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Long-term effects of air pollution on ankle-brachial index

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ABSTRACT

Background: Ankle-brachial index (ABI) has been linked to the risk of cardiovascular events. However, the association between long-term exposure to air pollution and abnormal ABI has not been fully investigated.

Methods: This cross-sectional study involved 4544 participants from the KORA Study (2004–2008) in the region of Augsburg, Germany. Participants' residential annual mean concentrations of particulate matter (PM) and nitrogen dioxide (NO_2) were predicted with land-use regression models, and the traffic information was collected from geographic information systems. We applied multinomial logistic regression models to assess the effects of air pollution on the prevalence of low and high ABI, and quantile regression models to explore the non-monotonic relationship between air pollution and ABI. We also examined effect modification by individual characteristics.

Results: Long-term exposure to PM with an aerodynamic diameter ≤ 10 μm (PM_{10}) and ≤ 2.5 μm ($PM_{2.5}$) was significantly associated with a higher prevalence of low ABI, with the respective odds ratios (ORs) of 1.82 (95%CI: 1.11–2.97) and 1.59 (95%CI: 1.01–2.51) for a 5th to 95th percentile increment in pollutants. Positive associations with the prevalence of high ABI were observed for PM (e.g., PM_{10}: OR = 1.63, 95%CI: 1.07–2.50) and NO_2 (OR = 1.84, 95%CI: 1.15–2.94). Quantile regression analyses revealed similar non-monotonic results. The effects of air pollution on having abnormal ABI were stronger in physically inactive, hypertensive, or non-diabetic participants.

Conclusions: Long-term exposure to PM and NO_2 was associated with a higher prevalence of both low and high ABI, indicating the adverse effects of air pollution on atherosclerosis and arterial stiffness in the lower extremities.

1. Introduction

The ankle-brachial index (ABI) is the ratio of systolic blood pressure at the ankle to that at the brachial artery. A low ABI indicates the presence of atherosclerosis and is used clinically in the diagnosis of peripheral artery disease (PAD) (Heald et al., 2006). A high ABI implies the incompressibility of vessels due to arterial stiffness in the lower extremities (Aboyans et al., 2012). Epidemiological studies have found that both low and high ABI are associated with increased risk of cardiovascular disease and mortality (Resnick et al., 2004; O'Hare et al., 2006; Lamina et al., 2006; Ankle Brachial Index Collaboration, 2008). In addition, individuals with low ABI show greater deterioration of physical function (McDermott et al., 2004).

As a major underlying pathology of cardiovascular disease, the prevalence and progression of atherosclerosis have been linked to air pollution, mainly by using carotid intima-media thickness (CIMT), coronary arterial or aortic calcification as indicators (Adar et al., 2013; Kaufman et al., 2016; Kälsch et al., 2014). The atherosclerotic effects of air pollution on different vascular beds are heterogeneous (Diez Roux et al., 2008; Wang et al., 2016). So far, only a few studies investigated the chronic effects of air pollution on low ABI, and yielded inconsistent results. A study from Germany found that living within 50 m of a main road was associated with a higher prevalence of low ABI (Hoffmann et al., 2009). However, the North-American Multi-Ethnic Study of Atherosclerosis (MESA) reported lower prevalence of low ABI among participants exposed to elevated particulate matter (PM) (Diez Roux et al., 2008).

Despite the association between arterial stiffness and atherosclerosis

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(van Popele et al., 2001), the air pollution effects on low and high ABI could be distinct. A study from Spain observed significantly positive associations of residential nitrogen dioxide (NO_2), traffic load, and traffic intensity with the prevalence of high ABI, while no associations with low ABI (Rivera et al., 2013). Arterial stiffness was found to be associated with acute exposure to air pollution in observational and experimental studies (Mehta et al., 2014; Schneider et al., 2008; Lundback et al., 2009); yet evidence of the long-term effects of air pollution is limited, especially on the stiffness in lower extremity arteries (O'Neill et al., 2011; Lenters et al., 2010).

Given the different pathologies of atherosclerosis and arterial stiffness, we hypothesized a non-monotonic relationship between air pollution and ABI, in which long-term exposure to air pollution would increase the prevalence of both low and high ABI. In the framework of the KORA Cohort (Cooperative Health Research in the Region of Augsburg), we conducted this cross-sectional study to test our hypothesis for air pollution measures including PM with an aerodynamic diameter ≤ 10 μm (PM_{10}), 2.5–10 μm (PM_{coarse}), ≤ 2.5 μm ($PM_{2.5}$), $PM_{2.5}$ absorbance ($PM_{2.5abs}$) as a proxy of elemental carbon levels related to traffic exhaust, NO_2, traffic intensity on the nearest major road, and traffic load within 100 m of the residence.

2. Methods

2.1. Study population

The data for this cross-sectional study were taken from KORA F3 (2004–2005) and F4 (2006–2008), which are population-based surveys among registered German residents in Augsburg and its two adjacent counties (Southern Germany) (Holle et al., 2005). The KORA Study was approved by the ethics committee and all participants gave written informed consent.

