SHORT COMMUNICATION

Effects of interval and sprint training under hypobaric hypoxia on aerobic, anaerobic, and time trial performance in elite Korean national male mountain bike cyclists—a pilot study

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Abstract
The purpose of our study to determine the effects of interval hypoxic training (IHT) and repeated sprint training in hypoxia (RSH) on metabolic and cardiac function during submaximal exercise, aerobic and anaerobic performance, and time trial performance in elite Korean national male mountain bike (MTB) cyclists. The participants included elite Korean national male MTB cyclists (n = 4) preparing for the 19th Asian Games in Hangzhou 2022. The hypoxic training frequency was 90 min (3 days per week for 4 weeks). Before and after hypoxic training, metabolic and cardiac functions during submaximal exercise, aerobic performance, anaerobic performance, and time trial performance were measured. Oxygen uptake, carbon dioxide excretion, and heart rate tended to decrease, and stroke volume, end-diastolic volume and cardiac output tended to increase. In aerobic, anaerobic and time trial performances, the peak torque in aerobic performance significantly increased (p = 0.046). Maximal oxygen uptake and exercise time in aerobic performance, relative peak power, relative mean power, post-exercise blood lactate level, fatigue index in anaerobic performance, and time trial performance showed an improved tendency (all p = 0.068). Our pilot study confirmed that although the sample size was small, IHT and RSH can potentially improve athletic performance in elite Korean national male MTB cyclists.

Keywords
Athletic performance; Hemodynamic function; Interval hypoxic training; Mountain bike cyclists; Repeated sprint training in hypoxia

1. Introduction

Hypoxic exercise training is commonly accepted as a training method that enhances athletic performance, and there is varied evidence to support this [1–7]. However, the effect of hypoxic training on the athletic performance of elite athletes in the national team is highly contested [8].

Among hypoxic training methods, the most popular is the living-low, training-high (LLTH) method, where the athlete lives at sea level and trains in a high-altitude environment [4, 9, 10]. LLTH is characterized by repetitive brief exposures to hypoxic environments (2–5 times of exercise training sessions per week) that has less cost, and requires less time and effort [9, 11]. LLTH, which typically comprises continuous hypoxic training, interval hypoxic training (IHT), and repeated sprint training in hypoxia (RSH), is structured according to a specific event to improve aerobic and anaerobic performance [3, 9, 11–16].

IHT is a training method that involves repeated exposure to progressive hypoxia, lasting 5 to 7 minutes during a training session, interrupted by an equal recovery period [17, 18]. IHT is known to enhance aerobic and anaerobic performance via enhanced oxygen transporting and utilizing capacity, metabolic abilities such as anaerobic glycolysis and lactate tolerance, hemodynamic function, nitric oxide level and vascular endothelial growth factor [17–20]. Alternatively, RSH comprises maximal, short-duration (typically ≤30 s) efforts interspersed with incomplete recovery periods (≤60 s) in hypoxia. The fundamental difference between RSH and IHT is the total effort required due to the high mobilization of fast muscle fibers [21]. IHT often aims to induce physiological adaptations related to endurance and aerobic capacity. RSH focuses on repeated bouts of high-intensity sprints or efforts in a hypoxic environment. The emphasis is on improving anaerobic performance and sustaining high-intensity efforts under hypoxic conditions. RSH contributes to the maintenance of oxygen delivery to the heart and peripheral tissues by increasing the recruitment rate of fast muscle fibers, improving metabolic function through specific muscle transcriptional responses, and increasing blood flow to active skeletal muscles and coronary arteries.
arteries through compensatory vasodilation [1, 12, 21]. In other words, RSH is considered to potentially enhance aerobic and anaerobic performance through improved oxygen delivery and utilization, the activation of transcription factors for mitochondrial metabolic enzymes, and compensatory vasodilation and faster creatine phosphate resynthesis [3, 21–25]. As mentioned above, when compared to training under normoxia both IHT and RSH are effective training methods that can enhance exercise performance in athletes who require aerobic and anaerobic performance in time trial performance using either IHT or RSH. Therefore, there are limited studies that examine how the combination of IHT and RSH affects aerobic/anaerobic and time trial performance, and hemodynamic function during exercise in elite national athletes.

