



# Effects of L-arginine Supplementation and Aerobic Training on Hemodynamic Indices of Obese Men

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Received 2018 December 21; Revised 2018 December 28; Accepted 2019 February 22.

## Abstract

**Background:** L-arginine is a precursor to nitric oxide, which can affect some hemodynamic indices.

**Objectives:** The purpose of this study was to investigate the effect of one-month aerobic training with and without supplementation of L-arginine on hemodynamic indices in obese men.

**Methods:** A quasi-experimental double-blind, study was carried out. Subjects (age, 30 - 45 years; BMI, 38 - 40 kg.m<sup>-2</sup>) were randomly assigned to an exercise and L-arginine supplementation group (n = 10) and placebo group (n = 10). Before and after four weeks of aerobic exercise (three 90 - 120 min sessions per week at 65% - 85% of maximal heart rate), systolic and diastolic blood pressure, and rate pressure product (RPP) were measured at rest. The analysis of variance was used to determine the interaction between the two factors of exercise and supplementation of L-arginine on the dependent variables at P < 0.05.

**Results:** Four weeks of aerobic exercise reduced the RPP in both groups (P ≤ 0.05), while the L-arginine group significantly reduced systolic blood pressure (116.6 ± 3.40), diastolic blood pressure (76 ± 2.29) and RPP (8918.2 ± 722.86).

**Conclusions:** L-arginine supplementation along with four weeks of aerobic exercise can be effective in controlling hypertensive of obese men.

**Keywords:** Aerobic Exercises, L-arginine, Blood Pressure

## 1. Background

It has been predicted that roughly half of the world's population will be overweight by the year 2030. Several factors such as genetic factors, increased intake of energy versus consumption, sedentary lifestyle, environmental-social and psychological factors, neurodegenerative disorders and excessive feeding in early childhood are associated with the development of obesity (1).

Hypertension is a prevalent disease in Iran (2). Approximately, 6.6 million Iranians in the range of 25 - 64 years old are suffering from hypertension and about 12 million people are at the risk of hypertension and cardiovascular diseases at the same age range (2). Obesity, in particular abdominal obesity, plays an important role in the pathology of high blood pressure, and this issue should not be ignored when treating high blood pressure. In this regard, the results from previous studies indicated that in 6.5% of people with high blood pressure, the waistline (waist circumference) was associated more with systolic and diastolic blood pressure compared to other factors including insulin resistance and fasting blood glucose.

The major part of the renin-angiotensin system is carried out in the human body fat tissue. Obesity causes structural changes in the kidneys, impedes the function of some neurons and increases blood pressure. Therefore, fatty sediment in the renal sinus that is measured by CT can be a factor of increased blood pressure (3). Given the high prevalence of hypertension and cardiovascular disease, numerous complications and their considerable costs, it is of tremendous importance to look for new strategies for the prevention and control of these diseases, as well as the finding new treatment that are effective and have less side effects. Non-pharmacological approaches include lifestyle modification aimed at reducing weight by diet, reducing sodium intake, reducing stress and increasing physical activity. Sports exercises in particular are considered as a non-pharmacological strategy for high blood pressure control (4, 5). It has been illustrated that aerobic exercises can reduce blood pressure by 5 to 7 mmHg in people having high blood pressure (6). In the same vein, the results of studies by Murphy et al. showed that walking for at least 4 weeks decreased systolic and diastolic blood pressure by 8

and 2% respectively (7).

In addition, the results of previous studies indicated that active and physically fit individuals with high physical fitness levels have a lower resting rate due to high parasympathetic activity or low sympathetic activity compared to inactive people. On the other hand, venous return and high systolic volumes have been reported in patients with a better endurance status due to low resting heart rate (8).

