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EFFECTS OF VARIOUS HYPOBARIC HYPOXIA ON METABOLIC RESPONSE, SKELETAL MUSCLE OXYGENATION, AND EXERCISE PERFORMANCE IN HEALTHY MALES

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ABSTRACT

Objective

This study aimed to evaluate the effect of various levels of hypoxia versus normoxia on exercise performance, measured by metabolic parameters and skeletal muscle oxygenation profiles during graded exercise test (GXT) in healthy men.

Methods

In this randomized crossover trial, 11 healthy male participants (age 21.5 ± 2.3 years) performed the GXT using a cycle ergometer at sea-level (760 torr) and at various hypobaric hypoxia: 633, 526, and 433 torr, corresponding to simulated altitudes of 1500, 3000, and 4500 m, respectively. The GXT was started at 50 W and increased by 25 W every 2 min until the participants were exhausted. The pedal frequency was set to 60 rpm. Metabolic parameters (heart rate, HR; minute ventilation, VE; carbon dioxide excretion, VCO_2; respiratory exchange ratio, RER; peripheral capillary saturation, SpO_2; oxygen consumption, VO_2; and blood lactate, O_2 pulse) and skeletal muscle oxygen profiles (oxygenated hemoglobin and myoglobin, OxyHb; deoxygenated hemoglobin and myoglobin, DeoxyHb; and tissue oxygen saturation, StO_2) were measured for every 2 min during the GXT. Exercise performance was evaluated by maximal oxygen consumption, peak power, and duration of exercise time obtained through GXT.

Results

Regarding metabolic parameters, HR ($P < 0.05$), VE, ($P < 0.05$), VCO_2 ($P < 0.05$), RER ($P < 0.05$), and blood lactate ($P < 0.05$) showed significant increase under hypoxia compared to normoxia. Moreover,

the increase was more pronounced as hypoxia became more severe. However, the S_pO_2 ($P < 0.05$) and O_2 pulse ($P < 0.05$) presented a significant decrease under hypoxia compared to normoxia. Similarly, the decrease was more pronounced as hypoxia became more severe. VO_2 ($P > 0.05$) did not show significant difference under different environmental conditions. In skeletal muscle oxygen profiles, none of the parameters showed noticeable changes. Regarding exercise performance, VO_2max ($P < 0.05$) and exercise time ($P < 0.05$) decreased significantly as hypoxia became more severe, and peak power ($P < 0.05$) decreased significantly at simulated altitudes of 3000 and 4500 m compared to normoxia.

Conclusion

A decrease in exercise performance is due to a decrease in metabolic function under various hypoxia compared to normoxia and the decrease was more pronounced as hypoxia became more severe.

Keywords: *exercise performance; graded exercise test; hypoxia; metabolic function; NIRS; skeletal muscle oxygenation*

INTRODUCTION

Under hypobaric hypoxia, the partial pressure of oxygen decreases due to low atmospheric pressure. This results in reduction of alveolar oxygen partial pressure, arterial oxygen saturation, and arteriovenous oxygen difference, thereby diminishing the capacity of oxygen delivery and utilization.[1–4] These physiological changes under hypobaric hypoxia are known to cause deterioration in energy metabolism, hemodynamic function, and vascular function, and reduce oxygen transportation and utilization, thereby reducing exercise performance.[5]

In the previous studies, the exercise time, maximal oxygen consumption (VO_2max), and exercise load were reduced when graded exercise tests (GXT) were performed at various simulation altitudes with 75% maximal heart rate (HRmax). It has been consistently reported that acute exposure to various hypobaric hypoxia affects exercise performance negatively.[6,7] Furthermore, hypoxia reduces oxygen consumption (VO_2) in skeletal muscles during exercise and accelerates the accumulation of fatigue-related metabolites because of reduced oxidative phosphorylation ability.[8] In addition, as the altitude increases, the respiratory exchange rate (RER) and blood lactate concentration increase significantly. The researchers explained that exercise under hypoxia reduces oxygen transport and utilization to active muscles because of low oxygen partial pressure in the alveoli, thereby increasing substrate-level phosphorylation and carbon dioxide excretion (VCO_2) by hypoxic ventilation response (HVR).[9,10]

Many aspects of hemodynamic and hemorheological functions, as well as energy metabolism, are considered while conducting studies on the mechanism of exercise performance reduction during hypoxia.[11,12] In a study assessing cardiac function and hemodynamics, the cardiac output (CO) and stroke volume (SV) were significantly lower when performing the GXT under hypoxia than those measured under normoxia.[13,14] It was reported that exercise during hypoxia might be associated with a decrease in end-diastolic volume (EDV) and end-systolic volume (ESV) and an increase in heart rate (HR), ejection fraction (EF), and CO during submaximal exercise.[15] These hemodynamic changes are an acute compensation response to decreased oxygen delivery and utilization capacities under hypobaric hypoxia.[16] Furthermore, under severe hypoxia, the RBC deformability, a hemorheological index that indicates ability to deliver oxygen to tissues, decreases.[6] This decrease in hemorheological function plays a key role in reducing exercise performance because it lowers oxygen supply to microvessels and tissues.[7,17]

Near-infrared spectroscopy (NIRS) is used to identify the physiological mechanisms of changes in exercise performance during exercise. NIRS enables the measurement of skeletal muscle oxygenation profiles and the ability to deliver and use oxygen in muscle tissues.[18] The NIRS signal reflects a dynamic balance between muscle capillary blood flow and muscular VO_2 in microcirculation.[18,19] In this regard, another study reported a static correlation between exercise performance and skeletal muscle oxygenation.[20] Also, it was reported that assessing oxygen-transporting and utilizing capacity in muscles through NIRS is vital because it is highly associated with exercise performance ability.[21] Most of the previously conducted studies have confirmed skeletal muscle oxygenation profiles in a single hypoxic condition using NIRS. However, there are few studies evaluating skeletal muscle oxygenation during exercise under various hypoxic conditions.[3]

Therefore, the purpose of this study was to evaluate the effects of various hypobaric hypoxia (simulated altitude) versus normoxia (sea-level) on exercise performance via metabolic parameters and skeletal muscle oxygenation profiles during GXT in healthy men.

