Published online 2019 June 19.

**Research Article** 

# Effects of Eight-Week Resistance Training in Different Environmental Conditions on Arterial Factors in Overweight Men

Sahar Kamankesh 💿<sup>1</sup>, Vahid Tadibi 💿<sup>1,\*</sup>, Naser Behpoor 💿<sup>1</sup> and Farhad Naleini 💿<sup>2</sup>

<sup>1</sup>Razi University, Kermanshah, Iran

<sup>2</sup>University of Medical Sciences, Kermanshah, Iran

<sup>\*</sup>Corresponding author: Razi University, Kermanshah, Iran. Email: vahidtadibi@razi.ac.ir

Received 2018 October 08; Revised 2019 April 09; Accepted 2019 April 15.

## Abstract

**Background:** The present study was conducted to investigate the effects of eight weeks of resistance training in different environmental conditions on arterial factors in overweight men.

**Methods:** The present study was conducted in Kermanshah, Iran, on thirty overweight males with a mean body mass index (BMI) of 27.4  $\pm$  1.57 kg/m<sup>2</sup>, who voluntarily participated in this study. The subjects were randomly divided into a hypoxic and a normoxic resistance training group and a hypoxia exposure group, and performed the training protocols for eight weeks. Vascular endothelial growth factor (VEGF), high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol (TC) and triglyceride (TG) were measured before and after performing the intervention.

**Results:** The results showed a significant increase in the level of VEGF in all the three groups (P < 0.05). Significant differences were also observed between the groups in terms of changes in VEGF (P < 0.05). In the hypoxic resistance training group, HDL increased and LDL, TC and TG significantly decreased (P < 0.05). No significant changes were, however, observed in lipid profile in the hypoxia exposure and normoxic resistance training groups.

**Conclusions:** The present findings suggest that hypoxic and normoxic resistance trainings and hypoxia exposure positively affect the level of VEGF, and only the hypoxic resistance training could improve lipid profile in overweight subjects. Hypoxic resistance training is concluded to be a more effective method for improving arterial factors in overweight men.

Keywords: VEGF, Lipid Profile, Hypoxia, Resistance Training

### 1. Background

Atherosclerosis is a pathologic condition that directly affects obesity and overweight, and is associated with the thickening of the inner layer of vessels caused by fat deposits and platelets (1). The progression of atherosclerosis disrupts the blood supply to the brain and other organs (2). A major function of vascular endothelial cells is the secretion regulation of growth factors such as VEGF, which plays a key role in the process of blood supply and angiogenesis, and is negatively correlated with obesity and atherosclerosis (3). Research suggests that stimulants such as hypoxia and training can increase the stimulation of VEGF (4), and the shear stress due to blood flow is a major cause of endothelial vascular endothelial growth factor (VEGF) secretion (5). Obesity reduces the vascular endothelial function, and is associated with impaired mechanisms, including lipid metabolism and hypertension (6). A review study demonstrated correlations between the femoral arterial thickness and factors involved in atherosclerosis, including ankle-brachial index (ABI) and cholesterol (7).

Different training methods proposed in recent years to prevent and treat obesity and overweight-associated diseases include the new method of training under hypoxic conditions. Research suggests improvements in the metabolism of fats and carbohydrate in hypoxic conditions (8, 9). Resistance exercise significantly increases the metabolic and angiogenesis responses, and adding a hypoxic stimulus has been proposed for increasing metabolic and angiogenesis responses to resistance exercise (3, 10, 11). Women with breast cancer showed significant increases in the level of VEGF, fibroblast growth factor (FGF) and nitric oxide (NO) after eight weeks of resistance training (12). A significant decrease was also observed in VEGF in female older adults after eight weeks of resistance training (13). In other study, for angiogenesis factors in healthy subjects, the eight weeks of resistance training under hypoxic conditions had significantly higher level of VEGF and capillary ratio to muscle mass than the normoxic

Copyright © 2019, Journal of Clinical Research in Paramedical Sciences. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, provided the original work is properly cited.

resistance training (3).

