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Acute Moderate-Intensity Aerobic Exercise under High PM_{2.5} Levels Does Not Influence the Pulmonary Function and Lung Diffusion Capacity in Healthy Young Men

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Abstract: Exposure to fine particulate matter (PM_{2.5}) impairs the respiratory system and increases the morbidity and mortality of respiratory diseases. Even though aerobic exercise is known to improve pulmonary function in diverse populations, it can lead to an increase in the inhalation of PM_{2.5} in polluted environments. We aimed to investigate the effects of aerobic exercise under high PM_{2.5} conditions on the pulmonary function in young adults. Nine healthy young men performed indoor treadmill running in both high and low PM_{2.5} conditions (59.0 ± 2.1 vs. 7.8 ± 1.0 $\mu\text{g}/\text{m}^3$) by a crossover study design. Pulmonary function was assessed by spirometry and diffusing capacity for carbon monoxide (DLCO) at pre- and 1-h post-exercise. There was no difference in the response of pulmonary function and lung diffusion capacity to the acute aerobic exercise in high and low PM_{2.5} conditions ($p \geq 0.09$). These findings indicate that aerobic exercise in high PM_{2.5} conditions may not adversely affect pulmonary function in healthy young adults.

Keywords: fine particulate matter; aerobic exercise; pulmonary function; lung diffusion capacity

Citation: Kim, J.-S.; Lee, D.G.; Wang, L.; Kang, H.; Hwang, M.-H. Acute Moderate-Intensity Aerobic Exercise under High PM_{2.5} Levels Does Not Influence the Pulmonary Function and Lung Diffusion Capacity in Healthy Young Men. *Appl. Sci.* **2022**, *12*, 10080. <https://doi.org/10.3390/app121910080>

Academic Editor: Simone Morais

Received: 28 July 2022

Accepted: 4 October 2022

Published: 7 October 2022

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1. Introduction

Exposure to air pollution is widely known to increase all-cause morbidity and mortality. Particulate matter (PM), one of the constituents of air pollution, adversely affects the human cardiorespiratory system, and as a result, the incident rate of cardiopulmonary complications and their mortality can increase with augmented PM levels [1–4]. Due to its harmful influence on human health and wellbeing, the International Agency for Research on Cancer (IARC) categorized outdoor air pollution and PM as a carcinogen to humans [5]. In an outdoor environment, PM is mainly derived from traffic output, industrial activities, and biomass burning [6]. Furthermore, particles from the outdoor environment can rapidly penetrate the indoor environment, making people inevitably suffer from PM exposure in their daily lives [7].

PM is mainly classified as PM₁₀, PM_{2.5}, and PM₁ according to the particles' aerodynamic diameter (PM ≤ 10 μm , 2.5 μm , and 1 μm in diameter, respectively), and its effects on the cardiorespiratory system are determined by its size. PM₁₀ can only penetrate and deposit in the upper respiratory tract [8]. However, PM_{2.5} can seep into the alveolar region, the deepest part of the lung, which can trigger negative influences on the whole respiratory system [8,9]. Short-term exposure to PM_{2.5} impairs the respiratory tract by inducing

inflammation and oxidative stress, which may induce bronchoconstriction and temporarily decrease pulmonary function [10]. Furthermore, long-term exposure to PM_{2.5} engenders morphological changes in nasal airways and increases the risk of respiratory diseases [10].

Aerobic exercise is known to improve pulmonary function in asthmatic patients [11]. Even in healthy individuals, pulmonary function was enhanced after participating in regular aerobic exercise [12–14]. However, performing aerobic exercise under high PM_{2.5} conditions might annul the positive effect of the exercise and impair the respiratory system. Substantially increased minute ventilation during aerobic exercise is likely to increase the number of inhaled particles into the lungs [15,16]. In addition, increased velocity of air-flow during exercise can cause particles to reach a deeper region of the respiratory system [15]. Previous findings on the effect of aerobic exercise on pulmonary function in high PM_{2.5} conditions are limited, and their results are still controversial [17–21]. Hence, this study aimed to demonstrate the effect of acute moderate-intensity aerobic exercise on pulmonary function under high PM_{2.5} conditions compared with low PM_{2.5} conditions. We hypothesized that exposure to high PM_{2.5} conditions during aerobic exercise would negatively affect pulmonary function due to the elevated PM_{2.5} inhalation caused by the increased minute ventilation during exercise. Moreover, our study controlled indoor PM_{2.5} conditions with penetrated particles from the outdoor environment to emphasize that the influx of outside ambient air has a negative effect on indoor air quality.

2. Materials and Methods

2.1. Participants

Nine healthy young men (24.6 ± 0.4 years) participated in this study and they were recruited by word of mouth at Incheon National University. All participants were free of clinical diseases and non-smokers with normal lung function - over 80% of predicted forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV₁) for sex, age, height, and ethnicity [22]. Participants were excluded if they were taking any medications that might affect cardiovascular and pulmonary function, and if they have or had a history of musculoskeletal, cardiovascular, or respiratory diseases. We confirmed via interview that all participants were recreationally active before initiating the study. This study observed the ethical standards of the Declaration of Helsinki. The purpose and risks of the study were fully explained to each participant, and they voluntarily signed an informed consent form before participating in the study. This study was reviewed and approved by the Institutional Review Board of Incheon National University.

