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Long-term exposure to airborne particulate matter and NO_2 and prevalent and incident metabolic syndrome – Results from the Heinz Nixdorf Recall Study

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ABSTRACT

Introduction: Recently, epidemiological studies have found a link between air pollution (AP) and individual components of the metabolic syndrome (MetS), a condition predisposing to cardiometabolic diseases. However, very few studies have explored a possible association between air pollution and MetS.

Objective: We analyzed the effects of long-term exposure to airborne particulate matter and NO_2 on prevalence and incidence of MetS.

Methods: We used data of the population-based prospective Heinz Nixdorf Recall study (baseline 2000–2003) to investigate the association(s) between AP exposure and MetS prevalence at baseline (n = 4457) and MetS incidence at first follow-up visit (n = 3074; average follow-up: 5.1 years). Mean annual exposure to size-fractioned particulate matter (PM_{10}, $PM_{2.5}$, PM_{coarse}, and $PM_{2.5}$abs) and nitrogen dioxide (NO_2) was assessed using a land use regression model. MetS was defined as central obesity plus two out of four additional risk factors (i.e., elevated triglycerides, reduced high-density lipoprotein cholesterol, elevated blood pressure or elevated plasma glucose). We estimated odds ratios (ORs) of MetS prevalence and incidence per interquartile range (IQR) of exposure, adjusting for demographic and lifestyle variables.

Results: We observed a MetS prevalence of 20.7% (n = 922) and an incidence of 9.7% (n = 299). NO_2 was positively associated with MetS prevalence, with an OR increase per IQR of 1.12 (95%-CI 1.02–1.24, IQR = 6.1 μg/m^3). PM_{10} and $PM_{2.5}$ were both borderline positively associated with MetS incidence, with ORs of 1.14 (95%-CI 0.99–1.32, IQR = 2.1 μg/m^3) and 1.19 (95%-CI 0.98–1.44, IQR = 1.5 μg/m^3) per IQR, respectively.

Conclusion: In summary, we found a weak positive association between air pollution and MetS. The strongest and most consistent effects were observed between NO_2 and prevalent MetS.

1. Introduction

The metabolic syndrome (MetS) is considered to be a major public health problem, as it increases the risk of atherosclerotic cardiovascular diseases (CVD), type 2 diabetes mellitus (T2D), and all-cause mortality (Alberti et al., 2009; Kaur, 2014). Overall, the International Diabetes Federation (IDF) estimates that around 25% of the world's adult population has MetS (IDF, 2006). MetS is defined as a collection of

Abbreviations: AP, Air Pollution; ATC, Anatomical Therapeutic Chemical Classification System; ATP III, Adult Treatment Panel III; BMI, Body Mass Index; BP, Blood Pressure; CTM, Chemistry Transport Model; CVD, Cardiovascular Disease; ESCAPE, European Study of Cohorts for Air Pollution Effects; EMI, Dietary Pattern Index/"Ernährungsmusterindex"; ETS, Environmental Tobacco Smoking; EURAD, European Air Pollution Dispersion; FPG, Fasting Plasma Glucose; HDL, High-Density Lipoprotein; HNR, Heinz Nixdorf Recall; IDF, International Diabetes Federation; IQR, Interquartile Range; LUR, Land Use Regression; MetS, Metabolic Syndrome; NO_2, Nitrogen Dioxide; OR, Odds Ratio; PM, Particulate Matter (size-fractioned PM_{10}, $PM_{2.5}$, PM_{coarse}, $PM_{2.5}$abs); RR, Relative Risk; SES, Socioeconomic Status; TG, Triglycerides; T2D, Type 2 Diabetes Mellitus; t_0, Baseline Examination; t_1, First Follow-up Examination; T/Wk, Times per Week; WC, Waist Circumference; WHO, World Health Organization; Yrs, Years

