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ORIGINAL ARTICLE

Short-Term Exposure to Sulfur Dioxide and Nitrogen Monoxide and Risk of Out-of-Hospital Cardiac Arrest

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Background & Aims Over the past decades, particulate matter (PM), especially fine PM <2.5 μm in aerodynamic diameter ($PM_{2.5}$) has been a major research focus. However, the air pollutant is a mixture of gases or vapour-phase compounds, such as carbon monoxide (C), nitrogen oxides (NO_x), photochemical oxidants (Ox), and sulfur dioxide (SO_2). Little is known about their cardiovascular effect, individually or in combination with PM. Thus, we aimed to determine the associations between the incidence of acute cardiac events and both gaseous and PM using a case-crossover design.

Methods Cardiovascular cases were identified through the Gunma Prefectural Ambulance Activity Database in Japan in 2015 (1,512 out-of-hospital cardiac arrest [OHCA] and 1,002 heart failures from 53,006 ambulance cases). Air quality data from the nearest station was for day of the arrest (lag0) and 1-2 days before the arrest (lag1, lag2) and the moving average across days 0-1 (lag0-1). Conditional logistic regression was used for unadjusted and adjusted analysis for temperature and humidity.

Results Independent associations of OHCA were daily concentrations of SO_2 at lag1 (OR 1.173, 95%CI 1.004, 1.370; p=0.044) and lag0-1 (OR 1.203, 95%CI 1.015, 1.425; p=0.033); and daily NO concentrations at lag2 (OR 1.039, 95%CI 1.007, 1.072; p=0.016). The incidence of heart failure was significantly associated with daily concentrations of O_x on the day of the event in univariable model but not after adjustment for temperature and humidity. No associations were found for other pollutants.

Conclusions Short-term exposure to SO_2 and NO are associated with an increased risk of OHCA.

Keywords Air pollution • Out-of-hospital cardiac arrest • Heart failure • Particulate matter • Sulfur dioxide

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Introduction

Ambient air pollution is recognised as a major risk for the global burden of disease. In 2015, ambient particulate matter (PM) in both developed and developing countries was estimated to account for 4.2 million premature deaths and 103.1 million disability-adjusted life-years (DALYs) [1]. Cardiovascular diseases attributed to air pollution have been identified as the main contributor to worldwide mortality and morbidity [2–4].

Epidemiological studies have highlighted the acute effects of air pollution on cardiovascular events, including ischaemic heart disease [5–8], out-of-hospital cardiac arrest (OHCA) [9–13], heart failure [14,15] and stroke [16–18]. There are, however, still some neutral results [19–22], necessitating further research on the association between ambient air pollution and cardiovascular outcomes. Particulate matter smaller than 2.5 μm in aerodynamic diameter ($PM_{2.5}$; also known as fine PM) is small enough to travel deep into the alveoli and even into the bloodstream when inhaled, with an adverse effect on human health [3]. Thus, there is a rapidly growing focus on $PM_{2.5}$. However, the risk of other common constituents, such as oxides of nitrogen and sulfur, cannot be neglected. Sulfur dioxide (SO_2) is a colourless gas that is emitted mainly from the combustion of fuels; the resulting formation of sulfur-containing particulates plays a critical role in triggering related diseases [2]. Ambient nitrogen oxides (NO_x) are primarily attributed to motor vehicle emissions. They may act alone or together with PM to influence the progression of cardiovascular diseases [3]. The chemical components that make up PM may also play different roles and need to be identified from various sources of air pollution [2].

To test our hypothesis that exposure to $PM_{2.5}$ and common gaseous pollutants would precipitate cardiovascular disease events, we conducted this case-crossover study in a Japanese prefecture. In view of the diverse pathogenesis of different cardiovascular conditions, we selected OHCA and heart failure as the main health outcomes for this study, based on Zones of evidence linking air pollution and CV disease [23,24]. Data were obtained from ambulance records. To obtain comprehensive knowledge of air pollution patterns, we examined $PM_{2.5}$, nitric oxide (NO), NO_x, nitrogen dioxide (NO_2), photochemical oxidant (O_x) and SO_2 across the entire prefecture.

