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The effects of ambient temperature on non-accidental mortality in the elderly hypertensive subjects, a cohort-based study

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Abstract

Background The association between ambient temperature and mortality has yielded inconclusive results with previous studies relying on in-patient data to assess the health effects of temperature. Therefore, we aimed to estimate the effect of ambient temperature on non-accidental mortality among elderly hypertensive patients through a prospective cohort study conducted in northeastern China.

Methods A total of 9634 elderly hypertensive patients from the Kailuan research who participated in the baseline survey and follow-up from January 1, 2006 to December 31, 2017, were included in the study. We employed a Poisson generalized linear regression model to estimate the effects of monthly ambient temperature and temperature variations on non-accidental mortality.

Results After adjusting for meteorological parameters, the monthly mean temperature (RR = 0.989, 95% CI: 0.984–0.993, $p < 0.001$), minimum temperature (RR = 0.987, 95% CI: 0.983–0.992, $p < 0.001$) and maximum temperature (RR = 0.989, 95% CI: 0.985–0.994, $p < 0.001$) exhibited a negative association with an increased risk of non-accidental mortality. The presence of higher monthly temperature variation was significantly associated with an elevated risk of mortality (RR = 1.097, 95% CI:1.051–1.146, $p < 0.001$). Further stratified analysis revealed that these associations were more pronounced during colder months as well as among male and older individuals.

Conclusions Decreased temperature and greater variations in ambient temperature were observed to be linked with non-accidental mortality among elderly hypertensive patients, particularly notable within aging populations and males. These understanding regarding the effects of ambient temperature on mortality holds clinical significance for appropriate treatment strategies targeting these individuals while also serving as an indicator for heightened risk of death.

Keywords Ambient temperature, Non-accidental mortality, Hypertension, Geriatrics

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Background

Both short-term and long-term exposure to decreased ambient temperature can lead to an elevation in blood pressure (BP). Previous studies have reported a 0.2—0.4 mmHg increase in systolic blood pressure (SBP) and a 0.1—0.3 mmHg increase in diastolic blood pressure (DBP) per 1 °C decrease in the ambient temperature [1]. Experimental evidence has also demonstrated that sudden exposure to cold temperatures can result in a substantial rise of up to 20–30 mmHg in BP [2]. Furthermore, BP tends to be higher during cold seasons, with an average increase of approximately 5/3 (SBP/DBP) mmHg observed. This effect appears more pronounced among hypertensive patients and older individuals [3]. Additionally, emerging evidence suggests that temperature variation may further contribute to increased BP variability [1].

The elevated levels of BP and its variability associated with decreased temperature or temperature fluctuations could potentially play a crucial role in the excess morbidity and mortality observed during cold weather conditions, particularly regarding adverse cerebrovascular and cardiovascular events [4, 5]. Hypertensive patients may exhibit heightened susceptibility to ambient temperature, as exposure to decreased temperature or temperature variation could amplify BP fluctuations, exacerbate symptoms, worsen disease progression, and consequently elevate the risk of cerebro-cardiovascular events along with additional mortality risks [6]. Moreover, aging is known to impair blood pressure regulation while increasing its variability, thus advancing age might further intensify the manifestation of cold-related symptoms and complaints among hypertensive patients [7].

Most of the previous studies have focuses on assessing the effect of temperature on mortality using in-patient data, such as the number of cases or deaths [8, 9]. In this study, we aimed to investigate the relationship between ambient temperature and non-accidental mortality among elderly individuals with hypertension, based on a prospective cohort study conducted in northeast China.