Some researchers have reported improvements in terms of the effect of resistance training on lipid profile and some have demonstrated the lack of significant changes. The correlation between training intensity and changes in lipid profile have also been demonstrated (14, 15). A study of six-week aerobic exercise under hypoxia in two groups with 14.5% and 16.5% oxygen saturations found a significant increase in high density lipoprotein (HDL) levels and a significant decrease in low density lipoprotein (LDL), triglyceride (TG) and total cholesterol (TC) compared to the normoxic resistance training group (16). The chronic effects of hypoxia and hypoxic resistance training on these factors have rarely been addressed in literature. Given the effectiveness of hypoxia in angiogenesis and lipid profile, resistance training under hypoxia conditions can increase arterial responses to resistance exercise.

## 2. Objectives

The present research was therefore performed to evaluate and compare the effects of eight weeks of hypoxic and normoxic resistance training and hypoxia exposure on arterial factors in overweight men.

## 3. Methods

#### 3.1. Participants

Thirty overweight none-athletic males in Kermanshah voluntarily participated in the present study. The subjects had no history of cardiorespiratory diseases and had not gone to altitudes of over 2500 meters in the two months prior to the intervention. They also visited the research laboratory of the Faculty of Physical Education of Razi University in Kermanshah two days before the intervention to get familiar with the study procedure, 1RM and demographic measurements. In addition, informed written and oral consent was obtained from all the subjects, and they were informed of any potential risks associated with the experiments.

#### 3.2. Study Design

The subjects participated in 24 sessions of training protocols and hypoxia exposure, three sessions a week. The subjects were randomly assigned to three groups, namely hypoxic resistance, normoxic resistance and hypoxia exposure, the day they visited the laboratory. The maximum repetition of resistance was determined for squat and lunge using submaximal repetitions up to fatigue as follows (14).

$$1 - RM = \frac{(moved weights) kg}{(1.0278 - repetition to exhaustion \times 0.0278)}$$

The levels of VEGF, LDL, HDL, TG and TC were measured one day before and two days after the eight-week intervention.

#### 3.3. Normoxic Resistance Training

This training program initially began by performing five minutes of stretching and warm-up exercises and a 15repeat set with about 50% of 1RM. Three sets of ten repeats were performed in the first week, four sets of ten repeats in the second week, and from the third week, five sets of ten repeats with 70% of 1RM were performed for both the squat and lunge. All the sets and exercises were separated by 90-second rest intervals (3, 17).

#### 3.4. Hypoxia Exposure

The subjects were placed in a sitting position breathing for twenty minutes using a mask attached to a Douglass Bag (Australian, model: Model ERA II GO2 Altitude) and filled with 14% oxygen. A pulse oximeter (Nonin Medical INC.Plymouth MN USA) was used to monitor arterial blood saturation in each subject from the beginning to the end of the intervention. The minimum arterial blood saturation was found to be 75% for continuous exercise or hypoxia exposure. In case the oxygen saturation dropped below this threshold during the intervention, or the subjects suffered breathing difficulties and dizziness, they were prevented from continuing the task.

#### 3.5. Hypoxic Resistance Training

This type of training was performed in a similar fashion as resistance training in normoxic conditions. The subjects put on the mask after warm-up in a completely similar manner to the hypoxia exposure, and performed the resistance training protocol.

#### 3.6. Sampling

Seven ml of fasting blood samples were collected between 8 am and 10 am one day before and two days after the intervention. VEGF levels were measured using ELIZA kits (Boster Biological, sensitivity of 1 pg/Ml >, made in USA), HDL, TG and TC using Pars kits, and LDL using the Friedwold formula.

## 3.7. Statistical Analyses

To investigate the research hypotheses, the dependent t-test was used for normally-distributed data and Wilcoxon, Kruskal-Wallis and Mann-Whitney U tests for the data with a non-normal distribution. The data collected were analyzed in SPSS-22.

