The effect of air pollution on hospitalization of individuals with respiratory and cardiovascular diseases in Jinan, China

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Abstract
To analyze the short-term effects of air pollution on the hospitalization rates of individuals with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), stroke, and myocardial infarction (MI) after adjusting for confounding factors including weather, day of the week, holidays, and long-term trends in Jinan, China.

Hospitalization information was extracted based on data from the primary class 3-A hospitals in Jinan from 2013 to 2015. The concentrations of PM$_{2.5}$, PM$_{10}$, SO$_2$, NO$_2$, and O$_3$ were obtained from Jinan Environment Monitoring Center. The relative risk and 95% confidence intervals of AECOPD, stroke, and MI were estimated using generalized additive models with quasi-Poisson distribution in the mgcv package, using R software, version 1.0.136.

The incremental increased concentrations of particulate pollutants including PM$_{2.5}$ and PM$_{10}$ were significantly associated with increased risk of hospitalization of AECOPD, stroke, and MI, and the adverse influences of PM$_{2.5}$ on these diseases were generally stronger than that of PM$_{10}$. The incremental increased concentrations of gaseous pollutants including SO$_2$, NO$_2$, and O$_3$ were significantly associated with increased risk of hospitalization of stroke and MI in this population.

Air pollution has significant adverse effects on hospitalization rates of individuals with AECOPD, stroke, and MI in Jinan, China.

Abbreviations: AECOPD = acute exacerbation of chronic obstructive pulmonary disease, CI = confidence interval, MI = myocardial infarction, NO$_2$ = nitrogen dioxide, O$_3$ = Ozone, RR = relative risk, SO$_2$ = sulfur dioxide.

Keywords: acute exacerbation of chronic obstructive pulmonary disease, ambient pollutants, generalized additive model, myocardial infarction, stroke

1. Introduction
Accumulating evidence suggests that air pollution is a primary risk factor for hospitalization of individuals with respiratory and cardiovascular diseases in the general population.

Moreover, to the best of our knowledge, none of the previous studies have fully explored the associations of ambient pollutants and hospitalization rates of these diseases in developing countries like China. Previous studies have focused on developed countries such as in Europe and North America.

However, for developing countries like China, research has been inconsistent, probably due to the limited sample sizes of the studies. Moreover, to the best of our knowledge, none of the previous studies have fully explored the associations of ambient pollutants and hospitalization rates of these diseases in developing countries like China.

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Medicine (2019) 98:22(e15634)

Received: 15 October 2018 / Received in final form: 29 March 2019 / Accepted: 18 April 2019

http://dx.doi.org/10.1097/MD.0000000000015634
studies simultaneously evaluated the influence of ground-level ambient pollutants on the hospitalization rate of AECOPD, stroke, and MI. Therefore, large epidemiologic studies are needed to determine the effects of ground-level ambient pollutants on hospitalization rates of individuals with AECOPD, stroke, and MI in China.

Jinan, the capital city of Shandong Province in China, has been reported to be one of the most polluted cities in China in recent years. Overall, Jinan is a northern inland city with complex natural terrain and poor airflow and ventilation, which ranks it among the top 10 cities with the worst air quality in China. The characteristic terrain in Jinan includes higher elevations in the southern area and lower elevations in the northern area, surrounded by mountains that hinder the management and diffusion of ambient pollutants. Accordingly, the objective of this study is to explore the association between the air pollution and hospitalization rates of individuals with AECOPD, stroke, and MI in Jinan from 2013 to 2015. Results of our study are expected to clarify the influence of ground-level ambient pollutants on hospitalizations attributed to acute respiratory and cardiovascular diseases in China, and to provide pertinent advice and guidance for the prevention of acute respiratory and cardiovascular diseases.

