



## **Introduction**

Billions of people worldwide are exposed to environments with air pollution (AP) [

(4) no history of pulmonary or cardiovascular diseases; (5) absence of symptoms such as cold or fever; (6) non-smokers; (7) voluntary participation and cooperation with researchers throughout the study. Exclusion criteria included: (1) nasal allergy sufferers; (2) participants experiencing discomfort such as cold or fever during the trial period; (3) participants who consumed alcohol the day before the trial; (4) inability to tolerate moderate-to-high-intensity exercise; (5) female participants menstruating during the exercise period. All participants provided voluntary informed consent after agreeing to participate in the study. The study received approval from the Ethics Committee of Shanghai University of Sport (Approval No.: 102772019RT001).

The experiments were conducted between September 2023 and December 2023. Participants were instructed to abstain from alcohol consumption and vigorous physical exercise 24 h before the experiment and avoid exposure to high pollution levels in the air. Additionally, coffee and soy milk intake were prohibited within 3 h before testing. To minimize the influence of different measurement times on the results, all experiments and measurements were conducted at the same time of day, and participants were required to consume a standardized meal to reduce interference from the diet. On the day of the experiment, participants arrived at the laboratory at 7:30 a.m., having already consumed their meal prior to arrival. After a brief rest of at least 30 min, they underwent baseline health indicator measurements. Subsequently, they walked to the 100-meter playground for a 90-minute moderate-intensity exercise session, which took place from 9:30 a.m. to 11:00 a.m. The exercise regimen included warm-up running (5 min), warm-up exercises (5 min), aerobic exercises (40 min), games (30 min), and stretching and relaxation (10 min). The entire exercise intervention was led by experienced coaches.

After the 90-minute exercise intervention, participants returned to the laboratory immediately for post-intervention health indicator measurements. Blood samples were collected first, with venous blood collection completed within 15 min after exercise, followed by the measurement of cardiorespiratory health indicators within 30 min after the exercise intervention. Each participant completed PE under three different AP environments, and between each experiment, participants underwent a washout period of at least 2 weeks.

#### Physical exercise monitoring

Before the exercise, participants uniformly wore Polar heart rate monitors to objectively monitor their exercise

Fractional exhaled nitric oxide (FeNO) was measured using the portable NIOX MINO Analyzer (Aerocrine AB, Solna, Sweden).

#### Blood sample collection

irty minutes before the start of the exercise and within 15 min after its completion, trained medical personnel collected venous blood samples from the study participants. Blood samples were drawn using Ethylenediaminetetraacetic Acid (EDTA) anticoagulant tubes for routine blood tests. Serum samples for the measurement of IL-1 , IL-10, IL-6, TNF- , and CRP were centrifuged and aliquoted within 4 h after blood collection and stored at -80 °C.

#### Ethical considerations

Ethics approval for the study was obtained from the Ethics Committee of Shanghai University of Sport (Ethics approval no: 102772019RT001) and registered in the Chinese Clinical Trial Registry (Registered No: ChiCTR2000031851). Written informed consent was obtained from participants before they participated in the study.

#### Statistical analysis

Statistical analysis of the data was conducted using R 4.3.2 software. Descriptive analysis was primarily focused on the basic information of the study participants, pollutant concentrations, and fundamental characteristics of health indicators. Continuous variables were described using arithmetic means and standard deviations, while categorical variables were described using proportions. Changes in health indicators before and after exercise were expressed as relative differences  $((\text{post-exercise} - \text{baseline}) / \text{baseline})$ , where a relative difference  $< 0\%$  indicated a decrease after exercise. The Shapiro-Wilk test was employed to assess the distribution of data. Paired t-tests were used to evaluate the statistical significance of differences between pre- and post-exercise measurements in each experiment. Due to the non-normal distribution of pollutant concentrations, Wilcoxon rank-sum tests were utilized to assess differences between the three different AP levels. Considering the repeated study design, linear mixed-effects models (LME) were constructed using the 'lme4' package in R. These models analyzed changes relative to baseline values after exercise across the three experiments. The study participants' ID was included as

while mean values of PEF and  $FEF_{25-75\%}$  also increased, albeit without significant differences. Additionally, post-exercise FVC still showed a weak significant increase in the medium pollution level environment ( $0.3 \pm 0.5$ ,  $P=0.05$ ). However, post-exercise mean values of FEV1 significantly decreased in the high-level AP environment ( $-0.2 \pm 0.4$ ,  $P=0.031$ ), with other lung function indicators also showing a tendency of decreases in the high pollution level environment.

