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ORIGINAL RESEARCH

Association of Daily Mean Temperature and Temperature Variability With Onset Risks of Acute Aortic Dissection

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BACKGROUND: The association between ambient temperature and cardiovascular diseases has been well established, but evidence of temporal changes in the risk of acute aortic dissection (AAD) onset is lacking.

METHODS AND RESULTS: We conducted an 8-year time-series study based on data from 2120 patients diagnosed with AAD at Tongji Hospital (Wuhan, China). Daily meteorological parameters were measured in the study area. Spearman's rank correlation analysis was applied to measure the associations between daily meteorological data and air pollution indicators. A distributed lag nonlinear model following quasi-Poisson regression was used to express the nonlinear exposure-response relationships and lag effects of daily mean temperature and temperature variability on the occurrence of AAD. Considering a 25-day lag effect, lower or higher temperatures with reference to 25°C did not alter the onset risk of AAD. The lag effect of daily mean temperature on the incidence of AAD is statistically significant within 2 days, and the impact of daily mean temperature on the risk is most influential on the day. The exposure-response curve between daily mean temperature and onset risks of AAD at lag 0 showed that the extremely cold temperature (2.5th percentile, 0.5°C) significantly increased the AAD risk for the total (relative risk, 1.733; 95% CI, 1.130–2.658) and type A dissection (relative risk, 3.951; 95% CI, 1.657–9.418). Temperature variability within 1 week did not affect the onset risks of AAD for the total.

CONCLUSIONS: We confirmed that extremely cold temperatures significantly increased the AAD risk, which could contribute to early prevention and timely diagnosis of the disease.

Key Words: aortic dissection ■ daily mean temperature ■ temperature variability

Acute aortic dissection (AAD) is a life-threatening vascular disease mainly manifested by a sudden onset of severe chest pain.[1] Population-based studies reported an annual incidence of AAD of 3 to 20 per 100 000 people worldwide.[1,2] The highest mortality from AAD occurs in the first 48 hours after symptom onset, and thus, an immediate diagnosis is lifesaving.[2] To achieve early prevention and timely diagnosis of the disease, studies were committed to identifying triggering factors for AAD.[3-5] Retrospective observational studies suggested that occurrences of AAD followed a chronologic pattern, and the frequency significantly increased in relatively colder months of the year.[6,7] Since the incidence of the disease was negatively correlated to daily mean temperature,[5-7] AAD might be triggered by low temperatures.

Recently, studies identified nonlinear associations of ambient daily mean temperature with morbidity and mortality of myocardial infarction,[8-10] heart failure,[11] and stroke.[12-14] A U- or V-shaped exposure-response

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CLINICAL PERSPECTIVE

What Is New?

- The lag effect of daily mean temperature on the incidence of acute aortic dissection is statistically significant within 2 days, and the impact of daily mean temperature on the risk is most influential on the day.
- We observed that there was no statistically significant association between short-term temperature fluctuations and the onset risk of acute aortic dissection.

What Are the Clinical Implications?

- Regardless of lag effect, extremely cold temperature (2.5th percentile, 0.5°C) significantly increased the acute aortic dissection risk for the total (relative risk, 1.733; 95% CI, 1.130–2.658) and type A dissection (relative risk, 3.951; 95% CI, 1.657–9.418), suggesting the need for more resource allocation for acute aortic dissection rescue at extremely cold temperatures.

Nonstandard Abbreviations and Acronyms

AAD	acute aortic dissection
DLNM	distributed lag nonlinear model
TV	temperature variation

curve of the temperature effect on cardiovascular disease was found, which meant an extremely cold or hot climate significantly increased risks of several cardiovascular diseases.[8,10,15] The temperature effect had a noticeable delayed effect,[8] which was that the impact of ambient temperature on the onset of diseases did not occur until a few days later. Besides, temperature variability (TV) was also proven to increase the onset risks of ischemic heart disease, heart failure, heart rhythm disturbances, and ischemic stroke.[16] TV is an essential meteorological indicator reflecting rapid temperature fluctuations within a certain period (eg, inter- and intraday changes of ambient temperature).[15-17] Therefore, ambient temperature has a significant and complicated influence on the morbidity of cardiovascular disease, which would be of great value for early prevention and first aid intervention.

Although a statistically significant association between low temperatures and the onset of AAD was observed under a linear regression analysis,[5,6,18] the exposure-response relationship between daily mean temperature and occurrence of AAD is still nubilous, and whether the temperature has a lag effect on the disease remains unexplored. Short-term temperature fluctuation could alter heart rate, blood pressure, and inflammatory reaction,[16,19,20] and these physiological changes may trigger the onset of AAD. Nevertheless, no study has analyzed how short-term temperature fluctuations affect dissection of the aorta.

To address these knowledge gaps, we conducted an 8-year time series study based on validated and detailed medical records of AAD cases. We used a distributed lag nonlinear model (DLNM) following quasi-Poisson regression to (1) elucidate the exposure-response relationship between daily mean temperature and the onset risk of AAD, (2) analyze whether a lag effect exists in the impact of temperature, and (3) investigate whether TV affects the incidence of AAD.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

We enrolled patients diagnosed with AAD in Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (Wuhan, China) from 2011 to 2018. Tongji Hospital is one of the largest general hospitals in Wuhan, and it lies in the Hubei province of central China. We defined AAD as dissection onset within 14 days (subacute aortic dissection: 15–90 days, chronic aortic dissection: >90 days). Because AAD shares the typical pathophysiological process and clinical characteristics with intramural hematoma and penetrating atherosclerotic aortic ulcer, which are collectively known as the acute aortic syndrome, we screened all patients admitted to Tongji Hospital with acute aortic syndrome from January 1, 2011, to December 31, 2018. We checked electronic medical records and identified AAD cases through validated, detailed records. We further stratified AAD by Stanford classification of aortic dissection depending on medical imaging information or surgical records. For each case, characteristics were extracted on sex, age, onset time (when typical symptoms like acute chest/back/abdominal pain occurred), hypertension, and diabetes mellitus.

The study was approved by the Research Ethics Committee in Tongji Medical College, Huazhong University of Science and Technology (2019, S1149), and performed following the Declaration of Helsinki. The informed consent form was not applicable for this study.

Data Collection and Exposure Definition

Daily meteorological data in the study area from January 1, 2011, to December 31, 2018, were obtained from the website of the National Meteorological Information Centre of China (http://data.cma.cn), including daily mean temperature, daily maximum temperature, daily minimum temperature, daily mean atmospheric pressure, maximum atmospheric pressure, minimum atmospheric pressure, and relative humidity. The daily mean temperature was widely used to estimate the effect of ambient temperature on morbidity and mortality of cardiovascular disease.[8,21] TV was another important meteorological indicator defined as the SD of daily maximum and minimum temperature over different exposure days (2–7 days).[16] For example, TV of 2 days' exposure (TV_{0-1}) was SD ($MinTemp_{lag0}$, $MaxTemp_{lag0}$, $MinTemp_{lag1}$, $MaxTemp_{lag1}$), $MinTemp_{lagi}$ and $MaxTemp_{lagi}$ represented the daily minimum and maximum temperature for the preceding day i; temperature variability of 4 days' exposure (TV_{0-3}) was expressed as SD ($MinTemp_{lag0}$, $MaxTemp_{lag0}$, $MinTemp_{lag1}$, $MaxTemp_{lag1}$, $MinTemp_{lag2}$, $MaxTemp_{lag2}$, $MinTemp_{lag3}$, $MaxTemp_{lag3}$). This indicator could fully represent both inter- and intraday temperature fluctuations. Because TV was immediate but not tardive, it was pointless to explore the lag effect of TV. Daily average concentrations for particulate matter with an aerodynamic diameter <10 μm, SO_2, and NO_2 were obtained from China National Environmental Monitoring Centre.

Statistical Analysis

We applied a DLNM following quasi-Poisson regression to study the impact of daily mean temperature and temperature variability on the occurrence of AAD. The DLNM model was widely used to investigate the association between environmental factors and health events, as it can simultaneously express nonlinear exposure-response relationships and lag effects.[16,22,23] Previous studies indicated that TV is almost linearly elevated with increases in mortality of cardiovascular disease. Thus, we also investigated the effect of TV in the model. Furthermore, we considered several confounders in the model: day of the week, relative humidity, average atmospheric pressure, and public holidays. The full model was shown as below:

$$\begin{aligned}\text{Log}\left[\text{E}\left(\text{Y}_t\right)\right] &= \beta \text{ temperature} + \gamma \text{ temperature variability} \\ &+ \text{day of the week} + \text{public holidays} + \text{atmospheric pressure} \\ &+ \text{ns}\,(\text{calendar time}, df = 7\times 8) + \text{ns}\,(\text{relative humidity}, df = 3) \\ &+ \text{ns}\left(\text{PM}_{10}, df = 3\right) + \text{ns}\left(\text{NO}_2, df = 3\right) + \text{ns}\left(\text{SO}_2, df = 3\right) + \alpha\end{aligned}$$

where β represents the log-relative risk of the onset of AAD associated with 1°C increase of daily mean temperature; γ stands for the log-relative risk correlated with 1 unit increase of temperature variability; $E(Y_t)$ is the expected onset events of AAD on day *t*; temperature is a 2-dimensional cross-basis matrix produced by DLNM; *ns*() indicates natural cubic spline function; public holidays and day of the week were included in the model as indicator variables; relative humidity indicates 3-day moving average relative humidity; atmospheric pressure is daily mean atmospheric pressure; particulate matter with particle size below 10 microns (PM_{10}), NO_2, and SO_2 represent daily average concentrations for air pollutants; α stands for the intercept. We conducted separate analyses for TV during distinct exposure days from TV_{0-1} to TV_{0-7}. To investigate the exposure-response relationship between daily mean temperature and occurrence of AAD, we brought TV_{0-1} to TV in the model.