2.2. Outcome measurement

Systolic blood pressure was measured in supine position after resting for at least 15 min. The measurements were taken twice in the posterior tibial artery of each ankle and the brachial artery of the right arm using a Doppler probe for pulse detection. We inflated the cuff to about 30 mmHg above the usual systolic blood pressure of the participant and then deflated it by 2–3 mmHg per second. The blood pressure at which the Doppler probe redetected the pulse was recorded as the systolic blood pressure of the limb. The order of measurements was right arm, right leg and left leg, and repeated measurements were in the same order. If the two values of one limb differed by > 10 mmHg, a third measurement was taken. We calculated the ABI of each side separately as the ratio of average systolic blood pressure at the ankle to that at the right arm. We defined participants having normal ABI as participants with $0.9 < ABI \leq 1.4$ in both legs. Participants with $ABI \leq 0.9$ in one or both legs were defined as having low ABI; participants with $ABI > 1.4$ in one leg and normal ABI in the contralateral leg, or with $ABI > 1.4$ in both legs were defined as having high ABI (Aboyans et al., 2012; Rooke et al., 2011; Allison et al., 2008). For participants with ABI values only in one leg, the available ABI value was classified into low ($ABI \leq 0.9$), normal ($0.9 < ABI \leq 1.4$) and high ($ABI > 1.4$).

2.3. Exposure assessment

We estimated the annual average concentration of air pollutants within the European Study of Cohorts for Air Pollutant Effects (ESCAPE) based on standardized protocols (Eeftens et al., 2012; Beelen et al., 2013). In brief, PM and nitrogen oxides were monitored at 20 and 40 sites, respectively, in the region of Augsburg and Munich. Three two-week measurements were taken in different seasons between October 2008 and July 2009, and the monitored values were used to calculate annual mean concentration for each site. Meanwhile, geographic variables from the geographic information system (GIS) were collected to build land-use regression (LUR) models to estimate the individual outdoor pollutant concentrations, including PM_{10}, PM_{coarse}, $PM_{2.5}$, $PM_{2.5abs}$ and NO_2 at each participant's home address. The model explained variance (R^2) for the investigated pollutants ranged from 78% ($PM_{2.5}$) to 91% ($PM_{2.5abs}$), and the leave-one-out cross validation R^2 ranged from 62% ($PM_{2.5}$) to 82% ($PM_{2.5abs}$). Residential background NO_2 levels were predicted using a similar method except that the LUR model was developed with only background monitoring data and GIS predictors. Traffic intensity on the nearest major road (> 5000 vehicles/day) and traffic load within 100 m of the residence (sum of traffic intensity multiplied by length of major roads in a 100 m buffer), were also analyzed in this study.

To control the effect of long-term road traffic noise, annual average Day-Night Sound Level (dB(A) Leq) was estimated for each participant's residential address using the model developed by ACCON GmbH (Pitchika et al., 2017).

2.4. Potential confounding and mediating factors

Trained medical staff administered a standardized face-to-face interview to collect information on sociodemographic characteristics (age, sex, marital status, years of education, current occupation, and income), lifestyle variables (smoking status, smoking pack years, alcohol consumption, and physical activity), self-reported medical history (hypertension, diabetes, myocardial infarction, angina pectoris, and stroke), and medication intake (antihypertensive drugs, antidiabetic drugs, anticoagulants, antiplatelet drugs, and statins). In addition, physical examinations and laboratory tests were conducted to obtain anthropometric data (height, weight, waist and hip circumference), systolic and diastolic blood pressure, blood lipid levels, and glomerular filtration rate (Meisinger et al., 2002). We also assessed neighborhood socioeconomic status (SES) by the percentage of households with low income (< 1250 €) in $(5\,km)^2$ grid cells based on participants' home addresses.

We defined smoking pack years as the number of packs of cigarettes (20 cigarettes per pack) smoked per day multiplied by the number of years the participant had smoked, which is an indicator of the lifelong cumulative exposure to tobacco smoke. Body mass index (BMI) was calculated as weight divided by height squared. Waist-hip ratio was calculated as waist circumference divided by hip circumference. We categorized physical activity based on the time spent on physical exercise and converted it into low level (no or almost no physical exercise), medium level (about one hour per week), and high level (more than two hours per week). Hypertension was defined by blood pressure ≥ 140/90 mmHg or taking antihypertensive medication in people reporting a previous diagnosis of hypertension. Participants who reported doctor-diagnosed diabetes or taking antidiabetic medication were defined as having diabetes.

2.5. Statistical analysis

We applied multinomial logistic regression to investigate the association between air pollution and abnormal ABI. The minimum model was adjusted for age, sex, time trend, and a dummy variable for study. The time trend was modeled as a penalized spline of day of year with three degrees of freedom. Other covariates were chosen by minimizing Bayesian Information Criterion. The main model additionally adjusted for years of education, neighborhood SES, smoking pack years, and smoking status. The extended model further adjusted for diabetes and hypertension. When analyzing the effects of traffic indicators, background NO_2 level was additionally controlled for. Results are presented as odds ratio (OR) of low ABI and high ABI with reference to normal ABI for increments from 5th to 95th percentiles in exposure with a 95% confidence interval (95%CI).