Environment International 121 (2018) 139–147

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Long- and short-term air pollution exposure and measures of arterial stiffness in the Framingham Heart Study

Petter L.S. Ljungman[a,b,c,*], Wenyuan Li[b,d], Mary B. Rice[b,e], Elissa H. Wilker[b,d], Joel Schwartz[f], Diane R. Gold[f,g], Petros Koutrakis[f], Emelia J. Benjamin[h,i,j], Ramachandran S. Vasan[h,i,j], Gary F. Mitchell[k], Naomi M. Hamburg[h,i,j], Murray A. Mittleman[b,d]

[a] Environmental Epidemiology Unit, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden
[b] Cardiovascular Epidemiology Research Unit, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA
[c] Department of Cardiology, Danderyds Hospital, Stockholm, Sweden
[d] Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA, USA
[e] Division of Pulmonary, Critical Care and Sleep Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA
[f] Department of Environmental Health, Harvard T. H. Chan School of Public Health, Boston, MA, USA
[g] Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA
[h] National Heart, Lung, and Blood Institute's and Boston University's Framingham Heart Study, MA, USA
[i] Preventive Medicine and Cardiology Sections, Department of Medicine, Boston University School of Medicine, MA, USA
[j] Department of Epidemiology, Boston University School of Public Health, MA, USA
[k] Cardiovascular Engineering Inc., Norwood, MA, USA

ARTICLE INFO

Handling Editor: Xavier Querol

Keywords:
Arterial stiffness
Air pollution
Applanation tonometry
Epidemiology

ABSTRACT

Background: Studies of air pollution exposure and arterial stiffness have reported inconsistent results and large studies employing the reference standard of arterial stiffness, carotid-femoral pulse-wave velocity (CFPWV), have not been conducted.

Aim: To study long-term exposure to ambient fine particles ($PM_{2.5}$), proximity to roadway, and short-term air pollution exposures in relation to multiple measures of arterial stiffness in the Framingham Heart Study.

Methods: We assessed central arterial stiffness using CFPWV, forward pressure wave amplitude, mean arterial pressure and augmentation index. We investigated long-and short-term air pollution exposure associations with arterial stiffness with linear regressions using long-term residential $PM_{2.5}$ (2003 average from a spatiotemporal model using satellite data) and proximity to roadway in addition to short-term averages of $PM_{2.5}$, black carbon, particle number, sulfate, nitrogen oxides, and ozone from stationary monitors.

Results: We examined 5842 participants (mean age 51 ± 16, 54% women). Living closer to a major roadway was associated with higher arterial stiffness (0.11 m/s higher CFPWV [95% CI: 0.01, 0.22] living < 50 m vs 400 ≤ 1000 m). We did not observe association between arterial stiffness measures and long-term $PM_{2.5}$ or short-term levels of $PM_{2.5}$, particle number, sulfate or ozone. Higher levels of black carbon and nitrogen oxides in the previous days were unexpectedly associated with lower arterial stiffness.

Conclusions: Long-term exposure to $PM_{2.5}$ was not associated with arterial stiffness but positive associations with living close to a major road may suggest that pollutant mixtures very nearby major roads, rather than $PM_{2.5}$, may affect arterial stiffness. Furthermore, short-term air pollution exposures were not associated with higher arterial stiffness.

1. Introduction

Exposure to air pollution has been associated with cardiovascular morbidity and mortality in many studies (Brook et al., 2004). Atherosclerosis and vascular dysfunction contribute to the development of cardiovascular events and may represent a pathway by which air pollution may exert effects both as a result of short- and long-term exposure (Newby et al., 2015). Long-term exposure to particulate matter pollution over months to years has been associated with vascular risk factors and subclinical disease including high blood pressure (Zhang et al., 2018), carotid intima media thickness (Wilker et al., 2013; Bauer et al., 2010) and increased calcification of arteries

* Corresponding author at: Institute of Environmental Medicine, Karolinska Institute, 171 77 Stockholm, Sweden.
E-mail address: petter.ljungman@ki.se (P.L.S. Ljungman).

https://doi.org/10.1016/j.envint.2018.08.060
Received 4 June 2018; Received in revised form 24 August 2018; Accepted 27 August 2018

(Hoffmann et al., 2007), although associations were not consistent for these measures in all studies (Diez Roux et al., 2008; Dorans et al., 2017).

Increased central arterial stiffness, another measure of vascular dysfunction, is a risk factor for the development of cardiovascular events and may be a precursor to hypertension (Kaess et al., 2012; Mitchell, 2009). To date, studies of long-term air pollution exposure and arterial stiffness have reported inconsistent results (Breton et al., 2016; Endes et al., 2017; Iannuzzi et al., 2010; Jiang et al., 2016; Lenters et al., 2010; O'Neill et al., 2011; Weng et al., 2015) but only one study measured carotid femoral pulse wave velocity (CFPWV), considered the reference standard measure of arterial stiffness (Lenters et al., 2010). Instead most studies used measures such as augmentation index, that with age becomes a less sensitive marker for arterial stiffness and future CVD risk (Mitchell, 2009).

Short-term exposures to air pollution on the order of days, including both gaseous and particulate components, also have been associated with measures of vascular function including changes in blood pressure (Yang et al., 2018), peripheral vascular function (Ljungman et al., 2016; Zanobetti et al., 2014; Sack et al., 2016; Schneider et al., 2008), and coronary ischemia (Mills et al., 2007). Changes in arterial stiffness also have been studied in relation to short-term air pollution exposure in previous studies but with varying results and a lack of large-scale studies using CFPWV (Adamopoulos et al., 2010; Hunter et al., 2014; Langrish et al., 2013; Lundback et al., 2009; Mehta et al., 2014).

