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ORIGINAL RESEARCH

The effects of wearing KF94 masks on cardiorespiratory function and hemorheological response during moderate intensity exercise in adult males

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Abstract

The purpose of this study was to examine the effect of wearing a Korea filter 94 (KF94) mask on cardiorespiratory function and hemorheological responses during moderate intensity exercise in men during the Coronavirus disease 2019 (COVID-19) pandemic. 12 healthy males aged 20 to 29 years (28.3 $\pm$ 3.6 yr) were recruited for this study. The exercise intensity corresponding to the anaerobic threshold level was determined following a maximum graded exercise test, and exercise was performed for 40 minutes with a cycle ergometer at the target exercise intensity. Cardiorespiratory function, blood pressure, and hemorheological responses were measured every 10 minutes at rest and during exercise. Our results indicated no differences between conditions in respiratory frequency (Rf), tidal volume (TV), minute ventilation (VE), carbon dioxide production ($\dot{V}CO_2$), and partial pressure of arterial oxygen (PaO_2). However, oxygen consumption ($\dot{V}O_2$) was significantly lower in the KF94 mask group compared to the control. There were no differences in systolic blood pressure (SBP), diastolic blood pressure (DBP), rate pressure product (RPP), aggregation index (AI), and blood critical stress (BCS) between the two groups. The mask group had a significant respiratory exchange ratio (R) at rest and during 10 minutes exercise compared to the control. The elongation index was higher at rest, 10 minutes, and 30 minutes in the mask group than control group ($p <$ 0.05). Overall, our results suggest that although $\dot{V}O_2$ was decreased and R values were increased, the effects of other physiological parameters and hemorheological responses imposed by face masks during moderate intensity exercise are small. Thus, although negative effects of using face masks affect exercise capacity (*i.e.*, exercise tolerance), our findings suggest that individuals wearing KF94 could safely exercise and get some health benefits from physical activities during the COVID-19 pandemic.

Keywords

COVID-19; Cardiorespiratory function; Hemorheological responses; KF94 masks

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, which caused a global public health emergency in 2020, exerted adverse effects throughout all aspects of society. The World health organization (WHO) recommended proper hand hygiene and face mask use as a preemptive precaution to prevent the spread of COVID-19 [1]. Government policies to prevent the spread of the coronavirus included reducing social interaction thorough partial city blockades, travel bans, restricted meetings, online schools, and international border closures. With the implementation of various policies to prevent transmission, normal daily life was limited, sedentary behaviors increased, and the amount of daily physical activity sharply decreased. The resulting lack of exercise is a well-known risk factor for future diseases and will negatively affect the country, society, and individuals [2]. Evidence suggests that high fitness lowers the rate of hospitalization and the rate of mortality due to COVID-19 [3, 4]. Accordingly, adequate exercise can help prevent or reduce the likelihood of acute respiratory distress syndrome associated with COVID-19 [5].

During the COVID-19 pandemic, the Korea National Occupational Safety and Health Agency approved the KF94, a mask designed to decrease transmission of the virus. The KF94 was originally used by infectious patients, but has recently become common for everyone to wear. The mask not only filters small particles in the air such as viruses from reaching the respiratory system but also acts as a personal protective device that can prevent transmission between individuals. As a result of the pandemic, face masks have integrated themselves as a part of our daily lives. Wearing them during exercise has become a common phenomenon because gymnasiums and other enclosed areas increase the spread of COVID-19. Conversely, wearing a face mask like a N95 during exercise can also induce a hypoxic condition, leading to changes in alveolar and blood metabolism, immune mechanisms, and physiologic changes in the brain and nervous system [6]. A decrease in alveolar oxygen (O_2) partial pressure (PO_2) due to hypoxic aerobic exercise limits pulmonary O_2 diffusion capacity which reduces the saturation of percutaneous oxygen (SpO_2) in the arteries [7]. Furthermore, ventilation (VE) increases with heart rate (HR) within a few minutes [7]. This response is considered a part of the compensatory mechanism for hypoxia with reduced O_2 delivery to peripheral tissues. Thus, these effects could induce a hypoxic condition during exercise. Further studies are needed to reveal the physiological responses to hypoxic exercise due to safety associated with wearing a mask specifically.

