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Original article

Long-term exposure to fine particulate matter modifies the association between physical activity and hypertension incidence

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Abstract

Background: The trade-off between the benefits of regular physical activity (PA) and the potentially detrimental effects of augmented exposure to air pollution in highly polluted regions remains unclear. This study aimed to examine whether ambient fine particulate matter ($PM_{2.5}$) exposure modified the impacts of PA volume and intensity on hypertension risk.

Methods: We included 54,797 participants without hypertension at baseline in a nationwide cohort of the Prediction for Atherosclerotic Cardiovascular Disease Risk in China (China-PAR) project. PA volume and intensity were assessed by questionnaire, and high-resolution (1 km ×1 km) $PM_{2.5}$ estimates were generated using a satellite-based model.

Results: During 413,516 person-years of follow-up, 12,100 incident hypertension cases were identified. $PM_{2.5}$ significantly modified the relationship between PA and hypertension incidence ($p_{interaction} < 0.001$). Increased PA volume was negatively associated with incident hypertension in the low $PM_{2.5}$ stratum (<59.8 μg/m^3, $p_{trend} < 0.001$), with a hazard ratio of 0.81 (95% confidence interval (95%CI): 0.74−0.88) when comparing the fourth with the first quartile of PA volume. However, the health benefits were not observed in the high $PM_{2.5}$ stratum (≥59.8 μg/m^3, $p_{trend} = 0.370$). Moreover, compared with light PA intensity, vigorous intensity was related to a 20% (95%CI: 9%−29%) decreased risk of hypertension for participants exposed to low $PM_{2.5}$, but a 17% (95%CI: 4%−33%) increased risk for those with high $PM_{2.5}$ levels.

Conclusion: PA was associated with a reduced risk of hypertension only among participants with low $PM_{2.5}$ exposure. Our findings recommended regular PA to prevent hypertension in less polluted regions and reinforced the importance of air quality improvement.

Keywords: Air pollution; Cohort study; Hypertension; Particulate matter; Physical activity

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1. Introduction

Hypertension is the leading risk factor for cardiovascular disease and the most important contributor to the global disease burden.[1] The number of people with hypertension rose by 90% worldwide from 1975 to 2015, with the increase largely occurring in low- and middle-income countries.[2] Thus, preventive approaches for hypertension are essential to fight this epidemic.

Physical activity (PA) is beneficial to cardiovascular health,[3] whereas air pollution, especially ambient fine particulate matter ($PM_{2.5}$), elevates the risk of various diseases, including hypertension.[4,5] PA markedly increases the inhalation of air pollutants, which might, in turn, reduce or even negate its health benefits.[6,7] Globally, 80% of countries have made national policies or plans to promote regular PA,[8] meanwhile, more than half of the world's population lives in areas exceeding the least stringent air quality target (annual mean $PM_{2.5} \leq 35$ $\mu g/m^3$) of the World Health Organization (WHO).[9] Therefore, it is a public concern whether or not regular PA should be recommended in highly polluted areas.

Results from recent studies on whether long-term exposure to air pollution modified the protective effects of regular PA remain inconsistent.[10–15] In addition, these studies were generally conducted in areas meeting the WHO's least stringent air quality target (annual mean $PM_{2.5} \leq 35$ $\mu g/m^3$), thus limiting its generalization to seriously polluted areas, including the mainland of China. Besides, the only study regarding hypertension was further limited by its retrospective design and selection bias, including only participants who were well-educated and had healthy lifestyles.[12] Furthermore, previous studies merely pertained to the volume or type of PA but lacked information on PA intensity, which was an evidence gap identified by the 2020 European Society of Cardiology guidelines on cardiology and exercise.[16]

Using data from satellite-based $PM_{2.5}$ estimates at high spatial resolution combined with a national scale population-based prospective cohort of the Prediction for Atherosclerotic Cardiovascular Disease Risk in China (China-PAR) project over a 16-year period, we investigated whether long-term exposure to $PM_{2.5}$ altered the associations between regular PA and incident hypertension.

