The cold effect of ambient temperature on acute aortic dissection hospital admission: utilizing distributed lag nonlinear analysis

Qian-Ru Zhang
Anhui Medical University
Kai-Di Li
Anhui Medical University
Yi-Yu Wang
Anhui Medical University
Hua Wang
Anhui Medical University
Xian-Bao Li
Anhui Medical University
Ji-Rong Zhu
Anhui Provincial Hospital
Bao-Zhu Li (lbz88730@163.com)
Anhui Medical University

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Abstract

The effects of ambient temperature on acute aortic dissection (AAD) admissions in China have not been well addressed. So, the aim of study was to explore the effect of ambient daily mean temperature for AAD admissions, especially in Hefei, China. Data on daily mean temperature, daily maximum temperature, daily minimum temperature, air pressure, relative humidity and AAD admissions in Hefei were obtained between 2015 and 2020. Distributed lag non-linear model was employed to determine the association between daily ambient temperature and AAD admissions. Relative risk (RR) with 95% confidence interval (CI) were calculated based on gender, age group and hypertensive status. A total number of 1648 AAD admitted cases were documented. A non-linear acute effect of cold temperature on AAD was evaluated. Compared with median reference temperature (17.56 °C), the cumulative RR of extreme low temperature increased the risk of AAD admissions. The cumulative effect was at lag 0 day (RR: 1.639, 95% CI: 1.120, 2.398), and got the peak at lag 3 days (RR: 2.176, 95% CI: 1.345, 3.519). Then the effect size was gradually reduced until lag 8 days (RR: 1.953, 95% CI: 1.010, 3.776). The impact of extreme low temperature on AAD admissions was found to be more obvious in male, the elderly, and hypertensive patients. Overall, exposure to extreme low temperature was associated with increasing AAD daily admissions risk in Hefei, China.

Introduction

Acute aortic dissection (AAD) is the clinical manifestation of acute aortic syndrome, and it is also one of the most life-threatening cardiovascular emergencies (Guo et al., 2021). Once the symptoms of AAD onset, they could threaten human life and have a high mortality. Although the treatment of AAD with advanced treatments, and the mortality rate of AAD is still high (Erbel, 2018; Pape et al., 2015). In China, the total number of AAD cases is increasing, which has brought a heavy burden to the government and the public. Thus, the factors that affecting AAD need to be identified for AAD prevention.

At present, the impact of ambient temperature on humans has received more and more attention. The direct evidence shows that there is a significant association between ambient temperature and cardiovascular disease. For example, Tian et al. analyzed the national time series and found that exposure to short-term variability of temperature can increase the risk of cardiovascular disease (Tian et al., 2019). Mohammad et al. discovered that low temperature is linked to cardiovascular disease (Mohammad et al., 2020). Temperature change between neighbouring days has been found to be linked with adverse cardiovascular outcomes (Lei et al., 2021). Published articles reported that the changes in hemodynamics and the increased risk of thrombosis at the low temperature environment may account for the occurrence of cardiovascular disease and mortality (Cheng et al., 2020; Park et al., 2020; Phung et al., 2016). However, the conclusions in published articles are inconsistent. A study has found that the admissions for cardiovascular disease is related to high temperature, which may increase the burden especially in the context of global warming (Lu et al., 2020). The incidence rate of AAD was the highest in winter and the lowest in summer (Xia et al., 2020). A study has found that a low temperature environment can increase the risk of AAD (Yu et al., 2021), and a significant association between cold temperature and the AAD was discovered by a linear regression analysis (Sadamatsu et al., 2020). Seasonal variation suggests that ambient temperature may be an important environmental risk factor for AAD. But insufficient evidence between AAD and the temporal changes of temperature. Furthermore, exposure-response relationship between daily mean temperature and first admissions for AAD is still unclear. Therefore, we want to explore the correlation between admissions of AAD and the daily mean temperature in Hefei.

To address these knowledge gaps, we conducted a statistical analysis of 6-year time series study based on AAD admissions. Moreover, the temperature effect has an obvious delay, the influence of the ambient temperature on the disease not only appear in a short-term but also after some days (Bao et al., 2016). In order to make our results more robust and credible, we need to use flexible statistical models to perform temperature and AAD admissions time series studies. Here, the Poisson regression model combined with distributed lag nonlinear model (DLNM) is utilized, which can simultaneously represent the nonlinear exposure-response dependence and delay effects. This method is based on a "cross basis" with a two-dimensional function space (Gasparrini et al., 2010). Regarding this method, it has been widely used to discover the relationship between environmental pollution and human health or disease. For example, extreme temperatures on cerebrovascular mortality (Rodrigues et al., 2019) and the association between ambient temperature and preterm birth (Liang et al., 2016). The aim of our study is to analyze the correlation between daily mean temperature and AAD admissions with DLNM.