Cardiopulmonary function is limited by several factors such as the capacity of lung O_2 diffusion, cardiac output (CO), the volume of blood to carry O_2, and the capacity of the muscles to extract and use O_2 for adenosine triphosphate resynthesis (ATP) [8]. Oxygen intake ($\dot{V}O_2$) is a product of CO and arteriovenous O_2 content difference (a-$\dot{V}O_2$ difference). The rate at which O_2 is delivered to the muscle depends on the content in the blood and the rate of blood flow. The rate of blood flow depends on pressure changes and blood flow resistance [9]. In addition, hemorheological factors such as red blood cell (RBC) aggregation and deformability are known as physiological indicators that indirectly affect O_2 transport and O_2 utilization to peripheral tissues through blood vessels. For example, Doyle and Walker [10] reported that acute exposure to hypoxia negatively affected RBC transformation and RBC aggregation due to reduction of $\dot{V}O_{2max}$ and a-$\dot{V}O_2$ difference and red blood cell membrane damage, resulting in decreased aerobic capacity. However, even though there is a change in blood rheological response in the hypoxic state, there have been no reports regarding the effects of wearing a KF94 mask on cardiopulmonary function during exercise.

The KF94 mask is not completely enclosed but forms a closed circuit for air intake. Rebreathing of unclean remaining air increases arterial CO_2 concentration and increases acidity [11]. In consequence, individuals who exercise with a face mask exhibit physiological effects such as discomfort, fatigue, dizziness, headache, and shortness of breath [12]. Such effects can be greater when performing aerobic exercise for longer periods, causing physiological damage to muscle and a change in the ratio of fibers, as well as psychological effects on the exercising individual. Previous studies examining the impact of mask wearing during exercise have been limited to respiratory muscle training [13] and hypoxia exercise. The effects of wearing a KF94 mask on cardiorespiratory function and hemorheological response during exercise have not been examined. Therefore, the purpose of this study was to assess cardiorespiratory function, and the blood rheological (RBC deformability, RBC aggregation, blood critical stress) responses when wearing a KF94 mask during prolonged aerobic exercise at an anaerobic threshold (AT) level in men. Our findings would provide exercise professionals with relevant information on the impact of masks to the body during exercise. We hypothesized that wearing a KF94 mask during prolonged exercise would not affect cardiorespiratory function, blood pressure, and hemorheological responses.

2. Materials and methods

2.1 Participants

Twelve male college students (28.3 ± 3.6 yr) were recruited *via* advertisements within the university. All subjects gave written informed consent forms and were screened for conditions that may affect the cardiopulmonary function and blood rheological responses such as physical activity difficulties or taking cardiovascular disease-related drugs through a health history questionnaire (HHQ). Based on the information provided by the subjects, they were in good health and recreationally active. They were asked to refrain from strenuous exercise, caffeine, and alcohol at least 24 hours before each data collection.

2.2 Experimental procedures

Table 1 indicated the physical characteristics of subjects. All subjects reported to the laboratory 3 times during the study. Subjects were randomly assigned *via* a crossover design. On the first visit, the fat mass, body fat percentage, and fat-free mass were measured by bioelectrical impedance analysis (Inbody 720, Korea). While the subjects sat on a chair with their feet flat on the floor for at least 5 minutes, blood pressure (BP) was measured using a sphygmomanometer and pressure cuff placed on the left arm at heart level. Two measurements were taken, 5 minutes apart, and the mean of 2 measurements was recorded.

TABLE 1. Physical characteristics of subjects.

Variables	Subjects (n = 12)
Age (yr)	28.3 ± 3.6
Height (cm)	179.4 ± 7.0
Weight (kg)	82.2 ± 11.2
BMI (kg/m^2)	25.4 ± 1.9
Fat-free mass (kg)	65.4 ± 9.4
Fat mass (kg)	16.8 ± 5.5
Body fat (%)	20.3 ± 5.8
$\dot{V}O_{2AT}$ (mL/kg/min)	23.7 ± 3.3
$\dot{V}O_{2peak}$ (mL/kg/min)	39.3 ± 4.4

BMI: body mass index; $\dot{V}O_{2peak}$: peak oxygen consumption; $\dot{V}O_{2AT}$: oxygen consumption at the AT level.

