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Association of short-term exposure to fine particulate matter and nitrogen dioxide with acute cardiovascular effects

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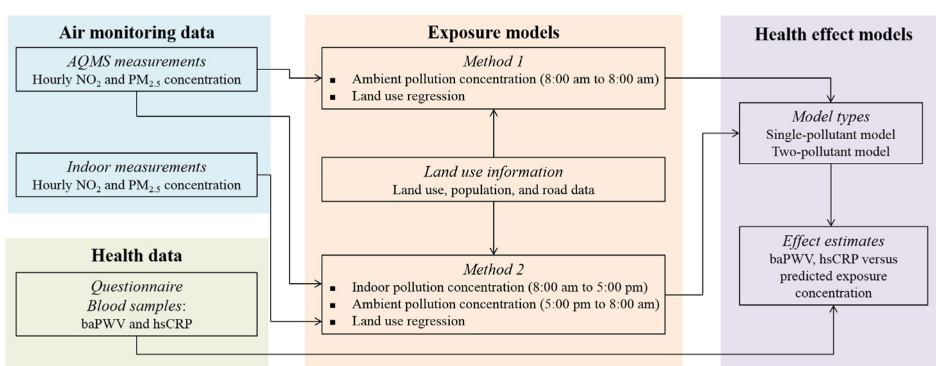
HIGHLIGHTS

- Acute cardiovascular effects from exposures to $PM_{2.5}$ and NO_2 were investigated.
- Exposures were estimated from land use regression models and indoor measurements.
- Arterial stiffness was positively associated with $PM_{2.5}$ exposures.
- Inflammation was positively associated with NO_2 exposures.
- Arterial stiffness might be more sensitive to $PM_{2.5}$ exposure than is inflammation.

GRAPHICAL ABSTRACT



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ABSTRACT

This study evaluated whether exposure to fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) is associated with cardiovascular effects by examining a panel of 89 healthy subjects in Taipei, Taiwan. The subjects received two health examinations approximately 8 months apart in 2013. Brachial–ankle pulse wave velocity (baPWV), a physiological indicator of arterial stiffness, and high-sensitivity C-reactive protein (hsCRP), a biomarker of vascular inflammations, were measured during each examination. Two exposure assessment methods were used for estimating the subjects' exposure to $PM_{2.5}$ and NO_2. The first method involved constructing daily land use regression (LUR) models according to measurements collected at ambient air quality

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monitoring stations. The second method required combining the LUR estimates with indoor monitoring data at the workplace of the subjects. Linear mixed models were used to examine the association between the exposure estimates and health outcomes. The results showed that a 10-μg/m^3 increase in $PM_{2.5}$ concentration at a 1-day lag was associated with 2.1% (95% confidence interval: 0.7%–3.6%) and 2.4% (0.8%–4.0%) increases in baPWV based on the two exposure assessment methods, whereas no significant association was observed for NO_2. The significant effects of $PM_{2.5}$ remained in the two-pollutant models. By contrast, NO_2, but not $PM_{2.5}$, was significantly associated with increased hsCRP levels (16.0%–37.3% in single-pollutant models and 26.4%–44.6% in two-pollutant models, per 10-ppb increase in NO_2). In conclusion, arterial stiffness might be more sensitive to short-term $PM_{2.5}$ exposure than is inflammation.

1. Introduction

Previous epidemiological studies have identified associations between air pollution and cardiovascular mortality and morbidity, particularly for traffic-related air pollutants (Gan et al., 2012; Chen et al., 2013; Franklin et al., 2015). Nitrogen dioxide (NO_2) and particulate matter with aerodynamic diameter smaller than 2.5 μm ($PM_{2.5}$) were found to be associated with cardiovascular diseases (Barnett et al., 2006; Tsai et al., 2010; Raaschou-Nielsen et al., 2012). In previous epidemiological studies, the exposure of study subjects has usually been determined according to monitoring data collected at one or few air quality monitoring stations (AQMSs) (Katsouyanni et al., 1995; Peel et al., 2005; Chuang et al., 2007). However, this approach may lead to exposure misclassification and potentially biased health risk results (Wilson et al., 2005).