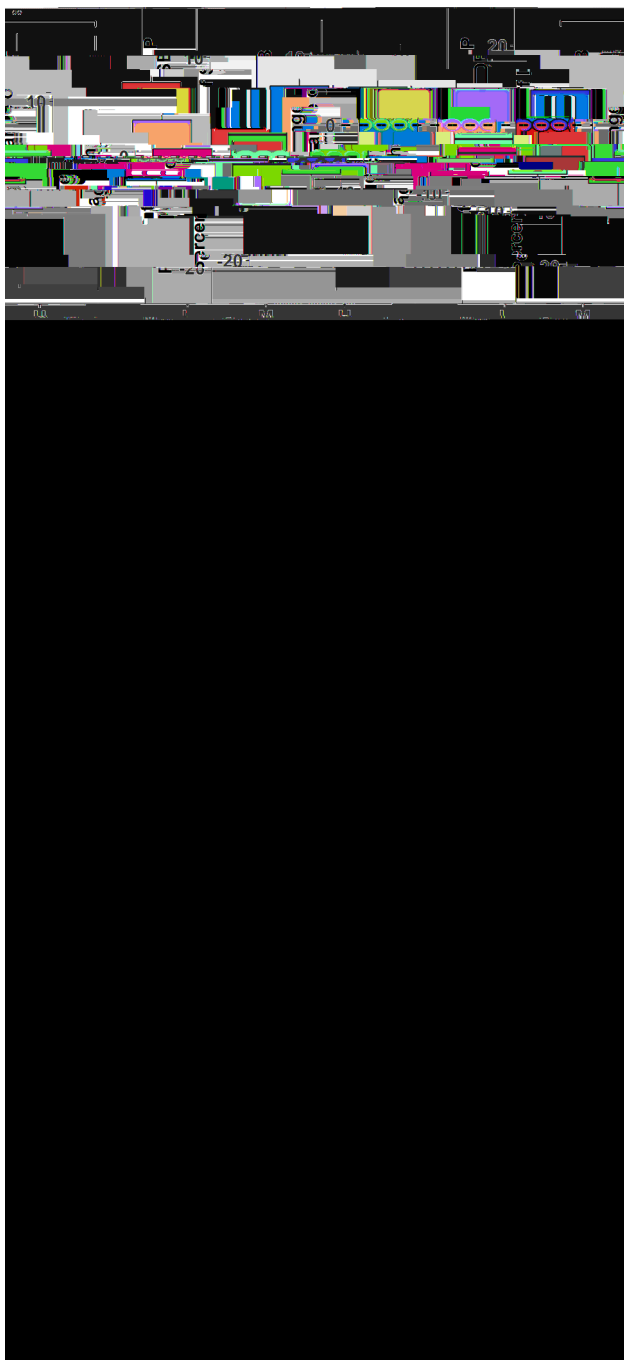
For airway inflammation indicators, we found that FeNO significantly decreased after exercise in both the

low pollution level ( $-3$  ppb,  $p<0.001$ ) and medium pollution level ( $-1.7$  ppb,  $p=0.038$ ) environments, while it tends to be increased in the high pollution level environment, although without significant differences. Moreover, after exposure to environments with three different concentrations of pollution, the percentage change in FeNO values showed an increasing trend.

Based on the observed changes in cardiorespiratory function indicators pre- and post-exercise, it is evident that exercising in medium-level AP environments may not lead to as beneficial significant changes in cardiorespiratory function indicators as seen with exercise in low pollution environments. Conversely, exercising in high pollution environments yields adverse effects. This suggests that AP may diminish the benefits of PE on cardiorespiratory function.