## 4. Results

The present study participants comprised overweight male subjects with a mean body mass (weight) of 85.2  $\pm$  6.53 kg, a mean age of 19.8  $\pm$  1.13 years and a BMI of 27.4  $\pm$  1.57 kg/m<sup>2</sup>. Table 1 presents the pre-test and post-test results obtained in each of the three groups, suggesting a significant increase in VEGF in all the groups, and showing a significant increase in HDL and a significant decrease in LDL, TC and TG only in the hypoxic resistance group.

The increase in the level of VEGF was found to be 75.8% ( $z = -2.803^{b}$ , P = 0.005) in hypoxic resistance training, 51.6% ( $z = -2.701^{b}$ , P = 0.007) in hypoxia exposure and 25.2% ( $z = -2.803^{b}$ , P = 0.005) in normoxic resistance training. The Kruskal-Wallis test showed a significant difference ( $x^{2}(2) = 6.382$ , P = 0.041) between the groups. The Mann-Whitney U test used for the pairwise comparison of the groups suggested no significant differences between the hypoxic resistance and hypoxia exposure groups (P = 0.631) and between the hypoxia exposure and hypoxia exposure groups (P = 0.075), while showing significant differences between the hypoxic resistance and the normoxic resistance groups (P = 0.015).

A significant increase of 7.4% ( $t_9 = -4.9$ , P = 0.001) was observed in the level of HDL in the hypoxic resistance training group, although no significant changes were observed in the hypoxia exposure ( $t_9 = -1.2$ , P = 0.256) and the normoxic resistance training group ( $t_9 = -1.3$ , P = 0.222). A significant decrease of -5.3% ( $t_9 = 3.1$ , P = 0.012) was observed in the level of LDL in the hypoxic resistance training group, although no significant changes were observed in the hypoxia exposure ( $t_9 = 0.889$ , P = 0.397) and the normoxic resistance group ( $t_9 = 1.62$ , P = 0.139). A significant decrease of -5.2% ( $t_9 = 3.1$ , P = 0.11) was observed in the level of TG in the hypoxic resistance training group, although no significant changes were observed in the hypoxia exposure ( $t_9 =$ 0.324, P = 0.753) and the normoxic resistance group ( $t_9 =$ 0.589, P = 0.570). A significant decrease of -4.6% ( $t_9 = 4.1$ , P = 0.002) was observed in the level of TC in the hypoxic resistance training group, although no significant changes were observed in the hypoxia exposure ( $t_9 = 1.3$ , P = 0.220) and the normoxic resistance group ( $t_9 = 0.327$ , P = 0.751).

## 5. Discussion

The present study was conducted to investigate the effects of eight weeks of hypoxic and normoxic resistance exercises and hypoxia exposure on arterial factors in overweight men. After eight weeks, the level of VEGF increased in all the three groups, and significant differences were observed between the groups in terms of changes in the level of VEGF. The present findings suggested an increase in the level of VEGF following normoxic and hypoxic resistance trainings, which is consistent with literature (3, 12, 18). Kon et al. reported significant changes in the level of VEGF in hypoxic resistance training compared to in normoxic resistance training. They used an increasing intensity of exercise during the sessions, whereas the present study used a constant exercise intensity. The present study found the hypoxic resistance training group to be significantly different from the normoxic resistance training group, although it was found not to be significantly different from the hypoxia exposure group. Hypoxia can be concluded to affect the arterial function in overweight individuals (3). In contrast to the present study, no significant changes were observed in the level of VEGF in certain studies (13, 19, 20). Exercise duration and intensity have been proposed as the factors affecting the results (20). Research suggests that resistance training stimulates the secretion of cytokines (21), as a reason for increasing VEGF following resistance training. Moreover, exercise-induced ischemic induces a local hypoxia in muscles (18). Shear stress, cytokine secretion and local hypoxia can therefore significantly contribute to stimulating VEGF after resistance training. Hypoxia is a major factor contributing to angiogenesis stimulation (4). Systemic hypoxia such as angiogenesis can be considered an internal stimulus for endurance adaptation (22). A major function of hypoxia is to stimulate hypoxia-inducible factor-1 (HIF-1), which is responsible for transcribing different hypoxia-compatible genes, including angiogensis and glycolysis. Stimulating the expression of VEGF and erythropoietin (EPO) is an important regulatory effect of HIF-1(23). Evidence suggests increased cytokines in hypoxia conditions, which can stimulate the expression of VEGF, as in the case of resistance training (24).

