Original Article

The effects of high-intensity interval training on fibrinolytic factors, D-dimer, and fibrinogen in men with type 2 diabetes

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Abstract

Background and Objective: Sudden cardiac events and thrombophilia are dominant diseases in diabetic patients. Due to the role of exercise on the homeostatic system, the effect of high intensity interval training (HIIT) on some fibrinolytic, dimer and fibrinogen factors in men with type 2 diabetes was investigated in this study. Methods: For this purpose, 24 men with type 2 diabetes who were able to participate in regular physical activity were voluntarily selected and randomly divided into two groups of HIIT (n=12) and control (n=12). These two groups were same in terms of weight and body mass index. The experimental group did exercise 8 weeks, 3 sessions per week. Changes in t-PA, TAFI, t-PA/PAI-1 complex, D-dimer and fibrinogen were analyzed before and after training using covariance statistical test at $P<0.05$. Results: Intergroup comparison showed that resting levels of TAFI antigen decreased (P=0.033) and t-PA/PAI-1 complex (P=0.032) increased significantly. Intergroup comparison showed that resting values of t-PA (P=0.036) increased significantly and TAFI (P=0.01), D-dimer (P=0.007) and fibrinogen (P=0.001) showed a significant decrease in the experimental group. Conclusion: It seems that the implementation of HIIT has promising effects on the fibrinolytic system of type 2 diabetic patients and may decrease the cardiovascular risks in this group of patients.

Keywords: High intensity interval training, t-PA, TAFI, t-PA/PAI-1 complex, D-dimer

Introduction

A sedentary life reduces physical activity and performance. The link between physical activity and health has a long history. Therefore, decreased physical activity increases the risk of diseases [1]. Diabetes is the most common metabolic disease in the world and its prevalence increases with increasing age [2]. Insulin resistance in target tissues and chronic hyperglycemia are the most important features of diabetes and its associated complications [3]. Although insulin resistance has not symptom, it is associated with an increased risk of coronary arterial disease (CAD), cardiovascular system dysfunction, and their associated mortality [4]. Diabetes has many complications, one of which is the homeostasis system disorder. Type 2 diabetic patients are more likely than others to have CAD and are also more likely to have atherothrombotic events [5]. CAD is more widespread than any other diseases in the world and has the great life and financial losses. In this disease, the coronary arteries of the heart are narrowed due to plaque formation and the heart muscle is deprived of sufficient blood and oxygen [6]. Some of the inflammatory markers predicting cardiovascular disease include the level of serum fibrinogen, cytokines, CRP, and amyloid A [7]. According to the results of some studies, in addition to the above-mentioned factors, alterations in the fibrinolysis system play a very important role in cardiovascular events [8]. The fibrinolytic system is an important physiological mechanism whose function is to break down fibrin filaments in blood vessels and to remove and destroy the clot [9]. Thus, by activating the coagulation system, the fibrinolysis system is also activated [10]. D-dimer is one of the factors used to diagnose thrombosis [11]. The presence of soluble D-dimer indicates that the thrombin has been formed first, then coagulation has occurred and eventually, the plasmin has been formed and has cut the fibrin clot [12]. t-PA is the first plasminogen activator that acts

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How to cite this article: Rezaeimanesh, D. The effects of high-intensity interval training on fibrinolytic factors, D-dimer, and fibrinogen in men with type 2 diabetes. Arch Pharma Pract 2020;11(S1):154-160.

