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Effectiveness of Eight Weeks Aerobic and Aerobic-resistance Cardiac Rehabilitation Exercise Training on Hemorheologic Variables among Middle-aged Men with Coronary Artery Disease

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Abstract

Introduction: Hemorheologic disorders are the most important causes of impaired circulation and cardiovascular events. It is also documented that regular and continuous exercise training could improve vascular adaptation to exercise and provide protection against major cardiovascular events. The aim of this study was to evaluate effectiveness of eight-week cardiac rehabilitation exercise by aerobic and aerobic-resistance methods on hemorheologic variables among middle-aged men with coronary artery disease (CAD). **Materials and Methods**: The present quasi-experimental study was carried out on 51 middle-aged men with CAD aged 45-65 years. Participants were randomly divided into three groups including aerobic exercise, aerobic-resistance exercise, and control group. The experimental groups performed sub-maximal aerobic exercises for eight weeks. Exercise protocol consisted rehabilitation exercises for three sessions a week. In addition to aerobic exercise, aerobic-resistance group received two sessions of resistance exercise using free weights per week for 15 minutes. **Results**: There was a significant improvement in all hemorheologic variables including fibrinogen concentration (P=0.001), hematocrit concentration (P=0.002), and erythrocyte sedimentation rate (P=0.001) in both aerobic and aerobic-resistance exercise groups compared to the control group. There was also a significant decrease of mentioned hemorheologic variables in aerobic-resistance group compared to aerobic group. **Conclusion**: Our study showed that eight-week cardiac rehabilitation exercises, especially aerobic-resistance exercise training, could improve the blood hematologic variables in middle-aged men with CAD.

Keywords: Cardiac rehabilitation; Coronary artery disease; Hematologic tests

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Introduction

Coronary artery disease (CAD) is the most common etiology of cardiovascular disease occurring in adults due to atherosclerosis of the coronary arteries (1). Atherosclerosis is an inflammatory response that begins with damage to vascular endothelium and, as the disease progresses, causes blockage, narrowing of the arteries, and reduced myocardial blood flow (1), thereby leading to ischemia of myocardial cells and consequently myocardial infarction. It is documented that hemorheologic disorders are among primary etiological factors in the occurrence and spread of cardiovascular complications. It also plays an important role in pathogenesis of atherosclerosis and thrombotic diseases such as ischemic heart disease (IHD) (2-5).

Although efforts to prevent cardiovascular disease and common medical treatments such as medication and surgery (as primary and secondary steps) are taken into account for the management of cardiovascular patients, cardiac rehabilitation along with pharmacological and surgical treatments is of great importance (6, 7). It has been documented that regular and continuous exercises can improve vascular adaptation to exercise and provide protection against major cardiovascular events (8). While the effectiveness of exercise training programs in cardiac rehabilitation is obvious, there have been fewer studies on effects of exercise training programs on hemorheologic variables among patients with CAD (9). Also, absence of high quality research studies investigating the effectiveness of regular exercise training on the rheological function of cardiovascular disease has limited its definitive effective capacity (10).

