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Exercising under particulate matter exposure: Providing theoretical support for lung deposition and its relationship with COVID-19

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ABSTRACT

The aim of the present study was to investigate lung particulate matter (PM) deposition during endurance exercise and provide a new insight concerning how SARS-CoV-2 could be carried into the respiratory tract. The anatomical and physiological characteristics of the Human Respiratory Tract model were considered for modeling the lung PM deposition during exercise. The Monte Carlo method was performed to randomly generate different values of PM concentrations (1.0, 2.5, and 10.0 μm) per minute of exercise at moderate, heavy, and severe exercise intensity domains. Compared to moderate and severe intensities, during heavy exercise (75–115 L·min⁻¹, duration of 10.0–60.0 min) there is greater lung deposition in the bronchiolar region (p < 0.01). In turn, there is greater deposition per minute of exercise at the severe intensity domain (115.0–145.0 L·min⁻¹, duration of 10.0–20.0 min, p < 0.01). Considering that SARS-CoV-2 could be adsorbed on the particles exercising under PM exposure, mainly at the severe domain, could be harmful concerning the virus. In conclusion, beyond the traditional minute ventilation assumption, there is a time vs intensity dependence for PM deposition, whereby the severe domain presents greater deposition per minute of exercise. The results observed for PM deposition are alarming since SARS-CoV-2 could be adsorbed by particles and carried into the deeper respiratory tract.

1. Introduction

A contemporary paradox of the health benefits of physical exercise and adverse environmental factors has been established; while the positive health adaptations from exercise practice are widely known (Bull et al., 2020; Garber et al., 2011), the threat imposed by air pollution exposure may negate these positive gains (Cutrufello et al., 2012; Giles and Koehle, 2014; Marmett et al., 2020; Nyhan et al., 2014). Although several studies have addressed this issue (Giles et al., 2018; Pasqua et al., 2018, 2020), the way in which exercising under air pollution exposure impacts health needs further clarification. For instance, the extent to which exercise may switch from beneficial to harmful in a polluted environment could depend on exercise intensity and exercise duration. In this sense, previous studies have indicated no differences in pulmonary function comparing low- and high-intensities of exercise under PM exposure (Giles et al., 2018). In addition, prolonged exercise has also been considered as a health threat, although cardiovascular and inflammation cytokines were only affected by air pollution after 90-min of low-intensity exercise (Pasqua et al., 2020).

Greater exposure to pollutants is observed in endurance exercises due to a physiological adaptation in respiratory pattern during the transition from rest to effort, where there is an exponential and positive relationship between the intensity of exercise and minute ventilation (Cruz et al., 2020; Nyhan et al., 2014). Nevertheless, it remains unknown whether the balance between the total amount of pollutants inhaled and the values of minute ventilation could or could not determine negative health outcomes, mainly for exercises with short duration (e.g. 10–30 min) and higher intensity (close to maximal oxygen consumption, VO2max). In addition, the anatomical filters present in the respiratory tract must be considered (ICRP, 1994; McNabola et al., 2008; Nyhan et al., 2014) to broaden understanding of the air pollution, health, and exercise interface. Beyond the health-related issues caused by air pollution exposure, severe acute respiratory...
syndrome coronavirus 2 (SARS-CoV-2) causes the novel coronavirus disease 2019 (COVID-19), establishing a pandemic health condition. In this sense, it has been proposed that a virus may be carried on the PM, which will assist in the transport of the virus throughout the respiratory tract (Lolli et al., 2020; Tung et al., 2021). Indeed, previous studies suggest that air pollution (mainly PM) could lead to the spread of the SARS-CoV2 virus (Tung et al., 2021).

From the point of view of environmental physiology, it is still unclear how lung filtration level could be related to intensity and duration of exercise as well as the ratio of PM deposition at each lung level. Beyond the health risks imposed by PM when exercises are performed, since the pandemic started, poor air quality could also increase the virus threat. Understanding how PM is deposited in the lung during endurance exercise, how lung filtration level could be related to intensity and duration of exercise as well as the ratio of PM deposition at each lung level, is critical to the transport of the virus throughout the respiratory tract. Thus, a mathematical modeling approach was proposed to understand how PM is deposited in the lung during endurance exercise, and how deep the SARS-CoV-2 could be carried into the respiratory tract by the PM.

