European Review for Medical and Pharmacological Sciences 2020; 24: 5633-5643

Temperature decline is a trigger of subarachnoid hemorrhage: case-crossover study with distributed lag model

D.-X. YAO[1], Y.-B. LIU[2], Q.-M. WU[3], N. GUO[4], F. PAN[5], H.-L. YU[6]

[1]Department of Interventional Radiography, Rizhao People's Hospital, Rizhao, P.R. China
[2]Department of Neurology, Qingdao Central Hospital, Qingdao University, Qingdao, P.R. China
[3]Health Management Center, Qingdao Central Hospital, Qingdao University, Qingdao, P.R. China
[4]Blood Transfusion Department, The People's Hospital of Zhangqiu Area, Jinan, P.R. China
[5]Department of Ward, The People's Hospital of Zhangqiu Area, Jinan, P.R. China
[6]Medical Insurance Department, Yantaishan Hospital, Yantai, P.R. China

Abstract. – OBJECTIVE: The aim was to use a novel statistical test to predict the trend of subarachnoid hemorrhage (SAH) incidence in response to temperature change and demonstrate its delayed effect in a short hazard period.

PATIENTS AND METHODS: In a retrospective study, data collected between January 2005 and September 2019 were analyzed and 1682 consecutive SAH patients from one hospital were enrolled. Meteorological data in this period including temperature, atmospheric pressure, and humidity were obtained from the China Surface Meteorological Station. Using a case-crossover analysis and distributed lag linear model (DLM) with 4 days lag period to assess the association of temperature change from the previous day (TCP) and risk of SAH. Results were presented as overall cumulative odds ratios (ORs) and 95% CI.

RESULTS: Temperature decline was associated with increased risks of SAH: overall cumulative OR was 1.14 (95% CI: 1.05-1.23) for -1.1°C; 2.11 (95% CI: 1.37-3.25) for -6.2°C, as compared with a reference TCP of 0°C. Temperature decline on the day of SAH onset was significantly associated with SAH incidence days, ORs 1.34 (95% CI: 1.19-1.52). In addition, December, ORs 1.49 (95% CI: 1.17-1.90) in winter was the ictus peak in Rizhao throughout the year.

CONCLUSIONS: Temperature decline from the previous day is a trigger for the occurrence of SAH. Its effect was most apparent on the day of exposure.

Key Words:
Temperature decline, Subarachnoid hemorrhage, Meteorological variation, Case-crossover study, Distributed lag linear model, Delayed effect.

Abbreviations

SAH: subarachnoid hemorrhage; TCP: temperature change from the previous day; CI: Confidence interval; ORs: odds ratios; DLM: distributed lag linear model; DLNM: distributed lag non-linear model; AIC: akaike information criterion.

Introduction

Subarachnoid hemorrhage is a major global health issue which affects approximately 9 per 100 000 of the global population every year[1]. It accounts for 0.8%-7% of cerebral strokes[2]. Despite its relative rarity, SAH has a large impact because of the relatively young age of onset and poor outcome[3]. The risk factors of smoking, hypertension, excessive alcohol intake, female sex and familial preponderance of SAH are supported by strong evidence[4-6]. Possible associations between meteorological variables and their changes and the incidences and characteristics of SAH have been largely investigated. The most studied variable groups were: atmospheric pressure[7-9], ambient air temperature[7-11], seasons[12-14], meteorological variations[15-20] and duration of sunshine[21]. Although several environmental factors have been reported to be correlated with the incidence of SAH, some researchers have not reported such association[22-26] and the controversy is persistent[27,28]. These inconsistencies may be due to the small number of included patients. Beseoglu et al[23] only retrospectively examined 183 patients, resulting in low precision. Moreover, many studies that compared the meteorological variables with the SAH incidence in univariate and multivariate models with-

Corresponding Author: Hongling Yu, MD; e-mail: zhaolongslyy@163.com

out taking delayed effect into consideration, which may have been subject to statistic defects[24,26]. In addition, failure to show any seasonal or meteorological associations may be due to the characteristics of regional differences in a SAH occurrence or climate[22,25]. Therefore, it is more accurate and practical to analyze meteorological factors that trigger SAH in different areas and climates. To the best of our knowledge, no publication researching varying risks of subarachnoid hemorrhage in response to temperature change in the continental monsoon climate zone and further, no studies have used a case-crossover design to examine linear and distributed lag effects of meteorological variables on ictus of SAH.

