**Original Article**
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# INFLUENCES OF SHORT-TERM NORMOBARIC HYPOXIC TRAINING ON METABOLIC SYNDROME-RELATED MARKERS IN OVERWEIGHT AND NORMAL-WEIGHT MEN

## Normobaric Hypoxic Training on Metabolic Syndrome

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### Abstract

**Background and Objective**

This study examined the influence of short-term normobaric hypoxic training on metabolic syndrome-related markers in overweight and normal-weight men.

**Material and Methods**

Forty-one Japanese men were included and divided into two groups based on their body mass indices (BMIs): BMI≥25 or BMI<25. Participants in the overweight and normal-weight groups were randomly classified into the hypoxic exercise group (hypoxic overweight, HO; hypoxic normal-weight, HN) and the normoxic exercise group (normoxic overweight, NO; normoxic normal-weight, NN). Subjects performed treadmill exercise three days per week for four weeks at an exercise intensity of 60% of maximum heart rate, under either normobaric hypoxic or normobaric normoxic conditions, for 50 min (including 5 minute warm-up and cool-down periods) after a 30-min rest period. The study parameters included weight, body fat percentage, BMI, heart rate, waist circumference, ankle-brachial pulse wave velocity (PWV), blood sugar, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) scores, and adiponectin levels. Repeated measures two-way analysis of variance was used to examine differences in the mean parameter values between the two groups (overweight and normal-weight) before and after training.

**Results**
Hypoxic training improved the weight, body fat percentage, BMI, waist circumference, PWV, TC, LDL-C levels, and HOMA-IR scores in the overweight and normal-weight groups ($p$<0.05). In addition, TG level, HDL-C level, and HOMA-IR scores showed significant interactions with hypoxic training, as these parameters improved in the hypoxic overweight group ($p$<0.05).

**Conclusion**
These results suggest that hypoxic training could be useful for improving arterial stiffness, circulatory system function, body composition, and energy metabolism in adult males.

Obesity and metabolic syndrome are pressing worldwide epidemics that are growing at an alarming rate, with one in three individuals at risk of these conditions.[1] Aerobic and muscle-strength exercises are effective at improving lifestyle-related diseases, including obesity.[1] However, middle-aged or elderly people with a motor system disease who perform exercise that strain their back or knees for an extended period can experience increased pain and difficulty in everyday life. An important question is how training stimuli can be optimized to maximize metabolic and cardiovascular benefits and minimize their risk of injury, particularly in overweight individuals.[2] Previous studies have suggested that hypoxic training elicits a similar cardiovascular stimulus to normoxic training at a lower workload.[2,3] Although the workload is reduced in hypoxic training, its benefits are similar to or greater than those of normoxic training in terms of improvements to cardiovascular and metabolic risk factors.

Hypoxic training, although not commonly used, may be beneficial in individuals with clinical conditions, such as coronary artery disease and chronic obstructive pulmonary disease.[4] However, the effects of hypoxic training vary greatly according to the oxygen concentration, exercise intensity, time and duration, and among individuals. However, there is disagreement regarding the effects of exercise in a hypoxic environment on lipid metabolism, with some studies reporting no change and others reporting improvements in markers. Hence, further studies are needed to develop effective and safe hypoxic training programs for the prevention and improvement of metabolic syndrome.

Recently, there have been many reports that hypoxic training can effectively alleviate obesity and improve metabolic syndrome in overweight and obese people. Shi et al. examined the effect of hypoxic training on high-sensitivity C-reactive protein (hs-CRP) levels, an inflammatory marker, in healthy adult males and reported that hs-CRP levels were significantly lower in the hypoxic group than in the control group after the training.[5] Therefore, hypoxic training may have positive, anti-inflammatory effects on metabolic syndrome-related factors.

Most previous hypoxic training studies have focused on specific groups, such as obese individuals,[6,7] athletes,[8] college students,[5,9,10] and general adults,[11] and the effects of hypoxic training have varied according to the physical fitness and physical characteristics of the subjects. Since obese people are at greater risk of developing metabolic syndrome than are those of a normal weight, the effects of hypoxic training on metabolic syndrome-related factors might be more pronounced in obese individuals. It is also necessary to investigate whether metabolic syndrome markers are improved following hypoxic training in normal-weight people. However, no hypoxic training studies have compared obese and normal-weight groups with one another.