Results of previous studies have confirmed that one of the most important causes of circulatory damage and cardiovascular events is impaired blood rheology (2-5). Major blood rheology factors, including fibrinogen, hematocrit, and erythrocyte sedimentation rate (ESR), are independent risk factors for cardiovascular complications and mortality (11). Fibrinogen, a positive acute phase protein is upregulated in response to systemic inflammation, tissue damage, and certain cardiovascular events. It has also been reported that increased fibrinogen levels occur due to inflammation, thrombosis, and vascular damage; therefore, increasing plasma fibrinogen levels are associated with an increased risk of CAD and myocardial infarction (12). Topics as to whether fibrinogen is a causative agent or merely a marker of CAD still need further studies to investigate the relationship between fibrinogen and CAD (13, 14). Epidemiological studies have shown that hematocrit level, as a major determinant of blood viscosity, is an important blood rheology indicator (11, 15, 16). Hematocrit, as an indicator of blood erythrocyte level, plays an important role in venous return and platelet adhesion (17). Although there is limited information on exact mechanism of hematocrit related to cardiovascular risk factors, its abnormal level can result in circulatory disorders, altered capillary circulatory perfusion, increased atherosclerosis, increased plaque rupture, and subsequent ischemia (10). Although basically hematocrit levels in people with cardiovascular risk factors are higher than those without risk factors (11), after cardiac rehabilitation, CAD patients have shown decreased level of plasma viscosity and hematocrit level (18). It is documented that ESR plays an important role in the inflammatory etiology of CAD, while it is also increased in CAD patients in the long run (19). Since ESR provides strong prognostic information in people with CAD, increase in ESR gradient is associated with an increased risk of mortality among patients with cardiovascular disorders (20). Exercise training can reduce inflammatory markers by improving endothelial function indirectly (21). Therefore, since the beneficial effects of exercise on CAD may decrease inflammatory markers, further relevant studies may be of considerable help to treat cardiovascular patients.

Assuming effectiveness of cardiac rehabilitation exercises on rheological blood function, an attempt was made in the present study to answer the question of how cardiac rehabilitation exercises in both aerobic and aerobic-resistance methods affect the hemorheologic variables of patients with CAD? Therefore, the aim of present study was to evaluate the effectiveness of exercise training on the blood rheological variables (fibrinogen, hematocrit, and erythrocyte sedimentation rate).

Methods and Materials:

This was a prospective quasi-experimental study with pre-and post-test design. Inclusion criteria were male patients of 45-65 years-old with CAD (myocardial infarction and patients undergoing coronary artery bypass graft surgery and percutaneous coronary intervention) who referred to Sadr Heart Clinic in Tehran and were low-risk patients. Considering exclusion criteria of smoking, alcohol abuse, and taking drugs affecting research variables, with the use of G-Power software with power of 0.95 and alpha of 0.05, a total of 51 patients were selected as the study participants under the supervision of a nurse familiar with cardiac monitoring., Participants were selected using purposive sampling and were randomly divided into three groups, including two experimental groups; aerobic exercise group (n=17), aerobic-resistance exercise group (n=17), and a control group (n=17). After explaining the purpose of research, subjects completed the informed consent form, personal information questionnaire, and cardiac health history questionnaire. Blood samples were taken as initial tests to determine the concentration of fibrinogen, hematocrit, and ESR. Study protocol was approved by ethics committee with number of IR.AJAUMS.REC.1398.133.

Experimental groups practiced sub-maximal aerobic exercise for eight weeks, three times a week, first with an intensity of 60-65% of the heart rate reserve according to the Karvonen formula and under the supervision of a specialist in rehabilitation medicine (22). Target heart rate or ratio of heart rate reserve to exercise intensity was calculated for each subject separately using the Karvonen equation (23). In addition to aerobic exercise, the aerobic-resistance group performed resistance exercise training using free weights twice a week for 15 minutes each time. The control group did not have any regular exercise training during these eight weeks.

Table 1. Mean (SD) of demographic and clinical characteristics of participants before cardiac rehabilitation (N=17 patients in each group)

Parameter	Aerobic Group	Aerobic-Resistance Group	Control Group	Sig.
Age (years)	53.41 (5.97)	56.88 (5.91)	56.88 (5.52)	0.823
Height (cm)	176.76 (5.04)	172.94 (7.45)	175.29 (5.62)	0.188
Weight (kg)	81.18 (9.00)	78.41 (9.17)	76.47 (6.01)	0.192
BMI (kg/m^2)	25.93 (2.04)	26.23 (1.87)	24.88 (1.29)	0.235
BSI	1.99 (0.13)	1.94 (0.15)	1.93 (1.00)	0.257
METs	7.13 (1.91)	6.58 (3.13)	5.36 (1.95)	0.011
MI (n)	2 person	1 person	2 person	-
CABG (n)	4 person	4 person	6 person	-
PCI (n)	11 person	12 person	9 person	-