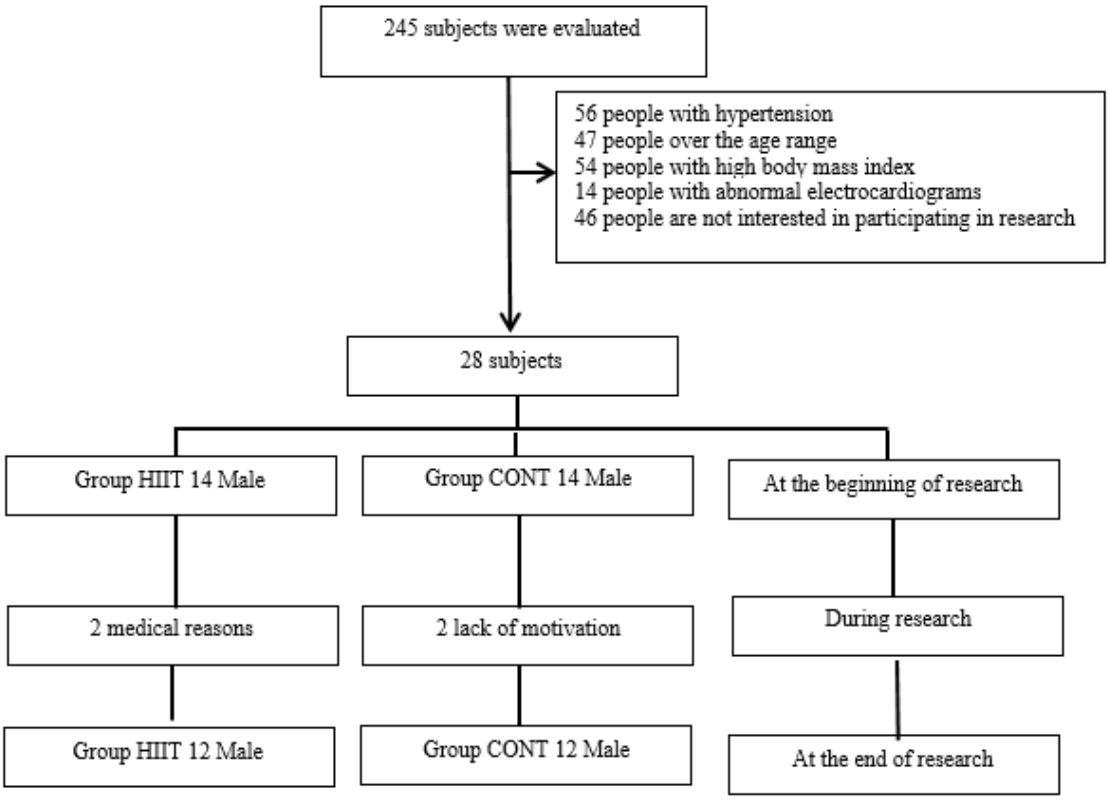
directly and forms the plasmin molecule [10]. The major inhibitor of t-PA is plasminogen activator inhibitor (PAI-1) [13], which is mainly produced by endothelial cells lining the inner wall of blood vessels, but is also secreted from other tissues including fats [14]. The ratio of these two indices is called t-PA/PAI-1 complex, which has received little attention. The t-PA/PAI-1 complex indicates the amount of t-PA activity that is inhibited by PAI-1. As this ratio tends to favor t-PA, the body is actually prone to fibrinolysis [15]. In fact, the capacity of fibrinolysis is shown by t-PA, PAI-1 and t-PA/PAI-1 complex [16]. Some studies show that t-PA activity decreases as PAI-1 concentration increases [17]. Thus, both t-PA and PAI-1, which are released from endothelial cells, along with fibrinogen, play important roles in homeostasis and cardiovascular disease and are stimulated and activated by various factors [18]. Another fibrinolysis inhibitor, which has recently received attention, is thrombin activable fibrinolysis inhibitor (TAFI). Unlike PAI-1, this antigen exerts its inhibitory effect by removing the lysine and arginine heads on the C terminus of the fibrin clot and prevents plasminogen from adhering to the fibrin clot [19]. Thrombin converts TAFI it into activated form of TAFIa by stimulating it. On the other hand, plasmin also activates TAFI, so TAFI appears to play a key role in regulating the balance between fibrinolytic system and coagulation [20]. Elevated plasma levels of TAFI antigen have been reported in CAD and diabetic patients compared to healthy individuals [21].

The results of some research indicate that the activity of the fibrinolysis system increases with the intensity of exercise [22]. This appears to be due to an increase in plasminogen activators as the intensity of activity increases and products of fibrin degradation increase during intense exercise [14]. According to previous research, acute and vigorous activity increases fibrinolytic potential by increasing catecholamine secretion and decreasing hepatic blood flow [23]. In most studies, the intensity of exercise activity has been a major offecting factor on the activity of the fibrinolysis system. Exercise training plays an important role in improving cardiovascular complications in type 2 diabetes patients. In general, the beneficial effects of exercise training on diabetes are related to glycemic control and various cardiovascular risk factors. This is especially important in diabetic patients with elevated platelet activity [24].

One of the physical activity protocols that has recently attracted attention of researchers in the field of various physical adaptations is High Intensity Intermittent Exercise (HIIT). Implementation of HIIT involves intermittences of intense exercise and active to moderate intensity breaks [25]. Previous studies have shown that HIIT has led to similar metabolic adaptation comparing to traditional endurance training in adults [26]. Therefore, due to the high potential of this exercise method in fat reduction and its efficiency in terms of time interval compared to other exercise methods, this protocol was used. Whether this exercise has a positive effect on fibrinolytic, D-dimer and fibrinogen indices in diabetic subjects has not been investigated. Therefore, the aim of this study was to investigate the effect of 8 weeks of HIIT on some fibrinolytic, D-dimer and fibrinogen factors in men with type 2 diabetes.

