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Cardiovascular benefits of short-term indoor air filtration intervention in elderly living in Beijing: An extended analysis of BIAPSY study

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ABSTRACT

Background: Adverse cardiovascular effects associated with air pollution exposure have been widely demonstrated. However, inconsistent cardiovascular responses were observed from reducing indoor air pollution exposure. We aimed to assess whether short-term air filtration intervention could benefit cardiovascular health in elderly living in high pollution area.
Methods: A randomized crossover intervention study of short-term indoor air filtration intervention on cardiovascular health was conducted among 35 non-smoking elderly participants living in Beijing in the winter of 2013, as part of Beijing Indoor Air Purifier StudY (BIAPSY). Portable air filtration units were randomly allocated to active filtration for 2 weeks and sham filtration for 2 weeks in the households. Twelve-hour daytime ambulatory heart rate variability (HRV) and blood pressure (ABP) were measured during active and sham filtration. Concurrently, real-time indoor and outdoor particulate matter with diameter less than 2.5 µm ($PM_{2.5}$) and indoor black carbon (BC) concentrations were measured. We applied generalized additive mixed models to evaluate the associations of 1- to 10-h moving average (MA) exposures of indoor $PM_{2.5}$ and BC with HRV and ABP indices, and to explore whether these associations could be modified by air filtration.
Results: We observed decreases of 34.8% in indoor $PM_{2.5}$ and 35.3% in indoor BC concentrations during active filtration. Indoor $PM_{2.5}$ and BC exposures were significantly associated with reduced HRV and increased ABP indices, and greater changes were observed during sham filtration. In specific, each 10 µg/m^3 increase in indoor $PM_{2.5}$ at MA8-h was associated with a significant reduction of 1.34% (95% CI: −2.42, −0.26) in SDNN during sham filtration, compared with a non-significant reduction of 0.81% (95% CI: −6.00, 4.68) during active filtration ($P_{inter} <$ 0.001). Each 1 µg/m^3 increase in indoor BC at MA8-h was associated with a significant increase of 2.41% (95% CI: 0.38, 4.47) in SBP during sham filtration, compared with a non-significant increase of −1.09% (95% CI: −4.06, 1.96) during active filtration (P_{inter} = 0.135). Nonlinear inverse exposure-response relationships of indoor air pollution exposures with predicted HRV and ABP indices also confirmed some cardiovascular benefits of short-term air filtration intervention.
Conclusions: Our results suggested that short-term indoor air filtration intervention can be of some cardiovascular benefits in elderly living with high pollution episodes.

Abbreviations: BC, black carbon; BIAPSY, Beijing Indoor Air Purifier StudY; BMI, body mass index (weight(kg)/height(m)^2); BP, blood pressure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; ECG, electrocardiographic; GAMM, generalized additive mixed models; GBD, Global Burden of Disease; HEPA, high efficiency particulate air; HF, high frequency; IRB, Institutional Review Board; LF, low frequency; MA, moving average; MA-8h, 8 h moving average; MAP, mean arterial pressure; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than 2.5 µm; PUHSC, Peking University Health Science Center; PUTH, Peking University Third Hospital; RMSSD, the square root of the mean of the squared differences between adjacent normal-to-normal intervals; SBP, systolic blood pressure; SD, standard deviation; SDNN, the standard deviation of normal-to-normal intervals; TP, total power; WHO, World Health Organization

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1. Introduction

Previous epidemiological studies have elucidated consistent and significant associations between ambient air pollution exposure and cardiovascular morbidity and mortality (Newby et al., 2015; Brook et al., 2010; Pope et al., 2004). Potential biological mechanisms linking air pollution to cardiovascular diseases have been investigated and are yet to be fully illuminated (Brook et al., 2010). Particulate matter with an aerodynamic diameter less than 2.5 µm ($PM_{2.5}$) is of particular concern due to its adverse cardiovascular consequences (Pope et al., 2004, 2006; Coogan et al., 2016; O'Donnell et al., 2011). A wealth of population-based epidemiological studies have shown that short-term exposure to ambient $PM_{2.5}$ is associated with reduced heart rate variability (HRV) (Huang et al., 2012; Baccarelli et al., 2008; Pope et al., 1999), a putative marker reflecting the activity of autonomic nervous system function, and increased blood pressure (BP) (Liang et al., 2014; Dvonch et al., 2009; Brook et al., 2009). Both of the changes are known for increasing cardiovascular risk.

