



EFFECT OF COMBINED SPORTS ACTIVITIES ON CARDIOVASCULAR HEALTH STRUCTURES OF INACTIVE MEN FOLLOWING ADDICTION WITHDRAWAL

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Abstract

Background and purpose: In fact, one of the concerns in drug treatment is related to the aspect of weight gain, body mass index (BMI), cholesterol increase and nutritional disorders after drug withdrawal. The purpose of this research is to investigate the effect of 8 weeks of combined sports activity on the structures of cardiovascular health in inactive men after quitting drugs.

Materials and methods: The statistical population of this study was formed by inactive male drug addicts in Khorramabad city, who had been abstinent from drugs for at least two months, and 30 of them agreed to cooperate as a sample and were randomly selected in a ratio of 1: 1. They were divided into two experimental groups (15 people) and control (15 people). Sports activity of walking with 50-70% of the maximum heart rate and weight work with 45-50% of a maximum repetition was performed for eight weeks. 48 hours before and after eight weeks of sports activity, blood samples were taken to measure homocysteine, apoprotein A, HDL, and LDL. , fibrinogen of vulcocytes was performed. Analysis of covariance (ANCOVA) and Pearson's moment correlation coefficient were used for the inferential analysis of the data.

Findings: 8 weeks of combined sports activity caused a significant decrease in the values of homocysteine, fibrinogen, and LDL leukocytes ($P < 0.05$). 8 weeks of combined sports activity



caused a significant increase in the values of apoprotein A and HDL ($P = 0.0001$). The peak after eight weeks of combined sports activity increased significantly ($P=0.0001$). The inverse and significant relationship between fibrinogen ($r=-0.76$, $P=0.001$) and homocysteine ($P=0.67$, 0.001) ($r=-$), leukocyte count ($r=-0.81$, $P=0.001$) and BMI ($r=-0.86$, $P=0.001$), with peak VO_2 after eight weeks.

Discussion and conclusion: Eight weeks of combined sports activity reduces cardiovascular risk structures and improves cardiorespiratory fitness in inactive men after quitting drugs.

Keywords: Sports Activities, Cardiovascular, Health Structures , Inactive Men ,Addiction

Introduction

Addiction is one of the major complications in human societies, which not only causes behavioral and social disorders but also causes substantial financial losses to the individual, family, and society by affecting various aspects of physical health (1). However, heart disease and atherosclerosis are still the number one cause. Moreover, in developed and developing countries such as Iran, approx. %40 of death and disability counts by heart disease. In 2020, coronary artery diseases, particularly atherosclerosis, are among the world's diseases that reduce individuals' efficiency and helpful life due to disability and premature death. Significant success has been in reducing complications and deaths from acute coronary events in recent years. However, it is possible to treat the underlying process of CAD1 and prevent complications, which is considered a challenge for researchers.

With a molecular weight of 135.2 Daltons, homocysteine is an amino acid that contains sulfur and is produced during the metabolism of methionine. Epidemiological studies show that an increase in homocysteine from the optimal level is independently associated with the risk of cardiovascular diseases, and a decrease in homocysteine levels reduces heart attacks and strokes (3). Lipoproteins are particles composed of lipids and proteins. Proteins in the structure of lipoproteins are called apoproteins or apolipoproteins. Each lipoprotein contains one or more apoproteins. The apoprotein in HDL is called HDL A, and the major apoprotein in low-density lipoprotein (LDL) is called LDL subclass pattern B (LDL B). Consequently, the ratio of apolipoprotein B to apolipoprotein A significantly predicts heart muscle damage. Most researchers have shown that the metabolism, amount, and type of lipids, particularly blood lipoproteins, play a significant role in aggravating cardiovascular diseases; therefore, regulation of blood lipids is considered an essential factor in health (3-4) due to the direct relationship between fats and heart attack.

The results of a study by Naderi show that Lipoprotein-a (Lpa), apoprotein B, and fibrinogen levels in drug abusers are considerably higher than in the control group, and HDL levels and antioxidant capacity are lower in drug addicts compared to the control group. Control group (4); therefore, it seems drug abusers are more prone to cardiovascular attacks than other individuals, and there are many precarious structures in them.