To overcome these limitations, recent studies have used various geostatistical models and obtained improved exposure estimates (Jerrett et al., 2005). A well-accepted technique is land use regression (LUR) modeling, which was developed on the basis of air monitoring data collected at multiple locations and incorporated predictor variables obtained through the geographic information system (GIS) (Hoek et al., 2008). Although LUR models have been used to study individual-level exposure, these generally have been applied to investigate chronic effects (e.g., Eeftens et al., 2012; Adam et al., 2015; Wolf et al., 2015). The relationship between short-term exposure predicted using LUR models and health outcomes has rarely been discussed (Johnson et al., 2013), particularly on acute cardiovascular effects. To evaluate acute effects, personal monitoring provides accurate exposure estimates. However, the required resources may increase substantially when having a large study population.

This study evaluated the association of exposure to $PM_{2.5}$ and NO_2 with cardiovascular effects. LUR models were used to predict exposure to air pollutants. We further combined indoor measurements with LUR predictions to improve individual exposure estimates.

2. Materials and methods

2.1. Study design

This was a prospective panel study examining the acute cardiovascular effects of short-term exposure to $PM_{2.5}$ and NO_2. The subjects were healthy adults working at a bank in the metropolitan area of Taipei, Taiwan. In total, 117 adults received two health examinations approximately 8 months apart at the workplace. The examinations included a general medical examination and cardiovascular screening.

Ambient concentrations of traffic-related air pollutants ($PM_{2.5}$ and NO_2) were measured at multiple AQMSs within the Taipei metropolitan area. The daily concentration measurements of these two air pollutants were used to develop the LUR models. The corresponding indoor concentrations at the workplace were also monitored during the study period. Predictions from these LUR models along with the indoor monitoring data were compared with the subjects' health data to investigate whether $PM_{2.5}$ and NO_2 were associated with cardiovascular endpoints.

2.2. Study area

Greater Taipei, including Taipei City and New Taipei City, is a basin located in Northern Taiwan. It is a hub of major commercial and residential areas with busy freeway and road networks. The study area, monitoring station locations, and subjects' homes are presented in Fig. S1 in the Supplementary information.

2.3. Health data collection

The first and follow-up health examination sessions were conducted during February 20–26 and September 13–18, 2013, respectively, with 14–22 subjects scheduled to undergo examination in a quiet meeting room within the bank each day. Data regarding lifestyle and medical history were obtained using questionnaires. The health examinations included measurement of weight, height, and waist, along with blood sampling and cardiovascular screening. Blood samples were taken and analyzed for high-sensitivity C-reactive protein (hsCRP) levels by using a chemiluminescent enzyme immunometric assay (IMMULITE hsCRP; Diagnostic Products Corp., CA, USA), and total cholesterol (T-CHO) levels were also recorded. Cardiovascular screening was performed by monitoring brachial–ankle pulse wave velocity (baPWV; VP1000 Plus; Omron Colin, Japan). The research protocols and consent forms were approved by the Institutional Review Board of National Taiwan University Hospital.

2.4. Pollutant measurement

The ambient $PM_{2.5}$ and NO_2 concentrations within the study area were measured at AQMSs (n = 18 and 25, respectively) by governmental agencies (Fig. S1, Supplementary information). Hourly measurements were used to calculate the daily averages. For indoor measurements, the sampling site was located within the workplace in a finance building in Taipei City. Continuous hourly $PM_{2.5}$ and NO_2 concentrations were measured by the research team during the two health examination sessions. $PM_{2.5}$ concentrations were measured using a personal dust monitor (DUST-check portable dust monitor, model 1.108; Grimm Labortechnik Ltd., Ainring, Germany). NO_2 concentrations were measured using the chemiluminescence method (API-200A analyzer, Teledyne Technologies Inc., San Diego, USA).

2.5. LUR predictor variables

We included land use, population, and road data as potential predictors in the LUR models, similar to our previous study (Ho et al., 2015). The land use data were as follows: the surface area of high-density residential land, low-density residential land, industry, port, urban green space and semi-nature. Land use and population data were obtained from the National Land Survey and Mapping Center of Taiwan and the Ministry of the Interior, respectively. The buffer sizes of these variables were 100, 300, 500, and 1000 m. Road data were obtained from the Institute of Traffic and Transportation, Ministry of Transportation and Communications. The lengths of all roads, lengths of major roads,