Spearman's rank correlation analysis was applied to measure the direction and strength of monotonic associations between daily meteorological data and air pollution indicators. We used R (version 3.6.1, R Foundation for Statistical Computing, Vienna, Austria) and IBM SPSS Statistics (version 24.0, IBM Co., Armonk, NY) to build the model and conducted statistical analyses. The estimated effects and corresponding 95% CIs were calculated and represented in artworks produced by DLNMs. To test the statistical difference between relative risks, we calculated the *Z* score of 2 relative risk estimates.[10] Two-sided *P* values of <0.05 were considered statistically significant in this study.

Subgroup Analyses

We performed subgroup analyses to identify subpopulations that were susceptible to daily ambient temperature and TV. Planned subgroup analysis for the association included the following subsets: patients with Stanford type A or type B aortic dissection, patients of different ages (<55 years, ≥55 years), patients of different sexes, and patients with or without hypertension.

RESULTS

Study Population and Exposure Characteristics

From January 1, 2011, to December 31, 2018, 3665 patients hospitalized in Tongji Hospital were identified with acute aortic syndrome. After excluding 1193 patients with only intramural hematoma, penetrating atherosclerotic ulcer, or subacute/chronic symptoms, 352 patients with traumatic, pregnancy-induced, or asymptomatic aortic dissection, we included 2120 AAD patients confirmed by preoperative imaging and surgery records in the final time series (see Figure 1). Baseline characteristics of enrolled patients were summarized in Table 1. Of included patients, the median age was 53 years (interquartile range, 46–61), ranging from 21 to 91 years, and 1704 (80.4%) were men. The median systolic/diastolic

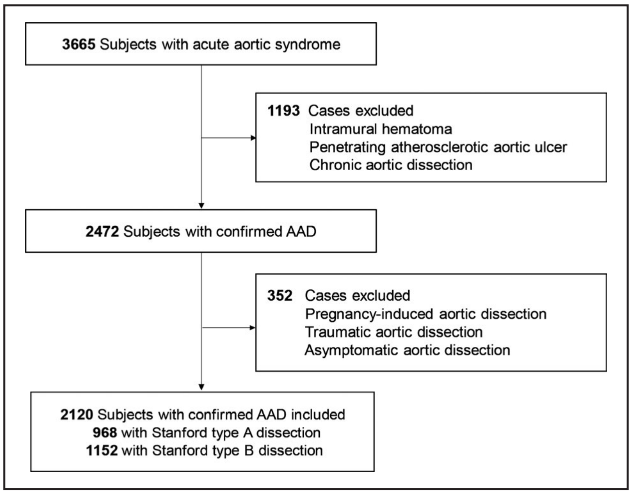

Figure 1. Patient selection flow diagram.
A total of 2120 patients with AAD confirmed by preoperative imaging and surgery records were included in the final study. AAD indicates acute aortic dissection.

blood pressure of inclusion was 142/79 mm Hg (interquartile range, 122–160/68–90 mm Hg). Of the 2120 patients, 968 had Stanford type A dissection, and 1152 had Stanford type B dissection. After checking and confirming the patients' comorbidities, we found that 1244 (58.7%) patients had hypertension, and 39 (1.8%) patients had diabetes mellitus. Statistically significant differences were observed in age, blood pressures, and the proportion of cases with hypertension between male and female subjects. Table S1 summarizes the daily indicators of meteorology and air pollution particles in Wuhan, China, from 2011 to 2018. The magnitudes of TVs varied slightly over different exposure days. Spearman's rank correlation coefficients (Table S2) showed that daily mean temperature had a strong negative correlation with average atmospheric pressure ($\rho=-0.913$; $P<0.001$), with weak to moderate negative associations with the daily concentration of SO_2 ($\rho=-0.356$; $P<0.001$) and NO_2 ($\rho=-0.400$; $P<0.001$). Indicators for TV are negatively associated with relative humidity and positively correlated with particulate matter with an aerodynamic diameter <10 μm, SO_2, and NO_2.

Daily Mean Temperature and Onset of AAD

The time-series distributions of monthly AAD cases and daily ambient temperature during 2011 to 2018 are depicted in Figures S1 and S2. Considering lag effects of daily mean temperature on diseases over 25 days, during the 8 years, lower and higher temperature with reference to 25°C did not alter onset risks of AAD for the total, type A dissection, and type B dissection (Figure S3, Table S3). Contour and 3-dimensional plots provided comprehensive summaries of the bidimensional exposure-lag-response relationships between the onset of AAD and daily mean temperature (Figures S4 and S5). The extremely cold temperature (0.5°C, 2.5th percentile) significantly increased the risk of AAD within 2 days (1.733; 95% CI, 1.130–2.658 for lag 0; 1.252; 95% CI, 1.040–1.09 for lag 1), and the extremely hot temperature (32.0°C, 97.5th percentile) had no significant effect on the onset risk of AAD within 26 days (lag 0 to lag 25) (see Figure 2, Figure S6, Table S4). Regardless of the lag effect, the exposure-response curves (lag 0, reference 25°C) between daily mean temperature and AAD for the total, type A dissection, and type B dissection are displayed in Figure 3 and Table S5. The effect peaked at 0.7°C, with a relative risk of 1.734 (95% CI, 1.133–2.653) for the total. The extremely cold temperature (0.5°C) significantly increased risks of AAD for the total (1.733; 95% CI, 1.130–2.658) and type A dissection (3.951; 95% CI,

Table 1. Baseline Characteristics of Study Population

	No. (%)					*P* Value*
	Total (N=2120)	Male (n=1704)	Female (n=416)	Type A (n=968)	Type B (n=1152)	
Age, y, median (IQR)	53 (46–61)	52 (45–61)	55 (50–63)	52 (46–61)	54 (47–62)	<0.001
Stanford type A, n (%)	968 (45.7)	751 (44.1)	217 (52.1)	968 (100.0)	0 (0.0)	<0.001
Hypertension, n (%)	1244 (58.7)	1030 (60.4)	214 (51.4)	535 (55.3)	709 (61.5)	0.001
Diabetes mellitus, n (%)	39 (1.8)	29 (1.7)	10 (2.4)	19 (2.0)	20 (1.7)	0.347
Systolic blood pressure, mm Hg, median (IQR)	142 (122–160)	142 (123–162)	136 (119–159)	132 (114–152)	148 (131–167)	0.016
Diastolic blood pressure, mm Hg, median (IQR)	79 (68–90)	80 (69–92)	76 (67–88)	74 (63–85)	84 (75–97)	<0.001

P<0.05 is considered statistically significant. IQR indicates interquartile range.
**P* values indicate differences between men and women.

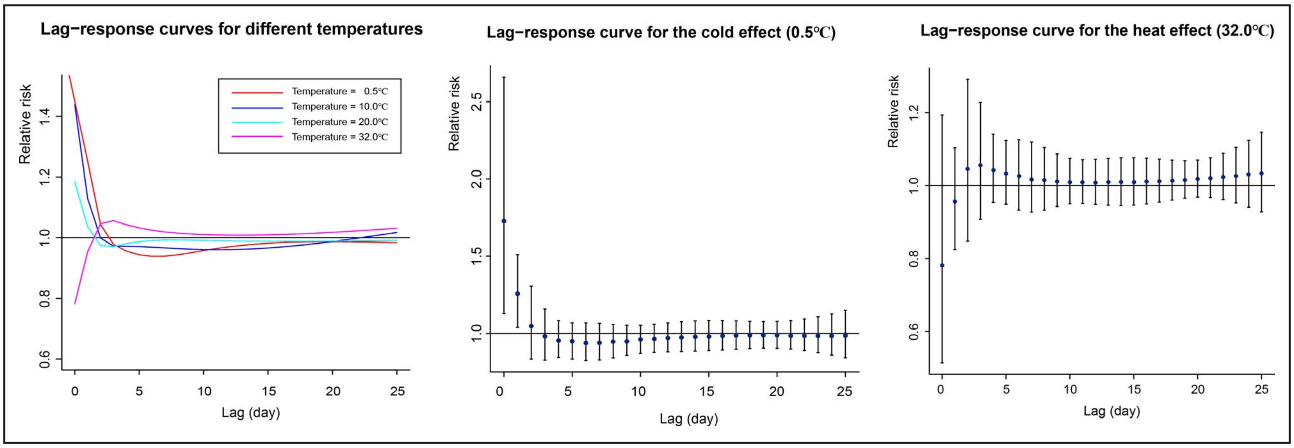

Figure 2. Lag-response curves for different temperatures.
The lag effect of daily mean temperature on the incidence of AAD is statistically significant within 2 days at the extremely cold temperature (0.5°C, 2.5th percentile), and the lag effect is not significant at the extremely hot temperature (32.0°C, 97.5th percentile). The dots represent the relative risks, and vertical lines represent corresponding 95% CIs. AAD indicates acute aortic dissection.

1.657–9.418). Significant heat-related AAD risk was not observed for the total, type A dissection, type B dissection (Table S5).

Subgroup analyses were conducted on the basis of sex, age, history of hypertension, and Stanford type of AAD (see Table 2, Figure S7, Table S6). Significantly increased cold-related AAD risks were observed in men, people aged <55 years, and people with type A aortic dissection. The extremely hot temperature was associated with a decreased onset risk of AAD among women and patients without hypertension. The heat-related effect on the risk was statistically different between men and women (*P*=0.006).