2. Methods

2.1. Study design and participants

Participants were derived from 3 sub-cohorts in the China-PAR project, including China Multi-Center Collaborative Study of Cardiovascular Epidemiology (China MUCA (1998)), International Collaborative Study of Cardiovascular disease in Asia (InterASIA), and Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study (CIMIC). A detailed description of the study design was published elsewhere.[17] Briefly, China MUCA (1998) was established in 1998 and selected participants aged 35–59 years from 15 clusters in China with a cluster random sampling method. InterASIA was initiated in 2000–2001 and selected a nationally representative sample using a 4-stage stratified sampling method based on geographic region (northern *vs.* southern China, divided by the Yangtze River) and urbanicity (urban *vs.* rural). CIMIC was set up during 2007–2008, using a cluster random sampling method to recruit participants aged ≥18 years in 4 survey sites from central and eastern China. Together, the 3 sub-cohorts covered 15 Chinese provinces and were last followed up between 2012 and 2015. The China-PAR project was approved by the Institutional Review Board at Fuwai Hospital in Beijing (No. 2018-1061). Written informed consent was obtained from all participants before data collection.

A total of 113,448 adults were enrolled for the baseline examinations, of which 8185 (7.2%) were lost to follow-up. Because the $PM_{2.5}$ exposure data were available beginning in 2000, the follow-up information after that year was used. We excluded deaths prior to 2000 ($n = 67$), subjects with cardiovascular disease ($n = 2218$) or hypertension ($n = 35{,}151$) at baseline or before 2000, participants with missing blood pressure (BP) information during follow-up ($n = 11{,}439$), and those with missing baseline information for BP ($n = 28$), PA ($n = 1562$), or residential address ($n = 1$). Finally, 54,797 participants were included in the analysis (Supplementary Fig. 1).

2.2. $PM_{2.5}$ exposure and temperature assessment

The detailed $PM_{2.5}$ exposure assessment has been published elsewhere and applied in previous environmental epidemiology studies.[18,19] In brief, a spatiotemporal model was used to estimate ambient $PM_{2.5}$ levels at 1 km×1 km spatial resolution across China from 2000 to 2015, based on high-resolution satellite aerosol optical depth data retrieved through the Multi-Angle Implementation of Atmospheric Correction algorithm, land use information, roads, meteorology, and population density data. We validated the model using ground-level $PM_{2.5}$ measurements from 2013 to 2016 acquired from the China Environmental Monitoring Center (www.cnemc.cn/), with an overall 10-fold cross-validation R^2 of 0.95 at the annual level. To assess the prediction accuracy of the period without national ground measurements (before 2013), we compared model predictions with available monitoring data from Hong Kong, China; Taiwan, China; and the US Embassy in China; and the prediction R^2 was 0.80 at the annual level. The monthly mean temperature at 2-m height was extracted from the European Center for Medium-Range Weather Forecast Atmospheric Re-analysis dataset Version 5.[20]

Residential addresses for all participants were collected at baseline and at follow-up visits and were geocoded into latitude and longitude data. Considering the changing residential history over the follow-up period, for each participant time-weighted averages of $PM_{2.5}$ and temperature from 2000 to 2015 were used as indicators of long-term exposure, with weights defined as the duration spent at each residence. We divided participants into 2 groups according to the median of $PM_{2.5}$ exposure: low (31.2 to <59.8 $\mu g/m^3$) and high (59.8 to 88.8 $\mu g/m^3$).

2.3. PA assessment

For InterASIA and CIMIC sub-cohorts, we collected the daily duration of light, moderate, and vigorous PA on weekdays and weekends over the previous year. China MUCA (1998) covered more detailed PA information, collecting the daily time spent on specific types of PA in occupation, household, transportation, and leisure-time domains on weekdays and weekends over the previous year. The intensity of each activity was expressed in metabolic equivalent (MET), which was equivalent to 1 kcal/kg of body weight per hour. For InterASIA and CIMIC, we assigned 2 MET, 4 MET, and 8 MET values to activities with light PA, moderate PA, and vigorous PA, respectively; we assigned MET values to each activity in China MUCA (1998) according to the 2011 Compendium of Physical Activities.[21] For every individual, time spent on each activity was multiplied by its MET value, and the sum of all activities was used as the measurement of daily PA volume (MET-h/day). We classified participants into 4 groups ($\leq$18.0 MET-h/day, $>$18.0$-$32.0 MET-h/day, $>$32.0$-$54.5 MET-h/day, and $>$54.5 MET-h/day) according to the quartiles of PA volume. The average PA intensity for each subject was created by dividing the daily PA volume by the total daily hours spent on PA.[22] Participants were categorized by average PA intensity as follows: light (1.6$-<$3.0 MET), moderate (3.0$-<$6.0 MET), and vigorous ($\geq$6.0 MET).