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concurrent abnormal body measurements and laboratory tests that are hypothesized to result from a common underlying pathological mechanism, including elevated fasting plasma glucose, abdominal obesity, high total cholesterol, and high blood pressure (BP) (IDF, 2006; Kaur, 2014). Modifiable risk factors for MetS are insulin resistance, central obesity, a proinflammatory state, physical inactivity, and hormonal changes (IDF, 2006). Environmental exposures, such as air pollution (AP), have rarely been investigated as potential risk factors to develop MetS, although AP has been shown to have a wide range of acute and chronic health impacts related to MetS (Thurston et al., 2017). Most studies have focused on the association between AP and cardiopulmonary morbidity and mortality (Brook et al., 2010; Pope III and Dockery, 2006), while recent studies have also suggested that exposure to major air pollutants (e.g. particulate matter (PM_{10} and $PM_{2.5}$) and nitrogen dioxide (NO_2)) may increase the risk of T2D (Eze et al., 2014; Rao et al., 2015; Thiering and Heinrich, 2015; Wang et al., 2014; Weinmayr et al., 2015; Yan and Wang, 2014). Furthermore, two studies have observed that persons with MetS may be particularly vulnerable to the effects of AP (Chen and Schwartz, 2008; Park et al., 2010). Epidemiological studies have also observed associations between AP and specific components of MetS, such as obesity and insulin resistance (Li et al., 2016; Wolf et al., 2016; Brook et al., 2015; Thiering et al., 2013). However, to our knowledge only two epidemiological studies have looked at AP exposure and MetS as an outcome itself. (Eze et al., 2015; Wallwork et al., 2016). Both studies looked at long-term AP, one in a cross-sectional and one in a longitudinal design, and observed a positive association between AP and MetS.

The aim of this study was to investigate whether long-term exposure of AP (airborne particulate matter and NO_2) at a person's residence increases the chance to have or to develop MetS (prevalence and incidence), using data from the baseline (t_0) and first follow-up (t_1) examinations of the Heinz Nixdorf Recall (HNR) cohort study in Germany.

2. Materials and methods

2.1. Study design

This study was conducted using data from the baseline (t_0:2000–2003) and first follow-up (t_1:2006–2008) examinations of the Heinz Nixdorf Recall (risk factors, evaluation of coronary calcium and lifestyle) study, an ongoing prospective population-based cohort study located in three adjacent cities (Bochum, Essen, and Mülheim) within the highly urbanized German Ruhr Area. The rationale and design of the cohort study have been described in detail in another paper (Schmermund et al., 2002). In short, a sample of individuals aged 45–75 years were identified through a random selection process using local residency registries. In total, 4814 participants were enrolled into the HNR study between December 2000 and August 2003 (recruitment efficacy proportion: 55.8%), and 4157 participants returned for a follow-up examination between 2006 and 2008. Assessment at both examinations included a self-administered questionnaire, face-to-face interviews for personal risk factor assessment, clinical examinations, and comprehensive laboratory tests following standard protocols. Participants were also mailed yearly questionnaires. The study was approved by the institutional ethics committees of the University of Duisburg-Essen and the University Hospital of Essen and adhered to strict internal and external quality assurance protocols. All participants gave their written informed consent.