TV and Onset Risk of AAD

Figure 4 and Table S7 summarizes the onset risks of AAD associated with TV in different populations. The indicator significantly decreased AAD risks at 0 to 2 and 0 to 3 exposure days among female patients.

Sensitivity Analyses

We conducted sensitivity analyses to assess the robustness of the results by changing the maximum lag effect of temperature from 20 to 30 days, *df* for daily mean temperature (3–6), and *df* for time trend (6–8/y). The results of the study among the total population did not change significantly.

DISCUSSION

In this 8-year time-series study, we found that considering a 25-day lag effect, lower or higher temperature with reference to 25°C did not alter the onset risk of AAD. The lag effect of daily mean temperature on

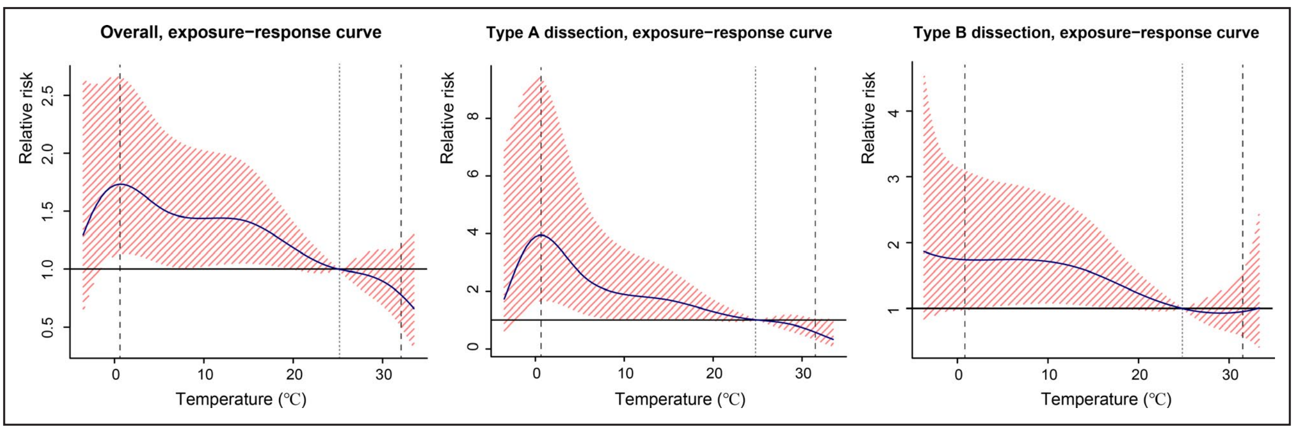

Figure 3. Exposure-response relationships between temperature and risks of AAD at lag 0.
The extremely cold temperature (0.5°C), instead of the extremely hot temperature (32.0°C), significantly increased the risk of AAD in the overall population (RR, 1.733; 95% CI, 1.130–2.658) and in patients with type A dissection (RR, 3.951; 95% CI, 1.657–9.418). The vertical dotted lines represent the extremely cold temperature (0.5°C, 2.5th percentile) and the extremely hot temperature (32.0°C, 97.5th percentile). The blue curve represents RRs, and the red dashed line represents corresponding 95% CIs. AAD indicates acute aortic dissection; and RR, relative risk.

Table 2. Subgroup Analyses

Group	Cold-Related Effect RR (95% CI)	Cold-Related Effect *P* Value	Heat-Related Effect RR (95% CI)	Heat-Related Effect *P* Value
Overall	1.733 (1.130–2.658)		0.783 (0.513–1.193)	
Subtype				
Type A	3.951 (1.657–9.418)	0.125	0.513 (0.257–1.024)	0.161
Type B	1.745 (0.976–3.121)		0.960 (0.560–1.647)	
Sex				
Male	1.923 (1.193–3.101)	0.607	0.989 (0.627–1.562)	0.006*
Female	2.747 (0.769–9.812)		0.178 (0.057–0.549)	
Age				
<55 y	2.340 (1.322–4.140)	0.131	0.858 (0.488–1.509)	0.673
≥55 y	1.203 (0.629–2.303)		0.714 (0.376–1.354)	
Hypertension				
Yes	2.778 (1.301–5.932)	0.495	0.961 (0.546–1.692)	0.131
No	1.956 (1.008–3.795)		0.497 (0.262–0.945)	

RR indicates relative risk.
*Heat-related effect on the risk was statistically different between males and females ($P < 0.05$).

the incidence of AAD is statistically significant within 2 days, and the impact of daily mean temperature on the risk is most influential on the day (lag 0). We mapped the exposure-response curve between daily mean temperature and onset risks of AAD at lag 0, and the extremely cold temperature (2.5th percentile,

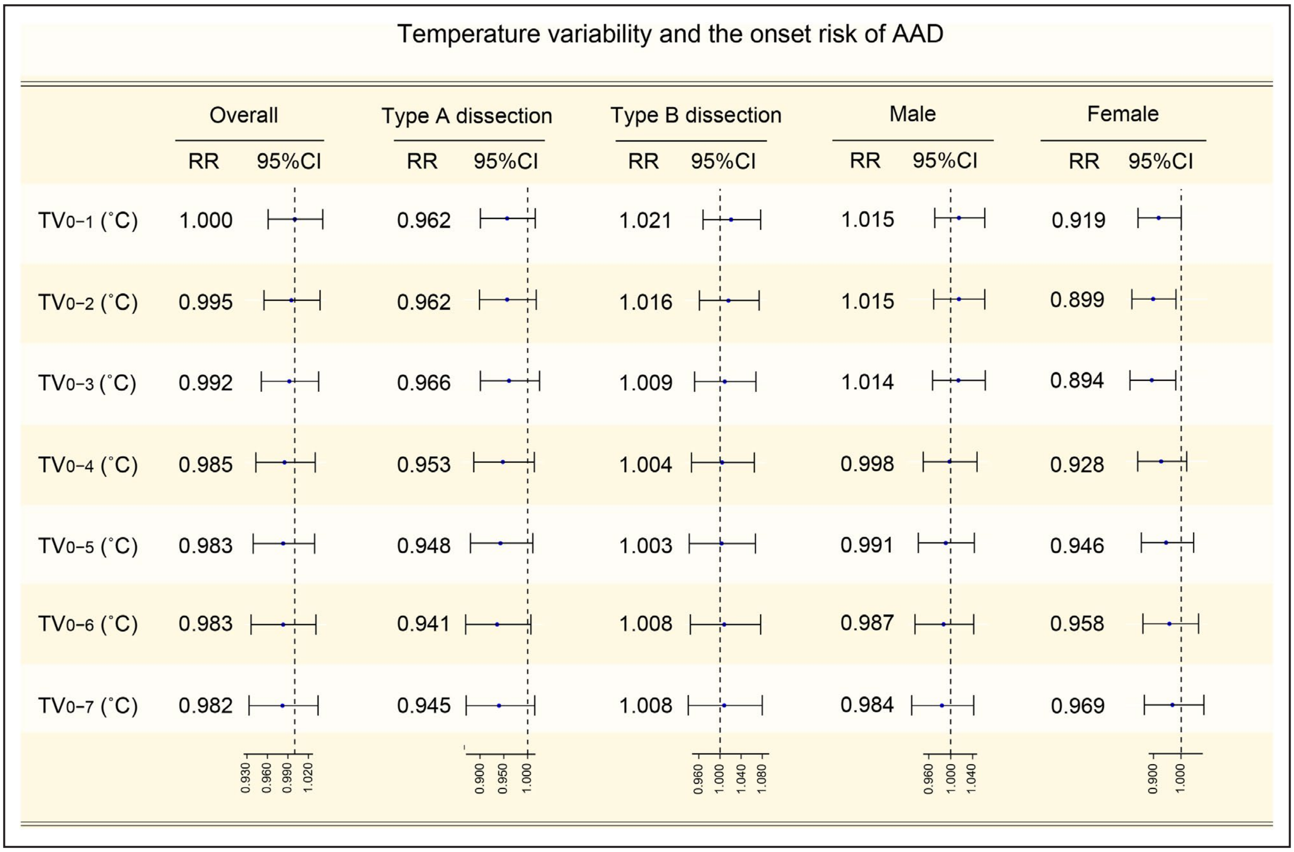

Figure 4. Effect of the temperature variability on the risks of AAD in different populations.
Temperature variability was an important meteorological indicator defined as the SD of daily maximum and minimum temperature over different exposure days (2–7 days). Temperature variability over 3 days ($TV_{0–2}$) and 4 days ($TV_{0–3}$) was associated with lower risks among female patients. Dots indicate RR and the bars indicate the 95% CI. AAD indicates acute aortic dissection; RR, relative risk; and $TV_{0–n}$, the standard deviation of daily maximum and minimum temperature over n+1 days.

0.5°C), but not the extremely hot temperature (97.5th percentile, 32.0°C), significantly increased the AAD risk for the total and type A dissection (see Figure 5). The heat-related effects on the risk were statistically different between men and women. Additionally, TV within 1 week did not affect the onset risks of AAD for the total.