2. Methods

2.1. Study design

Mathematical modeling for lung air pollutant deposition was performed to estimate the lung deposition of PM at moderate, heavy, and severe exercise-intensity domains. This type of modeling was established by The International Commission for Radiological Protection (ICRP, 1994) and widely applied in previous studies (McNabola et al., 2008; Nyhan et al., 2014). The anatomical and physiological characteristics of the Human Respiratory Tract model were considered for modeling the lung PM deposition in the respiratory tract at four levels, as follows:

i. The extra thoracic region, comprising the anterior nasal (ET1) and posterior nasal passages, larynx, pharynx, and mouth (ET2);
ii. The bronchial region (BB), consisting of the trachea and bronchi from which deposited material is cleared by ciliary action;
iii. The bronchiolar region (bb), consisting of the bronchioles and terminal bronchioles;
iv. The alveolar-interstitial region (AI), consisting of the respiratory bronchioles (bronchioles with some alveoli apposed), the alveolar ducts and sacs with their alveoli, and the interstitial connective tissue.

Eleven parameters were considered for data modeling, as described by (ICRP, 1994). Table 1 summarizes the parameter values of the lung deposition model used in the present paper.

Tidal volume (Tv) and the fraction of total ventilatory airflow ($f_{tota}$) were calculated as functions of minute ventilation (VE) (Equations (1) and (2))

Table 1: Parameter values considered in the lung deposition modeling.

| Parameter | Value |
|-----------|-------|
| Particle density | $2 \text{ g cm}^{-3}$ |
| Air density | $1.14 \text{ kg m}^{-3}$ |
| Kalman coefficient | $1.3806 \times 10^{-13}$ |
| Air dynamic viscosity | $1.9 \times 10^{-5} \text{ kg m}^{-1} \text{s}^{-1}$ |
| Air temperature inside lung | $37 \text{ C}$ |
| Functional residual capacity | $3.392 \text{ L}$ |
| Anatomical dead space in BB | $0.049 \text{ L}$ |
| Anatomical dead space in bb | $0.047 \text{ L}$ |
| Anatomical dead space in ET | $0.05 \text{ L}$ |
| Person age | 30 years |
| Person height | 1.80 m |

$$T_v = \frac{VE}{28} + 0.32$$

$$f_{tota} = \frac{287 \times VE^{-0.45}}{100}$$

The Monte Carlo method was performed to randomly generate different values of minute ventilation and duration of exercise at moderate, heavy, and severe exercise-intensity domains. The method generated 10,000 values of minute ventilation between 40 and 145 L/min and exercise duration from 5 to 90 min. These limits cover a wide range of possibilities found during exercise practice. PM of 1.0, 2.5, and 10.0 μm in diameter were considered to characterize the air pollution present in a metropolitan city. We chose these fractions of PM to represent different pollution sources, formation mechanisms, and penetration capacity through the respiratory tract (Wilson and Suh, 1997).

The fraction between 10 and 2.5 μm of PM$_{10}$ is the coarse mode of inhalable particles. Coarse particles generally result from mechanical disruption processes, such as crushing and grinding. Soil resuspension induced by wind and traffic flow turbulence is the major source of PM$_{10}$ in urban areas. PM$_{2.5}$ represents the fine particles of PM, which are emitted from combustion and originate from complex reactions of chemicals. PM$_{1.0}$ are a major part of PM$_{2.5}$ and explain most of the health effects of PM$_{2.5}$ (Chen et al., 2017). The Monte Carlo method was also used to generate 10,000 values of PM$_{10}$, PM$_{2.5}$, and PM$_{1.0}$ concentrations ranging from 10 to 150 μg·m$^{-3}$. According to the WHO (WHO, 2005), values smaller than 50 for PM$_{10}$ and 10 for PM$_{2.5}$ are desirable and health risks associated with short-term exposure are minimized. The present study did not discriminate between indoor and outdoor physical activities.

2.2. Exercise intensity domains and minute ventilation

The three exercise intensity domains were named as previously recommended (Poole and Richardson, 1997; Xu and Rhodes, 1999). The moderate exercise domain is considered as exercise intensities performed below the Gas Exchange Threshold, the heavy exercise domain as exercise intensities between the Gas Exchange Threshold and respiratory compensation point, and the severe exercise domain as exercise intensities above the respiratory compensation point. Estimated minute ventilation for moderate, heavy, and severe exercise domains were: 40.0–75.0 L·min$^{-1}$, 75–115 L·min$^{-1}$, and 115–145.0 L·min$^{-1}$. The model was applied for exercise of different durations (10–90 min for moderate, 10–60 min for heavy, and 10–20 min for severe exercise
The range values of minute ventilation at each intensity domain were established based on a graded incremental running test, as previously described (Bertuzzi et al., 2013).

