Letter to the Editor

Ambient Particulate Matter Pollution and Hospital Visits for Cardiac Arrhythmia in Beijing, China*

WU Jun Hui[1], WU Yao[1], WANG Zi Jing[1], TIAN Yao Hua[1], WU Yi Qun[1], WU Tao[1], WANG Meng Ying[1], WANG Xiao Wen[1], WANG Jia Ting[1], and HU Yong Hua[1,2,#]

Cardiac arrhythmia is a serious public health problem in many countries[1]. Previous studies estimated that 33.5 million people are affected by cardiac arrhythmia worldwide, and this number will continue to grow as society ages[2]. Despite improvements in diagnostic and therapeutic interventions in electrophysiology, the disease burden, incidence and prevalence of cardiac arrhythmia continue to increase and have aroused public health concern. Increasing evidence has indicated that air pollution may be associated with cardiac autonomic nervous system[3]. Among air pollutants, particulate matter with an aerodynamic diameter of ≤ 2.5 μm ($PM_{2.5}$) is considered exert more toxicity than other air pollutants, as it provides a larger surface area and absorbs or condenses more toxic substances per unit mass[4].

However, most of previous studies were performed in western countries where $PM_{2.5}$ concentrations are much lower than those in developing countries[5]. Furthermore, these studies focused primarily on hospital admissions, which may affected by many factors like scheduled appointments and availability of hospital beds. Thus, we use a time-series design to evaluate whether $PM_{2.5}$ pollution levels were related to the risk of cardiac arrhythmia between 2010 and 2012 in Beijing, China. To our knowledge, this is the first time that the short-term effects of $PM_{2.5}$ levels on arrhythmia-associated outpatient visits, hospital admissions, and emergency admissions have been studied simultaneously at the city level.

We obtained the daily numbers of hospital visits for cardiac arrhythmia from the citywide database, Beijing Medical Claim Data for Employees (BMCDE), which records medical claim data for all working or retired employees (aged ≥ 18 years) who are covered by basic medical insurance in Beijing. By the end of 2017, nearly 80% of Beijing's residents (17.8 million) were included in the database. Basic characteristics (e.g., sex and age) of individuals diagnosed with cardiac arrhythmia were obtained from the BMCDE between January 1, 2010 and June 30, 2012 (912 days). As in previous studies, cardiac arrhythmia was identified by ICD-10 codes (Supplementary Material available in www.besjournal.com)[3]. Patients younger than 18 years old were excluded.

Daily $PM_{2.5}$ concentration data were retrieved from an air-monitoring station of the US Embassy (http://www.stateair.net) in Chaoyang District, Beijing. China did not include $PM_{2.5}$ in the national first-report monitoring data until 2013; thus, the monitoring data from the US Embassy were the only open source of $PM_{2.5}$ concentration data during the study period. Previous studies have reported that the $PM_{2.5}$ levels detected by the US Embassy were approximately comparable with citywide $PM_{2.5}$ levels in Beijing[6]. In order to reduce exposure misclassification, it could be considered that the maximum distance from the US Embassy to the hospital is about 40 km[7]. Within that radius, the monitoring data covering all the region with high population density in Beijing (> 5,000 residents/km^2) and 79.2% of Beijing's residents[6]. In the present study, we used the daily average $PM_{2.5}$ concentrations (24 h) as a proxy for population exposure levels. Moreover, daily meteorological data including temperature (°C) and relative humidity (%) were collected from the Chinese Meteorological Bureau.

The association between $PM_{2.5}$ concentrations and cardiac arrhythmia-associated hospital visits was assessed using a quasi-Poisson regression model,

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1. Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing 100191, China; 2. Medical Informatics Center, Peking University, Beijing 100191, China

which has been widely adopted in time-series studies[8]. The following covariates were included in the main model: a penalized spline function of calendar time with 7 degrees of freedom (*df*) per year to control for underlying time trends, public holiday, and day of the week as categorical variables to account for short-term variations, and penalized spline functions with 3 *df* for temperature and 3 *df* for relative humidity. The formula applied in the present study is as follows:

$$\begin{aligned}\text{Log}\,[E(Y_t)] = \alpha + \beta\text{PM}_{2.5} &+ \text{day of the week}\\ &+ \text{public holiday}\\ &+ s(\text{calendar time, 7 per year})\\ &+ s(\text{temperature}, 3)\\ &+ s(\text{humidity}_{01}, 3)\end{aligned}$$

where $E(Y_t)$ refers to the expected number of cardiac arrhythmia-associated hospital visits on day *t*, α represents the model intercept, β denotes the log (relative risk) of morbidity relative to unit increase in $PM_{2.5}$ level; and *s* represents a smoother based on the penalized splines. Following the approaches applied in previous studies, we selected the degrees of freedom (*df*) for calendar time, temperature, and relative humidity[3].