The purpose of this study was to examine the effects of hypoxic training on factors related to metabolic syndrome. In this study, participants were divided into either an overweight or a normal-weight group, and the effects of regular normobaric hypoxic training on metabolic syndrome-related factors were examined according to physique.

## METHODS

### *Participants*

Forty-one Japanese men were included in this study. Information on aerobic and hypoxic exercise programs were posted on notice boards in the Gifu University and Gifu University hospital in order to recruit participants, and those who wanted to participate in this exercise program were included in this study. Participants were divided into two groups based on their body mass indices (BMIs): BMI≥25 or BMI<25. The overweight and normal-weight groups were randomly subdivided into the hypoxic exercise group (hypoxic overweight, HO; hypoxic normal-weight, HN) and the normoxic exercise group (normoxic overweight, NO; normoxic normal-weight, NN). The sample sizes were 8, 12, 9, and 12 in the HO, HN, NO, and NN groups, respectively. Participant characteristics are shown in Table 1.

The exclusion criteria included a history of coronary heart disease, cardiac insufficiency, pulmonary disease, or uncontrolled hypertension. Only men were included in this study since certain blood parameters differ across sexes. The purpose and procedures of the study were explained in detail to all participants, and written informed consent was obtained prior to their participation. This study was approved by the institutional review board of the Gifu University School of Medicine (reference number 24-392) and was performed in accordance with the ethical standards established in the 1964 Declaration of Helsinki.

***Measurements***

Baseline and follow-up investigations were performed in the laboratory. Body weight and body fat were measured to the nearest 0.1 kg with a BC-118D body composition analyzer (TANITA Co., Tokyo, Japan). Heart rate was measured with an automated blood pressure cuff (HEM-7500F, OMRON Healthcare Co., Ltd., Kyoto, Japan). Waist circumference was measured in the standing position to the nearest 0.1 cm with a vinyl tape, at the narrowest circumference between the lowest rib and the iliac crest.

Ankle-brachial pulse wave velocity (PWV), representing arterial stiffness, was measured noninvasively with a form-I automated PWV/ABI analyzer (Colin Co. Ltd., Komaki, Japan) attached to the four limbs with subjects in the supine position.[13] PWV is generally assessed as the time required for a pulse wave to travel a given distance along the blood vessel, and serves as an objective index of atherosclerosis.[14]

A fasting blood sample was taken at 12:30 P.M. on the day of the experiment from the antecubital vein. The study parameters included blood sugar, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) scores, and adiponectin levels. HOMA-IR scores were calculated based on fasting insulin and glucose levels using the following formula: insulin (μU/mL) × glucose (mmol/L) / 22.5.[12]

based on the protocol of Shi et al.[5] They trained on a treadmill 3 days per week for 4 weeks, under either normobaric hypoxic (15.4% $O_2$, equivalent to an altitude of 2500 m) or normobaric normoxic (20.9% $O_2$, equivalent to sea level) conditions for 50 min (including 5-minute warm-up and cool-down periods). In both environmental conditions, a 30-minute rest period preceded and followed each exercise

**TABLE 1** Characteristics of Participants

| | **Hypoxic Training** | | | | | **Normoxic Training** | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Overweight (*n*=8)** | | **Normal weight (*n*=12)** | | | **Overweight (*n*=9)** | | **Normal weight (*n*=12)** | |
| Parameters | Mean | SD | Mean | SD | | Mean | SD | Mean | SD |
| Age, years | 45.6 | 20.9 | 28.6 | 15.6 | | 46.0 | 20.5 | 27.8 | 13.0 |
| Height, cm | 170.9 | 6.2 | 174.2 | 6.3 | | 171.8 | 5.6 | 173.7 | 5.6 |
| Weight, kg | 78.3 | 8.4 | 65.2 | 8.0 | | 79.8 | 11.0 | 63.8 | 8.3 |
| BMI, kg/m$^2$ | 26.8 | 2.3 | 21.5 | 1.9 | | 27.0 | 3.0 | 21.1 | 2.0 |