BMI=Body mass index, BSI=Body surface index, METs=Metabolic Equivalents, MI = Myocardial Infarction, CABG = Coronary Artery Bypass Grafting, PCI = Percutaneous Coronary Intervention

Karvonen heart rate formula is as follows:

$$THR = RHR + [(\text{Percentage of desired intensity}) \times (MHR - RHR)]$$

Each exercise session included warm-up, main exercise training, and cooling down phase in the end.

A. Warm-up: It included walking and light cycling to gradually increase the heart rate in two 5-minute steps, and stretching activity including stretching upper and lower body muscles. Each stretching exercise was performed for 10 to 15 seconds.

B. Main exercise training: Main exercise training was performed with the aim of maintaining the heart rate for 20 to 40 minutes. Aerobic exercise consisted of working on leg ergometer, hand ergometer, and treadmill with intensity of 50-80% of the maximum heart rate. As the physical fitness was improved, exercise training time was increased (one minute per session) and its intensity was also increased approximately 4% of the maximum heart rate each week (the duration of the first exercise session was 20 minutes). Heart rate, blood pressure, and possible electrocardiogram changes were monitored during each exercise training session.

C. Cool down: It included stretching exercises aimed to gradually reduce the heart rate and return body to a resting state. Stretching exercises of cooling down phase were completed within 10 minutes.

After completing eight weeks of cardiac rehabilitation program, participants underwent blood tests similar to the pre-test. Considering the nature of hemorheologic variables (fibrinogen, hematocrit, and ESR), any reduction in these variables after cardiac rehabilitation period was considered as an improvement.

Descriptive analysis was performed using mean and standard deviation. Shapiro-Wilk test was used to check the normal distribution of data. Levene's test was used to determine the homogeneity of variance of groups. One-way ANOVA and Tukey's test were performed for intra- and inter-group comparisons, respectively. P-value<0.05 was considered as level of significance. All statistical studies were performed using SPSS ver. 23.

Results

Mean and standard deviation of demographic and clinical characteristics of patients are presented in Table 1. It is noteworthy that none of the patients in the experimental and control groups had a recurrent cardiac event during the study period. Shapiro-Wilk test showed that all measured variables had a normal distribution.

Mean and standard deviation of variables, effect size of exercise intervention, and significant level of changes in pre- and post-test and inter-group differences are presented in Tables 2 and 3. The results of blood rheological indices in the variables of fibrinogen, hematocrit, and ESR showed a significant decrease between pre-test and post-test, respectively ($P<0.05$). Moreover, reduction in these three variables was significant in aerobic-resistance exercise group compared to aerobic exercise training group ($P<0.05$).

The findings of the present study showed a significant reduction in plasma fibrinogen levels after aerobic and aerobic-resistance exercises in CAD patients ($P<0.05$). The results also indicated a significant reduction in fibrinogen level in the aerobic exercise training group (-15.765±4.657) and the aerobic-resistance group (-20.588±6.246). These changes were significant in both experimental groups compared to control group ($P<0.05$). Results also revealed a more significant reduction in fibrinogen levels in the aerobic-resistance exercise group compared to the aerobic group (P<0.05), which confirmed the superiority of aerobic-resistance exercises over aerobic exercises as the findings of present study.