2. Materials

2.1. Study population

Information on 6981 AECOPD, 56,922 stroke, and 11,583 MI patients, including age, gender, date of admission, date of discharge, clinical symptoms, disease classification, workplace, and current residence, were obtained from Jinan Qilu Hospital, the Provincial Hospital of Shandong Province, and the Central Hospital of Shandong Province database, respectively. Patients who did not reside or work in Jinan were excluded from the present study. According to epidemiological studies about AECOPD, stroke, and MI in China,[8–10] patients who met the following criteria were included:

(1) ≥18 years of age;
(2) resided and worked in the study area (Jinan City) during study period.

The exclusion criteria were as follows:

(1) <18 years old;
(2) not residing and working in Jinan during the study period;
(3) patients with duplicate records;
(4) more than 1 patient admission per week.

The study was approved by the ethic committees of the 3 hospitals.

2.2. Data source

Data reflecting the daily average concentrations of fine particles (PM_{2.5}), inhalable particles (PM_{10}), sulfur dioxide (SO_{2}), nitrogen dioxide (NO_{2}) for 24-hours, and Ozone (O_{3}) for 8-hours, acquired from the 14 fix-sited monitoring stations in urban areas of Jinan, during 2013 to 2015 were obtained from Jinan Environment Monitoring Center. The expectation-maximization method was used to impute missing data. Daily average air temperatures and relative humidity in the corresponding period were obtained from the Jinan Bureau of Meteorology.

2.3. Methods

The generalized additive model with the link function of Poisson distribution was established to assess the impact of air pollution on the hospitalization rates of individuals with AECOPD, stroke, and MI. Because of the application of link function of Poisson distribution and the emergence of extreme values in the data, the quasi-Poisson regression model was applied to reduce the influence of over-dispersion of the results.[11] Confounding factors such as day of the week, holidays, and long-term trends were included as dummy variables and subsequently adjusted.

2.4. Degree of freedom of basic model

The basic models of AECOPD, stroke, and MI were as follows:

For AECOPD:

\[ \log(\hat{E}(Y_t)) = \alpha + \beta_1C_t + \text{ns}(\text{Temperature}, \text{df}=3) + \text{ns}(\text{Humidity}, \text{df}=5) + \text{ns}(\text{Time}, \text{df}=6*3) + \beta_2 \text{factor (DOW)} + \beta_3 \text{factor (Holiday)} \]

For stroke:

\[ \log(\hat{E}(Y_t)) = \alpha + \beta_1C_t + \text{ns}(\text{Temperature}, \text{df}=4) + \text{ns}(\text{Humidity}, \text{df}=6) + \text{ns}(\text{Time}, \text{df}=7*3) + \beta_2 \text{factor (DOW)} + \beta_3 \text{factor (Holiday)} \]

For MI:

\[ \log(\hat{E}(Y_t)) = \alpha + \beta_1C_t + \text{ns}(\text{Temperature}, \text{df}=3) + \text{ns}(\text{Humidity}, \text{df}=6) + \text{ns}(\text{Time}, \text{df}=7*3) + \beta_2 \text{factor (DOW)} + \beta_3 \text{factor (Holiday)} \]

Y_{t} represents the number of hospitalized patients on t days; E(Y_t) represents the expected number of hospitalized patients on t days; \beta_1 represents the daily average concentration coefficient of pollutants on t days or lag t days; C_t represents the daily average concentration of pollutants on t days or lag t days; ns represents a natural spline smooth function; Time represents the long-term trend of the date; the dummy variables DOW and Holiday represent the effect of “day of the week” and the statutory holidays, respectively, and the \beta_2 and \beta_3 represent the coefficients of factor variables DOW and Holiday, respectively.

The basic model without pollutants was established, and the natural spline smooth function of time, daily temperature, and relative humidity were included to fit the nonlinear effects of the model. The degree of freedom for time, daily temperature, and relative humidity were determined according to the akaike information criterion.[12]

The single-pollutant composed of basic model and daily concentrations of major ambient pollutants were established to estimate the relative risk (RR) and 95% confidence interval for the associations between major ambient pollutants with an increment of 10 μg/m³ and the risk of hospitalizations of the above diseases. A P<.05 was considered statistically significant.