Subsequently, we utilized LME to adjust for participants' gender, age, and BMI. Using the percentage change in cardiorespiratory health indicators after exercising in

further confirmed the aforementioned results. The spe-



**Fig. 3** Percentage change in cardiorespiratory health measurements relative to baseline

**Effects on circulating inflammation markers**

Figure 4 illustrates the percentage change relative to baseline in inflammation markers following exercise across three different levels of AP. Overall, the change in inflammation markers after exercise in environments with high pollution concentrations was notably higher than those in medium and low concentrations, while the changes between medium and low concentrations were small.

Moreover, the majority of inflammation markers showed an increase after exercise regardless of the AP concentration, except monocytes and eosinophils, which exhibited a slight decrease in change after exercise in environments with medium and low concentrations.

Table 4 presents the results of LME analysis comparing the differences in percentage change of inflammation markers between medium and high levels of AP with reference to the percentage change at the low pollution level. The results indicate that compared to the changes observed after exercise in the low pollution environment, there was a significant increase in the levels of white blood cells (27.0,  $p < 0.001$ ), neutrophils (26.8,  $p < 0.001$ ), lymphocytes (32.2,  $p < 0.001$ ), monocytes (28.2,  $p < 0.001$ ), eosinophils (48.9,  $p < 0.001$ ), IL-1 (0.76,  $P = 0.003$ ), IL-10 (0.17,  $P = 0.02$ ), IL-6 (0.1,  $P = 0.17$ ), TNF- (0.97,  $P = 0.011$ ), and CRP(0.17,  $P = 0.003$ ) after exercise in the high pollution environment. Additionally, only eosinophils exhibited a significant increase (25.6,  $p = 0.022$ ) in the medium-pollution environment, while the percentage change in other inflammation cells after exercise in the medium-pollution environment did not significantly differ from that in the low pollution environment. The results above suggest that high levels of AP significantly increase inflammation in the body, while the difference in inflammation levels between medium and low pollution levels is smaller.

**Discussion**

This study conducted a self-controlled crossover design to assess the effects of moderate-intensity PE on the cardiorespiratory health of healthy young adults in environments with low, medium, and high AP concentrations. Our findings indicate that PE in medium and low-level AP environments seems relatively safe for cardiorespiratory health among healthy young adults. However, PE in high-level AP environments can be detrimental to cardiorespiratory health, significantly increasing the body's inflammatory response.

**Pollution levels**

Reviewing previous studies, it is evident that different studies have varied definitions for low- and high-concentration ranges. Some studies classify pollution levels as high, while other studies might consider them low, potentially contributing to inconsistent research conclusions [22]. For instance, a significant discrepancy in the classification of pollutant levels was observed between the study by Kocot et al. [12] and the study by Matt et al. Kocot et al. primarily categorize pollutant levels based on low and high traffic flow, whereas Matt et al. define low and high pollutant levels using a PM<sub>10</sub> threshold of 50 µg/m<sup>3</sup>. In the research conducted by Matt et al. [13], the difference between low and high levels of exposure was

**Table 3** Differences in cardiorespiratory health among three different AP levels

	SBP				DBP			
	Coefficient	95% CI		p Value*	Coefficient	95% CI		p Value*
M	-0.62	-4.76	3.41	0.770	-3.44	5.21	7.66	0.685
H	-1.44	-5.58	2.59	0.496	6.45	2.11	10.75	0.005
	FVC				FEV1			
	Coefficient	95% CI		p Value*	Coefficient	95% CI		p Value*
M	<b>-0.43</b>	<b>0.02</b>	6.0	<b>0.9</b>	-6.57	-13.44	0.01	0.062

43  $\mu\text{g}/\text{m}^3$  for  $\text{PM}_{2.5}$  and 58  $\mu\text{g}/\text{m}^3$  for  $\text{PM}_{10}$ . In contrast, the study by Kocot et al. reported a discrepancy of 49  $\mu\text{g}/\text{m}^3$  for  $\text{PM}_{2.5}$  and 156  $\mu\text{g}/\text{m}^3$  for  $\text{PM}_{10}$  between low and high levels of exposure. Consequently, the findings of the two studies were markedly different. Our study clearly distinguishes between low, medium, and high levels of AP concentrations. For instance, in the study by Kocot et al. [12], a threshold of  $\text{PM}_{10}$  at 50  $\mu\text{g}/\text{m}^3$  was used to differentiate between good and poor air quality, categorizing pollution levels as poor that aligns with our high pollution exposure levels. However, our  $\text{PM}_{2.5}$  exposure concentrations are higher than those reported by Kocot et al. Additionally, in our study, medium pollution exposure levels are comparable to high pollution exposure levels in other experimental studies [13, 17]. Therefore, our classification of AP levels is more refined, accurately reflecting the impact of PE on health benefits under different levels of AP environments.