The results of the present study also indicated that both aerobic and aerobic-resistance exercises significantly reduced hematocrit level ($P<0.05$). A significant reduction in blood hematocrit was found in aerobic exercise group (-4.484±0.534) and aerobic-resistance exercise group (-4.782±0.666). These changes were significant in both experimental groups compared

Table 2. Intra- and inter-group analysis of variances regarding comparing effectiveness of aerobic and aerobic-resistance exercise on rheological indices of patients before and after attending cardiac rehabilitation program

Selected Variable	Test	Groups	Mean (SD)	Sum of Squares	mean squares	F	Sig.
Fibrinogen (mg/dl)	Before	Aerobic	276.12 (52.38)	4703.569	2351.784	0.682	0.510
		Aerobic-Resistance	296.41 (58.82)	165450.941	3446.895		
		Control	278.76 (64.32)	170154.510			
	After	Aerobic	258.35 (48.41)	4416.745	2208.373	94.904	0.001*
		Aerobic-Resistance	275.82 (53.30)	1115.882	23.270		
		Control	279.88 (62.54)	5533.686			
Hematocrit (%)	Before	Aerobic	44.19 (5.50)	69.391	34.695	0.895	0.415
		Aerobic-Resistance	46.33 (6.83	1861.149	38.774		
		Control	43.62 (6.28)	1930.540			
	After	Aerobic	39.71 (7.23)	329.777	164.888	6.992	0.002*
		Aerobic-Resistance	41.55 (4.73)	1131.885	23.581		
		Control	44.37 (6.08)	1461.662			
ESR(mm/h)	Before	Aerobic	8.47 (3.34)	4.039	2.020	0.187	0.830
		Aerobic-Resistance	9.00 (3.61)	518.118	10.794		
		Control	8.35 (2.87)	522.157			
	After	Aerobic	6.41 (2.35)	198.471	99.23	59.545	0.001*
		Aerobic-Resistance	5.77 (2.22)	80.118	1.66		
		Control	9.76 (2.03)	278.588			

** Significant difference (P≤0.05)*

Table 3. Tukey or Games-Howell post-hoc tests for selected hemorrhagic variables

Selected Variable	Post-Hoc Analysis	Test	Group (I)	Group (J)	Mean difference (I-J)	Sig.
Fibrinogen (mg/dL)	Games-Howell	Pre	Control	Aerobic	4.647	0.971
			Control	Aerobic-Resistance	-17.647	0.658
			Aerobic	Aerobic-Resistance	-22.294	0.514
	Tukey	Post	Control	Aerobic	16.88	0.001*
			Control	Aerobic-Resistance	21.70	0.001*
			Aerobic	Aerobic-Resistance	4.82	0.015*
Hematocrit (%)	Games-Howell	Pre	Control	Aerobic	-0.57647	0.961
			Control	Aerobic-Resistance	-2.71176	0.419
			Aerobic	Aerobic-Resistance	-2.13529	0.581
	Tukey	Post	Control	Aerobic	5.24	0.029*
			Control	Aerobic-Resistance	5.53	0.001*
			Aerobic	Aerobic-Resistance	0.29	0.989
ESR (mm/h)	Games-Howell	Pre	Control	Aerobic	-0.11765	0.994
			Control	Aerobic-Resistance	-0.64706	0.834
			Aerobic	Aerobic-Resistance	-0.52941	0.886
	Tukey	Post	Control	Aerobic	3.47	0.001*
			Control	Aerobic-Resistance	4.67	0.001*
			Aerobic	Aerobic-Resistance	1.17	0.028*

** Significant difference (P≤0.05).*

to control group ($P<0.05$). Findings also revealed a more significant reduction in hematocrit levels in aerobic-resistance exercise training group compared to the aerobic group ($P<0.05$), which confirmed the superiority of aerobic-resistance exercise over aerobic exercise in the present study.

The results of the present study also indicated that both aerobic and aerobic-resistance exercises significantly reduced ESR level ($P<0.05$). A significant reduction in blood ESR was found in the aerobic exercise group (-2.059±1.345) and the aerobic-resistance exercise group (-3.235±1.522). These changes were significant in both experimental groups compared to the control group ($P<0.05$). Findings also revealed a more significant reduction in ESR levels in the aerobic-resistance exercise group compared to the aerobic group ($P<0.05$), which confirmed the superiority of aerobic-resistance exercises over aerobic exercises in the present study.