Methods

Study Population and Outcome Data

Gunma is a landlocked prefecture of Japan located on Honshu Island; it has a total area of 6,366.16 square kilometres and a population of 2.0 million [25]. Ambulance records from 1 January 2015 to 31 December in 2015 were extracted from the Gunma Prefectural Comprehensive Medical Information System. This 24/7 system collects and provides emergency medical information and data via a web-based format; it links all public ambulance systems and all hospitals/institutions providing emergency medical services in Gunma Prefecture. One of the main aims of this system is to provide better logistics when patients require transfer to hospitals with appropriate medical and human resources. Thus, every single ambulance record in Gunma Prefecture is captured immediately with the following patient information: location, date, time, age, sex, initial diagnosis, severity of disease at the time, classification of disease and plausible aetiology entered by the emergency department physicians. The time recorded is the time to the nearest hour of the first call to the ambulance service.

Cardiac arrest was defined as the unexpected cessation of cardiac mechanical activity, which may have been restored by cardiopulmonary resuscitation and a defibrillator. Cardiac arrest has a high mortality rate. We included cases from outside the hospital setting that were presumed to have cardiac aetiology. The exclusion criteria included arrests with an obvious preceding non-cardiac event, such as trauma, poisoning, drowning, overdose, asphyxia, electrocution, or primary respiratory arrests. We also included cases with an initial diagnosis of heart failure. Heart failure is a clinical syndrome resulting from abnormality in cardiac structure and/or function, affecting cardiac output and intracardiac filling pressure. The inclusion criteria included rapid onset or acute worsening of chronic heart failure requiring urgent medical evaluation and treatment.

This study preceded our nationwide study [26] to test feasibility of our study design and to assess more granular level evidence in smaller scale. This study was approved by the Tasmanian Human Research Ethics Committee (reference H0017657).

Air Quality and Meteorological Data

We obtained hourly air quality and meteorological data from eight 24-hour monitoring sites (Figure 1) during the study period; data were obtained from a public database published by the Gunma Prefectural Environmental Protection Department [27]. This dataset contained information concerning NO, NO_x, NO_2, O_x, SO_2 and $PM_{2.5}$. Meteorological data consisted of hourly temperature and humidity measurements. Hourly data were then averaged to produce daily mean values for all air quality and meteorological variables.

Statistical Analysis

All continuous variables are presented as mean ± SD or median (interquartile range; IQR), as appropriate. Categorical variables are presented as absolute and relative frequencies (%). The time stratified case-crossover design is an established and standard study design to investigate the relationship between transient environmental exposures and acute health outcomes; it was first proposed by Maclure in 1991 [28], and has been widely used in studies of air pollution [19,20,22]. In this study design, the case period is defined as the day of onset of the identified case. The control periods were defined as non-case days that were on the same day of