The present study showed a significant increase in HDL and significant reductions in LDL, TG and TC in the hypoxic resistance group, although it did not suggest any changes in lipid profile in the hypoxia exposure and normoxic resistance training groups. Both significant improvements and no changes in lipid profile have been reported in literature (14, 15). Evidence shows that the intensity, duration and volume of exercise affect the changes in lipid profile. Moreover, a minimum duration of eight weeks has been proposed for exercise to affect lipid profile, whereas the majority of researchers using protocols based on below eight weeks of training did not report significant changes (15). Compared to previous studies on resistance training protocols, the present research focused only on two types of training, i.e. lunge and squat. The low volume of exercise can explain the lack of changes in lipid profile obtained in the normoxic resistance exercise group. Investigating the effect of hypoxia exposure on lipid profile in patients with coronary heart disease showed that intermit-

	Hypoxic Resistance	Hypoxia Exposure	Normoxic Resistance
GF, mg/L			
Pre-test	$958.1 \pm 499.1$	1149.1 ± 609.6	1198 $\pm$ 907.6
Post-test	$1620\pm893.8^{\rm b}$	$1655.5 \pm 793.58^{\rm b}$	$1438.4\pm1008^{b}$
DL, mg/dL			
Pre-test	$94.8\pm11.3$	$95.8\pm10.9$	$96.2\pm11.9$
Post-test	$89.7\pm10.7^{c}$	$94.8\pm9.9$	$95.1\pm12$
DL, mg/dL			
Pre-test	$44\pm3.7$	$46.1\pm3.8$	$43.6\pm4.1$
Post-test	$47.3\pm3.88$	$46.6\pm3.8$	$44.3\pm4.2$
C, mg/dL			
Pre-test	$163.4\pm10.3$	164.4 $\pm$ 11.7	$163.4\pm10.5$
Post-test	$155.6\pm10^{\circ}$	$163 \pm 12.2$	$162.7\pm11.1$
G, mg/dL			
Pre-test	148.1 ± 10.3	$148.2 \pm 12.7$	$147.2\pm11.5$
Post-test	$140.3 \pm 12.8^{\circ}$	$147.8 \pm 12.1$	$146.6\pm11.1$

Table 1. The Pre-Test and Post-Test Results Associated with VEGF, HDL, LDL, TG and TC in All the Groups<sup>a</sup>

Abbreviations: HDL, high density lipoprotein; LDL, low density lipoprotein; TC, total cholesterol; TG, triglyceride; VEGF, Vascular endothelial growth factor; <sup>a</sup>Values are expressed as mean  $\pm$  standard deviation (SD).

<sup>b</sup>A significant increase compared to the pre-test (P < 0.01).

<sup>c</sup>A significant decrease compared to the pre-test (P < 0.01).

tent hypoxia significantly improves lipid profile after 22 sessions (3 hours per day) (25), which is inconsistent with the present study that reported no significant changes, as the subjects were exposed to hypoxia for only 20 minutes each session. Evidence suggests the critical role of HIF-1 in regulating the metabolism of carbohydrates and fats. In addition, using fat as a substrate required for metabolism has been observed in hypoxia conditions (26).

## 5.1. Conclusions

Normoxic and hypoxic resistance training and hypoxia exposure generally increased the level of VEGF. Hypoxic resistance training also significantly increased lipid profile. Hypoxia can therefore be proposed as a more prominent factor in terms of improving the arterial function. Exercises under hypoxia conditions and their effects on the arterial function have rarely been addressed in literature. Numerous discrepancies observed in the obtained results can be explained by the differences in the intensity and duration of trainings or the type of exercise. Overweight subjects at risk for cardiovascular diseases can generally prevent the disease by employing appropriate training protocols. Optimal training programs are therefore recommended to be provided for these individuals.