Mountain bike (MTB) cycling is a sport, using a rough track mimicking a mountain road, that is a high-intensity intermittent activity requiring both aerobic and anaerobic energy systems and athletic performance [26–28]. It is known that MTB cyclists show high levels of maximal oxygen uptake (VO2 max) and require effective training strategies to improve high-intensity submaximal aerobic performance [29, 30]. Therefore, elite MTB cyclists typically utilize high-intensity of interval training and repeated sprint training under normoxia that is thought to enhance aerobic and anaerobic performance and time trial performance by improving skeletal muscle buffering capacity, high intensity continuous exercise capacity, and buffering oxidative capacity [31–34]. The combined application of interval training and repeated sprint training has been reported to be the most effective manner for MTB cyclists to enhance their athletic performance [30].

To summarize, interval training and repeated sprint training under hypoxia clearly show potential as an effective training method to maximize MTB cyclist’s aerobic, anaerobic and time trial performance in evaluating the effects of hypoxic training combining IHT and RSH for elite national level mountain cyclists is crucial in enhancing performance in international competitions and facilitating international competitiveness.

Therefore, the purpose of our pilot study is to evaluate the effects of a 4-week IHT and RSH program on elite Korean national male MTB cyclist’s metabolic and cardiac function during submaximal exercise, aerobic, anaerobic and time trial performance. We hypothesized that combined IHT and RSH would enhance metabolic and cardiac function during submaximal exercise, aerobic and anaerobic performance, and time trial performance among elite Korean national male MTB cyclists.

2.2 Study design

This study was designed by modifying the exercise program of previous studies [35]. The design of this study is shown in Fig. 1; all male MTB cyclists underwent 3 days of pre-testing (i.e., 3 testing days and 1 day of rest between testing days), a 4-week hypoxic training session consisted of warm-up, IHT, RSH and cool-down, and a 3-day post-test session. The post-testing began 3 days after the last training session.

During the first pre- and post-test sessions, anthropometry, body composition and blood pressure (BP) were measured between 8:00 AM and 9:00 AM. Subsequently, the male MTB cyclists performed the Wingate test for 30 s to assess anaerobic performance under normoxia. After the participants were allowed to eat and relax for 4 h, a graded exercise test (GXT) to assess aerobic performance was conducted under normoxia. In the second pre- and post-test sessions, metabolic and cardiac function parameters were measured during a 30-min bout of submaximal cycle ergometer exercise under normoxia. For all participants, the exercise intensity was set to load equivalent to 80% VO2 max (258.0 ± 34.1 watts) measured during pre-test period. On the third testing day, a 3.8 km time trial was conducted on an authorized MTB stadium in Korea.

All male MTB cyclists conducted the following four training regimes for 90 min: warm-up, IHT, RSH and cool-down. This study’s design was based on the hypoxic training of previous studies [36]. Hypoxic training was performed under hypobaric hypoxia (week 1: 596 torr; 2000 m simulated altitude; week 2: 526 torr; 3000 m simulated altitude) created by an environmental control chamber (NCTC-1, Nara Controls, Seoul, Korea). The hypoxic training frequency was 90 min 3 days per week for 4 weeks. Warm-up and cool-down were set at 50% VO2 max under normoxic conditions for 15 min. The IHT session consisted of 10 repetitions of interval workouts, each 2 min of exercise at 85% VO2 max measured under normoxia and 1 min of rest. The RSH utilized the Wingate sprint protocol, a repeated sprint training regime that involved an effort of 30 s close to maximum, where the male MTB cyclists performed six repetitions of repeated sprints of 30 s with a load of 100–110% VO2 max and a 4 min recovery workout with a load of 50% VO2 max. All male MTB cyclists continuously maintained the maximum pedaling frequency corresponding to 100 rpm or more for 30 s and 60 rpm in the recovery workout for 4 min. All hypoxic training sessions were managed by coaches, directors and the researchers.