2.2. Study Design

This study used a crossover design and all participants visited the laboratory three times. In the initial visit, the participants performed a maximal graded exercise test with a modified Bruce protocol to assess their maximal oxygen consumption (VO₂max) and heart rate (HRmax) [23]. Since not all participants met at least three of the following criteria: (1) a heart rate within 10 bpm of age-predicted max heart rate ($220 - \text{age}$); (2) a score of at least 18 on the Borg rating of perceived exertion scale; (3) above 1.15 of maximal respiratory exchange ratio; (4) a plateau of oxygen consumption with increasing exercise intensity; we defined the VO₂max as peak oxygen consumption (VO₂peak) and HRmax as peak heart rate (HRpeak). In the second and third visits, the participants performed acute moderate-intensity aerobic exercise in high and low PM_{2.5} conditions in an indoor training facility. A randomized crossover study design could not be employed because the decision as to whether or not to run the planned experiments on the same day depended on the external weather conditions. But luckily, four of nine participants executed their second visit in low PM_{2.5} conditions and five participants completed the second visit in high PM_{2.5} conditions. We measured clinical pulmonary function parameters before and 1-h after an established aerobic exercise session in each condition. In both second and third visits, we

used air purifiers with high-efficiency particulate absorbing (HEPA) filters to minimize the PM_{2.5} exposure in the laboratory during pulmonary function measures at pre- and post-exercise intervention. The aerobic exercise intervention consisted of 30 min of treadmill running at 70% of HR_{peak}. Heart rate was measured by Polar H7 (Polar Electro Oy, Finland) devices and was continuously monitored by using the Polar Team App (version 1.8.8, Polar Electro Oy, Finland) during the exercise intervention. Participants were asked to refrain from alcohol consumption and any moderate to vigorous physical activity for at least 24 h and to fast for 12 h prior to the second and third visits. To avoid any confounding effect of aerobic exercise and PM_{2.5} inhalation between the second and third visits, the participants had at least 7 days of wash-out period.

2.3. PM_{2.5} Concentration

Concomitant outdoor and indoor PM_{2.5} concentrations were continuously monitored during the exercise intervention by using a light-scattering laser photometer device (SIDEPAK™ AM520 Personal Aerosol Monitor, TSI Ltd., USA). The light-scattering laser photometers were placed at the same spots throughout the research. PM_{2.5} concentrations were averaged every minute with continuously recorded values during the exercise intervention.

2.4. Height, Body Mass and Body Composition

Height was measured to the nearest 0.1 cm by a conventional stadiometer and body mass was measured with an Inbody 720 Scale (Biospace, Korea). Body composition was measured and assessed by dual-energy X-ray absorptiometry (Prodigy, GE Healthcare, USA). Body mass index (BMI) was calculated using the following equation; body mass (kg)/height² (m²). All anthropometric measurements were performed before the exercise intervention in the second and third visits.

2.5. Pulmonary Function

Spirometry and DLCO were measured to assess the basic pulmonary function parameters and the lung's capability to transfer the inhaled gas to the alveolar capillary vessels by using a Quark PFT system connected with its respiratory chamber (COSMED, Italy). The same research staff continuously monitored the participant's mouthpiece (Proguard EX, GMS KOREA, Korea) and nose clip position to ensure that there was no gas leakage during the test. The spirometry measurement was performed to assess FVC, FEV₁, FEV₁/FVC, and forced expiratory flow between 25% and 75% of the FVC (FEF₂₅₋₇₅) in a standing position following the American Thoracic Society (ATS) guidelines [24]. The DLCO was measured using a gas containing 0.3% CO, 0.3% CH₄, 20.85% O₂, and Bal N₂ while sitting on a chair in the respiratory chamber. The participants exhaled fully before maximal gas inhalation and then held their breath for 10 s before exhaling the gas normally during the DLCO procedure. In our laboratory, the day-to-day coefficient of variation for spirometry variables were lower than 0.9% and DLCO variables were less than 3.8%.

2.6. Statistical Analysis

All statistical analyses were performed with SPSS version 27 (IBM SPSS Inc., USA). Data are presented as mean ± standard error. We confirmed the normality of data by using the Shapiro–Wilk test. We used a paired *t*-test to confirm whether there were changes in the body composition and pulmonary function at pre-exercise intervention between the second and third visits. The Mann–Whitney U test was used to compare the outdoor and indoor PM_{2.5} concentrations between high and low PM_{2.5} conditions. We employed the analysis of variance (ANOVA) with repeated measures to demonstrate the PM_{2.5} conditions (high vs. low) × time (pre- vs. post-exercise) interaction effect on pulmonary function. All statistical significance was set as *p* < 0.05.

3. Results

3.1. Participants' Characteristics and PM_{2.5} Concentration

The characteristics of participants are shown in Table 1. They were all healthy young men ($n = 9$; 24.6 ± 0.4 years) without abnormal lung function.

Table 1. Participant's characteristics.