Several epidemiologic studies have evaluated the association between ambient temperature and AAD risks.[5-7,18,24,25] Most of them[6,18,24,26] found that cold temperature increased the onset risk of AAD with a small sample size (no more than 400 cases). Ma and colleagues[5] supported an inverse correlation between daily mean temperature and incidence of AAD using data from 1642 patients. In line with previous studies, we observed a cold-related effect on AAD incidence based on a single population of 2120 cases. Cold-related effects on myocardial infarction had a delay of 2 to 5 days,[10] while the impact on AAD was within 2 days, and it was most evident on the first day. Cold temperatures would induce increased sympathetic activity, elevated blood pressure, and escalated blood viscosity,[19] which can enhance the forces that act to produce wall deformation and increase friction and shear stress on the internal surface of the aorta.[27] Thus, hypothermia is deemed to be a trigger of AAD. Thrombosis formation in myocardial infarction takes a period. Still, the onset of AAD is an instant event of intimal tearing, which may explain why cold temperature has a much shorter delay effect on the latter.

Cumulative 25-day cold or heat effects (low temperature and high temperature) had no significant impact on the onset of AAD, which could be attributable to a short

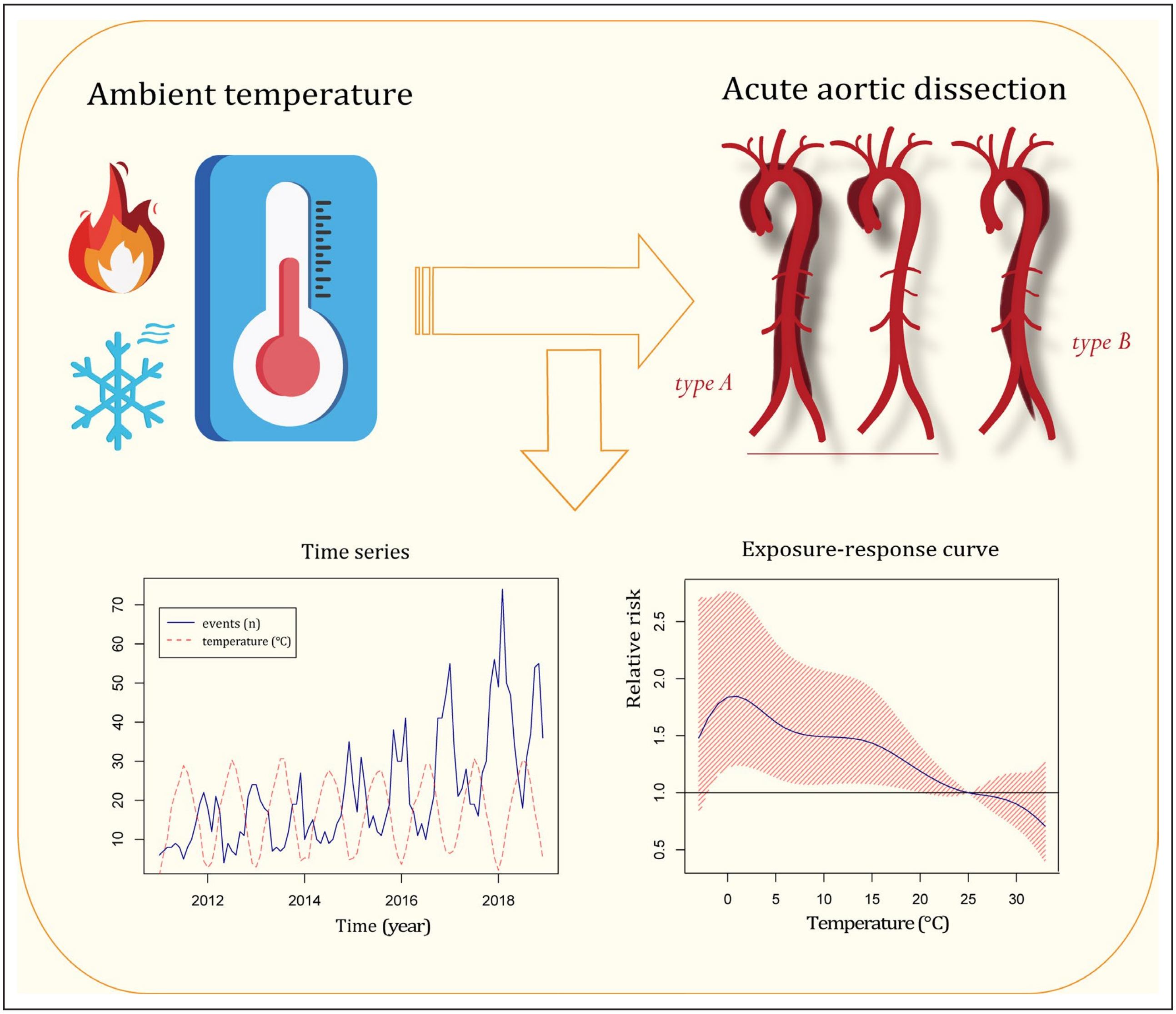

Figure 5. Extremely cold temperature (2.5th percentile, 0.5°C) significantly increased the AAD onset risk.
The lag effect for the association between daily ambient temperature and AAD was not obvious. AAD indicates acute aortic dissection.

delay effect of temperature on AAD within 2 days. Thus, we should pay more attention to the temperature effect on the day (lag 0), rather than the cumulative effect. The exposure-response relationship between daily mean temperature and myocardial infarction was described as U- or V- shaped.[8] For AAD cases, we obtained a hooklike curve with 1 peak at lag 0. At 0.7°C, the curve reached its peak, and every 1°C decrease in temperature corresponded to a 7.3% (95% CI, 1.3%–16.5%) increased incidence of AAD. Exposure to cold should be considered as an environmental trigger of AAD, suggesting the need for more resource allocation for AAD rescue at extremely cold temperatures. This finding should be relevant for cardiac surgeons, policymakers, and high-risk populations of AAD.

Furthermore, a nationwide study in China reported a significantly positive relationship between 1-week TV and daily hospital admissions for ischemic heart disease, heart failure, heart rhythm disturbances, and ischemic stroke.[16] However, our results indicated that TV within 1 week did not alter the incidence of AAD. He and colleagues[7] showed that the difference between maximal and minimal temperature within 1 day was higher in days with AAD than those without. However, this indicator could not fully reflect inter- and intraday variations of temperature compared with TV.

Through further analyses in subpopulations, we found that female patients were more susceptible to changes in daily mean temperature as well as TV. Nonetheless, female patients made up only one-fifth of the study population, and the sample size was 416, which could significantly reduce the statistical power compared with that of male patients. Thus, more studies are required to confirm the results. If this phenomenon does exist, the underlying mechanism needs to be further explored. In our analyses, we adjusted for air pollutants, atmospheric pressure, and humidity, which might be related to the occurrence of AAD.[18,28]

Our study explored the impacts of daily mean temperature and TV on the occurrence of AAD in a single population of 2120 cases during 8 years. There are several limitations. First, because of the single-center retrospective design, an inevitable selection bias exists in this study. Second, meteorological data and air pollutant indicators were obtained from outdoor monitoring stations, which could lead to a measurement error. Meanwhile, the data represented the entire city and was not correlated with individuals, which was also an important source of bias. Finally, the small sample size in subpopulations reduced the statistical power in subgroup analyses.

CONCLUSIONS

Overall, our study mapped the exposure-response relationship between daily mean temperature and onsets of AAD, and we confirmed that cold temperature significantly increased the AAD risk. In addition, we found that the lag effect of daily mean temperature on the incidence of AAD is statistically significant within only 2 days. Also, we found no statistically significant association between short-term temperature fluctuations and the onset risk of AAD.

ARTICLE INFORMATION

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Drs Yu, Feng, and Wei contributed to the conception or design of the work. Drs Yu and Xia contributed to the acquisition, analysis, or interpretation of data for the work. Drs Yu and Xia drafted the manuscript. Drs Xiao and Zheng critically revised the manuscript. All gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

Disclosures

None.

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Supplementary Material

Tables S1–S7
Figures S1–S7

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SUPPLEMENTAL MATERIAL

Table S1. Summary statistics of daily indicators of meteorology and air pollution particles in Wuhan, China from 2011 to 2018.

	Mean (SD)	Percentile	
		2.5 th	97.5 th
Daily mean temperature (℃)	17.0 (9.3)	0.5	32.0
Daily maximum temperature (℃)	22.0 (9.5)	4.3	36.4
Daily minimum temperature (℃)	13.0 (9.5)	-3.9	28.0
Relative humidity (%)	79.3 (10.8)	55.0	97.0
Average atmospheric pressure (kPa)	101.5 (6.0)	99.8	103.0
PM_{10} (μg/m^3)	98.8 (55.0)	21.0	226.0
SO_2 (μg/m^3)	23.1 (18.8)	4.0	74.0
NO_2 (μg/m^3)	51.8 (22.1)	21.0	103.0
Temperature variability			
TV_{0-1} (℃)	4.7	1.4	8.2
TV_{0-2} (℃)	4.9	1.8	8.1
TV_{0-3} (℃)	5.0	2.1	8.0

$TV_{0\text{-}4}$ (℃)	5.1	2.4	7.9
$TV_{0\text{-}5}$ (℃)	5.2	2.7	7.9
$TV_{0\text{-}6}$ (℃)	5.2	3.0	7.9
$TV_{0\text{-}7}$ (℃)	5.3	3.1	7.9

Table S2. Spearman's rank correlation coefficients between daily meteorological metrics and daily concentrations of air pollution particles in Wuhan, China from Jan 1, 2011, to Dec, 31, 2018.

