

# Effect of eight weeks low intensity aerobic exercise on endothelin-1 plasma level, blood pressure and heart rate in healthy people and patients with coronary artery disease

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## Abstract

**Introduction:** Cardiovascular homeostasis such as tonicity of vessels and blood flow can be affected by activities and hormones. The purpose of the present study was to investigate the effect of 8 weeks low intensity aerobic exercise on plasma endothelin-1 (ET-1), blood pressure and heart rate (HR) in healthy men and women and coronary artery disease (CAD) patients.

**Methods:** In this quasi-experimental study, the experimental group consisted of 30 CAD patients (15 males and 15 females). The control group included 15 healthy males and 15 healthy females. These groups were chosen randomly. Participants did aerobic exercises with the intensity of 30%-40% of maximum HR. Blood samples were taken from participants in three stages (before, immediately and 24 hours after 8 weeks of exercise) and ET-1 plasma level was measured by ELISA method.

**Results:** There was no significant alteration in ET-1 plasma level during the experiment. However, there was a significant difference in the systolic blood pressure (SBP) at the three stages in all groups ( $P=0.01$ ). In addition, we could observe a significant difference in the diastolic blood pressure (DBP) at the three stages in CAD men and healthy women ( $P=0.03$ ). Conversely, no significant difference was observed in the DBP of other groups. There was a significant difference in the blood pressure of three groups ( $P=0.002$ ) except for healthy men.

**Conclusion:** The results demonstrated that, as there is a threshold in terms of time or intensity to stimulate the secretion of hormone; when the intensity and duration of exercise is below the stimulation threshold, no significant change can be observed in the level of ET-1.

**Keywords:** Aerobic exercise, Endothelin-1, Heart rate, Blood pressure, Coronary artery disease

## Introduction

Endothelial and vasodilation disorders are the first signs of cardiovascular disease and the predictive factors of cardiovascular problems. Therefore, many researchers and physicians have been attracted to vascular function assessment. Their main purpose is to identify vulnerable individuals prior to the disease. Smooth muscle contraction of vessel intermediate layer is the indication of vascular tonus. Endothelial, which covers arteries and arterioles, plays a significant role in the regulation of smooth muscle contraction (1). Human body contains various hormones which cause vasoconstriction or vasodilation and, thus,

can change the level of blood flow. Factors influencing vessel diameter can also affect vascular resistance and blood pressure regulation. Vascular endothelial cells play an important role in vessel activity regulation by releasing vascular active substances such as endothelin-1 (ET-1) and nitric oxide (1). It is one of the most important active substances in ET-1. With regard to the influencing role of ET in cardiovascular homeostasis, many have focused on the physiological and pharmacological importance of ET. ET-1 is a peptide vasoconstrictor which is made in endothelial cells (2). A peptide vasoconstrictor, known as ET, was discovered in 1985 (3). After refining this peptide,



Yanagisawa et al (4) reached the conclusion that this hormone, with a sequence of 21 amino acids, is a complete model of cDNA and gave the name of ET to this endothelium derived relaxing factor(s) (EDRF). In general, ET contains three isoforms of ET-1, endothelin-2 (ET-2) and endothelin-3 (ET-3) which are coded by three different genes. ET-1 is responsible for cardiovascular changes (5) and is secreted by cardiac myocytes, cardiac endothelial cells and cardiac fibroblasts (6). ET-1, as a primitive isoform of cardiovascular system, is the strongest and most prolonged human vasoconstrictor that has been known so far (4). ET-1 is involved in most cardiovascular diseases and, in just a few hours, severe cardiac ischemia can increase ET-1 density by five (7). ET-1 is also effective in the progress of arteriosclerosis. In most cases, the density of ET-1 is increased (8). With regard to the fact that physical activity can change the blood flow of different organs (active or inactive), physical activity could be considered as the most potential factor in secretion of these hormones. A recent study investigated the ET-1 plasma density in young athletic males after using ergometer bicycle (during a 30-minute session). Based on the results of this study, ET-1 plasma increases after a physical workout (9). Evaluation of seven cardiovascular patients by Kopeć et al (10) also showed that after a 6-minute walk, left ventricle voluminosity and ET-1 level increase. On the other hand, after 3 months of aerobic exercise in older females with 80% of reserved HR, Boghabadi et al (11) found that regular periods of aerobic exercise can reduce blood pressure and ET-1 level which can exert positive changes in the cardiovascular system. Moreover, Maeda et al investigated the effects of resistance training on ET-1 plasma level on six 25-27 year-old young men. Participants were involved in a resistance training course for 8 weeks and 3 days. The results showed that, although there was no difference between body composition, blood pressure, HR and maximum oxygen consumption before or after training, the level of ET-1 plasma level decreased significantly (12). On the other hand, Cosenzi et al (13) found that after a 15-minute use of ergometer bicycle with moderate intensity by young adults, the level of ET-1 plasma did not change. Based on the results of Callaerts et al, 8 weeks of aerobic exercise had no influence on cardiovascular patients ET-1 level (14).