*BMI = body mass index; SD = standard deviation.*

session. Exercise was performed at an intensity corresponding to 60% of the maximum heart rate (HR max), which was calculated from the age and heart rate at rest (HRrest) using the following formula: [(220−age−HRrest)×0.6+HRrest)]. All subjects were required to rest for 30 minutes after exercise. During the exercise session, HR was monitored to ensure that the exercise intensity did not exceed 60% of HR max. Subjects were asked to report any symptoms of acute altitude sickness (e.g., headache, nausea, or a typical weakness in the legs). Percutaneous oxygen saturation ($SpO_2$) was also monitored for safety with a PULSOX-M24 pulse oximeter (Teijin Pharma Limited, Tokyo, Japan).

***Statistical Analyses***

Values are presented as the mean ± standard deviation. A two-factor analysis of variance (ANOVA) with repeated measures of one factor (before and after training) was used to examine differences in the mean parameter values between the two groups (overweight and normal-weight) and before and after training. A two-way ANOVA was conducted for hypoxic and normoxic training. Multiple post-hoc comparisons were performed with Tukey's honestly significant difference test if a significant main effect or interaction was identified. A probability level of $p<0.05$ was considered statistically significant. STATISTICA 10.0 software (StatSoft Inc., Tulsa, OK, USA) was used for all statistical analyses.

## RESULTS

Table 2 displays the differences in parameters between the overweight and normal-weight hypoxic groups before and after training. Significant main effects were observed before and after training for weight, body fat percentage, BMI, waist circumference, PWV, TC, LDL-C levels, and HOMA-IR scores, as indicated by the elevated levels for these values in the HO group compared to the HN group ($p<0.05$). Significant main effects were observed between the groups for weight, body fat percentage, BMI, heart rate, waist circumference, PWV, TG, HDL-C, and HOMA-IR scores, as indicated by the lower levels for these values after training in both groups ($p<0.05$). Significant interactions were observed with TG, HDL-C, and HOMA-IR scores ($p<0.05$). In the HO group, TG and HOMA-IR levels were lower after the training than before the training, and HDL-C levels were higher after the training than before the training ($p<0.05$).

Table 3 displays the differences in parameters between the overweight and normal-weight normoxic groups before and after training. Significant main effects were observed before and after training for weight, body fat percentage, BMI, waist circumference, PWV, blood sugar, TG, LDL-C, HOMA-IR, and adiponectin levels, as indicated by the elevated levels for these values in the NO group compared to the NN group ($p<0.05$). A significant main effect was observed between the groups for heart rate since it was lower after training compared to before training ($p<0.05$). A significant interaction was observed with waist circumference, which was smaller after training than before training in the NO group ($p<0.05$).

## DISCUSSION

This study evaluated the effects of regular normobaric hypoxic training on metabolic syndrome related-factors according to physique. First, the weight, body fat percentage, BMI, waist circumference, PWV, and TC and LDL levels were reduced by hypoxic training in both groups, regardless of body weight. The improvements in body composition and reduction in body weight associated with hypoxic training may correlate with the increased basal metabolic rate observed under hypoxic conditions.[4] An increased metabolic rate may result from improved substrate utilization and mitochondrial oxidation,[15] via signalling pathways that stimulate GLUT-4 transport.[4,16] Hypoxic conditions are also associated with increased leptin production,[17,18] which can suppress appetite and hence improve body composition.[16] A previous study involving hypoxic training ($O_2$, 15%) for middle-aged obese subjects over 4 weeks indicated that the reduction in body fat content with training was greater in the hypoxic group than in the normoxic group.[18,19] In this study, the weight, BMI, body fat percentage and waist circumference were reduced after hypoxic training, regardless of physique, supporting the results of previous studies.