Methods

Study population

A total of 126,847 inhabitants who underwent their initial health examination in Kailuan reach from 2006 to 2009 (ChiCTR-TNRC-11001489) were selected as the study cohort. Inclusion criteria comprised individuals aged over 65 with a history of hypertension who consented to participate in the Kailuan research and provided informed consent. Hypertension was defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or current use of antihypertensive medication [10]. Exclusion criteria included individuals with a history of myocardial infarction, stroke, tumor, or missing information. Ultimately, a total of 9634 elderly subjects with essential hypertension were included for analysis (Fig. 1). This prospective study adhered to the principles outlined in the Helsinki Declaration and received approval from the Ethics Committee of Kailuan General Hospital. Written informed consent was obtained from all participants. The first physical examination conducted between January 1, 2006, and December 31, 2009 marked the commencement of

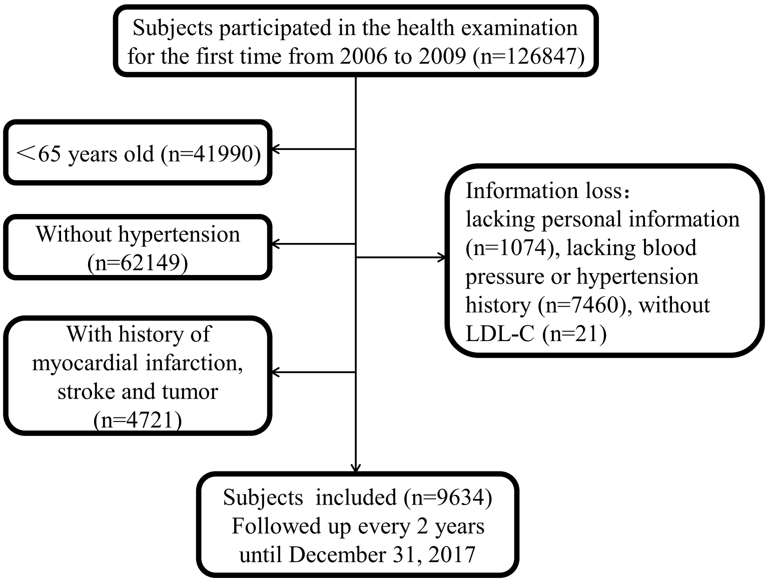

Fig. 1 Flow-chart of the study

follow-up. Non-accidental mortality served as the endpoint. The final follow-up date was December 31, 2017.

Subjects assessments

The demographic characteristics and clinical history of each subject were documented, including age, sex, body mass index (BMI), alcohol consumption, smoking habits, diabetes status, and hyperlipidemia. Additionally, the SBP, DBP, and total cholesterol levels of the subjects were recorded. The 10-year ischemic cardiovascular diseases (ICVD) risk assessment system was utilized to assess the ICVD risk in the study population. This risk assessment tool for ischemic stroke and coronary events was specifically developed for the Chinese population [11]. The evaluation system primarily considered seven cerebro-cardiovascular risk factors, including age, sex, SBP, BMI, total cholesterol level, smoking status, and diabetes. The absolute10-year ICVD risk was categorized based on the total score as follows: extremely high risk (score > 40%), high risk (20% < score ≤ 40%), medium risk (10% < score ≤ 20%), low risk (5% < score ≤ 10%) and very low risk (score ≤ 5%). Subjects who had occupational exposure to pulverized coal prior to retirement were classified as having dust exposure. All health examination data were recorded by trained health workers. Non-accidental mortality was defined as death resulting from any cause other than accidental injury during the follow-up period, and was obtained through Kailuan Social Security Information System.

Meteorological data

Tangshan is situated in the northern region of China (117°31′ – 119°19′ E and 38°55′ – 40°28′ N) and experiences a warm temperate semi-humid monsoon continental climate. The Tianjin Meteorological Bureau provided the meteorological data from the Tangshan Climate Monitoring Station, situated at 117°95′ E and 40°20′ N. The meteorological observations were collected from January 1, 2006, to December 31, 2017, encompassing monthly average temperature, maximum temperature, minimum temperature, relative humidity, precipitation, and wind speed. Monthly temperature variation was calculated using the standard deviation of daily average temperatures [12, 13].