We applied a penalized cubic regression spline of the $PM_{2.5}$ concentration with 3 *df* to assess the concentration-response association. We also explored the relationship between $PM_{2.5}$ and cardiac arrhythmia-associated hospital visits by building models with a single-day lag from the current day (lag 0) up to the previous 3 days (lag 1, lag 2, and lag 3), and with 2-day (lag 0–1), 3-day (lag 0–2), and 4-day (lag 0–3) moving average concentrations. To examine potential effects per subgroup, analyses were stratified by age, sex, and season. The warm season was defined as April to September, and the cool season was defined as October to March. We used the Z-test to assess the statistical significance of the subgroup differences.

All results were presented as the percentage change and 95% *CI* of the daily cardiac arrhythmia-associated hospital visits for each 10-μg/m^3 increase in ambient $PM_{2.5}$. We applied the "mgcv" and "nlme" packages in R 3.2.2 for all the analyses[9].

In total, 1,435,139 outpatient visits, 29,837 hospital admissions, and 43,347 emergency visits between January 1, 2010 to June 30, 2012 were identified from the BMCDE database. Table 1 summarizes the descriptive statistics for the cardiac arrhythmia-associated hospital visits, $PM_{2.5}$ concentrations, and weather conditions. The daily mean counts for the outpatient visits, hospital admissions and emergency visits were 1,573 (1,132), 33 (22), and 48 (27) respectively. For $PM_{2.5}$ concentration, the annual average was 99.5 (75.3) μg/m^3, and the maximum was 493.0 μg/m^3.

Table 2 presents the acute elevations in $PM_{2.5}$ concentrations were related to increased hospital

Table 1. Summary statistics for daily cardiac arrhythmia-associated hospital visits, daily $PM_{2.5}$ concentrations and meteorological data

Variable	Mean ± SD	Percentiles				
		Minimum	P25	P50	P75	Maximum
Outpatient visits	1,573 ± 1,132	1	575	1,391	2,304	5,055
Cool season	1,565 ± 1,232	1	439	1,470	2,473	5,055
Warm season	1,587 ± 966	1	777	1,348	2,249	4,124
Hospital admissions	33 ± 22	1	5	39	51	84
Cool season	34 ± 30	1	5	39	52	84
Warm season	43 ± 21	1	5	39	49	81
Emergency visits	48 ± 27	1	28	48	66	120
Cool season	49 ± 29	1	24	52	71	120
Warm season	46 ± 22	8	29	43	57	107
$PM_{2.5}$ (μg/m^3)	99.5 ± 75.3	7.2	42.5	82.8	133.0	493.0
Temperature (℃)	12.6 ± 11.6	−12.5	1.5	14.1	23.8	34.5
Relative humidity (%)	48.6 ± 20.3	9	30	48	66	92

Note. SD: standard deviation.

visits for cardiac arrhythmia. A 10-μg/m^3 increase in $PM_{2.5}$ level on lag days 0–3 corresponded with 0.71% (95% *CI*: 0.43%–0.47%) and 0.48% (95% *CI*: 0.59%–0.82%) increases in outpatient and hospital admissions for cardiac arrhythmia, respectively. A 10 μg/m^3 increase in $PM_{2.5}$ level on current day corresponded with 0.17% (95% *CI*: 0.10%–0.23%) increases in emergency visits for cardiac arrhythmia. Our findings provide new evidence which may help improve targeted intervention strategies for cardiac arrhythmia in China. Previous western studies have explored associations between $PM_{2.5}$ and hospitalizations for cardiac arrhythmia, which support the results of our study. A recent meta-analysis of $PM_{2.5}$ and daily hospitalizations for cardiac arrhythmia reported that arrhythmia-associated hospitalizations were related to increases in $PM_{2.5}$ (relative risk = 1.02 per 10 μg/m^3)[5]. However, most of previous studies have been conducted in the US and Europe, while Beijing has higher $PM_{2.5}$ levels than those areas, which might lead to differences in effect estimates.

Table 3 lists the estimates for subgroup analyses. The association between $PM_{2.5}$ and arrhythmia-associated outpatient visits was greater during the warm season (0.94%, 95% *CI*: 0.91%–0.97%), and the estimated $PM_{2.5}$ effect was stronger in men (0.82%, 95% *CI*: 0.66%–0.99%). For hospital admissions, the estimates were higher for men (0.48%, 95% *CI*: 0.45%–0.51%) and during the warm season (0.52%, 95% *CI*: 0.50%–0.54%). For emergency visits, the estimates were greater for men (0.19%, 95% *CI*: 0.10%–0.29%) and during the warm season (0.22%, 95% *CI*: 0.14%–0.30%). Similarly, a recent study reported that the short-term effect of $PM_{2.5}$ on arrhythmias was relatively stronger for men than for women in all lag models[10], but the underlying mechanism of the sex difference remains elusive and requires more study. Differences in seasonal estimates may be due to the behavioral differences. Beijing residents are more likely to participate in outdoor activities and ventilate their homes during

Table 2. Percentage change with 95% confidence interval in cardiac arrhythmia-associated hospital visits for each 10 μg/m^3 increase in $PM_{2.5}$ levels for different lag days