**TABLE 2** Differences between the Overweight and Normal-Weight Hypoxic Groups Before and After Training

| | | Before Training | | After Training | | Two-Way Analysis of Variance | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Parameters** | **Group** | **Mean** | **SD** | **Mean** | **SD** | | **F-value** | ***p*-value** | **Tukey's honestly significant difference** |
| Weight, kg | HO | 78.34 | 8.43 | 76.46 | 8.80 | F1 | 11.300 | 0.003** | |
| | HN | 65.22 | 8.03 | 64.99 | 7.34 | F2 | 6.250 | 0.022* | |
| | | | | | | F3 | 3.860 | 0.065 | |
| Body fat, % | HO | 26.75 | 5.17 | 25.46 | 6.24 | F1 | 10.860 | 0.004** | |
| | HN | 18.52 | 5.41 | 17.72 | 4.79 | F2 | 10.400 | 0.005** | |
| | | | | | | F3 | 0.570 | 0.461 | |
| Body mass index, kg $m^2$ | HO | 26.83 | 2.41 | 26.24 | 2.76 | F1 | 26.960 | <0.001*** | |
| | HN | 21.48 | 1.98 | 21.37 | 1.73 | F2 | 6.900 | 0.017* | |
| | | | | | | F3 | 3.200 | 0.091 | |
| Heart rate, bpm | HO | 76.38 | 17.99 | 69.75 | 12.28 | F1 | 0.820 | 0.377 | |
| | HN | 70.50 | 10.62 | 65.67 | 9.20 | F2 | 20.950 | <0.001*** | |
| | | | | | | F3 | 0.510 | 0.483 | |
| Waist circumference, cm | HO | 95.75 | 6.90 | 92.44 | 7.64 | F1 | 26.630 | <0.001*** | |
| | HN | 77.58 | 8.24 | 75.86 | 7.65 | F2 | 9.020 | 0.008** | |
| | | | | | | F3 | 3.490 | 0.079 | |
| PWV, cm $sec^{-1}$ | HO | 1425.19 | 396.92 | 1330.75 | 311.28 | F1 | 5.151 | 0.036* | |
| | HN | 1135.67 | 181.84 | 1094.04 | 163.18 | F2 | 6.925 | 0.017* | |
| | | | | | | F3 | 1.043 | 0.321 | |
| Blood sugar, mmol $L^{-1}$ | HO | 100.75 | 38.49 | 97.50 | 13.22 | F1 | 0.035 | 0.854 | |
| | HN | 96.58 | 15.59 | 98.42 | 16.82 | F2 | 0.020 | 0.889 | |
| | | | | | | F3 | 0.256 | 0.619 | |
| Triglycerides, mg $mL^{-1}$ | HO | 198.57 | 179.30 | 109.71 | 70.95 | F1 | 4.404 | 0.051 | Before : HO>HN |
| | HN | 73.67 | 29.54 | 75.92 | 50.90 | F2 | 6.092 | 0.024* | HO : Before>After |
| | | | | | | F3 | 6.741 | 0.019* | |
| Total cholesterol, mg $dL^{-1}$ | HO | 191.00 | 31.08 | 187.75 | 28.56 | F1 | 9.043 | 0.008** | |
| | HN | 159.75 | 22.63 | 155.83 | 19.02 | F2 | 0.733 | 0.403 | |
| | | | | | | F3 | 0.006 | 0.937 | |
| HDL-C, mg $dL^{-1}$ | HO | 45.13 | 16.57 | 50.50 | 15.81 | F1 | 2.380 | 0.140 | |
| | HN | 56.02 | 11.35 | 57.27 | 8.12 | F2 | 12.260 | 0.003** | HO : Before<After |
| | | | | | | F3 | 4.750 | 0.043* | |
| LDL-C, mg $dL^{-1}$ | HO | 113.25 | 25.71 | 112.88 | 34.78 | F1 | 6.876 | 0.017* | |
| | HN | 88.92 | 18.62 | 84.25 | 16.22 | F2 | 0.503 | 0.487 | |
| | | | | | | F3 | 0.364 | 0.554 | |
| Fasting Insulin, μU $mL^{-1}$ | HO | 15.01 | 12.32 | 9.58 | 6.88 | F1 | 1.729 | 0.205 | |
| | HN | 9.58 | 12.67 | 5.65 | 4.00 | F2 | 3.307 | 0.086 | |
| | | | | | | F3 | 0.086 | 0.772 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| HOMA-IR, units | HO | 3.44 | 2.34 | 2.31 | 1.64 | F1 | 5.465 | 0.031* | Before : HO>HN |
| | HN | 1.41 | 0.69 | 1.43 | 1.17 | F2 | 5.128 | 0.036* | HO : Before>After |
| | | | | | | F3 | 5.473 | 0.031* | |
| Adiponectin, μg mL$^{-1}$ | HO | 5.88 | 3.23 | 6.14 | 4.04 | F1 | 3.887 | 0.066 | |
| | HN | 8.64 | 1.63 | 9.16 | 3.00 | F2 | 0.080 | 0.781 | |
| | | | | | | F3 | 0.281 | 0.603 | |