2.4. Outcome measurements

Blood pressure (BP) measurements were obtained by trained and certified staff according to the protocol recommended by the American Heart Association.[23] BP (mmHg) was read with a standardized mercury sphygmomanometer (XJ11D; Yutu, Shanghai, China) for China MUCA (1998) and InterASIA, and an electronic sphygmomanometer (HEM-770A; Omron, Kyoto, Japan) for CIMIC. We required participants to rest for 5 min in a sitting position and to avoid alcohol, cigarette smoking, coffee/tea, and exercising for at least 30 min before their BP measurements. The average of 3 right-arm BP measurements obtained within 30 s intervals was used in the analysis. We used the unified protocol to collect information on antihypertensive drugs at each survey for all sub-cohorts. Hypertension was defined as systolic BP $\geq$ 140 mmHg or diastolic BP $\geq$ 90 mmHg or self-reported taking of antihypertensive medication within the past 2 weeks. The incident date of hypertension was identified as the date of first diagnosis or initial use of antihypertensive agents.

2.5. Covariates

Information on demographics, residential addresses, lifestyle risk factors, and medical history was obtained using similar questionnaires at baseline for all sub-cohorts. Smoking was defined as having smoked more than 400 cigarettes or at least 1 cigarette per day for 1 year or more. Smokers were further categorized as current and former smokers by asking whether the smoker had quit smoking by the time of survey. Alcohol drinking was defined as alcohol consumption at least once per week during the previous year. Height and weight were measured with light indoor clothing and without shoes, using a standardized soft tape measure and platform scale, respectively. Body mass index was calculated as weight divided by squared height (kg/m^2). Blood samples after overnight fasting of at least 10 h were drawn to measure serum glucose and lipids levels. Diabetes mellitus was defined as fasting glucose level of $\geq$7.0 mmol/L and/or the use of insulin or oral hypoglycemic agents and/or diagnosed medical history of diabetes.

2.6. Statistical analysis

The baseline characteristics are presented as mean $\pm$ SD for continuous variables or as numbers (percentages) for categorical variables. Person-years of follow-up were calculated from baseline date or from January 1, 2000 (if baseline date was earlier than 2000), to the date of incident hypertension, death, or the last follow-up, whichever came first.

We used Cox proportional hazards models stratified by sub-cohorts to assess the hazard ratios (HRs) and 95% confidence intervals (95%CIs) of incident hypertension with PA volume, average PA intensity, and $PM_{2.5}$. The proportional hazards assumption was tested by evaluating the weighted Schoenfeld residuals and no violations were observed ($p > 0.05$). Covariates in the Cox model included age, sex, education level (less than high school, or high school or above), urbanization (urban or rural), geographic region (north, east, north eastern, south, central, south western, or north western), smoking status (never, former, or current), alcohol drinking (yes or no), body mass index, systolic BP, diabetes mellitus, total cholesterol, temperature, and $PM_{2.5}$ (for the association with PA volume), PA volume (for the association with $PM_{2.5}$), or both $PM_{2.5}$ and PA volume (for the association with PA intensity). To account for the nonlinear association of temperature with hypertension, we used a regression spline with 3 degrees of freedom. Stratified analyses were conducted to examine the associations between PA and the risk of hypertension in each $PM_{2.5}$ stratum. Tests for trend were performed by including the median of each PA category as a continuous variable in the models. Interaction effects of $PM_{2.5}$ and PA (volume or intensity) were detected by including both the main effects and the interaction terms of $PM_{2.5}$ groups and PA (volume or intensity) categories in the model. The effects of 8 joint categories of $PM_{2.5}$ (low and high) and PA volume (first to fourth quartiles) were calculated by comparing each group with reference to the participants who were in the first quartile of PA volume and exposed to low $PM_{2.5}$. Similarly, subjects were cross-classified into 6 groups to estimate the combined effects of $PM_{2.5}$ (low and high) and PA intensity (light, moderate, and vigorous), with the group of light PA intensity and low $PM_{2.5}$ as reference.