Hospital visits	Lag days	Percentage change (%)	95% Confidence interval (%)	*P* value
Outpatient visits	0	0.15	0.17–0.19	< 0.001
	1	0.51	0.19–0.22	< 0.001
	2	0.48	0.25–0.27	< 0.001
	3	0.26	0.16–0.18	< 0.001
	0–1	0.39	0.24–0.27	< 0.001
	0–2	0.64	0.38–0.41	< 0.001
	0–3	0.71	0.43–0.47	< 0.001
Hospital admissions	0	0.18	0.07–0.22	< 0.001
	1	0.21	0.42–0.60	< 0.001
	2	0.26	0.40–0.56	< 0.001
	3	0.17	0.18–0.34	0.001
	0–1	0.26	0.30–0.49	< 0.001
	0–2	0.40	0.53–0.75	< 0.001
	0–3	0.45	0.59–0.82	< 0.001
Emergency visits	0	0.17	0.10–0.23	0.012
	1	−0.11	0.10 to −0.03	0.173
	2	−0.26	−0.33 to −0.19	0.100
	3	−0.11	−0.18 to −0.04	0.098
	0–1	0.07	−0.01 to −0.16	0.380
	0–2	−0.09	−0.19 to −0.01	0.345
	0–3	−0.15	−0.26 to −0.05	0.154

the warm season, bringing monitoring data closer to their individual exposure levels. Another explanation for the higher correlation is that high temperatures may affect the chemical conversion and deposition processes of air pollutants.

In the present citywide time-series analysis, significant and positive associations between $PM_{2.5}$ levels and hospital visits for cardiac arrhythmia were found in Beijing. To our knowledge, this is the first citywide research in Beijing, or even in other highly air polluted region, to comprehensively reveal the acute effect of $PM_{2.5}$ on cardiac arrhythmia-associated outpatient, emergency, and hospital admissions in a same study.

Some limitations should be acknowledged. First, data from one fixed monitoring station could not

Table 3. Increases in cardiac arrhythmia-associated hospital visits for each 10 μg/m^3 increase in $PM_{2.5}$ for lag days 0–3 (for outpatient visits and hospital admissions) and current-day (for emergency visits) with stratification

Hospital visits	Percentage change (%)	95% *CI* (%)	*P*	P^a
Outpatient visits				
Sex				< 0.001
Male	0.82	0.66–0.99	< 0.001	
Female	0.65	0.48–0.83	< 0.001	
Age (years)				0.010
< 65	0.91	0.71–1.10	< 0.001	
≥ 65	0.67	0.52–0.82	< 0.001	
Season				0.014
Cool	0.64	0.38–0.90	< 0.001	
Warm	0.94	0.91–0.97	< 0.001	
Hospital admissions				
Sex				0.017
Male	0.48	0.45–0.51	< 0.001	
Female	0.42	0.40–0.45	< 0.001	
Age (years)				< 0.001
< 65	0.39	0.36–0.42	< 0.001	
≥ 65	0.50	0.48–0.53	< 0.001	
Season				0.029
Cool	0.39	0.35–0.42	< 0.001	
Warm	0.52	0.50–0.54	< 0.001	
Emergency visits				
Sex				0.004
Male	0.19	0.10–0.29	0.044	
Female	0.14	0.04–0.23	0.140	
Age (years)				0.016
< 65	0.27	0.17–0.37	0.006	
≥ 65	0.08	−0.01 to −0.17	0.376	
Season				0.025
Cool	−0.21	−0.36 to −0.07	0.139	
Warm	0.22	0.14 to −0.30	0.004	

Note. ^{a}*P*: Z-test for the difference between the two risk estimates in subgroup analyses.

exactly represent the actual situation of personal exposure to $PM_{2.5}$. Second, because the information was limited, we did not explore other potential modifiers, including health-related and nutritional factors, which are reported to be associated with arrhythmias[3]. Third, the US Embassy only provided $PM_{2.5}$ monitoring data during the study period. The lack of authoritative records of other air pollutants has limited our exploration of the independent effects of $PM_{2.5}$. Finally, due to information limitations, we are unable to distinguish all subtypes of arrhythmias. Future research is warranted to investigate the modification effect between different cardiac arrhythmia subtypes.

#Correspondence should be addressed to Professor HU Yong Hua, PHD, MD, Tel: 86-10-82801189, E-mail: yhhu@bjmu.edu.cn

Biographical note of the first author: WU Jun Hui, female, born in 1992, PHD Candidate, majoring in genetic epidemiology.

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Supplementary Material

We used ICD-10 codes to identify cardiac arrhythmia and these codes included I44 (atrioventricular and left bundle-branch block), I45 (other conduction disorders), I46 (cardiac arrest), I47 (paroxysmal tachycardia), I48 (atrial fibrillation and flutter), and I49 (other cardiac arrhythmia)(Dominici et al. 2006[1], Zheng et al. 2018[2]).

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