While most population appears to be at risk, the health risk associated with ambient air pollution is more severe in developing countries than that reported in north American and European countries (van Donkelaar et al., 2015; Forouzanfar et al., 2015). The Global Burden of Disease (GBD) study estimated that ambient $PM_{2.5}$ resulted in more than 0.9 million premature deaths annually and ranked fourth in risk factors for disease burden in China (van Donkelaar et al., 2015). Indoor air pollution is highly correlated with outdoor air pollution due to high infiltration rate (Han et al., 2015). Various indoor sources such as cooking and cleaning activities also contribute to indoor pollution (He et al., 2004). World Health Organization (WHO) has considered indoor air pollution as the third leading risk factor contributing to 4.3% of the global burden of disease (Lim et al., 2012). Given vulnerable people, including elderly and children who tend to spend the majority of their daily time indoors (Duan, 2013; Klepeis et al., 2001), indoor air pollution exposure may also cause almost as large or greater cardiovascular effects compared with ambient air pollution exposure (Mitter et al., 2016; Karottki et al., 2014).

Portable filter-based air filtration units are now being widely used to reduce indoor air pollution concentrations, of either outdoor or indoor origins. A previous review has suggested that reductions on indoor exposure to outdoor sourced particles following both short-term and long-term air filtration intervention are associated with decreases in morbidity and mortality risks (Fisk, 2013). Recently, several intervention studies have assessed the impacts of short-term indoor air filtration intervention between 2 and 14 days on biomarker changes in China (Shao et al., 2017; Li et al., 2017; Chen et al., 2015). However, due to a diversity of intervention designs and study participants, these findings were not directly comparable and reported inconsistent effects of indoor air filtration on cardiovascular health.

Previously, we conducted a randomized cross-over air filtration intervention study, known as the Beijing Indoor Air Purifier StudY (BIAPSY), in 35 currently non-smoking elderly with or without chronic obstructive pulmonary disease (COPD) living in their own households in the winter of 2013 in Beijing, China (Shao et al., 2017). In previous analysis, we focused on the changes on lung function, systemic inflammation and oxidative stress, and cardiovascular function levels following air filtration intervention. However, non-significant improvements on HRV and BP levels were observed, in which both indices were analyzed as averages of 12-h ambulatory HRV and blood pressure (ABP) measurements (Shao et al., 2017). The averaged transformation might not capture the temporal variations of ambulatory monitoring and reduced power to examine time-varying exposure-response relationships (Ringrose et al., 2018; Drawz et al., 2017). In this extended analysis on 12-h real-time air pollution monitoring and concurrent ambulatory HRV and ABP data, we aimed to evaluate whether short-term air filtration intervention could benefit cardiovascular health in elderly who spend large amount of time indoors.

2. Materials and methods

2.1. Study participants and design

Current analysis was based on the data collected in BIAPSY and the detailed study protocol has been published previously (Shao et al., 2017). In brief, a panel of 35 currently non-smoking elderly (15 couples and 5 single individuals) from 20 households were recruited from the Respiratory Department of Peking University Third Hospital (PUTH) between December 2013 and March 2014 in Beijing, China. All participants resided within 5 km from PUTH. The participants were on average of 66.26 years old including 20 COPD patients and their non-COPD partners (only 15 couples). The severity for COPD patients was ranked following Global Initiative for Chronic Obstructive Lung Disease criteria (Vestbo et al., 2013), and all patients were free from exacerbations over the prior 6 weeks. All participants participated in the entire period of 4-week observational intervention, including a consecutive 2-week of active filtration (with filter) and another consecutive 2-week of sham filtration (without filter). Two types of high efficiency particulate air (HEPA) filtration units (AC4374 and AC4016, Philips Lifestyle Ltd. equipped with HEPA and activated carbon filters) were used in each study household, in which one was allocated in the living room and another in the bedroom. Participants were asked to close their residential windows and doors during active and sham filtration intervention periods, and to keep daily activities as usual for free-living condition. At baseline, each study participant's basic information was recorded from questionnaires and measurements, including demographic characteristics, anthropometrics and medical history (Shao et al., 2017).

Nested within this 4-week intervention, we measured 12-h ambulatory HRV and ABP of each participant at the end of each 2-week active- and sham-filtration periods in this study. Participants were required to stay at home throughout the monitoring during the day. Concurrently, air pollution monitoring devices were set up in their living rooms to measure the corresponding 12-h real-time indoor $PM_{2.5}$ and BC concentrations. Outdoor $PM_{2.5}$ concentrations were also continuously measured during active and sham filtration. The study protocol was approved by the Institutional Review Board (IRB) of Peking University Health Science Center (PUHSC) (IRB #00001052–13,070). Each participant signed the written informed consent before participation. This study had been registered at http://www.clinicaltrials.gov (NCT02509000).