	Tmean	Tmax	Tmin	RH	AP	PM_{10}	SO_2	NO_2	TV_{0-1}	TV_{0-2}	TV_{0-3}	TV_{0-4}	TV_{0-5}	TV_{0-6}	TV_{0-7}
Tmean	**1.000**														
Tmax	**0.970**	**1.000**													
Tmin	**0.978**	**0.909**	**1.000**												
RH	-0.040	-0.144	0.075	**1.000**											
AP	**-0.913**	**-0.871**	**-0.906**	-0.096	**1.000**										
PM_{10}	-0.277	-0.157	-0.372	-0.331	0.301	**1.000**									
SO_2	-0.356	-0.266	-0.422	-0.300	0.337	0.642	**1.000**								
NO_2	-0.400	-0.280	-0.489	-0.156	0.396	**0.780**	0.643	**1.000**							
TV_{0-1}	-0.061	0.130	-0.224	-0.494	0.101	0.590	0.431	0.568	**1.000**						
TV_{0-2}	-0.101	0.057	-0.234	-0.451	0.122	0.568	0.412	0.528	**0.908**	**1.000**					
TV_{0-3}	-0.137	-0.002	-0.249	-0.402	0.145	0.531	0.383	0.488	**0.791**	**0.935**	**1.000**				
TV_{0-4}	-0.169	-0.050	-0.267	-0.357	0.167	0.493	0.357	0.459	0.698	**0.842**	**0.951**	**1.000**			
TV_{0-5}	-0.196	-0.088	-0.284	-0.318	0.186	0.462	0.333	0.438	0.631	**0.765**	**0.878**	**0.962**	**1.000**		
TV_{0-6}	-0.219	-0.119	-0.300	-0.287	0.201	0.439	0.318	0.422	0.583	**0.709**	**0.815**	**0.904**	**0.970**	**1.000**	
TV_{0-7}	-0.241	-0.150	-0.314	-0.260	0.218	0.424	0.308	0.413	0.543	0.664	**0.765**	**0.850**	**0.922**	**0.976**	**1.000**

A strong correlation is considered when absolute value of the Spearman's rank correlation coefficient between two factors is greater than 0.7, and a moderate correlation is considered when absolute value of the coefficient is greater than 0.4. The results indicated that daily mean temperature had a strong negative correlation with average atmospheric pressure (ρ= -0.913; $p<0.001$), while weak to moderate negative associations with the daily concentration of SO_2 (ρ= -0.356; $p<0.001$) and NO_2 (ρ= -0.400; $p<0.001$). Tmean, daily mean temperature; Tmax, daily maximum temperature; Tmin, daily minimum temperature; RH, relative humidity; AP, average atmospheric pressure; PM_{10}, particulate matter with particle size below 10 µm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; TV, temperature variability.

Table S3. **The overall lag-cumulative exposure-response relationship between daily mean temperature and the occurrence of AAD.**

Temperature (℃)	Cumulative relative risk (95% confidence interval)	Temperature (℃)	Cumulative relative risk (95% confidence interval)	Temperature (℃)	Cumulative relative risk (95% confidence interval)
-2	0.222 (0.027, 1.829)	*10*	0.942 (0.212, 4.184)	*22*	0.915 (0.568, 1.473)
-1	0.528 (0.079, 3.551)	*11*	0.939 (0.226, 3.906)	*23*	0.928 (0.652, 1.321)
0	0.944 (0.144, 6.205)	*12*	0.944 (0.243, 3.667)	*24*	0.955 (0.783, 1.164)
1	1.332 (0.201, 8.852)	*13*	0.954 (0.264, 3.448)	*25*	1.000 (1.000, 1.000)
2	1.556 (0.237,10.200)	*14*	0.963 (0.287, 3.230)	*26*	1.062 (0.840, 1.343)
3	1.579 (0.251, 9.923)	*15*	0.968 (0.313, 2.996)	*27*	1.134 (0.703, 1.831)
4	1.462 (0.246, 8.692)	*16*	0.965 (0.341, 2.737)	*28*	1.206 (0.596, 2.438)
5	1.294 (0.229, 7.316)	*17*	0.956 (0.370, 2.472)	*29*	1.264 (0.522, 3.063)
6	1.151 (0.212, 6.234)	*18*	0.943 (0.400, 2.222)	*30*	1.296 (0.475, 3.534)
7	1.054 (0.203, 5.486)	*19*	0.930 (0.433, 1.997)	*31*	1.285 (0.444, 3.724)
8	0.994 (0.200, 4.940)	*20*	0.919 (0.468, 1.802)	*32*	1.223 (0.400, 3.740)
9	0.959 (0.203, 4.520)	*21*	0.913 (0.511, 1.630)	*33*	1.106 (0.301, 4.063)

Considering lag effects of daily mean temperature on diseases over 25 days, during the eight years, lower and higher temperature with reference to 25 ℃ did not alter onset risks of AAD for the total, type A dissection, and type B dissection. In this table, cumulative relative risk is based on 25 days of temperature exposure.

Table S4. Overall lag-response relationships for the association between daily mean temperature and occurrence of AAD.

Lag (day)	Relative risk (95% CI) of the cold effect	Relative risk (95% CI) of the heat effect	Lag (day)	Relative risk (95% CI) of the cold effect	Relative risk (95% CI) of the heat effect
0	**1.733 (1.130, 2.658)***	0.783 (0.513, 1.193)	*13*	0.975 (0.884, 1.076)	1.008 (0.946, 1.075)
1	**1.252 (1.040, 1.509)***	0.954 (0.824, 1.103)	*14*	0.979 (0.886, 1.081)	1.009 (0.945, 1.077)
2	1.043 (0.834, 1.306)	1.046 (0.847, 1.292)	*15*	0.982 (0.890, 1.084)	1.009 (0.946, 1.077)
3	0.978 (0.827, 1.158)	1.056 (0.907, 1.229)	*16*	0.984 (0.894, 1.084)	1.010 (0.949, 1.075)
4	0.956 (0.844, 1.083)	1.043 (0.954, 1.141)	*17*	0.986 (0.899, 1.081)	1.012 (0.954, 1.073)
5	0.944 (0.833, 1.068)	1.033 (0.949, 1.124)	*18*	0.987 (0.903, 1.079)	1.014 (0.960, 1.070)
6	0.938 (0.824, 1.068)	1.025 (0.933, 1.126)	*19*	0.987 (0.906, 1.077)	1.016 (0.965, 1.068)
7	0.939 (0.828, 1.065)	1.019 (0.927, 1.120)	*20*	0.987 (0.905, 1.078)	1.018 (0.968, 1.070)
8	0.944 (0.841, 1.058)	1.015 (0.933, 1.104)	*21*	0.987 (0.900, 1.083)	1.020 (0.967, 1.077)
9	0.950 (0.858, 1.052)	1.012 (0.943, 1.087)	*22*	0.987 (0.890, 1.094)	1.023 (0.961, 1.088)
10	0.958 (0.871, 1.053)	1.010 (0.950, 1.075)	*23*	0.986 (0.876, 1.109)	1.026 (0.952, 1.105)
11	0.965 (0.878, 1.059)	1.009 (0.951, 1.071)	*24*	0.985 (0.860, 1.128)	1.028 (0.941, 1.124)
12	0.970 (0.881, 1.068)	1.009 (0.948, 1.072)	*25*	0.984 (0.842, 1.149)	1.031 (0.928, 1.146)

The lag effect of daily mean temperature on the incidence of AAD is statistically significant within two days at the extremely cold temperature. Cold effect was the impact of extreme cold temperature (0.5℃, 2.5th percentile) on occurrence of AAD, and heat effect was the impact of extreme heat temperature (32.0℃, 97.5th percentile) on AAD. AAD, acute aortic dissection; CI, confidence interval. * statistically significant

Table S5. **The exposure-response relationship (lag 0) between daily mean temperature and the occurrence of AAD.**