With regard to the controversial results of these studies, it could be said that more studies are required in this area. In the present study the authors seek to answer questions such as: whether 8 weeks of moderate aerobic activity can cause any meaningful difference in ET-1; whether the preliminary conditions of individuals can affect study results; whether there is a relationship among HR, blood pressure and changes of ET-1; and whether gender can influence the effects of physical activity on ET-1. This study aimed to investigate the effects of an 8 week moderate aerobic activity program on the plasma level of ET-1 hormone, blood pressure and HR in coronary artery patients and healthy males and females.

## Methods

In this quasi-experimental study, 15 males and 15 females with CAD were assigned to experimental group. By the same token, the control group included 15 healthy males and 15 healthy females. Participants were enrolled into the study after receiving complete description of the study and signing the consent form. The age range of participants was from 50 to 65 and included non-athlete and non-smoker individuals. No signs of cardiovascular diseases were observed in the control group and all participants were interested to take part in the study. Participant demographics are shown in Table 1.

Since all subjects gave consent to participate in the study and had the required criteria, we used targeted sampling and voluntary participation. In each session, participants would first warm up for 10 minutes, start the main activity and at the end cool down for another 10 minutes. For the main activity, they were asked to use ergometer bicycle for 8 weeks (3 days a week). In the first week, participants used the bicycle for 15 minutes with 30% to 40% of their maximum HR. Afterwards (from the fourth session), 5 minutes were added to the duration of main activity. Exercise intensity was static during all sessions; therefore, in the last week of the program, participants exercised for 50 minutes with 30% to 40% of their maximum HR. ET-1 hormone level was measured during three stages (before the first session, immediately after the last session and 24 hours after the last session) and was assessed by means of CASOBIO company ET-1 kit and by using ELISA experimental method in ELISA reader machine. To

**Table 1.** Participants' demographic characteristics

	Min.	Max.	Mean	SD
<b>Women</b>				
<b>Control group (n=15)</b>				
Age	50	64	56.57	6.9010
Height	149	165	160.30	6.0749
Weight	54.2	88.5	69.92	10.4086
BMI	19.9	39.8	27.47	6.0461
PBF	26.7	45.2	35.90	5.4363
<b>Experimental group (n=15)</b>				
Age	50	64	56.50	6.8870
Height	151.5	163	156.22	4.1479
Weight	51.6	74.5	67.15	8.1551
BMI	23.3	30.7	27.70	2.8430
PBF	32.6	39.5	36.65	2.4940
<b>Men</b>				
<b>Control group (n=15)</b>				
Age	50	63	51.50	9.1380
Height	171	181	176.50	3.2711
Weight	62	81	71.83	6.4936
BMI	21.2	25.5	22.95	1.6134
PBF	16.7	22.7	19.40	2.1854
<b>Experimental group (n=15)</b>				
Age	50	65	57.89	9.2120
Height	165	180	171.77	5.4493
Weight	68	103.3	81.33	11.1471
BMI	24.3	33.5	27.47	3.2062
PBF	20.9	30.2	24.47	3.4139

measure blood pressure and HR with digital barometer, the patients were asked to keep their right elbow in line with their heart. Blood samples were also taken in three stages (before the first session, immediately after the last session and 24 hours after the last session) from participants' left elbow. Blood sample serums were gathered by means of centrifuge machines with 4000 rpm and were kept in  $-20^{\circ}\text{C}$ . Descriptive statistics were used to calculate mean and standard deviation. Parametric repeated measures test was used to assess the changes in ET-1, blood pressure and HR. To investigate the relationship between ET-1 with blood pressure and HR, Pearson correlation coefficient was used. Statistical analysis showed a  $\alpha < 0.05$  level of significance. SPSS software version 16 was used to analyze the data.