Methods

Data resource

Hefei is the capital of Anhui province and located in the middle of Anhui. It occupies a total area of 11,445 square kilometers, with a permanent population of 5,118,200 in the urban area (http://www.hefei.gov.cn/mlhf/index.html). In this study, we obtained all AAD admissions in the First Affiliated Hospital of University of Science and Technology of China (Anhui provincial hospital) from January 1, 2015 to December 31, 2020. The collected hospitalization information of AAD patients includes age, gender, home address, hospitalization date, and hypertension status. In addition, AAD is defined as dissection onset no more than 14 days (Yu et al., 2021) and the gold standard is CT angiography of the aorta. The exclusion criteria were as follows. (1) Iatrogenic aortic disease secondary to previous cardiac surgery or interventional repair. (2) Unidentified atherosclerosis without any evidence of multi-row computed tomography or echocardiography. (3) Traumatic AAD. (4) Exclude chronic dissection; more than 14 days is chronic aortic dissection. (5) Permanent residence outside Hefei. (6) Patients with congenital arterial malformations, Marfan syndrome, connective tissue disease, vasculitis and Loeys-Dietz syndrome.

Our meteorological data includes daily mean temperature, daily maximum temperature, daily minimum temperature, air pressure and relative humidity. Daily air quality data includes aerodynamic diameter < 10μm (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2). The above data comes from China Meteorological Data Network (http://data.cma.cn/) and China National Environmental Monitoring Center (https://www.aqistudy.cn/historydata/).

Time Series Analyses

Meteorological factors (daily mean temperature, daily maximum temperature, daily minimum temperature, air pressure, relative humidity) and air pollutants (PM_{10}, SO_2, NO_2). Median, standard deviation, minimum, maximum, 25th percentile (P25) and 75th percentile (P75) parameters were used to describe data in descriptive analysis. Spearman correlation analysis was used to explore meteorological and air pollutants variables. If variables have a strong correlation, and we selectively eliminated during model fitting to avoid possible collinearity problems. As far as we know, the association between temperature and disease generally shows a non-linear trend (Chen et al., 2018). The DLNM statistical model was used to evaluate the two-dimensional relationship for the data with "cross-basis" function. DLNM not only can express the relationship of exposure-response between temperature and AAD, but also imply the non-linear hysteresis effect for both (Gasparrini et al., 2010). As in previous studies, we use a natural cubic spline to control the influence of air pollutants, including PM_{10}, NO_2, SO_2, air pressure and relative humidity (Zhang et al., 2020). Furthermore, based on the conclusions of published articles that the cold effect can last for several weeks, we used a 28-day lag period for AAD (Li et al., 2016). According to the quasi-Poisson Akaike information criterion (Q-AIC) for temperature and lag with 3 degrees of freedom. We control long-term trends with 7 degrees of freedom per year (Pan et al., 2021). The basic model is shown as below:

$Y_t \sim \text{Poisson}(\mu_t)$

$\text{Log}(\mu_t) = \alpha + \beta * \text{temp}_{t,l} + \text{ns}(PM_{10}, 3) + \text{ns}(SO_2, 3) + \text{ns}(NO_2, 3) + \text{Air pressure} + \text{ns}(\text{relative humidity}, 3) + (\text{time}, 7/\text{year}) + DOW_t$

Where t represents the day of observation; Yt is the expected daily counts of AAD on day t (1,2,3,...2192); α is the model intercept and β is the coefficient in DLNM; $\text{temp}_{t,l}$ represents the "cross-basis" function and lag effect from lag 0 to lag l days, the maximum of l was set to 28 days (Guo et al., 2014); ns ( ) means a natural cubic spline, we control long-term trends with 7 degrees of freedom per year and 3 degrees of freedom for relative humidity, PM_{10}, SO_2 and NO_2; a dichotomous variable representing the day of the week (*DOW*) in the model.

The DLNM model was used to fit the lag effect of ambient temperature (daily maximum temperature, daily mean temperature, daily minimum temperature) and AAD. Based on multiple analyses of the data, we choose the percentile of the daily average temperature to calculate the effect of AAD (cold effect: 10th ; hot effect: 90th) and the median was used as the reference temperature (17.56°C) (Anderson and Bell, 2009).Through the comparison of the results of three temperature variables, the risk effect between daily mean temperature and AAD was significant. Thus, here we mainly report lag effect of daily average temperature on AAD (Yang et al., 2012).

In order to discover people who are susceptible to ambient temperature, we conducted a stratified analyses of gender, age, and presence or absence of hypertension. Among them, gender was divided into two groups: male and female; age was divided into group of < 55 years old and ≥ 55 years old due to the characteristics of AAD onset; existing evidence indicated that a positive correlation between hypertension and the onset of AAD, so, hypertension is a key risk factor that we should to be considered (Dong et al., 2019). Analyses were conducted by R software, packages "dlnm" and "splines".

Sensitivity Analysis

Since conclusions usually vary with model specifications, sensitivity analysis needs to be performed to verify that risk estimates were robust. The degree of freedom was adjusted to 5 to control the confounding effect of the time trend, and the degree of freedom was adjusted to 4 and 5 to control the factors of weather and pollutants (Lin et al., 2013). The results have not changed substantially.