Lag structures (from lag 0 day to lag 7 day) were defined as lag 0 to lag 7, and the multi-day moving averages lag structures (from lag 0–1 day [average] to lag 0–7 day [average]) were defined as lag 01 to lag 07. The time lag and cumulative time lag effects of major ambient pollutants were included in the model.

The 2-pollutant models of pollutants and O_{3} with multi-day moving averages lag structures (from lag 0–1 day [average] to lag 0–7 day [average]) were established for sensitive analysis and to confirm model stability.

The stratification analyses of pollutants exposure based on gender (male or female) and age (<65 years and ≥65 years) were conducted to explore the influence of age and gender on the
Positive correlations were detected among PM2.5, PM10, SO2, and concentrations of air pollutants, temperature, and relative humidity. Table 3 shows the Spearman correlation coefficients among these pollutants and O3, temperature, and relative humidity. The strongest associations for PM2.5, PM10, and O3 were 94% (1.018–1.040), 2.0% (1.009–1.031), and 3.5% (1.031–1.039), respectively (Table 5). Stratified analysis based on gender and age showed the impact of concentrations of PM2.5, PM10, and O3 on the hospitalization risk of AECOPD was stronger for males compared to females and stronger for older participants (≥65 years) compared to younger participants (Fig. 2).

### 2.5. Spearman correlation analysis

Spearman correlation was applied to describe the correlation of daily concentrations of air pollutants, temperature, and relative humidity.

### 3. Results

#### 3.1. Distribution of ambient pollutants and weather data

The annual average concentrations of PM2.5, PM10, SO2, NO2, and O3 were 94 μg/m3, 188 μg/m3, 79 μg/m3, 57 μg/m3, and 104 μg/m3, respectively, during 2013 to 2015, which were 2.7, 2.7, 1.3, 1.4, and 0.7-fold greater than the Annual Secondary National Ambient Air Quality Standards (GB3095-2013). The distribution of daily data on ambient pollutants and weather parameters is shown in Table 1. The distribution of daily ambient pollutant concentrations and temperature is shown in Figure 1.

#### 3.2. Data description

Table 2 shows the demographic characteristic of patients with respiratory and cardiovascular diseases. A total of 6981 AECOPD hospitalizations (4920 males and 2061 females), and 56,922 stroke hospitalizations (36,516 males and 20,406 females), and 11,583 MI hospitalizations (8085 males and 3498 females), were obtained from the databases of the primary class 3-A hospitals in Jinan from 2013 to 2015. The percentage of patients aged <65 years was 44.4% (33,492/75,486), while that of patients aged ≥65 years was 55.6% (41,994/75,486).

#### 3.3. Spearman correlation analysis

Table 3 shows the Spearman correlation coefficients among daily concentrations of air pollutants, temperature, and relative humidity. Positive correlations were detected among PM2.5, PM10, SO2, and NO2, while there was a significant negative association between these pollutants and O3, temperature, and relative humidity. The Spearman correlations between PM2.5 and PM10 (r = 0.802), SO2 and NO2 (r = 0.783), PM2.5 and NO2 (r = 0.694), and O3 and temperature (r = 0.840) were statistically significant (P < .01).

#### 3.4. Daily hospitalizations: AECOPD, stroke, and MI

##### 3.4.1. AECOPD

The strongest associations for PM2.5, PM10, and O3 and the risk of AECOPD hospitalizations were observed on lag 3, lag 2, and lag 3 with an increment of 3.1% (1.017–1.044), 1.6% (1.070–1.025), and 2.8% (1.026–1.030), respectively (Table 4). For moving averages lag structures, the strongest associations for PM2.5, PM10, and O3 and the risk of AECOPD hospitalizations were observed in lag 0, lag 2, and lag 3 with an increment of 2.9% (1.018–1.040), 2.0% (1.009–1.031), and 3.5% (1.031–1.039), respectively (Table 5). Stratified analysis based on gender and age showed that the impact of concentrations of PM2.5, PM10, and O3 on the hospitalization risk of AECOPD was significantly stronger in patients <65 years of age compared to patients ≥65 years of age, while the impact of concentrations of SO2 and NO2 on stroke hospitalization was significantly stronger in patients ≥65 years of age compared to patients <65 years of age. Stratified analysis based on gender showed that the impact of concentrations of PM2.5, PM10, and SO2 on stroke hospitalization was significantly stronger in males, while the impact of concentrations of NO2 and O3 on stroke hospitalization was significantly stronger in females (Fig. 3).