However, the liver produces fibrinogen, a high molecular weight protein; its normal level is 250 mg/dL on average. The amount of plasma fibrinogen, moreover, amplifies inflammatory and liver malfunctions. Increased plasma fibrinogen may be considered a precursor to increased clot formation.

Advanced plasma fibrinogen is linked to other coronary artery disease risk factors, such as age, smoking, hypertension, hyperlipidemia, diabetes, and obesity, but it also acts as a stand-alone risk factor for the development of atherosclerosis. (5). However, blood plays a key role, and due to its influence on the red blood cell aggregation process, blood is proposed as one of the main factors determining blood rheology (6). Atherosclerotic changes in coronary and peripheral vessels also reduce cardiorespiratory fitness (7). A positive correlation between cardiorespiratory fitness and high aerobic fitness was reported with a reduction in coronary artery disease (7). Different phases of the inflammatory process include leukocyte migration through the endothelium to the vessel wall and adhesion of neutrophils, monocytes, and leukocytes to the endothelium. Circulating leukocyte counts correlate with the severity of coronary artery disease, and high circulating leukocyte levels are a factor. Furthermore, it is considered a risk factor for subsequent occurrence of ischemic heart diseases (8).

Bani Talebi et al. studied the effect of a period of physical activity on the cardiovascular risk factors of drug addicts following addiction withdrawal. The results showed that selected physical activity positively affects the body composition and physical fitness factors of individuals with a substance use disorder (SUD) following quitting and prevents cardiovascular risk factors (9). The studies by Gorji (10) and Saidipour (11) showed that routine physical activity is suitable for preventing and treating drug-dependent patients. Cardiovascular fitness is the ability to participate in aerobic exercise activities, and it is associated with low clinical factors such as stroke, metabolic syndrome, myocardial infarction, and other cardiovascular diseases (12), which may be measured by $\max 2V_o$ (7).

Moreover, $\max 2V_o$ predicts the exercise capacity of individuals and is a strong predictor of cardiovascular function (7). Low cardiovascular fitness is likely to lead to atherosclerotic changes in peripheral or coronary arteries theoretically. Additionally, Iftikhar et al. have shown that the inflammatory indices of adults have an inverse relationship with their level of aerobic fitness (13).

Daneshmandi et al. studied the physical condition and aerobic capacity of individuals with SUD. They showed that the aerobic capacity of individuals with SUD is lower than that of healthy individuals (14). Moreover, Bani Talebi et al. stated that physical activity improves the aerobic capacity of individuals with SUD following addiction withdrawal (9). Therefore, it seems routine sports activity may increase the maximum oxygen consumption, and increasing the maximum oxygen consumption in individuals freed from drugs reduces the cardiovascular risk structures in these individuals. Additionally, combined sports activities, including physical exercises, cause physiological adaptations such as increasing oxidative enzymes, reducing fat tissue, reducing

inflammatory factors, increasing anabolic hormones, increasing capillary density, increasing the number of mitochondria, and increasing maximum oxygen consumption and efficiency.

Cardiovascular system and mass increase, although the actual mechanism of the effect of routine and controlled strength training in reducing the amount of fibrinogen and homocysteine is not known; however, probably this decrease is a kind of adaptation due to exercise and routine activity, which directly or indirectly through the control of the production of this glycoprotein in the liver, reduces the production of cytokines and causes inflammation.

Few studies have examined inflammatory markers in recovering individuals with addiction; therefore, this study seeks to answer the question, "*Does eight weeks of combined exercise activity affect the cardiovascular health structures of inactive men following addiction withdrawal?*".

The statistical population consists of inactive men who were members in Lorestan province following addiction withdrawal, and at least two months had passed since addiction withdrawal. Among them, 30 men who recovered from drug use were willing to cooperate and were divided into two experimental groups (15 individuals) and a control group (15 individuals) in a simple random manner at a ratio of 1:1.

