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Low ambient temperature and air pollution are associated with hospitalization incidence of coronary artery disease: Insights from a cross-sectional study in Northeast China

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Abstract

Background: Previous studies have established a link between fluctuations in climate and increased mortality due to coronary artery disease (CAD). However, there remains a need to explore and clarify the evidence for associations between meteorological changes and hospitalization incidences related to CAD and its subtypes, especially in cold regions. This study aimed to systematically investigate the relationship between exposure to meteorological changes, air pollutants, and hospitalization for CAD in cold regions. **Methods:** We conducted a cross-sectional study using hospitalization records of 86,483 CAD patients between January 1, 2009, and December 31, 2019. Poisson regression analysis, based on generalized additive models, was applied to estimating the influence of hospitalization for CAD. **Results:** Significant associations were found between low ambient temperature [-10°C, *RR* = 1.65; 95% CI: (1.28–2.13)] and the incidence of hospitalization for CAD within a lag of 0–14 days. Furthermore, O_3 [95.50 μg/m^3, *RR* = 12; 95% CI: (1.03–1.21)] and NO_2 [48.70 μg/m^3, *RR* = 1.0895% CI: (1.01–1.15)] levels were identified as primary air pollutants affecting the incidence of CAD, ST-segment-elevation myocardial infarction (STEMI), and non-STEMI (NSTEMI) within the same lag period. Furthermore, O_3 [95.50 μg/m^3, *RR* = 1.12; 95% CI: (1.03–1.21)] and NO_2 [48.70 μg/m^3, *RR* = 1.0895% CI: (1.01–1.15)] levels were identified as primary air pollutants affecting the incidence of CAD, ST-segment-elevation myocardial infarction (STEMI), and non-STEMI (NSTEMI) within the same lag period. The effect curve of CAD hospitalization incidence significantly increased at lag days 2 and 4 when NO_2 and O_3 concentrations were higher, with a pronounced effect at 7 days, dissipating by lag 14 days. No significant associations were observed between exposure to PM, SO_2, air pressure, humidity, or wind speed and hospitalization incidences due to CAD and its subtypes. **Conclusion:** Our findings suggest a positive correlation between short-term exposure to low ambient temperatures or air pollutants (O_3 and NO_2) and hospitalizations for CAD, STEMI, and NSTEMI. These results could aid the development of effective preparedness strategies for frequent extreme weather events and support clinical and public health practices aimed at reducing the disease burden associated with current and future abnormal weather events.

Keywords

meteorological changes; ambient temperature; air pollution; coronary heart disease; Poisson regression analysis

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1 Introduction

Amidst the backdrop of global climate change, a growing body of epidemiological and clinical evidence has heightened concerns about the potential adverse impacts of the environment on cardiovascular health, especially the risk of coronary artery disease (CAD)[1-2]. CAD encompasses a wide spectrum of ischemia-related conditions, including ST-segment-elevation myocardial infarction (STEMI), non-ST-segment-elevation myocardial infarction (NSTEMI), unstable angina, and stable angina. Previous studies have revealed a U-shaped exposure-response relationship between temperature and cardiovascular mortality, indicating elevated risk at both high and low daily temperatures[3-5]. Globally, the majority of temperature-related mortality is significantly higher in colder climates compared to warmer conditions[6-7]. While numerous studies have scrutinized the association with increased mortality, there has been limited evaluation of the links between meteorological changes in cold regions and the onset of CAD and its subtypes.

Air pollution has emerged as a pressing global public health concern, consistently linked to increased morbidity and mortality[8-9]. Nationwide and multinational studies increasingly highlight the detrimental impact of air pollution on both circulatory and respiratory systems[10-13]. Outdoor air pollutants constitute a complex blend of various components, including crucial components like airborne particulate matter (PM) and gaseous pollutants such as nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3). While many epidemiological studies have primarily focused on air pollution's association with mortality—revealing robust chronic and acute robust correlations—only a subset have adequately adjusted for potential important confounding variables. Furthermore, limited research has holistically explored the connections between multiple air pollutants in cold regions and the onset of CAD and its diverse subtypes. Both meteorological variables and air pollution stand as pivotal risk factors, demanding further investigation to enhance our understanding of their collective health impacts in cold regions. This understanding holds crucial significance for devising effective public health interventions and establishing dependable forecasts concerning the health ramifications of climate change.

Our aim in this study was to comprehensively evaluate the relationship between meteorological variables, air pollution, and the incidence of hospitalization due to CAD and its subtypes in Heilongjiang province. Situated in Northeast China, this region serves as a representative cold area. The study period spanned from 2009–2019. Employing a standard time-series Poisson model, we controlled for trends and day-to-day variations, effectively minimizing potential confounding factors stemming from long-term, seasonal, and daily patterns. To analyze these relationships, we utilized distributed lag non-linear models, providing estimates in terms of relative risk (*RR*) and 95% confidence intervals (CIs). Specifically, our examination of the meteorological variables and hospital admissions involved a distributed lag non-linear model considering a lag of 14 days. Furthermore, we assessed exposure-response relationships within this framework.