## Results

Pearson correlation coefficient showed that there was no significant relationship between HR, systolic blood pressure (SBP), diastolic blood pressure (DBP) and ET-1 for female patients in the first stage, respectively, ( $r=0.09$ ,  $P=0.73$ ), ( $r=-0.16$ ,  $P=0.56$ ) and ( $r=-0.36$ ,  $P=0.18$ ), HR; second stage, respectively, ( $r=-0.27$ ,  $P=0.32$ ), ( $r=0.18$ ,  $P=0.51$ ) and ( $r=-0.24$ ,  $P=0.93$ ); and third stage, respectively, ( $r=0.02$ ,  $P=0.91$ ), ( $r=-0.09$ ,  $P=0.73$ ) and ( $r=-0.20$ ,  $P=0.45$ ). In addition, there was no significant relationship between HR, SBP, DBP and ET-1 for healthy females in the first stage, respectively, ( $r=0.40$ ,  $P=0.14$ ), ( $r=-0.23$ ,  $P=0.40$ ) and ( $r=0.30$ ,  $P=0.26$ ); second stage, respectively, ( $r=-0.09$ ,  $P=0.73$ ), ( $r=0.25$ ,  $P=0.13$ ) and ( $r=-0.37$ ,  $P=0.16$ ); and third stage, respectively, ( $r=0.02$ ,  $P=0.94$ ), ( $r=0.29$ ,  $P=0.28$ ) and ( $r=0.09$ ,  $P=0.74$ ). Correlation coefficient between HR, SBP, DBP and ET-1 for male patients in stage one were, respectively, ( $r=0.41$ ,  $P=0.12$ ), ( $r=0.35$ ,  $P=0.19$ ) and ( $r=0.04$ ,  $P=0.87$ ); second stage, respectively, ( $r=-0.28$ ,  $P=0.28$ ), ( $r=0.17$ ,  $P=0.54$ ) and ( $r=-0.26$ ,  $P=0.33$ ); third stage, respectively, ( $r=-0.28$ ,  $P=0.31$ ), ( $r=-0.15$ ,  $P=0.59$ ) and ( $r=0.20$ ,  $P=0.45$ ); which was an indication of no significant relationship between the patients of this group. Moreover, there was no sig-

nificant relationship between HR, SBP, DBP and ET-1 for healthy males in the first stage, respectively, ( $r=-0.26$ ,  $P=0.92$ ), ( $r=0.47$ ,  $P=0.07$ ) and ( $r=0.13$ ,  $P=0.62$ ); second stage, respectively, ( $r=-0.15$ ,  $P=0.59$ ), ( $r=0.23$ ,  $P=0.39$ ) and ( $r=0.18$ ,  $P=0.51$ ); and third stage, respectively, ( $r=-0.67$ ,  $P=0.81$ ), ( $r=0.26$ ,  $P=0.34$ ) and ( $r=-0.04$ ,  $P=0.88$ ) (Table 2).

## Discussion

Assessment of vascular function is conducted to determine the role of endothelial and vascular smooth muscle in regulation of cardiovascular physiology and to make progress in the field of cardiovascular disease diagnosis. Pathological changes of endothelial function and structure can severely affect our health. Nowadays it is believed that endothelium disorder is a primary disorder of atherosclerosis and is directly connected with increased cardiac problems. Evidence shows that physical activities can increase the risk of endothelial disorder. Therefore, endothelial disorder plays an important role in the initiation of coronary artery disease (CAD) and its clinical side effects. In addition, this factor is essential for medical practices, such as physical activities (1). By assessing severe heart stroke patients (CHF) with the average age of  $9\pm 60$ , Genth-Zotz et al concluded that after one session of hard exercise on ergometer bicycle (for 2-12 minutes, starting from 30 W and increasing by 10 W per minute, until complete exhaustion), the level of ET-1 plasma changed significantly among control and experiment groups (15). In this study, when participants performed the activity in one session and with increasing intensity, there was a significant relationship in ET-1 levels of both groups. This shows that in the present study, patients did not continue until complete exhaustion since our training program was designed based on participants' abilities and, during the program, the intensity did not proceed 30% to 40% of maximum HR. Another study on male athletes showed that by using the ergometer bicycle for 30 minutes with intensity of 90% to 130% in anaerobic conditions for one session, the ET-1 plasma density can increase (9). It could