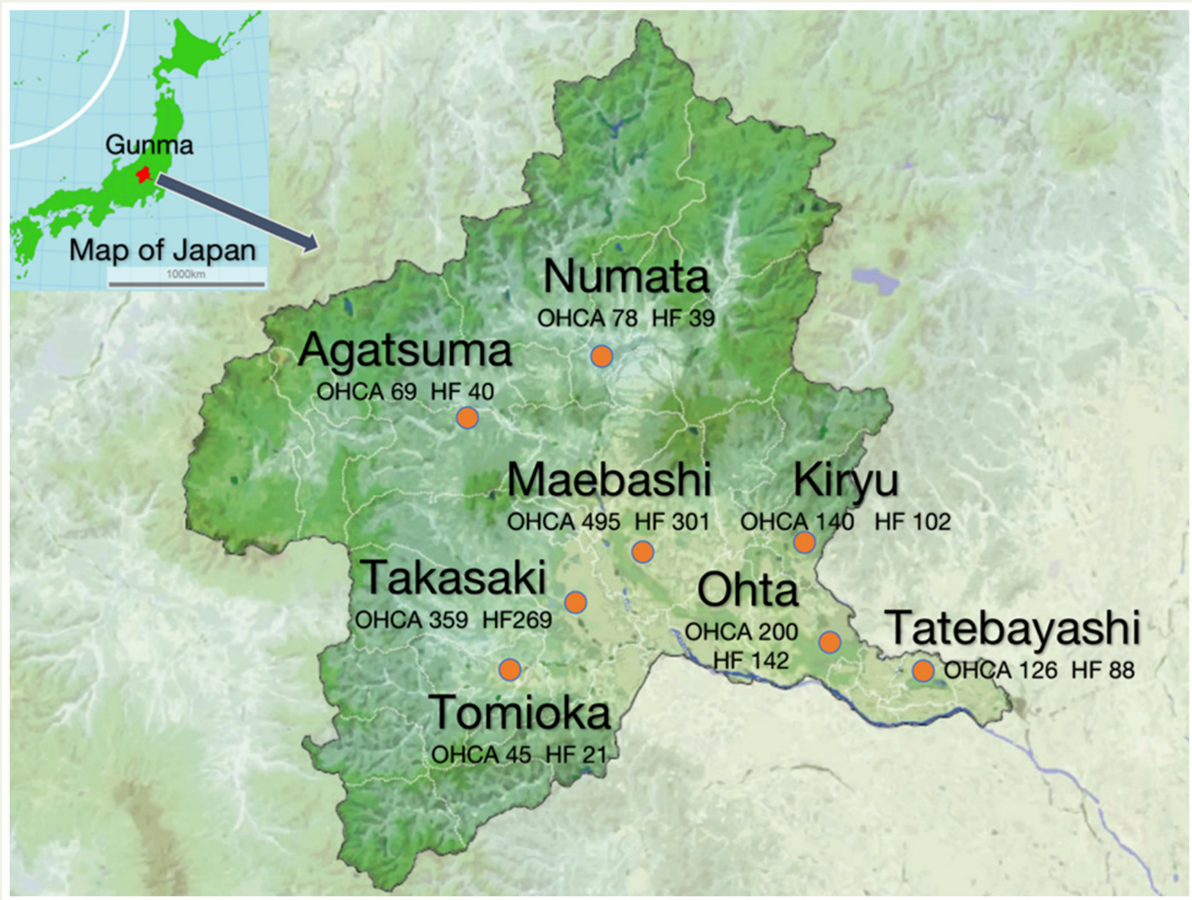

Figure 1 Map of eight 24-hr air monitoring sites in Gunma, Japan.
This figure illustrates the distribution of air monitoring sites in Gunma and the breakdown of the out-of-hospital cardiac arrest (OHCA)/heart failure (HF) by region.

the week during the same month as the case. Hence, this study compared exposure levels on the day of the case with exposure levels before and after the case during the same month. Every patient served as his or her own control, which reduced the influence of personal confounding factors such as sex or smoking status, which rarely change within a single month.

Conditional logistic regression models were used to analyse the association between air pollutants and the incidence of OHCA and heart failure, respectively. As there may be a certain response time between exposure to air pollutants and the associated outcome, we investigated lagged exposures. The average exposure level on the day of case onset was defined as lag 0; the average exposure level 1 day before the day of case onset was lag 1; the average exposure level 2 days before the day of case onset was lag 2 and lag 0-1 was the average exposure level on the day of case onset and the day prior to case onset.

Correlations between air pollutants and meteorological variables were also examined. The air quality and meteorological data from the nearest air monitoring station were merged with the health outcome data to calculate the odds ratios (OR) and the 95% confidence intervals (CI) per unit change in each air pollutant separately; both unadjusted and adjusted analyses (for temperature and humidity) were performed. We used the natural cubic spline of temperature and humidity with two degrees of freedom in the multivariable model. In addition to the single pollutants examined in the main analysis, the models were further adjusted for $PM_{2.5}$ when needed, as a sensitivity analysis for multiple pollutants. A p-value of 0.05 was considered statistically significant. All analyses were conducted using R version 3.2.3 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Study Subjects and Exposure Characteristics

In 2015, a total of 53,006 emergency ambulance cases were collected by the Gunma Prefectural Health Department. There was a greater number of male than female patients. The average age of the patients was 64±26 years; the oldest patient was 108 years. Nearly 40% of ambulance events occurred in the cold season (Nov-Mar) and 68.8% of the cases