Rizhao is on the East coast of China, latitude 35°04′-36°04′N and longitude 118°25′-119°39′E. Its climate is typical continental monsoon climate characterized by hot and rainy summers, cold and dry winters. During the fall, winter, and spring, the cold currents of air from Siberia can bring temperature variability from high to low, which generally occurs in the nighttime or early in the morning. Among meteorological factors, daily temperature changes may disrupt and violate homeostasis and predispose to SAH[15,20,29,30]. We observed noticeable clusters of patients with SAH in hospital after daily temperature change from the previous day. Thus, we hypothesized that temperature change from the previous day to the event day, may trigger SAH. We performed a case-crossover study with distributed lag model to investigate changes in the incidence of SAH during a brief hazard period after exposure to decrements or increments in ambient temperature.

Patients and Methods

Compliance With Ethical Standards

The study protocol was approved by the Biomedical Research Ethics Committee of Qingdao University.

Patient Population

Medical Data collected between January 2005 and September 2019 were analyzed and 1682 consecutive SAH patients were enrolled. The Clinic of Neurosurgery, Clinical Centre of Rizhao, is a referral center for patients with SAH. Members of it attend to patients from the Rizhao city area and the surrounding area within a radius of approximately 50 km for about 1.9 million people. Due to its vicinity, the remaining population of 1.1 million people from Western Rizhao goes to Linyi city. Admission electronic medical record database was used to gather SAH patients admitted to our hospital. All SAH admissions (International Classification of Diseases, 10th revision, I60.0- I60.7 codes) records were collected. Patients with SAH due to trauma were excluded. SAH was diagnosed using clinical symptoms, cerebral angiography, a head CT scan, and lumbar puncture was performed when the head CT scan was negative. For all records meeting these inclusion and exclusion criteria, patients' age, gender, timing of SAH onset, Modified Fisher Scale, Hunt and Hess Scale were extracted from electronic medical record database. These data were gathered and verified by one individual. 1682 patients were categorized as having SAH.

Meteorological Data Collection

Meteorological data, including daily mean ambient temperature (°C), temperature change from the previous day (mean temperature of today-mean temperature of previous day, °C), daily mean barometric pressure (Pa), daily mean humidity (%) were obtained from the Rizhao Surface Meteorological Station (Station code: 54945, Latitude: 35°26′N and longitude 119°32′E, elevation 369m) and the China Meteorological Data Sharing Service System (http://www.escience.gov.cn). The temperature data obtained at the Rizhao Surface Meteorological Station was representative, since Rizhao is relatively small in latitude and the meteorological conditions are homogeneous throughout the region. In addition, approximately 86% of Rizhao residents, except residents from the Western part of Rizhao (dark areas without red points), live within a 50-kilometers radius from Rizhao weather station (Figure 1). The year was divided into seasons based on similarities in the group months (spring: March to May; summer: June to August; autumn: September to November; winter: December to February) in accordance with other researches[9,19].

Statistical Analysis

Continuous variables are presented as mean ± standard deviation or median value and interquartile range as appropriate. Categorical variables are shown as number or percentages. Student's *t*-tests were used to examine patient differences in continuous variables, and χ^2-tests were used to compare patient differences in dichotomous variables. The Lagrange Multiplier Test was applied to test overdispersion of the data[31]. Univariate