Group	Participants ($n = 9$)
Age (years)	24.6 ± 0.4
Height (cm)	177.4 ± 1.5
Body mass (kg)	77.9 ± 1.6
BMI (kg/m ²)	24.8 ± 0.6
VO ₂ peak (mL/kg/min)	55.0 ± 18.3

Note. Data are mean $\pm$ standard error. BMI, body mass index; VO₂peak, peak oxygen consumption.

Outdoor and indoor PM_{2.5} concentrations in high PM_{2.5} conditions were significantly higher than those in low PM_{2.5} conditions during the aerobic exercise session ($p < 0.001$; Table 2). According to the air quality index (AQI) issued by Environmental Protection Agency (EPA), the concentration of indoor PM_{2.5} was categorized as 'good' in low PM_{2.5} conditions and 'unhealthy for sensitive groups or unhealthy' in high PM_{2.5} conditions during exercise. Additionally, indoor PM_{2.5} concentration in high PM_{2.5} conditions was higher than the recommended U.S. National Ambient Air Quality Standards (NAAQS) for PM_{2.5} of 35 $\mu\text{g}/\text{m}^3$ (mean: 59 $\mu\text{g}/\text{m}^3$, range: 50–73 $\mu\text{g}/\text{m}^3$). There were no adverse events during or after the exercise interventions in both high and low PM_{2.5} conditions.

Table 2. Outdoor and indoor PM_{2.5} concentrations during exercise intervention.

	HPM	LPM
Outdoor PM _{2.5} concentration ($\mu\text{g}/\text{m}^3$)	150.9 ± 27.1 (71, 280)	17.6 ± 4.7 (5, 40) *
Indoor PM _{2.5} concentration ($\mu\text{g}/\text{m}^3$)	59.0 ± 2.1 (50, 73)	7.8 ± 1.0 (5, 13) *

Note. Data are mean $\pm$ standard error (minimum, maximum). HPM, high PM_{2.5} condition; LPM, low PM_{2.5} condition. * $p < 0.001$ vs. HPM.

3.2. Pulmonary Function

Performing acute moderate-intensity aerobic exercise did not have any notable difference in FVC, FEV₁, FEV₁/FVC, and FEF_{25–75} between high and low PM_{2.5} conditions ($p \geq 0.24$; Table 3, Figure 1). Additionally, there was no effect of high PM_{2.5} conditions on DLCO and DLCO/VA in response to acute moderate-intensity aerobic exercise compared with low PM_{2.5} conditions ($p \geq 0.09$; Table 3, Figure 2).

Table 3. Pulmonary function measures at pre- and post-exercise intervention.

	HPM		LPM	
	Pre	Post	Pre	Post
FVC (L)	5.22 ± 0.16	5.23 ± 0.15	5.27 ± 0.19	5.30 ± 0.18
(% predicted)	106.67 ± 2.84	106.78 ± 2.84	107.44 ± 3.22	108.22 ± 3.20
FEV ₁ (L)	4.47 ± 0.13	4.43 ± 0.16	4.49 ± 0.13	4.58 ± 0.13
(% predicted)	106.22 ± 3.08	105.33 ± 3.33	106.56 ± 3.12	108.67 ± 3.30
FEV ₁ /FVC (%)	86.01 ± 2.49	85.16 ± 3.68	85.76 ± 2.44	86.76 ± 2.39
(% predicted)	99.33 ± 2.81	98.44 ± 4.14	98.89 ± 2.61	100.00 ± 2.60
FEF _{25–75} (%)	5.01 ± 0.43	4.94 ± 0.47	4.96 ± 0.38	5.21 ± 0.42
(% predicted)	105.33 ± 9.28	101.56 ± 9.85	104.00 ± 8.30	109.00 ± 9.19

DLCO				
(mL/min/mmHg)	36.41 ± 1.66	35.05 ± 1.83	35.66 ± 1.64	34.94 ± 1.70
(% predicted)	101.44 ± 4.11	97.56 ± 4.50	99.33 ± 4.53	97.33 ± 4.46
DLCO/VA				
(mL/min/mmHg/L)	5.40 ± 0.12	5.24 ± 0.13	5.25 ± 0.13	5.02 ± 0.11
(% predicted)	104.56 ± 2.27	101.44 ± 2.56	101.44 ± 2.29	97.33 ± 2.11

Note. Data are mean ± standard error. HPM, high PM_{2.5} condition; LPM, low PM_{2.5} condition; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; FEV_{25–75}, forced expiratory flow between 25% and 75% of the FVC; DLCO, diffusing capacity for carbon monoxide; DLCO/VA, DLCO corrected by alveolar volume.