MATERIALS AND METHODS

Participants

We included 11 healthy men (age, 21.5 ± 2.1 years; height, 178.3 ± 5.5 cm; weight, 71.1 ± 4.2 kg) who did not participate in any planned exercise program for the past 6 months, did not take dietary supplements, and did not live at high altitudes for 3 months. The subjects were nonsmokers and had no history of musculoskeletal, cardiovascular, pulmonary, or metabolic disease. All subjects received information about the purpose and process of this study and provided informed consent prior to the start of the study. The characteristics of the subjects are presented in Table 1. This study was approved by the IRB at Konkuk University (7001355-201805-HR-241) and was performed in accordance with the provisions of the Declaration of Helsinki.

TABLE 1 Participant Characteristics (n = 11).

Variable	Mean ± SD
Age (years)	21.5 ± 2.16
Height (cm)	178.3 ± 5.52
Weight (kg)	71.1 ± 4.22
BMI (kg/m^2)	22.3 ± 1.32
Muscle mass (kg)	57.8 ± 4.82
Lean body mass (kg)	61.4 ± 5.08
Fat mass (kg)	9.6 ± 2.46
Body fat (%)	13.5 ± 3.57

BMI, body mass index, SD, standard deviation.

Study Design

The study design of this study is shown in Figure 1. The subjects visited the laboratory for five times during the experimental period. The subjects' body composition was measured during the first visit at sea-level (760 torr). To minimize the adaptation effect of each condition during the main experiments, sea-level (760 torr) and various hypobaric hypoxia (1500 m, 634 torr; 3000 m, 526 torr; and 4500 m, 433 torr) were randomly selected, and each condition was set up with a wash-out period of 2 weeks. The GXT of exercise performance (started at 50 W and increased by 25 W every 2 min) was conducted with a bicycle ergometer (Monark Ergomedc 828E, Monark, Sweden) at sea-level (760 torr) and various simulated altitudes after resting for 30 min. Once the subjects began their exercise, HR, VE, VO_2, VCO_2, RER, O_2 pulse (K5, COSMED, Monte Savello, Italy), oxygen saturation (% S_pO_2, Radical-7 pulse oximeter, MASIMO, CA, USA) and NIRS (Astem, Mizonokuchi, Japan), which are the subjects' energy metabolism parameters, were measured at every 10 s, while blood lactate concentration was measured at every 1 min. The average values at each exercise load during 2 min were used for all results. The GXT was performed in a chamber with environmental control, at a mean

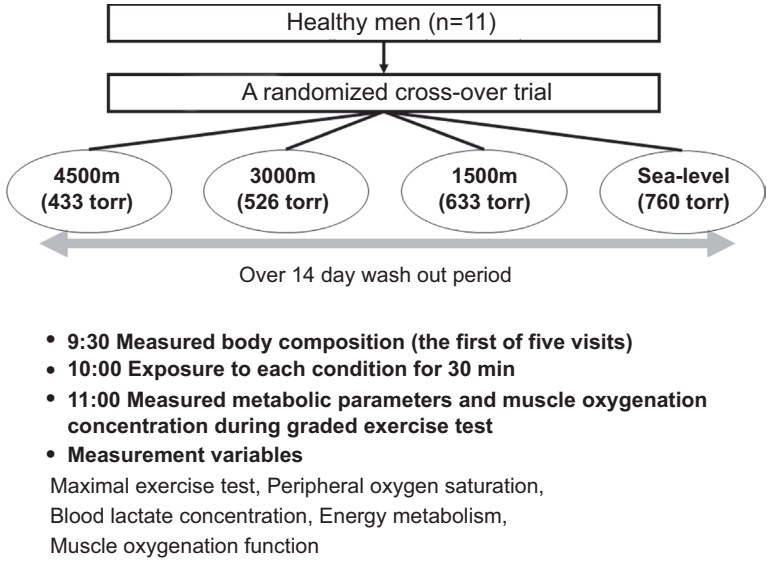

FIGURE 1 Study design.

temperature of 23 ± 1°C, and a mean humidity of 50 ± 5%. The dimensions of the chamber were 9 m (width) × 7 m (length) × 3 m (height).

Measurement

Body composition (fat mass, lean body mass, percentage of body fat, weight, and height) was measured using Inbody 770 (Inbody, Seoul, South Korea). Body mass index (BMI) was calculated by dividing the body weight (kg) by the square of body height (m^2). The subjects wore lightweight clothing and were asked to remove any metal items.

Peripheral capillary oxygen saturation was measured after the subjects had adapted to sea-level for 30 min and at various hypobaric hypoxia. The sensors of the Radical-7 pulse oximeter (MASIMO, CA, USA) were placed on the bicycle ergometer seat and fixed on the index finger. The analysis was performed at an average of 2 min each with identical load during rest and GXT every 10 s.

