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RESEARCH ARTICLE

Short-term effects of ambient air pollutants and myocardial infarction in Changzhou, China

Yongquan Yu[1] · Shen Yao[1] · Huibin Dong[2] · Minghui Ji[1] · Zhiyong Chen[2] · Guiying Li[2] · Xingjuan Yao[2] · Shou-Lin Wang[1] · Zhan Zhang[3]

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Abstract

Ambient air pollution had been shown strongly associated with cardiovascular diseases. However, the association between air pollution and myocardial infarction (MI) is inconsistent. In the present study, we conducted a time-series study to investigate the association between air pollution and MI. Daily air pollutants, weather data, and MI data were collected from January 2015 to December 2016 in Changzhou, China. Generalized linear model (GLM) was used to assess the immediate effects of air pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3) on MI. We identified a total of 5545 cases for MI, and a 10-μg/m^3 increment in concentrations of $PM_{2.5}$ and PM_{10} was associated with respective increases of 1.636% (95% confidence interval [CI] 0.537–2.740%) and 0.805% (95% CI 0.037–1.574%) for daily MI with 2-day cumulative effects. The associations were more robust among males and in the warm season versus the cold one. No significant effect was found in SO_2, NO_2, or O_3. This study suggested that short-term exposure to $PM_{2.5}$ and PM_{10} was associated with the increased MI risks. Our results might be useful for the primary prevention of MI exacerbated by air pollutants.

Keywords Air pollution · Myocardial infarction · Time-series study · Generalized linear model · $PM_{2.5}$ · PM_{10}

Introduction

Ambient air pollution, a heterogeneous group of particulate matters (PMs) and gaseous pollutants, represents a modifiable threat to human health (Chen et al. 2012; Gurung and Bell 2013) and has aroused general concern of the academia recently. Numerous epidemiological studies have demonstrated that exposure to air pollutants may increase the mortality, hospital admissions, and emergency visits for patients with cardiovascular diseases (Argacha et al. 2016; Nuvolone et al. 2011; Zhang et al. 2016). In specific, PMs with aerodynamic diameters < 10 μm (PM_{10}) and < 2.5 ($PM_{2.5}$) have been linked to deleterious effects on cardiovascular health. Transient elevations of $PM_{2.5}$ and PM_{10} could increase the occurrence of ischemic heart disease hospital admissions, and moreover, increased cardiovascular mortality has also been associated with hourly peak $PM_{2.5}$ concentration (Lin et al. 2017; Sohn et al. 2016; Stockfelt et al. 2017; Weber et al. 2016).

Myocardial infarction (MI), an acute and severe cardiovascular event, can cause damage to the heart and induce heart failure (Krumholz and Normand 2008). It is the leading cause of morbidity and mortality in Chinese populations (Zhou et al. 2016). MI caused more than 1 million deaths annually; this number in China will increase to 23 million by 2030 (Li et al. 2015; Yang et al. 2013). Without immediate medical attention, MI may result in a poor prognosis with nearly 25% dying within minutes and 40% within the first month (Ibanez et al. 2015). Due to the limitation in therapeutic regimen and the fatal outcomes, identifying modifiable risk factors for MI and taking effective countermeasures is of critical public health problem (Thiele et al.

Yongquan Yu and Shen Yao contributed equally to this work.

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✉ Zhan Zhang
zhanzhang@njmu.edu.cn

[1] Department of Occupational Medicine and Environmental Health, School of Public Health, Nanjing Medical University, 101 Longmian Avenue, Nanjing, Jiangsu 211166, People's Republic of China

[2] Department of Chronic Disease Control and Prevention, Changzhou Center for Disease Control and Prevention, 203 Taishan Road, Changzhou, Jiangsu 213022, People's Republic of China

[3] Department of Hygiene Analysis and Detection, School of Public Health, Nanjing Medical University, 101 Longmian Avenue, Nanjing, Jiangsu 211166, People's Republic of China

2015). The previous studies indicated that diabetes, hypertension, obesity, smoking, high cholesterol levels, and physical inactivity contributed to MI (Mehta et al. 2015). Recently, MI was linked to air pollution (Roswall et al. 2017; Talbott et al. 2014). However, few studies, especially in China, have discussed the differences in the effects of the main air pollutants on MI risk.