Nabilpour and Mayhew stated that the resistance exercises significantly reduce the blood pressure of the participants (5). In addition to exercising and controlling the diet, some studies have suggested that the use of supplements can also have beneficial effects in this regard. One of these supplements is the L-arginine supplement. L-arginine or 2-amino-5-guanidino-valeric acid is an essential amino acid because it can be synthesized in the kidney and the liver. It has been revealed that L-arginine levels have been decreased in some patients, such as obese people or people with metabolic syndrome. This decrease in L-arginine in endothelial cells can hinder the ability to produce nitric oxide, thereby increasing blood pressure and the risk of cardiovascular difficulties (9). In fact, it has been argued that L-arginine is important for the production of nitric oxide, a potent vasodilator, by increasing the concentration of guanosine monophosphate (cGMP) (10). Other possible L-arginine-related effects include decreased blood pressure and homocysteine levels, increased body mass and adiponectin, and reduced fat mass and endothelin levels (11). Furthermore, a number of studies have demonstrated the beneficial effects of L-arginine supplementation in lowering blood pressure (12). The results of Yaman et al. (13) studies with a dose of 6 grams per day and Orozco-Gutierrez et al. (14) with a dose of 8 grams per day suggest a substantial reduction in blood pressure due to administration of L-arginine supplements. Nevertheless, in other studies with a dose of 6 and 12 grams per day, L-arginine did not affect blood pressure (15, 16).

## 2. Objectives

Since the effects of aerobic exercise along with L-arginine supplementation on hemodynamic indices have not been studied comprehensively, and given the existence of a handful of contradictory results from other studies, this study intends to investigate the simultaneous effect of a month of aerobic training, along with the addition of L-arginine, on hemodynamic indices of obese men.

## 3. Methods

The present study was conducted in the form of a quasi-experimental double-blind experiment after obtaining the research ethics license, No. 93103, from the vice-chancellor for research and technology of the University of Medical

Sciences. The statistical population consisted of 20 obese volunteers from the city of Tabriz. After completing the consent form, they participated in the study. The criteria for entering the study include: being male, non-smoking and no alcohol consumption during the past year, no history of regular exercise, no acute or chronic illness, not using any type of medicine or supplementation, a body mass index (BMI)  $\geq 29.9$  kg.m<sup>-2</sup>, systolic blood pressure between 110 and 140 mmHg, and diastolic blood pressure between 63 to 95 mmHg. After basal measurements, participants were randomly assigned to homogeneous groups.

TOOLS STATE software was utilized to homogenise the two groups, each consisting of 10 subjects (complementary group: exercise + L-arginine daily 6 g/day and placebo: exercise + dextrose daily 6 g/day). The BMI was measured in kilograms per square meter by the Fat detector device. The systolic and diastolic blood pressure of the participants were measured three times by the physician in two stages of pre-test and post-test in sitting position after ten minutes of rest from the left arm of the subjects. In addition, the rate pressure product was calculated using the formula (systolic pressure \* heart rate = RPP). Since the participants were not athletic, a researcher-made health questionnaire was used in addition to conducting the medical tests.

Prior to the start of the training program, the subjects attended two sessions to get acquainted with sports devices and the nature of their work at the training site. All tests were performed 24 hours preceding the start of the program. A 24-hour nutritional questionnaire was also used to control the nutrition relatively. After four weeks of aerobic exercise at 65% - 85% heart rate using the Karunen method and consuming L-arginine, measurements of the research variables were performed based on the first stage of the study.

Both groups participated in a program, which included treadmill, bike, elliptical-trainer, and rhythmic movements in a circle of severity. The intensity of continuous exercises was monitored by pulverizer pulse rate and pulse rate meter on sports devices in the target range, and if necessary, descriptions were provided to the subjects. The exercise program with an intensity of 65% of the heart rate in the first and second weeks began and gradually increased to 85% in the third and fourth weeks, with an understanding of the severity (13-17) of the Borg scale. The daily supplement group received 6 L-arginine capsules, comprised of a gram in three meals (17), the placebo group also ingested the same amount of dextrose capsules.

### 3.1. Statistical Methods

Initially, the Shapiro-Wilk test was applied to confirm the normal distribution of data. Then analysis of variance was used to determine the interactions between the two factors of exercise and supplementation of L-arginine with the variables of the research. To determine the difference

between the pre-test in each group, independent *t* test was used to determine the difference between the groups. A significant level was considered at a 5% error rate. Statistical analysis was performed using SPSS (version 20) software.