2 Methods

2.1 Clinical data

Clinical data encompassing all hospital admissions with a primary diagnosis of CAD, including its subtypes (STEMI, NSTEMI, unstable angina, and stable angina), coded as ICD-10 I20-I25, were retrieved from the case management system at The Second Affiliated Hospital of Harbin Medical University. The study period ranged from January 2009 to December 2019. Additionally, individual characteristics such as sex, age, and marital status were collected. Exclusion criteria included cases not meeting the primary diagnosis and missing meteorological data. The study area comprised Harbin city, situated in the southwest of Heilongjiang Province, Northeast China, characterized by a moderate temperate continental monsoon climate (latitude 44°04′–46°40′N, longitude 125°42′–130°10′E). Harbin experiences long winters and short summers typical of cold regions, with an annual precipitation of 423 mm, concentrated mainly in June–September, and 168 frost-free days. The city covers an area of 53,100 km^2, with 1.977 million hectares of arable land. The Medical Ethics Committee of the Second Affiliated Hospital of Harbin Medical University approved the study (KY2022-276).

2.2 Meteorology and air pollution data

Daily meteorological variables (mean temperature, mean relative humidity, mean barometric pressure, and mean wind speed) were obtained from Harbin Meteorological Observatory (126º57'E, 45º93'N). Data on environmental air pollutants including $PM_{2.5}$, PM_{10}, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3) were sourced from the Ministry of Ecology and Environment of the People's Republic of China (https: //air.cnemc.cn: 18007/), covering the period from 2013 to 2019. The monitoring station provided hourly air pollutant data, presenting 24-hour average daily concentrations.

2.3 Statistical methods

Separate Poisson generalized additive models (GAMs)[14] for time series were used to analyze data from 86,483 CAD hospitalizations. Meteorological predictors (ambient temperature, humidity, barometric pressure, and wind speed) and air pollutants, namely, NO_2, SO_2, O_3, $PM_{2.5}$, and PM_{10}, were initially modeled using non-linear polynomial constrained distributed lag models[2,15]. The associations between climatic parameters, air pollutants, and CAD occurrence were analyzed using Poisson regression as a time series model of count data[6]. We utilized distributed lag non-linear models to assess the impact of meteorological variables on CAD hospitalization and to analyze the nonlinear and delayed effects of temperature and air pollutants. Cross-basis functions were used to account for variable dimensions and lag days[16]. In CAD simulations, the impact of a specific meteorological factor is analyzed while controlling for other meteorological factors acting as confounding variables. Similarly, when studying the effects of a particular pollution factor on coronary heart disease, meteorological factors and other pollution factors are also set as confounding variables to isolate the impact of the variable of interest. The smoothing spline was used with three degrees of freedom (df) for the meteorological elements and atmospheric pollutants. Natural cubic spline (NS) DLNM models were used to analyze the nonlinear and delayed effects of temperature and air pollutants. The cross-basis function contains the dimensions of variables and lag days. The covariates tested were penalized regression splines of movement (to control for long-term trends, seasonality, and changes in the baseline rate) and meteorology (daily temperature, humidness, air pressure, and the difference between current day temperature and the mean temperature of the previous three days), as well as indicators of weekdays, vacation periods, or week, holidays, and season. According to similar studies[3], a non-linear relationship was assumed between the explanatory variable of interest and the outcome variables, considered as hospitalizations for CAD. Consider air pressure, for instance, we constructed a quasi-Poisson function that allows for overdispersion in daily CAD admissions:

$$Y_t \sim quasiPossion(\mu_t)$$

$$\begin{aligned} log(\mu_t) = \alpha + Tt,l + ns(time,df) + ns(temperature,df) + ns(air\ pressure,df) + \\ ns(humidity,df) + ns(wind\ speed,df) + \beta DOW \end{aligned}$$

Yt is the number of CAD admissions on day t, which is assumed to have followed a discrete Poisson distribution. Our study used a NS function with three degrees of freedom to smooth meteorological elements and air pollutants. A NS function with seven degrees of freedom was used to control the long-term trend over time, setting the lag period of variable exposure to 14 days. CB (air pressure) is a two-dimensional cross-basis matrix representing the mean temperature and the number of days lag included a natural cubic spline with three degrees of freedom reflecting the air pressure dimension effect and a NS function with three degrees of freedom reflecting the air pressure hysteresis effect. α represents the intercept term, and DOW denotes the week effect.

We applied multiple non-linear regression analysis models to assess the effect of each meteorological variable on CAD hospitalization. Lags of 0–14 days were considered because the impact of exposure on ambient temperature and air pollutants were evidenced not only on the same day but also days after exposure.

The correlation between air pollutants and weather conditions was estimated using the Spearman correlation. Modeling coped with overdispersion for the response variable and collinearity for the explanatory variables. The Akaike information criteria was used to select the best model. Data analysis was conducted using the R software (The Comprehensive Archive Network: http: //cran.r-project.org/) applying the "mgcv" and "dlnm" packages. The Kolmogorov-Smirnov method was used to test the normality of the measurement data, and the standard deviation of the mean was used when following the normal distribution, the *T*-test was used for the comparison between groups, and the median and quartile interval were used when the normal distribution was not obeyed. Counting data is expressed as a percentage of examples. A *P*-value ≤ 0.05 was considered statistically significant.

3 Results

3.1 Descriptive statistics for study variables

A total of 86,483 cases of CAD were included in our study at the Second Affiliated Hospital of Harbin Medical University between January 1, 2009, and December 31, 2019. These comprised 12,030 (13.91%) cases of STEMI, 5,864 (6.78%) of NSTEMI, 57,243 (66.19%) of unstable angina, and 11,346 (13.12%) of stable angina. Of the cases, 48,663 (56.27%) were male and 37,820 (43.73%) were female, with an average age of 62.0 years (range: 55.0–69.0 years). The daily average of hospitalization for CAD was 7.0 (5.0–10.0) days.