2.2. Environmental exposures

2.2.1. LUR exposure assessment

Exposure to PM_{10}, $PM_{2.5}$, PM_{coarse}, $PM_{2.5}$ absorbance ($PM_{2.5}$abs), and NO_2 was estimated with a Land Use Regression (LUR) model according to the European Study of Cohorts for Air Pollution Effects (ESCAPE) standardized procedure (ESCAPE-LUR) (Beelen et al., 2013; Eeftens et al., 2012). The ESCAPE-LUR is a linear prediction model developed after a standardized procedure, including annual mean air pollution concentrations as a dependent variable and geographic data on traffic, industry, and population density as potential predictors (independent variables). Predictor data were collected in a Geographical Information System (GIS), based on CORINE 2000 definitions (Keil et al., 2011). Particulate matter of varying aerodynamic diameter d (PM_{10} ($d \leq 10\,\mu m$), $PM_{2.5}$ ($d \leq 2.5\,\mu m$), PM_{coarse} ($2.5 \leq d \leq 10\,\mu m$)) and $PM_{2.5}$abs were measured at 20 sites (Harvard Impactors) (Eeftens et al., 2012). In addition to the commonly used size fractions PM_{10} and $PM_{2.5}$, PM_{coarse} is the size fraction that represents specifically larger particles that come from earth crustal material or resuspension of dust, while $PM_{2.5}$abs is a measure representing the blackness of the $PM_{2.5}$ exposed filter and serving as a marker for soot and black carbon (Eeftens et al., 2012). Concentration of NO_2 was measured at 40 sites with Ogawa passive samplers. Assuming a temporally stable spatial distribution for air pollution concentrations, annual air pollution concentrations were based on a measurement campaign in the study area, including three periods of a 14-day measurement to cover all seasons (cold, warm, and one intermediate temperature season) from October 2008 until October 2009 (Beelen et al., 2013; Eeftens et al., 2012;). Measurements were conducted at 20–40 monitoring sites, which were placed at designated “high traffic” or “background” air pollution locations, for PM-fractions (at 20 sites) and NO_2 (at 40 sites). One additional background reference site was chosen to measure PM and NO_2 continuously during a complete year (starting in October 2008) in order to generate a long-term annual average from all discontinuous site-specific measurements. For each air pollutant, a separate LUR model was developed and validated to estimate point-specific AP concentration (Beelen et al., 2013; Eeftens et al., 2012). The model for $PM_{2.5}$ included heavy traffic load, industry, population density and the x-coordinate of the participant's baseline address with an explained variance of $R^2 = 0.85$. The model for PM_{10} included heavy traffic and population density ($R^2 = 0.66$), while the model for NO_2 included industry, population density, inland or seaport and traffic load ($R^2 = 0.88$). The leave-one-out cross-validation R^2 values were 0.74, 0.59 and 0.82, respectively (Hennig et al., 2016).

2.2.2. CTM-based exposure assessment

In addition to AP concentrations based on the point-specific LUR-Model, we repeated the analysis in sensitivity analysis with the European Air Pollution Dispersion and Chemistry Transport Model (EURAD-CTM), which represents urban background air-pollution on a grid of $1\,km^2$ (Memmesheimer et al., 2004). The EURAD-CTM uses input data from official emission inventories from different sources (e.g. transport, industry) to estimate PM_{10}, $PM_{2.5}$, and NO_2 concentrations on a spatial resolution of $1\,km^2$ grid cells. The particulate matter sizes are defined by aerodynamic diameter as in the ESCAPE-LUR model. The EURAD-CTM daily output is calibrated on a daily basis against the measured values from all monitoring stations in the study area for PM_{10} and NO_2. Therefore, correlations of the EURAD-CTM long-term values for PM_{10} and NO_2 with the measured values are > 0.9. Each participant of HNR was assigned the daily mean PM and NO_2 concentrations of the $1\,km^2$ grid cell corresponding to his/her given residential address (Hennig et al., 2016; Nonnemacher et al., 2014). From these daily values, concentrations for longer exposure periods were calculated. For this study, mean exposure concentrations for the years 2001–2003 were used. Air pollution in the Ruhr Area is mainly influenced by traffic, heavy industry and energy production (coal), agriculture, and domestic heating. Similar to in other European countries, the fraction of $PM_{2.5}$ ranges between 60 and 70% of PM_{10} (Beelen et al., 2013). In the EURAD-CTM, the fraction of $PM_{2.5}$ is approximately 80%. This results in part from the fact that the PM_{10} model output is assimilated (data fusion) with the measured PM_{10} concentrations from the monitoring stations, whereas the $PM_{2.5}$ values are not. $PM_{2.5}$ was not measured on a regular basis because of lacking regulations and therefore no data for assimilation is available for the time period under consideration.