Tem (℃)	Relative risk (95% CI) for the total	Relative risk (95% CI) for type A dissection	Relative risk (95% CI) for type B dissection	Tem (℃)	Relative risk (95% CI) for the total	Relative risk (95% CI) for type A dissection	Relative risk (95% CI) for type B dissection
-2	1.558 (0.936, 2.592)	2.927 (1.034, 8.286)*	1.798 (0.922, 3.508)	16	1.376 (1.046, 1.812)*	1.629 (1.039, 2.555)*	1.491 (1.026, 2.167)*
-1	1.668 (1.057, 2.631)*	3.553 (1.392, 9.068)*	1.770 (0.960, 3.263)	17	1.335 (1.038, 1.716)*	1.550 (1.029, 2.335)*	1.430 (1.017, 2.012)*
0	1.724 (1.117, 2.660)*	3.896 (1.607, 9.448)*	1.751 (0.972, 3.155)	18	1.287 (1.028, 1.611)*	1.465 (1.016, 2.111)*	1.366 (1.007, 1.853)*
0.5	**1.733 (1.130, 2.658)***	**3.951 (1.657, 9.418)***	**1.745 (0.976, 3.121)**	19	1.236 (1.014, 1.505)*	1.378 (1.000, 1.898)	1.302 (0.998, 1.701)
1	1.732 (1.136, 2.642)*	3.934 (1.675, 9.237)*	1.741 (0.981, 3.091)	20	1.185 (1.000, 1.404)	1.293 (0.982, 1.703)	1.240 (0.986, 1.559)
2	1.704 (1.131, 2.569)*	3.730 (1.637, 8.498)*	1.737 (0.995, 3.034)	21	1.136 (0.985, 1.310)	1.215 (0.964, 1.530)	1.181 (0.975, 1.431)
3	1.654 (1.111, 2.461)*	3.386 (1.534, 7.475)*	1.737 (1.012, 2.982)*	22	1.091 (0.972, 1.225)	1.144 (0.951, 1.378)	1.127 (0.965, 1.315)
4	1.593 (1.083, 2.345)*	3.002 (1.403, 6.423)*	1.740 (1.030, 2.940)*	23	1.053 (0.967, 1.147)	1.084 (0.947, 1.242)	1.078 (0.962, 1.208)
5	1.535 (1.052, 2.240)*	2.650 (1.274, 5.512)*	1.743 (1.044, 2.911)*	24	1.022 (0.974, 1.072)	1.036 (0.960, 1.118)	1.035 (0.971, 1.104)
6	1.490 (1.028, 2.161)*	2.374 (1.171, 4.815)*	1.745 (1.054, 2.889)*	25	1.000 (1.000, 1.000)	1.000 (1.000, 1.000)	1.000 (1.000, 1.000)
7	1.462 (1.015, 2.105)*	2.181 (1.102, 4.315)*	1.744 (1.063, 2.862)*	26	0.984 (0.930, 1.043)	0.971 (0.888, 1.062)	0.972 (0.900, 1.049)
8	1.446 (1.011, 2.067)*	2.047 (1.061, 3.948)*	1.740 (1.071, 2.827)*	27	0.971 (0.864, 1.092)	0.939 (0.783, 1.127)	0.951 (0.813, 1.112)
9	1.439 (1.015, 2.040)*	1.955 (1.040, 3.675)*	1.731 (1.078, 2.782)*	28	0.954 (0.803, 1.134)	0.895 (0.684, 1.170)	0.937 (0.744, 1.180)
10	1.438 (1.023, 2.022)*	1.893 (1.033, 3.468)*	1.717 (1.081, 2.729)*	29	0.930 (0.747, 1.160)	0.831 (0.589, 1.172)	0.931 (0.693, 1.250)
11	1.440 (1.033, 2.008)*	1.849 (1.034, 3.306)*	1.698 (1.080, 2.669)*	30	0.896 (0.687, 1.167)	0.744 (0.490, 1.130)	0.932 (0.656, 1.324)

12	1.441 (1.042, 1.994)*	1.815 (1.038, 3.172)*	1.671 (1.074, 2.601)*	31	0.857 (0.614, 1.168)	0.636 (0.379, 1.067)	0.942 (0.619, 1.434)
13	1.439 (1.048, 1.975)*	1.783 (1.043, 3.047)*	1.637 (1.063, 2.521)*	32	**0.783 (0.513, 1.193)**	**0.513 (0.257, 1.024)**	**0.960 (0.560, 1.647)**
14	1.429 (1.051, 1.942)*	1.745 (1.046, 2.913)*	1.596 (1.051, 2.425)*	33	0.704 (0.389, 1.275)	0.386 (0.145, 1.028)	0.989 (0.467, 2.090)
15	1.409 (1.050, 1.889)*	1.695 (1.044, 2.752)*	1.547 (1.037, 2.308)*				

The extremely cold temperature (0.5℃), instead of the extremely hot temperature, significantly increased risks of AAD for the total (RR, 1.733; 95% CI, 1.130-2.658) and type A dissection (RR, 3.951; 95%CI, 1.657-9.418). Cold effect was the impact of extreme cold temperature (0.5°C, 2.5th percentile) on occurrence of AAD, and heat effect was the impact of extreme heat temperature (32.0°C, 97.5th percentile) on AAD. AAD, acute aortic dissection; Tem, daily mean temperature; RR, relative risk; CI, confidence interval.

* statistically significant

Table S6. Subgroup analyses.

Group	Cold-related effect		Heat-related effect	
	RR (95% CI)	*P* value	RR (95% CI)	*P* value
Overall	1.733 (1.130, 2.658)		0.783 (0.513, 1.193)	
Subtype				
Type A	3.951 (1.657, 9.418)	0.125	0.513 (0.257, 1.024)	0.161
Type B	1.745 (0.976, 3.121)		0.960 (0.560, 1.647)	
Sex				
Male	1.923 (1.193, 3.101)	0.607	0.989 (0.627, 1.562)	**0.006**
Female	2.747 (0.769, 9.812)		0.178 (0.057, 0.549)	
Age				
$<$55 years	2.340 (1.322, 4.140)	0.131	0.858 (0.488, 1.509)	0.673
$\geq$55 years	1.203 (0.629, 2.303)		0.714 (0.376, 1.354)	
Hypertension				
Yes	2.778 (1.301, 5.932)	0.495	0.961 (0.546, 1.692)	0.131
No	1.956 (1.008, 3.795)		0.497 (0.262, 0.945)	

Table S7. **Effect of temperature variability on the occurrence of AAD.**

	Relative risk (95% CI) in different groups								
	Overall	Type A dissection	Type B dissection	Male	Female	Younger than 55	Older or equal to 55	With hypertension	Without hypertension
TV_{0-1}	1.000 (0.961,1.041)	0.962 (0.906,1.021)	1.021 (0.968,1.077)	1.015 (0.971,1.062)	0.919 (0.844,1.001)	0.993 (0.942,1.047)	1.008 (0.949,1.071)	1.004 (0.953,1.058)	0.979 (0.921,1.041)
TV_{0-2}	0.995 (0.955,1.037)	0.962 (0.904,1.023)	1.016 (0.961,1.074)	1.015 (0.969,1.062)	**0.899* (0.822,0.982)**	0.976 (0.923,1.031)	1.019 (0.957,1.084)	0.993 (0.941,1.048)	0.980 (0.919,1.044)
TV_{0-3}	0.992 (0.951,1.035)	0.966 (0.906,1.030)	1.009 (0.952,1.068)	1.014 (0.967,1.063)	**0.894* (0.815,0.981)**	0.982 (0.928,1.040)	1.002 (0.940,1.068)	0.983 (0.930,1.039)	0.989 (0.926,1.056)
TV_{0-4}	0.985 (0.943,1.030)	0.953 (0.892,1.019)	1.004 (0.946,1.065)	0.998 (0.950,1.048)	0.928 (0.843,1.021)	0.991 (0.934,1.051)	0.976 (0.913,1.042)	0.974 (0.919,1.031)	0.987 (0.921,1.056)
TV_{0-5}	0.983 (0.939,1.029	0.948 (0.885,1.016)	1.003 (0.942,1.067)	0.991 (0.941,1.043)	0.946 (0.856,1.046)	0.999 (0.939,1.063)	0.960 (0.896,1.029)	0.975 (0.918,1.035)	0.980 (0.912,1.052)
TV_{0-6}	0.983 (0.936,1.031)	0.941 (0.875,1.012)	1.008 (0.944,1.077)	0.987 (0.935,1.042)	0.958 (0.862,1.064)	1.009 (0.945,1.077)	0.948 (0.882,1.019)	0.984 (0.924,1.048)	0.966 (0.896,1.042)
TV_{0-7}	0.982 (0.933,1.034)	0.945 (0.876,1.020)	1.008 (0.940,1.080)	0.984 (0.929,1.042)	0.969 (0.867,1.083)	1.018 (0.950,1.090)	0.938 (0.869,1.012)	0.982 (0.919,1.049)	0.970 (0.895,1.050)

The indicator significantly decreased AAD risks at 0-2 and 0-3 exposure days among female patients. AAD, acute aortic dissection; RR, relative risk; CI, confidence interval; TV, temperature variability.

* statistically significant

Figure S1. Time series distributions for daily mean temperature and monthly onset cases of acute aortic dissection.

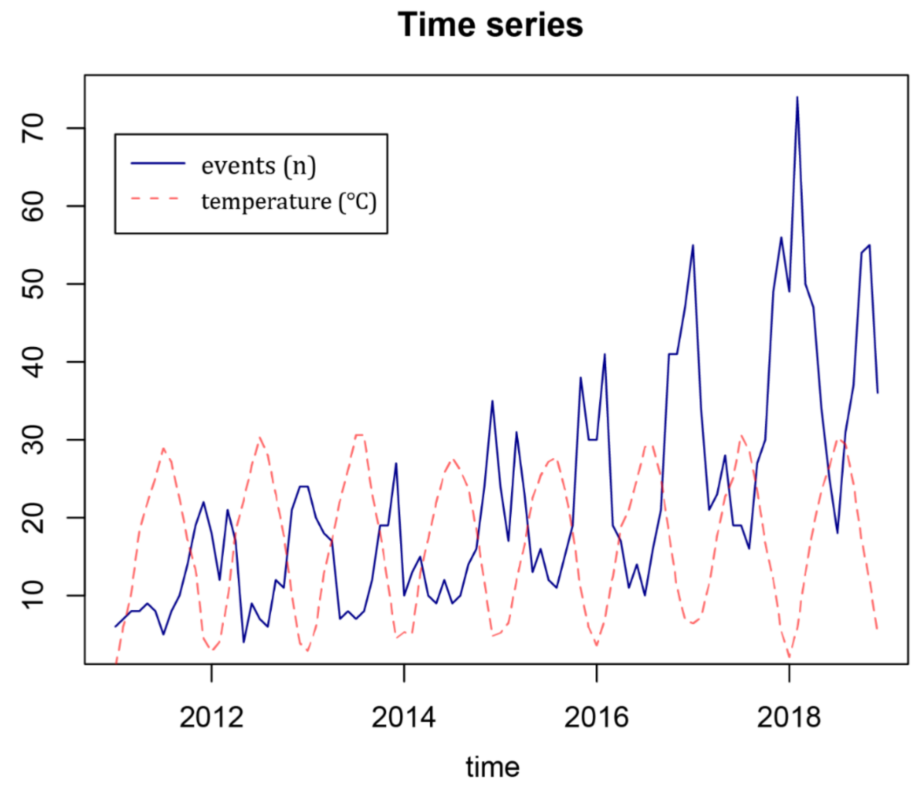


Figure S2. Seasonal decomposition analysis of time series of monthly onset cases of acute aortic dissection.