On the second visit, a $\dot{V}O_{2peak}$ test was performed using a cycle ergometer using an intensity that corresponded to the AT level determined for each subject. A warm-up exercise was performed for 2 minutes at 0 watts and a rotational speed of 60 rpm per minute using an automatic respiration metabolic analyzer (Quark CPET, COSMED Sr, The Metabolic Company, Albano Laziale, Italy) and a bicycle ergometer (Monark 828E, Uppsala, Sweden). A multi-step graded exercise was used to increase the load by 30 watts per minute [14]. The rating of perceived exertion (RPE) was measured 8 times at 5-minute intervals. The heart rate (HR) was measured using a polar monitor every minute. The $\dot{V}O_{2peak}$ was determined when it met three criteria: (1) the point of the rapid rise of VE and $\dot{V}CO_2$, (2) the point where O_2 rises without change in CO_2,

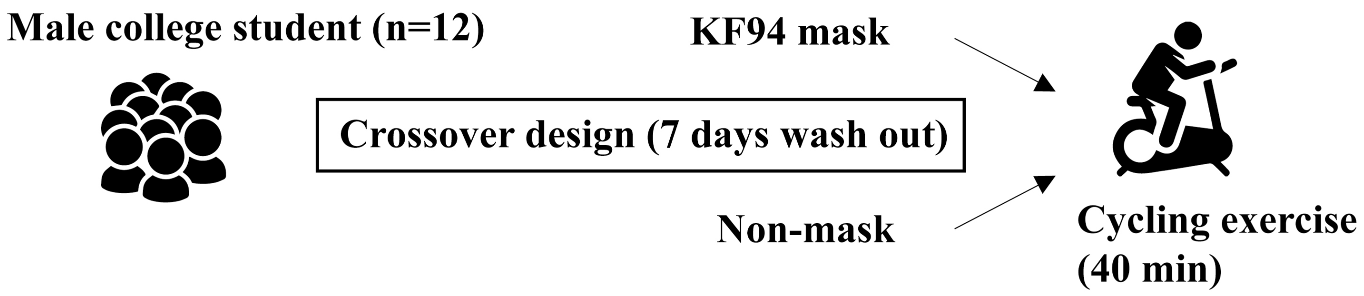

FIGURE 1. Experimental design.

and (3) the point where $\dot{V}O_2$ levels off [15]. The AT level met the exercise intensity (40~70% $\dot{V}O_{2peak}$) necessary to maintain and promote the body composition, muscle strength, and endurance of the respiratory circulatory system for healthy persons [16]. The AT was determined using the V-slope method [17]. When the V-slope method was not applicable, the AT was determined as the lowest point of VE (VE/$\dot{V}O_2$) for O_2. Carbohydrate and fat utilization reflected by R values were determined using the respiratory quotient [18].

2.3 Exercise protocols

On the third visit, 40 minutes of aerobic exercise at the AT level intensity of their predetermined $\dot{V}O_{2peak}$ values was performed randomly by wearing a mask (MASK) or without wearing a mask (CON). Subjects were instructed to fast for 12 hours and visited the laboratory at 9:00 AM. Cardiopulmonary function and PaO_2 were measured throughout the experiment *via* a metabolic cart, and BP was measured at rest, 10 minutes, 20 minutes, 30 minutes, and 40 minutes (Fig. 1). Systolic (BP) and diastolic (BP) were measured every 10 minutes using a standing mercury sphygmomanometer. Exercises of MASK and CON were carried out at intervals of 7 days. Subjects were instructed to continue their normal activities and not to change their exercise habits. The AT level determined in this study was 60.4% (range 50.8~69.3% of $\dot{V}O_{2peak}$) and the HR corresponding to the AT was used to monitor moderate intensity exercise. In previous studies, the duration of long-term exercise varied from 40 to 120 minutes [19, 20]. In this study, exercise duration was limited to 40 minutes to minimize negative effects of wearing a mask.

2.4 Blood collection and analysis for hemorehological response

Subjects were instructed to fast for 12 hours and visited the laboratory at 9:00 AM. Blood was collected at rest and during prolonged aerobic exercise at 10, 20, 30 and 40 minutes of exercise respectively *via* a 20 G Catheter (Gyeonggi Medical Industry, Korea) inserted into the brachial vein. Venous blood samples were obtained from the antecubital vein and collected in vacutainer ethylenediaminetetraacetic acid (EDTA) tubes. The hemorheological response of the RBC elongation index, RBC aggregation index, and the RBC critical were measured *via* a microchip stirring system by light transmission [21] and calculated using Rheoscan-D (Rheo Meditech, Korea).