Before the interventions and homogenizing, the two groups were compared based on age, height, weight, duration of drug abuse, addiction withdrawal interval, body mass index (BMI), and aerobic fitness, and there was no considerable difference between the factors (Table 1). All participants received written information about the research and were asked to sign a printed consent form after the study. However, ethical permits required for the implementation of this research and cooperation with addiction treatment centers were obtained from the Lorestan Province Welfare Organization. Additionally, the current research was conducted under the supervision of an expert doctor and sports physiology expert. All subjects completed the health questionnaire and were approved by the physician. According to an analysis of the medical records, there was no history of diabetes, high blood pressure, heart disease, kidney, or liver disorders that could have affected the immune system or fibrinogen levels.

Blood sampling

In one session, the subjects learned how to exercise and take blood. Moreover, to reduce some interfering and influential factors in the research results and reduce the effect of the type of food on the inflammatory and immune indicators, the subjects were asked to refrain from eating prepared diets for a minimum of 24 hours in this session before the exercise schedules and blood sampling. Moreover, the subjects were banned from drinking caffeinated drinks (14). The subjects' blood samples were measured in two stages: before training (stage 1) and immediately after training (stage 2). In each phase, 5ccs of blood were collected in the fasting state (8 hours). Subsequently, after 3 hours, serum was separated from plasma by centrifugation at 1500 rpm to measure the investigated variables.

Sports exercises protocols

Sports exercises were merely for the experimental group; the control group received no sports intervention. Considering the physical conditions of the subjects and the passage of two months after quitting drugs, the researchers of this study chose the sports activity of walking and exercising with lifts. Furthermore, the walking training schedules were implemented for eight weeks and three sessions per week with low to moderate intensity. The researchers controlled the exercise intensity using a polar heart rate monitor by determining the subjects' heart rates before the exercises started, during, and after the activity in each session (Table 1). The strength training schedule was implemented for eight weeks and three sessions per week with low to moderate intensity. The resistance training movements were two rounds of 10 repetitions and %30 of one repetition maximum RM (1), which changed to 3 rounds of 6 repetitions and %50-60 of one repetition maximum at the end of the training period. Additionally, 3-5 minutes rest was considered in the middle of rounds. The performed movements were chest press, leg press, leg back press, underarm stretch, forearm stretch, and two-way downward stretch 1, which comprises the large muscles of the upper and lower body (9-15).

To comply with the principle of overload and gradual progression, the RM1 of these movements was measured again at weeks 4, 2, and 6. Moreover, the subjects did walking exercises on one day and resistance exercises on the other day. However, the control group had no sports activities during these eight weeks; their only activity was doing daily tasks as before.

Table 1. Specifications of the walking program

Weeks	days (number)	percentage of heart rate	average distance	time (minutes) traveled
The first and second week (adaptation to training)	3	%45-50	20	700-1400
The third and fourth week	3	50-55%	30	1400-1800
The fifth and sixth week	3	55-65%	45	1900-2100
Seventh and eighth week	3	65-75%	55	2100-2400

Methodology

Research Instruments

BMI, however, was achieved by dividing weight (kg) by the square of height (in meters). To measure the peak oxygen consumption, the *Rockport 1-Mile Fitness Walking Test* was exploited using the heart rate polar pacing device and the corresponding equation at the beginning and end of the course (7). Moreover, since the subjects were in a relatively weak condition regarding physical fitness, and the current study's researchers could not source the high intensity of the exercises to determine the max2Vo indices, peak2Vo was used instead of max2Vo. Additionally, the index was measured 24 hours before blood sampling in the pre-test and 24 hours after the end of eight weeks of training in the post-test. The highest 2vo obtained during the test was peak2Vo (12). Maximum oxygen consumption is the subjects' maximum oxygen consumption in ml/kg/min.

The heart rate of 7 subjects was randomly measured with a pulse counter to determine the training intensity (12).

Laboratory analysis

Forty-eight hours before and 48 hours after sports activity and after 8 to 10 hours of fasting, blood samples were taken from subjects at rest to determine homocysteine, apoprotein A, HDL, LDL, fibrinogen, and the number of leukocytes (WBC).

