## ORIGINAL ARTICLE



# Association Between Air Pollution and Coronary Heart Disease Hospitalizations in Lanzhou City, 2013–2020: a Time Series Analysis

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Abstract Coronary heart disease (CHD) is one of the most serious public health problems. However, few studies have focused on the effects of exposure to particulate matter and gaseous air pollutants on CHD. This study aimed to explore the relationship between air pollutants and the number of hospitalized patients with CHD in Lanzhou, and we collected daily data on the number of hospitalized patients with CHD, daily air pollutants, and meteorological factors from 2013 to 2020. A distributed lag nonlinear model (DLNM) combined with a quasi-Poisson regression model was applied to evaluate the relationship between air pollutants and the number of hospitalized patients with CHD. The results indicated that the hysteresis effect of all pollutants except O<sub>3</sub>8h reached its maximum at lag3, and the relative risk of coronary heart disease admission was 1.0014 (95%CI: 1.0004, 1.0023), 1.0003 (95%CI: 1.0000, 1.0006), 1.0020 (95%CI: 1.0004, 1.0035), and 1.0053 (95%CI: 1.0026, 1.0080) when PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and SO<sub>2</sub> concentrations were increased by 10  $\mu$ g/m<sup>3</sup>, respectively. Each 1 mg/m<sup>3</sup> increase in CO concentration was associated with a

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School of Public Health, Lanzhou University, Lanzhou 730000, People's Republic of China e-mail: ruany1203@163.com relative risk of coronary heart disease; hospitalization risk was 1.1076 (95%CI: 1.0530, 1.1650). We observed a relative risk of 0.9991 (95%CI: 0.9986, 0.9999) for each 10  $\mu$ g/m<sup>3</sup> increase in O<sub>3</sub>8h for coronary heart disease admission at lag1. Women and elderly were more susceptible to the impact of air pollution, and the impact was greater during cold seasons. Our results indicate that air pollution increased the risk of hospitalization for CHD in a short term. The research findings can provide strategic insights into the impact of current and future air pollution on CHD.

**Keywords** Air pollutants  $\cdot$  Coronary heart disease  $\cdot$  Lagged effect  $\cdot$  Short-term exposure  $\cdot$  Hospitalization

## Abbreviations

CHD Coronary heart disease Distributed lag non-linear models DLNM Relative risk RR SD Standard deviation IQR Inter quartile range Q-AIC Quasi Akaike information criterion CI Confidence intervals WHO World Health Organization

## Introduction

Coronary heart disease (CHD) is a heart disease caused by stenosis or occlusion of coronary artery lumen. According to the American Heart Association,

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coronary heart disease is the leading cause of death globally [1], and the cases of coronary heart disease would increase nearly 100% by 2030 [2]. According to the data released by the World Health Organization in 2019, the number of people who die from cardiovascular diseases each year accounts for 31% of the total number of deaths worldwide, more than any other cause of death [3]. According to the Health China Action (2019–2030), there are currently 11 million patients with coronary heart disease in China, and more than 700,000 patients die of coronary heart disease. Coronary heart disease, with its high incidence rate, high mortality, and high treatment costs, has seriously restricted the further improvement of people's living standards.

Lanzhou was one of the cities with the most serious air pollution in China and even in the world. Sand and dust weather was common in Lanzhou in spring, but after decades of treatment, the frequency of sand and dust occurrence has been greatly reduced, and the level of particulate pollution has been greatly reduced. At the same time, Lanzhou is a famous chemical city, and the car ownership is high. By the end of 2021, the car ownership in Lanzhou has exceeded 1.03 million, which also makes the air condition in Lanzhou not optimistic. To sum up, Lanzhou is a city with characteristic air pollution. Therefore, we conducted a study on the relationship between air pollutants and coronary heart disease in Lanzhou.

The prevalence of coronary heart disease in 2019 was 24 times that in 1980 [4]. Facing the high burden and high pollution level of coronary heart disease, it is urgent to clarify the relationship between air pollution and coronary heart disease.

Many evidences show that air pollutants may have delayed effects on health outcomes, and the exposureresponse relationship is usually nonlinear [5]. Distributed lag nonlinear model (DLNM) is more feasible and flexible among the various methods that have been proposed to deal with delays. It has been widely used to analyze the impact of air pollution on various healthy tissues in recent years [6, 7]. But few studies have applied this model to evaluate the relationship between exposure to six air pollutants (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>8h, CO) and the risk of coronary heart disease.