Statistical methods

Continuous variables normally distributed were presented as mean ± standard deviation, while categorical variables were reported as counts and percentages. To analyze the differences in risk factors between groups, a t-test was utilized for continuous variables and the Chi-square test for categorical variables. The non-accidental mortality rate was expressed as the average number of deaths that occurred during the study period per 1,000 people per month. A Poisson generalized linear regression model was applied to analyze the impact of ambient temperature on the monthly mortality risk of the study population. The log of the monthly population base from 2006 to 2017 was used as the log-linkage function offset in the statistical model [14]. The effect of monthly temperature on the non-accidental mortality in the elderly hypertensive population was estimated by relative risk (RR) and 95% confidence interval (CI). The models were fitted for each meteorological variable (monthly mean temperature, monthly minimum temperature, monthly maximum temperature) after adjusting for the relative humidity, wind speed and precipitation. The model fitted for monthly temperature variation further adjusted for the monthly mean temperature. Tangshan experiences hot, wet summers and cold, dry winters, thus, all months were categorized into warm season (May through October) and cold season (November through April) based on meteorological reports and previous findings [15, 16]. Further stratified analysis was conducted to investigate the differential effects of monthly temperature on non-accidental mortality during warm and cold seasons and among subjects with varying risk factors stratified by age, sex 10-years ICVD risk, and dust exposure. A two-tailed *P* value less than 0.05 was considered statistically significant. All analyses were performed using SPSS 25.0.

Results

Baseline characteristics of the subjects

A total of 9634 elderly hypertensive subjects were included in the analysis, with 3254 deaths during the follow-up. The mean age of the surviving subjects was 70.9 ($SD = 5.3$, $n = 6380$). Subjects who died during the follow-up exhibited higher baseline age (73.1 ± 5.6), a higher proportion of males, diabetes, smoking, dust exposure and elevated levels of SBP and DBP ($p < 0.05$) at baseline. Those who died also had higher mid-, high- and very high-risk 10-year ICVD absolute risk levels compared to survivors ($p < 0.001$). There was no difference in terms of hyperlipidemia and alcohol consumption between the two groups ($p > 0.05$), as indicated in Table 1. The differences in baseline characteristics among deceased subjects stratified by warm and cold seasons was presented in Table 2. However, no significant differences were found between the two groups.

The monthly distribution of meteorological factors and non-accidental mortality

The mean monthly temperature reached its minimum in January (-5.26℃), and the maximum monthly temperature was recorded in July (26.27℃). The minimum monthly temperature variation occurred in July (standard

Table 1 The baseline characteristics of the study subjects with or without death

Characteristic	**Without death (*n* = 6380)**	**Death (*n* = 3254)**	***P* value**
Age, mean ± SD	70.9 ± 5.3	73.1 ± 5.6	< 0.001
≤ 70, n (%)	3659 (57.4%)	1283 (39.4%)	< 0.001
> 70, n (%)	2721 (42.6%)	1971 (60.6%)	
Sex			
Male, n (%)	5412 (84.8%)	3027 (93.0%)	< 0.001
Female, n (%)	968 (15.2%)	227 (7.0%)	
Diabetes, n (%)	872 (13.7%)	589 (18.1%)	< 0.001
Hyperlipidemia, n (%)	2061 (32.3%)	1045 (32.1%)	0.851
SBP (mmHg), mean ± SD	153.0 ± 17.0	155.4 ± 18.7	< 0.001
DBP (mmHg), mean ± SD	88.3 ± 10.3	88.7 ± 11.2	0.037
BMI, mean ± SD	25.3 ± 3.5	25.0 ± 3.7	0.010
Smoking, n (%)	1936 (30.3%)	1052 (32.3%)	0.046
Alcohol drinking, n (%)	2027 (31.8%)	1030 (31.7%)	0.906
10-years ICVD absolute risk grade			
Very low risk, n (%)	150 (2.4%)	48 (1.5%)	< 0.001
Low risk, n (%)	2243 (35.2%)	859 (26.4%)	
Middle risk, n (%)	2014 (31.6%)	1070 (32.9%)	
High risk, n (%)	1464 (22.9%)	899 (27.6%)	
Very high risk, n (%)	509 (8.0%)	378 (11.6%)	
Dust exposure, n (%)	1023 (16.0%)	675 (20.7%)	< 0.001