Laboratory analysis utilized an ELISA kit manufactured by Axis-Shield Diagonist, Germany. The study measured apoprotein A utilizing the turbidimetric method. Moreover, using a Pars test kit in Iran, the enzymatic photometric method measured high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterols. The coagulometric method was applied to measure fibrinogen levels; a Quattron coagulometer was also utilized. First, a package of 10 TEC lots of Glaso coagulation method was applied to determine the amount of fibrinogen in plasma. White blood cells were measured in plasma through cell counter one and isotone solution method 2.

Statistical analysis

The paper studied each research variable's frequency, mean, and standard deviation (Table 1). Furthermore, the Smirnov column graph test was applied to determine the data distribution. Due to the normality of data distribution, the ANCOA test was used to compare between groups. The correlation of each variable of homocysteine, apoprotein A, HDL, LDL, fibrinogen, and the number of leukocytes was investigated separately with peak2VO in the post-test, applying Pearson's correlation coefficient. Statistical calculations were performed with *SPSS v.16* at a significant level ($P < 0.05$).

Results:

Table 2 shows the results of the covariance test (ANCOA) for the intergroup comparison of the variables with the control pre-test in the two experimental and control groups.

Table 2. Demographic characteristics of inactive men after quitting drugs (mean \pm standard deviation)

Variables,	experimental group	control group	P value
Age	1.16 \pm 28/90	1.06 \pm 28.73	0.6
Weight	1.17 \pm 61.33	0.86 \pm 61	0.3
height	172/2 \pm 2/70	171/2 \pm 2/54	0.3
Duration of drug use	0/31 \pm 7/5	0/33 \pm 7/4	0.2
Duration of leaving the material	0.39 \pm 2/13	0/26 \pm 2	0.1 0.2

(ml/kg/min)Vo ₂ peak	0/27±28/1	0/25±27/90	0.3
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Eight weeks of physical activity in the experimental group caused a significant decrease in homocysteine, fibrinogen, and LDL leukocytes (P=0.0001), which showed a significant increase in body mass index and maximum oxygen consumption (P=0.0001).

Table 3. Intergroup comparison of research variables using ANCOVA test

variable	group	Pre-test	Post-test	F	P
Homocysteine (micromol/liter)	experimental	0.63±18/06	0/25±16/93	416/01	0.0001
	Control	0.27±18/27	0/26±18/23		
Apoprotein A (mg/dL)	experimental	17/81±98/20	29/31±198/1	85/27	0.0001
	Control	16/40±96/30	29/31±162/1		
HDL(mg/dL)	experimental	10/37±35/37	9/45±36/87	91/26	0.0001
	Control	10/43±35/20	9/25±35/40		
LDL(mg/dL)	experimental	45/51±131/68	43/61±129/06	276/48	0.0001
	Control	29/84±127/86	28/86±128/66		
Fibrinogen (mg/dL)	experimental	431/8±49/55	30/11±233/33	17/39	0.0001
	Control	450/66±49/55	7626/66±196/42		
Leukocyte (number in ml cubic meter)	experimental	12540/33±747/18	9700/16±196/42	26/41	0.0001
	Control	20/48±0/62	22±0/44		
BMI(kg/m ²)	experimental	21±0/71	21/45±0/44	88/45	0.0001
	Control	28/15±0/27	29/03±0/22		
$V_{2peak}(\frac{m}{kg})$	experimental	27/10±0/23	27/23±0/24	81/61	0.0001
	Control				

Significant and inverse correlation between fibrinogen ($r=-0.76$, $P=0.03$), homocysteine ($r=-0.67$, $P=0.01$), leukocyte count ($r=0.61$, $P=0.03$) and LDL ($r=0.71$) $p = 0.71$) with a 2VO peak. However, there was a significant and direct relationship between apoprotein ($r=0.79$ ($p=0.79$), HDL001 ($p=0.75$), and 2VO peak (Table 4).