With the rapid economic development that has occurred in the past years and as one of the most populous developing country, China is experiencing exacerbating air quality due to emissions from manufacturing industries, traffic, agriculture, and forest fires (Kan et al. 2009; Petaja et al. 2016; Rohde and Muller 2015). Changzhou is a prefecture-level city in southern Jiangsu province of China and locates on the southern bank of the Yangtze River. It is a part of the highly developed Yangtze Delta region of China extending from Shanghai going northwest, which now has more than 36 million inhabitants (Kerstens et al. 2009). The concentrations of $PM_{2.5}$ and PM_{10} in Changzhou were higher than the national ambient air quality standard (35 μg/m^3 for $PM_{2.5}$ and 50 μg/m^3 for PM_{10}) (Li et al. 2008). Thus, Changzhou was chosen to study the effect of air pollutants on MI.

In this study, we performed an epidemiological time-series design to estimate the effect of main air pollutants on MI in Changzhou, China. In addition, the association of possible modifiers, including meteorological factors, demographic characteristics between air pollutants and MI were also evaluated. This work will help provide insights into the relationship between MI and air pollutants, especially particulate matters and implications for prevention of MI in Changzhou, China.

Methods

Data collection

Air pollution data, including PM_{10}, $PM_{2.5}$, nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3), were obtained from the database of Changzhou Environmental Monitoring Center, from January 1, 2015 to December 31, 2016. This center established ten air quality monitoring stations in different administrative districts of Changzhou (Fig. 1). These stations are located away from major roads, industrial sources, buildings, or residential sources of emissions including coal, waste, or oil. Thus, the daily air pollution data collected from the monitoring stations can represent the background urban air pollution level. Furthermore, all the cases identified in this study resided less than 40 km from the nearest monitoring station, and it is appropriate to use the monitoring data to represent a good indicator of individual exposures (Dockery et al. 2005; Wellenius et al. 2012; Xie et al. 2015). Weather data regarding temperature (°C), wind speed (m/s), and relative humidity (%) were collected from Changzhou Meteorological Bureau and averaged daily.

Daily MI data from January 1, 2015 to December 31, 2016 were obtained from the database of Changzhou Center for Disease Control and Prevention (CDC), which is a part of Changzhou-controlled network reporting system for chronic diseases. The data in this study were recorded according to The International Classification of Diseases, Revision 10 (ICD-10) and further categorized into acute myocardial infarction (I21) and subsequent myocardial infarction (I22). Daily MI counts were also classified by gender and age group (< 65, 66–85, and > 85 years old). Demographic data were collected from Changzhou Municipal Bureau of Statistics.

Statistical analysis

Daily MI counts, air pollutants concentrations, and meteorological data were linked by date for the subsequent time-series design, which was applied to explore the effects of each air pollutant on MI. Spearman's correlation coefficient was used to determine the association between air pollutants and meteorological variables. To develop the basic model, the distribution pattern of daily MI numbers was investigated. Since the data followed a Poisson distribution, Poisson regression was applied in the generalized linear model (GLM) to analyze the effect of air pollutants on daily MI counts. To control the potential confounding effect, multivariable regression model was used, including the following: (1) a natural cubic smooth function of calendar time with three degrees of freedom (df) per year to exclude unmeasured long-term and seasonal trends; (2) natural smooth functions of the current day-to-day relative humidity (3 df) and average temperature (3 df) to control the weather confounding effects; (3) indicator variable was used for "day of the week (DOW)". In addition, data with different modifiers stratified by sex and season (warm season as 1 May to 31 October and cold season as 1 November to 30 April) were also tested to separately analyze the effect of air pollutants on MI.