Table 1 **Breakdown of out-of-hospital cardiac arrests and heart failures.**

Variable	OHCA (n=1,512)	Heart Failure (n=1,002)
Age		
Mean (SD)	77 (15)	81 (11)
<40	35 (2.3)	4 (0.4)
40-60	151 (10.0)	37 (3.7)
61-80	574 (38.0)	353 (35.2)
>80	736 (48.7)	603 (60.2)
Missing	16 (1.0)	5 (0.5)
Sex		
Female	666 (44.0)	501 (50.0)
Male	842 (55.7)	498 (49.7)
Missing	4 (0.3)	3 (0.3)
Season		
Spring (March-May)	391 (25.8)	337 (33.6)
Summer (June-August)	313 (20.7)	146 (14.6)
Autumn (September-November)	344 (22.8)	189 (18.9)
Winter (December-February)	464 (30.7)	330 (32.9)

Values are the number (percentage) of respondents, unless otherwise stated.

occurred at home. Table 1 summarises the breakdown of OHCAs and heart failures. Daily average data for air pollutants, temperature and humidity are shown in Table 2. Correlations between air pollutants and meteorological factors are shown in Table 3 to avoid any potential collinearity issue. Atmospheric pollutants tended to be moderately positively correlated with each other, aside from O_x which was negatively correlated. NO_x, NO_2 and NO were strongly correlated with each other. Meteorological variables exhibited weak correlations with pollutant levels, except O_x which exhibited a moderate negative correlation with humidity.

Air Pollution and OHCA

In 2015, there were 1,512 OHCAs that met the selection criteria; these eligible OHCAs comprised 2.8% of the total number of emergency ambulance cases. After adjusting for meteorological variables, the association between OHCA and SO_2 concentration was statistically significant at lag 1 (OR 1.173, 95%CI [1.004, 1.370], p=0.044) and lag 0-1 (OR 1.203, [1.015, 1.425], p=0.033), and the association between OHCA and NO was statistically significant at lag 2 (OR 1.039, [1.007, 1.072], p=0.016). No significant associations were found for the other pollutants (Table 4). These results were not meaningfully changed when $PM_{2.5}$ was included in the sensitivity analysis model (Table S1 and Table S2).

Air Pollution and Heart Failure

There were 1,002 cases of heart failure (1.9%) during the study period. The daily rate of heart failure cases was significantly associated with the O_x concentration on the day of the event in the unadjusted model (OR 1.008, [1.001, 1.016], p=0.031), but not after adjusting for temperature and humidity. No associations were found for the other pollutants (Table 5).

Discussion

The main finding of this case-crossover study is that short-term exposure to ambient SO_2 and NO, respectively, was independently associated with the incidence of OHCA in Gunma, Japan. After adjusting for temperature and humidity, the odds of an OHCA event were 1.173 and 1.203 times higher with a 1 part per billion (ppb) increase in SO_2 in lag 1 and lag 0-1, respectively. An increase of 1 ppb in NO 2 days before the event was also associated with 1.039 times higher odds of an OHCA event. No significant associations were detected between OHCA and other pollutants. In addition, there were no independent associations between the occurrence of heart failure and ambient air pollution.

Associations of SO_2 and NO With OHCA

SO_2 is recognised as a major air pollutant from the combustion of fuels in the atmosphere and has been linked to all-cause and cardiac mortality [29], cardio respiratory mortality [30], coronary heart diseases [31,32], hypertension [33] and cardiac arrhythmia [34]. NO is a result of high temperature combustion, mainly from vehicular exhausts [2]. Because most NO gets transformed into NO_2, NO_2 has become the principle research target among all NO_x [2]. The proportion of vehicle owners in Gunma is the highest among all prefectures in Japan (68.4 cars per 100 persons in 2015) [35]. This might partly explain the null findings regarding associations between air pollution and heart failure in Gunma; specifically, given the high number of vehicle owners, patients may be transferred to hospital by private car rather than seeking assistance from the ambulance despatch centre. OHCA patients are generally unable to self-present, because onset occurs without warning and results in sudden loss of consciousness. One study investigated the mode of presentation among 1,068 acute decompensated heart failure patients and found that 78% self-presented and 22% presented via ambulance [36]. Recently, Ha et al. [37] conducted a case-crossover study in the United States to investigate the association between air pollution and cardiovascular events during labour and delivery. The main finding was that higher concentrations of $PM_{2.5}$, SO_2 and NO_x in the previous days were associated with a higher proportion of deliveries affected by cardiovascular events such as heart failure or cardiac arrest during labour. These results, together with the results of our study, support the idea that short-term exposure to gaseous air pollutants may be associated with an increased occurrence of serious cardiovascular outcomes. Although the aerodynamic size of air pollutants such as $PM_{2.5}$ has been the main focus of research to date, our data suggests that the individual components of pollution should

Table 2 Description of daily air quality and meteorological data from 8 stations (1 January 2015 to 31 December 2015).