2.3. Statistical analysis

The rate of PM deposition was analyzed using mixed model ANOVA with intensity of exercise (moderate, heavy, and severe domains) and lung level of deposition (ET1, ET2, BB, bb, and Al). To establish the intensity with the greatest ratio of deposition per minute of exercise, a time-correction adjustment was performed (ratio of lung deposition by duration of exercise). The Tukey's post hoc test was performed to identify the differences when necessary. The significance level was set at $p < 0.05$ and the effect size (ES, 0.20–0.49 small, 0.50–0.79 medium, > 0.80 large) and ETA-squared - $\eta^2$ (0.01–0.05 small, 0.06–0.13 medium, > 0.14 large) of all analyses were reported.

3. Results

The rate of lung deposition for PM1.0, PM2.5, and PM10 at each lung level are presented through the heat maps in Figs. 1–3, respectively. The strongest colors can be observed in the upper limits of each box.

The comparisons between each intensity of exercise showed that the most particles are deposited during the heavy exercise for bb_inh and Al levels ($p < 0.001$), as presented in Fig. 4.

After performing time-correction adjustments, the severe domain presents higher values of ratio of deposition per minute of exercise. Fig. 5 presents all comparisons.

4. Discussion

As the main results, the present study demonstrates that heavy exercise promotes absolute greater PM deposition than moderate and severe domains. The time-correction adjustment shows that the severe
domain provides the greatest deposition in the bronchial region. Considering that SARs-CoV-2 could be adsorbed in the particles, even with only a few minutes of high-intensity exercise (e.g. severe intensity domain), the virus could reach a deep level in the respiratory tract. The novel findings of the study indicate that as well as the minute ventilation to promote greater PM exposure, the time vs intensity must be considered due to the deposition of pollutants at each level of the respiratory tract.

Mathematical modeling has been considered for environmental health studies (Deng et al., 2019). In fact, our study considered the Monte Carlo method to establish how the air pollutants could be deposited in the respiratory tract. Nevertheless, it is important to highlight that the physiological parameter of minute ventilation was based on a previous experimental study (Bertuzzi et al., 2013). Furthermore, the efficiency to retain the pollutants and the lung deposition ratio were based on the theoretical model for lung deposition pollutants established by The International Commission for Radiological Protection (ICRP, 1994; Wilson and Suh, 1997) and widely applied in previous studies (McNabola et al., 2008; Nyhan et al., 2014). Additionally, our methodological approach to the problem allowed a wide range of exercise intensity and time-correction adjustments. Therefore, the results observed in the present study support the inference related to deposition in the respiratory tract in accordance with the intensity and duration of exercise.

The association between air pollution and virus spread/deposition provides an insight into how the SARs-CoV-2 could reach the respiratory tract in accordance with the intensity of exercise. The hypothesis that increasing PM concentration would also increase the probability of infection is derived from recent studies reporting that SARs-CoV-2 might be adsorbed in particles, which could provide a platform for intermixing with the virus (Comunian et al., 2020; Lolli et al., 2020; Tung et al., 2021; Zoran et al., 2020).

The mechanism that increases exposure to PM is established, since at higher physical intensities there is oral predominance, with a higher
volume of air inhaled, bronchial dilation, and dryness of mucosa present in the respiratory tract (Giles and Koehle, 2014; Giorgini et al., 2016; Niinimaa et al., 1980; Zuurbier et al., 2009). Nevertheless, there was no further suggestion of anatomical deposition and efficiency to retain the particles in accordance with intensity and duration of exercise. In fact, the results describing the air pollution, health, and exercise interface are inconsistent (Bos et al., 2013; Giles et al., 2018; Nyhan et al., 2014; Pasqua et al., 2018, 2020). In a recent study, it was demonstrated that prolonged cycling exercise under traffic-related exposure elicits pro-inflammatory cytokines and impairs blood pressure (Pasqua et al., 2020). In turn, it was suggested that cycling under PM$_{2.5}$ exposure did not affect blood pressure and heart rate variability (Pasqua et al., 2018, 2020). In a recent study, it was demonstrated that prolonged cycling exercise under traffic-related exposure elicits pro-inflammatory cytokines and impairs blood pressure (Pasqua et al., 2020). In turn, it was suggested that cycling under PM$_{2.5}$ exposure did not affect blood pressure and heart rate variability (Pasqua et al., 2018, 2020). In a recent study, it was demonstrated that prolonged cycling exercise under traffic-related exposure elicits pro-inflammatory cytokines and impairs blood pressure (Pasqua et al., 2020). In turn, it was suggested that cycling under PM$_{2.5}$ exposure did not affect blood pressure and heart rate variability (Pasqua et al., 2018, 2020).