Moreover, a single-pollutant model was performed to explore the air pollution's effects on MI with single-day lags (lag 0, 1, 2, 3, 4, 5, 6) and multiple-day lags (lag 0–1, 0–2, 0–3, 0–4, 0–5, 0–6). Two-pollutant model was developed to examine the stability of results. Smoothing function was applied to analyze the exposure-response relationship between the log-relative risk of daily MI numbers and air pollutant concentrations using a 0 df in single-pollutant model.

Statistical software R (version 3.2.3, R Foundation for Statistical Computing, Austria) was used for data analysis and result output. The baseline data were presented as mean ± standard deviation (SD) for continuous variables. All tests were two-sided, and $P < 0.05$ was considered as statistically significant.

Fig. 1 Locations of air quality monitoring stations and weather monitoring station in Changzhou, 2015–2016

Results

Descriptive analysis

Table 1 shows the basic demographic information of MI. There were 5545 MI cases recorded; of these, 63% were males and 81.1% were aged between 65 and 85. The daily average MI counts were 7.6 during study period (data not shown).

Table 2 reveals the summary statistics of daily air pollutants and weather conditions. The daily average concentrations for $PM_{2.5}$, PM_{10}, SO_2, NO_2, and O_3 were 52.4, 86.0, 22.6, 38.9, and 90.2 μg/m^3, respectively. The corresponding average concentrations of $PM_{2.5}$ and PM_{10} in Changzhou were 2.1 and 1.6 times higher than the national ambient air quality standard (35 μg/m^3 for $PM_{2.5}$ and 50 μg/m^3 for PM_{10}). The daily temperature, wind speed, and relative humidity were 17.0 °C, 2.2 m/s, and 75.0%, respectively.

Table 3 illustrates the Spearman correlation coefficients among the air pollutants and weather conditions. They were positively correlated among five air pollutants, except O_3. In addition, they were negatively correlated with temperature, wind speed, and humidity.

Estimated effects of air pollutants

Figure 2 summarizes the estimated changes in daily MI counts associated with a 10-μg/m^3 increase in air pollutant concentrations with different lag days in single-pollutant models. The cumulative effects of $PM_{2.5}$ and PM_{10} were more significantly associated with percent increment in MI numbers than single

Table 1 Demographic characteristics of daily MI counts (%) in Changzhou, 2015–2016

Variable	All year	Cold season	Warm season
Total	5545	2975 (53.7%)	2570 (46.3%)
Gender			
Male	3492 (63.0%)	1857 (53.7%)	1617 (46.3%)
Female	2053 (37.0%)	1100 (53.6%)	953 (46.4%)
Age (years)			
< 65	223 (4.0%)	113 (50.7%)	110 (49.3%)
65–85	4497 (81.1%)	2398 (53.3%)	2099 (46.7%)
> 85	825 (14.9%)	464 (56.2%)	361 (43.8%)

Table 2 Summary of daily weather conditions and air pollutants in Changzhou, 2015–2016

Variable	Mean ± SD	Min	Median	Max
Air pollution (μg/m^3)				
$PM_{2.5}$	52.4 ± 1.2	6.8	44.8	181.1
PM_{10}	86.0 ± 1.6	10.5	77.5	289.1
SO_2	22.6 ± 0.4	6.9	20.3	78.1
NO_2	38.9 ± 0.6	10.9	35.9	117.3
O_3	90.2 ± 1.6	10.6	79.9	252.2
Weather condition				
Temperature (°C)	17.0 ± 0.3	− 6.6	18.1	34.6
Wind speed (m/s)	2.2 ± 0.0	0.0	2.2	6.1
Relative humidity (%)	75.0 ± 0.5	35.0	76.0	100.0

day effects. And the highest association was identified for lag 0–1 (1.636%, 95%CI: 0.537–2.740%; 0.805%, 95%CI: 0.037–1.574%). Moreover, for lag 4, lag 0–5, lag 0–6, and lag 0–7, significantly negative associations were identified in 10-μg/m^3 increase of SO_2 and NO_2. And no significant association was observed regarding O_3 for any lag days. A 2-day moving average of the concentrations (lag 0–1 days) was used in the subsequent analysis.