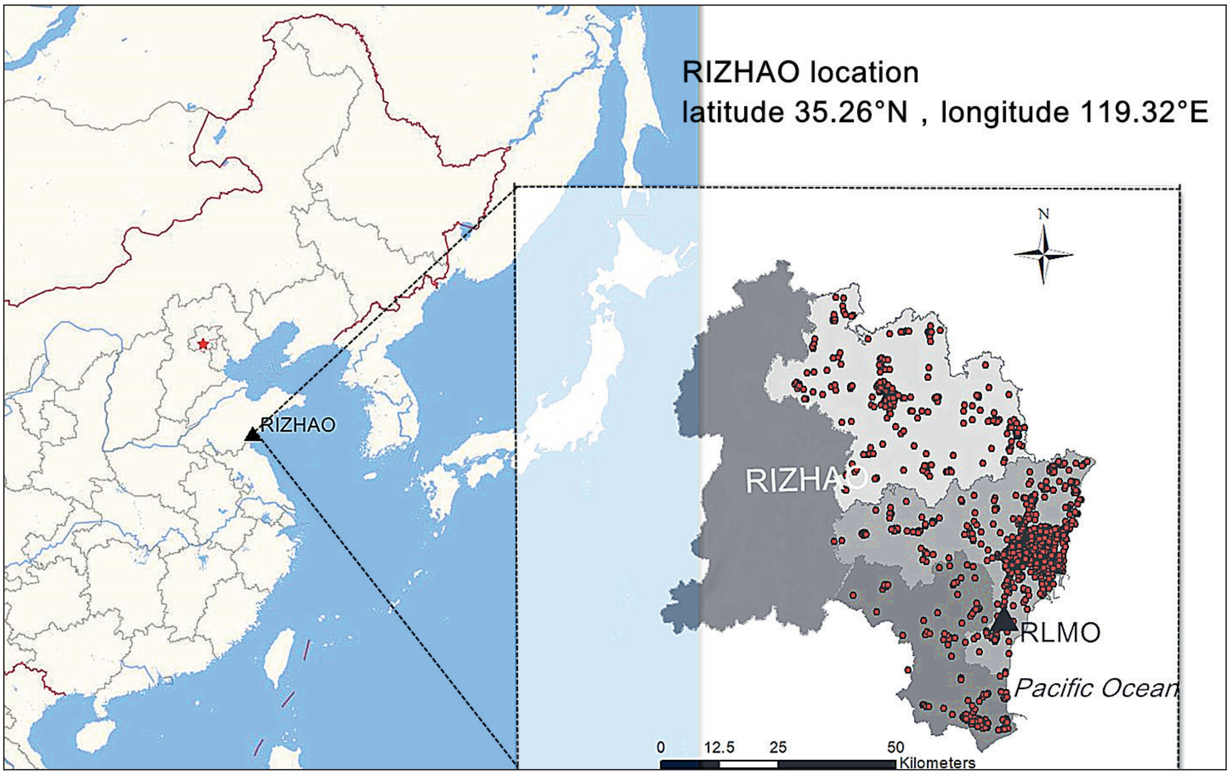

Figure 1. Locations of Rizhao city and Rizhao Local Meteorological Observatory (RLMO). The Rizhao area is showed in the right part of the picture and RLMO is indicated by a triangle. Red dots in the Rizhao city show population included in our referral network. The population dot data are obtained from Rizhao Bureau of Statistics.

Poisson regression was used to calculate ORs with corresponding 95% confidence interval (CI) to compare the frequency of a SAH between the months and seasons of the year. Meanwhile, correlation analysis was conducted to assess the associations between meteorological variables and SAH cases. Generally, variables with correlation coefficient over 0.8 were not included in the analysis simultaneously to avoid multicollinearity in multivariate analysis.

We applied a time-stratified, case-crossover analysis to investigate the association between exposure to TCP and SAH risk[32-34]. TCP was calculated by subtracting the mean temperature of the day from the previous day. A negative value signals temperature decline from the previous warmer day to the subsequent cooler day and a positive one indicates temperature increase. Since several studies[4,7,9,29,30,35,36] consistently demonstrate that the frequencies of stroke exhibit high risk ratio when temperature, barometric pressure change in 0-4 days prior to the onset. We examined the lag effect from day 0 to day 4 to seek the day TCP had a great impact on the incidence of SAH in a short hazard period. The day of the SAH onset and preceding 3d period time were selected as the case period for each SAH event. Control periods were chosen such that exposures during the case period were compared with exposures occurring on other days of the same month falling on the same day of the week[37-40]. Because environmental factors were compared within each individual case, time-invariant confounders including patients' age, sex, and habitus were intrinsically controlled and thus were not included in the model[32,41].

Distributed lag linear model (DLM) is a time-series modelling framework. This methodology rests on the definition of a cross-basis, a bi-dimensional space of functions describing the dependency along the space of the predictor and along lags. It has been widely used to examine the relationships and delayed effects of meteorological variables on human health[42]. We used a univariate conditional Poisson regression model that allows for overdispersion to combine a DLM with the case-crossover design[43]. The general model is shown below:

$$g[E(y_t)] = \alpha + \beta TCP_{t,l} + \gamma Strata_t + \eta DOW_t$$

Where y_t represents the number of daily SAH cases on day t (t =1,2,3,4, …, 5386) and $E(y_t)$ is the expected number on a corresponding day; α is the model intercept; $TCP_{t,l}$ is the cross-basis function of the TCP and SAH cases over the current day to lag l days to model linear and lag effects and β is the coefficient. $Strata_t$ is a categorical parameter to control seasonality and long-term trends; the day of week (DOW_t) was used to adjust weekly confounding in the model. As described, several studies have reported a delayed relationship between temperature, barometric pressure changes and an increased risk of SAH 0 to 4 days after exposure. We assumed a lag 4 days between the TCP and SAH in order to completely capture their association. We used the mean of TCP as the reference to report overall cumulative ORs and 95% confidence intervals (CI) that were computed by the sum of the lag-specific risk contributions for a given value of TCP exposures during the 4 days lag period.

To check the robustness of the study results, several sensitivity analyses were performed: using a Poisson univariate conditional regression model which combines a DLM with the case-crossover design to female, age≤65, aneurismal subarachnoid hemorrhage patients (aSAH); building multivariable conditional Poisson regression models to control confounding environmental factors of daily mean temperature, barometric pressure, and humidity and extending the maximum lag length from 4 to 6 d. The goodness of fit for multivariable models was estimated with the Akaike information criterion (AIC). At last, distributed lag non-linear models (DLNM) further detailed the nonlinear relationships between TCP and SAH. All statistical tests were two-sided, and values of $p < 0.05$ were considered statistically significant. All statistical analyses were performed by using R software (version 3.6.1) with the 'dlnm' package to fit the models.