Lactate concentration was tested by drawing 80 μL of blood from the capillaries of the fingertip and analyzed using the Lactate pro2 Lactic Acid Analyzer (Arkray, Kyoto, Japan). The test recorded the average value measured at every 1 min during rest and until exhaustion, consistently, giving the average value of every 2 min.

The HR, VE, VO_2, VCO_2, RER, O_2 pulse, and VO_2max values were measured using the automatic metabolism analyzer K5 (COSMED, Monte Savello, Italy). The analysis performed indicated an average value of 2 min at each identical load during rest and GXT every 10 s. The K5 equipment was calibrated in each condition before the experiment started. The measured VO_2max was compared for each condition.

The analysis of levels of oxygenated hemoglobin (Oxy_Hb), deoxygenated hemoglobin (Deoxy_Hb), total hemoglobin (Total_Hb), and tissue oxygen saturation (StO_2) was performed using multi-channel tissue oxygenation monitor (Near Infrared Spectroscopy (NIRS), Astem, Mizonokuchi, Japan) by reviewing laser signals (wave length: 775, 810, and 850 nm). The signals were shot from the light-emitting area of the subject's vastus lateralis muscle and were received at the absorber after it had returned penetrating the muscle tissues. The test recorded the average value measured every 10 s

while at rest and until exhaustion, consistently, giving an average value every 2 min.

In order to measure VO_2max, an automatic analyzer K5 (COSMED, Monte Savello, Italy) and a bicycle ergometer (Monark Ergomedc 828E, Monark, Sweden) were prepared, after which the GXT was conducted. In each environment, the GXT was terminated when two or more criteria were met. The criteria used for achieving a threshold for exhaustion are plateau in VO_2 as workload increases, an RER greater than 1.15, and maximal HR is the predicted maximal HR (220 – age).

Statistical Analysis

All data obtained in the present study were analyzed using SPSS software version 25.0 for Windows (IBM Corp., Armonk, NY, USA). Data were presented as mean ± standard deviation. The assumption of normality and homoscedasticity was verified using the Sharpiro–Wilks W-test before parametric tests. First, a two-way analysis of variance (ANOVA) with repeated measures was used to elucidate the interaction effects between environmental conditions and exercise time. Second, repeated one-way ANOVA was used to evaluate differences in dependent variables between all environmental conditions at each time point, and the post hoc test was used the Bonferroni test. A significance level of $P < 0.05$ was used to determine the statistical difference.

RESULTS

Energy Metabolism during GXT

Energy metabolism parameters at rest and during exercise are shown in Figure 2. A significant interaction ($n^2 = 0.236$, $P < 0.001$) was observed between environmental conditions and exercise time in S_pO_2. As a result of post hoc analysis, S_pO_2 was significantly lower ($P < 0.05$) at hypobaric hypoxia (433 torr) than all environmental conditions at most exercise loads. Furthermore, S_pO_2 was significantly lower ($P < 0.05$) at hypobaric hypoxia (623 torr) than at sea-level (760 torr) and hypobaric hypoxia (633 torr), but hypobaric hypoxia (633 torr) was significantly lower ($P < 0.05$) than sea-level (760 torr) (Figure 2A).

Heart rate showed a significant interaction ($n^2 = 0.336$, $P < 0.001$) between environmental condition and exercise time. HR was significantly higher ($P < 0.05$) at hypobaric hypoxia (433 torr) and hypobaric hypoxia (623 torr) than at sea-level (760 torr) at most exercise loads. Furthermore, HR was significantly higher ($P < 0.05$) at hypobaric hypoxia (433 torr) than hypobaric hypoxia (633 torr) (Figure 2B).

Minute ventilation presented a significant interaction ($n^2 = 0.679$, $P < 0.001$) between environmental condition and exercise time. VE was significantly higher ($P < 0.05$) at hypobaric hypoxia (526 torr) and hypobaric hypoxia (433 torr) than hypobaric hypoxia (633 torr) and at sea-level (760 torr) at most exercise loads (Figure 2C).

VO_2 presented a significant interaction ($n^2 = 0.374$, $P < 0.001$) between environmental condition and exercise time. Post hoc analyses found that VO_2 increased ($P < 0.05$) significantly at hypobaric hypoxia (433 torr) than all other environmental conditions at rest. However, no main effect in environmental condition was observed ($n^2 = 0.147$, $P = 0.184$) and there was no significant difference between sea-level and various simulated altitudes at most exercise loads (Figure 2D).

There was a significant interaction ($n^2 = 0.551$, $P < 0.001$) between environmental condition and exercise time in O_2 pulse. Post hoc analyses found that O_2 pulse was significantly lower ($P < 0.05$) at hypobaric hypoxia (526 torr) and hypobaric hypoxia (422 torr) than other environmental conditions at most exercise loads (Figure 2E).

VCO_2 showed a significant interaction ($n^2 = 0.299$, $P < 0.001$) between environmental condition and exercise time. VCO_2 was significantly higher ($P < 0.05$) at hypobaric hypoxia (433 torr) than all other environmental conditions at most exercise loads. Furthermore, VCO_2 was significantly higher ($P < 0.05$) at hypobaric hypoxia (526 torr) than hypobaric hypoxia (633 torr) (Figure 2F).