Discussion

The aim of present study was to evaluate the effectiveness of eight-week cardiac rehabilitation exercise including aerobic and aerobic-resistance exercise training on rheological variables in middle-aged male patients with CAD. Overall, the findings demonstrated that cardiac rehabilitation exercises had a positive effect on rheological blood variables among these patients.

Research findings indicated the effectiveness of aerobic and aerobic-resistance exercises with significant reduction of plasma fibrinogen levels after eight weeks of cardiac rehabilitation exercises in patients with CAD. Increased circulating plasma fibrinogen levels have been considered as a risk factor for cardiovascular diseases (24). Epidemiological studies have reported a high correlation between the plasma viscosity and the fibrinogen concentration (25, 26). Studies have also shown that increasing circulating plasma fibrinogen levels, thereby increasing blood viscosity, is strongly associated with increased risk of CAD (11, 24, 27). Decreased fibrinogen level, which is due to a direct effect of exercises on blood viscosity, can improve abnormal hemorheologic blood parameters and also reduce risk of cardiovascular diseases. This effect is probably due to direct effects of exercise training on blood viscosity. Therefore, it can be said that this variable can positively react to exercise and reduce blood viscosity (28-35). In other studies, Pabsiak et al. (22), Lee et al. (29), and Sweetnam et al. (30) reported a decrease in the fibrinogen concentration following completion of cardiac rehabilitation program. They also observed beneficial changes in the blood rheology and the blood content following cardiac rehabilitation program. They showed that the greatest decrease in fibrinogen level was in the aerobic exercise group compared to the aerobic-resistance exercise group. The results of the present study demonstrated that cardiac rehabilitation exercises reduced the blood fibrinogen concentration of patients, which could lead to beneficial changes in blood content and blood rheology of patients.

These findings also indicated the effectiveness of aerobic and aerobic-resistance exercises with significant reduction of blood hematocrit in CAD patients after eight weeks of cardiac rehabilitation exercise training. Hematocrit, as one of the important factors in changing blood viscosity, has a direct and strong relationship with occurring coronary heart diseases (11). Normally, the blood viscosity does not affect blood flow, but since the critical shear stress threshold for the onset of blood flow (yield shear stress) depends on the hematocrit level, when the hematocrit increases, it increases the blood viscosity. In this case, the blood flow decreases (27). Instead, a decrease in hematocrit concentration may cause an increase in the blood flow (27). Improvement in capillary circulation and blood rheology, decreased hematocrit, decreased blood and plasma viscosity, and increased red blood cell transport efficiency are observed in cardiovascular patients after cardiac rehabilitation. In addition, these improvements may contribute to increased functional capacity and reduced mortality and incidence rate, which depend on participating in cardiac rehabilitation exercise programs (18, 22). In other studies, Pabsiak et al. (22), Sandor et al. (31), Adachi et al. (24), and Sweetnam et al. (30) reported decreased blood hematocrit levels and reduced risk of cardiovascular diseases following patients' participation in cardiac rehabilitation exercises. However, the results of the present study were not consistent with findings of some studies by Najarian et al. (27), Brun et al. (32), Church et al. (18), and Adachi et al. (24).

The results of the present study indicated that hemorheologic parameters such as hematocrit positively react to exercise and we observed an improvement in the abnormal rheological blood parameters. Besides, considering the effect of exercises on blood hematocrit, we could observe a decrease in plasma viscosity, an increase in the red blood cells transport efficiency, and finally an increase in blood flow after these exercises.