In the analysis of meteorological variables and air pollutant concentration 14 days preceding the onset of disease in patients, significant associations were observed with short-term exposure to NO_2 [37.04 μg/m^3, range: 27.9–48.7 μg/m^3, *RR* = 1.08; 95% CI: (1.01–1.15)], O_3 [68.25 μg/m^3, range: 46.6–95.50 μg/m^3, *RR* = 1.2; 95% CI: (1.03–1.21)], and low-temperature levels [6.8°C, range: -10°C–19°C, *RR* = 1.65; 95% CI: (1.28–2.13)]. These findings were significant in relation to the incidence of CAD, STEMI, and NSTEMI, as presented in Fig. 1.

As illustrated in Fig. 1, the collective influence of NO_2, O_3, and low temperature on the lag time of CAD onset spanning from 2006 to 2011 was evaluated. The results indicate a nonlinear effect of NO_2 on incidence, revealing that the risk of CAD onset increases when NO_2 levels are low (below 38 μg/m^3) with an *RR* of less than 1. Calculating the cumulative effect revealed that the risk of incidence increased within a temperature range between -20 degrees and 8 degrees, with an *RR* and 95% CI exceeding 1. However, once the temperature surpassed 22 degrees, the risk of CAD onset declined with escalating daily average temperature, as evidenced by the curve positioned below the reference line.

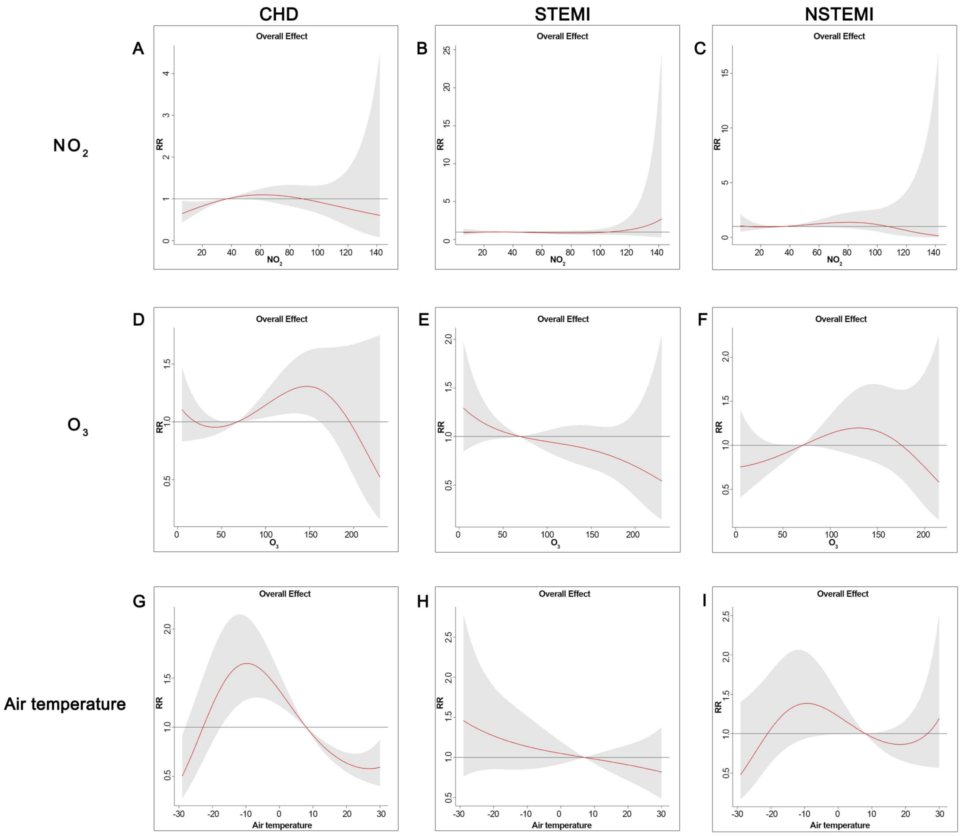

Fig. 1 Cumulative relative risk (*RR*) over lag 0–14 days and 95% empirical CI (shaded grey) of NO_2, O_3, and air temperature on hospitalization incidences of CAD, STEMI, and NSTEMI. Smooth red lines (A–C) represent *RR*s for nitrogen dioxide (NO_2); (D–F) denote O_3; (G–I) depict air temperature. CAD: coronary heart disease; STEMI: ST-segment-elevation myocardial infarction; NSTEMI: non-ST-segment-elevation myocardial infarction; NO_2: nitrogen dioxide.

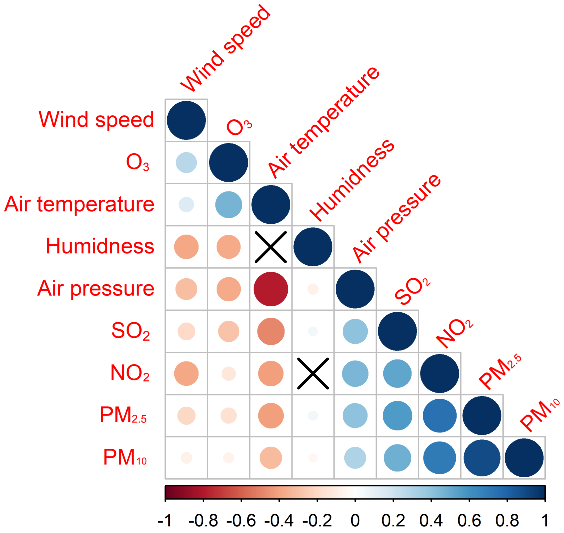

Fig. 2 Spearman correlations between variables. $PM_{2.5}$: particulate matter with aerodynamic diameter ≤ 2.5 μm; PM_{10}: particulate matter with aerodynamic diameter ≤ 10 μm; SO_2: sulfur dioxide; NO_2: nitrogen dioxide.