##### 3.6. MI

The strongest associations between PM2.5 and PM10 and the risk of MI hospitalizations were both observed in lag 0 with an increment of 1.8% (1.009–1.028) and 4.7% (1.041–1.052), respectively. In addition, the strongest associations for SO2 and O3 and the risk of MI hospitalizations were both observed in lag 1...
with an increment of 4.8% (1.035–1.060) and 0.8% (1.007–1.009) (Table 8). For moving averages lag structures, the strongest associations for PM10, SO2, and O3 and the risk of MI hospitalizations were all observed in lag 01 with an increment of 0.3% (1.002–1.004), 3.7% (1.022–1.050), and 0.8% (1.006–1.010), respectively (Table 9).

Stratified analysis based on gender and age showed that the impact of concentrations of PM2.5, PM10, SO2, and O3 and MI hospitalizations in females was stronger compared to males, and stronger in older participants (≥65 years) compared to younger (<65 years) participants (Fig. 4).

3.7. Sensitive analysis

Sensitive analysis showed no significant changes in RR due to concentrations of airborne particulates for AECOPD, stroke, and MI hospitalizations after inclusion of O3 in multi-day moving averages lag structures, which indicated that the effect of the single-pollutant model was robust (Figs. 5–7).

4. Discussion

In this epidemiological study from Jinan, China, we found that air pollution has significant adverse effects on the hospitalization rates of individuals with AECOPD, stroke, and MI. These results

### Table 2

Demographic characteristics of patients with respiratory and cardiovascular diseases in Jinan, 2013–2015.

| Variable | AECOPD | Stroke | MI |
|----------|--------|--------|----|
| Total    | 6981   | 56922  | 11583 |
| Gender   |        |        |     |
| Male     | 4920   | 36516  | 8085 |
| Female   | 2061   | 20406  | 3498 |
| Age (X±S) |       |        |     |
| <65      | 58±6   | 55±8   | 54±8 |
| ≥65      | 77±7   | 76±8   | 75±7 |

AECOPD = acute exacerbation of chronic obstructive pulmonary disease, MI = myocardial infarction, S = standard deviation, X = mean value.
suggest that air pollution has become a major contributor to the incidence and exacerbation of acute respiratory and cardiovascular diseases in developing countries. These results highlight the importance of management of air pollution for the prevention of acute respiratory and cardiovascular diseases.

4.1. AECOPD

Our findings are consistent with previous reports. Xu et al included patients with respiratory disease who visited emergency hospitals in Beijing and showed that the severe adverse effect of PM$_{2.5}$ on the hospitalization of patients with AECOPD was the

Table 3

| Variable | PM$_{2.5}$ | PM$_{10}$ | SO$_2$ | NO$_2$ | O$_3$ | Temp | Hum |
|----------|------------|-----------|--------|--------|-------|------|-----|
| PM$_{2.5}$ | 1.000 | 0.802** | 0.554** | 0.649** | −0.222** | −0.207** | 0.216** |
| PM$_{10}$ | − | 1.000 | 0.638** | 0.694** | −0.253** | −0.288** | −0.104** |
| SO$_2$ | − | − | 1.000 | 0.783** | −0.495** | −0.598** | −0.223** |
| NO$_2$ | − | − | − | 1.000 | −0.555** | −0.580** | −0.062** |
| O$_3$ | − | − | − | − | 1.000 | 0.840** | −0.092** |
| Temp | − | − | − | − | − | 1.000 | 0.156 |
| Hum | − | − | − | − | − | − | 1.000 |

∗ P < .05.
** P < .01.