2.2. 12-h ambulatory HRV and ABP measurements

HRV measurements were monitored for each participant during the 12-h daytime (from 8:00 a.m. to 20:00 p.m.) on the last day of each intervention, using a 7-lead ambulatory electrocardiographic (ECG) monitoring device (Model MGY H7, DM Software Inc., USA). Each participant wore the device by trained personnel and proceeded a normally daily activity. The ECG digital recordings were reviewed and analyzed by professional clinical technologists using a personal computer-based software (Holter System, version 12. Net for Windows, DM Software). Complete 5-min segments of normal-to-normal (NN) intervals were taken to compute the following five HRV indices: time-domain indices, including standard deviation of NN intervals (SDNN), and the square root of the mean of the squared differences between adjacent NN intervals (RMSSD); as well as frequency-domain indices, including low frequency (LF) (0.04–0.15 H_Z), high frequency (HF) (0.15–0.40 H_Z), and total power (TP) (0.01–0.40 Hz). For each HRV index, approximately 288 valid measurements were obtained for each participant (144 measurements for each intervention) and a total of 10,080 measurements for all participants.

ABP measurements were concurrently monitored for each participant throughout the 12-h daytime, using a portable BP monitoring device with a self-inflating cuff (MGY-ABP1, DM Software Inc., USA).

Ambulatory systolic blood pressure (SBP) and diastolic blood pressure (DBP) were repeatedly measured every 30 min and then reviewed through a personal computer-based software (Ambulatory Blood Pressure Monitor Analysis Software 1.0 for Windows, DM Software). Ambulatory mean arterial pressure (MAP) was also derived as (SBP + 2 × DBP)/3 for further analyses. For each ABP index, approximately 48 valid measurements were obtained for each participant (24 measurements for each intervention) and a total of 1680 measurements for all participants.

2.3. Real-time indoor and outdoor air pollutants

Concurrently with 12-h ambulatory HRV and ABP monitoring, minute-to-minute indoor $PM_{2.5}$ and BC concentrations were measured during the 12-h daytime, using portable monitors PDR-1500 (Thermo Scientific Inc., U.S.) and Aethlabs AE-51 (Magee Inc., U.S.). The 5-min and 30-min average concentrations from minute-to-minute $PM_{2.5}$ and BC were also calculated to match with HRV and ABP indices. For averaged indoor $PM_{2.5}$ and BC, 1- to 10-h moving average (MA) concentrations preceding each HRV or ABP measurement were constructed for further statistical analyses. For example, the 8-h moving average (MA-8 h) concentrations meant averages of air pollutant concentrations for preceding 8 h to each measurement.

In addition, outdoor hourly $PM_{2.5}$ concentrations were determined continuously using a β-ray method (BAM-1020, MetOne Instruments, Inc., U.S.) at a fixed air monitoring station located on the campus of PUHSC (adjacent to PUTH) since mid-January 2014. To compare with outdoor $PM_{2.5}$ concentrations, hourly indoor $PM_{2.5}$ and BC concentrations were also calculated for descriptive analyses.

2.4. Statistical analysis

Descriptive statistics were performed for demographic characteristics, health indices and air pollution exposures. Paired Wilcoxon-test was conducted to compare the differences of health indices between the intervention (active and sham filtration). All HRV and ABP indices were log transformed (natural log) prior statistical analyses due to skewed distributions assessed by Shapiro–Wilk Normality Test.

To evaluate potential health effects of indoor air pollution, generalized additive mixed models (GAMM) were applied to investigate the associations of 1- to 10-h air pollution exposures with HRV and ABP indices. The first-order autoregressive covariance structure was selected based on the minimizing Akaike's information criterion. The participant was fitted as a random intercept to account for within participant correlation between active and sham filtration interventions. Age, gender, body mass index (BMI) and air filtration (yes vs. no) were adjusted as fixed-effect covariates for all models. To control for nonlinear fixed-effect of monitoring time, we adjusted for a penalized cubic regression spline function of time of day. We did not adjust for indoor temperature and relative humidity in the models, because these parameters remained consistent in study households throughout central heating winter in Beijing (Shao et al., 2017). Stratification analyses were then performed on the associations of indoor air pollution exposures at MA-8 h with HRV and ABP indices by air filtration (yes vs. no). The effect modifications were evaluated by including multiplicative interaction terms between air filtration (yes vs. no) and all covariates, and then the interaction terms between air filtration (yes vs. no) and indoor air pollutants were selected. Finally, smooth curves were derived to graphically evaluate the exposure–response relationships between indoor air pollutants and predicted HRV and ABP indices, using a restricted cubic spline function with 3 degrees of freedom (df).

The effect estimates of air pollution exposure on HRV and ABP indices were back transformed and presented as percentage changes with 95% confidence intervals (95% CIs) per 10- or 1-μg/m^3 increases in $PM_{2.5}$ or BC, respectively. Two-sided Wald test with a significant level of $\alpha < 0.05$ was assessed to evaluate the statistical significance. All statistical analyses were performed using R statistical software (version 3.2.2; http://www.r-project.org).

Table 1
Participants' characteristics (N = 35) and health indices' levels during the 12-h active and sham filtration. #: Statistically non-significant differences ($P > 0.05$) between active and sham filtration (N-paired = 35) using paired Wilcoxon-test.