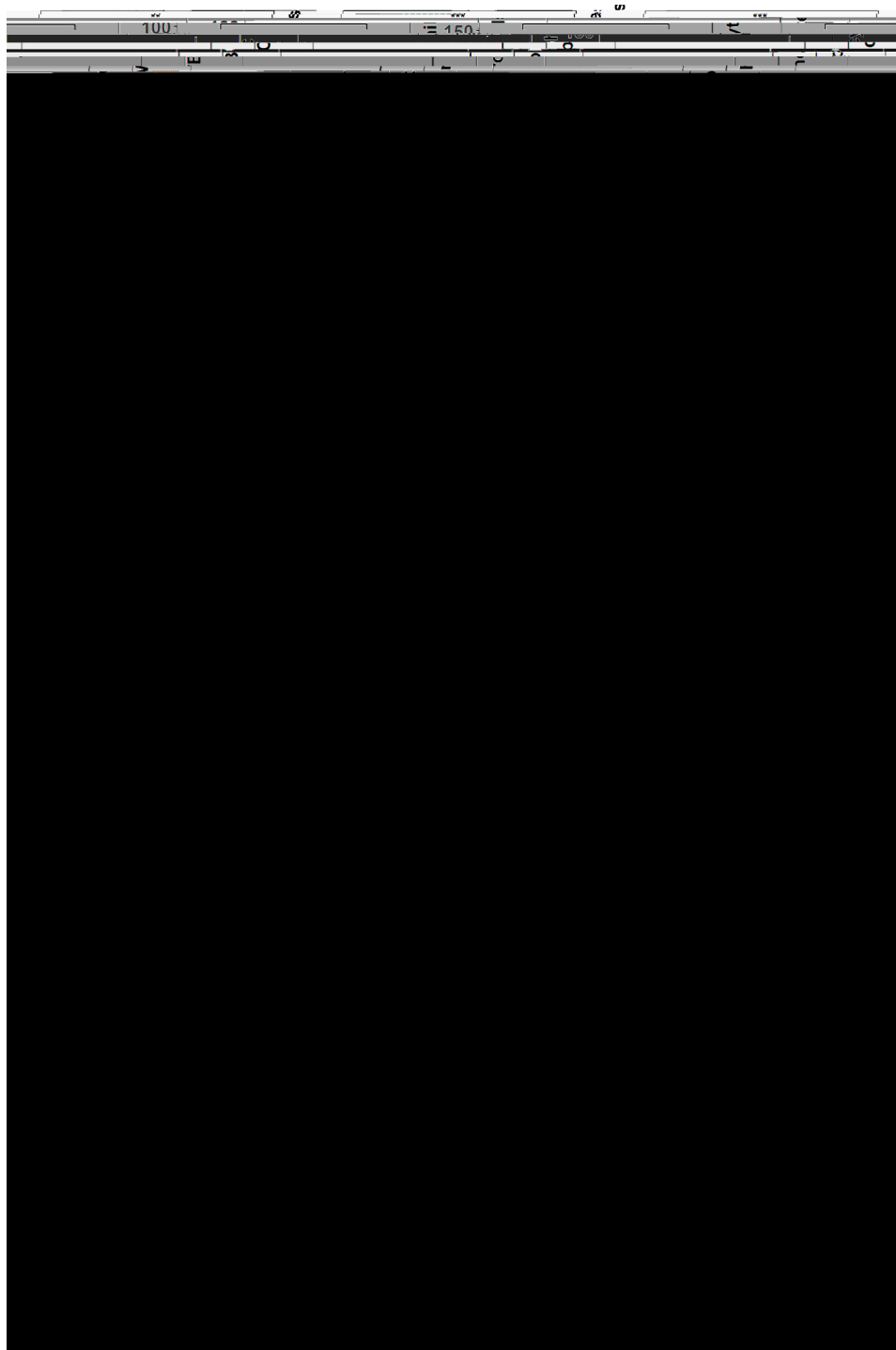
#### Effects of combined exercise and AP exposure on cardiorespiratory function