Three sensitivity analyses were performed. First, we excluded hypertension cases occurring within the first year of follow-up. Second, we used county-level averaged years of education (demographic census of China, 2000) as a surrogate for socioeconomic status and further adjusted for it in the Cox model. Third, $PM_{2.5}$ exposure was dichotomized by the 75th percentile of the exposure range (77.7 μg/m^3) in order to

explore whether different cutoff points would differentiate the main findings.

Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) software. All statistical tests were two-sided, with a p value of <0.05 considered to be significant.

3. Results

3.1. Baseline characteristics

The average annual $PM_{2.5}$ concentration from 2000 to 2015 at participants' residences was 65.4 μg/m^3, ranging from 31.2 μg/m^3 to 88.8 μg/m^3. Table 1 presents the baseline characteristics overall and according to quartiles of PA volume. At baseline, the mean age of participants was 48.8 years and 38.5% were men. Participants with higher PA volume were more likely to smoke and drink alcohol, to have a lower education level and lower prevalence of diabetes, and to do PA with greater intensity.

3.2. Associations of PA or $PM_{2.5}$ with hypertension

During 413,516 person-years, 12,100 incident hypertension events were identified. Table 2 shows the independent associations of long-term exposure to $PM_{2.5}$ and PA with incident hypertension. High $PM_{2.5}$ was associated with a 53% (95%CI: 43%−64%) elevated risk of developing hypertension after adjusting for multiple covariates, including regular PA volume. By contrast, higher volume and intensity of habitual PA were related to a reduced risk after adjusting for a wide range of covariates, including $PM_{2.5}$. With the first quartile of PA volume as reference, the adjusted HRs (95%CI) were 1.01 (0.96−1.06), 0.87 (0.82−0.92), and 0.82 (0.77−0.87) in the second to fourth quartiles of PA volume, respectively. Compared with light intensity, the multivariable-adjusted HRs (95%CIs) were 0.93 (0.88−0.99) for moderate intensity PA and 0.93 (0.85−1.01) for vigorous intensity PA.

Table 2
HR and 95%CI of hypertension associated with the volume and intensity of PA and long-term exposure to $PM_{2.5}$.

	HR (95%CI)[a]
PA volume (MET-h/day)	
Quartile 1 (≤18.0)	1.00
Quartile 2 (>18.0−32.0)	1.01 (0.96−1.06)
Quartile 3 (>32.0−54.5)	0.87 (0.82−0.92)
Quartile 4 (>54.5)	0.82 (0.77−0.87)
Average PA intensity (MET)	
Light (1.6−<3.0)	1.00
Moderate (3.0−<6.0)	0.93 (0.88−0.99)
Vigorous (≥6.0)	0.93 (0.85−1.01)
$PM_{2.5}$ level (μg/m^3)	
Low (<59.8)	1.00
High (≥59.8)	1.53 (1.43−1.64)

[a] Cox proportional hazard model, stratified by cohort and adjusted for age, sex, education level, urbanicity, geographic region, temperature, smoking status, alcohol drinking, body mass index, systolic blood pressure, diabetes mellitus, total cholesterol, and $PM_{2.5}$ (for the association with PA volume) or PA volume (for the association with $PM_{2.5}$) or both $PM_{2.5}$ and PA volume (for the association with PA intensity).
Abbreviations: 95%CI = 95% confidence interval; HR = hazard ratio; MET = metabolic equivalent; PA = physical activity; $PM_{2.5}$ = fine particulate matter.

3.3. Associations of PA with hypertension stratified by $PM_{2.5}$ level

There was a significant interaction between $PM_{2.5}$ and PA volume in association with incident hypertension ($p_{interaction} < 0.001$, Table 3). Among participants exposed to low $PM_{2.5}$, the adjusted

Table 1
Baseline characteristics of participants overall and according to quartiles of PA volume.