**p<0.05, **p<0.01, ***p<0.001.*
*F1 = difference between groups; F2 = difference before and after training; F3 = interaction; HDL-C = high-density lipoprotein cholesterol; HO = hypoxic overweight group; HN = hypoxic normal-weight group; HOMA-IR = homeostatic model analysis ratio; LDL-C = low-density lipoprotein cholesterol; PWV = ankle-brachial pulse wave velocity; SD = standard deviation.*

**TABLE 3** Differences between the Overweight and Normal-Weight Normoxic Groups Before and After Training

| | | Before Training | | After Training | | Two-Way Analysis of Variance | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Parameters** | **Group** | **Mean** | **SD** | **Mean** | **SD** | | **F-value** | ***p*-value** | **Tukey's honestly significant difference** |
| Weight, kg | **NO** | 79.78 | 10.98 | 79.62 | 9.62 | F1 | 16.140 | 0.001** | |
| | **NN** | 63.79 | 8.29 | 63.28 | 8.07 | F2 | 1.790 | 0.197 | |
| | | | | | | F3 | 0.520 | 0.481 | |
| Body fat, % | **NO** | 29.13 | 5.88 | 29.16 | 4.45 | F1 | 34.310 | <0.001*** | |
| | **NN** | 17.07 | 4.84 | 16.41 | 4.40 | F2 | 0.680 | 0.420 | |
| | | | | | | F3 | 0.780 | 0.389 | |
| Body mass index, kg m$^2$ | **NO** | 26.99 | 3.13 | 26.95 | 2.78 | F1 | 29.480 | <0.001*** | |
| | **NN** | 21.11 | 2.12 | 20.93 | 2.06 | F2 | 1.610 | 0.219 | |
| | | | | | | F3 | 0.790 | 0.384 | |
| Heart rate, bpm | **NO** | 78.67 | 14.46 | 73.11 | 13.66 | F1 | 2.067 | 0.168 | |
| | **NN** | 70.67 | 11.67 | 65.91 | 9.93 | F2 | 6.060 | 0.024* | |
| | | | | | | F3 | 0.017 | 0.898 | |
| Waist circumference, cm | **NO** | 96.22 | 6.80 | 94.61 | 6.85 | F1 | 50.870 | <0.001*** | |
| | **NN** | 74.88 | 6.48 | 74.79 | 5.91 | F2 | 3.000 | 0.100 | NO: Before>After |
| | | | | | | F3 | 6.220 | 0.023* | |
| PWV, cm sec$^{-1}$ | **NO** | 1499.94 | 416.29 | 1481.61 | 397.56 | F1 | 9.934 | 0.005** | |
| | **NN** | 1090.08 | 150.90 | 1104.21 | 166.30 | F2 | 0.006 | 0.942 | |
| | | | | | | F3 | 0.327 | 0.574 | |
| Blood sugar, mmol L$^{-1}$ | **NO** | 106.71 | 23.21 | 102.57 | 14.70 | F1 | 10.420 | 0.005** | |
| | **NN** | 86.64 | 5.94 | 85.45 | 6.12 | F2 | 1.360 | 0.261 | |
| | | | | | | F3 | 0.420 | 0.526 | |
| Triglycerides, mg mL$^{-1}$ | **NO** | 149.43 | 62.77 | 143.14 | 97.26 | F1 | 7.570 | 0.014* | |
| | **NN** | 85.00 | 36.95 | 71.64 | 26.00 | F2 | 0.765 | 0.395 | |
| | | | | | | F3 | 0.099 | 0.757 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Total cholesterol, mg dL$^{-1}$ | **NO** | 208.43 | 32.66 | 198.57 | 23.67 | F1 | 3.859 | 0.067 | |
| | **NN** | 174.36 | 25.22 | 179.55 | 32.97 | F2 | 0.375 | 0.549 | |
| | | | | | | F3 | 3.881 | 0.066 | |
| HDL-C, mg dL$^{-1}$ | **NO** | 50.14 | 11.94 | 52.43 | 13.33 | F1 | 4.352 | 0.053 | |
| | **NN** | 61.86 | 11.26 | 64.64 | 12.34 | F2 | 4.188 | 0.058 | |
| | | | | | | F3 | 0.039 | 0.846 | |
| LDL-C, mg dL$^{-1}$ | **NO** | 131.43 | 33.75 | 122.71 | 23.72 | F1 | 5.143 | 0.038* | |
| | **NN** | 95.45 | 23.67 | 99.00 | 30.30 | F2 | 0.713 | 0.411 | |
| | | | | | | F3 | 4.012 | 0.062 | |
| Fasting Insulin, μU mL$^{-1}$ | **NO** | 10.76 | 8.49 | 9.91 | 9.42 | F1 | 3.478 | 0.081 | |
| | **NN** | 6.85 | 8.05 | 4.05 | 1.96 | F2 | 0.635 | 0.437 | |
| | | | | | | F3 | 0.182 | 0.675 | |
| HOMA-IR, units | **NO** | 2.81 | 2.17 | 2.59 | 2.50 | F1 | 5.570 | 0.031* | |
| | **NN** | 1.50 | 1.85 | 0.87 | 0.43 | F2 | 0.550 | 0.469 | |
| | | | | | | F3 | 0.127 | 0.726 | |
| Adiponectin, μg mL$^{-1}$ | **NO** | 4.99 | 2.87 | 5.50 | 3.68 | F1 | 9.674 | 0.008* | |
| | **NN** | 9.71 | 2.35 | 9.51 | 2.45 | F2 | 0.007 | 0.936 | |
| | | | | | | F3 | 2.168 | 0.165 | |