Variable	No.	Missing	Mean	Percentile					IQR
				5%	25%	50%	75%	95%	
$PM_{2.5}$ (μg/m^3)	2,874	46	13.08	3.17	7.25	11.83	17.96	27.18	10.71
O_x (ppb)	2,919	1	32.20	12.79	23.12	31.00	40.77	54.67	17.65
NO_x (ppb)	2,534	386	9.51	2.04	5.01	8.06	12.00	21.79	6.99
NO_2 (ppb)	2,534	386	7.82	1.54	4.17	6.83	10.34	17.42	6.18
NO (ppb)	2,534	386	1.70	0.07	0.61	1.12	1.88	5.28	1.27
SO_2 (ppb)	2,181	739	1.33	0.42	1.00	1.21	1.71	2.29	0.71
Temperature (°C)	2,900	20	14.6	1.8	7.0	15.6	21.3	28.1	14.3
Humidity (%)	2,920	0	69.7	42.5	57.3	69.1	82.6	96.6	25.3

Abbreviations: NO_x, nitrogen oxides; NO_2, nitrogen dioxide; NO, nitric oxide; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than 2.5 micrometres; O_x, photochemical oxidants; SO_2, sulfur dioxide; ppb, parts per billion.

be taken into account. Further studies of pollution components as well as the combination of various air pollutants are required, as these could have different adverse impacts on cardiovascular health [3].

No Statistically Significant Association Between $PM_{2.5}$ and OHCA

The lack of association between $PM_{2.5}$ and OHCAs in this study did not support our hypothesis. However, there has been inconsistency in findings among previous case-crossover studies. Most studies [9–12,22,38] have reported a relationship between elevated $PM_{2.5}$ and increased risk of OHCA, while others have reported no association [13,20,21]. There are several possible explanations for this. First, our sample size (n=1,512) might have been too small and our statistical power might not have been adequate, although power was sufficient to detect a significant association between OHCA with SO_2. The numbers of OHCAs in the negative studies were lower, at 362 [20] and 1,206 [21], than those in the positive studies, which ranged from 2,000 [12] to 11,677 [22]. Second, one study from the United States reported no association between $PM_{2.5}$ and OHCA among the whole population, but found significant associations among current smokers with histories of previous heart disease [21]. This suggests there may be sub-groups who are more sensitive to $PM_{2.5}$ exposure. Third, the mixed results in the literature may be due to differences in pollution exposure and/or composition, or measurement differences, or the methods used to select study subjects. Thus, standard protocols for reporting should be developed and applied. Finally, publication bias could be present, as significant results are more likely to be published. An international registry would be helpful to better characterise possible associations between $PM_{2.5}$ on OHCA. We only found two studies that investigated the association between Asian desert dust and acute cardiac events in Japan. One suggested that dust had no association with OHCA [39], while the one found that Asian dust was associated with the incidence of acute myocardial infarction [40].

Strengths and Limitations

A time stratified case-crossover design is an appropriate approach to investigate associations between transient environmental pollutant exposure and acute health

Table 3 Correlations between air pollutants and meteorological variables.

	NO	NO_2	NO_x	O_x	$PM_{2.5}$	SO_2	Temperature	Humidity
NO	1.00							
NO_2	0.66	1.00						
NO_x	0.85	0.96	1.00					
O_x	-0.53	-0.41	-0.49	1.00				
$PM_{2.5}$	0.22	0.49	0.43	0.18	1.00			
SO_2	0.14	0.33	0.29	0.08	0.32	1.00		
Temperature	-0.24	-0.24	-0.26	0.33	0.21	-0.01	1.00	
Humidity	0.12	0.12	0.13	-0.46	0.02	-0.20	0.25	1.00

Abbreviations: NO_x, nitrogen oxides; NO_2, nitrogen dioxide; NO, nitric oxide; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than 2.5 micrometres; O_x, photochemical oxidants; SO_2, sulfur dioxide.