SD Standard deviation, *SBP* Systolic blood pressure, *BMI* Body mass index, *ICVD* Ischemic cardiovascular diseases. The 10-year ICVD absolute risk grade was evaluated by age, sex, SBP, total cholesterol level, BMI, smoking and diabetes

deviation 1.85), while the greatest variation was observed in March (standard deviation 3.98). The highest monthly non-accidental mortality rate among elderly individuals with hypertension occurred in December, at 32.80 ‰ (95% CI: 29.24–36.36), whereas the lowest monthly non-accidental mortality rate was reported in April, at 24.39 ‰ (95% CI: 21.31–27.47), as detailed in Table 3.

The effect of monthly temperature on non-accidental mortality

We analyzed the relationship between monthly temperature and non-accidental mortality risk among the elderly hypertensive subjects by Poisson generalized linear regression model after adjusting for the monthly mean relative humidity, wind speed and precipitation. Our findings revealed that there was a negative association between the monthly mean temperature, minimum temperature and maximum temperature with the increase in non-accidental mortality among the subjects. Specifically, we observed that a decrease of 1 °C in the monthly mean temperature, minimum temperature and maximum temperature correlated with an increase of 1.1%, 1.3% and 1.1% respectively in non-accidental mortality. Furthermore, we found that higher monthly temperature variation was significantly associated with increased non-accidental mortality risk in elderly hypertensive subjects. For every 1 °C increase in the standard deviation of monthly temperature, there was a corresponding 9.7% increase in non-accidental mortality risk within the study population. Upon conducting stratified analysis, it became evident that the effect of the monthly temperature on non-accidental mortality among elderly subjects with hypertension was more pronounced during the cold season, except for the monthly maximum temperature (RR = 0.993, 95% CI: 0.984–1.001, $p = 0.080$). However, it is worth noting that there was no significant correlation between monthly mean temperature, maximum temperature, or temperature variation and the risk of non-accidental mortality among the study population during warm seasons. Nevertheless, we found that during warm seasons there was a correlation between monthly minimum temperature and increased mortality risk (RR = 0.987, 95% CI: 0.976–0.998, $p = 0.019$), as shown in Table 4.

Table 2 Distribution of risk factors of the subjects with death in different warm and cold seasons

Characteristic	**May–October (*n* = 1610)**	**November–April (*n* = 1644)**	***P* value**
Male, n (%)	1496 (92.9%)	1531 (93.1%)	0.816
> 70, n (%)	976 (60.6%)	995 (60.5%)	0.954
SBP (mmHg), mean ± SD	155.7 ± 18.8	155.2 ± 18.7	0.379
DBP (mmHg), mean ± SD	88.6 ± 11.3	88.9 ± 11.2	0.411
BMI, mean ± SD	25.0 ± 3.7	25.1 ± 3.6	0.698
Diabetes, n (%)	292 (18.1%)	297 (18.1%)	0.958
Hyperlipidemia, n (%)	511 (31.7%)	534 (32.5%)	0.650
Smoking, n (%)	531 (33.0%)	521 (31.7%)	0.431
Alcohol drinking, n (%)	506 (31.4%)	524 (31.9%)	0.785
10-years ICVD absolute risk grade			
Very low risk, n (%)	22 (1.4%)	26 (1.6%)	0.943
Low risk, n (%)	423 (26.3%)	436 (26.5%)	
Middle risk, n (%)	539 (33.5%)	531 (32.3%)	
High risk, n (%)	439 (27.3%)	460 (28.0%)	
Very high risk, n (%)	187 (11.6%)	191 (11.6%)	
Dust exposure, n (%)	322 (20.0%)	353 (21.5%)	0.300