#### Acknowledgments

The authors would like to express their gratitude to all the study participants and the authorities of the Faculty of Physical Education at Razi University, who helped conduct the present research project. The present article was extracted from a Ph.D. dissertation on sport physiology, and the authors declare no sponsorship.

#### Footnotes

**Conflict of Interests:** The authors declare no conflict of interests regarding the publication of the present article.

**Ethical Approval:** This study was approved by the Ethics Committee of Kermanshah University of Medical Sciences (code: IR.KUMS.REC.1396.751).

Funding/Support: The authors declare no sponsorship.

#### References

- Ip JH, Fuster V, Badimon L, Badimon J, Taubman MB, Chesebro JH. Syndromes of accelerated atherosclerosis: Role of vascular injury and smooth muscle cell proliferation. *J Am Coll Cardiol*. 1990;**15**(7):1667-87. doi: 10.1016/0735-1097(90)92845-S. [PubMed: 2188991].
- Properzi G, Francavilla F, Bellini C, D'Abrizio P, Mangiacotti B, Ferri C, et al. Blood endothelin-1 levels before and after carotid endoarterectomy for atherosclerotic stenosis. *Atherosclerosis*. 2001;**154**(1):137–40. doi: 10.1016/S0021-9150(00)00445-7. [PubMed: 11137092].

- Kon M, Ohiwa N, Honda A, Matsubayashi T, Ikeda T, Akimoto T, et al. Effects of systemic hypoxia on human muscular adaptations to resistance exercise training. *Physiol Rep.* 2014;2(6). doi: 10.14814/phy2.12033. [PubMed: 24907297]. [PubMed Central: PMC4208656].
- Rostami A, Khazaei M. [Inflammation and angiogenesis: Role of inflammatory cells and mediators]. *J Isfahan Med Sch.* 2016;**34**(384):612– 22. Persian.
- Ferrara N, Gerber HP, LeCouter J. The biology of VEGF and its receptors. *Nat Med*. 2003;9(6):669–76. doi: 10.1038/nm0603-669. [PubMed: 12778165].
- Weil BR, Stauffer BL, Mestek ML, DeSouza CA. Influence of abdominal obesity on vascular endothelial function in overweight/obese adult men. *Obesity (Silver Spring)*. 2011;19(9):1742–6. doi: 10.1038/oby.2011.189. [PubMed: 21738236].
- Thijssen DH, Cable NT, Green DJ. Impact of exercise training on arterial wall thickness in humans. *Clin Sci (Lond)*. 2012;**122**(7):311– 22. doi: 10.1042/CS20110469. [PubMed: 22150253]. [PubMed Central: PMC3233305].
- Wood IS, Wang B, Lorente-Cebrian S, Trayhurn P. Hypoxia increases expression of selective facilitative glucose transporters (GLUT) and 2-deoxy-D-glucose uptake in human adipocytes. *Biochem Biophys Res Commun.* 2007;**361**(2):468-73. doi: 10.1016/j.bbrc.2007.07.032. [PubMed: 17658463]. [PubMed Central: PMC2211375].
- Grosfeld A, Zilberfarb V, Turban S, Andre J, Guerre-Millo M, Issad T. Hypoxia increases leptin expression in human PAZ6 adipose cells. *Diabetologia*. 2002;45(4):527–30. doi: 10.1007/s00125-002-0804y. [PubMed: 12032628].
- Vedam H, Phillips CL, Wang D, Barnes DJ, Hedner JA, Unger G, et al. Short-term hypoxia reduces arterial stiffness in healthy men. *Eur J Appl Physiol*. 2009;**105**(1):19–25. doi: 10.1007/s00421-008-0868-6. [PubMed: 18815804].
- Ross MD, Wekesa AL, Phelan JP, Harrison M. Resistance exercise increases endothelial progenitor cells and angiogenic factors. *Med Sci Sports Exerc.* 2014;46(1):16–23. doi: 10.1249/MSS.0b013e3182a142da. [PubMed: 24346188].
- Fathollahi Shourabeh F, Tarverdizadeh B, Keihani M. [The impact of eight weeks of resistance training on some angiogenesis indicators in women with breast cancer]. *Iran J Obstet Gynecol Infertil*. 2017;20(3):9– 17. Persian.
- Behjati A, Babai Mazrae No A, Faramarzi M. [The effect of resistance training on vascular endothelial growth factor (VEGF) in older women]. *Iran J Ageing*. 2015;10(3):156–65. Persian.
- Nayebifar S, Afzalpour M, Saghebjoo M, Hedayati M, Shirzaee P. [The effect of aerobic and resistance trainings on serum C-Reactive Protein, lipid profile and body composition in overweight women]. *Mod Care* J. 2012;8(4):186–96. Persian.