Research Method

The research method was quasi-experimental research involves pretest-posttest design and control group. Subjects were selected voluntary and purposeful among the male patients with type 2 diabetes aged 30-40 years referred to the clinic. The objectives and conditions of the study were explained to the volunteers and consent form given to them, if they agreed. Finally, they referred to a specialist physician for permission to participate in the research. 24 men with type 2 diabetes who were able to participate in regular exercise programs were selected based on inclusion criteria and were randomly divided into two groups of training (n=12) and control (n=12). The training group performed HIIT for 8 weeks and three sessions per week. However, the subjects in the control group continued their sedentary lifestyle during the study period. Inclusion criteria included type 2 diabetes defined as 126 mg/dl by the American Diabetes Association (2015), no complications of diabetes, no specific disease such as heart, kidney, liver or metabolic disease, no participation in regular exercise for more than 2 hours per week over the past 6 months, no blood pressure above 140/90 mm Hg, diabetes for at least 2 years, no consumption of more than one type of anti-diabetic pill at night, and no consumption of insulin. These criteria were assessed through PAR-Q demographic questionnaire, health and physical activity questionnaire and medical history questionnaire. All coordination in terms of medical ethics and supervision was done by diabetes specialist and patients were informed.



Research Flodiogram

High-intensity interval training (HIIT)

After a week of preparation and familiarity with the protocol implementation method, the participants performed their training programs, including Shuttle Run Test for a distance of 20 m, shown by 3 cones, for 8 weeks in training hall at a temperature of 26 °C during fall according to the following procedure. After warming up, including 10 min of jogging and 5 min of active stretching exercise, the participants ran from the starting point (cone 1) towards the cone 2 (path 1) with a maximum speed, and then returned and ran in the inverse direction towards the cone 3 (path B) with a maximum speed of 20 m. Finally, they re-returned, and ran towards the starting point (cone 1) with a maximum speed (path C) to complete the 40-m distance. The participants continued the trend with a maximum speed and completed a 30-second period of training protocol, and repeated the training protocol after 30 seconds of rest. The training was progressed by increasing frequency of 30-second repetition from 4 times in the first and second weeks to five times in the third to fourth weeks, six times in fifth and sixth weeks, and eight times in the seventh and eighth weeks. The training intensity was measured for all participants at all protocol stages, over a Heart Rate Maximum (HRmax) of 90% using a formula of HRmax= 220-age, and it was controlled by a heart rate monitor, made in Finland. The training program was derived from a 40-m Shuttle Run Test with a maximum speed as it was a valid test for evaluating the anaerobic performance [15]. At the end of each training session, the participants walked and did stretching training and exercise for cooling down during 10 minutes.

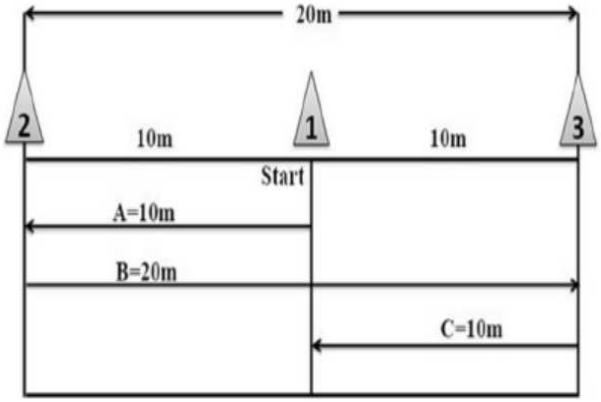


Figure 1. Schematic diagram of HIIT protocol

Blood sampling

In order to determine the levels of the research variables, all subjects were present in the laboratory between 8am and 10am before the start of the training program and 12 hours fasting (according to the physician recommendation). After 30 minutes rest in sitting position, 10-ml blood samples were taken from the brachial vein of individuals. The training group then participated in the exercise protocol. The control group did not participate in any regular exercise program

during the study. 48 hours after the last training session, all subjects participated in blood sampling under condition similar to pretest condition to avoid the possible acute effect (posttest phase). Variables were measured in both training and control groups simultaneously. At each phase, blood samples were immediately poured into EDTA-containing tubes. After centrifugation for 10 min at 3000 rpm, the blood plasma was isolated and poured in special microtubes and frozen at -80 °C until the evaluation day.