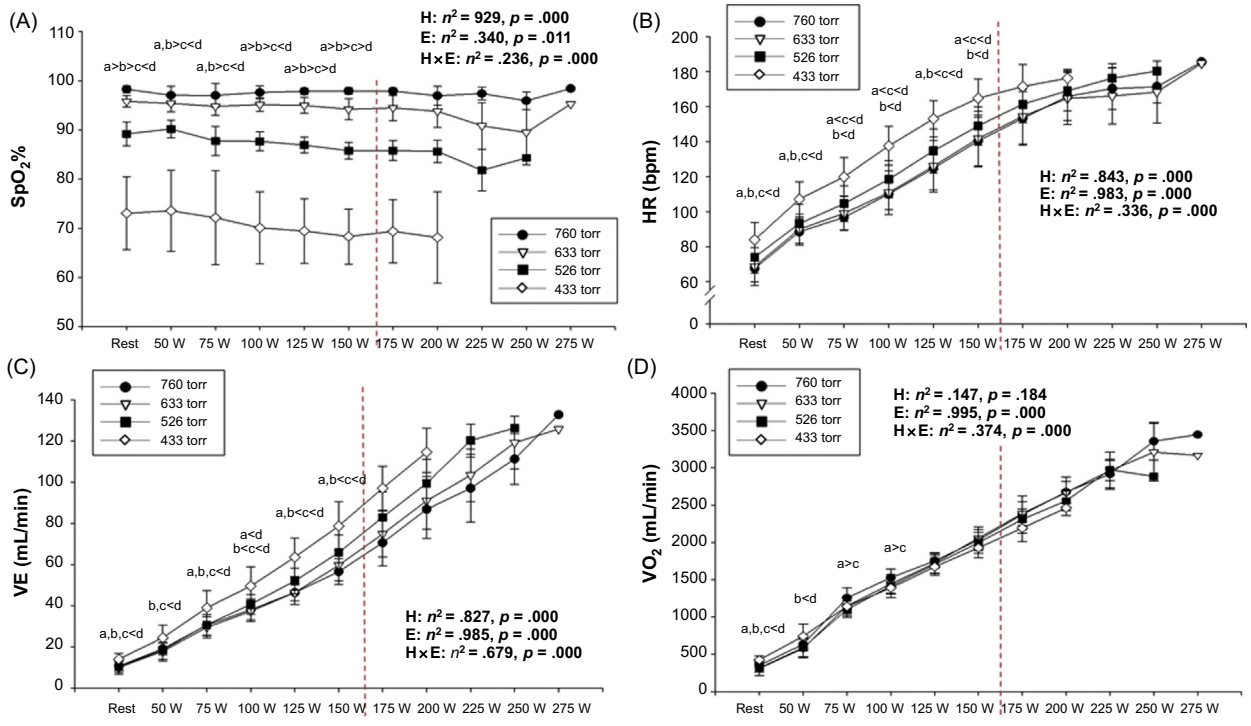

FIGURE 2 Changes in metabolic parameters at rest and during GXT. (A) Change in S_pO_2 (%), (B) change in HR (bpm), (C) change in VE (L/min), (D) change in VO_2 (mL/min), (E) change in O_2 pulse (mL/min), (F) change in VCO_2 (mL/min), (G) change in RER, (H) change in blood lactate level (mmol/L); a =760 torr, b = 633 torr, c = 526 torr, d = 433 torr; greater than (>) or less than (<) indicates significant difference. Different lowercase letters indicate significant differences in hypoxia groups. No alphabet of time indicates not significant. Red line: For comparison of each condition, statistical analysis was conducted with the results of up to 10 min; all subjects completed the GXT. GXT: graded exercise test, n^2: partial eta squared, H: hypoxia, E: exercise, S_pO_2: peripheral capillary oxygen saturation, HR: heart rate, VE: minute ventilation, VO_2: oxygen uptake, O_2 pulse: oxygen pulse, VCO_2: carbon dioxide exertion, RER: respiratory exchange ratio. *Continues*

There was a significant interaction in RER (n^2 = 0.312, P < 0.001) between environmental condition and exercise time. RER was significantly higher (P < 0.05) at hypobaric hypoxia (433 torr) than all other environmental conditions. It was also significantly higher (P < 0.05) at hypobaric hypoxia (526 torr) than hypobaric hypoxia (533 torr) and sea-level (760 torr) at most exercise loads (Figure 2G).

Blood lactate level showed a significant interaction (n^2 = 0.740, P < 0.001) between environmental condition and exercise time. Blood lactate level was significantly higher (P < 0.05) at hypobaric hypoxia (433 torr) than all other environmental conditions at most exercise loads. It was significantly higher (P < 0.05) at hypobaric hypoxia (526 torr) than at sea-level (760 torr) (Figure 2H).