	All	Quartiles of PA volume (MET-h/day)			
		First (≤18.0)	Second (>18.0−32.0)	Third (>32.0−54.5)	Fourth (>54.5)
No. of participants	54,797	14,594	12,938	13,566	13,699
Age (year)	48.8 ± 11.5	49.3 ± 12.8	47.0 ± 11.3	48.6 ± 11.0	50.2 ± 10.5
Male	21,099 (38.5)	5334 (36.5)	4621 (35.7)	5099 (37.6)	6045 (44.1)
Urban	5914 (10.8)	3654 (25.0)	1765 (13.6)	421 (3.1)	74 (0.5)
Education level>high school	8530 (15.6)	3828 (26.2)	2543 (19.7)	1249 (9.2)	910 (6.6)
Smoking[a]					
Never smoker	40,478 (73.9)	10,953 (75.1)	9682 (74.8)	10,134 (74.7)	9709 (70.9)
Former smoker	1748 (3.2)	553 (3.8)	421 (3.3)	361 (2.7)	413 (3.0)
Current smoker	12,375 (22.6)	3026 (20.7)	2762 (21.3)	3030 (22.3)	3557 (26.0)
Alcohol consumption	9534 (17.4)	2233 (15.3)	2049 (15.8)	2370 (17.5)	2882 (21.0)
Body mass index (kg/m^2)	23.1 ± 3.3	23.3 ± 3.4	23.1 ± 3.3	23.1 ± 3.3	23.0 ± 3.3
Systolic blood pressure (mmHg)	117.0 ± 11.5	116.9 ± 11.8	116.6 ± 11.5	117.0 ± 11.2	117.5 ± 11.3
Diastolic blood pressure (mmHg)	73.6 ± 8.0	74.0 ± 7.8	73.9 ± 7.9	73.3 ± 8.0	73.3 ± 8.0
Diabetes mellitus	2252 (4.1)	816 (5.6)	534 (4.1)	473 (3.5)	429 (3.1)
Total cholesterol (mg/dL)	171.5 ± 34.3	175.2 ± 35.9	170.2 ± 34.5	169.4 ± 33.6	170.9 ± 32.6
PA volume (MET-h/day)	37.1 ± 23.3	11.2 ± 5.3	25.1 ± 4.4	43.2 ± 6.0	70.1 ± 10.8
PA intensity (MET)	4.2 ± 2.0	2.3 ± 0.8	3.2 ± 1.4	4.7 ± 1.3	6.6 ± 1.1
$PM_{2.5}$ exposure (μg/m^3)	65.4 ± 13.6	66.4 ± 14.5	64.5 ± 12.7	64.5 ± 12.8	66.0 ± 14.0

Note: Values are presented as mean ± SD for continuous variables or as n (%) for categorical variables.
[a] A total of 196 participants had missing information on smoking status.
Abbreviations: MET = metabolic equivalent; PA = physical activity; $PM_{2.5}$ = fine particulate matter.

Table 3
HR and 95%CI for hypertension associated with the volume of PA stratified by long-term exposure to $PM_{2.5}$.

	Quartiles of PA volume (MET-h/day)				p_{trend}
	First (≤18.0)	Second (>18.0−32.0)	Third (>32.0−54.5)	Fourth (>54.5)	
Low $PM_{2.5}$ (<59.8 μg/m³)					
Cases number	1741	1477	1522	1535	
Person-years	46,967	46,685	52,313	50,095	
HR (95%CI)[a]	1.00	0.93 (0.86−1.00)	0.86 (0.80−0.94)	0.81 (0.74−0.88)	<0.001
High $PM_{2.5}$ (≥59.8 μg/m³)					
Cases number	2049	1487	1150	1139	
Person-years	62,409	45,653	39,541	41,492	
HR (95%CI)	1.00	1.10 (1.03−1.18)	1.04 (0.96−1.13)	1.06 (0.97−1.15)	0.370

[a] Cox proportional hazard model, stratified by cohort and adjusted for age, sex, education level, urbanicity, geographic region, temperature, smoking status, alcohol drinking, body mass index, systolic blood pressure, diabetes mellitus, and total cholesterol.
Abbreviations: 95%CI = 95% confidence interval; HR = hazard ratio; MET = metabolic equivalent; PA = physical activity; $PM_{2.5}$ = fine particulate matter.