Plasma levels of t-PA were measured by enzyme linked immunosorbent assay (ELISA) method and kits with accuracy of 10 pg/ml (Boster Company, USA). Plasma levels of TAFI and t-PA/PAI-1 complex were measured by ELISA using Mybiosource kits (USA). D-dimer was measured by Coagulometry using the French BIOMERIEUX kit. Mahsa Yaran kit was used for quantitative determination of fibrinogen by coagulometry method.

Statistical method

Shapiro-Wilk test was used to determine the normality of the data distribution. After making sure the data is natural, analysis of covariance (ANCOVA) and paired t-test at P <0.05 were used to compare averages of variables between groups with respect to homogeneity of slopes. Data were analyzed using SPSS 23 software.

Findings

The results of the general characteristics of the subjects have been presented in Table (1). After 8 weeks of exercise, weight (P=0.001) and BMI (P=0.015) decreased significantly in the periodic group.

Table 1. general characteristics of the subjects.

Variables	Group	Post-test Mean and SD	Pre-test Mean and SD	P In-group
age	HIIT	35.1±4.1	35.1±4.1	-
	control	34.7±5.5	34.7±5.5	-
High (cm)	HIIT	178±6.7	178±6.7	-
	control	176±6.2	176±6.2	-
Weight (kg)	HIIT	80±6.4	77.6±5.4	0.001*
	control	80±4.1	79.5±3.6	0.212
BMI (kg/m^2)	HIIT	25.1±3.4	24.4±2.5	0.015*
	control	25.6±2.6	25.3±2.8	0.247

*In-group Statistical significance

Statistical analysis of data showed that after 8 weeks of HIIT, there was a significant difference between the two groups at resting levels of TAFI antigen (P=0.033, $F_{1,21}$=5.19), (Fig.2) and t-PA/PAI-1 complex (P=0.032, $F_{1,21}$=5.3), (Fig.3). However, after 8 weeks of HIIT, there was not a significant difference in the levels of t-PA antigen (P=0.054, $F_{1,21}$=4.15), D-dimer (P= 0.081, $F_{1,21}$=3.35) and fibrinogen (P=0.074, $F_{1,21}$=3.54). Table (2).

Table 2. Investigation of inter- and intra-group changes in variables in two groups, HIITand Control groups

Variables	Group	Pre-test Mean and SD	Post-test Mean and SD	In-group t	In-group P	Intergroup F	Intergroup P
t-PA (ng/ml)	HIIT	12.2±2.3	14.7±4.4	2.38	*0.036	**4.14**	**0.054**
	control	12.9±3.1	13.1±2.6	0.89	0.39		
TAFI (ng/ml)	HIIT	11.9±3.1	10.6±2.5	3.08	*0.01	**5.19**	**¥0.033**
	control	11.3±2.7	11.1±2.6	0.82	0.42		
t-PA/PAI-1(ng/ml)	HIIT	11.5±3.1	12.9±2.9	2.02	0.068	**5.3**	**¥0.032**
	control	11.1±3.2	11±2.9	0.33	0.74		
D-dimer (ng/ml)	HIIT	192±40	183±37	3.26	*0.007	**3.35**	**0.081**
	control	195±37	193±36	0.56	0.52		
Fibrinogen (mg/dl)	HIIT	219±32	205±35	4.63	*0.001	**3.54**	**0.074**
	control	218±34	212±37	2.05	0.065		

*In-group Statistical significance; ¥ intergroup Statistical significance

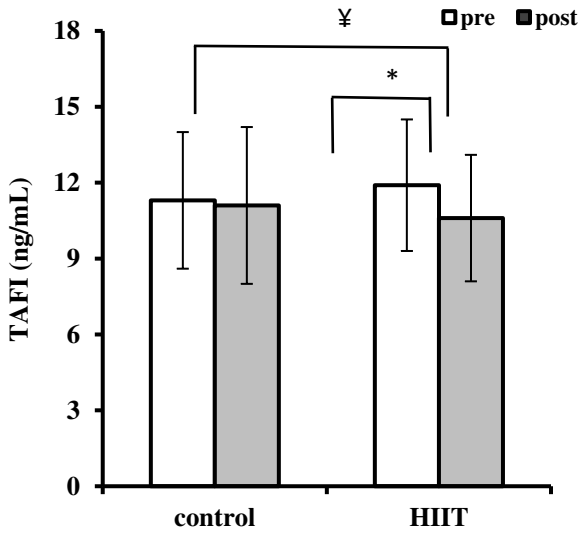


Figure 2. Mean (±Standard error) of TAFI before and after training in control and HIIT groups. *In-group Statistical significance; ¥ intergroup Statistical significance.