SD Standard deviation, *SBP* Systolic blood pressure, *BMI* Body mass index, *ICVD* Ischemic cardiovascular diseases. The 10-year ICVD absolute risk grade was evaluated by age, sex, SBP, total cholesterol level, BMI, smoking and diabetes

Further stratified analysis was conducted to investigate the variation in the effects of monthly temperature on non-accidental mortality in the elderly hypertensive subjects with different risk factors stratified by age, sex, 10-year ICVD risk and dust exposure in warm and

Table 3 Monthly all-cause mortality and monthly ambient temperature data from January 1, 2014 to December 31, 2017

Month	All-cause mortality rate (‰)	Mean temperature (℃)	Minimum temperature (℃)	Maximum temperature (℃)	Temperature variation (℃)
January	27.9	-5.3	-11.5	0.2	2.8
February	28.8	-1.5	-7.7	4.8	3.3
March	27.0	5.8	-1.4	14.0	4.0
April	24.4	13.5	7.2	20.8	3.5
May	24.8	20.4	14.1	26.0	3.0
June	27.9	24.0	19.2	28.4	2.3
July	28.1	26.3	22.1	29.6	1.9
August	29.6	25.3	20.7	28.9	2.0
September	27.3	20.3	13.6	24.7	2.8
October	29.4	12.9	5.3	19.8	3.6
November	29.8	3.8	-3.5	11.2	3.9
December	32.8	-3.1	-9.3	1.7	2.9

The temperature variation was presented as the standard variation of the daily mean temperature of each month

Table 4 The effect of monthly temperature and temperature variation on all-cause mortality of the subjects

	Overall ($n = 3254$)		**May–October ($n = 1610$)**		**November–April ($n = 1644$)**	
	RR (95% CI)	***P* value**	**RR (95% CI)**	***P* value**	**RR (95% CI)**	***P* value**
Monthly mean temperature	0.989 (0.984, 0.993)	< 0.001	0.986 (0.972, 1.000)	0.051	0.988 (0.979, 0.997)	0.009
Monthly minimum temperature	0.987 (0.983, 0.992)	< 0.001	0.987 (0.976, 0.998)	0.019	0.983 (0.974, 0.991)	< 0.001
Monthly maximum temperature	0.989 (0.985, 0.994)	< 0.001	0.984 (0.967, 1.001)	0.061	0.993 (0.984, 1.001)	0.080
Monthly temperature variation[a]	1.097 (1.051, 1.146)	< 0.001	1.070 (0.972, 1.179)	0.168	1.159 (1.094, 1.228)	< 0.001

Poisson generalized linear models were fitted for each meteorological variable after adjusting for the relative humidity, wind speed and precipitation

RR Relative risk, *CI* Confidence interval

[a] Further adjusted for the monthly mean temperature

cold seasons. We observed a more pronounced effect of monthly mean temperature, maximum temperature, minimum temperature and temperature variation on hypertensive individuals over 70 years old and those who were male and had dust exposure. However, there was no significant difference in the effect of monthly temperature on non-accidental mortality among the study population with varying 10-year ICVD risks. Although the effect of monthly temperature on subjects with dust exposure was more evident, all results reached statistical significance (Fig. 2A). Subsequent exploration into the distinct effects of monthly temperature on subjects with different risk factors during warm (Fig. 2B) and cold seasons (Fig. 2C) demonstrated a greater impact during cold seasons, except for females in the warm season. The subgroup analysis indicated that monthly minimum and maximum temperatures were negatively associated with non-accidental mortality in males but positively associated with non-accidental mortality in females.