2.3 Body composition

All male MTB cyclists fasted for 4 h before the measuring body composition parameters, including height, weight, free fat mass and percent body fat. All participants were asked to wear light clothing and remove all metallic objects. Inbody 770 (Inbody, Seoul, Korea) was used to measure all parameters under normoxic conditions.
**TABLE 1. Participants’ characteristics.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before hypoxic training</th>
<th>After hypoxic training</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (n)</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>22.0 ± 4.3</td>
<td>22.0 ± 4.3</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.0 ± 5.8</td>
<td>172.0 ± 5.8</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66.70 ± 6.82</td>
<td>67.55 ± 6.53</td>
<td>0.144</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>56.93 ± 6.77</td>
<td>58.13 ± 7.21</td>
<td>0.068</td>
</tr>
<tr>
<td>Percent body fat (%)</td>
<td>14.60 ± 5.60</td>
<td>14.68 ± 5.03</td>
<td>1.000</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>120.00 ± 11.63</td>
<td>123.75 ± 10.47</td>
<td>0.068</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>60.00 ± 5.37</td>
<td>60.25 ± 7.32</td>
<td>0.715</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± standard deviation. DBP, diastolic blood pressure; FFM, free fat mass; SBP, systolic blood pressure.

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**FIGURE 1. Study design of the present study.** VO$_2$ max, maximal oxygen uptake; RPM, repetition per minute; MTB, mountain bike.

2.4 Blood pressure

BP was evaluated twice using an automatic BP monitor (HBP-9020, Omron, Tokyo, Japan) on the right brachial artery after resting for at least 20 min, and the average value was used as the result value.

2.5 Metabolic and cardiac function during submaximal exercise

Metabolic and cardiac functions were evaluated before and after hypoxic training using a submaximal cycle ergometer (Aerobike XLIII, Konami Corporation, Tokyo, Japan) at an individual cycle ergometer exercise load equivalent to 80% VO$_2$ max for 30 min under normoxia. Metabolic function parameters including minute ventilation (VE), oxygen uptake (VO$_2$), carbon dioxide excretion (VCO$_2$), and respiratory exchange ratio (RER) that were measured using the K5 auto metabolism analyzer (Cosmed, Rome, Italy) and a breathing valve in the form of a face mask. Cardiac function parameters (*i.e.*, heart rate, HR; stroke volume, SV; end-diastolic volume, EDV; end-systolic volume, ESV; cardiac output, CO; and ejection fraction, EF) were evaluated noninvasively with a
thoracic bioelectrical impedance device (PhysioFlow PF-05, Paris, France).

The metabolic and cardiac function parameters were measured every minute, and the total value was used for VE, VO$_2$, VCO$_2$, HR, SV, EDV, ESV and CO, while the average value was used for RER and EF.

2.6 Aerobic performance
To measure aerobic performance, including VO$_2$ max, peak torque and exercise time, GXT was performed with a cycle ergometer (Monark ergomedic 828E, Monark, Varberg, Sweden), the K5 auto metabolizer analyzer (Cosmed, Rome, Italy), and a breathing valve in the form of a facemask. The GXT protocol started at 900 kg/m/min (~150 W) and increased by 180 kg/m/min (~30 W) every 2 min until exhaustion. The pedal frequency was set to 60 rpm. The GXT was completed when the following four criteria were satisfied: (1) VO$_2$ plateau is defined as no further increase in oxygen use per minute as the work performed increases; (2) HR within 10 beats of age-predicted maximum heart rate (HRmax) as a basis for using the participant’s HRmax as a surrogate for VO$_2$ max when designing a personal training program; (3) RER ≥1.10 or higher; and (4) Borg scale score ≥17.

2.7 Anaerobic performance
To evaluate anaerobic performance, after a 10-min self-selected warm-up interspersed with three maximal sprints for approximately 5 s, the participants performed a 30 s Wingate test (Velotron Wingate version 1.0, Racermate Inc., Seattle, WA, USA) on a cycle ergometer (Monark ergomedic 828E, Monark, Varberg, Sweden), where they pedaled maximally against a constant load (male, 9.8% body weight) while seated, and the load was applied after an initial acceleration phase of 3 s [13]. Blood samples were obtained through the finger at the pre- and post-Wingate test and were analyzed for whole blood lactate using a portable lactate analyzer (Lactate Pro 2, Arkray Inc, Kyoto, Japan).