Muscle Oxygenation during GXT

Muscle oxygenation profiles at rest and during exercise are shown in Figure 3. There was a significant interaction between environmental condition

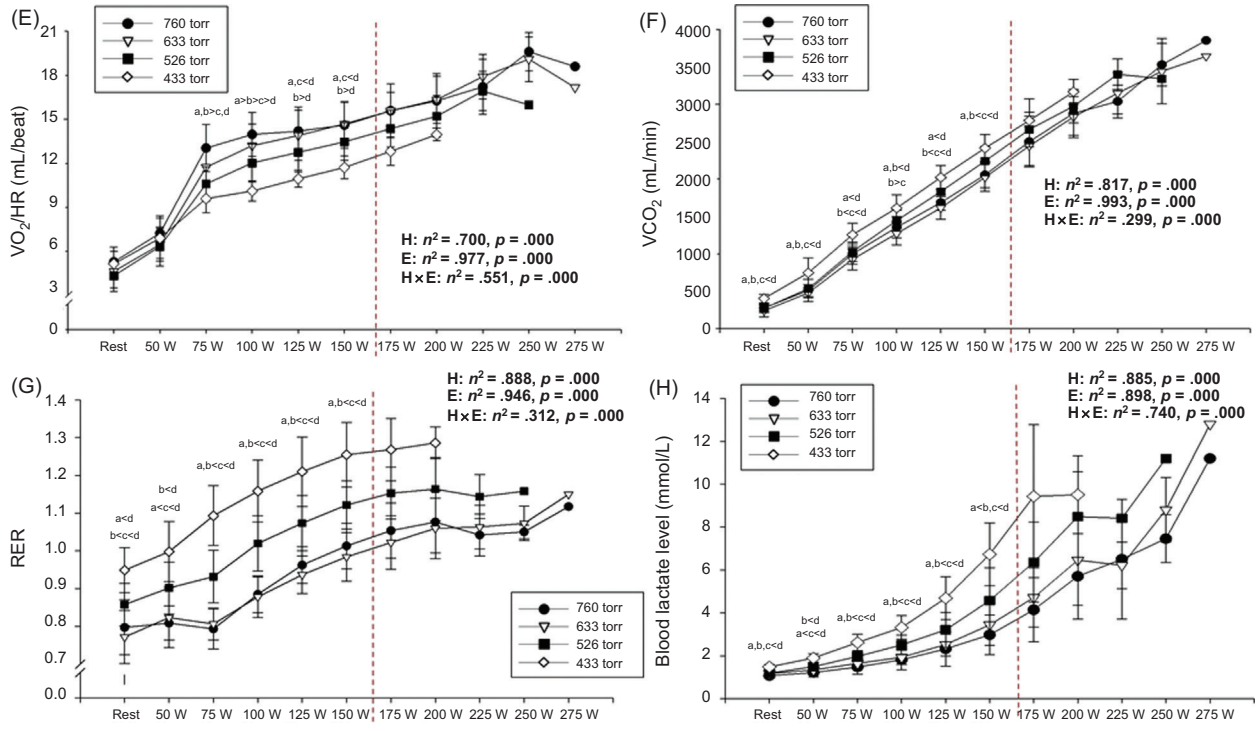

FIGURE 2 *Continued*

and exercise time in Oxy_Hb ($n^2 = 0.150$, $P = 0.045$) and StO_2 ($n^2 = 0.178$, $P = 0.010$). Post hoc analyses found that Oxy_Hb decreased ($P < 0.05$) significantly at hypobaric hypoxia (526 torr) than at sea-level (760 torr) at 50 and 75 watt of exercise load (Figure 3A). However, Oxy_Hb tended to be lower at sea-level than under most hypoxic conditions. StO_2 showed a significant decrease ($P < 0.05$) at hypobaric hypoxia (433 torr) than at hypobaric hypoxia (633 torr) at 100 watt of exercise load (Figure 3D). Overall, StO_2 presented a tendency similar to Oxy_Hb. Deoxy_Hb ($n^2 = 0.128$, $P = 0.124$) and Total_Hb ($n^2 = 0.063$, $P = 0.811$) showed no significant interaction between environmental condition and exercise time (Figures 3B and C).

Exercise Performance

There was a significant main effect within environmental condition in VO_2max ($n^2 = 0.941$, $P < 0.001$), peak power ($n^2 = 0.803$, $P < 0.001$), and exercise time ($n^2 = 0.921$, $P < 0.001$). As a result of post hoc analysis, VO_2max and exercise time showed a significant decrease ($P < 0.05$) proportionally with increase in simulated altitude (Figures 4A and C). Peak power also showed the same statistical changes as other exercise performance parameters (e.g., VO_2max and exercise time); however, there was no significant difference between sea-level (760 torr) and hypobaric hypoxia (633 torr) (Figure 4B).

DISCUSSION

Response to reduction phenomenon based on metabolic parameters and skeletal muscle oxygenation profiles for the change in exercise performance according to altitude was revealed. In metabolic parameters, HR, VE, VCO_2, RER, and blood lactate level increased, while O_2 pulse and SpO_2 decreased during the GXT at various hypobaric hypoxia