Table 4 Associations between out-of-hospital cardiac arrests and daily lag exposure to air pollutants.

		Lag0		Lag1		Lag2		Lag0-1	
		OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value
$PM_{2.5}$	Unadjusted	0.995 (0.987, 1.003)	0.2	0.993 (0.985, 1.001)	0.1	0.995 (0.987, 1.003)	0.26	0.993 (0.984, 1.002)	0.13
	Adjusted	1.0002 (0.988, 1.012)	0.97	0.998 (0.986, 1.010)	0.76	1.002 (0.990, 1.014)	0.8	0.999 (0.986, 1.014)	0.98
SO_2	Unadjusted	1.093 (0.948, 1.26)	0.22	1.069 (0.929, 1.23)	0.35	1.085 (0.945, 1.247)	0.25	1.098 (0.941, 1.282)	0.23
	Adjusted	1.155 (0.988, 1.352)	0.07	**1.173 (1.004, 1.370)**	**0.044**	1.122 (0.961, 1.309)	0.14	**1.203 (1.015, 1.425)**	**0.033**
NO	Unadjusted	0.999 (0.969, 1.032)	0.99	0.977 (0.945, 1.012)	0.19	1.028 (0.998, 1.058)	0.07	0.984 (0.943, 1.026)	0.44
	Adjusted	1.006 (0.971, 1.042)	0.75	0.976 (0.939, 1.015)	0.23	**1.039 (1.007, 1.072)**	**0.016**	0.987 (0.941, 1.035)	0.6
NO_2	Unadjusted	0.997 (0.981, 1.013)	0.68	0.990 (0.974, 1.007)	0.26	0.999 (0.983, 1.015)	0.88	0.990 (0.970, 1.011)	0.34
	Adjusted	1.006 (0.986, 1.027)	0.56	0.990 (0.970, 1.011)	0.35	1.008 (0.987, 1.029)	0.46	0.999 (0.973, 1.025)	0.92
NO_x	Unadjusted	0.998 (0.987, 1.01)	0.77	0.992 (0.981, 1.004)	0.21	1.004 (0.992, 1.015)	0.55	0.993 (0.979, 1.008)	0.35
	Adjusted	1.004 (0.990, 1.018)	0.59	0.992 (0.977, 1.006)	0.26	1.011 (0.997, 1.025)	0.12	0.997 (0.979, 1.016)	0.79
O_x	Unadjusted	0.998 (0.992, 1.005)	0.64	0.995 (0.989, 1.001)	0.12	0.998 (0.991, 1.004)	0.47	0.996 (0.988, 1.003)	0.25
	Adjusted	1.0002 (0.988, 1.012)	0.98	1.003 (0.991, 1.015)	0.64	0.992 (0.980, 1.004)	0.21	1.002 (0.988, 1.017)	0.75

Per unit change. Data in bold denotes statistically significant results. Single pollutant model was adjusted for temperature and humidity.

Abbreviations: NO_x, nitrogen oxides; NO_2, nitrogen dioxide; NO, nitric oxide; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than 2.5 micrometres; O_x, photochemical oxidants; SO_2, sulfur dioxide.

Table 5 Associations between heart failure and daily lag exposure to air pollutants.