In this study, DLNM was used to estimate the exposure-lag response relationship between the concentration of air pollutants and the risk of coronary heart disease; we also aim to provide strategic insights into the current and future impact of air pollution on CHD.

## **Material and Methods**

## Study Area and Period

We conducted this study in Lanzhou (102°35′-104°34′E, 35°34′-37°07′N), Gansu Province, from 1 Jan 2013 to 31 Dec 2020 (2922 days). Lanzhou has five districts and three counties under its jurisdiction (Figure S1). In 2021, Lanzhou has a permanent population of 4.3843 million. Lanzhou is located in the geometric center of northwest China and Chinese Mainland, in the middle of Gansu Province. The Yellow River flows from the southwest to the northeast, crosses the whole territory, cuts through mountains, and forms a beaded valley with valleys and basins. Lanzhou has a temperate continental climate. There is no extreme heat in summer and no severe cold in winter. It is a famous summer resort.

## The Data of Coronary Heart Disease

The inpatient data of coronary heart disease from January 1, 2013, to December 31, 2020 came from the admission and discharge data of Lanzhou local residents diagnosed as coronary heart disease in seven class III class A hospitals in Lanzhou, and these data include gender, age, home address, hospitalization date, discharge date, hospitalization diagnosis, and other information. According to the International Classification of Disease, 10th revision (ICD-10), all cases coded as coronary heart disease (I20-I25) were included in this study. The SPSS 27.0.0 was used to logically correct the inpatient data and eliminate the missing and duplicate data such as gender, age, date of visit, ICD code. Screening is carried out according to the registered residential address information of patients, and patients whose residential address is not Lanzhou City will be eliminated. Non-residents will be eliminated through the registered home address information of patients, so as to ensure that the research objects are from the local permanent residents of Lanzhou City.

#### Air Pollutants and Meteorology

The data of air pollutants (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>8h, CO) were collected from National Environmental Monitoring Station. There are four national air-quality monitoring stations in Lanzhou (Biological Products Institute, Railway Design Institute, Worker Hospital, and LanLian Hotel). These monitoring stations were far away from major roads, industrial sources, and pollutants, ensuring that the monitoring results reflect the overall air pollution level in Lanzhou. The measured data included 24-h average concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, CO, and 8-h maximum average concentrations of O<sub>3</sub>, and then the average of the four monitoring stations was used as the daily concentrations for each air pollutant, and all measurements of the ambient air pollutants were operated according to the China National Quality Control.

The type of all data was the daily municipal average. Ozone data was the maximum continuous 8-h average ozone concentration in a day

## Statistical Analysis

The daily number of inpatients with coronary heart disease was classified by sex and age, and the air pollutants and meteorological factors were expressed by maximum (Max), minimum (Min), median, mean, standard deviation (SD), and inter quartile range (IQR). Spearman's rank correlation analysis was used to estimate the relationship between air pollution and meteorological factors. The harmful effects of air pollutants on health were delayed, and the relationship was often nonlinear [8]. Therefore, DLNM was used to analyze the correlation between the daily count of coronary heart disease and the concentration of air pollutants. Both the exposure-response relationship and the hysteresis-response relationship were explained in one model [9, 10]. The event of hospitalization for coronary heart disease was a low-probability event, consistent with the occurrence of Poisson [9]. Therefore, DLNM combined with quasi-Poisson regression model was applied to the time series analysis of the impact of environmental air pollution [11]. Therefore, the specific formula is as follows:

$$Log[E(Yt)] = \alpha + \beta Xt, l + ns(Temp, df = 3) + ns(Rh, df = 3) + ns(Time, df = 7) + DOW + Holiday$$

where t is the lag day;  $Y_t$  means the number of inpatients for CHD on day t;  $E(Y_t)$  means the expected count of CHDs at day t;  $\alpha$  is the intercept;  $\beta$  represents the regression coefficient; ns is natural spline function; ns(Time) is natural cubic spline function used to control the long-term trend and seasonality of time; *ns*(*Temp*) is natural cubic spline function to control the average temperature; ns(Rh) is natural spline function to control the daily relative humidity; Holiday was utilized to control for the effect of holidays; DOW represents the indicator variable for the "day of the week effect"; df is the degree of freedom. Using ns fitted time functions, the choice of degrees of freedom is more critical, combining previous studies to choose df = 7, controlling for long-term trends and seasonality. In our study, we choose the degrees of freedom based on the minimum value of Quasi Akaike Information Criterion (Q-AIC), and a smaller value of Q-AIC indicates a better model.