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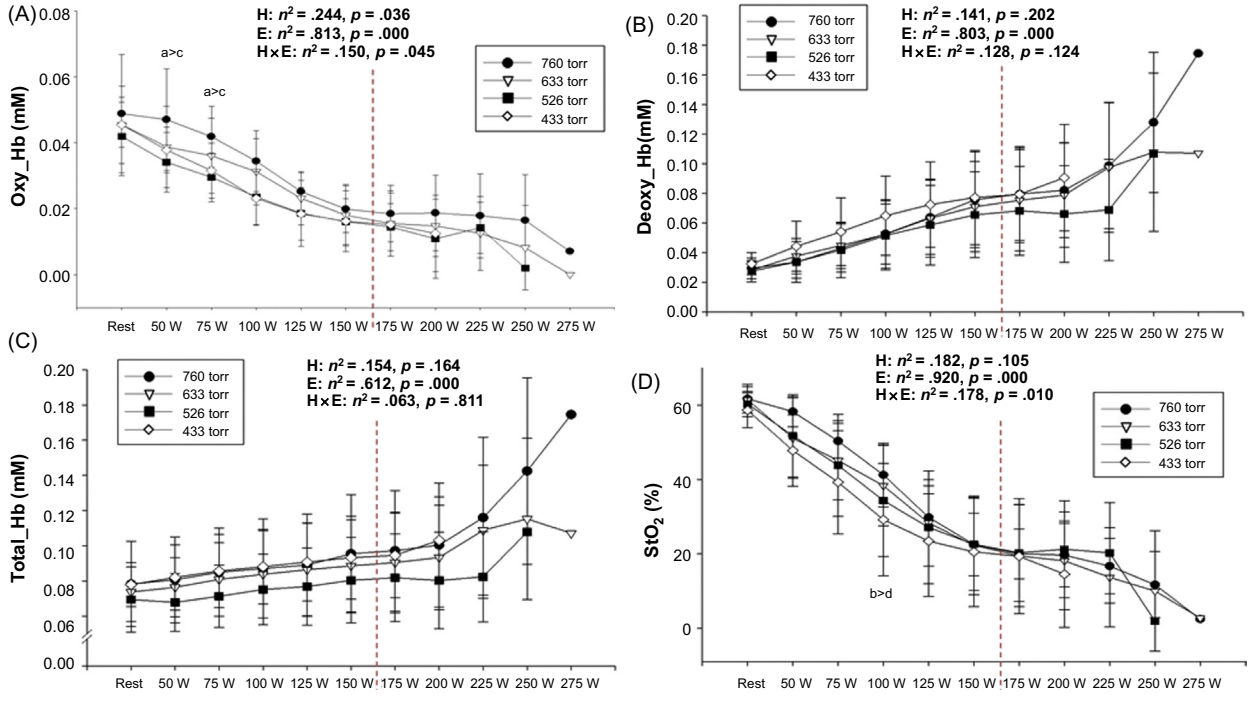

FIGURE 3 Changes in muscle oxygenation profiles at rest and during GXT. (A) Change in Oxy_Hb (%), (B) change in Deoxy_Hb (%), (C) change in total_Hb (%), (D) change in StO_2 (%); a = 760 torr, b = 633 torr, c = 526 torr, d = 433 torr; greater than (>) or less than (<) indicates significant difference. Different lowercase letters indicate significant differences in hypoxia groups. No alphabet of time indicates not significant. Red line: For comparison of each condition, statistical analysis was conducted with the results of up to 10 min; all subjects completed the GXT. GXT: graded exercise test, n^2: partial eta squared, H: hypoxia, E: exercise, Oxy_Hb: oxygenated hemoglobin, Deoxy_Hb: deoxygenated hemoglobin, Total_Hb: total hemoglobin, StO_2: tissue oxygen saturation.

compared with sea-level. However, VO_2 did not show any outstanding difference between environmental conditions. In muscle oxygenation profiles, no parameter (e.g., Oxy_Hb, Deoxy_Hb, Total_Hb, and StO_2) showed noticeable changes at various hypobaric hypoxia compared with sea-level. In exercise performance, VO_2max, peak power, and exercise time decreased proportionally with increase in simulated altitude.

Energy Metabolism

In our results, the level of S_pO_2 was significantly lower ($P < 0.05$) at various hypobaric hypoxia than at sea-level at all exercise loads. A previous study reported that the decrease in S_pO_2 is caused by the promotion of oxygen dissociation to compensate for the lack of oxygen in tissues.[22] Considering that the oxygen dissociation curve is an "S" shape curve, it can be understood that when PO_2 of the x-axis decreases, the oxygen saturation of hemoglobin drops rapidly.[23] It has been reported that individuals in hypoxic conditions have high respiratory frequency and increased dead space ventilation, which cause lower oxygen saturation than at sea-level.[24]

The RER results of this study showed no difference between sea-level and hypobaric hypoxia (633 torr) at all exercise loads. However, there was a significant difference ($P < 0.05$) at both hypobaric