Characteristics	Mean ± SD or N (%)	
Age, years	66.26 ± 7.71	
Woman	15 (43)	
BMI, kg/m^2	24.50 ± 3.72	
Chronic disease history		
COPD	20 (57)	
CVD	9 (26)	
Hypertension	11 (31)	
Diabetes	7 (20)	
	Active filtration	Sham filtration
Heart rate variability#		
SDNN, ms	36.88 ± 12.31	39.94 ± 13.31
RMSSD, ms	22.09 ± 15.93	21.29 ± 13.12
LF, ms^2	210.00 ± 132.85	245.22 ± 168.54
HF, ms^2	97.07 ± 145.78	103.23 ± 151.54
TP, ms^2	1348.29 ± 817.27	1532.97 ± 941.11
Ambulatory blood pressure#		
SBP, mmHg	127.70 ± 12.09	125.47 ± 11.58
DBP, mmHg	76.09 ± 9.06	72.98 ± 7.95
MAP, mmHg	92.99 ± 9.48	90.15 ± 8.55

3. Results

3.1. Descriptive statistics

Table 1 summarizes characteristics of all participants (N = 35), with more details elsewhere (Shao et al., 2017). The participants were on average 66.26 years old [standard deviation (SD), 7.71], with mean body mass index (BMI) 24.50 kg/m^2 (SD, 3.72), 43% female, and 57% COPD patients. 26% had diagnosed cardiovascular disease (CVD) including coronary heart disease, myocardial infarction and stroke, and 31% were reported with hypertension. The levels of HRV and ABP indices during the 12-h intervention were also present in Table 1. No statistically significant differences on the levels of HRV and ABP indices were observed between active and sham filtration.

Table 2 summarizes averaged real-time outdoor and indoor air pollution concentrations during the 12-h intervention. The mean concentration of outdoor $PM_{2.5}$ was 72.28 μg/m^3; however, outdoor BC was not monitored. During sham filtration, mean concentration of indoor $PM_{2.5}$ was 58.24 μg/m^3 and only slightly lower than outdoor $PM_{2.5}$ concentration. During active filtration, indoor $PM_{2.5}$ mean concentration was largely reduced to 37.99 μg/m^3. There was nearly 34.8% decrease in indoor $PM_{2.5}$ concentration. Similarly, during active filtration, there was about 35.3% decrease in indoor BC concentration compared with sham filtration (2.20 vs. 3.40 μg/m^3).

Fig. 1 presents temporal variations of average indoor and outdoor

Table 2
Summary of average real-time (12-h) outdoor and indoor air pollution concentrations (Mean ± SD).

Pollutants	Outdoor concentrations	Indoor concentrations		
		Active filtration	Sham filtration	Reduction (%)
$PM_{2.5}$, μg/m^3	72.28 ± 57.50	37.99 ± 45.89	58.24 ± 52.74	34.8
BC, μg/m^3	NA	2.20 ± 1.45	3.40 ± 2.14	35.3