**p<0.05, **p<0.01, ***p<0.001.*
*F1 = difference between groups; F2 = difference before and after training; F3 = interaction; HDL-C = high-density lipoprotein cholesterol; HOMA-IR = homeostatic model analysis ratio; LDL-C = low-density lipoprotein cholesterol; NN = normoxic normalweight group; NO = normoxic overweight group; PWV = ankle-brachial pulse wave velocity; SD = standard deviation.*

PWV is the rate at which blood leaving the heart circulates back to the heart, and is an indicator of the degree of arterial sclerosis (i.e., a faster rate indicates a greater risk of cardiovascular disease). Hirai et al. reported that arterial stiffness correlated highly with cardiovascular disease, and that PWV independently predicted cardiovascular risk.[20] In a crossover study by Shi et al. involving 4 weeks of aerobic exercise in a 2500-m hypoxic environment for male college students, PWV was significantly lower in the hypoxic group after training.[5] In addition, Nishiwaki et al. reported that hypoxic training increased flow-mediated vasodilation (FMD) (an indicator of increased blood flow) and reduced PWV, similar to the results of this study.[21] Katayama et al. reported that aerobic exercise improved vascular endothelial function to a greater extent in a hypoxic environment than in a sea-level environment.[3] Exercise-induced augmentation of blood flow and the subsequent increase in laminar shear stress have been reported to cause vasodilation and to upregulate endothelial nitric oxide (NO) synthase.[10,22,23] Systemic acute hypoxia induces vasodilation in conduit arteries. Furthermore, a combination of submaximal exercise and hypoxia also causes vasodilation. Casey et al. reported that vasodilation during exercise in hypoxia was due to NO from the endothelium.[24] These results are similar to the physiological adaptation induced by aerobic exercise, but regular aerobic exercise is expected to lead to more effective cardiovascular adaptation in hypoxic environments than under sea-level conditions.