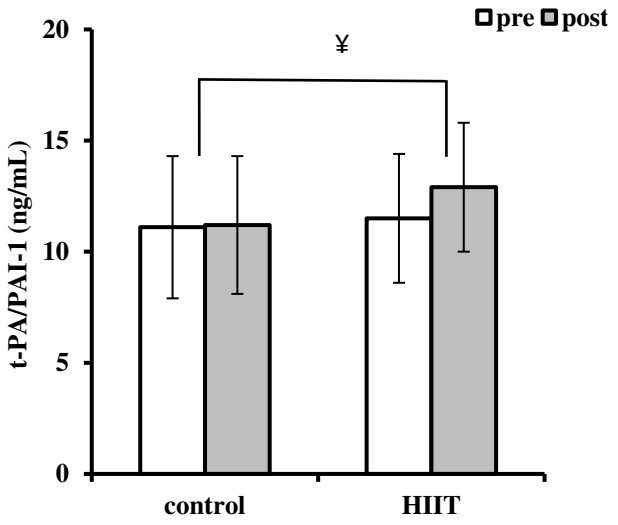


Figure 3. Mean (±Standard error) of t-PA/PAI-1 before and after training in control and HIIT groups. *In-group Statistical significance; ¥ intergroup Statistical significance.

Discussion

Performing regular exercise by modulating homeostasis is effective on the occurrence of prothrombotic events [22]. There is little research on the impact of HIIT on human fibrinolytic markers and this research is one of the first studies to investigate the simultaneous effect of HIIT on fibrinolytic and coagulation indices in patients with diabetes. The results showed that resting levels of TAFI antigen decreased and t-PA/PAI-1 complex increased after training intervention, but there was no significant difference in other variables. The results also showed that resting levels of t-PA increased significantly in the experimental group and resting values of TAFI, D-dimer and fibrinogen decreased significantly.

According to the findings of this study, the level of TAFI antigen decreased after intense intermittent exercise. There is not much research on the effect of exercise on TAFI antigen. Rajabi et al. investigated the effects of intermittent and continuous exercise on fibrinolytic agents such as TAFI in CAD patients and, contrary to the results of this study, they did not report any significant change in levels of TAFI antigen in the subjects [19]. This difference is probably due to the subjects and the intensity of the exercises used in this study. The results of past research indicate that the effect of training intensity is greater than the duration of training [19]. Certainly, the reduction of TAFI in the present study is a desirable adaptation to function the power of the fibrinolytic system in diabetic patients and in this regard, intense intermittent exercise are appropriate for diabetic patients. These results were consistent with results of [27, 28] but not with results of [19]. The mechanism of the effect of exercise intensity on changes of TAFI antigen and its precise mechanisms are unclear and need to be studied. Results of some studies show that adaptation to intermittent exercise decreases blood coagulation activity [22], decreases plasma levels of thrombin, fibrin and fibrinogen [22, 29, 30]. TAFI activator thrombin, TAFI junction fibrin and fibrinogen are precursor of fibrin. Changes in the coagulation system, especially thrombin depletion, may reduce TAFI secretion from the liver and increase the function of the fibrinolytic system in diabetic patients by reducing TAFI. Results of earlier research indicate that regular exercise provides the context for faster fibrinolytic activity comparing to thrombotic activity with increases in t-PA and t-PA/PAI-1 complex [22, 31]. Studies have shown that the effects of physical activity on different fibrinolysis and some inconsistencies depend to some extent on the protocol and method used to measure fibrinolysis indices, fitness, or health status of the subjects. Therefore, there are limitations to summarize the results of various studies. For example, some of these studies showed that exercise using different protocols had no significant effect on plasma level of t-PA [32], but other researchers reported an increase [12, 16, 22] or a significant decrease [7]. Based on the results of the present study, it can be concluded that the eight-week implementation of HIIT led to a relative improvement in fibrinolysis process under the break condition. Jong-Syhan Wang also found that long-term exercise had a favorable effect on fibrinolytic indices, but lack of training had a revers effect on the changes of intensity of these factors [33]. An increase in t-PA levels in response to regular exercise is directly related to the intensity and duration of exercise [22, 32]. Factors include improved liver clearance, t-PA/PAI-1 complex binding, increased endothelial susceptibility to t-PA secretion and reduced levels of PAI-1 are major factors of the effect of exercise on the function of the fibrinolysis system [9, 22, 34]. The higher intensity of the exercise results in more effectiveness of it [19]. Research shows that there is no significant increase in fibrinolysis activity until the heart rate reaches 50% of maximal oxygen consumption, and some researchers believe that the greatest increase is when the intensity is between 70% and 90% of heart rate [34]. Therefore, with respect to the training program of the present study, it is quite clear that the high intensity of exercises of HIIT implemented over eight weeks is probably one of the main reasons for the increase in fibrinolysis system performance. Increases in nitric oxide (NO) and prostacyclin (PGI_2) have been observed following prolonged activity [35]. Nitric oxide via vasodilatation increases production of t-PA and its release from endothelial cells and decreases PAI-1 production by vascular smooth muscle cells and platelets [36]. Therefore, given the intensity and volume of exercises of HIIT, it is likely that an increase in the resting levels of t-PA and a decrease in the amount of TAFI in the experimental group caused by an increase in NO and PGI_2 following exercise intervention.