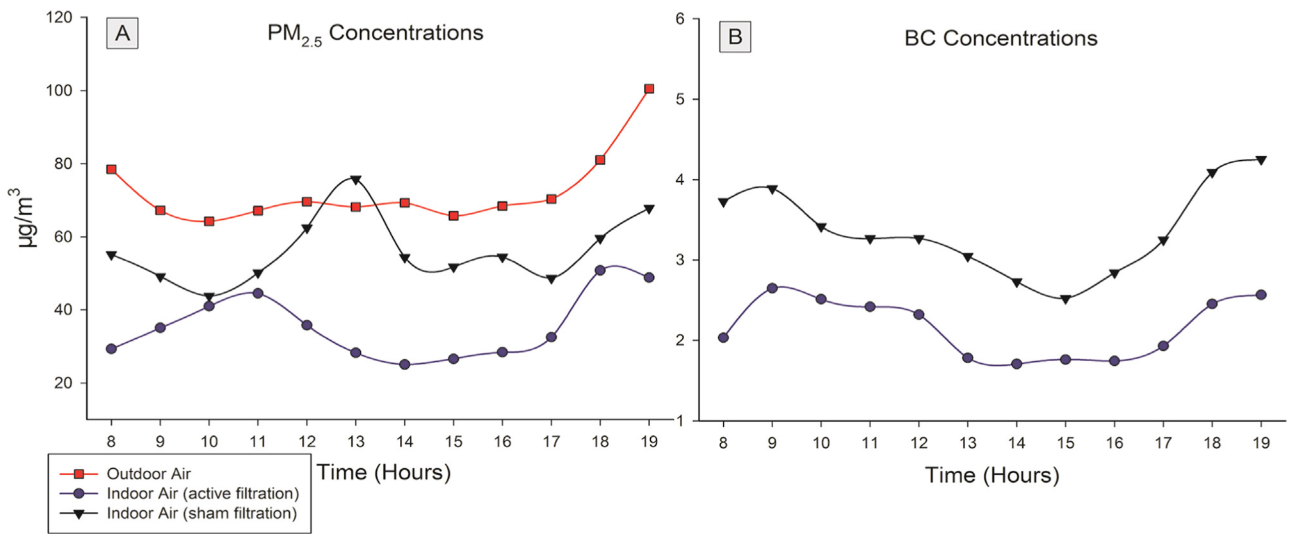

Fig. 1. Temporal variations of $PM_{2.5}$ and BC concentrations during the 12-h active and sham filtration. The hourly mean concentrations of outdoor and indoor $PM_{2.5}$ and indoor BC were the averages of all participants' measurements in each intervention mode.

$PM_{2.5}$ concentrations, as well as indoor BC concentrations during the 12-h intervention. As for indoor BC (shown in Fig. 1B), the differences and varying trends between active and sham filtration remained steady over the 12-h intervention. As for outdoor and indoor $PM_{2.5}$ (shown in Fig. 1A), similar patterns were observed between outdoor and indoor $PM_{2.5}$ over the 12-h active filtration. Interestingly, the concentrations of indoor $PM_{2.5}$ during sham filtration were elevated sharply from 11:00 a.m. to 13:00 p.m. and exceeded average outdoor $PM_{2.5}$ concentrations, indicating $PM_{2.5}$ emitted from indoor sources, such as home cooking.

3.2. Effects of $PM_{2.5}$ and BC on HRV and ABP indices

In Table 3, we present the associations of indoor $PM_{2.5}$ and BC exposures at MA-8 h with HRV and ABP indices estimated by generalized additive mixed mode. Indoor $PM_{2.5}$ exposures were significantly associated with reduced HRV indices and increased ABP indices. Likewise, indoor BC exposures were significantly associated with reduced RMSSD. In specific, each 10 μg/m^3 increase in indoor $PM_{2.5}$ at MA-8 h was significantly associated with a reduction of 1.25% [95% CI: −2.06, −0.42] in SDNN and an increase of 0.39% (95% CI: 0.03, 0.75) in SBP. Each 1 μg/m^3 increase in indoor BC at MA-8 h was significantly associated with a reduction of 5.93% (95% CI: −9.37, −2.35) in RMSSD. Results about the associations of indoor $PM_{2.5}$ and BC exposures at 1- to 10-h moving averages with HRV and ABP indices are presented in Supplemental Figs. S1 and S2, respectively.

3.3. Effect modifications by air filtration intervention

Effect modifications by air filtration on the associations of indoor air pollution exposures at MA-8 h with HRV and ABP indices are presented in Fig. 2. Overall, increases in indoor air pollution were associated with HRV reduction and blood pressure elevation in the stratified analyses (as shown in Fig. 2A and B).

As for HRV (shown in Fig. 2A), we observed some significant effect modifications by air filtration on the associations of indoor $PM_{2.5}$ exposures at MA-8 h with several HRV indices, including SDNN, LF and TP ($P_{inter} \leq 0.001$). During active filtration intervention, the associations between indoor $PM_{2.5}$ exposures at MA-8 h and reductions in SDNN, LF and TP became non-significant, whereas reductions in SDNN, LF and TP were significant during sham filtration. In specific, each 10 μg/m^3 increase in indoor $PM_{2.5}$ at MA-8 h was associated with a significant reduction of 1.34% (95% CI: −2.42, −0.26) in SDNN during sham filtration, compared with a non-significant reduction of 0.81% (95% CI: −6.00, 4.68) during active filtration. Non-significant effect modifications by air filtration were observed on the associations of indoor BC exposures at MA-8 h with HRV indices ($P_{inter} > 0.05$).

As for ABP indices (shown in Fig. 2B), we did not observe significant

Table 3
Associations between indoor $PM_{2.5}$ or BC exposures at MA-8 h and ambulatory HRV and ABP indices. Results were presented as percentage changes (95% CIs) in ambulatory HRV and ABP indices associated with 10- or 1-μg/m^3 increases in 8-h moving average exposures of indoor $PM_{2.5}$ or BC based on generalized additive mixed models among all participants. All models adjusted for age, gender, body mass index, air filtration (yes vs. no) and time of day. The 8-h moving average (MA-8 h) means the averages of pollutant concentrations for the prior 8 h to each index measurement.