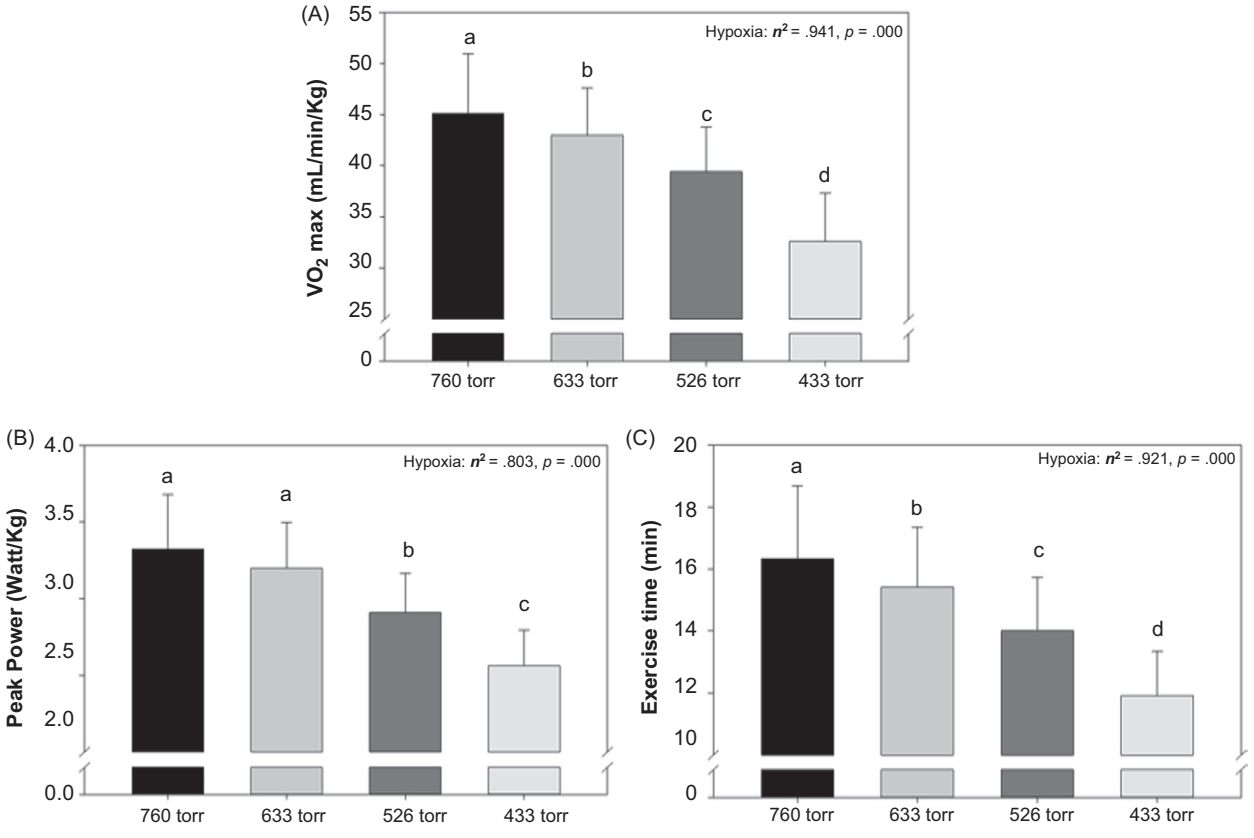

FIGURE 4 Exercise performance at all environmental conditions. (A) Change in VO_2max, (B) change in peak power, and (C) change in exercise time. a, b, c, and d: Different alphabets indicate significant difference, VO_2max: maximal oxygen consumption.

hypoxia (633 tor) and (433 torr) compared with other environmental conditions. In other words, the carbohydrate oxidation rate is high at hypobaric hypoxia (526 torr) and hypobaric hypoxia (433 torr) at all exercise loads. A previous study compared metabolic function during 60 min of aerobic exercise at 50% VO_2max at sea-level and normobaric hypoxia (inspired oxygen fraction, F_iO_2 = 12.4%).[25] The results showed a significant increase in RER and carbohydrate oxidation at normobaric hypoxia compared with sea-level, which is consistent with our findings. Regarding acute exposure to hypoxic conditions, glucose is the most oxygen-efficient substrate, and the use of glucose metabolism increases as the oxygen transport capacity is limited to tissues.[26] This can be explained by decrease in ability to generate aerobic energy because of low S_pO_2.[27] In addition, increase in carbohydrate oxidation with increase in altitude is due to the increased activity of the sympathetic nervous system, leading to increased secretion of epinephrine and norepinephrine, which promotes carbohydrate oxidation.[28] An increase in carbon dioxide emission due to a high respiratory frequency may lead to an increase in blood lactate and hydrogen, resulting in increased RER.[29] In this study, we found that carbohydrate oxidation increased with increase in simulated altitude. These results can be explained

by the fact that carbohydrates are more efficient in the use of oxygen in ATP production than fat oxidation. In addition, a previous study has reported that lactate production increased due to an imbalance in acetyl-CoA producing reactions because of accelerated glycolysis and decreased pyruvate dehydrogenase (PDH) activity during the GXT under hypoxic conditions.[30]

Compared to sea-level, the HR response was higher as the simulated altitudes increased at all points during exercise.[1] This increase in HR provides sufficient oxygen transfer to tissues, and the heart supplies more blood under hypoxia than normoxia.[27,31] In addition, increase in HR in hypoxia is mainly due to increased catecholamine secretion caused by activation of the sympathetic nervous system and the beta-adrenaline receptor stimulation by epinephrine.[32] In addition, as simulated altitude increases, breathing becomes faster, and oxygen through absorption increases the alveolar dead space rate without gas exchange in the pulmonary alveoli. It facilitates the transport of oxygen to tissues through increased HR.[33]

In VE, the reaction increased significantly ($P < 0.05$) during exercise with increase in simulated altitude. A previous study conducted GXT with seven trained and sedentary women at sea-level and various hypoxia (1000 m, F_iO_2 = 18.7%; 2500 m, F_iO_2 = 15.4%; 4500 m, F_iO_2 = 11.7%), and it reported results that were consistent with our findings.[34] An increase in VE due to hypoxia maintains VO_2, and an increase in anaerobic metabolism increases the stimulation of the respiratory control center and the elimination of VCO_2 through breathing.[27] There is less oxygen per volume of air in hypoxia than normoxia because hypoxia reduces air pressure. Therefore, to supply the same amount of oxygen for a given exercise intensity, more air must be exchanged in the lungs.[35] Another study explained that respiratory alkalosis, caused by hyperventilation at the simulated altitudes, increased the affinity of hemoglobin to oxygen. This reaction increases oxygen transport to pulmonary alveolar capillaries and is intended to regulate the transport of oxygen necessary for tissues.[36] Hypoxia is compensated by increasing VE to minimize decrease in the partial pressure of oxygen in arterial blood and reduction in oxygen saturation.[37]