Notably, no significant associations were found between unstable angina and stable angina concerning the cumulative effect (Fig. S1). Regarding other variables ($PM_{2.5}$, PM_{10}, SO_2, air pressure, humidness, and wind speed), the cumulative effect curve consistently exhibited non-significance for CAD and its subtypes (Fig. S2 and S3).

The meteorological data description and *RR* of hospitalization for CAD and its subtypes under different seasonal conditions are summarized in Table S1.

During the study period, the investigation into seasonal variations in CAD involved comparing hospitalizations across distinct seasonal groups. The year was segmented into four seasons: winter (December, January, and February), spring (March, April, and May), summer (June, July, and August), and autumn (September, October, and November). Based on the lag response curves (Fig. S4) and exposure-response curves (Fig. S5 and S6), no significant risks were observed in the overall CAD hospitalization incidence across different seasons.

3.2 Spearman's correlation coefficients between variables

Spearman's correlation coefficients for associations between various meteorological factors and air pollutants are presented in Fig. 2 and Table S2.

Daily mean concentrations of pollutants and meteorological factors were correlated. Fig. 2 illustrates a positive and statistically significant correlation among air pollutants SO_2, NO_2, $PM_{2.5}$, and PM_{10}. The correlation between $PM_{2.5}$ and PM_{10} is particularly strong, with a coefficient of 0.897. On the other hand, O_3 shows a negative correlation with other atmospheric pollutants, indicating potential collinearity. Furthermore, except for the air pressure, meteorological factors (humidity, temperature, wind speed) showcase a negative correlation with air pollutants.

3.3 Poisson time-series regression models

Descriptive data for meteorological variables and air pollution levels (*RR*s and 95% CI) regarding hospitalizations for CAD and its subtypes during the study period are outlined in Table 1. An increase in concentrations within the interquartile range of NO_2 [11.33 μg/m^3, *RR* = 1.08 (95%CI: 1.01–1.05)] and O_3 [68.25 μg/m^3, *RR* = 1.12 (95% CI: 1.03–1.21)] over the 0–14 days was significantly associated with a higher risk of CAD hospitalizations. Specifically, concentrations of 37.04 μg/m^3, *RR* = 1.16 (95%CI: 1.03–1.32) and 68.5 μg/m^3, *RR* = 1.24 (95% CI: 1.06–1.45) correlated with patients diagnosed with STEMI, while 36.38 μg/m^3, *RR* = 1.48 (95% CI: 1.22–1.81) was observed for patients with NSTEMI. The lag response effect is depicted in Fig. 3.

Our data revealed a significant association between low ambient temperature (6.8°C, range = 10°C–19°C, *RR* = 1.65, 95% CI: 1.28–2.13) and the risk of CAD hospitalizations. Conversely, relatively higher ambient temperatures were identified as a potential protective factor for hospitalization incidence of CAD (*RR* = 0.65, 95% CI: 0.57–0.75), STEMI (*RR* = 0.78, 95% CI: 0.63–0.95), and NSTEMI (*RR* = 0.68, 95% CI: 0.52–0.89).

Fig. 4 depicts the exposure-response relationships between O_3, NO_2, and low temperature concerning hospitalizations for CAD, STEMI, and NSTEMI, considering lagged days while controlling for confounders in time-series analysis. Significant associations were found between low-temperature levels and hospitalizations for CAD at lag 2, 4, 7, and 14 days, with the association disappearing at lag 14 days. However, no significant relationship was established between low temperature and the onset of STEMI or NSTEMI.

In single-pollutant models, elevated levels of NO_2 and O_3 were

Table 1 Descriptive summary statistics of meteorological variables and air pollutants, with relative risk (RR) of hospitalizations for CAD, STEMI, NSTEMI, Unstable angina, Stable angina from 2010-2020.