Indices	Indoor $PM_{2.5}$	Indoor BC
Heart rate variability (No. = 10,080)		
SDNN	−1.25 (−2.06, −0.42)*	−2.45 (−5.54, 0.75)
RMSSD	−2.77 (−3.78, −1.75)*	−5.93 (−9.37, −2.35)*
LF	−3.69 (−5.41, −1.94)*	−3.36 (−9.84, 3.58)
HF	−4.80 (−6.65, −2.91)*	−1.54 (−8.98, 6.51)
TP	−2.33 (−3.89, −0.75)*	−4.50 (−10.59, 2.01)
Ambulatory blood pressure (No. = 1680)		
SBP	0.39 (0.03, 0.75)*	0.86 (−0.76, 2.51)
DBP	0.57 (0.05, 1.10)*	0.66 (−1.48, 2.85)
MAP	0.49 (0.07, 0.92)*	0.71 (−1.11, 2.56)

* Statistically significant ($P < 0.05$).

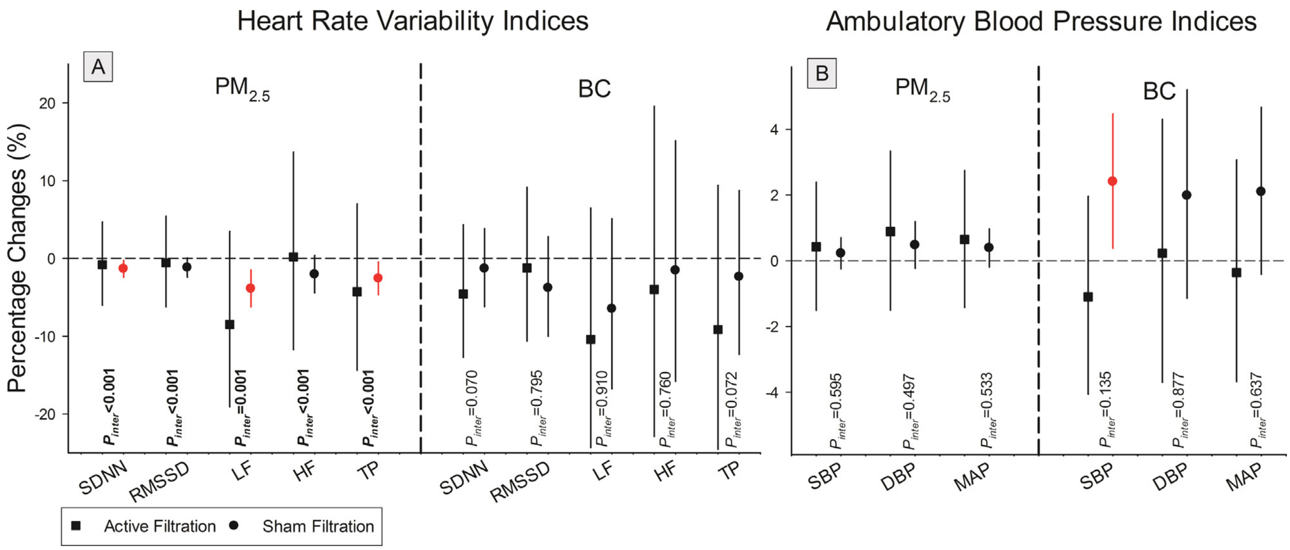

Fig. 2. Effect modifications by air filtration based on generalized additive mixed models. Results were presented as percentage changes (95% CIs) in ambulatory heart rate variability and blood pressure indices with 10- or 1-μg/m^3 increases in 8-h moving average exposures of indoor $PM_{2.5}$ or BC. All models adjusted for age, gender, body mass index and time of day. The 8-h moving average (MA-8 h) means the averages of pollutant concentrations for the prior 8 h to each index measurement. The bold P_{inter} values are presented as $P < 0.001$.

effect modifications on the associations of indoor $PM_{2.5}$ or BC exposures at MA-8 h with any ABP indices by air filtration ($P_{inter} > 0.05$), except for SBP. During active filtration intervention, the association between indoor BC exposure at MA-8 h and an increase in SBP became non-significant, whereas an increase in SBP was significant during sham filtration. In specific, each 1 μg/m^3 increase in indoor BC at MA-8 h was associated with a significant increase of 2.41% (95% CI: 0.38, 4.47) in SBP during sham filtration, compared with a non-significant increase of −1.09% (95% CI: −4.06, 1.96) during active filtration. However, the interaction term between indoor BC and air filtration on SBP was not significant (P_{inter} = 0.135).

3.4. Exposure-response relationships

The exposure-response relationships of indoor $PM_{2.5}$ and BC at MA-8 h with predicted HRV and ABP indices (95% CIs) for all participants are presented in Fig. 3, Supplemental Figs. S3 and S4. Smooth curves were modeled with a restricted cubic spline function with 3 degrees of freedom (df).