**Table 2.** Average of ET-1, HR, SBP and DBP following 8 weeks low intensity aerobics exercise

Groups		ET-1 (pg/ml)	HR Beat/min	SBP mm Hg	DBP mm Hg
Healthy women	Before exercise	21.0571	83.43	122.29	79.22
	Immediately after exercise	52.3000	92.71	116.86	77.43
	24 h after exercise	26.7571	82.14 <sup>a</sup>	114.00 <sup>a</sup>	74.76
Patient women	Before exercise	9.6375	69.25	124.38	73.00
	Immediately after exercise	11.7500	78.75	130.63	75.00
	24 h after exercise	8.7500	67.88 <sup>a</sup>	115.50 <sup>b</sup>	72.13 <sup>c</sup>
Healthy men	Before exercise	18.2833	69.33	119.33	76.67
	Immediately after exercise	24.3333	91.67	122.17	74.50
	24 h after exercise	27.0500	69.83	109.67 <sup>a</sup>	71.67
Patient men	Before exercise	11.0556	72.11	135.33	82.56
	Immediately after exercise	21.3556	82.67	124.67	74.89
	24 h after exercise	25.8111	70.67 <sup>d</sup>	112.22 <sup>a</sup>	72.22 <sup>b</sup>

Abbreviations: HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure.

<sup>a</sup>Significant in  $P=0.001$ . <sup>b</sup>Significant in  $P=0.001$ ; <sup>c</sup>Significant in  $P=0.01$ ; <sup>d</sup>Significant in  $P=0.002$ .

be said that if the session intensity reaches the point of ET secretion, some participants will not make any differences, since in Maeda et al (12) study (healthy people) and in Genth-Zotz et al (15) study (patients who participated in a severely intense training session), meaningful and similar changes in endothelial were observed. Training severity could be the cause of this (without considering healthy or sick individuals). Additionally, in a study by Donatoa et al (16), rats of the study were divided into four groups of sedentary young rats, sedentary old rats, trained young rats and trained old rats. The training program consisted of 12 weeks and 5 sessions a week (treadmill speed was 15 Mpm with a 15° tilt, for 1 hour a day). In the end, with regard to age, researchers faced an increase in capillaries healthy endothelial related to responsiveness and sensitivity of gemellus muscle to ET (16). Moreover, this study showed that the number of sessions can also influence ET-1 changes, since based on the previous study, 12 weeks of moderate training could make significant changes in ET. In addition, in this study, each week consisted of five training sessions, while our study contained three sessions a week, which could also result in meaningful changes of this hormone. We can also mention another study by Ahmadiasl et al with a training program exceeding 2 months. Ahmadiasl et al trained 20 Wistar male rats for 3 months (60 minutes a day) with the speed of 25 Mpm on treadmill. The results showed that ET-1 gene expression in experimental group was more than control group and this difference was statistically significant (17). In addition, we can also point to the duration of each session which was more than the present study. In Ahmadiasl et al (17) study the sessions started from 60 minutes, while our sessions started from 15 minutes. In another study, Maeda et al investigated 39 healthy and non-athlete females with an age range of 21 to 69 years old. The results showed that after 3 months of aerobic exercise on ergometer bicycle with moderate intensity (30 minutes for each session), for 5 sessions a week, a significant decrease of ET-1 level was observed in old females (18). The present study also shows that long training program (3 months) might significantly change ET levels. However, it should be noted that intensity might also play a role in these conclusions, since in previous studies (9,15) increased intensity resulted in increased changes of this hormone, while decreased intensity (18) resulted in decreased changes. Also, duration of each session in the previous study was less than 60 minutes sessions of Ahmadiasl et al which could result in increased ET in Ahmadiasl et al (17) study and decreased ET in Maeda et al study (18). After 24 weeks of aerobic exercise, Attipoe observed a significant change in ET-1 plasma level of older males (19). Results of this study are controversial with the present study which can originate from different durations of the training programs (24 weeks of aerobic training compared to 8 weeks of aerobic training). Based on this study, program duration (more than 12 weeks) and increased intensity of the training activity are the influencing factors that can result in increased ET hormone.

## Conclusion

Results of the present study and previous studies show that this hormone can be simulated by either time or intensity, since the high intensity of one session training program and long periods of training program can apply significant changes in endothelial. Moreover, based on the training program of this study, it could be said that with gradual and moderate increase of intensity, even coronary artery patients can follow regular training programs without facing any side effects.

## Ethical issues

The study was approved by the ethical committees of the Shiraz University, and all participants signed a written informed consent regarding participation in the research project.

## Authors' contributions

Authors equally contributed to the writing and revision of this paper.

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