The model calculated the relative risk (RR) and 95% confidence interval (CI) for each 10 µg/ m<sup>3</sup> increase in PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>8h and 1 mg/m<sup>3</sup> increase in CO under different conditions from 2013 to 2020. First, we used the single-pollution model to study the impact of different air pollutants on coronary heart disease. We set the maximum lag time to 7 days, fully study the short-term effect of air pollutants on coronary heart disease, and observe the impact of different lag days, including single-day lag (lag0-lag7) and cumulative lag (lag0-1~lag0-7). After that, we conducted subgroup analysis and divided hospitalized patients with coronary heart disease into different subgroups according to sex and age. Finally, in order to explore the impact of seasonal factors, we divided the year into cold seasons (January, February, March, October, November, and December) and warm seasons (April, May, June, July, August, and September) for analysis.

The R statistic software (version 4.2.1) and the "dlnm" package were adopted for all statistical analyses, and it is considered statistically significant when P < 0.05.

## Results

Table 1Descriptivestatistics of inpatients withCHD, air pollutants, andmeteorological factors inLanzhou during 2013–2020

Table 1 shows that from 2013 to 2020, 88,805 inpatients with coronary heart disease were included in this study, including 59,507 males (67.01%), 29,298 females (23.99%), 46,562 patients younger than 65 years old (52.43%), and 42,243 patients older than 65 years old (47.57%). And during the study, the average daily concentration of air pollutants from 2013 to 2020 was 49.70  $\mu$ g/m<sup>3</sup> (PM<sub>2.5</sub>), 114.45  $\mu$ g/m<sup>3</sup> (PM<sub>10</sub>), 21.64  $\mu$ g/m<sup>3</sup> (SO<sub>2</sub>), 45.94  $\mu$ g/m<sup>3</sup> (NO<sub>2</sub>), 1.16 mg/m<sup>3</sup> (CO), and 83.80  $\mu$ g/m<sup>3</sup> (O<sub>3</sub>8h). The average daily temperature and relative humidity were 11.13 °C and 51.19%.

Figure 1 shows the daily concentrations of different air pollutants in Lanzhou from 2013 to 2020, which showed a stable fluctuation, and the daily concentrations of  $O_3$ 8h and NO<sub>2</sub> showed an upward

Variables	Mean	SD	Min	Median	Max	IQR
Sex						
Man	20.44	15.86	0.00	16.00	103.00	21.00
Woman	10.06	8.41	0.00	8.00	57.00	11.00
Age						
Adult	16.00	13.01	0.00	13.00	87.00	17.00
Old	14.51	11.25	0.00	11.00	74.00	15.00
Total	30.51	23.54	1.00	24.00	151.00	31.00
All season						
$PM_{2.5} (\mu g/m^3)$	49.70	29.12	0.00	42.75	278.00	29.69
$PM_{10} (\mu g/m^3)$	114.45	82.37	16.00	98.63	1484.54	98.63
$SO_2 (\mu g/m^3)$	21.64	14.43	3.54	17.63	115.51	17.63
$NO_2 (\mu g/m^3)$	45.94	17.93	6.32	44.63	146.60	44.63
$O_{3}8h (\mu g/m^{3})$	83.80	43.57	8.00	76.00	462.00	76.00
$CO (mg/m^3)$	1.16	0.68	0.05	0.96	4.65	0.96
Temperature (°C)	11.13	9.87	-12.3	12.60	30.40	17.54
Rh (%)	51.19	15.28	11.71	51.85	96.09	22.00
Warm season						
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	38.73	22.87	9.00	34.61	278.00	20.78
$PM_{10} (\mu g/m^3)$	95.66	69.54	16.00	83.61	1250.00	57.08
$SO_2 (\mu g/m^3)$	14.05	8.23	3.54	12.00	67.07	8.99
$NO_2 (\mu g/m^3)$	40.22	13.18	6.32	40.82	86.00	18.48
$O_{3}8h (\mu g/m^{3})$	103.56	43.89	8.00	100.00	462.00	57.00
$CO (mg/m^3)$	0.82	0.33	0.12	0.79	2.95	0.38
Temperature (°C)	19.31	4.61	1.70	19.77	30.40	6.30
Rh (%)	51.79	15.75	11.71	52.00	96.09	22.79
Cold season						
$PM_{2.5} (\mu g/m^3)$	60.86	30.50	12.73	35.31	245.50	52.57
$PM_{10} (\mu g/m^3)$	133.58	89.65	28.00	70.41	1484.54	117.17
$SO_2 (\mu g/m^3)$	29.38	15.25	4.43	20.52	115.51	27.00
$NO_2 (\mu g/m^3)$	51.77	20.10	8.81	22.82	146.60	48.86
$O_{3}8h (\mu g/m^{3})$	63.64	32.60	11.00	32.50	442.00	59.00
CO (mg/m <sup>3</sup> )	1.52	0.77	0.05	1.04	4.65	1.35
Temperature (°C)	2.95	6.30	12.30	10.13	20.35	2.30
Rh (%)	50.62	14.78	14.33	21.81	87.90	51.00