HRs (95%CIs) were 1.00 (reference), 0.93 (0.86−1.00), 0.86 (0.80−0.94), and 0.81 (0.74−0.88) for the first to fourth quartile of PA volume, respectively (p_{trend} < 0.001). Among participants exposed to high $PM_{2.5}$, corresponding HRs (95%CIs) were 1.00 (reference), 1.10 (1.03−1.18), 1.04 (0.96−1.13), and 1.06 (0.97−1.15) (p_{trend} = 0.370). We also observed a significant interaction between PA intensity and $PM_{2.5}$ exposure ($p_{interaction}$ < 0.001, Table 4). Compared with light PA intensity, vigorous PA intensity was related to a 20% (95%CI: 9%−29%) decreased risk of hypertension for participants exposed to low $PM_{2.5}$, but a 17% (95%CI: 4%−33%) increased risk for those with high $PM_{2.5}$ levels.

3.4. Joint effects of PA and $PM_{2.5}$ on hypertension

The joint effects of PA (volume and intensity) and $PM_{2.5}$ exposure are presented in Fig. 1. Generally, participants exposed to high $PM_{2.5}$ levels had a consistently higher risk of hypertension compared with those exposed to low $PM_{2.5}$ levels, irrespective of PA volume or intensity. Furthermore, participants with low $PM_{2.5}$ exposure combined with the highest volume or vigorous intensity of PA had the lowest hypertension risk.

3.5. Sensitivity analyses

Sensitivity analyses yielded similar results after excluding those who developed hypertension during the first follow-up year (Supplementary Table 1), or considering the potential confounding effects of socioeconomic status (Supplementary Table 2), or grouping participants into low and high $PM_{2.5}$ categories by the 75th percentile of $PM_{2.5}$ concentration (77.7 μg/m³, Supplementary Table 3).

4. Discussion

To our knowledge, this is the first prospective cohort study to examine the joint effects of long-term $PM_{2.5}$ exposure with both PA volume and intensity on the development of hypertension in highly polluted regions. Among participants with low $PM_{2.5}$ exposure, habitual PA volume and intensity were inversely associated with the risk of incident hypertension. In contrast, among those exposed to high $PM_{2.5}$, insignificant or even positive associations between PA and hypertension risk were observed. The associations of PA volume and intensity with hypertension incidence were significantly modified by ambient $PM_{2.5}$ levels.

Previous cohort studies, typically conducted in settings with relatively good air quality, have found protective health effects

Table 4
HR and 95%CI for hypertension associated with the intensity of PA stratified by long-term exposure of $PM_{2.5}$.

	Average PA intensity (MET)			p_{trend}
	Light (1.6−<3.0)	Moderate (3.0−<6.0)	Vigorous (≥6.0)	
Low $PM_{2.5}$ (<59.8 μg/m³)				
Cases number	2503	2291	1403	
Person-years	71,973	77,185	44,905	
HR (95%CI)[a]	1.00	0.87 (0.80−0.94)	0.80 (0.71−0.91)	<0.001
High $PM_{2.5}$ (≥59.8 μg/m³)				
Cases number	2450	1992	1255	
Person-years	75,239	65,618	44,784	
HR (95%CI)	1.00	1.11 (1.02−1.20)	1.17 (1.04−1.33)	0.016

[a] Cox proportional hazard model, stratified by cohort and adjusted for age, sex, education level, urbanicity, geographic region, temperature, smoking status, alcohol drinking, body mass index, systolic blood pressure, diabetes mellitus, total cholesterol, and PA volume in MET-h/day.
Abbreviations: 95%CI = 95% confidence interval; HR = hazard ratio; MET = metabolic equivalent; PA = physical activity; $PM_{2.5}$ = fine particulate matter.