#### 4. Results

The results indicated that dual product in aerobic + placebo training group had a significant reduction in pre-test compared to pre-test ( $P < 0.05$ ). Yet, there was no significant change in systolic blood pressure indices ( $P < 0.41$ ;  $t = -0.88$ ) and diastolic ( $P > 0.05$ ). In the aerobic training group + L-arginine, all three hemodynamic indexes, systolic blood pressure, diastolic and dual product, showed a significant decrease compared to the pre-test ( $P < 0.05$ ) (Table 1).

Based on the results of two-in-two variance analysis, there was no significant difference ( $P = 0.48$ ,  $F = 0.53$ ) between the pattern of systolic blood pressure changes in obese men in the exercise + placebo + exercise + supplementation groups (Figure 1).

Based on the results of two-in-two variance analysis, there was no significant difference ( $P = 0.58$ ,  $P = 0.55$ ) between the pattern of diastolic blood pressure changes in obese men in exercise + placebo + exercise + supplementation groups (Figure 2).

Based on the results of two-in-two variance analysis, there was no significant difference ( $P = 0.58$ ,  $P = 0.55$ ) between the pattern of diastolic blood pressure changes in obese men in exercise + placebo + exercise + supplementation groups (Figure 2).

Based on the results of two-in-two variance analysis, there was no significant difference ( $P = 0.40$ ,  $P = 0.77$ ) between the pattern of systolic rate of pressure product changes in obese men in exercise + placebo + exercise + supplementation groups (Figure 3).

#### 5. Discussion

The results of the current study demonstrated that although there was no significant difference in the systolic and diastolic blood pressures before and after aerobic training in the exercise + placebo group, aerobic exercise significantly reduced RPP in this group. In contrast, administration of L-arginine along with exercise training significantly decreased systolic and diastolic blood pressures as well as RPP index in the obese men.

The rate of pressure product (RPP), which is the product of heart rate and systolic blood pressure, is usually used as the indirect and applied indicator of cardiac pressure. Since RPP is an appropriate indicator of the oxygen consumption of the heart muscle, it can be considered as a

prognostic indicator of coronary artery disease and myocardial ischemia (18). During exercise training, the RPP increases because of the increase in heart rate and blood pressure and reaches to five times greater than its rest level at the maximal exercise (19).

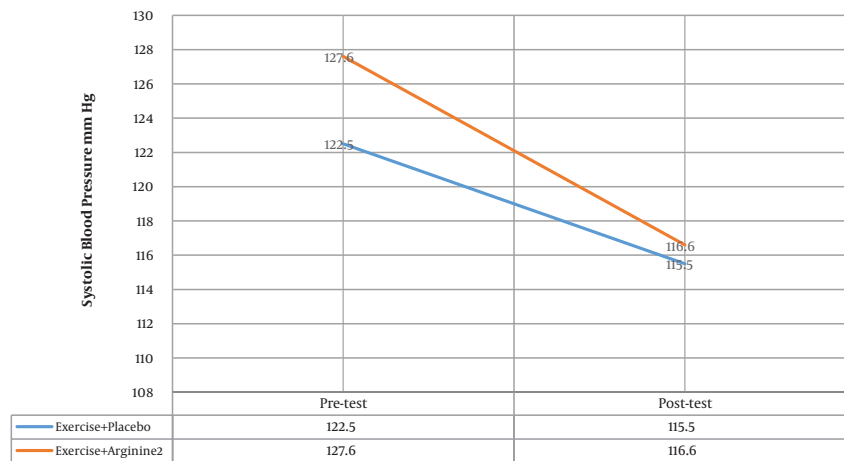
A number of studies have measured the effects of aerobic exercise on blood pressure in people with normal blood pressure and reported a hypotension only in systolic blood pressure with no or slight changes in the diastolic blood pressure (20, 21). Additionally, it has been reported that the reduction in systolic blood pressure after aerobic exercise is not significant in normotensive subjects (20).