SD standard deviation, Min minimum, Max maximum, IQR interquartile range, Rh relative humidity





trend. The daily concentration of air pollutants had obvious seasonality. The daily concentrations of  $PM_{2.5}$ ,  $SO_2$ , and CO showed a downward trend; the daily concentrations of  $PM_{10}$  showed an upward trend. The concentration of  $NO_2$ ,  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ , and CO was the highest in winter and the lowest in winter. However,  $O_3$ 8h showed the opposite trend and reached its peak in summer.

We also performed Spearman's correlation analysis for different air pollutants and meteorological factors, and the results show that the concentration of  $PM_{2.5}$ ,  $PM_{10}$ , SO<sub>2</sub>, and O<sub>3</sub>8h was positively correlated with each other,  $PM_{10}$  and  $PM_{2.5}$  were highly correlated (r = 0.850), followed by  $PM_{2.5}$ and SO<sub>2</sub> (r = 0.681), and NO<sub>2</sub> was lowly correlated with  $PM_{10}$ ,  $PM_{2.5}$ , and SO<sub>2</sub>. The concentration of CO was negatively correlated with other air pollutants. Except for O<sub>3</sub>-8h, all pollutants were negatively correlated with temperature, and the correlation coefficients ranged from - 0.578 to - 0.0358(Table S1).

Figure 2 shows the exposure-response relationship between the daily concentration of pollutants and the number of inpatients with coronary heart disease. The



relationship between the two shows a linear curve without threshold. The risk of hospitalization for coronary heart disease increases with the increase of the concentration of air pollutants ( $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ ,  $NO_2$ , CO), while the trend of  $O_3$ 8h is opposite.

Figure 3a shows the effect of 10  $\mu$ g/m<sup>3</sup> increase in air pollutant (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>8h) concentration and each 1 mg/m<sup>3</sup> increase in CO increment in single-pollutant exposure at different lag day; except for O<sub>3</sub>8h, all air pollutants contributed to the increase of the number of inpatients due to coronary heart disease. Among the five pollutants, NO<sub>2</sub> showed the strongest effect on the third day of delay, namely, CO (RR = 1.1076, 95% CI 1.0530–1.1500), SO<sub>2</sub> (RR = 1.0053, 95% CI 1.0026–1.0080), PM<sub>2.5</sub> (RR = 1.0014, 95% CI 1.053–1.165), PM<sub>10</sub> (RR = 1.0003, 95% CI 1.0001–1.0006), and NO<sub>2</sub> showed the strongest effect on the fourth day (RR = 1.0020, 95% CI 1.0004–1.0035), while O<sub>3</sub>8h showed the strongest effect on the 7th day, specifically (RR = 0.9999, 95% CI 0.9992–1.0006) (Table S3). Among all six pollutants, CO shows the strongest effect, while NO<sub>2</sub> and PM<sub>10</sub> have a weak effect. (The specific values can be seen in the supplementary table)



**Fig. 3** a Relative risk of single-day lag of CHD admissions in different gender and age for each 10  $\mu$ g/m<sup>3</sup> increase in air pollutant (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>8h) concentration and each 1 mg/m<sup>3</sup> increase in CO. **b** Relative risk of cumulative-

day lag of CHD admissions for each 10  $\mu$ g/m<sup>3</sup> increase in air pollutant (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub>8h) concentration and each 1 mg/m<sup>3</sup> increase in CO