- Foroutan Y, Daneshyar S, Tadibi V, Behpoor N. [Comparison of different concurrent protocols of lipid profile, insulin resistance index and some white adipose tissue hormones. Fats inactive men overweight]. *J Urmia Univ Med Sci.* 2018;**28**(12):805-16. Persian.
- Park HY, Lim K. The effects of aerobic exercise at hypoxic condition during 6 weeks on body composition, blood pressure, arterial stiffness, and blood lipid level in obese women. *Int J Sports Sci Med*. 2017;1:1– 5.
- Scott BR, Slattery KM, Dascombe BJ. Intermittent hypoxic resistance training: Does it provide added benefit? *Front Physiol.* 2014;5:397. doi:10.3389/fphys.2014.00397. [PubMed: 25352810]. [PubMed Central: PMC4195285].
- Alvar YM, Sayevand Z, Adab FE, Moghadam RH, Sharif MAS, Karami S. [The effects of five weeks' resistance training on some vascular growth factors in sedentary men]. *Exerc Physiol*. 2016;8(29):15–30. Persian.
- Friedmann B, Kinscherf R, Borisch S, Richter G, Bartsch P, Billeter R. Effects of low-resistance/high-repetition strength training in hypoxia on muscle structure and gene expression. *Pflugers Arch.* 2003;**446**(6):742–51. doi: 10.1007/s00424-003-1133-9. [PubMed: 12861415].
- 20. Shekarchizadeh P, Khazaei M, Gharakhanlou R, Karimian J, Safarzadeh AR. [The effects of resistance training on plasma angiogenic factors in normal rats]. *J Isfahan Med Sch.* 2012;**30**(176). Persian.
- Tzeng HE, Tsai CH, Chang ZL, Su CM, Wang SW, Hwang WL, et al. Interleukin-6 induces vascular endothelial growth factor expression and promotes angiogenesis through apoptosis signal-regulating kinase 1 in human osteosarcoma. *Biochem Pharmacol.* 2013;85(4):531–40. doi: 10.1016/j.bcp.2012.11.021. [PubMed: 23219526].
- Hudlicka O, Brown M, Egginton S. Angiogenesis in skeletal and cardiac muscle. *Physiol Rev.* 1992;72(2):369–417. doi: 10.1152/physrev.1992.72.2.369. [PubMed: 1372998].
- Ohno H, Shirato K, Sakurai T, Ogasawara J, Sumitani Y, Sato S, et al. Effect of exercise on HIF-1 and VEGF signaling. J Phys Fitness Sports Med. 2012;1(1):5–16. doi: 10.7600/jpfsm.1.5.
- Hempel SL, Monick MM, Hunninghake GW. Effect of hypoxia on release of IL-1 and TNF by human alveolar macrophages. *Am J Respir Cell Mol Biol*. 1996;14(2):170–6. doi: 10.1165/ajrcmb.14.2.8630267. [PubMed: 8630267].
- Tin'kov AN, Aksenov VA. Effects of intermittent hypobaric hypoxia on blood lipid concentrations in male coronary heart disease patients. *High Alt Med Biol.* 2002;3(3):277-82. doi: 10.1089/152702902320604250. [PubMed: 12396881].
- Park J, Park H. Effects of 6 months of aerobic and resistance exercise training on carotid artery intima media thickness in overweight and obese older women. *Geriatr Gerontol Int.* 2017;17(12):2304–10. doi: 10.1111/ggi.12972. [PubMed: 28060442].