Results showed a significant increase in resting values of t-PA/PAI-1 complex. Various researchers have reported that fibrinolytic markers such as t-PA and t-PA/PAI-1 complex may play a role in reducing atherothrombotic and cardiovascular diseases by modifying thrombotic markers [12,

[22, 31]. In this case, Bounameaux and Kruithof reported a strong relation between the t-PA/PAI-1 complex and activity of the t-PA and PAI-1 antigens, and they noted that negative changes in this complex were directly related to the increased risk of myocardial infarction and they related these changes to mechanisms such as increased endothelial cell activation and inflammation [37]. Therefore, it seems that performing moderate to high intensity aerobic exercises is a simple, healthy and practical strategy that can be used by individuals, especially patients with hemostatic disorders. High levels of t-PA antigen and t-PA/PAI-1 complex have also been suggested for individuals susceptible to atherosclerosis and cardiovascular events [38].

Resting levels of fibrinogen in the experimental group showed a significant decrease after eight weeks of HIIT without correction of plasma volume changes. Researchers have proposed different mechanisms as influencing factors for changes in plasma fibrinogen concentrations, including increases in neurotransmitters and catecholamines such as epinephrine and norepinephrine [39], changes in fibrinolytic system activity, decreased fibrinogen production by liver [22], plasma volume changes, lipid profile and BMI [40]. Eight weeks of HIIT may reduce and control this factor by reducing the activity of cytokines and reducing fibrinogen synthesis in the liver cells due to adaptation in the musculoskeletal system. Given the role of fibrinogen in platelet adhesion and aggregation [22], the positive effect of periodic exercise on these factors reduces the risk of thrombosis. Many researchers have studied the relationship between physical activity and fibrinogen levels in men and women [41, 42] and in line with the results of this study, an inverse relationship between this variable and cardiopulmonary fitness have been reported [43]. The reason for this is related to control of the production of hepatic glycoproteins after physical activity [44].

Conclusion

Based on the results of the present study, it can be said that the eight-weeks HIIT implementation leads to a relative improvement in the fibrinolysis and homeostasis process with favorable changes in some fibrinolytic markers such as t-PA, TAFI and t-PA/PAI-1 complex. In addition, intensity of exercise is probably one of the most important factors in improving the fibrinolysis process. As a result, HIIT training seems to be a time-efficient factor in preventing and improving cardiovascular risk factors in type 2 diabetic patients. Therefore, the results of the present study confirm once again the role of regular activity in reducing cardiovascular events.

Acknowledgment

This article is subtracted from the results of the executed research project under Contract No. 171 dated 2019/11/17 from the research credits of Khorramshahr University of Marine Science and Technology.