Variable	CAD		STEMI		NSTEMI		Unstable angina		Stable angina	
	Median (IQR)	*RR*	Median (IQR)	*RR*	Median (IQR)	*RR*	Median (IQR)	*RR*	Median (IQR)	*RR*
$PM_{2.5}$	31.330 (16.830, 64.920)	0.960 (0.930-1.000) 1.070 (0.990-1.160)	31.000 (16.790, 64.530)	1.010 (0.960-1.050) 0.970 (0.890-1.060)	54.300 (35.170, 89.790)	0.960 (0.890-1.020) 1.110 (0.950-1.290)	31.125 (16.690, 64.580)	0.950 (0.910-1.000) 1.100 (1.000-1.220)	31.290 (16.830, 64.810)	0.980 (0.920-1.030) 1.040 (0.930-1.150)
PM_{10}	58.120 (37.350, 69.200)	0.970 (0.930-1.000) 1.050 (0.980-1.130)	57.950 (37.230, 96.550)	1.010 (0.960-1.060) 0.970 (0.890-1.050)	27.080 (14.680, 54.920)	0.990 (0.930-1.050) 1.080 (0.890-1.330)	58.000 (37.330, 96.440)	0.950 (0.900-1.000) 1.100 (1.000-1.020)	58.120 (37.350, 96.600)	0.950 (0.890-1.010) 1.070 (0.960-1.180)
SO_2	37.040 (6.600, 23.200)	0.990 (0.920-1.070) 0.950 (0.830-1.090)	11.280 (6.540, 22.730)	0.900 (0.830-0.980) 1.190 (1.030-1.380)	9.890 (6.000, 18.300)	11.000 (0.990-1.230) 0.850 (0.710-1.010)	11.310 (6.540, 23.130)	1.070 (0.980-1.170) 0.820 (0.700-0.960)	11.330 (6.580, 23.150)	1.060 (0.990-1.150) 0.910 (0.800-1.030)
NO_2	11.330 (27.900, 48.700)	0.920 (0.870-0.970) 1.080 (1.010-1.150)	37.440 (27.830, 49.000)	0.910 (0.830-0.990) 1.160 (1.030-1.320)	36.380 (27.710, 47.820)	0.820 (0.690-0.980) 1.480 (1.220-1.810)	37.105 (27.920, 48.740)	0.940 (0.880-1.000)	37.040 (27.880, 48.710)	0.920 (0.850-0.990) 1.030 (0.950-1.120)
O_3	68.250 (46.600, 95.500)	0.960 (0.910-1.000) 1.120 (1.030-1.210)	68.500 (49.630, 96.060)	0.900 (0.830-0.990) 1.240 (1.060-1.450)	71.260 (48.000, 100.130)	0.790 (0.650-0.970) 1.010 (0.790-1.290)	68.250 (46.600, 95.620)	0.910 (0.850-0.970) 1.190 (1.060-1.340)	68.250 (46.600, 95.510)	0.960 (0.900-1.040) 1.220 (1.050-1.420)
Air pressure	1014.200 (1007.000, 1022.000)	0.930 (0.850-1.020) 1.080 (0.970-1.200)	1014.300 (1007.100, 1022.700)	1.010 (0.900-1.120) 1.050 (0.920-1.200)	1013.500 (1006.800, 1022.200)	0.850 (0.710-1.010) 1.250 (1.030-1.510)	1014.300 (1007.000, 1022.700)	0.970 (0.860-1.090) 1.040 (0.900-1.210)	1014.200 (1007.000, 1022.700)	1.080 (0.960-1.220) 0.920 (0.790-1.080)
Air temperature	6.800 (-10.000, 19.000)	1.650 (1.280-2.130) 0.650 (0.570-0.750)	6.800 (-10.000, 18.000)	1.070 (0.810-1.420) 0.780 (0.630-0.950)	8.500 (-7.850, 18.900)	1.080 (0.660-1.780) 0.680 (0.520-0.890)	6.800 (-10.000, 18.800)	0.950 (0.710-1.260) 0.680 (0.560-0.830)	6.800 (-10.000, 18.900)	0.840 (0.700-1.010) 0.970 (0.860-1.100)
Humidness	66.000 (55.000, 75.000)	1.010 (0.940-1.080) 1.020 (0.960-1.090)	66.000 (54.000, 75.000)	1.070 (0.960-1.180) 1.040 (0.970-1.180)	65.000 (52.000, 75.000)	0.910 (0.790-1.060) 1.020 (0.900-1.150)	66.000 (54.000, 75.000)	1.110 (1.000-1.230) 0.950 (0.880-1.030)	66.000 (54.000, 75.000)	0.960 (0.840-1.090) 0.980 (0.900-1.080)
Wind speed	2.600 (1.900, 3.600)	1.010 (0.930-1.080) 1.020 (1.000-1.050)	2.600 (1.900, 3.600)	1.000 (0.900-1.100) 1.040 (0.980-1.100)	2.700 (2.000, 3.600)	1.170 (1.010-1.360) 0.880 (0.820-0.960)	2.600 (1.900, 3.600)	0.860 (0.780-0.950) 0.940 (0.880-1.000)	2.600 (1.900, 3.600)	0.850 (0.750-0.970) 0.990 (0.910-1.070)

CAD: coronary artery disease; STEMI: ST-segment-elevation myocardial infarction; NSTEMI: non-ST-segment-elevation myocardial infarction; IQR: inter-quartile range; *RR*: Relative risk; $PM_{2.5}$: particulate matter with aerodynamic diameter ≤ 2.5μm; PM_{10}: particulate matter with aerodynamic diameter ≤ 10μm; SO_2: sulfur dioxide; NO_2: nitrogen dioxide.