Findings of the present study showed the effectiveness of aerobic and aerobic-resistance exercises in significantly reducing ESR after eight weeks of cardiac rehabilitation exercises in patients with CAD. Besides, the results of previous researches showed that erythrocyte aggregation positively reacted to exercise that may improve abnormal hemorheologic blood parameters (18, 29, 33, 36, 37). In sum, cardiac rehabilitation could lead to a decrease in the erythrocyte aggregation index and, as a result, a reduction in the risk of thrombogenesis, which in turn led to an improvement in the capillary circulation (22). Aerobic exercise essentially reduces erythrocyte aggregation and increases erythrocyte filtration capacity (10, 18). In other studies, Gwoździński *et al.* (34), Pabisiak *et al.* (22), Sandor *et al.* (31), Church *et al.* (18), and Ernest & Matray reported a reduction in ESR to the normal level after participating in a moderate-intensity cardiac rehabilitation program (18, 22, 34, 37, 38). Sandor *et al.* (31) and Narouki (38) also reported a decrease in blood viscosity after participating in rehabilitation exercises. Yalsin *et al.* (2) also claimed that, following one session of intense anaerobic exercise, hemorheologic parameters such as erythrocyte aggregation and erythrocyte deformability were significantly impaired immediately after exercise, and persisted for some time. Therefore, these changes should be considered in people with cardiovascular disorders. The present study concluded that cardiac rehabilitation program had beneficial changes in blood rheology and erythrocyte aggregation of heart patients. There was also an improvement in erythrocyte aggregation index, a decrease in ESR, a decrease in blood viscosity and, as a result, an increase in blood flow. In addition, a reduced ESR can decrease the risk of thrombosis.

Consistent with the present study, results of a number of previous studies have shown that hemorheologic variables positively reacted to exercise and these exercises improved hemorheologic profile by reducing total viscosity of blood and plasma, hematocrit, and fibrinogen level. Cardiac rehabilitation exercises also increased the effective red blood cells transport in CAD patients (18, 22, 38). Cardiac rehabilitation aims to limit progression of atherosclerosis, improves physical fitness, helps patients return to their normal life, relieves or reduces activity-related symptoms, improves patients' psychosocial status, prevents recurrent cardiac events, and reduces disability and mortality due to cardiovascular diseases (1, 39). According to previous studies, it seems that combined exercises (aerobic-resistance) are more effective than only resistance or aerobic exercises on reducing cardiovascular risk factors. In addition, increasing intensity of exercise, while improving the blood rheology, significantly reduced the onset of cardiovascular disease and subsequent mortality (40, 41).

There are some limitations for our study such as the subjects' sex studied only among male patients, small sample size, and short period of time constraints. Therefore, it is suggested that researchers apply the protocol used in the present study for both middle-aged and elderly men and women suffering from various coronary artery diseases and for longer periods of time in future studies.

Conclusion

According to results of the present study, eight weeks of cardiac rehabilitation program (aerobic and aerobic-resistance exercises) can be recommended for improving rheological variables, including fibrinogen concentration, platelet concentration, and red blood cells sedimentation, in middle-aged men with CAD. However, the aerobic-resistance exercise was superior to the aerobic exercise.