2.5 Statistical analysis

The mean and standard deviation (SD) of each variable were calculated and presented using the IBM SPSS Version 23.0 program (NY, USA). To compare the differences in each variable during the 40-minute cycling ergometer exercise, a two-way repeated measures analysis of variance (ANOVA) was performed regarding to the group variable (MASK *vs.* CON) and the time variable. When the interaction between group and time was significant, a repeated one-way ANOVA and least significant difference (LSD)'s post hoc test were performed for each mean difference analysis. The difference in the dependent variable between group and time was analyzed by a paired *t*-test. All statistical significance levels were set at $p < 0.05$. Effect size (ES) was calculated using Cohen's D formula as the mean difference divided by the pooled standard deviation.

3. Results

Table 2 indicates changes in cardiopulmonary function at rest and during exercise between the two groups. The time effect was observed for all variables. Rf, TV, VE, and $\dot{V}CO_2$, were significantly increased from rest to 40 minutes, but there were no differences between the two groups. The MASK group had significantly lower R values at rest, 10 minutes, and 20 minutes compared to the control (ES = 1.49, p = 0.03; ES = 0.94, p = 0.036; ES = 1.5, p = 0.026, respectively). $\dot{V}O_2$ was significantly lower in the MASK group compared to the control during exercise. Table 3 indicated changes in blood pressure and partial pressure of arterial oxygen. There were no differences in SBP, DBP, and PaO_2 between the two groups. Table 4 indicates changes in hemorheology at rest and during exercise between the two groups. There were no differences in the AI and BCS. The mask group had a significantly higher error indicator (EI) at rest and during 10 minutes and 30 minutes exercise compared to the control (ES = 1.0, p = 0.026; ES = 1.58, p = 0.01; ES = 1.58, p = 0.021, respectively).

4. Discussion

To our knowledge, this is the first study to assess the effects of MASK on cardiopulmonary function and hemorheological response during prolonged aerobic exercise. This study found that there were no differences in Rf, VT, $\dot{V}CO_2$, fraction of inspired oxygen (FiO_2), inspired fraction of carbon dioxide ($FiCO_2$), partial pressure of carbon dioxide ($PaCO_2$), VE, and PaO_2 during exercise between the two conditions. The MASK

TABLE 2. Indicates changes in cardiopulmonary function at rest and during exercise between the two groups.

	rest	10 min	20 min	30 min	40 min	*F*		*p*
Rf (beats/min)								
CON	15.3 ± 3.9	22.9 ± 7.2	26.8 ± 8.3	27.1 ± 8.2	27.8 ± 8.1	79.493	T	0.000*
						0.001	G	0.970
MASK	15.7 ± 4.1	23.3 ± 6.0	25.9 ± 5.8	26.6 ± 6.2	27.5 ± 6.3	0.315	T × G	0.868
TV (L)								
CON	1.0 ± 0.3	2.0 ± 1.2	2.1 ± 1.3	2.1 ± 1.1	1.9 ± 0.8	25.191	T	0.000*
						0.035	G	0.854
MASK	1.0 ± 0.3	1.9 ± 0.6	2.0 ± 0.7	2.0 ± 0.8	1.9 ± 0.6	0.086	T × G	0.987
VE (L/min)								
CON	15.3 ± 2.5	40.6 ± 9.3	49.3 ± 6.9	50.6 ± 8.5	50.6 ± 9.4	320.479	T	0.000*
						0.000	G	0.994
MASK	15.1 ± 2.0	40.9 ± 4.6	49.1 ± 7.1	51.3 ± 8.0	50.5 ± 5.0	0.089	T × G	0.986
$\dot{V}O_2$ (mL/kg/min)								
CON	8.7 ± 1.9	23.1 ± 2.8	26.3 ± 2.6	27.0 ± 2.4	27.2 ± 3.2	746.140	T	0.000*
						6.566	G	0.018*
MASK	5.9 ± 1.7	20.9 ± 2.9	23.6 ± 3.1	24.4 ± 3.0	24.8 ± 2.8	0.176	T × G	0.95
$\dot{V}CO_2$ (mL/kg/min)								
CON	6.4 ± 1.5	20.1 ± 2.7	23.3 ± 2.5	23.8 ± 2.1	23.7 ± 2.8	618.092	T	0.000*
						3.417	G	0.078
MASK	5.1 ± 1.5	18.9 ± 2.7	21.5 ± 2.8	21.9 ± 2.7	22.0 ± 2.4	0.232	T × G	0.920
R								
CON	0.73 ± 0.07#	0.86 ± 0.02#	0.88 ± 0.02#	0.88 ± 0.02	0.87 ± 0.02	20.034	T	0.000*
						20.070	G	0.000*
MASK	0.85 ± 0.09	0.89 ± 0.04	0.91 ± 0.02	0.90 ± 0.02	0.88 ± 0.03	5.484	T × G	0.001*