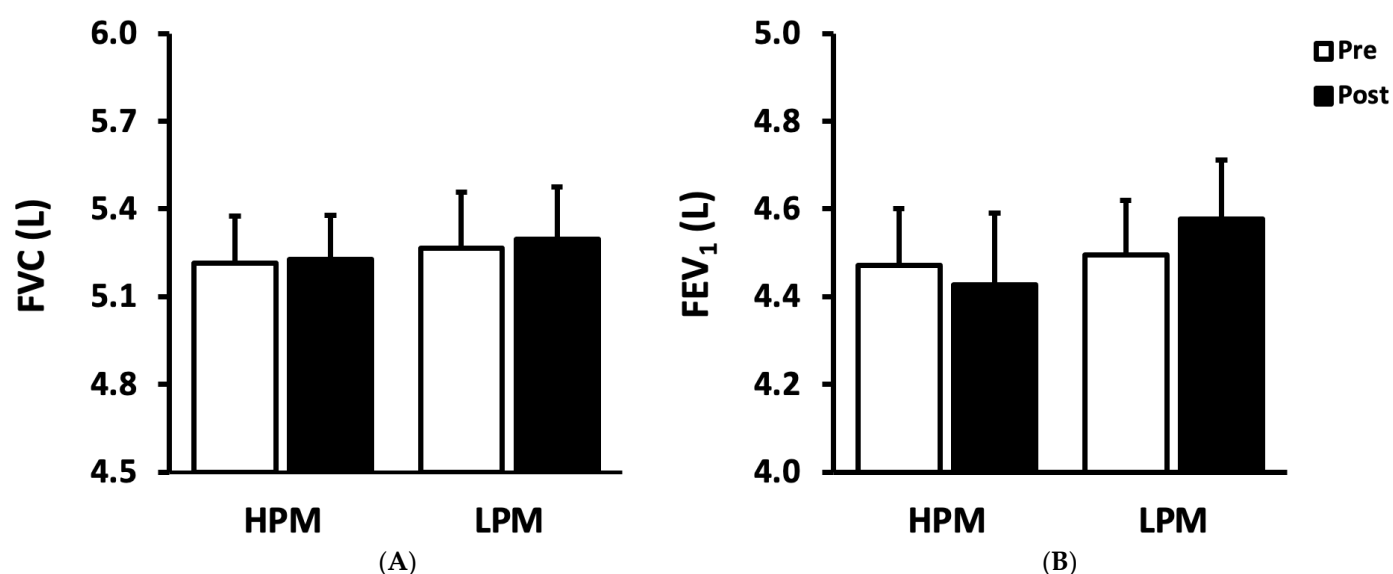


Figure 1. FVC (panel A) and FEV₁ (panel B) at pre- and post-exercise intervention. Data are mean ± standard error. FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; HPM, high PM_{2.5} condition; LPM, low PM_{2.5} condition. $p \geq 0.50$ for time-condition interaction.

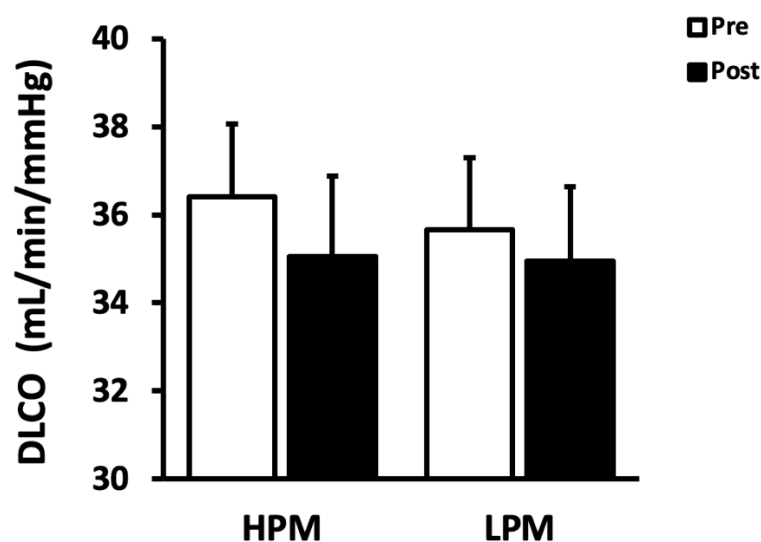


Figure 2. DLCO at pre- and post-exercise intervention. Data are mean ± standard error. DLCO, diffusing capacity of carbon monoxide; HPM, high PM_{2.5} condition; LPM, low PM_{2.5} condition. $p = 0.09$ for time-condition interaction.

4. Discussion

This study examined the effect of acute moderate-intensity aerobic exercise, which might substantially increase in the inhalation of PM_{2.5} particles, on the pulmonary function and lung diffusion capacity under high PM_{2.5} conditions compared with low PM_{2.5} conditions. To our knowledge, this is the first study to assess changes in DLCO with conventional pulmonary function parameters in response to aerobic exercise interventions in high PM_{2.5} conditions. Our results imply that performing moderate-intensity aerobic exercise even in high PM_{2.5} concentrations categorized as ‘unhealthy for sensitive groups or unhealthy’ level from AQI might not play a negative role on pulmonary function in healthy young men.