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References

1. Hinkle JL, KH C. Brunner and Suddarth's Textbook of Medical-Surgical Nursing. 14 ed: Lippincott Williams & Wilkins; 2017.
2. Yalcin O, Erman A, Muratli S, Bor-Kucukatay M, Baskurt OK. Time course of hemorheological alterations after heavy anaerobic exercise in untrained human subjects. Journal of Applied Physiology. 2003;94(3):997-1002.
3. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. Jama. 1998;279(18):1477-82.
4. Kensey KR. The mechanistic relationships between hemorheological characteristics and cardiovascular disease. Current medical research and opinion. 2003;19(7):587-96.
5. Ricci I, Sofi F, Liotta AA, Fedi S, Macchi C, Pratesi G, et al. Alterations of haemorheological parameters in patients with peripheral arterial disease. Clinical hemorheology and microcirculation. 2013;55(2):271-6.
6. Anderson L, Sharp GA, Norton RJ, Dalal H, Dean SG, Jolly K, et al. Home-based versus centre-based cardiac rehabilitation. Cochrane database of systematic reviews. 2017(6).
7. Risom SS, Zwisler AD, Johansen PP, Sibilitz KL, Lindschou J, Gluud C, et al. Exercise-based cardiac rehabilitation for adults with atrial fibrillation. Cochrane Database of Systematic Reviews. 2017(2).
8. Razaghi A, Sadeghi H. Effect of Exercise-based Cardiac Rehabilitation on Coronary Artery Biomechanical Variables in Atherosclerotic Patients: A Systematic Review Study. 2020.
9. Késmárky G, Kenyeres P, Rábai M, Tóth K. Plasma viscosity: a forgotten variable. Clinical hemorheology and microcirculation. 2008;39(1–4):243-6.
10. Connes P, Simmonds MJ, Brun J-F, Baskurt OK. Exercise hemorheology: classical data, recent findings and unresolved issues. Clinical hemorheology and microcirculation. 2013;53(1-2):187-99.
11. Jin YZ, Zheng DH, Duan ZY, Lin YZ, Zhang XY, Wang JR, et al. Relationship between hematocrit level and cardiovascular risk factors in a community-based population. Journal of clinical laboratory analysis. 2015;29(4):289-93.
12. Davalos D, Akassoglou K, editors. Fibrinogen as a key regulator of inflammation in disease. Seminars in immunopathology; 2012: Springer.