Our experimental findings indicate that exercise can reduce blood pressure, which is consistent with previous research results. Moreover, compared to exposure at medium to high concentrations, exercising at lower concentrations significantly lowers SBP. Similarly, in a crossover trial conducted in Barcelona, Spain, Kubesch et al. [23] found that intermittent PA was associated with lower SBP compared to resting, particularly following exposure to lower traffic-related air pollution (TRAP). Additionally, Kubesch et al. [23] demonstrated that exposure to higher TRAP was associated with higher DBP compared to lower TRAP. Kocot et al. [12] conducted a crossover

study on healthy adult males, which also showed significant differences in the relative changes of DBP between pollution exposure experiments and control experiments, with a greater increase during pollution exposure experiments. This finding aligns with ours. This suggests that even though exercise can regulate blood pressure, exercising in environments with higher pollution levels may still increase DBP. This could be attributed to the increased concentration of  $\text{PM}_{2.5}$ , which may weaken the blood pressure-lowering effect of exercise. Evidence suggests that inhaling PM may trigger acute autonomic imbalance, leading to acute endothelial/vascular dysfunction, favoring vasoconstriction and a sharp decline in aortic compliance, as well as increased bioactivity of endothelin or renin-angiotensin-aldosterone system activation [24, 25]. These factors, individually or collectively, may contribute to an elevation in blood pressure within hours of exposure to air particles. Therefore, elevated blood pressure may be a biomarker of adverse pathways leading to increased cardiovascular risk [24].

Regarding changes in lung function, Kubesch et al. [17] conducted a study involving 28 healthy adults, and their findings regarding low levels of AP concentration align with ours. They found that following PA during periods of low TRAP exposure, there was a significant increase in FEV1 and  $\text{FEF}_{25-75\%}$ . They also demonstrated that PA was associated with increases in FEV1, FVC, and  $\text{FEF}_{25-75\%}$  compared to rest, and even exercise in high TRAP environments had beneficial effects on lung function. Our research results also indicate that PE remains beneficial for lung function in environments with medium to low AP concentrations. Similarly, in a crossover study by Matt et al. [13] involving 30 healthy adults, immediate





**Fig. 4** Percentage change in inflammatory markers relative to baseline

post-exercise comparisons with baseline showed significant increases in FEV1 (48.5 mL,  $p=0.02$ ), FEV1/FVC (0.64%,  $p=0.01$ ), and FEF<sub>25-75%</sub> (97.8 mL,  $p=0.02$ ). However, in our study, the magnitude of respiratory responses was small, and these responses were observed only in healthy young adults.

Although exercise improves lung function, the benefits diminish with increasing pollutant concentrations. Kocot et al. [12] conducted a crossover experiment involving 15 min of submaximal exercise in healthy young adult males under conditions of poor and good air quality. The pollutant concentrations in their exposure group were similar to our medium-concentration pollutant levels.

ey compared the relative changes between the exposure and control groups and found no differences in FVC, FEV1, and FEV1/FVC after exercise, which is consistent with our findings. Unlike Kocot et al., we also compared the changes in cardiorespiratory health indicators after exercise in high and low AP concentration environments, finding significant decreases in FVC, FEV1, and PEF. Kocot et al. concluded that acute respiratory changes following exercise under exposure conditions depend on pollutant concentrations, with only participants exposed to particularly high levels showing acute decreases in FEV1/FVC post-exercise, and the relative changes in FEV1/FVC were significantly negatively correlated with pollutant concentrations. Strak et al. [26] investigated the effects of AP on the respiratory health of healthy cyclists and found a slight increase in lung function immediately after cycling, but a negative correlation with AP emerged six hours after cycling. Matt et al.'s study [13] also indicated that PA mitigates the negative effects of PM on the upper and lower respiratory tracts, with substantial

nitric oxide production through epigenetic changes, with the association between  $PM_{2.5}$  and FeNO being most significant with a one-day lag time [29]. Kocot et al. [30



