



## Fine particulate air pollution and hospital admissions and readmissions for acute myocardial infarction in 26 Chinese cities



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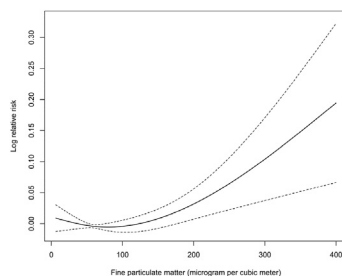
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### HIGHLIGHTS

- It is the first multicity study in China about the effect of PM<sub>2.5</sub> on AMI morbidity.
- Exposure to PM<sub>2.5</sub> increases risk of STEMI but not NSTEMI.
- AMI survivors are more sensitive to the effects of particulate air pollution.

### GRAPHICAL ABSTRACT



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### ABSTRACT

Monitoring data on fine particulate matter (PM<sub>2.5</sub>) level in China's major cities were available since 2013. We conducted a time-stratified case-crossover study to evaluate the association between short-term exposure to PM<sub>2.5</sub> and hospital admissions for acute myocardial infarction (AMI), as well as subsequent cardiac and AMI readmissions among AMI survivors. Hospital admissions for ST-elevation myocardial infarction (STEMI) and non ST-elevation myocardial infarction (NSTEMI) from 1 January 2014 through 31 December 2015 were identified from electronic Hospitalization Summary Reports. Conditional logistic regression was used to explore the relation between PM<sub>2.5</sub> and hospital admissions for AMI. Individuals discharged alive following STEMI in 2014 were followed up for subsequent readmissions through 31 December 2015. We used the Cox proportional hazards model to evaluate the effect of PM<sub>2.5</sub> pollution on subsequent cardiac and STEMI readmissions. Hospital admissions for STEMI (n = 106,467) and NSTEMI (n = 12,719) were examined separately. Exposure to an interquartile range (IQR) increase in PM<sub>2.5</sub> concentration (47.5 µg/m<sup>3</sup>) at lags 2, 3, 4 and 0–5 days corresponded with 0.6% (95% CI, 0.1%–1.1%), 0.8 (95% CI, 0.3%–1.3%), 0.6% (95% CI, 0.1%–1.1%) and 0.9% (95% CI, 0–1.8%) increases in STEMI admissions, respectively. For NSTEMI, no significant association was observed with PM<sub>2.5</sub>. We also observed significant associations of PM<sub>2.5</sub> concentration with both subsequent cardiac and STEMI readmissions among STEMI survivors. In conclusion, short-term elevations in PM<sub>2.5</sub> concentration may increase the risk of STEMI but not NSTEMI, and the association appeared to be more evident among STEMI survivors.

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## 1. Introduction

Acute myocardial infarction (AMI), one type of ischemic heart disease (IHD), is a major cause of death and adult disability worldwide ((Global et al., 2015)). A mounting body of evidence indicates that exposure to air pollution is closely associated with increased risk of cardiovascular mortality and morbidity (Peters et al., 2001; Barnett et al., 2006; Zanobetti et al., 2009). Air pollution is a complex mixture consisting of both suspended particulates and gaseous pollutants. The strongest evidence supporting such association comes from studies of fine particulate matter (PM<sub>2.5</sub>, PM with aerodynamic diameter  $\leq 2.5 \mu\text{m}$ ). Epidemiological and laboratory studies have indicated that PM<sub>2.5</sub> may be especially hazardous to human health, because it can be deposited more deeply in the lungs and carry higher concentrations of adsorbed or condensed toxic air pollutants per unit mass, owing to its greater surface area (Pope and Dockery, 2006). A meta-analysis that combined estimates from 13 studies demonstrated a close, quantitative association between PM<sub>2.5</sub> exposure and increases in mortality or hospital admissions due to myocardial infarction (Mustafic et al., 2012). However, all these 13 studies were conducted in developed countries. Because of considerable differences in PM<sub>2.5</sub> concentrations, characteristics of PM<sub>2.5</sub> and population susceptibility, there is still a need to assess the health effects of PM<sub>2.5</sub> on AMI in developing countries. Moreover, few studies have explored whether the acute effects of PM<sub>2.5</sub> differed across strata defined by AMI etiology (ST-elevation myocardial infarction: STEMI vs. non ST-elevation myocardial infarction: NSTEMI).