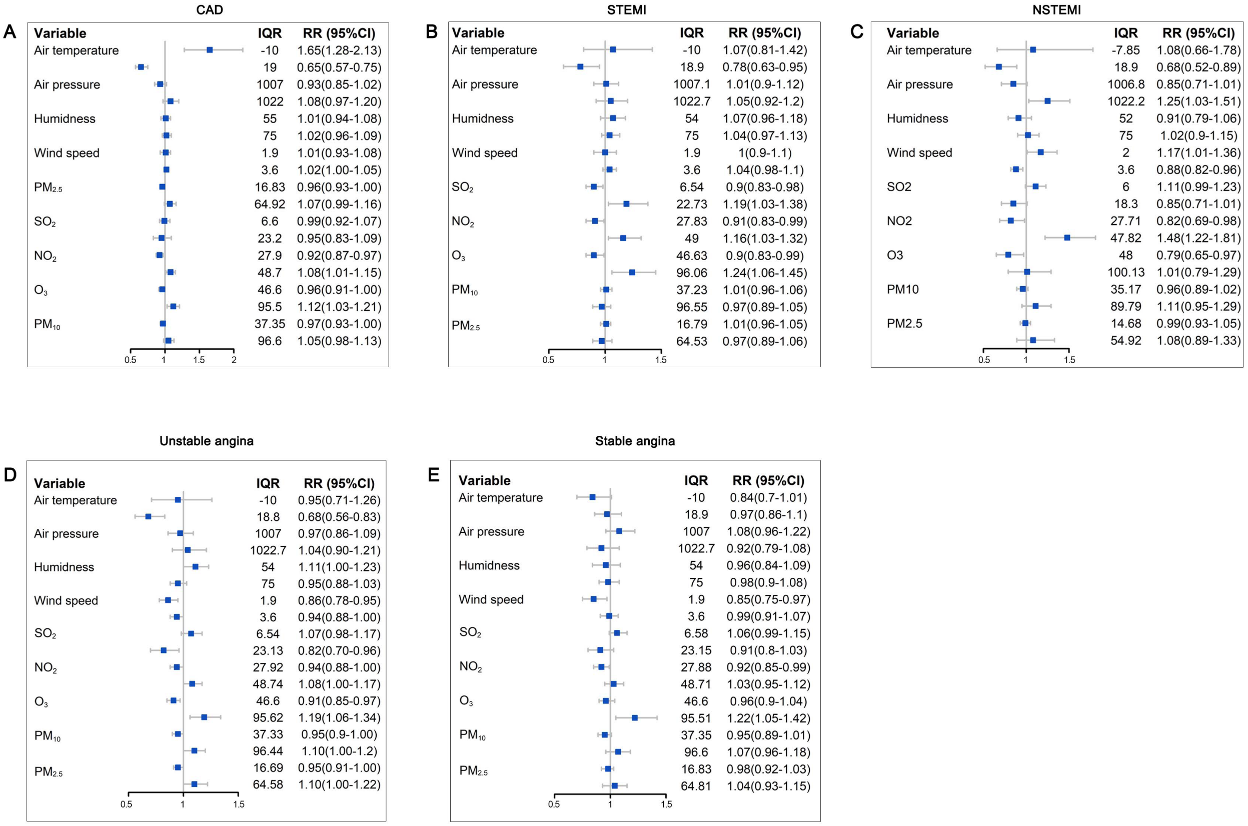

Fig. 3 Lag response for associations with hospitalizations for CAD and its subtypes with meteorological variables and air pollution concentrations. CAD: coronary artery disease; STEMI: ST-segment-elevation myocardial infarction; NSTEMI: non-ST-segment-elevation myocardial infarction; $PM_{2.5}$: particulate matter with aerodynamic diameter ≤ 2.5 μm; PM_{10}: particulate matter with aerodynamic diameter ≤ 10 μm; SO_2: sulfur dioxide; NO_2: nitrogen dioxide.

significantly associated with increased risks of CAD, STEMI, and NSTEMI at lags of 2, 4, 7, and 14 days. In contrast, higher concentrations of PM_{10} (*RR* = 1.05, 95% CI: 0.98–1.13) and $PM_{2.5}$ (*RR* = 1.07, 95% CI: 0.99–1.16) exhibited non-significant association with CAD hospitalizations across multiple lags. SO_2 exhibited no correlation with CAD incidence. Moreover, short-term exposure to climate parameters such as air pressure, humidity, or wind speed did not significantly correlate with CAD occurrences. The *RR* consistently demonstrated similar trends across various lag days, and no statistically significant relationship was found between air pressure, humidity, and wind speed concerning the onset of CAD (Fig. S7). Distributed lag models suggested that the risk of CAD hospitalizations escalated with increasing levels of O_3, NO_2, and low temperature during the study period, as observed in both meteorological variables and air pollutants.

4 Discussion

The present investigation delved into the impact of meteorological variables and air pollution on CAD hospitalizations in Heilongjiang province, northeast China, characterized by a moderate temperate continental monsoon climate. We analyzed the association between temperature, humidity, barometric pressure, wind speed, and air pollutant concentrations with CAD hospitalizations using time-series regression methods. Our analysis considered both non-linear and lagged effects for meteorological parameters, setting the maximum lag at 14 days to account for delayed and prolonged impacts, particularly notable in the context of cold temperature effects[17]. Hospitalization, being a countable and discrete event, led us to employ Poisson regression to estimate the *RR*s associated with exposure and hospital admissions. Our study robustly demonstrated robust associations between short-term exposures to low ambient temperature, O_3, and NO_2, and increased risks of hospitalizations for CAD and its subtypes.

The CI for the *RR* of CAD admission were computed based on values derived from the generalized linear model and their respective standard deviations. Notably, low ambient temperature emerged as a significant factor linked to CAD hospitalization, while the impact of O_3 and NO_2 concentrations on heightened