Table 4

| Variables | Lag 0 | Lag 1 | Lag 2 | Lag 3 |
|-----------|-------|-------|-------|-------|
| PM$_{2.5}$ | 0.989 | 0.986 | 1.025* | 1.031* |
| 95% CI | 0.973–1.005 | 0.971–1.001 | 1.011–1.039 | 1.017–1.044 |
| PM$_{10}$ | 0.994 | 0.996 | 1.016* | 0.996 |
| 95% CI | 0.987–1.001 | 0.983–1.008 | 1.070–1.025 | 0.997–0.998 |
| SO$_2$ | 1.018 | 0.987 | 0.988 | 0.984 |
| 95% CI | 0.997–1.039 | 0.966–1.008 | 0.965–1.011 | 0.959–1.009 |
| NO$_2$ | 0.981 | 0.973 | 1.020 | 0.980 |
| 95% CI | 0.940–1.022 | 0.932–1.014 | 0.998–1.042 | 0.937–1.023 |
| O$_3$ | 0.994 | 1.005 | 1.015* | 1.028* |
| 95% CI | 0.985–1.005 | 1.002–1.007 | 1.012–1.017 | 1.026–1.030 |

Table 5

| Variables | Lag 01 | Lag 02 | Lag 03 |
|-----------|--------|-------|-------|
| PM$_{2.5}$ | 0.982 | 1.023* | 1.029* |
| 95% CI | 0.961–1.003 | 1.010–1.036 | 1.018–1.040 |
| PM$_{10}$ | 0.994 | 1.020* | 0.993 |
| 95% CI | 0.978–1.010 | 1.000–1.031 | 0.985–1.001 |
| SO$_2$ | 0.993 | 0.986 | 0.975 |
| 95% CI | 0.962–1.004 | 0.958–1.014 | 0.935–1.015 |
| NO$_2$ | 0.970 | 0.975 | 0.962 |
| 95% CI | 0.958–0.982 | 0.952–1.017 | 0.911–1.013 |
| O$_3$ | 1.000 | 1.015* | 1.035* |
| 95% CI | 0.997–1.004 | 1.011–1.018 | 1.031–1.039 |

AECOPD = acute exacerbation of chronic obstructive pulmonary disease, CI = confidence interval, RR = relative risk.

* P < .05.
** P < .01.
cumulative lag 0 to 3 (Lag 03) day with an increment of 3.15% in the emergency hospital admission rate of AECOPD[13]. Ko et al also found significant associations between hospital admissions for COPD with PM2.5; the RR for admission for every 10 mg/m³ increase in PM2.5 was 1.031, at a lag day ranging from lag 0 to cumulative lag 0–5[14].

In our study, although no immediate effects were observed between PM2.5, PM10, O3, and hospitalizations of AECOPD, the effect on different lag days (lag 2, lag 3, lag 02, and lag 03) were statistically significant. As highly active oxidants with poor solubility, these airborne particulates can reach the depths of the lungs after being inhaled and subsequently cause inflammation of the epithelial cells of the respiratory tract. The certain reaction time of airway inflammation caused by oxidants could result in a cumulative effect, rather than an immediate effect[15] as previously indicated.

As a significant risk factor for AECOPD, SO2 dissolves easily in the upper respiratory tract and produces immediate stimulation to the mucosa[16,17]. However, the significant effects of SO2 on hospitalization risk in patients with AECOPD were not observed in this study. The annual average concentrations of SO2 in Jinan during 2013 to 2015 were 102 mg/m³, 79 mg/m³, and

| Variables | Lag 0 | Lag 1 | Lag 2 | Lag 3 |
|-----------|------|------|------|------|
| PM2.5     | 1.011* | 1.001* | 0.998 | 0.993 |
| RR        | 1.010–1.012 | 1.000–1.002 | 0.995–1.001 | 0.984–1.002 |
| 95% CI    | 1.005–1.007 | 1.000–1.002 | 0.999–1.003 | 0.991–1.001 |
| PM10      | 1.006* | 1.001* | 0.997 | 0.996 |
| RR        | 1.017–1.020 | 1.013–1.016 | 1.000–1.002 | 0.986–1.000 |
| 95% CI    | 1.023–1.027 | 1.000–1.004 | 0.971–1.001 | 0.968–1.000 |
| SO2       | 1.018* | 1.014* | 1.001 | 0.993 |
| RR        | 1.017–1.020 | 1.013–1.016 | 1.000–1.002 | 0.986–1.000 |
| 95% CI    | 1.001–1.003 | 1.004–1.006 | 1.001–1.003 | 0.993–1.001 |

CI = confidence interval, RR = relative risk.