*Values are expressed as means ± SD. *$p < 0.05$. Rf: respiratory frequency; TV: tidal volume; VE: minute ventilation; $\dot{V}O_2$: oxygen consumption; $\dot{V}CO_2$: validation of carbon dioxide production; R: respiratory exchange ratio. # indicate a significant different differences between the groups.*

TABLE 3. Changes in blood pressure and partial pressure of arterial oxygen. There were no differences in SBP, DBP, and PaO_2 between the two groups.

	rest	10 min	20 min	30 min	40 min	*F*		*p*
SBP (mmHg)								
CON	114.7 ± 10.8	154.3 ± 11.8	166.5 ± 11.3	171.3 ± 9.0	170.8 ± 13.4	79.493	T	0.000*
						0.001	G	0.706
MASK	114.0 ± 10.8	159.8 ± 12.3	166.9 ± 10.2	173.3 ± 12.3	171.4 ± 13.2	0.315	T × G	0.579
DBP (mmHg)								
CON	74.0 ± 7.5	86.4 ± 5.1	88.3 ± 3.3	90.0 ± 4.7	92.0 ± 4.8	64.454	T	0.000*
						1.033	G	0.320
MASK	72.6 ± 7.6	84.7 ± 6.6	86.0 ± 4.0	87.8 ± 6.7	90.0 ± 6.8	0.054	T × G	0.994
PaO_2 (mmHg)								
CON	119.0 ± 3.3	110.3 ± 2.1	109.6 ± 3.1	110.5 ± 3.8	111.5 ± 3.3	65.230	T	0.000*
						3.486	G	0.075
MASK	115.6 ± 3.9	108.3 ± 2.8	108.6 ± 2.7	109.3 ± 3.0	109.2 ± 3.0	1.265	T × G	0.290

*Values are expressed as means ± SD. *$p < 0.05$. SBP: systolic blood pressure; DBP: diastolic blood pressure; PaO_2: partial pressure of O_2 in arterial blood.*

TABLE 4. Indicates changes in hemorheology at rest and during exercise between the two groups.

	rest	10 min	20 min	30 min	40 min	F		p
Aggregation Index (au)								
CON	30.0 ± 4.6	31.0 ± 6.1	29.0 ± 4.7	29.9 ± 6.5	29.0 ± 5.8	0.682	T	0.054
						0.124	G	0.728
MASK	29.5 ± 5.8	31.0 ± 6.8	30.7 ± 4.6	30.3 ± 5.6	30.9 ± 5.0	0.761	T × G	0.553
Blood critical Stress (mPa)								
CON	217.2 ± 41.5	249.6 ± 54.3	246.8 ± 56.0	255.4 ± 59.8	249.1 ± 59.8	17.736	T	0.094
						0.220	G	0.644
MASK	209.6 ± 50.2	253.7 ± 55.7	261.0 ± 57.2	279.1 ± 87.5	269.5 ± 76.6	1.657	T × G	0.07
Elongation Index (au)								
CON	0.302 ± 0.026	0.304 ± 0.009	0.310 ± 0.011	0.304 ± 0.012	0.302 ± 0.013	1.046	T	0.000*
						4.263	G	0.051
MASK	0.322 ± 0.011#	0.319 ± 0.010#	0.317 ± 0.009	0.318 ± 0.015#	0.304 ± 0.054	0.871	T × G	0.038*

*Values are expressed as means ± SD. *p < 0.05. #indicate significant different between the two groups.*

condition had higher R values compared to the CON, reducing the muscle's oxidative capacity to get energy. $\dot{V}O_2$ was significantly decreased in the MASK condition compared to the CON. Regarding the ability of RBC to deform in response to shear forces, only the EI value was significantly higher at rest, 10 minutes, and 30 minutes in MASK condition than CON.

In this study, $\dot{V}O_2$ was significantly lower in MASK than CON ($p < 0.05$). This observation is consistent with previous findings that exercise without wearing a mask increased airway resistance [22]. Increased airway obstruction induced by adding resistance to the mouth increases respiratory resistance and decreases $\dot{V}O_2$ inhaled [23]. A previous study demonstrated that the dead space of the KF94 mask is a reservoir of exhaled gas that is re-breathed during continuous inhalation by mixing with the air entering through the mask. This can increase CO_2 and reduce O_2 entering the lungs [24]. Collectively, prolonged exercise with wearing KF94 masks likely decreases oxygen consumption.