		Lag0		Lag1		Lag2		Lag0-1	
		OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value
$PM_{2.5}$	Unadjusted	0.992 (0.982, 1.002)	0.1	0.994 (0.985, 1.004)	0.24	0.999 (0.989, 1.009)	0.84	0.992 (0.981, 1.003)	0.13
	Adjusted	0.998 (0.984, 1.013)	0.81	0.993 (0.979, 1.007)	0.3	0.992 (0.978, 1.007)	0.28	0.993 (0.976, 1.010)	0.4
SO_2	Unadjusted	1.031 (0.852, 1.247)	0.75	1.037 (0.860, 1.251)	0.7	1.065 (0.880, 1.289)	0.52	1.039 (0.843, 1.279)	0.72
	Adjusted	1.101 (0.886, 1.369)	0.39	1.118 (0.903, 1.383)	0.31	1.025 (0.825, 1.272)	0.83	1.105 (0.869, 1.406)	0.42
NO	Unadjusted	0.970 (0.935, 1.007)	0.11	1.008 (0.973, 1.044)	0.67	0.995 (0.958, 1.034)	0.81	0.981 (0.935, 1.029)	0.43
	Adjusted	0.998 (0.959, 1.038)	0.9	1.025 (0.986, 1.065)	0.21	1.003 (0.962, 1.046)	0.9	1.020 (0.967, 1.075)	0.47
NO_2	Unadjusted	0.986 (0.968, 1.005)	0.14	0.984 (0.966, 1.003)	0.09	0.991 (0.972, 1.01)	0.34	0.977 (0.954, 1)	0.05
	Adjusted	1.003 (0.979, 1.027)	0.81	0.993 (0.970, 1.017)	0.56	0.993 (0.969, 1.018)	0.59	0.996 (0.966, 1.027)	0.79
NO_x	Unadjusted	0.989 (0.976, 1.002)	0.11	0.993 (0.980, 1.006)	0.3	0.994 (0.981, 1.009)	0.44	0.986 (0.969, 1.003)	0.1
	Adjusted	1.001 (0.985, 1.017)	0.91	1.001 (0.985, 1.017)	0.92	0.997 (0.980, 1.014)	0.75	1.001 (0.980, 1.023)	0.92
O_x	Unadjusted	**1.008 (1.001, 1.016)**	**0.031**	1.003 (0.996, 1.011)	0.41	1.001 (0.993, 1.009)	0.75	1.008 (0.999, 1.017)	0.08
	Adjusted	0.997 (0.982, 1.012)	0.69	0.993 (0.977, 1.008)	0.35	0.994 (0.978, 1.010)	0.45	0.992 (0.974, 1.011)	0.4

Per unit change. Data in bold denotes statistically significant results. Single pollutant model was adjusted for temperature and humidity.

Abbreviations: NO_x, nitrogen oxides; NO_2, nitrogen dioxide; NO, nitric oxide; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than 2.5 micrometres; O_x, photochemical oxidants; SO_2, sulfur dioxide.

outcomes; further, it adjusted for potential confounding variables, such as personal characteristics. Exposure was well characterised with multiple air monitoring sites throughout the Prefecture. Further, the Gunma Prefectural Comprehensive Medical Information System includes information on every cardiovascular event attended by ambulance in Gunma, meaning that we had extensive data coverage.

However, our study also has several limitations. Information data on the cases not managed through the ambulance despatch centre was not available, i.e., those who used cars rather than ambulance services to seek medical care; this could introduce selection bias. Another limitation is that the measured concentrations of ambient air pollutants may introduce personal exposure misclassification, which would bias the results towards the null; this is a common limitation of outdoor air quality studies. Further, estimation of exposure based on the location of the nearest air monitoring station to the case, while appropriate for the time of the event, might not represent the previous days' exposure for people not usually residing in that area.

Implications

The findings of this study highlight that adverse effects of air pollution on cardiovascular diseases are measurable even in areas of lower-level pollution. Policies for improving air quality (e.g., encouraging the use of electric-powered vehicles and solar or wind power generation) are being developed and implemented in many developed countries, but it is still necessary to apply such measures more widely. As vehicles represent a significant source of urban outdoor air pollution, people should be encouraged to choose public transport to reduce the number of vehicles on the roads, thus improving air quality. Additionally, individuals, especially the elderly or those who already have cardiovascular disease [3], should take practical action to protect themselves. Because outdoor air pollution is an important source of poor indoor air quality, portable air cleaners can provide a practical and efficient way for residents to reduce their exposure to air pollution [41].

Conclusion

Our study results suggest that short-term exposure to SO_2 and NO is associated with increased risk of OHCA but not with other pollutants in Gunma, Japan. Exposure to ambient air pollutants was not associated with increased risk of heart failure in this study.

Conflict of Interest

The authors declare they do not have anything to disclose regarding conflicts of interest with respect to this manuscript.

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Appendices

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2022.08.010

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