In this study, changes in systolic blood pressure were miniscule, but changes in diastolic blood pressure were at a substantial level and extremely differed from the pre-test, which was not consistent with previous findings namely non-significant changes in systolic blood pressure in obese men. The practice + placebo group may be justified by highlighting the fact that as individuals age, their arterial rigidity also increases, which is associated with a rise in the systolic blood pressure. However, diastolic blood pressure remains constant, which can be attributed to the tightening of the vessel wall. On the other hand, the results of our study, with respect to the diastolic blood pressure, were consistent with the results of studies conducted by Murphy et al. (7) who examined the effect of aerobic training on hypertension in middle-aged women and men, and indicated a decrease in diastolic blood pressure, in contrast to the systolic blood pressure, which remained unaffected. Exercise can help reduce blood pressure in several ways. Reducing body fat and reducing stress are the indirect effects of exercises (22).

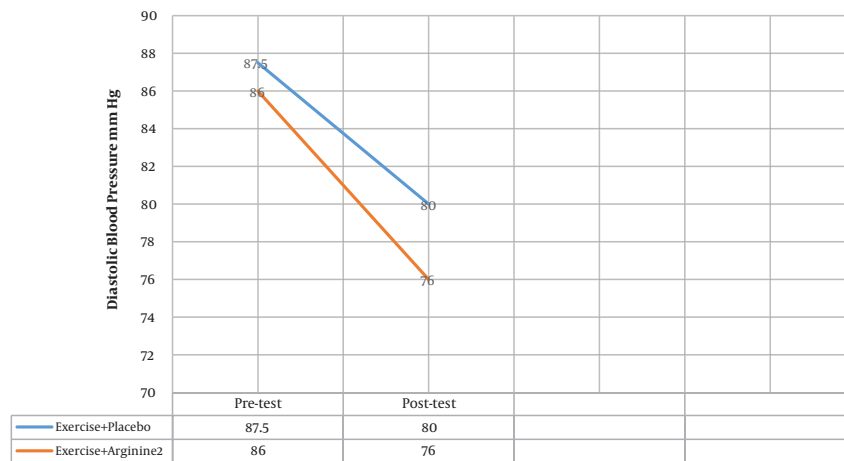
Likewise, the expansion of arterial dilatation due to the release of nitric oxide from endothelial cells, the expansion of compression reflection, the reduction of sympathetic activity, and the response of catecholamines to stress are direct results of sports activities (23). With increasing intensity and duration of exercise and when more muscle mass is contracted, simultaneously, the inactive parasympathetic system and sympathetic system are activated. The consequence of this is the increase in heart rate, myocardial contractility, and narrow veins on the one hand, and blood flow changes on the other (23). However, the results of this study showed that in the exercise group + L-arginine supplementation, all three hemodynamic indexes, systolic, diastolic, and rate of pressure product were significantly different. Nitric oxide precursor L-arginine acts as a vasodilator, which can lower blood pressure with this mechanism. In fact, nitric oxide produced from arginine is known as an important endothelial loosening factor, which activates guanosine cyclase, converting guanosine tri-phosphatase into guanosine monophosphate, resulting in a smooth muscle relaxation, which can ultimately decrease blood pressure (12). In a study conducted

**Table 1.** T Test Results in Rate of Pressure Product, Systolic Blood Pressure, Diastolic Blood Pressure Indices in Aerobic Training Group with and Without Supplementation of L-arginine

Indicator/Levels	Exercise + Placebo	Exercise + Arginine	Significance Between the Two Groups
<b>Rate of pressure product (RPP)</b>			
Pre-test	9532.5 ± 752.15	10410.2 ± 660.8	0.41
Post-test	8517 ± 745.71*	8918.2 ± 722.86*	0.71
<b>Systolic blood pressure</b>			
Pre-test	122.5 ± 3.23	127.6 ± 3.04	0.29
Post-test	115.75 ± 5.14	116.6 ± 3.40*	0.89
<b>Diastolic blood pressure</b>			
Pre-test	87.5 ± 2.5	86 ± 4.03	0.79
Post-test	80 ± 0.01	76 ± 2.29*	0.27



**Figure 1.** Pre-post changes in systolic blood pressure in obese men participating in aerobic exercises with and without