Spirometry is a pulmonary function test that assesses the volume and flow rate of air during inhalation and/or exhalation. FVC and FEV₁, the main results from spirometry, are helpful in distinguishing obstructive and restrictive respiratory diseases and categorizing the severity of asthma and chronic obstructive pulmonary disease (COPD). Inhalation of PM_{2.5} can impair the respiratory system by irritating the whole airway and inducing oxidative stress and inflammation [21,25–29]. Oxidative stress and inflammation may cause mucus hypersecretion and contraction of the airway smooth muscle, increasing airway resistance [29–31]. Moreover, long-term PM_{2.5} exposure is known to increase the risk of respiratory diseases, COPD, pneumonia, and lung cancer mortality [32]. However, even though aerobic exercise induces increased inhalation of PM_{2.5}, we could not find any changes in pulmonary function after exercise in high PM_{2.5} conditions. Previous studies have reported inconsistent findings on the effects of exercise on pulmonary function in polluted environments [17–21,33,34]. It is speculated that the inconsistent findings resulted from studies’ designs and the methodological differences among them; the source of air pollutants, exposure time, exercise type, exercise intensity, and time point of measuring pulmonary function varied. Moreover, our participants’ cardiorespiratory fitness might nullify the negative effect of PM_{2.5} on pulmonary function. They were recreationally active men with high VO_{2peak} values, which can be defined as an excellent group according to the American College of Sports Medicine (ACSM) fitness classification [35]. VO_{2peak} is negatively correlated with oxidative stress and inflammation, and positively related to total antioxidant capacity [36,37]. Therefore, an increased cardiorespiratory fitness level might protect the pulmonary function against oxidation stress and inflammation caused by PM_{2.5}.

We did not observe any changes in DLCO after acute moderate-intensity aerobic exercise in high PM_{2.5} conditions. In contrast to our findings, a previous study showed a decrease in DLCO after exposure to 50 µg/m³ of carbon ultrafine particles for two hours [38]. Pietropaoli et al. suggested that pulmonary gas diffusing capacity can be reduced owing to PM-induced pulmonary vasoconstriction [38]. Pulmonary endothelial dysfunction caused by exposure to high PM_{2.5} levels is considered a probable physiological mechanism for pulmonary vasoconstriction [39,40]. In a rodent model, the lumen to wall ratio in small pulmonary arteries was also reduced after exposure to ambient pollutants [41]. Regarding DLCO results, the reason for the differences between this study and the previous findings is also thought to be because of discrepancies in the experiment settings, major pollutants, pollutant exposure time, and post-exposure measurement time. Thus, the lack of related studies and unclear physiological mechanisms needs to be supplemented through well-designed future studies.

In the present study, we did not find any significant difference in pulmonary function and DLCO response to exercise in high and low PM_{2.5} conditions. This result implies that high levels of PM_{2.5} do not impair lung airways and pulmonary function in recreationally active healthy young individuals. However, these results should not be applied to older adults and patients with acute or chronic respiratory diseases because their lung airways are likely to be obstructed by high levels of PM_{2.5} exposure. This study was conducted in an indoor training facility where the ambient PM_{2.5} level changes every day according to

outside ambient PM_{2.5} concentration. Unlike laboratory settings in which only diesel exhaust gas is exposed in a chamber, the experimental design of this study may have the advantage that the local characteristics of real world air pollutants are reflected. Moreover, our study's data presenting the difference between the indoor and outdoor average PM_{2.5} concentrations can be helpful in establishing guidelines that help those who want to exercise safely in an indoor facility by referring to real-time outdoor air quality data provided by the country.

Despite this study's strengths, we admit there were several limitations in this study. First, contrary to our study plan, the difference in the wash-out period between the second and third visits varied among study participants because we scheduled them based on the weather forecast and real-time measurements of PM_{2.5} early in the morning of each visit. However, we asked our participants to keep their normal lifestyle throughout the study participation and confirmed that there was no difference in their body composition and pulmonary function parameters between the second and third visits. Second, even though we asked participants to wear masks to minimize PM_{2.5} exposure on the way to our laboratory, they might be unintentionally exposed to different PM_{2.5} conditions because of their different residences, distances from the laboratory, and the way in which they reached the laboratory. In addition, our findings cannot be generalized to other groups of people who have different age, gender, place of residence, health status, or physical activity levels because the sample size was small and all participants were recreationally active and healthy young men. Third, even if the exercise intervention in our study followed the ACSM's guideline [42], individuals might have different responses to the exercise and PM_{2.5} exposure depending on their lactate threshold. If the intensity of exercise intervention were above the lactate threshold, the participant would have increased ventilation due to lactate acid buffering and increased metabolism, causing an increase in PM_{2.5} inhalation. Fourth, since participants were exposed to the indoor ambient air penetrated from the outdoor environment, we could not maintain a constant PM_{2.5} concentration during the exercise and control the potential unexpected influence of other ambient gaseous pollutants, such as ozone, nitrogen dioxide, black carbon, and so on. Additionally, we admit that it would be very hard for this study to be replicated by future studies with the same concentrations and constituents of PM_{2.5} due to differences in regional PM_{2.5} conditions. However, future studies with similar study designs with our protocol can be conducted under similar PM_{2.5} concentrations in indoor facilities or environmental chambers using naturally formed PM_{2.5} or diesel exhaust. Lastly, this study had also planned to test the feasibility of whether we could conduct this type of functional study in natural, ambient settings without artificial manipulation of the environmental conditions. Thus, we could not get an insight into the physiological mechanisms involved in our new findings.