Discussion

We observed a significant association between monthly temperature and its variation with non-accidental mortality among the elderly hypertensive population in the Kailuan research cohort. Monthly mean temperature, minimum temperature and maximum temperature exhibited a tendency towards negative correlation with non-accidental mortality, while higher monthly temperature variation was correlated with an increased rate of non-accidental mortality, particularly during colder months. Subgroup analysis further suggested a greater impact of the monthly temperature and its variation on non-accidental mortality among the older and male subjects.

The absence of differences in the conventional cerebrovascular risk factors between subjects who died in warm and cold months suggested that other risk factors may contribute to the monthly variations in non-accidental mortality. Given the reported associations between meteorological factors and mortality due to climate

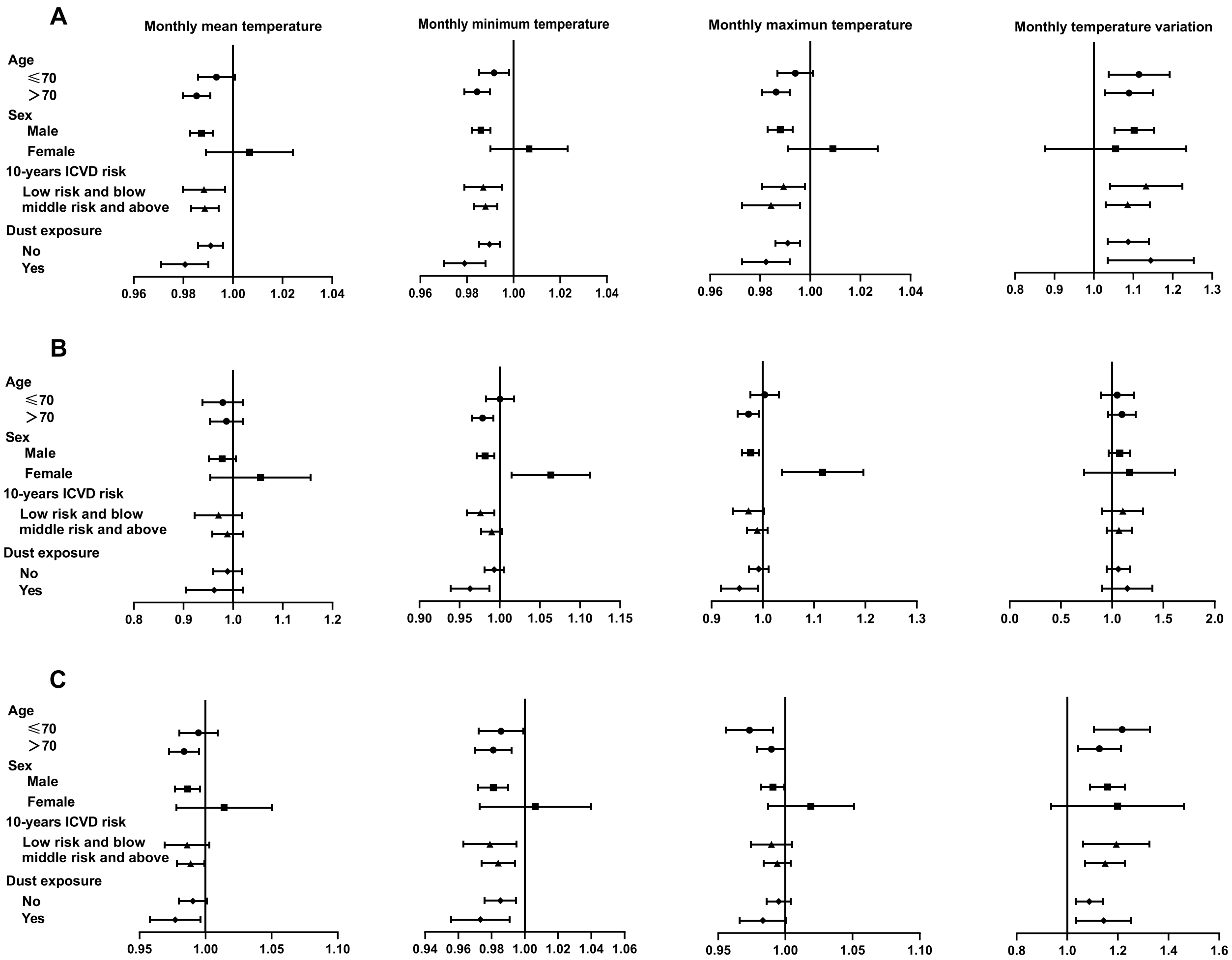

Fig. 2 Changes in mortality risk associated with every 1 °C change in the monthly temperature and temperature variations. **A** The effects of monthly ambient temperature and temperature variations on non-accidental mortality stratified by age, gender, 10-year ICVD risk and dust exposure. **B** The effects of monthly ambient temperature and temperature variations on non-accidental mortality stratified by age, gender, 10-year ICVD risk and dust exposure during warm seasons (May through October) and (**C**) cold seasons (November through April)

changes, it is plausible that meteorological factors may contribute to the differences in monthly mortality risk among elderly hypertensive subjects. Previous studies have shown inconsistent results regarding the effects of ambient temperature on non-accidental mortality due to variations in disease patterns, geographical locations and other contributing factors [8, 17]. While both high and low-temperatures increase mortality rates, the effects of cold generally outweigh those of heat on health [17]. The recent Global Burden of Disease Study estimated cause-specific relative risks of ambient temperature on mortality and found that cold effects were most pronounced in China [18]. In the study, we analyzed the effect of ambient temperature on elderly hypertensive subjects, who have been reported as more vulnerable to temperature changes [6]. The Poisson regression model revealed that lower monthly temperatures were associated with increased non-accidental mortality in elderly hypertensive subjects, particularly during cold months. Increased blood pressure during cold months may be a significant factor of the observed excess cold-related morbidity [4].