The decrease in ventilation threshold (VT) of the KF94 mask-wearing group was caused by changes in inhalation and exhalation time as well as a decrease in Rf compared to the non-masked group. This may also be due to respiratory protection devices or additional external respiratory resistance [23]. When the respiratory resistance increases, the individuals wearing masks require more work on the respiratory muscles than those without the KF94 mask, resulting in higher O_2 consumption. In addition, the cardiac load elevates because left ventricular pressure increases and myocardial O_2 consumption increases [25]. However, our results indicated that there was no difference in VT between the two conditions. Thus, this study indicates that wearing the KF94 mask during exercise can still maintain the tidal volume required by the exercise.

There was a significant difference between the KF94 MASK and the non-mask group (CON) in R during 10 minutes and 20 minutes exercise ($p < 0.05$). The gradual increase in R indicates a decrease in lipid utilization [26]. In our study, there were significant differences in relative carbohydrates (MASK: 4.40 kcal/min, 1.17 g/min; CON: 4.36 kcal/min, 1.20 g/min) and fat utilization (MASK: 2.47 kcal/min, 0.25 g/min; CON: 4.0 kcal/min, 0.41 g/min) between two conditions. This result suggests that our body leans on more carbohydrate metabolism to produce energy in the MASK condition during exercise compared to the normal condition.

This study also assessed whether the KF94 MASK worn during exercise could lead to health risks *via* the onset of acute or intermittent hypoxia. It was thought that BP would substantially be elevated since face covering-induced hypoxia triggers sympathetic nerve activity that leads to high BP [27]. In contrast, in this study, there were no differences in SBP, DBP, and PaO_2 between the two conditions, indicating that individuals can exercise safely in MASK conditions during the pandemic. Our findings are inconsistent with a study that reported higher SBP during high intensity exercise [28]. These changes in BP may be due to higher systemic vascular resistance or cardiac output (*i.e.*, Fick's law), but we did not measure these parameters.

Maintaining O_2 saturation and supplying O_2 to active muscles as well as physiological factors including blood viscosity and the ability to deform RBCs are the key factors for exercise performance [29]. The elevation of systemic vascular resistance induced by a decrease in red blood cell deformity leads to a decrease in oxygen carrying capacity, resulting in a decrease in aerobic exercise performance. Reduction of RBC deformability in the MASK group during exercise may reduce capillary perfusion and O_2 delivery to tissues which is consistent with most previous studies [30, 31]. The elongation index was higher in the MASK group than in CON ($p < 0.05$). Thus, O_2 delivery to tissues can be impaired in the MASK condition, reducing exercise performance. At low rates of RBCs (venous and small arterioles), blood viscosity is highly influenced by RBC aggregation. RBC aggregation depends on exposure to hypoxia and plasma factors such as fibrinogen levels. In this study, there were no significant differences in the aggregation index and blood critical stress between the two groups. Collectively, an impairment in O_2 delivery to tissues can be minimal since there were no differences in other factors such as RBC aggregation and blood critical stress.

The current study included healthy and physically active individuals. As such, the current study results are not applicable to other populations such as older adults, sedentary populations, and other at-risk patients. Another limitation is that this study did not evaluate the effects of the N95 mask during exercise at higher work intensities and over longer durations.

5. Conclusions

In conclusion, we found that the R-value was significantly higher in MASK conditions at 10 minutes and 20 minutes compared to CON. The elongation index evaluating the ability to transform RBC is higher in MASK conditions than that of CON. There was no significant change in the circulating VE and CO_2 concentration during prolonged exercise with a mask. There were no differences in SBP, DBP, and blood rheological responses between the two conditions. Overall, the findings indicate that the adverse effects of wearing a face mask during exercise appear to be small. Thus, our findings suggest that individuals wearing KF94 masks can safely exercise and receive health benefits from moderate physical activity during periods of seasonal illness such as COVID-19.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

CHP and SNL—designed the research study. SMK and JSL—performed the measurements. CHP, SMK, YKK, and SNL—processed the experimental data, performed the analysis, and designed the figures. CHP—drafted the manuscript. All authors read and approved the final version of the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study adhered to the ethical standards of the Declaration of Helsinki. The experimental procedure and analysis were explained to the subjects, and consent was obtained before continuing the experiment. The study was approved by the Institutional Review Board of Hanyang University (HYUIRB-202011-007).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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