*P < .05.

Figure 2. A stratified analysis of the effects of air pollutant concentrations at optimal lag on admission risk in patients with acute exacerbation of chronic obstructive pulmonary disease.
55 μg/m³, respectively, and the average annual concentration in 2015 was below the 2-level standard limit (60 μg/m³) of the national ambient air quality standard (GB 3095-2012) for the first time. The control of coal-fired volume and the improvement of technical treatment methods, such as desulphurization and denitrification, during the “13th 5-Year Plan” period in Jinan were highly effective.

The results of stratified analysis in gender and age showed that male patients aged ≥65 years were more sensitive to air pollutants and were at a consequently higher risk of hospitalization for AECOPD compared to women aged <65 years. It has been shown that the smoking rate is 74% among men aged >35 years in China. As China is one of the largest tobacco producing and consuming countries, the prevalence of chronic bronchitis among smokers is 2- to 8-fold higher than that of non-smokers. Meanwhile, the proportion of smoking in males has been significantly higher than that of females in underdeveloped and developing countries. Moreover, a previous report revealed that male patients with a history of smoking had a higher hospital admission risk and were more sensitive to varied concentrations of pollutants. Stratified analysis by age showed that patients ≥65 years of age were more sensitive to air pollutants exposure and had higher risk of hospital admission for AECOPD compared to patients <65 years of age. The weakness of the
immune system, the higher prevalence of chronic respiratory
diseases, and the increased sensitivities to the particles in the
elderly could be the underlying causes for the stronger association
between air pollution and risk of AECOPD hospitalization in
those older than 65 years of age.\(^{[19–21]}\)

### 4.2. Stroke

The strongest associations between particulate matter (PM\(_{2.5}\) and
PM\(_{10}\)) and hospitalizations of stroke were found on the day of
admission with an increment of 1.1% and 0.6%, respectively.
Our results were supplemented by experimental studies that
indicated that exposure to high concentrations of PM\(_{2.5}\) can lead
to pathophysiological changes related to the onset of cardiovas-
cular diseases, including increased blood pressure and heart rate,
reduced heart rate variability within 12 hours, changes in
coagulation factors, systemic inflammation, damaged endothelial
cells, and vascular dysfunction.\(^{[22]}\) Our study also showed that

#### Table 8

| Variables | Lag 0 | Lag 1 | Lag 2 | Lag 3 |
|-----------|-------|-------|-------|-------|
| PM\(_{2.5}\) | 1.018\(^*\) | 1.004 | 0.994 | 0.997 |
| RR 95% CI | 1.009–1.028 | 0.995–1.013 | 0.987–1.001 | 0.992–1.002 |
| PM\(_{10}\) | 1.047\(^*\) | 1.003 | 0.997 | 1.002 |
| RR 95% CI | 1.041–1.052 | 0.997–1.008 | 0.994–1.000 | 0.997–1.008 |
| SO\(_2\) | 0.999 | 1.048\(^*\) | 0.998 | 0.992 |
| RR 95% CI | 0.986–1.012 | 1.035–1.060 | 0.996–1.000 | 0.981–1.003 |
| NO\(_2\) | 0.988 | 0.988 | 0.981 | 0.989 |
| RR 95% CI | 0.968–1.008 | 0.976–1.000 | 0.960–1.002 | 0.977–1.001 |
| O\(_3\) | 1.002 | 1.008\(^*\) | 0.999 | 0.995 |
| RR 95% CI | 0.999–1.007 | 1.007–1.009 | 0.998–1.000 | 0.990–1.001 |