Figure 3 illustrates the concentration-response relationships of MI counts with air pollutants. The smoothing function curves for $PM_{2.5}$ and PM_{10} were linear positive and flat at higher concentrations, whereas the curves for other pollutants were linear without statistic positive correlation.

Table 4 shows the estimated changes in daily MI counts associated with a 10-μg/m^3 increase in air pollutant concentrations modified by seasons (warm and cold period) and gender. The estimated effects of $PM_{2.5}$ and PM_{10} were more pronounced in the warm season (2.296%, 95%CI: 0.671–3.929%; 1.135%, 95%CI: 0.004–2.269%) than that in the cold season. In addition, the association of $PM_{2.5}$ and MI numbers in males (2.733%, 95%CI: 0.986–4.487%) was more pronounced than that in females and for PM_{10}, though not statistically significant, the percentage increase was much higher in males than in females. No significant association was noted for other pollutants modified by seasons and gender.

The two-pollutant models were performed for lag 0–1 (Fig. 4). The effect estimate of all five pollutants did not change a lot in two-pollutant model. However, $PM_{2.5}$ was dramatically robust when adjusted for PM10 and PM_{10} produced the lower effect estimates for MI after adjusting for $PM_{2.5}$ than single-pollutant model.

Discussion

Our results described the short-term effects of air pollutant exposure on MI in Changzhou, China. To the best of our knowledge, in China, studies regarding the differences in the effects of the main air pollutants on MI counts are typically deficient. By identifying 5545 cases of MI in Changzhou, this study performed a comprehensive investigation on the association of exposure to main air pollutants with MI risk. In the present study, daily MI counts were found to tightly coincide with the elevation of $PM_{2.5}$ and PM_{10} concentrations. Of note, the males had greater estimated MI risk than females and the effect of $PM_{2.5}$ and PM_{10} in cold season has been attenuated than that in warm season. Moreover, SO_2 and NO_2 were found to be cardiovascular protective at seven cumulative days lag models (lag 0–7) and O_3 levels showed no significant association with MI counts.

Exposure to $PM_{2.5}$ and PM_{10} could induce the cardiovascular dysfunction of humans (McGuinn et al. 2017). For instance, numbers of MI admissions were statistically associated with higher $PM_{2.5}$ levels in a case-crossover

Table 3 Spearman correlation between air pollutants and weather conditions in Changzhou, 2015–2016

Variable	Temperature (°C)	Wind speed (m/s)	Relative humidity (%)	$PM_{2.5}$	PM_{10}	SO_2	NO_2	O_3
Temperature (°C)	–	− 0.025	.086*	− .479**	− .391**	− .315**	− .363**	.512**
Wind speed (m/s)	–	–	− 0.062	− .300**	− .278**	− .258**	− .390**	− 0.04
Relative humidity (%)	–	–	–	− .127**	− .278**	− .462**	− .145**	− .440**
$PM_{2.5}$	–	–	–	–	.940**	.697**	.705**	− .124**
PM_{10}	–	–	–	–	–	.764**	.741**	− 0.005
SO_2	–	–	–	–	–	–	.799**	0.064
NO_2	–	–	–	–	–	–	–	− .166**
O_3	–	–	–	–	–	–	–	–