13. Waite LR. Biofluid mechanics in cardiovascular systems. 2005.
14. Jiang P, Gao Z, Zhao W, Song Y, Tang X-F, Xu J-J, et al. Relationship between fibrinogen levels and cardiovascular events in patients receiving percutaneous coronary intervention: a large single-center study. Chinese medical journal. 2019;132(8):914.
15. Paul L, Jeemon P, Hewitt J, McCallum L, Higgins P, Walters M, et al. Hematocrit predicts long-term mortality in a nonlinear and sex-specific manner in hypertensive adults. Hypertension. 2012;60(3):631-8.
16. Skretteberg PT, Bodegård J, Kjeldsen SE, Erikssen G, Thaulow E, Sandvik L, et al. Interaction between inflammation and blood viscosity predicts cardiovascular mortality. Scandinavian Cardiovascular Journal. 2010;44(2):107-12.
17. Nemeth N, Alexy T, Furka A, Baskurt O, Meiselman H, Furka I, et al. Inter-species differences in hematocrit to blood viscosity ratio. Biorheology. 2009;46(2):155-65.
18. Church TS, Lavie CJ, Milani RV, Kirby GS. Improvements in blood rheology after cardiac rehabilitation and exercise training in patients with coronary heart disease. American heart journal. 2002;143(2):349-55.
19. Yayan J. Erythrocyte sedimentation rate as a marker for coronary heart disease. Vascular health and risk management. 2012;8:219.
20. Erikssen G, Liestøl K, Bjørnholt J, Stormorken H, Thaulow E, Erikssen J. Erythrocyte sedimentation rate: a possible marker of atherosclerosis and a strong predictor of coronary heart disease mortality. European heart journal. 2000;21(19):1614-20.
21. Kohandelanshahrenoei Y, Rashidlamir A, Ebrahimiatri A. Effect of 4 Weeks Circuit Training on Plasma Fibrinogen in Wrestlers. Journal of Rafsanjan University of Medical Sciences. 2014;12(12):1003-14.
22. Pabisiak A, Bromboszcz J, Kmiec S, Dendura M, Dabrowski Z, Smolenski O. Changes in the complete blood count and blood rheology in patients after myocardial infarction participating in the rehabilitation programme. Clinical hemorheology and microcirculation. 2015;61(3):541-7.
23. Karvonen J, Vuorimaa T. Heart rate and exercise intensity during sports activities. Sports medicine. 1988;5(5):303-11.
24. Adachi H, Sakurai S, Tanehata M, Oshima S, Taniguchi K. Effect of long-term exercise training on blood viscosity during endurance exercise at an anaerobic threshold intensity. Japanese circulation journal. 2000;64(11):848-50.
25. Koenig W, Sund M, Filipiak B, Doring A, Lowel H, Ernst E. Plasma viscosity and the risk of coronary heart disease: results from the MONICA-Augsburg Cohort Study, 1984 to 1992. Arteriosclerosis, thrombosis, and vascular biology. 1998;18(5):768-72.
26. Elwood PC, Yarnell J, Pickering J, Fehily AM, O'Brien JR. Exercise, fibrinogen, and other risk factors for ischaemic heart disease. Caerphilly Prospective Heart Disease Study. Heart. 1993;69(2):183-7.
27. Najarian S, Mostashfi H. Introdaction to biomedical engineering. 4 ed: Amirkabir University of Technology Branch; 2020.
28. Ahmadizad S, El-Sayed MS. The acute effects of resistance exercise on the main determinants of blood rheology. Journal of sports sciences. 2005;23(3):243-9.
29. Lee KW, Blann AD, Jolly K, Lip GY. Plasma haemostatic markers, endothelial function and ambulatory blood pressure changes with home versus hospital cardiac rehabilitation: the Birmingham Rehabilitation Uptake Maximisation Study. Heart. 2006;92(12):1732-8.
30. Sweetnam P, Thomas H, Yarnell J, Beswick A, Baker I, Elwood PC. Fibrinogen, viscosity and the 10-year incidence of ischaemic heart disease: The Caerphilly and Speedwell Studies. European heart journal. 1996;17(12):1814-20.
31. Sandor B, Nagy A, Toth A, Rabai M, Mezey B, Csatho A, et al. Effects of moderate aerobic exercise training on hemorheological and laboratory parameters in ischemic heart disease patients. PloS one. 2014;9(10):e110751.
32. Brun J-F, Varlet-Marie E, Connes P, Aloulou I. Hemorheological alterations related to training and overtraining. Biorheology. 2010;47(2):95-115.
33. Levine GN, O'Malley C, Balady GJ. Exercise Training and Bleed Viscosity in Patients With Ischemic Heart Disease. The American journal of cardiology. 1995;76(1-2):80-1.
34. Gwoździński K, Pieniążek A, Czepas J, Brzeszczyńska J, Jegier A, Pawlicki L. Cardiac rehabilitation improves the blood plasma properties of cardiac patients. Experimental Biology and Medicine. 2016;241(17):1997-2006.
35. Ernst E, Matrai A. Intermittent claudication, exercise, and blood rheology. Circulation. 1987;76(5):1110-4.
36. Jia B, Wang X, Kang A, Wang X, Wen Z, Yao W, et al. The effects of long term aerobic exercise on the hemorheology in rats fed with high-fat diet. Clinical hemorheology and microcirculation. 2012;51(2):117-27.
37. Mohammad Najad Panah Kandi Y, MohammadNajad Panah Kandi A, Shahidi F, Masoudian B. The effect of a maximal aerobic exercise session in the morning and afternoon on certain hematological factors in young athletes. Razi Journal of Medical Sciences. 2013;20(106).
38. Velzen MVN-v. The effect of a cardiac rehabiltation exercise program on plasma viscosity, fibrinogen concentration, Hematocrit, blood lipids and exercise capacity: University of British Columbia; 2004.
39. Pfeffer MA, Braunwald E. Ventricular remodeling after myocardial infarction. Experimental observations and clinical implications. Circulation. 1990;81(4):1161-72.
40. Lavie CJ, Thomas RJ, Squires RW, Allison TG, Milani RV, editors. Exercise training and cardiac rehabilitation in primary and secondary prevention of coronary heart disease. Mayo Clinic Proceedings; 2009: Elsevier.
41. Yektayar M, Mohammadi S, Deharshid KA, Khodamoradpour M. Comparison of the effects of resistance, endurance and combined exercises on lipid profile of non-athlete healthy middle aged men. Scientific Journal of Kurdistan University of Medical Sciences. 2011;16(4).