Recent studies discussed how the respiratory health outcomes of COVID-19 are aligned with air pollution (Bielecki et al., 2020; Comunian et al., 2020; Lolli et al., 2020; Zoran et al., 2020), wherein the systemic inflammation acts as a primary defense mechanism against a stressor agent. In this sense, it has been suggested that the severity of COVID-19 is related to higher activity of ACE-2 through the adhesion to the SARS-CoV-2 spike protein (Paital and Agrawal, 2020; Tung et al., 2021). Additionally, since higher values of PM 2.5 μm in diameter (or less) are

Fig. 3. Heat map of lung deposition at each lung stage and intensity of exercise for particulate matter 10. The boxes represent the range of minute ventilation and duration of exercise at each exercise intensity domain. ET1 = The extra thoracic region. ET2 = Posterior nasal passages, larynx, pharynx, and mouth. BB = Bronchial region. AI = Alveolar-interstitial region. Inh = Inhaled. Exh = Exhaled.
commonly observed in urban areas and the particles could be carriers of the virus (Lolli et al., 2020; Tung et al., 2021), our results demonstrate how these particles (2.5 and 1.0 μm of diameter) may reach the bronchiolar region, mainly for heavy and severe intensity domains. Recent studies have tried to establish how the chance of infection could be increased (Arslan et al., 2020; Qu et al., 2020) and PM adsorption could carry the virus to the lower respiratory tract level, which increases the chances of serious symptoms of COVID-19 (Venkata Mohan et al., 2020). Nevertheless, whether all particles could carry the virus is not yet fully elucidated. For instance, the presence of SARS-CoV-2 RNA has been reported in particles with a diameter lower than 2.5 μm (Nor et al., 2021), however another investigation failed to detect the virus in air samples (Ong et al., 2020).

Finally, the present study has some limitations to be considered. The aim of the study was to provide theoretical support on the understanding about how different intensities of exercise could promote the lung deposition as well as the SARs-CoV-2. In this sense, the results must be interpreted with caution and further experimental studies should be conducted. It is also important to highlight that virus transmission through the air demands further experimental studies, as well as which the physicochemical characteristics of the particles that could carry the virus need to be determined. The Monte Carlo method generates aleatory values within a specific range for particle concentration and minute ventilation values. In this sense, all the data considered in the mathematical model were based on original previous studies. The inferences related to COVID-19 and endurance exercise under PM exposure are preliminary, and the present study proposes an issue that may be important to human health. Even though, it has been reported that environmental condition has important implications in spreading the virus (Rowe et al., 2021). In this work, the atmospheric conditions were restricted to those presented in Table 1. Therefore, different environmental conditions that could influence the fate of the particles must also be considered in further investigations. Although we recognize that some mechanisms related to the disease remain unclear, the efforts of the scientific community to understand all the threats established by the pandemic are praiseworthy.
5. Conclusion

In this work, we present a combination of the lung deposition model and Monte Carlo method to estimate particle deposition in the lungs under a wide range of PM concentrations and three particle sizes. This approach represents a novelty to assess exposure while exercising. Our results suggest the existence of a time vs intensity dependence on particles, wherein the human domain represents the greatest absolute PM deposition, while the severe domain has the highest deposition after time-correction. In both intensities the particles reached the bronchial region, which is threatening since the SARs-CoV-2 could be adsorbed by particles carried into the deeper respiratory tract.

It is important to note that the present study has a theoretical approach and the mechanisms related to the presence of SARs-CoV-2 on particles is not fully elucidated. Thus, the extrapolation of the present results will demand further experimental studies. Despite these limitations, our findings contribute to future investigations in this field.

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