Results

Study population and exposure characteristics

As shown in Table 1, From January 1, 2015 to December 31, 2020, 1648 patients in the First Affiliated Hospital of University of Science and Technology of China (Anhui Provincial Hospital) were included for the first admissions with AAD. Male accounted for about 76.3%, and hypertension patients accounted for about 79.2%. Among meteorological factors, the average of daily maximum temperature, mean temperature, minimum temperature, relative humidity and atmospheric pressure were 21.81°C, 16.76°C, 11.70°C, 76.96% and 1024.60 (kpa), respectively. The 25th percentile and 75th percentile of the daily mean temperature were 8.72°C and 24.5°C. The mean concentration of pollutants PM_{10}, SO_2 and NO_2 was 77.10 (μg / m^3), 10.59 (μg·/ m^3), 41.44 (μg / m^3). Based on the results of Spearman's rank correlation coefficient, it was failed to find correlation between daily mean temperature and relative humidity, but association with other factors has been found (Table S1). Therefore, PM_{10}, NO_2, SO_2 and air pressure were regarded as confounding factors in the model.

Table 1
Daily distribution of AAD, meteorological and pollutant variables in Hefei during 2015 to 2020

Variables	Number (%)	Mean ± SD	Minimum	25th percentile	Median	75th percentile	Maximum
AAD cases							
Total	1648(100%)	0.75 ± 0.95	0	0	0	1	6
Male	1257(76.27%)	——	0	0	0	1	5
Famale	391(23.73)	——	0	0	0	0	3
Age (years-old)							
<50	636(38.59%)	——	0	0	0	0	3
≥ 50	1012(61.41%)	——	0	0	0	1	4
Hypertension							
Yes	1305(79.19%)	——	0	0	0	1	5
No	343(20.81%)	——	0	0	0	0	3
Daily meteorological measures							
Mean temperature (°C)	——	16.76 ± 9.22	-6.67	8.72	17.56	24.50	34.61
Maximum temperature (°C)	——	21.81 ± 9.72	-3.22	13.89	23.00	30.00	41.11
Minimum temperature (°C)	——	11.70 ± 9.45	-11.00	3.61	12.00	20.00	29.61
Relative humidity (%)	——	76.96 ± 12.25	33.00	69.00	78.00	86.00	100.00
Atmospheric pressure (kpa)	——	1024.60 ± 9.73	993.30	1007.90	1016.60	1024.10	1044.30
Daily concentrations of pollutants							
PM_{10}(μg/m^3)	——	77.10 ± 40.11	8.00	48.00	71.00	99.00	361.00
SO_2(μg/m^3)	——	10.59 ± 6.49	2.00	6.00	9.00	13.00	58.00
NO_2 (μg/m^3)	——	41.44 ± 18.44	9.00	28.00	37.00	52.00	137.00

Daily Mean Temperature And Total Aad Admissions

Based on the correlation between relative humidity, daily maximum temperature, daily average temperature, daily minimum temperature and time, it can be known that a certain periodicity in Fig. 1, except daily minimum temperature. Moreover, 3D shows that low temperature and high temperature can increase the risk of AAD admissions in the first few days of exposure, but cold effects were more significant (Fig. 2). The result of 3D was consistent with the contour plot (Figure S1). With reference to 17.56°C, there was a significant lag effect between AAD admissions and the daily mean temperature. In the cumulative day-lag model, when exposed to extremely low temperature, relative risks (RRs) emerged at lag 0–0 - lag 0–8 days. The smallest cumulative effect was at lag 0 day (RR: 1.639, 95% CI: 1.120, 2.398), and got the peak at lag 0–3 days (RR: 2.176, 95% CI: 1.345, 3.519). Then the effect size was gradually reduced until lag 0–8 days (RR: 1.953, 95% CI: 1.010, 3.776) (Table 2, Fig. 5). The exposure response correlation showed that the risk values decreased and lasted for four days in extremely low temperature, the largest effect at lag 0–0 day. Regarding heat effect, there was a correlation at lag0- 3 days, lasting about nine days, and the biggest risk was at lag 0–7 days (Fig. 3). Our results showed that the cumulative effect of low temperature on AAD admissions was the most significant. So, our stratified analysis focused on exploration of cumulative cold effects. The single day effects were showed in Table S2.

Table 2
The lag-cumulative effect between extremely low temperature and AAD admission (10th = 4°)