As for HRV indices, the exposure-response curve for indoor $PM_{2.5}$ and SDNN was similar to a left-skewed inverted U-shape with an increasing trend when indoor $PM_{2.5}$ concentration was below at about 20 μg/m^3 (shown in Fig. 3), and similar patterns were also observed for other HRV indices with indoor $PM_{2.5}$ (shown in Fig. S3). In addition,

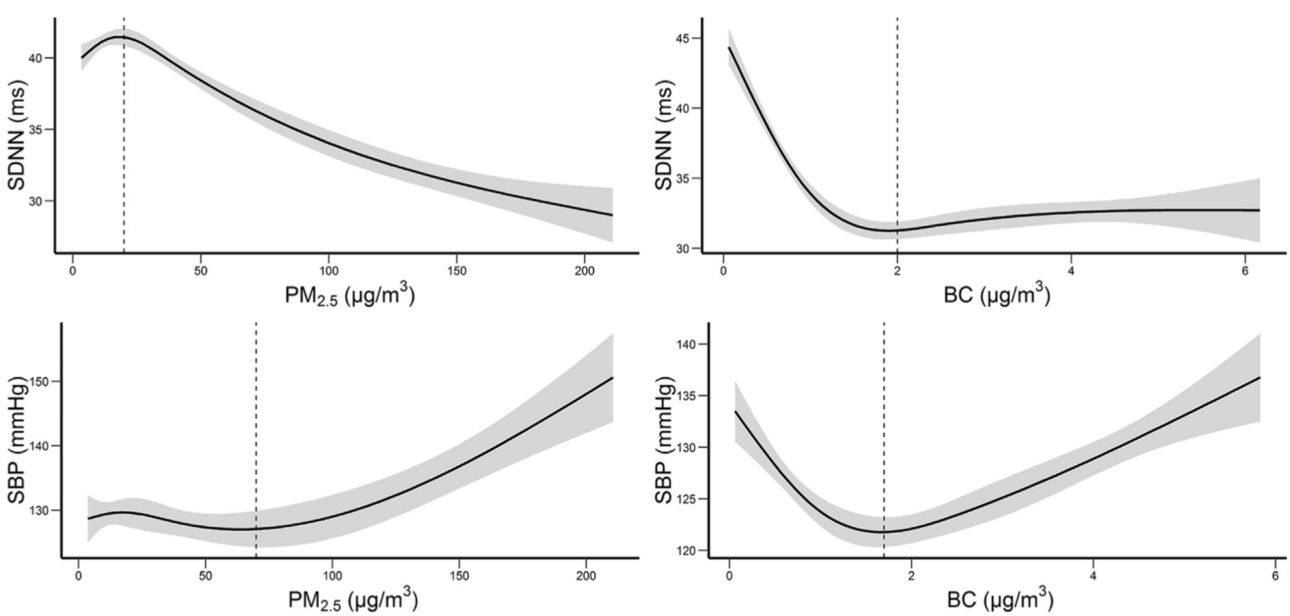

Fig. 3. Exposure-response relationships of indoor $PM_{2.5}$ and BC at MA-8 h with predicted ambulatory SDNN and SBP. The predicted ambulatory SDNN and SBP (95% CIs) were based on generalized additive mixed models after adjusting for age, gender, body mass index, air filtration (yes vs. no) and time of day for all participants. Smoothed curves were modeled using restricted cubic spline function with 3 degrees of freedom (df). The 8-h moving average (MA-8 h) means the averages of pollutant concentrations for the prior 8 h to each index measurement.

there was a segment of sharply decreasing trend in the exposure-response curve for indoor BC and SDNN when indoor BC concentration was below at about 2 μg/m^3 (shown in Fig. 3), and the patterns for other HRV indices with indoor BC differed (shown in Fig. S3).

As for ABP indices, the exposure-response curve for indoor $PM_{2.5}$ and SBP was almost linear with a slightly decreasing trend when indoor $PM_{2.5}$ concentration was below at approximately 70 μg/m^3 (shown in Fig. 3), and similar patterns were also observed for other ABP indices with indoor $PM_{2.5}$ (shown in Fig. S4). Moreover, the exposure-response curve for indoor BC and SBP was a slightly left-skewed U-shape with a decreasing trend when indoor BC concentration was below at about 1.7 μg/m^3 (shown in Fig. 3), and similar patterns were also observed for other ABP indices associated with indoor BC (shown in Fig. S4). Overall, these findings might provide insights on the differential effects of indoor $PM_{2.5}$ or BC observed on the same participants during active and sham filtration (Fig. 2), which were likely due to differential exposure-response slops over the broad range of exposures.

4. Discussion

In this extended analysis of BIAPSY, approximately 34.8% and 35.3% decreases were observed in 12-h indoor real-time $PM_{2.5}$ and BC concentrations during active filtration, compared with sham filtration. Our study demonstrated that increased indoor $PM_{2.5}$ as well as indoor BC exposures were positively associated with impaired autonomic nervous system function and increased blood pressure in currently non-smoking elderly with free-living in their own households in Beijing. These associations were modified by short-term air filtration intervention, and stronger effects of indoor air pollution exposures were observed on ambulatory HRV and ABP during sham filtration, suggesting short-term indoor air filtration intervention could be of some cardiovascular benefits in elderly. In addition, nonlinear inverse exposure-response relationships of indoor air pollution exposures with predicted HRV and ABP indices confirmed cardiovascular benefits of indoor air pollution reduction.