\(\text{CI} = \text{confidence interval}, \text{MI} = \text{myocardial infarction}, \text{RR} = \text{relative risk.}\)

\(\text{P}<.05.\)

#### Table 9

| Variables | Lag 0 | Lag 1 | Lag 2 | Lag 3 |
|-----------|-------|-------|-------|-------|
| PM\(_{2.5}\) | 0.998 | 0.997 | 0.996 | 0.996 |
| RR 95% CI | 0.996–1.000 | 0.993–1.001 | 0.991–1.001 | 0.991–1.001 |
| PM\(_{10}\) | 1.003\(^*\) | 1.001\(^*\) | 1.001\(^*\) | 1.001\(^*\) |
| RR 95% CI | 1.002–1.004 | 1.000–1.002 | 1.000–1.002 | 1.000–1.002 |
| SO\(_2\) | 1.037\(^*\) | 1.020\(^*\) | 0.998 | 0.998 |
| RR 95% CI | 1.022–1.050 | 1.003–1.040 | 0.996–1.000 | 0.996–1.000 |
| NO\(_2\) | 0.994 | 0.998 | 0.998 | 0.998 |
| RR 95% CI | 0.987–1.001 | 0.990–1.006 | 0.993–1.003 | 0.993–1.003 |
| O\(_3\) | 1.008\(^*\) | 1.005\(^*\) | 1.000 | 1.000 |
| RR 95% CI | 1.006–1.010 | 1.003–1.007 | 0.999–1.002 | 0.999–1.002 |

\(\text{CI} = \text{confidence interval}, \text{MI} = \text{myocardial infarction}, \text{RR} = \text{relative risk.}\)

\(\text{P}<.05.\)
pathophysiological effects and cause cerebral ischemia.\textsuperscript{[26]} Results of another meta-analysis also showed that hospitalization for ischemic stroke increased by 1.79\% (95\% CI = 1.0054–1.0306) with an incremental increase of SO\textsubscript{2}, which was in accordance with our findings.\textsuperscript{[20]} In addition, epidemiological studies from Denmark, Italy, Canada, and other countries consistently showed that variations in NO\textsubscript{2} concentration were significantly associated with the incidence of acute ischemic stroke.\textsuperscript{[27–29]} All of the above evidence supports a strong association between air pollution and the risk of stroke.

Moreover, we found that the association between SO\textsubscript{2} (RR = 1.018; 95\% CI = 1.017–1.020) and NO\textsubscript{2} (RR = 1.014; 95\% CI = 1.013–1.016) and stroke hospitalizations were stronger than the association between PM\textsubscript{2.5} and stroke admissions (RR = 1.011;...
95% CI = 1.010–1.012) and PM10 (RR = 1.006; 95% CI = 1.005–1.007). This finding is consistent with previous studies, which suggested that traffic pollution may cause ischemic stroke.\textsuperscript{[30–32]}

While the potential reasons for this association remains unclear, we hypothesize that gaseous pollutants exhausted from traffic in Jinan may have become one of the main sources of air pollutants. Stratified analysis by age showed that stroke patients ≥65 years of age were more sensitive to gaseous pollutants (SO\textsubscript{2} and NO\textsubscript{2})
exposure and were at higher risk of stroke-related hospitalizations. Similar results were supported by a previous case-crossover study from Beijing, which also showed that the increased daily concentrations of SO2 and NO2 were associated with a more significant increased risk of stroke hospitalizations of patients ≥65 years of age. Compared with the younger participants, the elderly are more sensitive to air pollution and have higher incidences of cardiovascular and cerebrovascular diseases. These findings are also supported by previous studies that showed that recurrent attacks of stroke were more frequent in elderly patients.\textsuperscript{[34]} Stratiﬁed analysis by gender showed that female patients were more sensitive to gaseous pollutants (NO2 and O3) exposure, while male patients were more sensitive to particulate matter (PM\textsubscript{2.5} and PM\textsubscript{10}) exposure. Qin et al. collected admission data of stroke patients from 3 cities in northern China in a case-crossover study and found that the signiﬁcant association between air pollution and stroke hospitalization was only observed in females.\textsuperscript{[35]} Moreover, a study in Beijing demonstrated that the impacts of PM\textsubscript{2.5} on the ﬁrst admission due to ischemic stroke did not different by gender.\textsuperscript{[36]} In addition, a study from Shanghai showed that male stroke patients were more sensitive to changes in concentrations of PM\textsubscript{10}, SO\textsubscript{2}, and NO2 than female patients.\textsuperscript{[37]} In summary, the potential gender differences underlying the association between air pollution and stroke remain to be determined.