References

1. Kumar A, Kar S, Fay WP. Thrombosis, physical activity, and acute coronary syndromes. J Appl Physiol 2011; 111(2):599-605.
2. Rayalam S, Della-Fera MA, Krieg PA, Cox CM, Robins A, and Baile CA. A putative role for apelin in the etiology of obesity. Biochem Biophys Res Commun 2008; 368:815-9.
3. Snowling NJ and Hopkins WG. Effects of Different Modes of Exercise Training on Glucose. Control and Risk Factors for Complications in Type 2 Diabetic Patients. Diabetes Care 2006; 29: 2518–2527.
4. Ingelsson E, Arnlov J, Lind L, Sundstrom J. Metabolic syndrome and risk for heart failure in middle-aged men. Heart 2006; 92:1409-13.
5. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA 2002; 287:2570-2581.
6. Katritsis DG, Ioannidis JP. Percutaneous coronary intervention versus conservative therapy in nonacute coronary artery disease: a meta-analysis. Circulation 2005;111(22):2906-12.
7. Hegde SS, Goldfarb AH, Hegde S. Clotting and fibrinolytic activity change during the 1 h after a submaximal run. Med Sci Sports Exerc.2011; 33(6):887-92.
8. Thompson PD. Exercise prescription and proscription for patients with coronary artery disease. Circulation. 2005; 112: 2354-63.
9. El-Sayed MS, El-Sayed Ali Z, Ahmadizad S. Exercise and training effects on blood haemostasis in health and disease: an update. Sports Med. 2004; 34(3):181-200.
10. Nascimento Dda C, Neto FR, de Santana FS, da Silva RA, Dos Santos-Neto L, Balsamo S. The interactions between hemostasis and resistance training: a review. Int J Gen Med. 2012; 5:249-54.
11. DeSouza CA, Jones PP, Seals DR. Physical activity status and adverse age-related differences in coagulation and fibrinolytic factors in women. Arterioscler Thromb Vasc Biol. 1998; 18(3):362-8.
12. Rezaeimanesh, D. and Amiri Farsani, P. 2018. The effect of eight weeks of aquatic exercise on fibrinolytic (t-PA, PAI-1, t-PA/PAI-1 complex and D-dimer) indexes in retired athletes. Journal of Marine Science and Technology, doi: 10.22113/jmst.2017.45297. [Full Text in Persian].
13. O'Keefe JH, Patil HR, Lavie CJ, Magalski A, Vogel RA, McCullough PA. Potential adverse cardiovascular effects from excessive endurance exercise. Mayo Clin Proc. 2012; 87(6):587-95.
14. Lip GY, Blann AD. Thrombogenesis and fibrinolysis in acute coronary syndromes. Important facets of a prothrombotic or hypercoagulable state?. J Am Coll Cardiol. 2000; 36(7):2044-6.
15. Ueshima S, Matsuo O. Development of new fibrinolytic agents. Current pharmaceutical Design. 2006; 12 (7):849-57.
16. Chandler W.L, M.C.Alessi, M.F.Aillaud, P.Henderson, MS;P.Vague; I.Juhan-Vague. "Clearance of tissue plaminogen activator (TPA) and TPA/Plasminogen activator inhibitor type 1(PAI-1) complex", Circulation. 1997; 96: PP: 761-768.
17. Oliver J,webb D. Stimulated tissue plasminogen activator release as a marker of endothelial function in humans. Arteriosclerosis,Thrombosis, and vascular Biology. 2005; 25(12)2470.
18. Ribeiro J, Almeida-Dias A, Ascensao A, Magalhaes J, Oliveira A, Carlson J, et al. Hemostatic response to acute physical exercise in healthy adolescents. Journal of Science and Medicine in sport. 2007; 10(3):164-9.
19. Rajabi H, Khedmatgozar E, Dastmalchi J, Dehkhoda MR. Comparison of High-Intensity Interval and Continuous Training Effects on Plasma Levels of Fibrinolytic Factors in CAD Patients. Jundishapur Sci Med J 2019; 18(3):287-300. [Full Text in Persian].
20. Verkleij CJ, Nieuwdorp M, Gerdes VE, Mörgelin M, Meijers JC, Marx PF. The effects of hyperglycaemia on thrombin-activatable fibrinolysis inhibitor. Thrombosis and haemostasis 2009;102(09):460-8.
21. Franco RF, Fagundes MG, Meijers J, Reitsma PH, Lourenço D, Morelli V, et al. Identification of polymorphisms in the 5'-untranslated region of the TAFI gene: relationship with plasma TAFI levels and risk of venous thrombosis. haematologica 2001;86(5):510-7.