5. Conclusions

In conclusion, performing acute moderate-intensity aerobic exercise under high PM_{2.5} levels may not negatively affect pulmonary function and lung diffusion capacity in healthy young adults. However, these findings must be cautiously interpreted due to the small sample size and participants' characteristics. Even though increased PM_{2.5} inhalation during aerobic exercise did not influence pulmonary function and lung diffusion capacity in recreationally active healthy young men, it might cause clinical or sub-clinical consequences in other populations more susceptible to air pollutants.

Author Contributions: Conceptualization, J.-S.K., D.G.L., L.W., H.K. and M.-H.H.; methodology, J.-S.K., D.G.L. and M.-H.H.; software, J.-S.K., D.G.L. and M.-H.H.; formal analysis, J.-S.K., D.G.L. and M.-H.H.; investigation, J.-S.K. and L.W.; resources, H.K. and M.-H.H.; data curation, J.-S.K.; writing—original draft preparation, J.-S.K. and M.-H.H.; writing—review and editing, D.G.L., L.W. and H.K.; visualization, J.-S.K.; supervision, M.-H.H.; project administration, H.K. and M.-H.H.; funding acquisition, H.K. and M.-H.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research was supported by the Incheon National University Institute of Convergence Science & Technology, 2018.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Incheon National University (7007971-201907-004-01-02 and 09/05/2019).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Acknowledgments: The authors thank the study participants for their time and effort.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References

1. Ni, L.; Chuang, C.C.; Zuo, L. Fine particulate matter in acute exacerbation of COPD. *Front. Physiol.* **2015**, *6*, 294. <https://doi.org/10.3389/fphys.2015.00294>.
2. Brook, R.D.; Rajagopalan, S.; Pope, C.A., 3rd; Brook, J.R.; Bhatnagar, A.; Diez-Roux, A.V.; Holguin, F.; Hong, Y.; Luepker, R.V.; Mittleman, M.A.; et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation* **2010**, *121*, 2331–2378. <https://doi.org/10.1161/CIR.0b013e3181dbee1>.
3. Ostro, B.; Broadwin, R.; Green, S.; Feng, W.-Y.; Lipsett, M. Fine particulate air pollution and mortality in nine California counties: Results from CALFINE. *Environ. Health Perspect.* **2006**, *114*, 29–33. <https://doi.org/10.1289/enh.8335>.
4. Schwartz, J.; Dockery, D.W.; Neas, L.M. Is daily mortality associated specifically with fine particles? *J. Air Waste Manag. Assoc.* **1996**, *46*, 927–939.
5. IARC. *Monographs on the Evaluation of Carcinogenic Risks to Human: Outdoor Air Pollution*; International Agency for Research on Cancer: Lyon, France, **2016**; Volume 109.
6. Karagulian, F.; Belis, C.A.; Dora, C.F.C.; Prüss-Ustün, A.M.; Bonjour, S.; Adair-Rohani, H.; Amann, M. Contributions to cities' ambient particulate matter (PM): A systematic review of local source contributions at global level. *Atmos. Environ.* **2015**, *120*, 475–483. <https://doi.org/10.1016/j.atmosenv.2015.08.087>.
7. Krebs, B.; Burney, J.; Zivin, J.G.; Neidell, M. Using Crowd-Sourced Data to Assess the Temporal and Spatial Relationship between Indoor and Outdoor Particulate Matter. *Environ. Sci. Technol.* **2021**, *55*, 6107–6115. <https://doi.org/10.1021/acs.est.0c08469>.
8. Miller, F.J.; Asgharian, B.; Schroeter, J.D.; Price, O. Improvements and additions to the Multiple Path Particle Dosimetry model. *J. Aerosol. Sci.* **2016**, *99*, 14–26. <https://doi.org/10.1016/j.jaerosci.2016.01.018>.
9. Nemmar, A.; Holme, J.A.; Rosas, I.; Schwarze, P.E.; Alfaro-Moreno, E. Recent advances in particulate matter and nanoparticle toxicology: A review of the in vivo and in vitro studies. *Biomed. Res. Int.* **2013**, *2013*, 279371. <https://doi.org/10.1155/2013/279371>.
10. EPA, U.S. *Integrated Science Assessment (ISA) for Particulate Matter (Final Report, Dec 2019)*; U.S. Environmental Protection Agency: Washington, DC, USA, **2019**.
11. Hansen, E.S.H.; Pitzner-Fabrizius, A.; Toennesen, L.L.; Rasmusen, H.K.; Hostrup, M.; Hellsten, Y.; Backer, V.; Henriksen, M. Effect of aerobic exercise training on asthma in adults: A systematic review and meta-analysis. *Eur. Respir. J.* **2020**, *56*, 2000146. <https://doi.org/10.1183/13993003.00146-2020>.
12. Giles, L.V.; Carlsten, C.; Koehle, M.S. The effect of pre-exercise diesel exhaust exposure on cycling performance and cardio-respiratory variables. *Inhal. Toxicol.* **2012**, *24*, 783–789. <https://doi.org/10.3109/08958378.2012.717649>.
13. Angane, E.Y.; Navare, A.A. Effects of aerobic exercise on pulmonary function tests in healthy adults. *Int. J. Res. Med. Sci.* **2017**, *4*, 2059–2063. <https://doi.org/10.18203/2320-6012.ijrms20161760>.
14. Munibuddin, A.; Khan, S.; Choudhari, S.; Doiphode, R. Effect of traditional aerobic exercises versus sprint interval training on pulmonary function tests in young sedentary males: A randomised controlled trial. *J. Clin. Diagn. Res.* **2013**, *7*, 1890. <https://doi.org/10.7860/JCDR/2013/5797.3343>.
15. McCafferty, W.B.; Horvath, S. *Air Pollution and Athletic Performance*; Thomas: Springfield, IL, USA, **1981**.
16. Daigle, C.C.; Chalupa, D.C.; Gibb, F.R.; Morrow, P.E.; Oberdorster, G.; Utell, M.J.; Frampton, M.W. Ultrafine particle deposition in humans during rest and exercise. *Inhal. Toxicol.* **2003**, *15*, 539–552. <https://doi.org/10.1080/089583703004468>.
17. Giles, L.V.; Carlsten, C.; Koehle, M.S. The pulmonary and autonomic effects of high-intensity and low-intensity exercise in diesel exhaust. *Environ. Health* **2018**, *17*, 87. <https://doi.org/10.1186/s12940-018-0434-6>.
18. Sinharay, R.; Gong, J.; Barratt, B.; Ohman-Strickland, P.; Ernst, S.; Kelly, F.J.; Zhang, J.J.; Collins, P.; Cullinan, P.; Chung, K.F. Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: A randomised, crossover study. *Lancet* **2018**, *391*, 339–349. [https://doi.org/10.1016/S0140-6736\(17\)32643-0](https://doi.org/10.1016/S0140-6736(17)32643-0).