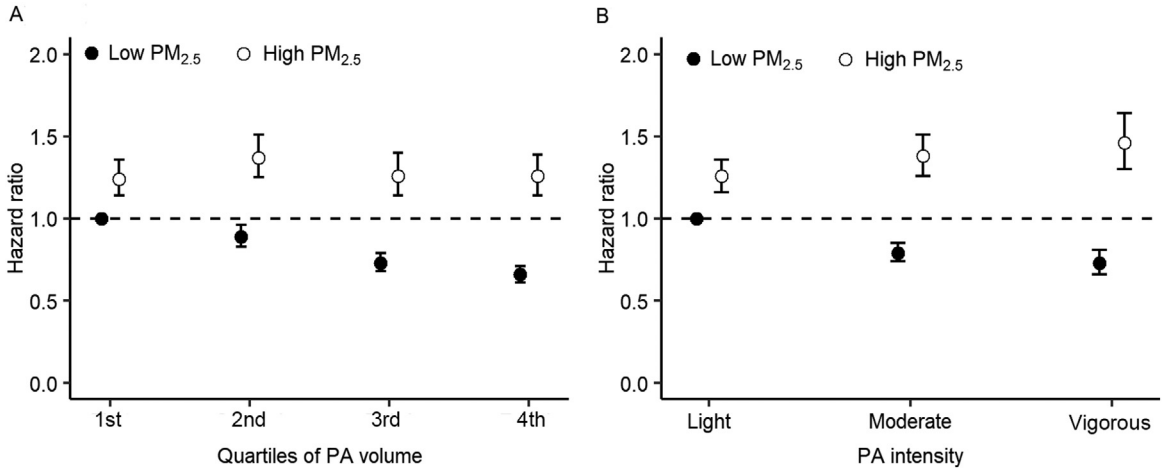

Fig. 1. Joint effects of $PM_{2.5}$ and (A) PA volume or (B) PA intensity on incident hypertension. Cox proportional hazard model was stratified by cohort and adjusted for age, sex, urbanicity, geographic region, temperature, education level, smoking status, alcohol drinking, body mass index, systolic blood pressure, diabetes mellitus, and total cholesterol (further adjusted for PA volume when analyzing the joint effects of $PM_{2.5}$ and PA intensity). PA = physical activity; $PM_{2.5}$ = fine particulate matter.

from higher PA volume across $PM_{2.5}$ levels.[10–12,24] For instance, a cohort in Taiwan, China found a reduced risk of developing hypertension associated with habitual PA volumes in people exposed to $PM_{2.5}$ levels ranging from 6 $\mu g/m^3$ to 50 $\mu g/m^3$.[12] In line with the existing evidence, our study demonstrated that individuals could benefit from higher PA volume when the $PM_{2.5}$ concentration was lower than approximately 60 $\mu g/m^3$. Therefore, we recommended higher PA volume for people residing in regions with low $PM_{2.5}$ concentrations.

High levels of air pollution prevent people from active outdoor exercise despite the clinical importance of PA,[25,26] thus it is very important to determine the optimal PA behaviors in highly polluted regions. Existing cohort studies suggested no evidence of interaction between regular PA volume and long-term $PM_{2.5}$ exposure.[10–12,24] However, the average $PM_{2.5}$ concentration for previous cohort studies was generally below the WHO's Interim Target 1 of 35 $\mu g/m^3$. Globally, the population-weighted $PM_{2.5}$ levels were 44.2 $\mu g/m^3$ in 2015, and 4 of the 10 most populous countries had estimated concentrations above the global level (e.g., 58.4 $\mu g/m^3$ for China).[27] Thus, findings from previous cohort studies had low generalization to a large proportion of the world's population in high $PM_{2.5}$ pollution settings, and our study filled this gap. This prospective cohort study, with a median $PM_{2.5}$ of approximately 60 $\mu g/m^3$, found that higher PA volume had no protective effects on incident hypertension among participants exposed to high $PM_{2.5}$. Similarly, a modeling study ($PM_{2.5}$ ranging from 5 to 200 $\mu g/m^3$)[28] and a cross-sectional study from Henan, China ($PM_{2.5}$ concentrations from 68 to 85 $\mu g/m^3$)[29] also found that a high level of ambient air pollution attenuated or negated the benefits of PA volume.