Recurrent AMI is associated with higher risk of complications, lower survival, and poorer quality of life relative to the initial AMI (Shotan et al., 2011). Despite best efforts at secondary prevention, the incidence rate of recurrent AMI remains high, accounting for ~20% of hospitalized patients with AMI (Mozaffarian et al., 2016). Studies have indicated that individuals with a history of cardiopulmonary conditions (Bateson and Schwartz, 2004). However, only a few studies have evaluated the effects of PM pollution on the risk of recurrent AMI, and their findings have been inconsistent (von Klot et al., 2005; Zanobetti and Schwartz, 2007; Koton et al., 2013). Not surprisingly, all studies to date have been conducted in developed countries, where air pollution was mild.

In this study, we evaluated the short-term effects of PM<sub>2.5</sub> on hospital admissions for AMI. We also investigated whether PM<sub>2.5</sub> was associated with subsequent cardiac and AMI readmissions of individuals discharged alive following AMI.

## 2. Materials and methods

### 2.1. Study population

The health data used in the present study were from electronic Hospitalization Summary Reports (HSRs) in top-ranked hospitals for care safety and quality as evaluated by the National Hospital Performance Evaluation Project in the National Healthcare Data Center. The hospital hierarchical management approach considers several aspects, including hospital infrastructure, medical service and management, technical level and efficiency, and quality and safety of clinical care. The HSR records data on basic demographics (e.g., sex and age), admission and discharge dates, hospitalization and discharge diagnoses (in Chinese) and their corresponding International Classification of Diseases, 10th Revision (ICD-10) codes (1 principle diagnosis and 10 accompanying diagnoses), treatments (mainly surgical information), discharge status (survival status, drug allergy, and hospitalization infection), and hospitalization costs.

We identified hospital admissions for STEMI (ICD-10 codes

I21.0–I21.3) and NSTEMI (ICD-10 code I21.4) from 1 January 2014 through 31 December 2015 based on the primary discharge diagnosis using ICD-10 codes. We also used the corresponding Chinese diagnoses to check the identified hospitalizations in order to reduce the influence of coding inaccuracy. In total, we identified 106,467 and 12,719 eligible hospital admissions for STEMI and NSTEMI, respectively, from 26 large cities across China. The 26 cities include all the four municipalities, 21 of 28 provincial capital cities, and Dalian city, as shown in Fig. S1 in the online supplement.

To evaluate the effects of PM<sub>2.5</sub> pollution on patients with STEMI, those discharged alive following STEMI between 1 January 2014 and 31 December 2014 were followed up for subsequent cardiac and STEMI readmissions through 31 December 2015.

### 2.2. Air pollution and meteorological data

Data on air pollution, including levels of PM<sub>2.5</sub>, carbon monoxide (CO), nitrogen dioxide (NO<sub>2</sub>), and sulfur dioxide (SO<sub>2</sub>) from 1 January 2014 through 31 December 2015, were obtained from the National Air Pollution Monitoring System, which is run by the Ministry of Environmental Protection. There are 4–15 fixed-site ambient air-monitoring stations in each city. To fulfill the quality assurance and quality control programs mandated by the Chinese government, each air-monitoring station must provide hourly air pollution data to the China National Air Pollution Monitoring System. For each city, the daily (24-h) mean concentrations for air pollutants were averaged from the available monitoring data across various stations. To allow the adjustment for weather conditions, daily meteorological data on temperature (°C) and relative humidity (%) for each city were obtained from the Chinese Meteorological Bureau.

### 2.3. Study design

We performed pooled analyses, for which observations for all cities were combined. Each city has a special indicator in the dataset. A time-stratified case-crossover study design was used to examine the association between ambient PM<sub>2.5</sub> concentrations and hospital admissions for AMI (Janes et al., 2005). The case-crossover design has been used as an alternative to time-series analysis (Fung et al., 2003; Lu and Zeger, 2007). In this design, cases serve as their own controls by using exposure on the days before or after the case day in the same city. For each case of AMI, ambient PM<sub>2.5</sub> exposure on the day of admission was compared to exposure up to four referent days that occurred on the same day of the week and in the same month and year. This approach allowed for controlling the influence of seasonal and long-term trends, day of the week, and slowly varying, individual-level risk factors (e.g., sex, genetics, and smoking status) (Janes et al., 2005; Carracedo-Martinez et al., 2010).

### 2.4. Statistical analysis

#### 2.4.1. PM<sub>2.5</sub> and AMI admissions

Spearman correlation tests were used to examine associations between air pollutants and meteorological variables. Conditional logistic regression was used to estimate associations between PM<sub>2.5</sub> concentrations and hospital admissions for AMI. To control the delayed and non-linear effects of temperature, we used the distributed lag non-linear models with three degrees of freedom in the natural cubic splines and 1-day lag (Krall et al., 2013). For adjustment of the spatial variations in the effects of meteorology, interactions between meteorology and cities were included in the model. We incorporated public holiday as a binary variable in the model to control for different baseline hospital visits for each day.

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