22. Rezaeimanesh D, Ahmadizad S, Ebrahim Kh. The effect of one season of preparation and competition on some factors of fibrinolysis, D-dimer, and CRP in professional athletes. Qom Univ Med Sci J 2017;11(9):32-41. [Full Text in Persian].
23. Ahmadizad S, EL-Sayed M. The Effects of Graded Resistance Exercison on Platelet Aggregation and Activation. Med Sci Sports Exerc. 2003; 35(6):1026-32.
24. De Meirelles L, Mendes-Ribeiro A, Mendes M, Da Silva M, John Clive Ellory J, Mann G, et al. Chronic exercise reduces platelet activation in hypertension: upregulation of the l-arginine-nitric oxide pathway. Scand J Med Sci Sports 2009; 19:67-74.
25. Gibala, M. J., & Ballantyne, C. High-intensity interval training: New insights. Sports Science Exchange. 2007; 20(2), 1-5.
26. Glaister M, Hauck H, Abraham CS, Merry KL, Beaver D, Woods B, et al. Familiarization, reliability, and comparability of a 40-m maximal shuttle run test. J of Sports Sci and Med. 2009; 8(1), PP: 77-82.
27. Meyer P, Gayda M, Juneau M, Nigam A. High-intensity aerobic interval exercise in chronic heart failure. Current heart failure reports. 2013;10(2):130-8.
28. Wisløff U, Støylen A, Loennechen J, Bruvold M, Rognmo Ø, Haram P, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: A randomized study. Circu. 2007; 115 (24): 3086-3094. CONCLUSÃO GERAL.
29. Ernst E. Regular exercise reduces fibrinogen levels: a review of longitudinal studies. British journal of sports medicine. 1993;27(3):175-6.
30. Wosornu D, Allardyce W, Ballantyne D, Tansey P. Influence of power and aerobic exercise training on haemostatic factors after coronary artery surgery. Heart. 1992;68(8):181-6.
31. Sugawara, J.; Hayashi, K.; Kurachi, S.; Tanaka, Yokoi T. and Kurachi, K. “Age-related effects of regular physical activity on hemostatic factors in men”. J Thromb Thrombolysis. 2008; 26.203-210.
32. Bodary PF, Yasuda N, Watson DD, Brown AS, Davis JM, Pate RR. Effects of short-term exercise training on plasminogen activator inhibitor (PAI-1). Med Sci Sports Exerc. 2003; 35(11): 1853-8.
33. Jong-Syhan Wang. "Exercise prescription and thrombogenesis". Journal of Biomedical Science. 2006; 13:753-761.
34. El-Sayed MS. Effects of exercise on blood coagulation, fibrinolysis and platelet aggregation. Sports Med. 1996; 22(5):282-98.
35. Killewich LA, Macko RF, Montgomery PS, Wiley LA, Gardner AW. Exercise training enhances endogenous fibrinolysis in peripheral arterial disease. J Vasc Surg. 2004; 40(4):741-5.
36. Stratton JR, Chandler WL, Schwartz R, Cerqueira M, Levy W, Kahn S, et al. Effects of physical conditioning on fibrinolytic variables and fibrinogen in young and old healthy adults. Circulation. 1991; 83(5):1692-7.
37. Bounameaux, Henri; Egbert, K. Kruithof. “On the Association of Elevated t-PA/PAI-1 complex and von Willebrand Factor with Recurrent myocardial Infraction”, Thrombosis and vascular biology. 2000; 20: 1857-1859.
38. Johansson L, Jansson J-H, Boman K, Nilsson TK, Stegmayr B, Hallmans G. Tissue plasminogen activator (tPA), plasminogen activator inhibitor (PAI-1) and tPA/PAI-1 complex as risk factors for the development of a ®rst stroke. Stroke. 2000; 1: 26±32.
39. Rezaeimanesh, D.; Amiri, P.; Saidian, S. The effect of 8- week’s anaerobic intermittent exercises on the amount of fibrinogen, CRP and VO2max in student athletes. Procedia- Social and Behavioral Sciences. 2011; 30: 2169 – 2172.
40. Myint PK, Luben RN, Wareham NJ, Welch AA, Bingham SA, Khaw KT. Physical activity and fibrinogen concentrations in 23,201 men and women in the EPIC-Norfolk population-based study. Atherosclerosis. 2008; 198(2):419-25.
41. Bahadursingh S, Beharry K, Maharaj K, Mootoo C, Sharma P, Singh J, et, al. C-reactive protein: adjunct to cardiovascular risk assessment. West Indian Med J. 2009; 58(6):551-5.
42. Calabro P, Willerson JT, Yeh ET. Inflammatory cytokines stimulated C-reactive protein production by human coronary artery smooth muscle cells. Circulation. 2003; 108(16):1930-2.
43. Zhang Z, Yang Y, Hill MA, Wu J. Does C-reactive protein contribute to atherothrombosis via oxidant-mediated release of pro-thrombotic factors and activation of platelets? Front Physiol. 2012; 16;3:433.
44. 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.