In addition to ambient temperature, temperature variability has also been identified as a potential trigger for additional mortality risks [12]. Our results indicated that monthly temperature variation was linked to non-accidental mortality risk in elderly subjects with hypertension, especially during cold months. Several epidemiological studies have demonstrated that changes in ambient temperature affect blood pressure variability [1, 19]. While this type of blood pressure variety has little medical relevance, patients with hypertension exhibit more pronounced blood pressure variability and are more susceptible to disruptions in blood pressure regulation due to temperature changes [1, 20]. Excessive blood pressure variability may increase the risk of diseases related to high blood and its complications. The current study suggests that the association between non-accidental mortality and monthly temperature variation could be influenced by the temperature-induced fluctuations in blood pressure. Furthermore, the stronger correlation between monthly temperature variation and mortality during cold months may attribute to the greater temperature variations during this period [19].

While deviations from the established core temperature can initiate a series of adverse physiological responses, the specific biological mechanism linking decreased temperature and temperature variability with an increased risk of mortality has not been fully elucidated, although several plausible explanations have been postulated. Mechanistically, both the sympathetic nervous system (SNS) and the renin–angiotensin–aldosterone axis (RAAS) play a central role in mediating cold-induced increases in mortality [21]. Additionally, various inflammatory or metabolic factors may also contribute to or result from cold-induced SNS/RAAS activation. These pathophysiologic changes can also be triggered by inefficiencies in the thermoregulatory system response to rapid temperature changes [22]. All these pathophysiological alterations will further lead to vasoconstriction, fluctuations in blood pressure, increased blood viscosity, elevated fibrinogen levels and platelet activation, all of which are associated with higher cardio-cerebrovascular risk and ultimately increase mortality [1, 23]. In our study, the higher mortality associated with decreased temperature and temperature variation may primarily be attributed to the effect of ambient temperature on cardio-cerebrovascular events in elderly hypertensive patients.