Multi-days	**total RR (95% CI)**	**Male (RR and 95% CI)**	**Female (RR and 95% CI)**	**< 55 years old**	**≥ 55 years old**	**Hypertension (Yes)**	**Hypert (No)**
lag0-0	**1.639(1.120,2.398)** *	**1.802(1.172,2.773)** *	1.315(0.597,2.899)	**1.876(1.030,3.417)** *	1.512(0.923,2.476)	**1.637(1.079,2.484)** *	1.681(
lag0-1	**2.021(1.272,3.209)** *	**2.236(1.325,3.776)** *	1.634(0.624,4.275)	**2.492(1.205,5.153)** *	1.787(0.979,3.260)	**2.122(1.278,3.524)** *	1.671(
lag0-2	**2.145(1.351,3.404)** *	**2.318(1.374,3.912)** *	1.869(0.715,4.886)	**2.740(1.328,5.650)** *	**1.863(1.021,3.399)** *	**2.389(1.440,3.963)** *	1.364(
lag0-3	**2.176(1.345,3.519)** *	**2.328(1.350,4.013)** *	1.951(0.718,5.304)	**2.816(1.325,5.987)** *	**1.881(1.006,3.516)** *	**2.520(1.489,4.265)** *	1.164(
lag0-4	**2.171(1.305,3.612)** *	**2.342(1.316,4.168)** *	1.886(0.654,5.441)	**2.806(1.262,6.240)** *	1.885(0.973,3.652)	**2.558(1.466,4.464)** *	1.076(
lag0-5	**2.139(1.245,3.672)** *	**2.357(1.278,4.348)** *	1.725(0.559,5.318)	**2.729(1.167,6.382)** *	1.876(0.929,3.786)	**2.523(1.397,4.559)** *	1.054(
lag0-6	**2.087(1.172,3.717)** *	**2.371(1.233,4.558)** *	1.519(0.456,5.055)	**2.609(1.053,6.465)** *	1.857(0.878,3.929)	**2.439(1.297,4.587)** *	1.071(
lag0-7	**2.023(1.091,3.753)** *	**2.381(1.182,4.793)** *	1.306(0.361,4.730)	2.464(0.932,6.512)	1.832(0.822,4.083)	**2.327(1.184,4.574)** *	1.112(
lag0-8	**1.953(1.010,3.776)** *	**2.385(1.130,5.036)** *	1.109(0.281,4.375)	2.309(0.818,6.519)	1.801(0.766,4.235)	**2.202(1.071,4.528)** *	1.167(
lag0-9	1.880(0.934,3.781)	**2.384(1.080,5.267)** *	0.938(0.219,4.006)	2.154(0.716,6.474)	1.767(0.714,4.370)	2.073(0.966,4.450)	1.230(
lag0-10	1.806(0.866,3.768)	**2.379(1.033,5.478)** *	0.792(0.172,3.642)	2.004(0.629,6.385)	1.731(0.668,4.484)	1.947(0.872,4.347)	1.298(
lag0-11	1.734(0.804,3.744)	2.369(0.989,5.674)	0.671(0.136,3.303)	1.862(0.553,6.269)	1.694(0.626,4.583)	1.826(0.789,4.229)	1.373(
lag0-12	1.666(0.747,3.716)	2.356(0.947,5.860)	0.571(0.109,3.002)	1.732(0.488,6.147)	1.657(0.587,4.674)	1.712(0.714,4.107)	1.454(
lag0-13	1.602(0.695,3.691)	2.341(0.907,6.045)	0.490(0.087,2.750)	1.613(0.431,6.039)	1.621(0.552,4.766)	1.606(0.646,3.991)	1.543(
lag0-14	1.542(0.647,3.675)	2.325(0.867,6.237)	0.424(0.070,2.547)	1.508(0.382,5.958)	1.588(0.518,4.867)	1.509(0.586,3.887)	1.640(
lag0-15	1.489(0.604,3.672)	2.309(0.828,6.441)	0.371(0.058,2.394)	1.415(0.339,5.915)	1.556(0.486,4.983)	1.422(0.532,3.801)	1.746(
lag0-16	1.442(0.564,3.685)	2.293(0.789,6.660)	0.329(0.047,2.289)	1.336(0.302,5.917)	1.528(0.456,5.118)	1.344(0.484,3.735)	1.863(
lag0-17	1.401(0.528,3.715)	2.277(0.752,6.897)	0.297(0.040,2.228)	1.269(0.270,5.968)	1.503(0.428,5.275)	1.276(0.441,3.690)	1.990(
lag0-18	1.367(0.496,3.765)	2.263(0.716,7.153)	0.272(0.034,2.210)	1.215(0.243,6.071)	1.482(0.403,5.455)	1.217(0.404,3.667)	2.131(
lag0-19	1.340(0.469,3.834)	2.251(0.683,7.426)	0.254(0.029,2.235)	1.173(0.221,6.231)	1.465(0.379,5.658)	1.168(0.372,3.666)	2.286(
lag0-20	1.321(0.445,3.924)	2.242(0.651,7.717)	0.242(0.025,2.306)	1.142(0.202,6.452)	1.452(0.358,5.887)	1.127(0.345,3.687)	2.456(
lag0-21	1.309(0.424,4.038)	2.235(0.622,8.026)	0.236(0.023,2.428)	1.124(0.187,6.743)	1.444(0.340,6.143)	1.095(0.321,3.733)	2.644(
lag0-22	1.305(0.408,4.178)	2.231(0.596,8.354)	0.234(0.021,2.611)	1.117(0.175,7.115)	1.442(0.323,6.430)	1.072(0.302,3.805)	2.852(
Continue							
lag0-23	1.309(0.394,4.349)	2.230(0.571,8.707)	0.238(0.020,2.872)	1.122(0.166,7.587)	1.444(0.309,6.753)	1.057(0.286,3.907)	3.082(
lag0-24	1.321(0.383,4.557)	2.233(0.549,9.092)	0.248(0.019,3.237)	1.141(0.159,8.187)	1.452(0.296,7.123)	1.050(0.273,4.045)	3.336(
lag0-25	1.342(0.374,4.813)	2.240(0.527,9.522)	0.265(0.019,3.749)	1.173(0.154,8.954)	1.465(0.284,7.555)	1.052(0.262,4.228)	3.619(
lag0-26	1.373(0.368,5.129)	2.251(0.506,10.015)	0.290(0.019,4.473)	1.221(0.150,9.949)	1.485(0.273,8.068)	1.063(0.253,4.468)	3.932(
lag0-27	1.414(0.362,5.525)	2.266(0.485,10.597)	0.326(0.019,5.519)	1.286(0.147,11.257)	1.511(0.263,8.694)	1.083(0.245,4.782)	4.281(
lag0-28	1.467(0.357,6.026)	2.286(0.462,11.300)	0.375(0.020,7.070)	1.371(0.145,13.007)	1.544(0.252,9.473)	1.112(0.238,5.194)	4.670(
* *P* < 0.05							