Meanwhile, significant interactions were observed in TG, HDL, and HOMA-IR levels. This suggests that the effects of hypoxic training are greater for people who are overweight than for those who are of a normal weight. The effects of hypoxic exercise on lipid metabolism vary with the study subjects and environmental conditions.[3] Our finding that hypoxic training did not increase LDL levels is consistent with the findings of a number of previous studies; however, our HDL results are inconsistent.[4] Wee and Climstein found that hypoxic training significantly reduced total cholesterol (TC) levels in obese subjects with dyslipidemia and metabolic syndrome.[4] However, the extent of the reduction beyond the effects of exercise has varied, and there have been few controlled studies. HDL and LDL levels have been strongly associated with metabolic syndrome, though no clear conclusions can be drawn on the effects of hypoxic training on these parameters.[25] Katayama reported that glucose metabolism increased with exercise in an acute hypoxic environment, while lipid metabolism improved marginally.[25] The improvement in HDL levels may be related to weight loss and improvements in body composition through an increase in the metabolic rate. Shin et al. reported that HDL significantly increased after training in the hypoxic group, but did not differ from that in the normoxic group.[11] HDL and TG levels are closely related to weight gain, and regular aerobic exercise induces weight loss and improves lipid metabolism. In the overweight group, the extent of weight loss and improvements in body composition by hypoxic training was relatively large, and the positive effects on both variables were also significant.

Although insulin sensitivity was not determined directly in this study, we obtained HOMA index values, which highly correlate with insulin sensitivity or resistance. The HOMA-IR index also significantly decreased in the HO group. Morishima et al. found that 4 weeks of hypoxic training in obese subjects suppressed elevated blood glucose levels more effectively than the same training under sea-level conditions.[26] Mackenzie et al. analyzed insulin sensitivity in sea-level and hypoxic environments in patients with type 2 diabetes, and reported that insulin sensitivity increased significantly after exercise under hypoxic conditions.[27]

Haufe et al. reported that HOMA index values as well as glucose and insulin responses to oral glucose tolerance testing improved with training, and even more so when training was combined with hypoxia.[2] The relative increase in the glucose oxidation rate during physical activity after hypoxic training was attributed to transactivation of hypoxia-inducible factor 1 (HIF-1).[28] Activation of the regulatory subunit HIF-1$\alpha$ leads to cellular adaptations that counteract the effects of the reduced oxygen supply to cells under hypoxic conditions.[2] These adaptations include the induction of several genes, such as those encoding phosphofructokinase, GLUT-1, and other proteins involved in glucose metabolism.[2,29] In this study, HOMA-IR decreased significantly with hypoxic training, thereby suggesting that insulin resistance had improved.

## LIMITATIONS

In this study, the effects of participant factors, such as social status, lifestyle, and exercise experience, on the training effect were not considered. The mean BMI of the normal and overweight groups in this study were 21.3 and 26.9, respectively. Generally, BMI averages of normal weight and overweight are 21.7 and 27.5, respectively, based on the BMI range of normal (18.5–24.9 BMI) and overweight (25.0–29.9) individuals. Therefore, the BMI of the participants were slightly lower than the averages of participants included in this study.

## CONCLUSION

This study investigated the effects of regular normobaric hypoxic training on metabolic syndrome-related factors according to physique. Hypoxic training improved the weight, body fat percentage, BMI, waist circumference, PWV, and TC and LDL levels in overweight and normal-weight men. In addition, there were significant interactions between improvements in TG, HDL, and HOMA-IR levels, and hypoxia exposure in the overweight group. These results indicate that hypoxic training can improve arterial stiffness, circulatory system function, body composition, and energy metabolism in adult males.

## DISCLOSURE

The authors have no conflicts of interest to declare.

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