Subgroup analysis revealed a stronger negative correlation between temperature and non-accidental mortality in subjects over 70-year old, possibly due to the higher prevalence of hypertensive complications and declining thermoregulatory function in older individuals with hypertension [7, 17]. The association between temperature variation and mortality across different age groups showed little difference, suggesting that temperature variation could have a greater estimated impact on mortality compared to decreased temperatures. The stronger association between monthly temperature and mortality in the elderly subjects during colder months may also be attributed to the detrimental effects of cold on health and greater temperature variation during this period [19]. Regarding gender-specificity, our results suggested that male hypertensive patients were more vulnerable to decreased temperature and temperature changes, especially during colder months. The positive association between monthly minimum and maximum temperatures and non-accidental mortality in female subjects during warm periods indicated that women were more susceptible to the effects of high temperatures compared to men. The observed differences in temperature-attributable mortality risk between men and women may be attributed to variations in the physiological characteristics of thermoregulation [24]. Our findings are consistent with previous studies [25, 26], but conflicting results from other research could stem from differences in social demographic characteristics of among subjects in different geographic regions [27–29]. Additionally, the higher likelihood of outdoor activities among men compared to women may also contribute to our results. Elderly hypertensive patients are more susceptible to stroke and coronary heart disease, thus we conducted subgroup analysis stratified by the 10-year ICVD risk. Moreover, a considerable proportion of the subjects in the study were coal miners who had previous exposure to dust in their work environment, therefore we carried out the subgroup analysis stratified by dust exposure. However, the subgroup analyses did not reveal any significant differences in mortality when stratified by 10-year ICVD risk and dust exposure, possibly due to the vulnerability of elderly hypertensive patients to ambient temperature effects [30, 31].

The strengths of our study lie in its prospective cohort design and comprehensive medical data collection within a homogeneous geographic area, allowing for a more robust understanding of the dynamic relationship between ambient temperature and mortality risk. Nevertheless, several limitations still exist. Firstly, the sample size of women was relatively small in the current study, however, the comparatively large overall sample size remains persuasive. Secondly, the detailed cause of death was not accessible, thus we did not analyze the effect of temperature on cause-specific mortality. Further studies are required to explore temperature-attributable cause-specific mortality among elderly hypertensive patients. Thirdly, we used outdoor temperature, thus there could be some biases in our results, which could be minimized after adjusting housing conditions [32].

Conclusions

In conclusion, the study demonstrated that both monthly temperature and monthly temperature variation were associated with the risk of non-accidental mortality among elderly hypertensive subjects. The associations were more pronounced among older males during cold months, indicating that the elderly and males were more susceptible to the mortality risk attributed to decreased temperature. Our findings emphasize the necessity for local governments and relevant agencies to formulate targeted recommendations for reducing mortality risks related to temperature in susceptible populations. This is particularly crucial when countries, such as China, are confronted with both significant cerebro-cardiovascular disease burdens and climate change events, especially those related to cold temperatures in northern China.

Abbreviations

BP	Blood pressure
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
BMI	Body mass index
ICVD	Ischemic cardiovascular diseases
SNS	Sympathetic nervous system
RAAS	Renin-angiotensin-aldosterone axis

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Authors' contributions

Study concept and Design: Xuemei Qi, Xin Li, Xiaoshuang Xia and Lin Wang; Acquisition of data: Xuemei Qi, Xiaobin Guo and Suqin Han; Analysis and interpretation of data: Xuemei Qi, Xiaobin Guo and Xin Li; Preparation of manuscript: Xuemei Qi, Xiaobin Guo Suqin Han Xiaoshuang Xia, Lin Wang and Xin Li. The authors report no conflicts of interest.

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Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study followed the Helsinki Declaration and was approved by the Ethics Committee of Kailuan General Hospital (ChiCTR-TNRC-11001489).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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