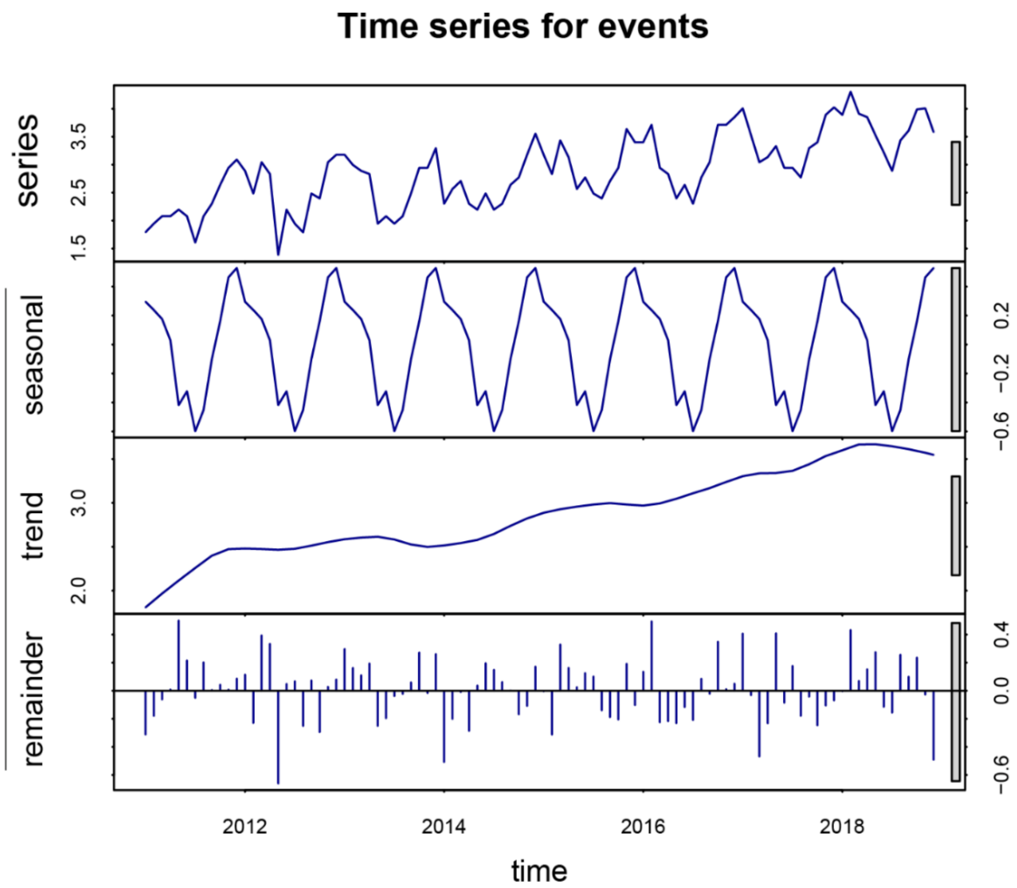
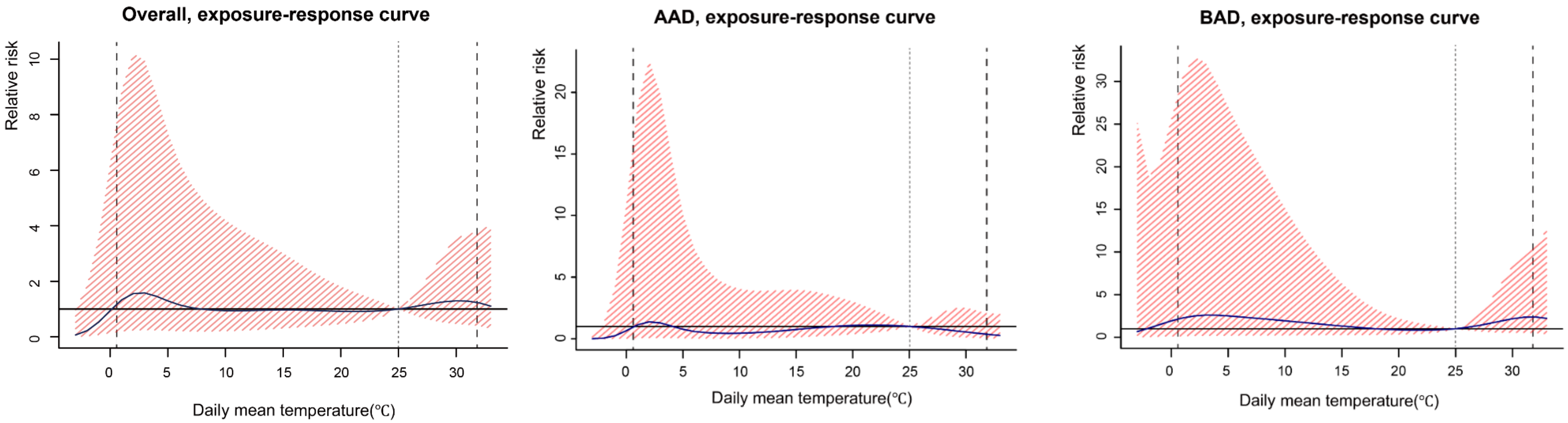
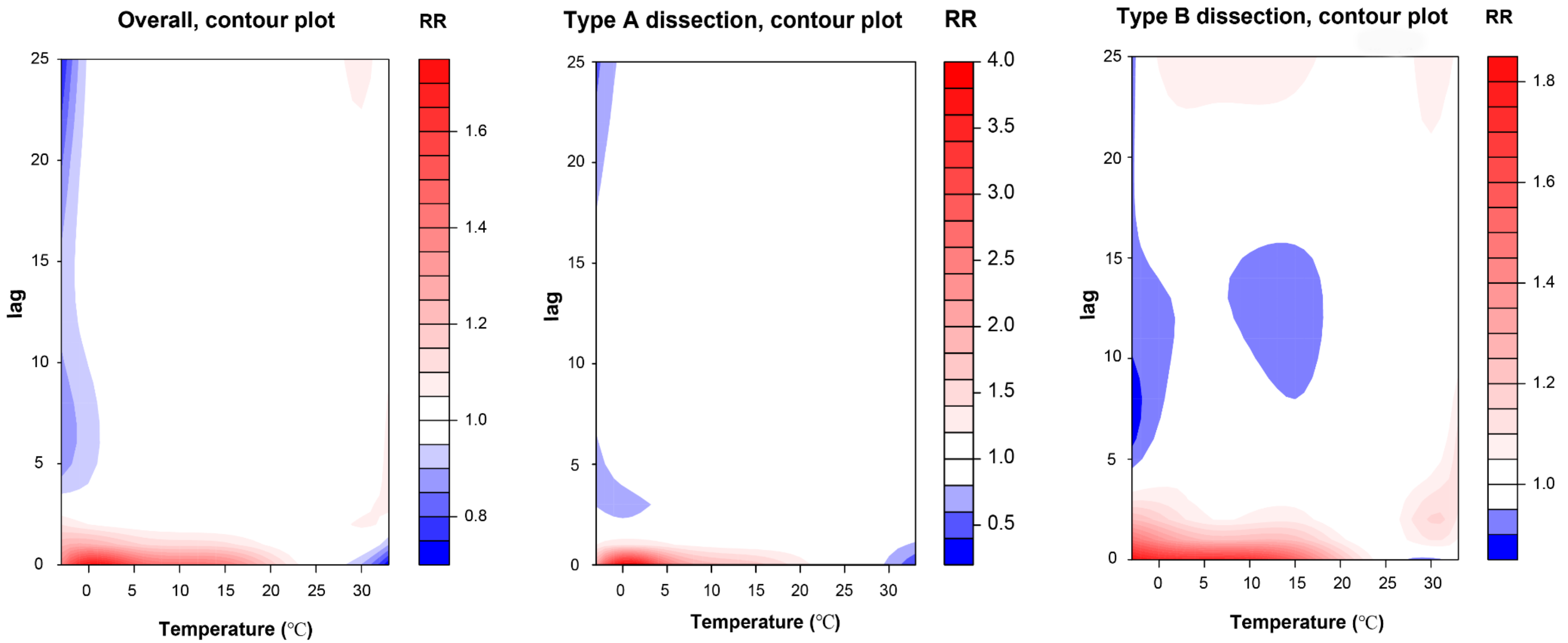


Figure S3. Lag-cumulative exposure-response relationships between daily mean temperature and occurrence of overall, Stanford type A and Stanford type B acute aortic dissection.