Whereas it is generally perceived that air pollution has an adverse effect on vascular function, resulting in increased risk of cardiovascular events in the short- and long-term, previous studies have yielded inconsistent results, possibly because the approach to measuring arterial stiffness has been problematic. Variation in study populations and constituents of air pollution mixtures may also explain inconsistencies across studies. In addition, none of the previous studies have assessed both long- and short-term air pollution exposure. We hypothesized that living close to a major road and at addresses with higher long-term averages of particulate matter is associated with higher arterial stiffness. We also hypothesized that higher short-term averages of particulate air pollution are associated with higher arterial stiffness. Therefore, we evaluated both long- and short-term exposure to air pollutants and traffic to the reference standard measure of arterial stiffness (and also several complementary measures) in a well-characterized large community-based cohort.

2. Methods

2.1. Study participants

Participants in the Framingham Heart Study Offspring and Third Generation cohorts were eligible based on having performed valid examinations of arterial stiffness in examination rounds 8 and 1 respectively and having a primary address in the Northeastern US corresponding to the catchment area of the spatially resolved fine particulate matter ($PM_{2.5}$) satellite model, resulting in 5842 participants. These cohorts have been described in detail previously (Kannel et al., 1979; Splansky et al., 2007). Ethical approval was obtained from the Institutional Review Boards of the Beth Israel Deaconess Medical Center and Boston University Medical Center. Written informed consent was obtained from all participants.

Individual-level covariates were collected through physician interview, blood draws, and physical examination. Neighborhood-level data concerning socio-economic characteristics were collected through the U.S. Census 2000 based on the primary residential address of each participant. These included median household income and median value of owner-occupied housing units, at the census tract level.

2.2. Measures of arterial stiffness

Offspring cohort examination round 8 was conducted between 2005 and 2008 and Third Generation cohort examination round 1 was conducted between 2002 and 2005. The methodology of arterial stiffness measures in the Framingham cohorts has been described in detail elsewhere (Mitchell et al., 2004; Mitchell et al., 2010). Briefly, using a custom transducer, electrocardiogram, and body-surface measurements, tonometric measurements were obtained from the carotid and femoral sites to calculate CFPWV. Left ventricular outflow tract diameter was measured with 2-dimensional echocardiography and Doppler flow velocity was multiplied by outflow tract area to obtain aortic volume flow. Wave separation analysis was used to determine the forward pressure wave amplitude (FWA) and carotid pressure waveform analysis was used to assess augmentation index. Mean arterial pressure was calculated from the brachial pressure wave form based on tonometry or oscillometric cuff waveform.

Of the several methods used to quantify arterial stiffness CFPWV is considered the reference standard. CFPWV is primarily a measure of aortic wall stiffness. FWA is a function of the peak systolic blood flow and aortic impedance and increases with greater aortic wall stiffness or in the presence of mismatch between aortic diameter and flow. Mean arterial pressure provides a measure of steady-flow load and is influenced by cardiac output and peripheral vascular resistance. Augmentation index is based on pulse wave analysis in the carotid artery and is used to measure relative wave reflection.

2.3. Exposure assessment

2.3.1. Long-term $PM_{2.5}$

We assessed annual averages of $PM_{2.5}$ exposure at the primary residential address of each participant recorded at the examination round using modeled estimates of daily $PM_{2.5}$ with a 1×1 km resolution. The basis of the model used satellite-derived aerosol optical depth (AOD), a quantitative measure of particle abundance in a column of air, to predict a $PM_{2.5}$ concentration for a 1×1 km grid (Kloog et al., 2014). These estimates were calibrated using 161 ground monitoring stations within 1 km of an AOD value and adjusted for meteorological parameters (temperature, daily visibility, sea land pressure, relative humidity, and wind speed) and local land-use regression parameters (distance to point source emissions, population density, percentage of land use, total area-source emissions, elevation, and traffic density). We then predicted daily $PM_{2.5}$ concentrations in grid cells without monitors but with available AOD using the model fit from the preceding model. Finally, for grid cells without AOD measurements on a given day, we used region-specific associations between grid-cell AOD and $PM_{2.5}$ levels using neighboring cells to calculate daily levels. The difference between ground-level $PM_{2.5}$ data and model predictions were regressed against temporal and spatial predictors of monitored $PM_{2.5}$ at a 200×200 m resolution including the following factors: distance to major roads, traffic density, percent urban, elevation, distance to point source emissions, population density, height of planetary boundary layer, and visibility. Our model predictions demonstrated an out-of-sample 10-fold cross-validated R^2 of 0.88 (0.82–0.90 between 2003 and 2011). We summed daily grid predictions and localized residual $PM_{2.5}$ predictions for each address and averaged them over a year.

We expected temporal trends for $PM_{2.5}$ levels over the years in which arterial measurements were collected (2002–2008) as well as lower arterial stiffness in the generally healthier and younger Third Generation cohort examined between 2002 and 2005 compared to higher arterial stiffness in the older Offspring cohort examined later between 2005 and 2008. In an effort to avoid introducing the bias of these temporal trends we used a similar strategy employed in previous studies (Miller et al., 2007; Rice et al., 2015), of assigning the annual $PM_{2.5}$ concentration of a fixed year (2003) as a measure of recent, longer-term $PM_{2.5}$ exposure. We used the address recorded at the time