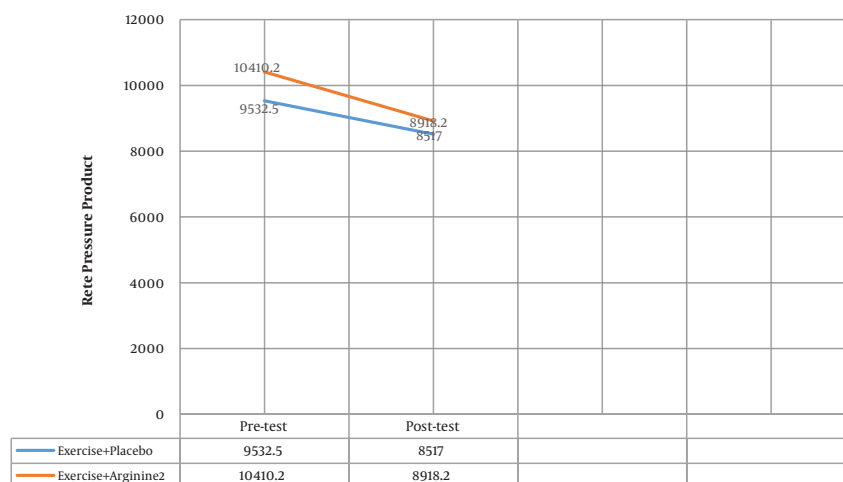


**Figure 2.** Pre-post changes in diastolic blood pressure in obese men participating in aerobic exercises with and without L-arginine supplementation

by Yaman et al. (13), the effect of one week of supplementation of L-arginine (6 g/day) on vascular dilatation in male football players was investigated and their results indi-

cated a significant increase in blood flow.

A study by Siani et al. (12) on six healthy people for one week showed that moderate increases in L-arginine re-



**Figure 3.** Rate of pressure product changes in the product of bipolar-systolic blood pressure of obese men participating in aerobic exercise with and without supplementation of L-arginine

duced blood pressure. The results of these studies are consistent with our study. Nonetheless, in some studies such as Forbes et al. (24), there was no significant difference in nitric oxide and blood pressure and heart rate between adjacent groups of L-arginine and placebo. Similarly, in the study by Lekakis et al. (16), 35 patients with high blood pressure were administered oral L-arginine (6 g/day), but their blood pressure remained untouched.

It is worth mentioning that this study diverges from others concerning race, sex, and the criteria for selecting subjects, methods for blood pressure measurement, the intensity and the duration of the exercise program, the method of L-arginine usage (oral versus intravenous injection), and the time spent conducting the research. Notwithstanding, further research in this area is required to analyse the effects of L-arginine supplementation with aerobic exercise activity on hemodynamic indices of obese men with more samples, and varying intensity and duration. Constraints limiting this study were uncontrolled factors such as possible changes to the quality of sleep and awakening by some subjects, as well as personality differences such as motivation and other psychological behaviours. Overall, the results of this study showed that the use of combined aerobic exercise program along with the use of L-arginine supplementation compared to aerobic exercise alone were more effective on reducing hemodynamic indices in obese men.

In conclusion, our findings elucidated that L-arginine supplementation in conjunction with aerobic improves blood pressure indices and can be effective in controlling high blood pressure in obese men. While this may be true, due to the small impact of one month of L-arginine supplementation on hemodynamic indices and aforementioned

limitations in the present study, further research is crucial to clarify the effects of L-arginine and its modus operandi.

### Acknowledgments

At the end, we would like to express our appreciation of the efforts of the Physical Education Department of the Faculty of Technology of Tabriz, and the subjects who collaborated in this research and wish them health and success.

### Footnotes

**Authors' Contribution:** Study concept and design: Majid Jahani, Maghsoud Nabilpour and Rodrigo Ramirez Campillo; analysis and interpretation of data: Majid Jahani.

**Conflict of Interests:** The authors were wholly responsible for the research conducted in this paper and present the work without conflict of interest.

**Ethical Approval:** This study is ethically approved by Tabriz University of Medical Sciences.

**Funding/Support:** The authors declare that there was no Funding or Support.

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