Figure 3 b shows the relationship between cumulative lag day and relative risk of CHD admissions for each 10 µg/m<sup>3</sup> increase in air pollutant (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>-8h) concentration and each 1 mg/ m<sup>3</sup> increase in CO. Except for O<sub>3</sub>8h, other pollutants will increase the number of inpatients with coronary heart disease, and all pollutants except NO<sub>2</sub> will reach a higher risk on the third day, namely, PM<sub>2.5</sub> (*RR* = 1.0019, 95% CI 1.0007–1.0020), PM<sub>10</sub> (*RR* = 1.0003, 95% CI 0.9999–1.0006), SO<sub>2</sub> (*RR* = 1.0046, 95% CI 1.0015–1.0078), and CO (*RR* = 1.1397, 95% CI 1.0774–1.2055), and the relative risk of NO<sub>2</sub> will reach the maximum on the fourth day (*RR* = 1.0047, 95% CI 1.0029–1.0064). However,  $O_3$ 8h showed the strongest effect on the 4th day, specifically (*RR* = 0.9984, 95% CI 0.9974–0.9994) (Table S4). Among all six pollutants, CO has the strongest effect. NO<sub>2</sub>, SO<sub>2</sub>, and PM<sub>2.5</sub> have significant cumulative effects on the risk of coronary heart disease, while PM<sub>10</sub> has a weak effect. (The specific values can be seen in the supplementary table)

We grouped the hospitalized patients with coronary heart disease according to sex and age and carried out subgroup analysis. The details can be seen in Fig. 4a and b. We find that when the concentration of five air pollutants increases by 10  $\mu$ g/m<sup>3</sup> and the concentration of CO increases by 1



**Fig. 4** a Relative risk of single-day lag of CHD admissions in different gender and age for each 10  $\mu$ g/m<sup>3</sup> increase in air pollutant (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>8h) concentration and each 1 mg/m<sup>3</sup> increase in CO. **b** Relative risk of cumulative-

 $mg/m^3$ , the risk of hospitalization due to coronary heart disease is higher in men than in women, and the risk of elderly people older than 65 years old is higher than that of adults younger than 65 years old. At the same time, we also divided the year into cold season and warm season and analyzed the number of inpatients due to coronary heart disease in these two periods. We found that the risk of hospitalization in cold season was higher than that in warm season. On this basis, we divided the risk of hospitalization due to coronary heart disease by sex and age and found that the risk of hospitalization due to coronary heart disease was higher for men than for women, and the risk of elderly people older than 65 years old was higher than that of adults younger than 65 years old, which was the same as the results of the above subgroup analysis. (See the supplementary Figure S2-S3)

The contour map of the relative risk (RR) of coronary heart disease and the concentration of air

day lag of CHD admissions in different gender and age for each 10  $\mu$ g/m<sup>3</sup> increase in air pollutant (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>8h) concentration and each 1 mg/m<sup>3</sup> increase in CO

pollutants and the delayed days is shown in Fig. 5. As the concentration of pollutants increases, the risk of coronary heart disease increases. However, the change trend of each pollutant is different.

We added additional pollutants to construct the double-pollutant model (Table S2). Except for CO, all other multi-pollutant models had a higher effect on CHD admissions.

The detailed results of the sensitivity analysis are shown in the supplementary documents. (Tables S3). In the range of 6–10, the change of df has no significant effect on the connection between air pollutions with CHD.

## Discussion

This study used the DLNM to study the short-term correlation between air pollutant exposure and coronary heart disease admission rate in Lanzhou City, Gansu Province, from 2013 to 2020. The results



Fig. 5 The contour map for the association of air pollutants and lag days and CHD

indicated that short-term exposure to  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ ,  $NO_2$ , and CO are positively correlated with an increase in hospitalization rates for coronary heart disease, and there is a significant lag effect of air pollutants on the onset of coronary heart disease. Among them, except for  $O_3$ , all pollutants have a slightly greater impact on women than men, and elderly people aged  $\geq 65$  are more susceptible to the impact of air pollutants. There are differences between cold and warm seasons. In cold seasons, people are more affected by air pollutants. There is a significant correlation between the increase in air pollutant concentration and the incidence of CHD in the entire population.

