like to thank Isfahan Cardiac Rehabilitation Research Center staff and are grateful to the patients who gave their time to participate in the study.

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