Cumulative literature demonstrated that light PA intensity was beneficial to cardiovascular health and that higher intensity conferred greater benefits.[3,22,30] Current PA guidelines generally recommended moderate or vigorous PA intensity for adults.[31,32] An experimental study found that greater PA intensity played a protective role with respect to the pulmonary and metabolic responses to exercise during short-term diesel exhaust exposure.[33] However, to our knowledge, previous studies have not examined the interactive effects of regular PA intensity and long-term air pollution. In this study, we found that greater PA intensity was related to a decreased risk of hypertension among participants with long-term low $PM_{2.5}$ exposure but to an increased risk among those exposed to long-term high $PM_{2.5}$. Our findings implied that people living in regions with high ambient $PM_{2.5}$ concentrations did not benefit from outdoor vigorous PA and that engaging in indoor PA while reducing air pollution with air filtration systems might be a good option for them. The difference between our study and previous short-term study results might be the findings of a delayed but cumulative effect. This suggests the need for further research to confirm our findings.

The health effects of $PM_{2.5}$ and PA had some mechanisms in common, such as changes in systemic inflammation and the autonomic nervous system.[4,34] PA augmented the intake of air pollutants due to increased ventilation rate, higher deposition fraction in airways, and switching from nasal breathing to oral,[35] and because of their shared pathways, the risks caused by extra $PM_{2.5}$ inhalation may nullify the benefits of PA. Moreover, PA intensity contributed to the extra inhalation of air pollutants. For example, previous research reported a 3- to 4.5-fold increase in the number of particles deposited in the airway during light-intensity exercise and a 6- to 10-fold increase during vigorous intensity exercise.[7,36] This might partly explain our results, which showed that greater intensity was related to a higher risk of developing hypertension among participants in highly polluted settings.

Our study had several strengths. First, because it covered a broader $PM_{2.5}$ concentration range (31.2–88.8 $\mu g/m^3$), our study filled the gap in research relative to serious ambient $PM_{2.5}$ levels, which means our findings are generalizable to other countries with similar $PM_{2.5}$ levels to China. Second, this study was based on a prospective cohort with a large sample size, high rate of follow-up (92.8%), long follow-up period, and stringent quality control procedures. Third, a satellite-based spatiotemporal model with high accuracy (1 km × 1 km

resolution) was used to estimate the concentration of ambient $PM_{2.5}$, which enabled us to capture the fine-scale $PM_{2.5}$ variability and assign the $PM_{2.5}$ concentrations prior to 2013.

Still, several limitations should be noted. First, we did not collect information to distinguish outdoor PA from indoor PA, hence we could not exclusively examine outdoor PA. However, Chinese people commonly exercise outdoors.[37] Second, we used the $PM_{2.5}$ at residence as a proxy of $PM_{2.5}$ levels encountered during PA, assuming that participants' daily activity mainly took place in proximity to their residences; this might lead to misclassification of $PM_{2.5}$ exposure. Third, the effects of gaseous pollutants, including sulfur dioxide, nitrogen dioxide, and ozone, were not examined due to lack of information.

5. Conclusion

This study provided the first prospective evidence from highly polluted settings that severe $PM_{2.5}$ exposure negates the benefits of regular PA against hypertension. Our study implies that regular outdoor PA, especially vigorous PA, should not be recommended for individuals in seriously polluted areas, and it reinforces the importance of air quality improvement for the prevention of hypertension.

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Authors' contributions

QL performed the formal analysis, drafted the original manuscript, and revised the manuscript; KH, FLiang, and XY performed data acquisition, contributed to the methodology, and revised the manuscript. JL, JChen, XLiu, JCao, CS, LY, YZ, YD, YLi, DH, and XLu collected data and revised the manuscript; YLiu contributed to the $PM_{2.5}$ exposure assessment protocol and methodology; DG implemented the study and revised the manuscript critically; FLiu and JH conceived the study, participated in its design and coordination, and revised the manuscript critically. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

Supplementary materials

Supplementary materials associated with this article can be found in the online version at doi:10.1016/j.jshs.2022.01.004.

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