The O_2 pulse refers to the amount of VO_2 per HR, which means that when the HR is low and the VO_2 is high, there is no stress on the heart, and the utilization of oxygen is positive.[38] Consequently, hypoxia-induced reduction in O_2 pulse affects exercise performance negatively by reducing the rate of oxygen transfer to tissues.[14]

Muscle Oxygenation

NIRS equipment was used to evaluate oxygen utilization rate in muscles during the GXT at sea-level and various hypobaric hypoxia. It was reported to have a high correlation with exercise performance as an index for evaluating oxygen utilization capacity in tissues.[39] The measurable variable of this equipment is the combination of oxygen and hemoglobin in Oxy_Hb and the separate amount of oxygen and hemoglobin in Deoxy_Hb. Basically, it is desirable to have higher Oxy_Hb and lower Deoxy_Hb in terms of exercise science.[40] Total_Hb is the amount of Oxy_Hb and Deoxy_Hb in total hemoglobin, and StO_2 is the amount of oxygen saturation carried to tissues.

A previous study reported a decrease in the amount of Oxy_Hb and an increase in Deoxy_Hb when performing leg resistance and submaximal exercise at various simulated altitudes.[7,41] This explains why hypoxia induces reduction in the arteriovenous oxygen difference by decreasing partial pressure of oxygen in the artery. This response is recorded as the oxygen dissociation curve moves to the right due to metabolic acidosis caused by the activation of glycolysis. The same result was observed when the GXT was performed, and this was explained as an increase in Deoxy_Hb in muscles due to a decrease in blood arterial oxygen saturation.[42] It has been reported that the oxygen utilization rate in tissues decreases by 7% for every 1000-m increase in

altitude and that limited oxygen accelerates peripheral muscle fatigue.[43] However, we confirmed that the use of oxygen in muscles did not significantly affect exercise performance. These findings show that decrease in exercise performance in hypoxia is more dependent on metabolic and cardiac functions than on muscle oxygenation functions. In order to clarify this, further studies are necessary.

Exercise Performance

In hypoxia, both the muscles and the brain have limited oxygen supply, so fatigue occurs earlier during exercise, affecting exercise performance.[44] It has been found that cerebral oxygen plays an important role in performance decline during exercise in hypoxia.[43] Acute exposure in a hypoxic condition also accelerates muscle fatigue by reducing alternative O_2 content and leg blood flow.[45] A previous study reported that exercise in hypoxia leads to low oxygen density, which means that the partial pressure of oxygen in the human body is low and affects VO_2max.[46] In addition, when acutely exposed to hypoxia, HR and VE are higher than at sea-level (760 torr) due to the stimulation of sympathetic nerve and relative increase in energy metabolism, which affects VO_2max.[47] In addition, the cause of decrease in VO_2max at a simulated altitude of 5000 m (F_iO_2 = 10.5%) was that the maximal CO and blood flow to the muscles were low.[48] Hypoxia revealed that hemoglobin concentration in the blood is low, causing a decrease in VO_2max.

In this study, VO_2max showed a significant decrease ($P < 0.05$) proportional to an increase in simulated altitude. In particular, VO_2max was at its lowest value at hypobaric hypoxia (433 torr). A previous study reported that when exposed to extreme hypoxia; oxygen saturation in the blood is less than 70%, which is equivalent to 4500 m (433 torr). This causes fatigue of the central nervous system and affects VO_2max, which is reported as one of the causes of its low value.[49] It was also reported that as the simulated altitude increased, oxygen diffusion was insufficient due to low diffusion in pulmonary capillaries, and relative exercise intensity increased when absolute intensity increased, resulting in lower VO_2max.[50] However, it has been reported that oxygen diffusion is limited to capillary mitochondria in muscles under severe hypoxia.[45] The decrease in VO_2max with altitude is believed to reduce the peak power and exercise time during hypoxia. In addition, it has been reported that VO_2max decreases by ~1.5–3.5% with every 300-m increase at altitudes above 1500 m.[51]

In acute exposure to a hypoxic condition, exercise performance is deteriorated by hypoxia in terms of energy metabolism and cardiac function as mentioned above. Nevertheless, when applying training in this hypoxic condition, plasma and blood cells increase, and therefore red blood cells increase, thereby increasing the exercise performance.[52] In addition, in the case of blood lactate concentration, it has the effect of showing a low value after training in a hypoxic condition.[53] Training in such a hypoxic condition brought benefits, but it was confirmed that exercise performance decreased during acute exposure. In the future studies, the analysis of protein and RNA changes at molecular level, which is not be confirmed in this study, could examine in multiple ways the causes of reduction in exercise performance in hypoxic conditions.

CONCLUSION

The results suggest that exercise performance decreased under various hypoxia compared to normoxia, and the decrease was more pronounced as hypoxia became more severe. In addition, it is confirmed that the difference between sea-level (760 torr) and hypoxia (633 torr) in a metabolic function is faint, but the difference is remarkable at hypoxia (526 torr) and above. From hypoxia (526 torr) and above, it has a greater negative impact on exercise performance because of a severe decrease in metabolic function. However, we confirm that muscle oxygenation profiles do not significantly affect the decrease in exercise performance.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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