*$P < 0.5$, **$P < 0.01$

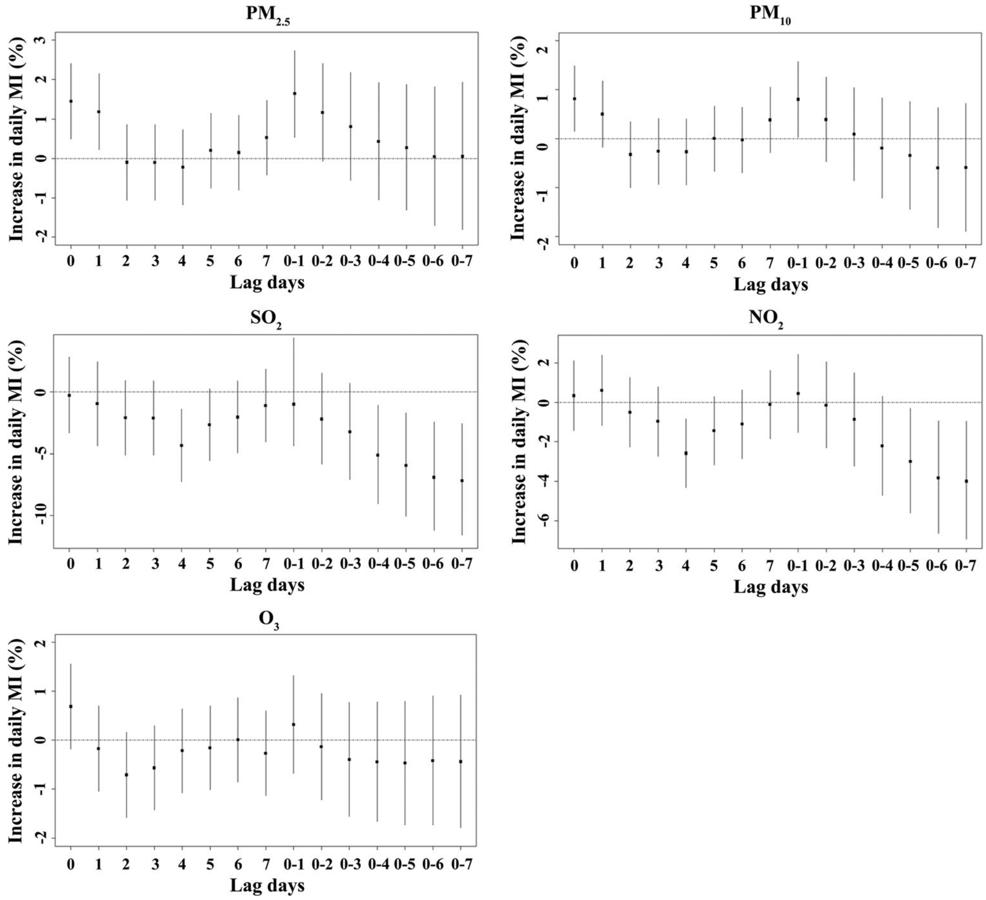

Fig. 2 Estimated changes with 95% confidence intervals in daily MI (myocardial infarction) percentage deviations (%) associated with an interquartile range increase in PM_{10}, $PM_{2.5}$, NO_2, SO_2, or O_3 concentrations with different lag days in single-pollutant model

study performed in Taiwan (Tsai and Yang 2014). Moreover, a Shanghai study demonstrated that a 10-μg/m^3 increment of $PM_{2.5}$ or PM_{10} was associated with a 0.25 or 0.57% increase in the hospitalizations of ischemic heart disease, respectively (Xu et al. 2017). A meta-analysis of 31 studies conducted recently, which indicated that risk of $PM_{2.5}$ (OR = 1.022) exposure was relatively greater than PM_{10} (OR = 1.005) (Luo et al. 2015). In the current study, a 10-μg/m^3 increase in $PM_{2.5}$ and PM_{10} concentrations increased the daily MI counts (1.636% for $PM_{2.5}$ and 0.805% for PM_{10}). In consistent with previous study (Zanobetti and Schwartz 2009), a cumulative effect of $PM_{2.5}$ and PM_{10} (lag 0–1) on the short-term effect with MI was also identified. And it was plausible that $PM_{2.5}$ was more deleterious to cardiovascular system than PM_{10}. In addition, the risk estimates from single-pollutant models found that SO_2 and NO_2 could exert protective effect on risk of MI, which was in accordance with previous report (Wang et al. 2016). It was also reported that SO_2 preconditioning could reduce MI injury in rats, and PI3K/Akt pathway was involved in the protective effects (Wang et al. 2011; Zhao et al. 2013). However, this should be interpreted with caution as limited study populations in this study. Further studies are required to explore the specific cardiovascular effects of SO_2 and NO_2.