Cold Effect On Stratified Analysis

Figure 4 showed the overall exposure-response relationship between AAD admission risk with different lag days in stratified groups. In addition, Table 3 also showed the exposure-response relationship between extremely low temperature and AAD admissions risk in subgroups at lag 0 day. In the subgroup analysis of gender, Males were susceptible people to AAD admissions risk. At extremely low temperature, the cumulative risk ranges from lag 0–0 day to lag 0–10 days, and the cumulative maximum effect value at lag 0–8 days (RR = 2.385, 95% CI: 1.130, 5.036) (Table 2). The results of the study showed no increased risk for AAD admissions, when female exposed to extremely low temperature. After subgroup analysis of age group, exposure to extremely cold temperature was detrimental to AAD admissions in each group. The effect started on the lag 0–0 day and gradually increased, reaching the maximum at lag0- 3 days (RR = 2.816, 95% CI: 1.325, 5.987) in age < 55 years old group. The RR of the extremely low temperature gradually decreased from lag 0–4 to lag 0–6 days. Therefore, the prevention of AAD admissions risk should be considered not only on elderly, but also on the young. In the age ≥ 55 years old, The cumulative effect from lag 0–2 days to lag 0–3 days, with the hazard effect (RR = 1.863, 95% CI: 1.021,3.399; RR = 1.881, 95% CI: 1.006, 3.516) and lasted two days. In the subgroup analysis of hypertension, the results showed that patients with hypertension were more likely to be vulnerable with AAD admissions. The risk effect lasted for nine days (from lag 0–0 days to lag0–9 days) and the largest risk at lag 5 days (RR = 2.558, 95% CI: 1.466, 4.464). Conversely, there was no increased risk without hypertension. Stratified analysis suggested that males, hypertension, and adults were at greater risk of AAD admissions at extremely low temperature.

Table 3
The effect of stratification analysis at lag of 0 day in the cumulative day-lag model (10th = 4°C; 90th = 28°C)

Group	RR and 95% CI (4°C)	RR and 95% CI (28°C)
Overall	1.639(1.120,2.398) *	0.754(0.532,1.068)
Sex		
Male	1.802(1.171,2.773) *	0.810(0.546,1.203)
Female	1.315(0.597,2.899)	0.602(0.294,1.233)
Age		
< 55 years	1.876(1.030,3.417) *	0.945(0.541,1.649)
≥ 55 years	1.512(0.923,2.476)	0.653(0.417,1.022)
Hypertension		
Yes	1.637(1.079,2.484) *	0.832(0.565,1.225)
No	1.681(0.706,4.004)	0.527(0.248,1.121)
** P < 0.05*		

Discussion

In a 6 yeas time-series study, a finding that extremely low temperature was associated with higher AAD admissions risk. The admissions risk of AAD is the highest, when the lag is 0 day in single days; the cumulative effect got the peak in lag 0–3 days. Moreover, this study also found that there were more male patients with AAD than female patients. A range of stratified analyses were conducted by patients' characteristics. It appears that patients with hypertension or male had higher risks of AAD associated with low temperature. These increased risks might be due to the fact that the history of hypertension or male patients, which may lead to the development of AAD.

Compared with existing studies, in the work of Yu et al., they found that extremely low ambient temperature is positively associated with the onset of AAD (Yu et al., 2021). In a study between incidence of AAD and climatic factors, it was found that the frequency of AAD reached its peak in winter (Ma et al., 2020). In addition, the study by Sadamatsu et al. showed that cold weather and a sudden drop in temperature may trigger the occurrence of aortic dissection (Sadamatsu et al., 2020). Our result is consistent with above studies. As far as we know, the biggest attributable risk factors for acute aortic dissection include male, eldely, long-term history of arterial hypertension, and aortic aneurysm (Gawinecka et al., 2017), extremely low temperature may be a potential risk factor.