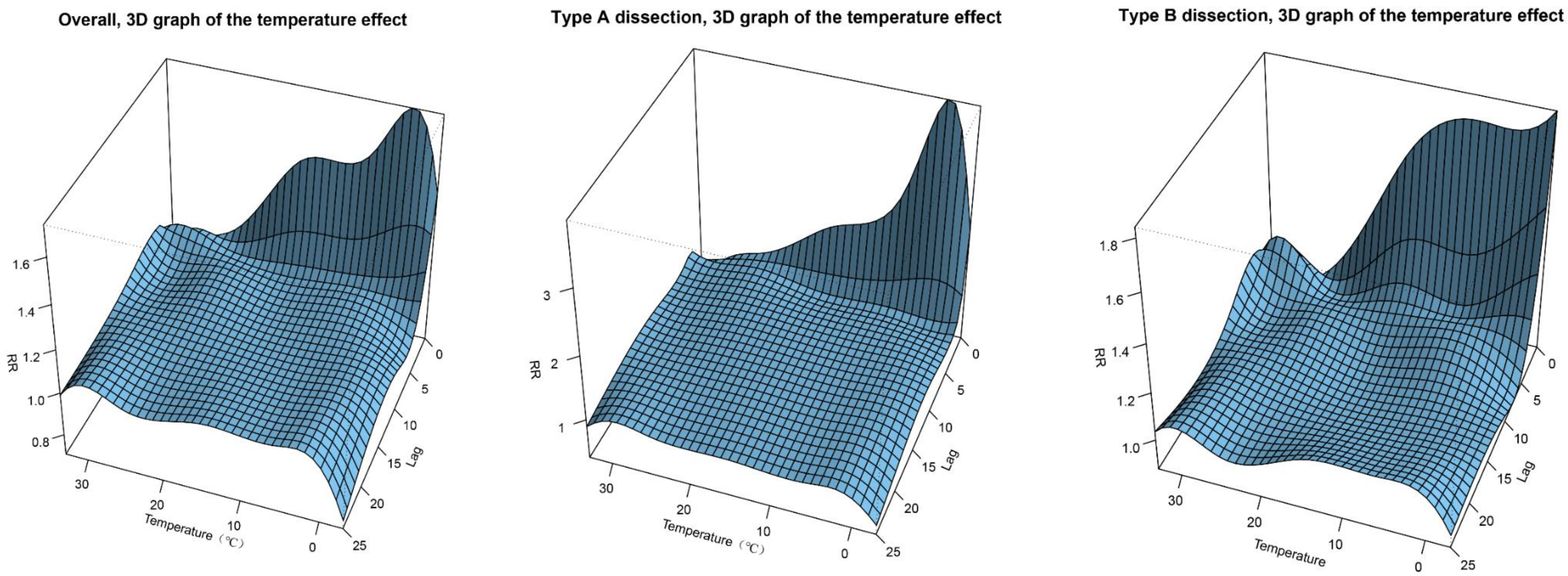
Considering lag effects of daily mean temperature on diseases over 25 days, during the eight years, lower and higher temperature with reference to 25 ℃ did not alter onset risks of AAD for the total, type A dissection, and type B dissection. The blue solid curve is the fitted curve of DLNM model, and the area covered by red oblique lines represents 95% confidence intervals of the curve. The vertical lines stand for reference temperature (25℃, dotted), and the 2.5th and the 97.5th percentiles of the distribution of daily mean temperature (dashed).

Figure S4. Bi-dimensional exposure-lag-response relationships between onset of AAD and daily mean temperature displayed in contour plots.



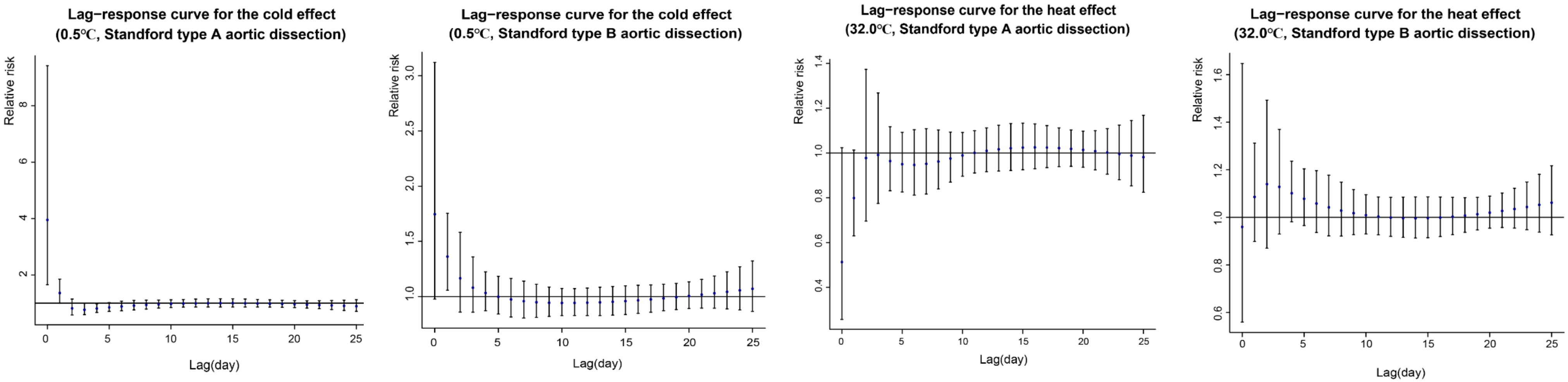
The contour plots could not show 95% confidence intervals of the fitted results.

Figure S5. Bi-dimensional exposure-lag-response relationships between onset of AAD and daily mean temperature displayed in 3-D graphs.



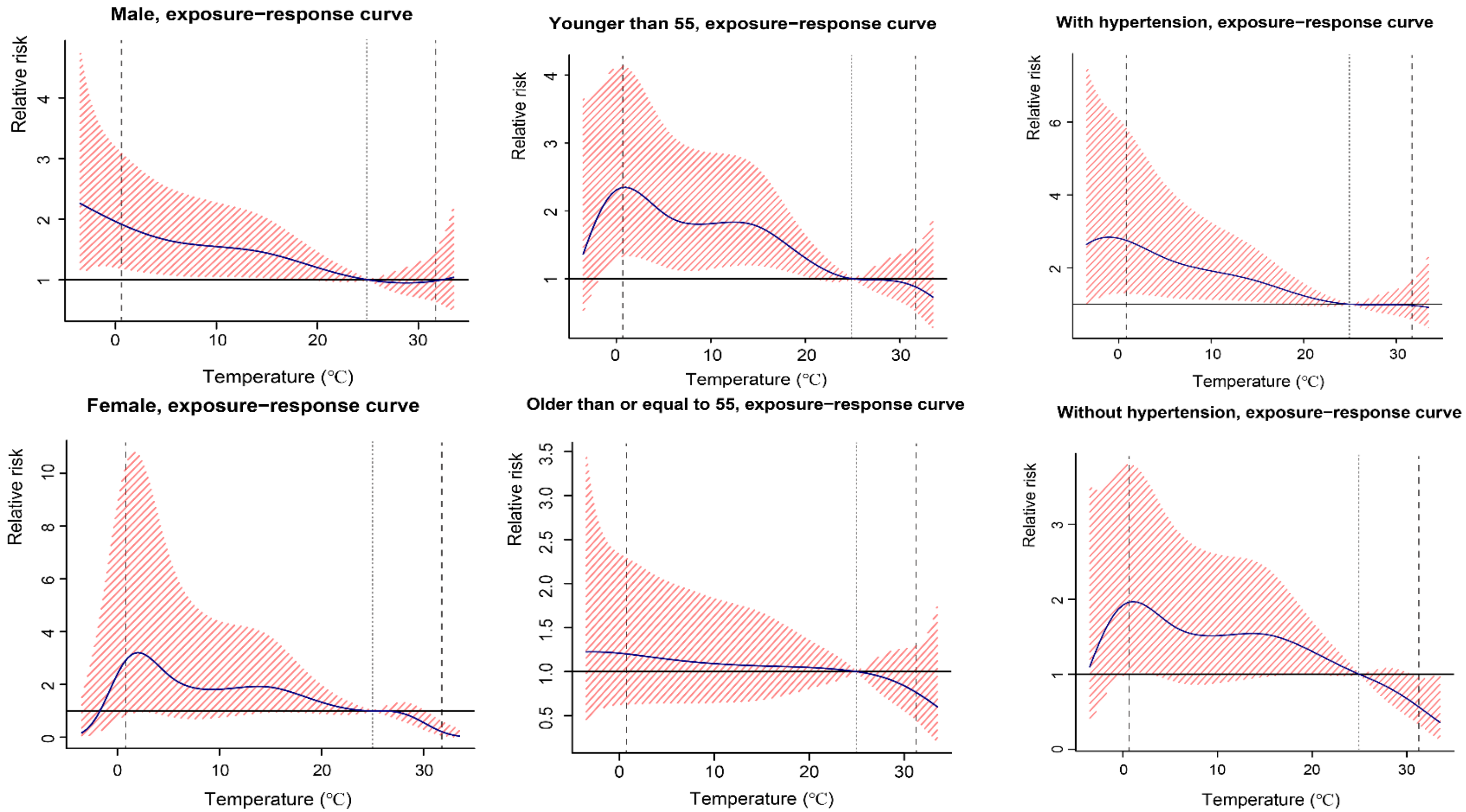
The 3-D graphs could not show 95% confidence intervals of the fitted results.

Figure S6. Lag-response relationships for the cold and heat effect among patients with Stanford type A and type B aortic dissection.



In these figures, vertical line segments estimate the 95% confidence intervals of relative risks.

Figure S7. Exposure-response curves (lag 0) for the association between daily mean temperature and AAD during the study period stratified by subgroups.



Significantly increased cold-related AAD risks were observed in males, people younger than 55, and people with type A aortic dissection. The blue solid curve is the fitted curve of DLNM model, and the area covered by red oblique lines represents 95% confidence intervals of the curve. The vertical lines stand for reference temperature (25℃, dotted), and the 2.5th and the 97.5th percentiles of the distribution of daily mean temperature (dashed).