The concentration-response relationship is important for assessment of the public health and determination of the adverse response pattern. In this study, the function curves for $PM_{2.5}$/MI and PM_{10}/MI were positive linear, with an estimated threshold of 100 μg/m^3 for $PM_{2.5}$ and 150 μg/m^3 for PM_{10}, respectively. The curves illustrated that the risks of the deterioration of MI could increase linearly corresponding to short-term increases in $PM_{2.5}$ and PM_{10} levels, and specifically, a sharp increase in MI counts was associated with the increment in moderate $PM_{2.5}$ (25 to 75 μg/m^3) and PM_{10} (50 to 125 μg/m^3) levels, suggesting that populations were more susceptible at that range.

Exploring the modifiers of the association between air pollution and MI is crucial to the primary prevention of MI (Dagres and Hindricks 2017). Males were found to have had greater estimated MI risk than females in this study, which was consistent with previous studies (Liu et al. 2017; Ye et al. 2001). A possible explanation for this observation may be that males are more likely to be exposed to air pollutants due to the higher rate of outdoor work and experience (Qiu et al. 2013). Furthermore, we found that the air pollutants ($PM_{2.5}$ and PM_{10})-MI associations varied by season. Despite of the higher levels of air pollutants in cold season, $PM_{2.5}$ and PM_{10} exhibited higher excess risk in the warm season. This was supported