2.8 Time trial performance
The 3.8 km time trial performance was measured at the Gumi Mountain Leisure Park on an authorized MTB course in Korea. This measurement method is a representative method of evaluating the exercise performance of MTB cyclists and consists of a combination of uphill and downhill courses.

2.9 Statistical analysis
Means and standard deviations were calculated for each primary dependent variable. Due to the small sample size, we used Wilcoxon’s signed-rank test as a nonparametric statistical method to evaluate the effects of hypoxic training. All analyses were performed using the Statistical Package for the Social Sciences version 28.0 (IBM Corp., Armonk, NY, USA). A p-value of < 0.05 was considered statistically significant.

3. Results

3.1 Metabolic and cardiac function during submaximal exercise
Fig. 2 depicts the pre- and post-training metabolic function data during the 30 min of submaximal exercise. No significant differences were observed in any of these parameters. However, VO$_2$ (p = 0.068, Δ% = −5.8) and VCO$_2$ (p = 0.068, Δ% = −7.41) tended to decrease over the 4-week IHT and RSH.

All cardiac function data during the 30 min of submaximal exercise also showed no significant difference between the 4-week IHT and RSH groups (Fig. 3). However, the HR (p = 0.068, Δ% = −3.74) tended to decrease after hypoxic training, and SV (p = 0.068, Δ% = 29.57), EDV (p = 0.068, Δ% = 23.46%), CO (p = 0.068, Δ% = 24.41%), and EF (p = 0.068, Δ% = 5.52%) tended to increase after hypoxic training.

3.2 Aerobic performance
The effects of the 4-week IHT and RSH on aerobic performance parameters are shown in Fig. 4. Peak torque after hypoxic training significantly increased (p = 0.046, Δ% = 8.2%). There was no significant difference in VO$_2$ max and exercise time via hypoxic training; however, VO$_2$ (p = 0.068, Δ% = 1.64) and exercise time (p = 0.068, Δ% = 11.33%) tended to decrease and increase via hypoxic training, respectively.

3.3 Anaerobic performance
As shown in Fig. 5, there were no significant differences in anaerobic performance parameters between the 4-week IHT and RSH groups. However, relative peak power (RPP; p = 0.068, Δ% = 9.72), relative mean power (RMP; p = 0.068, Δ% = 14.41), and blood lactate level (p = 0.068, Δ% = 73.98) after exercise showed a tendency to increase, and fatigue index (FI; p = 0.068, Δ% = −13.50) showed a tendency to decrease via hypoxic training.

3.4 3.8 km time trial performance
As shown in Fig. 6, there were no significant differences in the 3.8 km time trial performance between the 4-week IHT and RSH. However, 3.8 km time trial performance (p = 0.068, Δ% = −7.51) showed a tendency to be enhanced via hypoxic training.

4. Discussion
We hypothesized that hypoxic training consisting of IHT and RSH would enhance metabolic and cardiac function during submaximal exercise, aerobic and anaerobic performance, and time trial performance among elite Korean national male MTB cyclists. Our pilot study results demonstrated that interval training and repeated sprint training under hypobaric hypoxia (weeks 1–2, 596 torr; simulated 2000 m and week 3–4, 526 torr; simulated 3000 m) for 4 weeks presented the potential to enhance athletic performance in elite Korean national male MTB cyclists.

In general, IHT improves exercise economy via various structural and biochemical changes in the cardiac and skeletal muscles, such as increased blood transporting and utilizing to
FIGURE 2. Change in metabolic function during 30 min of submaximal exercise before and after the 4-week IHT and RSH. (A) Change in VE. (B) Change in VO$_2$. (C) Change in VCO$_2$. (D) Change in RER. RER, respiratory exchange ratio; VE, minute ventilation; VO$_2$, oxygen uptake; VCO$_2$, carbon dioxide excretion.