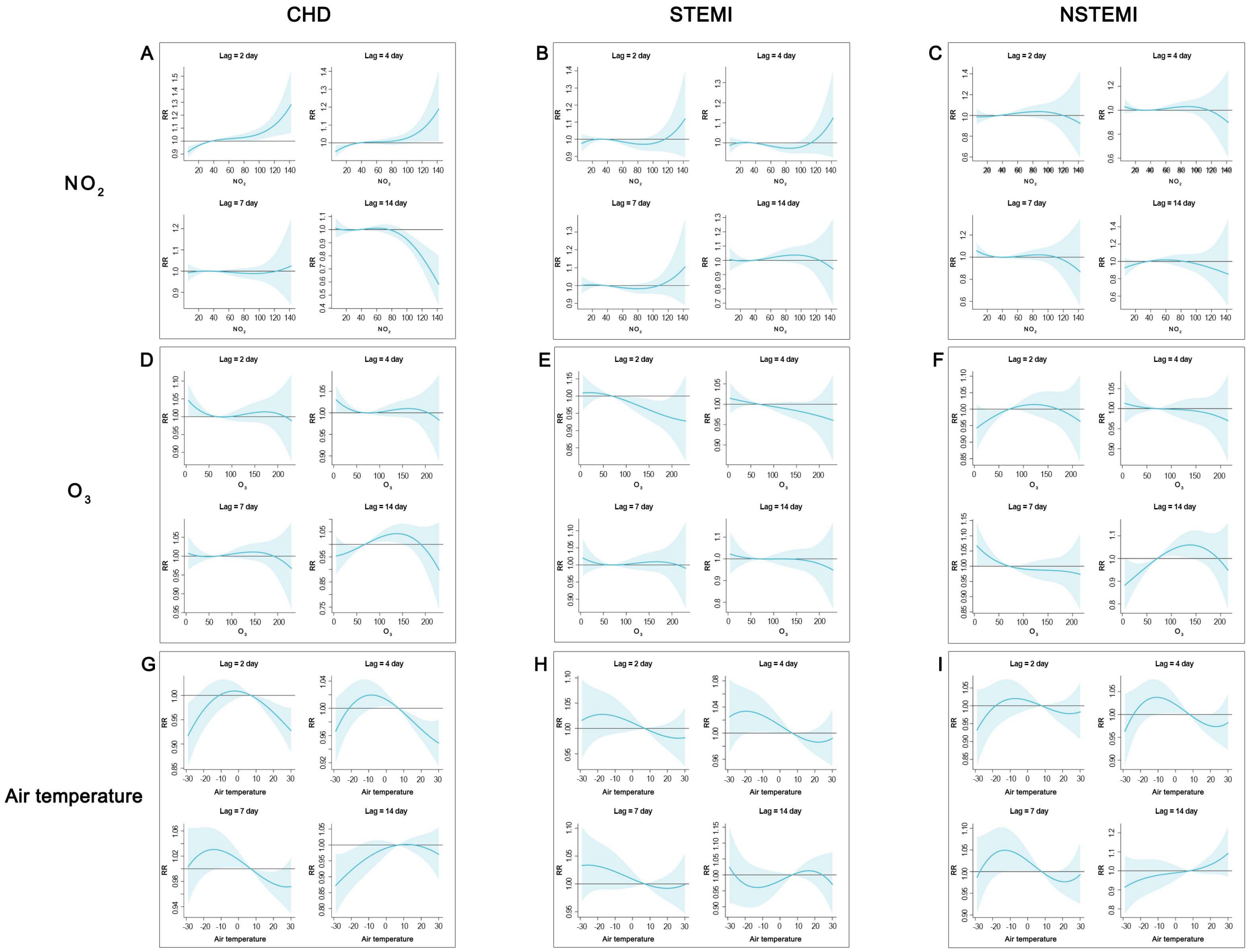

Fig. 4 Exposure-response curve for t hospitalizations due to CAD, STEMI, and NSTEMI in relation to NO_2, O_3, and air temperature at lag 2, 4, 7, 14 days. (A–C) Nitrogen dioxide (NO_2); (D–F) O_3; (G–I) O_3. *RR*: Relative Risk; CAD: coronary heart disease; STEMI: ST-segment-elevation myocardial infarction; NSTEMI: non-ST-segment-elevation myocardial infarction; NO_2: nitrogen dioxide.

CAD risk was more pronounced compared to other air pollutants. This observation implies that CAD-related hospitalizations are likely to rise within CAD within a few days. Throughout our analyses, PM_{10}, $PM_{2.5}$, SO_2 concentration, air pressure, humidity, and wind speed did not show any significant association with CAD hospitalization. This suggests either their minimal role or no direct contribution to the acute onset of CAD in this context. These results provide valuable insights into the impact of meteorological variables on health outcomes. They serve as a basis for informing the development of effective preparedness strategies, particularly in anticipation of frequent extreme weather events.