Although evidence suggested that cold weather could trigger the risk of AAD, the pathogenesis remains yet not to be elucidated. Low temperature might increase the risk of AAD admissions via several common pathways. Published articles have provided some evidence to explain the relationship for extremely low temperature and AAD admissions. AAD is one of the cardiovascular diseases and numerous studies have demonstrated that colder temperatures can increase the incidence of cardiovascular diseases (Park et al., 2020), due to exposure to colder temperatures may increase sympathetic nervous system activation and vasoconstriction (Widlansky et al., 2007), the sympathetic nervous system has been considered as a major regulator of cardiovascular physiology. The higher admission rate of AAD in males may be related to their exposure to risk factors, such as smoking and alcohol consumption. With the development of China's economy, unhealthy lifestyle, work pressure, mental stress and other factors, leading to the onset of hypertension earlier age. For people who suffering from hypertension, the onset of AAD is more significantly in cold weather. On the other hand, it is recognized that as the age increases, the organ function and immunity of the elderly decrease significantly compared with the younger (Dugan et al., 2020). In our stratified analysis, we also made it clear that elderly with hypertension should be a priority group for protection. In addition, ambient temperature is an environmental condition that is often ignored in studies of inflammatory/infectious mice, in order to verify the effect of temperature on the cardiac function of mice. Ndongson-Dongmo et al. conducted a study on the mechanism of myocardial function in mice and reported that temperature accelerated the adjustment of cardiac nerve function, which may lead to myocardial dysfunction (Ndongson-Dongmo et al., 2019). Yin et al. 's research background in mouse also clearly write that cold exposure leads to cardiac dysfunction (Yin et al., 2020). Therefore, we speculated that the frequent occurrence of AAD may be caused by low temperature exposure, which stimulates the sympathetic nervous system of the human body, and the sympathetic nervous system in turn plays a regulatory role in the heart nerve to increase arterial blood pressure and accelerate the heartbeat. Environmental temperature may play an indirect role in the process of mechanism, and further mechanism studies need to be carried out.

There were also some limitations in our study. Inevitable selection biases in the retrospective design of a single center. In the future, more representative cases should be collected in multiple regions to verify the robustness of the results. Due to the small sample size, and the results may be biased in the stratified analysis. This DLNM study cannot fully exclude confounding factors (e.g. physical activity, behavioural risk factors), which may affect the robust of the results. Despite it had some shortcomings in this study, results of this study were consistent with previous studies. The consistency of the outcomes indicates that the confounding factors were well controlled in the data analysis.

Conclusions

Overall, we used DLNM to predict the exposure-response relationship between daily mean temperature and the admissions of AAD. We disclosed that low ambient temperature increased the risk of AAD admissions significantly. Furthermore, male, the elderly and hypertensive patients were found to be high-risk people for AAD admissions.

Declarations

Ethics approval: This study has got the ethical approval from Anhui Medical University ethics committee (Ethical approval number: 2020H007).

Consent to participate: Not applicable.

Consent for publication: The authors declare that they agree with the publication of this paper in this journal.

Data availability: The datasets used and/or analyzed during the current study are available on reasonable request.

Code availability: No applicable.

Competing interests: There were no conflict interests in authors.

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Author contributions: Qian-Ru Zhang and Kai-Di Li: original draft, project administration, resources. Yi-Yu Wang and Hua Wang: investigation, methodology. Xian-Bao Li and Ji-Rong Zhu: data curation, software. Bao-Zhu Li: project administration, funding acquisition.

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Figures

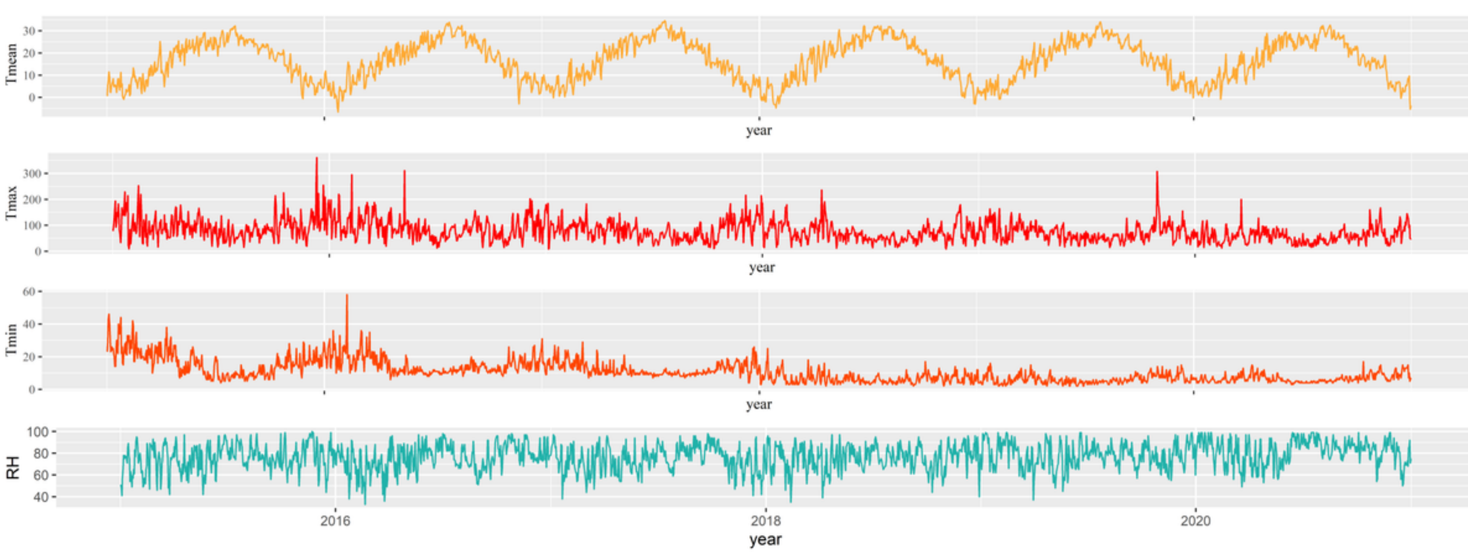

Figure 1

Distribution of daily mean temperature, maximum temperature, minimum temperature and relative humidity (RH) in 2015-2020.