FIGURE 3. Change in cardiac function during 30 min of submaximal exercise before and after the 4-week IHT and RSH. (A) Change in HR. (B) Change in SV. (C) Change in EDV. (D) Change in ESV. (E) Change in CO. (F) Change in EF. CO, cardiac output; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; HR, heart rate; SV, stroke volume.
**FIGURE 4.** Change in aerobic performance before and after the 4-week IHT and RSH. (A) Change in VO\textsubscript{2} max. (B) Change in peak torque. (C) Change in exercise time. VO\textsubscript{2} max, maximal oxygen uptake. *Significant difference between pre- and post-tests, \( p < 0.05 \).

**FIGURE 5.** Change in anaerobic performance before and after the 4-week IHT and RSH. (A) Change in RPP. (B) Change in RMP. (C) Change in FI. (D) Change in blood lactate level at pre-exercise. (E) Change in blood lactate level at post-exercise. FI, fatigue index; RMP, related mean power; RPP, related peak power.
tissues, increased mitochondrial and capillary density, and increased oxidative enzyme activity, thereby improving athletic performance [2, 4, 13, 18, 37]. In addition, IHT improves glycolytic enzymes, glucose transport and pH regulation, thereby increasing anaerobic power and enhancing repeated sprint ability [4, 13, 38, 39]. RSH also enhanced anaerobic performance with significantly greater molecular levels, whereby changes in blood perfusion in active skeletal muscle, improved lactate tolerance, improved acid-base equilibrium, and increased glycolysis enzyme activity have been reported [3, 21, 40]. MTB cycling is a sport that utilizes a rough track that mimics a mountain road and is a high-intensity intermittent activity that requires both aerobic and glycolytic energy systems and athletic performance [26–28]. It is therefore important for athletes to improve their metabolic and cardiac function, aerobic performance and anaerobic performance by performing IHT and RSH to enhance their athletic performance [31–34].

Athletic performance is highly correlated with exercise economy and hemodynamic function (improved flow rate of oxygen to skeletal muscle and mitochondrial oxygen utilizing capacity), and exercise economy and hemodynamic function are the main determinants of exercise performance along with VO\textsubscript{2} max [9, 18, 41, 42]. However, there is a lack of previous studies that have verified that hypoxic training consisting of IHT and RSH enhances athletic performance based on exercise economy and hemodynamic function through measurement of metabolic and cardiac function. Although our pilot study had a small sample size, the present study confirmed that hypoxic training consisting of IHT and RSH for 4 weeks showed the potential to improve exercise economy and hemodynamic function via decreasing HR, VO\textsubscript{2} and VCO\textsubscript{2} and increasing SV, EDV, CO and EF during submaximal exercise for 30 min in elite Korean national male MTB cyclists. The improvement in exercise economy is related to enhanced adenosine triphosphate resynthesis per 1 mol of oxygen and decreased adenosine triphosphate (ATP) levels at a given absolute intensity [9, 18, 41, 42]. The improvement in exercise economy and hemodynamic function increases the efficiency of oxygen transporting and utilizing capacity, that is, energy availability. It also activates the vagus and parasympathetic nerves of the cardiac muscle, increasing venous return and effectively improving cardiac function [9, 18, 20, 42]. In addition, high-intensity hypoxic training exercises economy and hemodynamic function, which in turn enhances VO\textsubscript{2} max [18, 42]. In the previous studies, Jung \textit{et al.} [18] measured the effects of IHT (526 torr, simulated 3000 m) for 6 weeks on exercise economy, hemodynamic function and exercise performance in middle- and long-distance runners. They reported that IHT was more efficient training modality to enhancing exercise performance via improving exercise economy and hemodynamic function. Kim \textit{et al.} [42] investigated the benefits of aerobic continuous and interval training under hypoxia (526 torr, simulated 3000 m) on the hemodynamic function and exercise performance of amateur male swimmers. They concluded that hypoxic training modality composed of aerobic continuous and interval exercises improves exercise performance with exercise economy and hemodynamic function. These previous studies show that the enhanced aerobic performance (e.g., VO\textsubscript{2} max, peak torque and exercise time) in the present study is the result of improvements in exercise economy and hemodynamic function.