19. Wagner, D.R.; Brandley, D.C. Exercise in Thermal Inversions: PM_{2.5} Air Pollution Effects on Pulmonary Function and Aerobic Performance. *Wilderness Environ. Med.* **2020**, *31*, 16–22. <https://doi.org/10.1016/j.wem.2019.10.005>.
20. Wagner, D.R.; Clark, N.W. Effects of ambient particulate matter on aerobic exercise performance. *J. Exerc. Sci. Fit.* **2018**, *16*, 12–15. <https://doi.org/10.1016/j.jesf.2018.01.002>.
21. Wyatt, L.H.; Devlin, R.B.; Rappold, A.G.; Case, M.W.; Diaz-Sanchez, D. Low levels of fine particulate matter increase vascular damage and reduce pulmonary function in young healthy adults. *Part Fibre Toxicol.* **2020**, *17*, 58. <https://doi.org/10.1186/s12989-020-00389-5>.
22. Quanjer, P.H.; Stanojevic, S.; Cole, T.J.; Baur, X.; Hall, G.L.; Culver, B.H.; Enright, P.L.; Hankinson, J.L.; Ip, M.S.; Zheng, J.; et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: The global lung function 2012 equations. *Eur. Respir. J.* **2012**, *40*, 1324–1343. <https://doi.org/10.1183/09031936.00080312>.
23. Stefani, L.; Mascherini, G.; Galanti, G. Aerobic threshold for exercise prescription. *Int. J. Clin. Med.* **2010**, *1*, 6–9. <https://doi.org/10.4236/ijcm.2010.11002>.
24. Miller, M.R.; Hankinson, J.; Brusasco, V.; Burgos, F.; Casaburi, R.; Coates, A.; Crapo, R.; Enright, P.; van der Grinten, C.P.M.; Gustafsson, P.; et al. Standardisation of spirometry. *Eur. Respir. J.* **2005**, *26*, 319–338. <https://doi.org/10.1183/09031936.05.00034805>.
25. Ghio, A.J.; Kim, C.; Devlin, R.B. Concentrated ambient air particles induce mild pulmonary inflammation in healthy human volunteers. *Am. J. Resp. Crit. Care* **2000**, *162*, 981–988. <https://doi.org/10.1164/ajrccm.162.3.9911115>.
26. Kocot, K.; Baranski, K.; Melaniuk-Wolny, E.; Zajusz-Zubek, E.; Kowalska, M. Acute FeNO and Blood Pressure Responses to Air Pollution Exposure in Young Adults during Physical Activity. *Int. J. Env. Res. Pub. Health* **2020**, *17*, 9012. <https://doi.org/10.3390/ijerph17239012>.
27. Riva, D.R.; Magalhaes, C.B.; Lopes, A.A.; Lancas, T.; Mauad, T.; Malm, O.; Valenca, S.S.; Saldiva, P.H.; Faffe, D.S.; Zin, W.A. Low dose of fine particulate matter (PM_{2.5}) can induce acute oxidative stress, inflammation and pulmonary impairment in healthy mice. *Inhal. Toxicol.* **2011**, *23*, 257–267. <https://doi.org/10.3109/08958378.2011.566290>.
28. Zhu, X.; Chen, C.; Zhang, B.; Ge, Y.; Wang, W.; Cai, J.; Kan, H. Acute effects of personal exposure to fine particulate matter on salivary and urinary biomarkers of inflammation and oxidative stress in healthy adults. *Chemosphere* **2021**, *272*, 129906. <https://doi.org/10.1016/j.chemosphere.2021.129906>.
29. Peixoto, M.S.; Galvao, M.F.D.; de Medeiros, S.R.B. Cell death pathways of particulate matter toxicity. *Chemosphere* **2017**, *188*, 32–48. <https://doi.org/10.1016/j.chemosphere.2017.08.076>.
30. Bousquet, J.; Jeffery, P.K.; Busse, W.W.; Johnson, M.; Vignola, A.M. Asthma—From bronchoconstriction to airways inflammation and remodeling. *Am. J. Resp. Crit. Care* **2000**, *161*, 1720–1745. <https://doi.org/10.1164/ajrccm.161.5.9903102>.