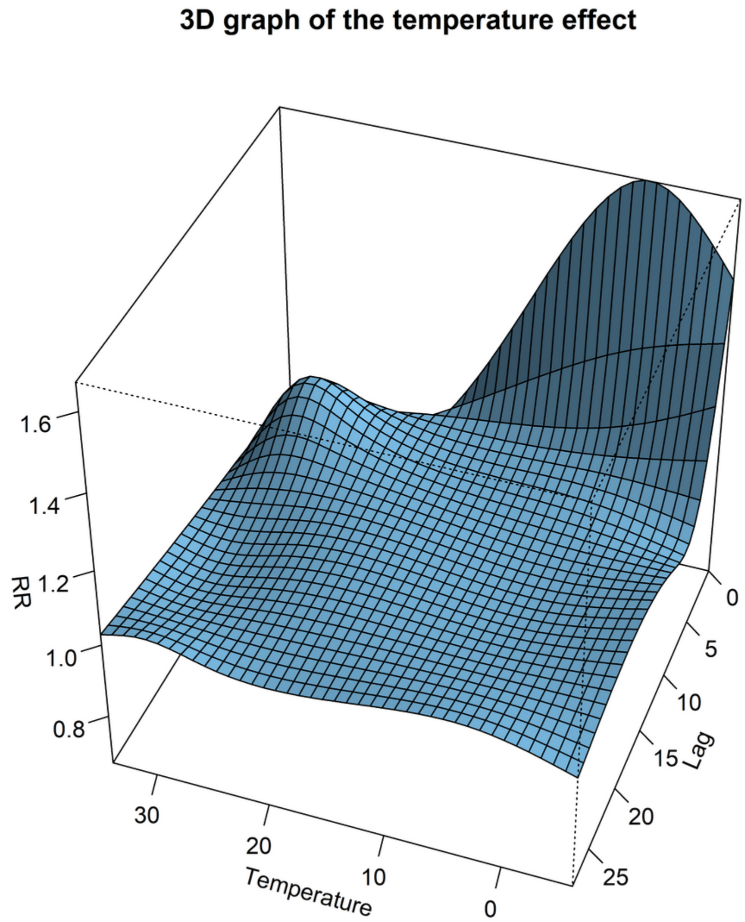

Figure 2

Three-dimensional graph of relative risk (RR) with temperature and lag time.

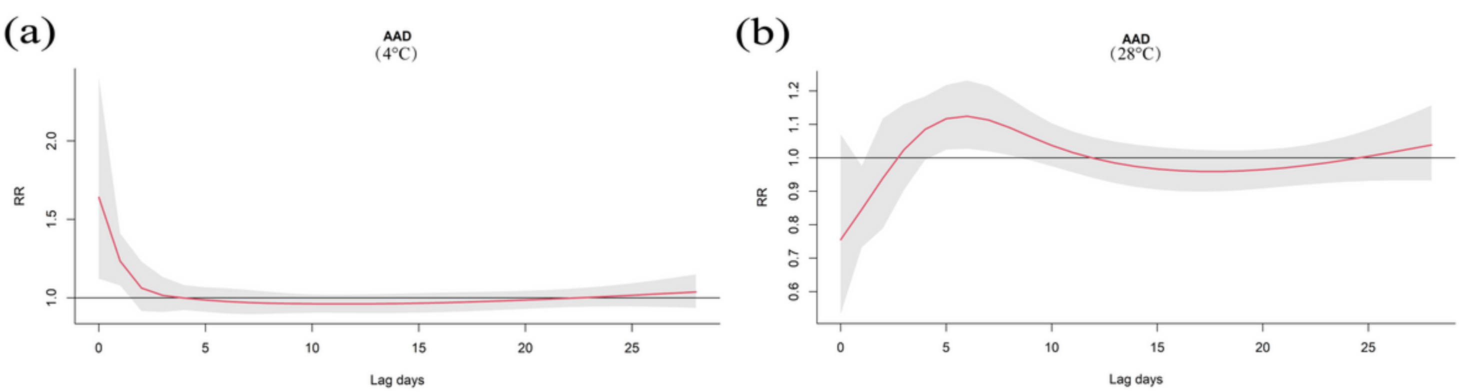

Figure 3

The cold effect (4°C) **(a)** and heat effect (28°C) **(b)** of ambient temperature on AAD admission under different lag days.