While numerous studies have predominantly focused only on assessing the mortality risks associated with cold temperatures, only a limited number have explored the effects of meteorological variables and air pollution on CAD-related hospitalizations. It is noteworthy that both high and low temperatures have demonstrated associations with all-cause mortality across diverse populations[18]. Several proposed mechanisms suggest how exposure to cold temperatures might elevate the risk of acute myocardial infarction. Cold stress has been linked to increased blood pressure, cardiac hypertrophy[19], blood viscosity[20], and platelet counts[21]. A prospective study investigating the relationship between air temperature and risk factors for ischemic heart disease highlighted the primary impact of cold temperatures on the hemostatic system, leading to increases in fibrinogen and α2 macroglobulin[22]. Moreover, our results align with previous studies examining the correlation between ambient temperature and cardiovascular mortality[23-25]. Notably, our data demonstrated no significant associations between other meteorological variables (air pressure, humidity, and wind speed) and CAD-related hospitalizations. It appears that the impact of temperature on CAD incidence is more long-term, spanning weeks or even months, unlike the more immediate effects observed with air pressure or wind speed. Establishing a direct cause-and-effect relationship becomes challenging without sufficient data delineating the potential impact of climate on the pathophysiological mechanisms underlying CAD. Future research endeavors and data collection efforts should emphasize specific geographical and environmental contexts to deepen our understanding of these relationships. Air pollution-triggered diseases have become a prominent global health concern. The World Health Organization reports a staggering toll of 4.3 million deaths annually attributable to indoor air pollution and 3.7 million deaths linked to outdoor air pollution[26]. Outdoor air pollution primarily stems from industry activities, transportation, and various combustion processes, such as those in heating and power-generation systems. This pollution comprises PMs and gaseous pollutants like SO_2 and NO_2. $PM_{2.5}$ and NO_2, primarily originating from motor vehicles in urban areas, a often serve as indicators of traffic-related pollution. Consistent with prior studies[10,13,27-28], our study corroborates a significant link between exposure to air pollution and the incidence of cardiovascular diseases. Specifically, our results indicate that elevated ambient concentrations of NO_2 and O_3 are associated with a short-term increased risk of CAD-related hospitalization. However, we did not observe convincing effects of SO_2 exposure. Previous studies have consistently reported an association between $PM_{2.5}$ and hospital admissions due to cardiac conditions within the general population[27,29]. Notably, a case-crossover study spanning 2009 to 2013 highlighted an association between STEMI and NO_2, demonstrating a significant impact[30]. The physiological mechanisms underpinning the relationship between air pollution and cardiovascular events are multifaceted. From a hemodynamic standpoint, this involves systemic and localized oxidative stress and inflammation, triggering endothelial dysfunction, platelet hyperreactivity, and impaired vascular fibrinolytic function[31]. These factors may suggest a predisposition to thrombotic phenomena or a hypercoagulable state. In addition, increased levels of high-sensitivity C-reactive protein levels due to air pollution, coupled with respiratory tract infections, are associated with stress and tachycardia. Given that virtually the entire population is exposed involuntarily to this risk factor, the collective health burden is amplified. The results of the current study underscore the critical importance of recognizing air pollution as a modifiable risk factor for cardiovascular diseases, which stand as the leading cause of mortality in China. This issue substantially contributes to a severe economic burden, leading to substantial loss of productivity and affecting the gross domestic product value.

The sensitivity of individuals in in developing countries to extreme temperatures can often surpass that of those in developed nations due to insufficient or absent public health infrastructure and limited coping abilities. China, as the largest developing country, faces a notably high incidence of CAD, contributing to 24.7% of global CAD deaths[32]. Numerous studies have documented increased morbidity and mortality from chronic diseases in regions with higher latitudes or colder climates[33-34]. China's expansive territory exhibits significant spatial heterogeneity in climatic conditions, economic development, and industrial structure across different regions[28]. The interplay of climatological, socioeconomic, demographic, and infrastructural factors has been identified as modifiers influencing the relationship between temperature and mortality[35]. On the other hand, these factors can inadvertently contribute to global warming through CO_2 emissions stemming from electricity consumption. Likewise, environmental factors linked to health risks hinge not solely on temperature but also on various other factors, including the level of urbanization, individual sensitivities, adaptability, and infrastructure conditions such as the availability of air conditioning, healthcare access, and medical resources. It is crucial to note that this study solely focuses on short- and intermediate-term risks, thereby potentially overlooking long-term risks. This limited scope might suggest that the effect of air pollution on CAD could be significantly greater than what this estimation of risk magnitude suggests independently. Future research is warranted to delineate the relationship between meteorological variables, air pollution, and CAD, along with identifying other conditions that might exacerbate vulnerability to these factors.

This study acknowledges several limitations that merit consideration. Firstly, we did not consider preexisting diseases, comorbidities, socioeconomic factors like income, education, or access to amenities such as air conditioning. These unaccounted factors might have influenced the estimated effects of temperature or air pollution on CAD admissions. Secondly, disparities in medical resources distribution and variations in patients' economic circumstances or treatment preferences might lead to some patients not seeking hospitalization. This selection bias complicates establishing a causal association between meteorological variables and CAD. Lastly, short-term fluctuations in meteorological conditions, including seasonal variations and temperature changes, may have impacted our study's conclusions. Validation through multicenter studies with expanded sample sizes would further solidify these findings. Nonetheless, the present study contributes significantly by providing a theoretical framework for public health decision-making, disease prevention, meteorological early warning systems in Heilongjiang province, and mitigating health and economic losses due to climate change.

5 Conclusion

In conclusion, our study presents robust evidence linking hospitalization for CAD, STEMI, and NSTEMI, with low ambient temperature, as well as O_3 and NO_2 concentrations. Conversely, the association with other meteorological variables (pressure, humidity, and wind speed) did not show statistical significance. Multiple intertwined mechanisms likely contribute to the phenomenon. Cold weather and exposure to air pollution emerge as noteworthy modifiable risk factors in preventing CAD and other chronic non-communicable diseases. However, further research is imperative to enhance our comprehension of how weather and climate directly and indirectly impact human health.

Author contribution

Conceived and designed the experiments: Rui J, Wang Y C. Data acquisition: Liu Y and Zhao G N. Data analysis and interpretation: Li Y Y. Manuscript writing and critical revision: Rui J and Wang Y C.

Ethnical Approval

The Medical Ethics Committee of the Second Affiliated Hospital of Harbin Medical University approved the study (KY2022-276).

Competing interests

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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Conflict of interest

Wang Y C is an Editorial Board Member of Frigid Zone Medicine. The article was subject to the journal's standard procedures, with peer review handled independently of him and his research groups.

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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