The concentrations of six air pollutants are 49.70  $\mu$ g/m<sup>3</sup> (PM<sub>2.5</sub>), 114.45  $\mu$ g/m<sup>3</sup> (PM<sub>10</sub>), 21.64  $\mu$ g/m<sup>3</sup> (SO<sub>2</sub>), 45.94  $\mu$ g/m<sup>3</sup> (NO<sub>2</sub>), 1.16 mg/m<sup>3</sup> (CO), and 83.80  $\mu$ g/m<sup>3</sup> (O<sub>3</sub>8h), respectively, with concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, and NO<sub>2</sub> higher than the World Health Organization's air quality guidelines (15  $\mu$ g/m<sup>3</sup>, 45  $\mu$ g/m<sup>3</sup>, 25  $\mu$ g/m<sup>3</sup>), while SO<sub>2</sub>, CO, and O<sub>3</sub>8h comply with the World Health Organization's air quality standards. PM<sub>2.5</sub> and PM<sub>10</sub> exceed the standard by 3–4 times, making them the main pollutants in Lanzhou.

In our study, we found that  $PM_{25}$  has short-term effects and affects coronary heart disease admission. In the single-pollutant model, the impact is greatest at lag 2(RR = 1.0014, 95% CI 1.0002, 1.0019). Elderly people are more susceptible to the impact of  $PM_{2.5}$  (*RR* = 1.0019, 95% CI: 1.0000, 1.0008). Meanwhile, in warm seasons, women are more susceptible to the influence of particulate matter such as  $PM_{2.5}$ . Studies have also confirmed that when  $PM_{2.5}$ increases by 10  $\mu$ g/m<sup>3</sup>, female is associated with an increased risks in coronary heart disease, which coincides with our research findings [12]. Elevated PM<sub>2.5</sub> levels may lead to coronary heart disease, as PM<sub>2.5</sub> pollution is associated with changes in hemodynamics [13], it may cause an increase in plasma viscosity, heart rate acceleration, and so on [14]. In addition, the impact of particulate matter pollution on health varies with different particle sizes, with different physical properties, chemical components, and biological activities [15, 16]. In our study, an increase in PM<sub>10</sub> concentration had a greater impact on women. Because women have smaller coronary arteries, microvascular dysfunction seems to be more common [17]. These results are consistent with some previous studies [18, 19].

This study found that the concentration of  $NO_2$ was increasing year by year. In the single pollution model, every 10% increase of NO<sub>2</sub>  $\mu$ g/m<sup>3</sup>, the impact is greatest at lag 2 (RR = 1.0020, 95% CI 1.0004, 1.0035). The risk for women is higher than that for men, and the risk for old people (RR = 1.0021, 95%CI = 1.0003, 1.0038) is higher than adult. At the same time, the incidence risk in cold season is significantly higher than that in warm season. At present, it is unclear why there is gender difference in the impact of NO<sub>2</sub> on cardiovascular disease mortality. Elderly people are more susceptible to the impact of NO<sub>2</sub>, mainly due to their low immune system and high incidence of related basic diseases such as heart and lung [20]. Our research results are also consistent with other previous studies [21, 22].

For  $SO_2$ , our conclusion is that in a single pollution model, we observed a relative risk of 1.0053 (95%Cl 1.0026,1.0080) for each 10µg/m<sup>3</sup> increase in SO<sub>2</sub> for coronary heart disease admission at lag2, and it has a greater impact on the elderly and men, which is consistent with most previous studies. In Beijing, the relative risk (95% CI) of admission to cardiovascular emergency rooms for every 10 mg/m<sup>3</sup> of  $SO_2$ is 1.008 (95%CI: 0.999, 1.018) [23]. In the atmosphere of six cities in China, the acute impact of sulfur dioxide on population mortality can be observed. We can observe that the impact of SO<sub>2</sub> on CHD mortality varies, but there is a clear correlation [24]. At the same time, research has found that inhalation of SO<sub>2</sub> in mice leads to an increase in lipid peroxidation levels in organs, and a significant decrease in SOD, GSH-Px enzyme activity, and GSH content, leading to oxidative stress and significant changes in antioxidant activity in nine organs of mice. In addition, studies have found that SO<sub>2</sub> derivatives can cause changes in  $Ca^{2+}$ ,  $K^+$ , and  $Na^+$  and channels in myocardial cells, which have adverse effects on the cardiovascular system.