Table 4. Relationship between homocysteine, apoprotein A, lipoprotein, fibrinogen, and leukocyte count with peak2VO after the test

Variables	correlation coefficient	P value
Homocysteine	-0.67	0.01
Apoprotein A	0.79	0.000
HDL	0.75	0.001
LDL	-0.71	0.005
Fibrinogen	-0.76	0.03
White blood cells	-0.61	0.03

Discussion

There is no study in the country on the effect of sports activity on changes in homocysteine, apoprotein A, HDL, LDL, fibrinogen, leukocytes, and its relationship with cardio-respiratory fitness in drug addicts. In the present study, homocysteine values significantly decreased after eight weeks of sports activities, including walking and exercising with lifts. The findings are consistent with those of Hairandova (16) and Schneider (17) on reducing homocysteine after exercise.

Studies by Nazim et al. (18) show no significant relationship between the amount of sports activity and serum homocysteine; this inconsistency may relate to the type of substances consumed, the type of physical activity (swimming), or the type of subjects (teenagers). Furthermore, the present paper showed an inverse relationship between homocysteine and 2VO peak even after adjusting mediators such as BMI.

However, the results are consistent with the results of Essing et al. (19), not with Nazim et al. (18). This contradiction may be related to the type of substances consumed, the preparation of the subjects, and the duration of the sports activity. One independent risk factor for cardiovascular disorders is elevated homocysteine. However, sports activity in addicted individuals reduced homocysteine after quitting sports.

By improving the homocysteine cycle's ability to absorb vitamins, particularly B vitamins, in the intestines of addicted individuals (which reduces the absorption of vitamins from their intestines), exercise helps to reduce the amount of homocysteine and prevents its accumulation in the blood (17).

Furthermore, combined sports activities reduce oxidative stress. The possible mechanism of the reductions may be an increase in the re-methylation of homocysteine, resulting in an increase in S-adenosylmethionine (SAM) levels and an increase in antioxidant capacity (17).

In this paper, eight weeks of sports activities, including walking and exercising with lifts, caused a significant increase in the amount of apoprotein A, consistent with results by Gaini et al. However, it is not consistent with the results of Wan (21); maybe this discrepancy is related to the type of subjects in the training protocol. Additionally, the present study showed a positive relationship between apoprotein A and 2VO peak. Moreover, it is expected that with the increase in HDL level, the amount of apoprotein A, which is the main protein of HDL, similarly increases.

Furthermore, by activating the lipoprotein lipase enzyme, apoprotein A causes the catabolism of LDL triglycerides in the walls of the body's blood vessels, especially the walls of the vessels of fatty tissues. In sports activities, catabolism of LDL occurs; for this reason, the increase of apoprotein A is necessary, which may justify the result of the present study on the effect of combined sports activity on the increase of Apolipoprotein A (22).

In this study, the level of HDL increased significantly after eight weeks of sports activities, including walking and exercising with lifts. Moreover, LDL values significantly decreased after eight weeks of sports activities, including walking and exercising with lifts. The findings are consistent with Afzalpour's (23) and Leon (24) findings. However, this difference may be related to individuals' exercise schedules.

The results showed an inverse relationship between LDL and peak2VO and a positive relationship between HDL and peak2VO. This increase in HDL is due to the activation of lipoprotein lipase and leucine cholesterol acyltransferase enzymes and a decrease in liver lipase activity (23). Clinical data have shown that interventions that increase high-density lipoprotein reduce risk. Coronary heart disease is up to 30-40%. Each 1 mg increase in high-density lipoprotein is associated with a 2-4% reduction in the risk of coronary heart disease (23).

In this paper, however, fibrinogen values of drug addicts showed a significant decrease after the eighth week of sports activities, including walking and exercising with lifts, which are consistent with the findings by Masoumi et al. (25) and Asgari et al. (26).

The studies by Lemora et al. (32) and Sharp et al. (28) show no significant relationship between the amount of exercise activity and serum fibrinogen, which may lack communication-related to the type of subjects. The subjects of this research were cardiovascular patients. Moreover, the present study showed an inverse relationship between fibrinogen and 2VO peak, even after adjusting for mediators such as BMI.