31. MacNee, W.; Rahman, I. Is oxidative stress central to the pathogenesis of chronic obstructive pulmonary disease? *Trends Mol. Med.* **2001**, *7*, 55–62. [https://doi.org/10.1016/S1471-4914\(01\)01912-8](https://doi.org/10.1016/S1471-4914(01)01912-8).
32. Pun, V.C.; Kazemiparkouhi, F.; Manjourides, J.; Suh, H.H. Long-Term PM_{2.5} Exposure and Respiratory, Cancer, and Cardiovascular Mortality in Older US Adults. *Am. J. Epidemiol.* **2017**, *186*, 961–969. <https://doi.org/10.1093/aje/kwx166>.
33. Gong, H.; Linn, W.S.; Clark, K.W.; Anderson, K.R.; Sioutas, C.; Alexis, N.E.; Cascio, W.E.; Devlin, R.B. Exposures of healthy and asthmatic volunteers to concentrated ambient ultrafine particles in los angeles. *Inhal. Toxicol.* **2008**, *20*, 533–545. <https://doi.org/10.1080/08958370801911340>.
34. Park, H.Y.; Gilbreath, S.; Barakatt, E. Respiratory outcomes of ultrafine particulate matter (UFP) as a surrogate measure of near-roadway exposures among bicyclists. *Environ. Health. Glob.* **2017**, *16*, 6. <https://doi.org/10.1186/s12940-017-0212-x>.
35. Medicine, A.C.o.S. *ACSM's Health-Related Physical Fitness Assessment Manual*; Lippincott Williams & Wilkins: Philadelphia, PA, USA, **2013**.
36. Child, R.; Wilkinson, D.; Fallowfield, J. Resting serum antioxidant status is positively correlated with peak oxygen uptake in endurance trained runners. *J. Sports Med. Phys. Fit.* **1999**, *39*, 282.
37. de Camargo, A.A.; de Castro, R.A.S.; Vieira, R.P.; Oliveira-Júnior, M.C.; Araujo, A.A.d.; De Angelis, K.; Rached, S.Z.; Athanazio, R.A.; Stelmach, R.; Corso, S.D. Systemic Inflammation and Oxidative Stress in Adults with Bronchiectasis: Association with Clinical and Functional Features. *Clinics* **2021**, *76*, e2474. <https://doi.org/10.6061/clinics/2021/e2474>.
38. Pietropaoli, A.P.; Frampton, M.W.; Hyde, R.W.; Morrow, P.E.; Oberdorster, G.; Cox, C.; Speers, D.M.; Frasier, L.M.; Chalupa, D.C.; Huang, L.S.; et al. Pulmonary function, diffusing capacity, and inflammation in healthy and asthmatic subjects exposed to ultrafine particles. *Inhal. Toxicol.* **2004**, *16 Suppl 1*, 59–72. <https://doi.org/10.1080/08958370490443079>.
39. Brook, R.D.; Brook, J.R.; Urch, B.; Vincent, R.; Rajagopalan, S.; Silverman, F. Inhalation of fine particulate air pollution and ozone causes acute arterial vasoconstriction in healthy adults. *Circulation* **2002**, *105*, 1534–1536. <https://doi.org/10.1161/01.cir.0000013838.94747.64>.
40. Cutrufello, P.T.; Rundell, K.W.; Smoliga, J.M.; Stylianides, G.A. Inhaled whole exhaust and its effect on exercise performance and vascular function. *Inhal. Toxicol.* **2011**, *23*, 658–667. <https://doi.org/10.3109/08958378.2011.604106>.

41. Batalha, J.R.; Saldiva, P.H.; Clarke, R.W.; Coull, B.A.; Stearns, R.C.; Lawrence, J.; Murthy, G.G.; Koutrakis, P.; Godleski, J.J. Concentrated ambient air particles induce vasoconstriction of small pulmonary arteries in rats. *Environ. Health Perspect.* **2002**, *110*, 1191–1197. <https://doi.org/10.1289/ehp.021101191>.
42. Garber, C.E.; Blissmer, B.; Deschenes, M.R.; Franklin, B.A.; Lamonte, M.J.; Lee, I.-M.; Nieman, D.C.; Swain, D.P. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med. Sci. Sports Exerc.* **2011**, *43*, 1334–1359. <https://doi.org/10.1249/MSS.0b013e318213febf>.