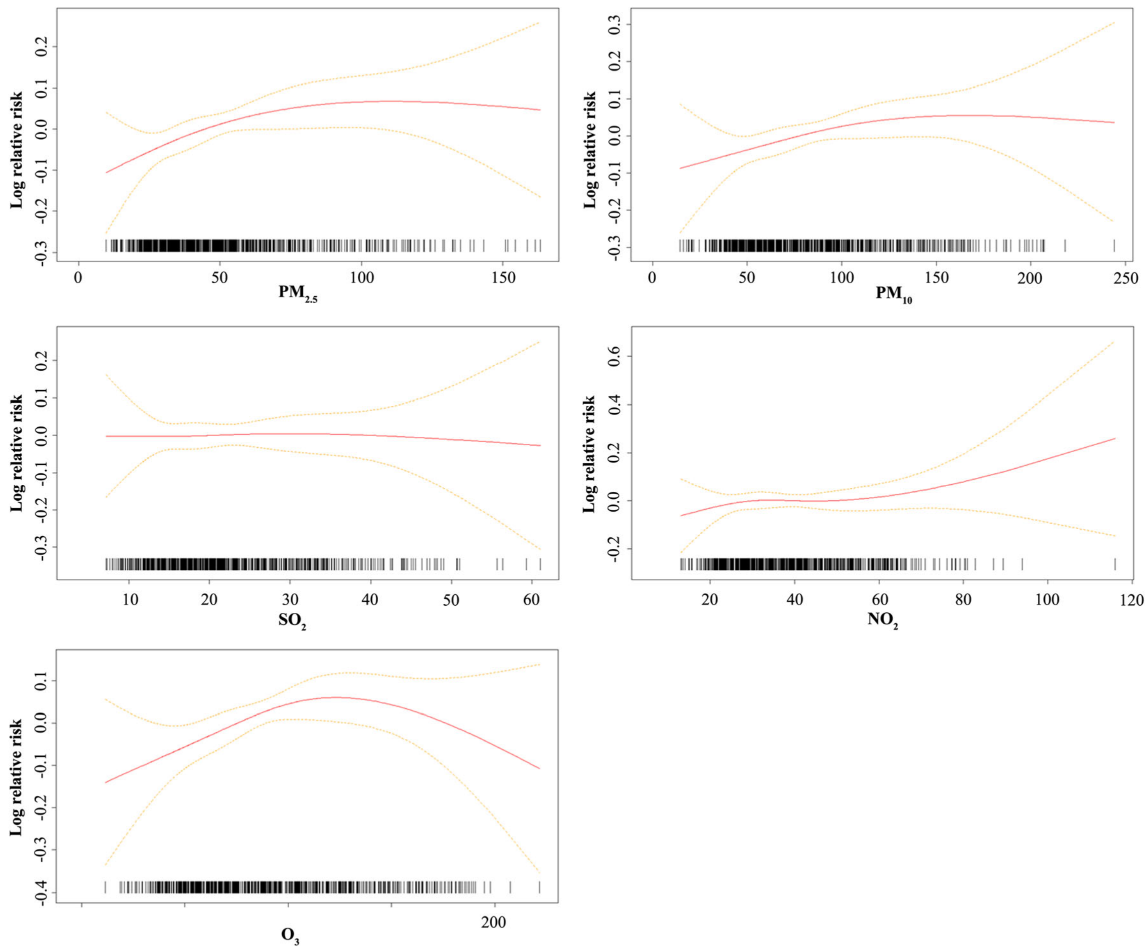

Fig. 3 The concentration-response curve of 2-day (lag 0–1) moving average air pollutants (df = 3) concentrations and MI counts in Changzhou, 2015–2016. Note: the *X*-axis is the 2-day (lag 0–1) moving air pollutants. *Y*-axis is the log relative risk (RR). The solid line represents the predicted log relative risk and the dotted lines represent the 95% CI

by Zanobetti but contrast to Kan and Chen's work (Chen et al. 2015; Kan et al. 2008; Zanobetti and Schwartz 2006). The underlying reasons may be the different population exposure patterns, differences in population susceptibilities, and lifestyles (Qiu et al. 2013).

However, the association between air pollution and near-term risk of MI remains controversial. No associations were recognized between the risk for onset of MI and air pollutant exposure in a case-crossover design conducted in Stockholm (PM_{10}, NO_2, CO, or O_3). Similarly, no significant associations between $PM_{2.5}$, NO_2, and CO and daily adults MI admissions were observed (Barnett et al. 2006; Berglind et al. 2010). However, a case-crossover study performed recently has demonstrated that per 5-μg/m^3 increment in 3-day mean $PM_{2.5}$

Table 4 Percent increase (mean and 95% confidence intervals) in daily MI counts with a 10-μg/m^3 increase in air pollutant concentrations modified by seasons and gender in Changzhou, 2015–2016

Variable	Seasons		Gender	
	Warm season	Cold season	Male	Female
$PM_{2.5}$	2.296 (0.671 to 3.929)*	1.123 (− 0.368 to 2.622)	2.733 (0.986 to 4.487)*	− 0.054 (− 1.650 to 1.558)
PM_{10}	1.135 (0.004 to 2.269)*	0.584 (− 0.460 to 1.630)	1.030 (− 0.043 to 2.102)	− 0.069 (− 1.289 to 1.163)
SO_2	0.690 (− 4.280 to 5.856)	− 2.115 (− 6.665 to 2.603)	0.432 (− 2.140 to 3.045)	− 3.531 (− 8.754 to 1.939)
NO_2	0.046 (− 2.835 to 2.982)	1.105 (− 1.581 to 3.841)	0.551 (− 3.902 to 5.158)	1.093 (− 2.413 to 4.715)
O_3	− 0.575 (− 2.010 to 0.879)	1.296 (− 0.079 to 2.687)	0.306 (− 0.770 to 1.391)	1.888 (− 1.131 to 4.994)