Regarding anaerobic performance and hypoxic training, high-intensity IHT and RSH increases the mobilization rate of fast-twitch muscle fibers, improves metabolic function through specific muscle transcriptional responses, and enhances lactate tolerance and polymerase chain reaction (PCR) resynthesis [1, 3, 21, 23, 24]. Czuba \textit{et al.} [2] evaluated the effects of the inspired oxygen fraction (FiO\textsubscript{2} = 15.5%, simulated 2500 m) on anaerobic capacity and swimming performance in well-trained swimmers. They concluded that IHT significantly enhanced anaerobic capacity and swimming performance. Faiss \textit{et al.} [3] verified the effects of RSH (FiO\textsubscript{2} = 14.6%, simulated 2950 m) for 4 weeks on anaerobic power and fatigue in male cyclists and confirmed that RSH improved anaerobic power and delayed exercise-induced fatigue. Galvin \textit{et al.} [40] measured the effects of RSH (FiO\textsubscript{2} = 13%, simulated 3800 m) for performing repetitive sprint exercises and passive recovery for 4 weeks on anaerobic performance in well-trained male academy rugby union and rugby league players and concluded that RSH resulted in twofold greater enhancements in capacity performed by repeated high-intensity workouts. Puyper \textit{et al.} [43] verified the effect of RSH (FiO\textsubscript{2} = 14.4%, simulated 3100 m) with an exercise intensity equivalent to 80% of the maximum sprint power for 4 weeks on glycolytic enzyme activity and anaerobic performance in healthy men. They reported that RSH upregulated muscle phosphofructokinase activity and the anaerobic threshold but did not enhance exercise performance, which is a result of the relatively low exercise intensity in RSH compared with other studies. In the present pilot study, our hypoxic training regimen consisting of high-intensity IHT and RSH for 4 weeks showed the potential to improve anaerobic performance (e.g., RPP, RMP and %Fi) and lactate tolerance. As reported in previous studies, enhanced anaerobic performance is probably due to compensatory vasodilation, increased glycolytic enzyme activity, increased ATP and PCR resynthesis, and increased lactate tolerance [1–3, 21, 23, 24, 40, 43].

In MTB cyclists, real game time trial performance is highly

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**FIGURE 6.** Change in 3.8 km time trial performance before and after the 4-week IHT and RSH.
correlated with high-intensity intermittent activity and requires both aerobic and anaerobic energy systems [26–28, 31–34]. Therefore, in our study, elite male MTB cyclists performed hypoxic training consisting of IHT and RSH to improve their athletic performance. As a result, all athletes showed the potential to enhance 3.8 km time trial performance with 4 weeks of IHT and RSH. This improvement in time trial performance in the real game is due to enhanced metabolic function (i.e., exercise economy and lactate tolerance), cardiac function during submaximal exercise, aerobic performance and anaerobic performance. In the future, our hypoxic training effect should be compared with normoxic training with a larger sample size to verify its efficacy more accurately.

In our pilot study, the participants were elite Korean national male MTB cyclists (n = 4) preparing for the 19th Asian Games in Hangzhou 2022, and the present study had a limited sample size. Therefore, our study was a single-trial pilot study without a control group. This study did not control for extraneous parameters such as diet, hydration, supplementation and total exercise amount for elite Korean national male MTB cyclists.

5. Conclusions

In our pilot study, we demonstrated that interval training and repeated sprint training under hypobaric hypoxia (weeks 1–2, 596 torr; simulated 2000 m and week 3–4: 526 torr; simulated 3000 m) for 4 weeks showed the potential to enhance metabolic and cardiac function during submaximal exercise, aerobic and anaerobic performance, and time trial performance in elite Korean national male MTB cyclists. In future studies, if biochemical analysis is conducted by exercise training under hypoxic conditions in a large number of study subjects, the effect of the intervention can be more clearly identified.

AVAILABILITY OF DATA AND MATERIALS

The data of this work will be made available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

SS, SWK and HYP—designed the research study. SS, JS, YS, HL and JHC—data curation, conducted the research investigation. SS, SWK, HL and HYP—analyzed the data. SS and HYP—wrote the original draft, approved the final version of the manuscript. All authors have read and agreed to the published version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Konkuk University (7001355-202111-HR-488), Korea. Informed consent was obtained from all the participants involved in the study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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