HRV indices are physiological measurements of variation in the inter-beat intervals on a continuous electrocardiogram. Reduced HRV has been regarded as a risk factor for cardiac morbidity and mortality (La Rovere et al., 2003; Lombardi et al., 2001). A balance of the parasympathetic and sympathetic nervous system regulates the heart rate for keeping a constant cardiac output at rest and responding to elevated demands during exercise. In this regard, air pollution-mediated elevated BP which is likely via cardiac autonomic dysfunction as a plausible mechanism. In our study, consistent with the findings of previous studies (Norris et al., 2016; Huang et al., 2014; H.C. Chuang et al., 2013; K.J. Chuang et al., 2013; Lin et al., 2009), we observed indoor air pollution exposures, especially $PM_{2.5}$, were associated with decreases in HRV indices and increases in ABP indices among currently non-smoking elderly.

The main finding of our study was that short-term air filtration intervention can modify some of the associations of indoor air pollution exposures with impaired autonomic nervous system function and increased blood pressure. These findings implied that short-term air filtration intervention might have some benefits, at least in part, on preventing the adverse effects of indoor air pollution exposure on sympathetic nervous system which is relative to elevated blood pressure. These results were consistent with several published short-term air filtration intervention studies (Lin et al., 2013, 2011; K.J. Chuang et al., 2013; H.C. Chuang et al., 2013). Lin et al. (2013) reported significant effect modifications of indoor $PM_{2.5}$ on 16-min resting SDNN and RMSSD according to 24-h air filtration in an intervention panel study of 300 healthy subjects in Taipei (both $P_{inter} < 0.05$). They found stronger effects of indoor $PM_{2.5}$ exposures on these two indices during air filtration off mode. H.C. Chuang et al. (2013) reported consistently significant effect modifications of in-car $PM_{2.5}$ on 2-h ambulatory SDNN and RMSSD by air filtration operation mode in an 2-h air filtration-based intervention study of 60 healthy citizens in Taipei (both $P_{inter} < 0.01$). They found stronger effects of in-car $PM_{2.5}$ on these two indices during air filtration off mode. Moreover, Lin et al. (2011) reported that 48-h air filtration intervention could significantly modify the effects of indoor $PM_{2.5}$ on 48-h ambulatory SBP and DBP in an air filtration-based intervention study of 60 young healthy students in Taipei (both $P_{inter} < 0.01$). The effects of indoor $PM_{2.5}$ exposures on BP were greater during the visits without air filtration. Recently, in Shanghai, China, two randomized double-blind crossover studies which conducted in healthy college students with 2- or 9-day air filtration periods reported that indoor air filtration could significantly reduce resting SBP and DBP or only resting SBP attributable to indoor air pollution exposures, respectively (Li et al., 2017; Chen et al., 2015).

Another finding was that exposure-response relationships between indoor air pollutants and predicted health indices were nonlinear. According to the exposure-response curves, the different curve slops over the broad range of exposures might provide a rational explanation for the differential health effects of indoor air pollution exposures on the same participants during the two different intervention modes. These results might also suggest that only when the concentrations of indoor air pollution were reduced to limited low levels, would the air filtration units offer benefits to cardiovascular health in elderly.

Besides the advantages that our intervention study was conducted under a real-world exposure scenario, we also restricted the study within one-month intervention to avoid some potential temporal confounding likely introduced by changes in participant behavior patterns. However, several limitations should be noted. First, we did not monitor indoor gaseous pollutants which might not be cleared by air filtration units and might have confounding impacts on the intervention effects of air filtration. Secondly, due to some missing values of continuous indoor air pollution measurements during active filtration period, the effect estimates during active-filtration tended to bias toward null and underestimate the potential impacts of active-filtration. Lastly, we did not collect detailed indoor activity information, such as ventilation and cooking habits, to address indoor and outdoor origins of air pollutants. However, our study could still contribute to the accumulation of evidences on the cardiovascular health effects by short-term indoor air filtration intervention.

5. Conclusions

Our study demonstrates the associations of indoor air pollution exposures with adverse cardiovascular effects among non-smoking elderly living with high outdoor air pollution. Some improvements on cardiovascular health can be obtained from reducing indoor air pollution concentrations by short-term air filtration intervention. Differential slops observed in the exposure-response curves over the broad range of exposures during active and sham filtration also confirm some cardiovascular benefits of short-term indoor air filtration intervention.

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Availability of data and materials

Please contact the corresponding author for data requests

Conflict of interest

The authors declare that they have no competing interests.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2018.08.026.

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