*$P < 0.5$

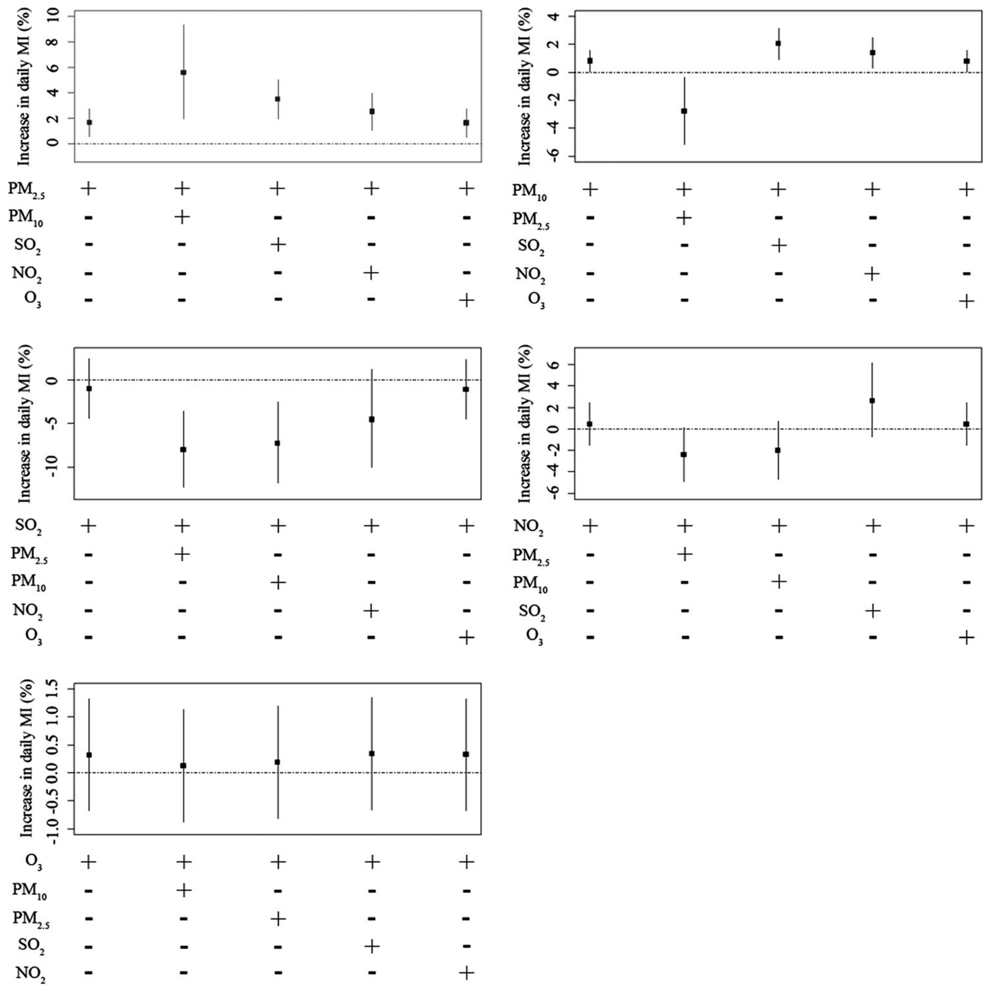

Fig. 4 Association between 10-μg/m^3 increment in air pollutants (lag 0–1 day) and MI counts using single- and two-pollutant models in Changzhou, 2015–2016

was associated with an increased risk of MI among elderly populations (Weichenthal et al. 2017). These differences might be attributed to the different levels of $PM_{2.5}$ concentrations: Stockholm and Australia experience a lower level of particulate matters.

This study had several strengths. Firstly, our study consisted of a large sample size of 5545 cases for MI and there were no missing data on air quality and meteorological figures during the study period, allowing for sufficient statistical power to detect a significant association. Secondly, it was the first time to investigate the hazardous effects of air pollutants on MI in Changzhou, China. Thirdly, the air quality and meteorological data were obtained from reliable sources and the results were consisted with many other studies. Herein, our work still had several limitations. First, we relied on routine measurements from fixed-site monitoring stations without data like the distance from the monitoring stations to the individual's residence and indoor exposure. Thus, the exact air pollutant exposure of individuals was unavailable. Second, individuals were recorded retrospectively from main hospitals in Changzhou, which may cause selection bias. Third, we obtained the data only from one city and the results were difficult to extrapolate.

In summary, we demonstrated that short-term exposure to $PM_{2.5}$ and PM_{10} were associated with daily MI counts in China. We believe that these findings have implications related to local environmental health risk assessment and early warning. And further studies should be conducted to validate our findings.

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Compliance with ethical standards

The present study was approved by the Institutional Review Board of Changzhou Center for Disease Control and Prevention, and all procedures were in accordance with prevailing ethical principles.

Conflict of interest The authors declare that they have no conflict of interest.

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