Ozone has shown a short-term protective effect in our research. The underlying mechanism needs further study. Some previous studies have proved that ozone can play the role of "protector" in some cases. Inject high-pressure ozone into the patient's blood and then inject it back into the patient's body. It can effectively improve the level of blood lipids and myocardial markers and improve exercise tolerance and cardiac ejection function. High-pressure ozone can also reduce the inflammatory reaction of vascular wall and the damage to vascular endothelium [25–27]. However, low concentration of ozone can inhibit enzyme activity, affect lipoprotein metabolism, induce systemic inflammatory reaction, and cause cardiovascular related diseases [28]. Therefore, ozone is a relatively contradictory air pollutant.

Our study found that CO was positively correlated with respiratory admission rate, and the relationship was the strongest in the cumulative lag model. When CO increases by  $1 \text{ mg/m}^3$ , the impact is greatest when the lag is 0-3 days (RR = 1.1397, 95% CI= 1.0774, 1.2055). At the same time, in the cumulative lag model, the effect of CO on women (RR = 1.1797, 95% CI = 1.1044, 1.2601) is higher than that of men, and the effect on older people older than 65 years old (RR = 1.1547, 95% CI = 1.0862, 1.2276) is higher than that of adults younger than 65 years old (RR = 1.1266, 95% CI = 1.0593, 1.1982) (see supplementary table). Many previous studies have shown that low exposure to carbon monoxide can increase blood carboxyhemoglobin concentration and aggravate myocardial ischemia [29]. Because the affinity of hemoglobin to carbon monoxide is more than 200 times that of oxygen, exposure to carbon monoxide will combine with hemoglobin, thus reducing the delivery of oxygen, leading to adverse health reactions [30]. Bell and his colleagues reported a positive and significant correlation between the day's exposure to carbon monoxide and the increased risk of hospitalization for cerebrovascular disease in the USA [31].

This study has the following advantages: First, this study was carried out in the whole city of Lanzhou, based on the total number of patients with coronary heart disease in seven tertiary hospitals in Lanzhou within 8 years, with a large sample size and complete data. Compared with some sample surveys, this study has no deviation and the results are stable. Secondly, DLNM was adopted in this study. DLNM can flexibly and conveniently analyze the lag effect between air pollution and disease, so as to conduct in-depth quantitative analysis of the relationship between the two. At the same time, quasi-Poisson regression is adopted, which has relatively loose requirements for variables. However, there are still some shortcomings in this study: First, coronary heart disease is a kind of disease caused by coronary atherosclerosis, and there are many subtypes. In our study, we only studied this kind of disease and did not further explore the relationship between air pollution and its subtypes; Secondly, our research had only explored the overall relationship between air pollution and the number of inpatients with coronary heart disease in Lanzhou. However, many people are exposed to more serious air pollution due to their occupational particularity, and our research has not taken this into account.

#### Conclusion

The results of this study show that exposure to  $PM_{2.5}$ ,  $PM_{10}$ ,  $NO_2$ ,  $SO_2$ , and CO is positively correlated with the risk of CHD, while exposure to  $O_3$  is associated with a reduced risk of CHD. Elderly people have a higher risk of developing diseases than adults. Except for  $O_3$ , women exposed to other pollutants have a higher risk of developing the disease than men. The interaction between air pollutants and CHD and its potential mechanisms needs further research. At the same time, more attention should be paid to the dangers brought by air pollution. Active measures should be taken to reduce the concentration of environmental air pollutants, thereby reducing the occurrence of CHD.

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**Data Availability** Air pollution data for this study are available at the China Environmental Monitoring General Station http://www.cnemc.cn/. Meteorological data can be accessed at http://data.cma.cn, which is managed by the National Meteorological Information Centre of China. Clinical hospital admission data are not available to the public. All analyses in this study were performed using R version 4.2.1 software, and licensing and other information are available at https://www.rproject.org. The package used to construct the distributed lag nonlinear model (DLNM) is publicly available at https://cran.r-project.

#### Declarations

**Competing Interests** We declare that we have no known competing interests or personal relationships that could have appeared to influence the work reported in this paper.

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