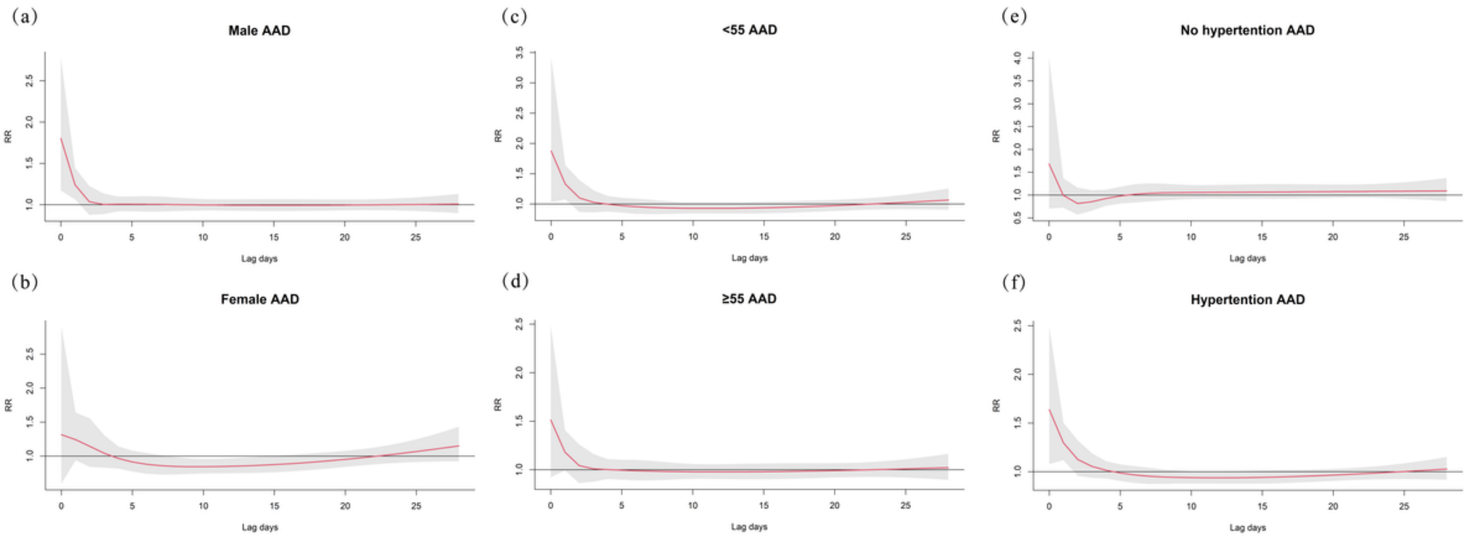

Figure 4

Exposure-response relationships between temperature and risks for AAD admission in subgroups (10th=4°C); **(a)** Male; **(b)** Female; **(c)** Age<55; **(d)** Age≥55; **(e)** Without hypertension; **(f)** Hypertension.

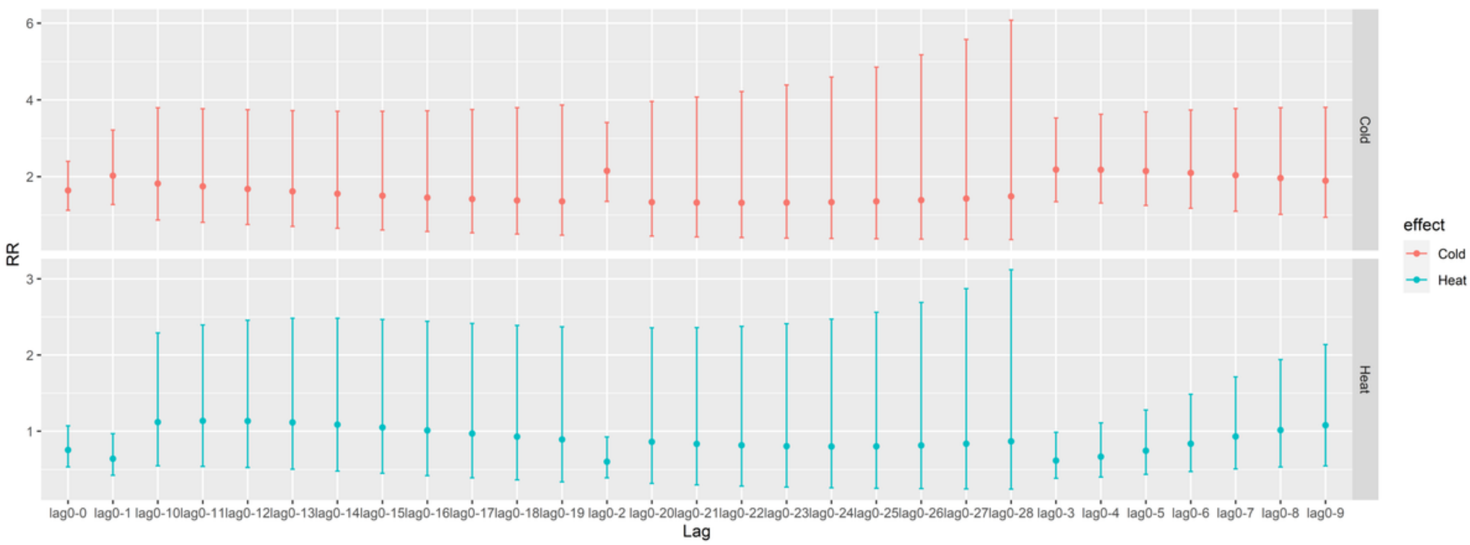

Figure 5

Cumulative-day lag effect and 95% confidence interval with cold and heat temperature (10th percentile=4°C; 90th percentile=28°C).

Supplementary Files

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- FigureS1.tif
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- TableS2.docx