4.3. MI

According to the results of this study, SO\textsubscript{2} has the strongest adverse impact on the admission of individuals with MI (RR = 1.048; 95\% CI = 1.035–1.060), which is consistent with the result of a similar study performed in Shanghai Pudong District during 2013 to 2014.\textsuperscript{[37]} This study showed that the incidence of acute MI increased by 5\% with an incremental 10 \textmu g/m\textsuperscript{3} increase in SO\textsubscript{2}.\textsuperscript{[36]}

However, we failed to detect a signiﬁcant effect of NO2 on admission rate of MI. Compared to the 4-quartile range of other pollutants (PM\textsubscript{2.5} = 56 \textmu g/m\textsuperscript{3}, PM\textsubscript{10} = 98 \textmu g/m\textsuperscript{3}, SO\textsubscript{2} = 57 \textmu g/m\textsuperscript{3}, and O3 = 96 \textmu g/m\textsuperscript{3}), the quartile range of NO2 only reached 29 \textmu g/m\textsuperscript{3}. The small variance in daily average concentrations of NO2 in Jinan might be the potential reason for the insigniﬁcant association between NO\textsubscript{2} and admission rate of MI.

Most previous studies have shown that there is no signiﬁcant association between short-term exposure to O3 and morbidity and mortality of MI\textsuperscript{[13,14,38,39]} In contrast to previous studies performed in Western countries, our study demonstrated a 0.8\% increased risk of hospitalizations for MI per 10 \textmu g/m\textsuperscript{3} increase in O3 concentration on lag 1 and a 0.8\%, 0.5\% increment on lag 01 and lag 02, respectively. The relatively high concentrations of O3 in Jinan could be one of the potential reasons underlying the variations between our results and the previous ﬁndings.

Although the inhalable particles (PM\textsubscript{2.5} and PM\textsubscript{10}) and O3 exposure could induce inﬂammatory effects, the results of this study showed that the adverse effects of particulate matter (especially for PM\textsubscript{10} [RR = 1.047; 95\% CI = 1.041–1.052]) were stronger than that of O3 (RR = 1.008; 95\% CI = 1.007–1.009). This is consistent with the study conducted by Rosenthal et al., who showed that, compared to O3, PM\textsubscript{10} plays a greater role in thrombosis.\textsuperscript{[7]}

The results of the stratified analysis showed that female patients ≥65 years of age were more sensitive to air pollutants exposure and suffered a higher risk of MI admissions than males <65 years of age. As a vulnerable group, the elderly often have atherosclerotic plaques and other cardiovascular diseases and are therefore more susceptible to the risks of air pollution exposure. Exposure to short-term air pollution is an important trigger of cardiovascular diseases, probably due to its ability to increase plaque vulnerability, platelet activation, and coagulation.\textsuperscript{[11]} Some studies suggested that many factors may underlying the potential gender differences regarding the association between air pollution and MI, such secretion of hormones, the physical build, and the range of activities\textsuperscript{[36]} The exact mechanisms deserve further investigation.

The limitation of our study was that we did not include patients <18 years of age.

5. Conclusions

In conclusion, results of our study indicate that air pollution is signiﬁcantly associated with an increased risk of hospitalization of individuals with AECOPD, stroke, and MI in Jinan, China. Future studies are needed to determine the potential mechanisms involved and explore the potential importance of management of air pollution for the prevention of acute respiratory and cardiovascular diseases.

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