The results of this study are consistent with those of Christopher et al. (29) however, not with those of Ahmadizad et al. (30) and Nikbakht et al. (31). They compared the relationship between physical activity level and serum fibrinogen in groups of active, inactive, and CAD middle-aged men. Increased plasma fibrinogen is an important and independent risk factor in developing and progressing some diseases, including coronary artery disease, stroke, and peripheral atherosclerosis (28). As the results show, the rate of clot formation in opium addicts is higher than in non-addicts (25). Several other studies showed a correlation between plasma fibrinogen levels and the severity of coronary artery disease in angiography (12). Most of these studies attribute this to vessel occlusion, indicating that increased plasma fibrinogen is a thrombogenic factor (31, 30). Other studies investigate some inflammatory indices' relationship with cardiovascular fitness in adults. Furthermore, numerous studies showed that routine exercise reduces inflammatory markers (13).

Since fibrinogen is one of the key determinants of plasma viscosity, however, routine exercise may increase plasma volume, increase blood rheology, decrease blood viscosity, and decrease plasma fibrinogen. (32). An increase in fibrinogen is associated with decreased cardiorespiratory fitness. Although the mechanism of increased fibrinogen in drug addicts is unknown (2), this concern is significant because increased plasma fibrinogen is considered an independent risk factor for coronary artery disease (25).

The results showed that routine exercise decreased the fibrinogen level in drug addicts compared to the control group, which may indicate the effectiveness of the training period on fibrinogen. However, the exact mechanism of the effect of routine and controlled exercise in reducing the amount of fibrinogen is not known (33); probably, this decrease is a kind of adaptation caused by exercise and routine sports activity, which directly or indirectly, by controlling the production of this glycoprotein in the liver, reduces the production of fibrinogen. Increasing peak oxygen consumption and weight ratio are all reasons for the effectiveness of these exercises and creating adaptation in reducing the amount of fibrinogen (33,31).

The results showed that peak2vo increases significantly after eight weeks of physical activity, including walking and exercising with lifts. Moreover, the findings are consistent with those of Duncan et al. (39), who studied the effect of physical activity on peak 2V levels in patients with coronary artery disease. The results showed that physical activity increased peak 2vo. Furthermore, atherosclerotic changes in coronary and peripheral arteries similarly reduce cardiorespiratory

fitness; there is documented evidence of a positive correlation between cardiorespiratory fitness and high aerobic fitness with reduced coronary artery disease (13).

In the current study, the increase in peak $\dot{V}O_2$ compared to before sports activities is attributed to adapting the cardiovascular, muscular, and metabolic systems to sports activities. Probably, these adaptations include increased muscle oxidative capacity, increased total hemoglobin, increased fat burning and decreased glycolysis, increased end-diastolic volume (cardiac preload), decreased end-diastolic volume, and increased stroke volume. In addition to increasing the oxygen difference between blood and veins, the activity of Krebs cycle enzymes and the electron transport system, the number and size of mitochondria, and the increase of muscle tissue and their efficiency increase (39). Emphasis on physical activity and cardiovascular fitness of addicted individuals is a crucial structure to prevent cardiovascular diseases after quitting drugs.

Conclusion

The level of inflammatory indicators is high in drug addicts, and exercise activity causes a significant decrease in homocysteine, LDL, plasma fibrinogen, and serum leukocytes and an increase in HDL and apoprotein A after addiction withdrawal, which reduces cardiovascular risk structures and improves cardiorespiratory fitness in men. It becomes inactive after stopping the drug. Based on the research results, it is possible to recommend walking with 50-70% of the maximum heart rate and working with weights with 50-60% of the maximum repetition of three sessions a week for this group.

Limitations and Future Research

One of the researchers' most important limitations in the present study was the strict control of the subjects' diet and daily activity levels. However, what intensity, speed, frequency, and many weeks of combined exercise activity with strict dietary control may lead to the most favorable response of cardiovascular health structures in inactive men following addiction withdrawal must be studied in future research. Additionally, the authors suggested that researchers benefit from larger samples.

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