Results

Demographics and Meteorological Characteristics

Table I shows baseline characteristics of the patients. There were 655 males (38.9%) and 1027 females (61.1%) in our cohort of 1682 patients with SAH. In the hospital-based series, the mean ages of patients were 56.9 years

Table I. Demographics and Meteorological Characteristics (2005-2019).

Patient Population	SAH
Number of cases, n	1682
Age (years),mean (SD)	56.90 (13.53)
Age ≤ 65, n	1232 (73.2%)
Age > 65, n	450 (26.8%)
Sex, n	
Male	655 (38.9%)
Female	1027 (61.1%)
Hunt-Hess Scale, n	
Grade 1	198 (11.8%)
Grade 2	497 (29.5%)
Grade 3	647 (38.5%)
Grade 4	282 (16.8%)
Grade 5	58 (3.4%)
Modified Fisher Scale, n	
1	91 (5.4%)
2	292 (17.4%)
3	1235 (73.4%)
4	64 (3.8%)

Meteorologic data	Mean (SD)	Median (interquartile range)	Minimum	Maximum
Temperature (°C)	13.99 (9.53)	15.20	-11.4	33.1
Change in tem-perature (°C)	0 (2.18)	0.20	-13.8	9.5
Pressure (Pa)	10116 (94.94)	10116	9796	10396
Humidity (%)	68.04 (19.26)	71	15	100

SD, standard deviation; SAH, subarachnoid hemorrhage; Change in temperature, temperature of today-temperature of previous day.

with most patients being younger than 65 years (73.2%). In 251 (14.9%) patients, no aneurysm was found on angiography (non-aneurysmal SAH), and in 81 (4.8%) patients, angiography was not performed due to poor clinical condition. The annual mean temperature was 13.99°C, atmospheric pressure was 10116 Pa, and humidity was 68.04%, respectively. The mean TCP was 0°C and the extreme was -13.8°C for the highest temperature decline, 9.5°C for the highest increase in temperature.

Month and Season

The average number of SAH in each month from 2005 to 2019 was shown in Figure 2A. In univariate Poisson regression analysis, December (ORs 1.49, 95% CI 1.17-1.90) was the ictus peak of SAH, whereas August was the trough throughout the year (Figure 2B). The seasonal difference of SAH onset was non-significant (p>0.05). Compared with fall, SAH occurrence in summer (ORs 0.87, 95% CI 0.76-1.01) was relatively low but the result was non-significant (p=0.06). The time series of admissions shows a weak and rather unregular series of peaks and troughs, with no apparent annual or seasonal patterns (Figure 3).

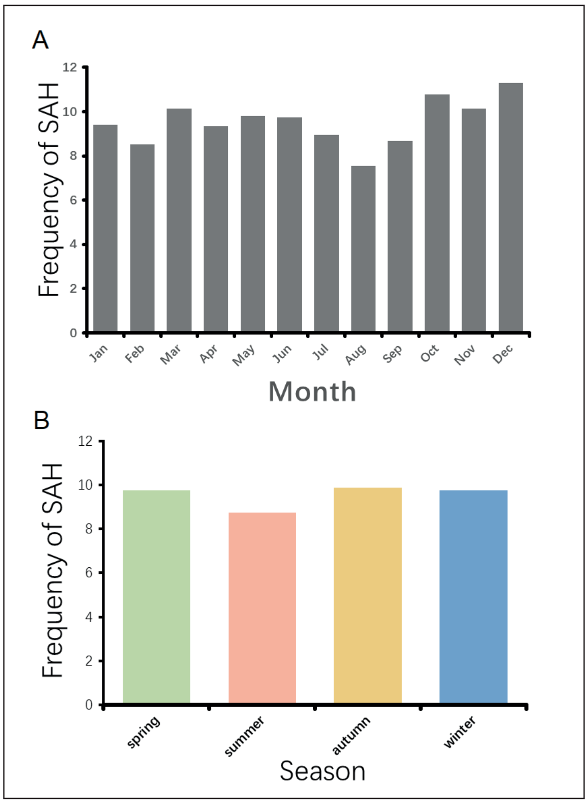

Figure 2. Month and season frequency. **A,** Monthly frequency of subarachnoid hemorrhage (SAH) in Rizhao (2005-2019). **B,** Seasonal frequency of SAH in Rizhao (2005-2019).

Meteorological Factors and SAH

The relationships between SAH incidence and meteorological parameters for each month of the year is shown in Figure 4. The Figure shows that, with marked temperature drop from previous day (TDP), the incidence of SAH increased significantly (Figure 4A); ictus was high in cold months and low in hot months (Figure 4B). In contrast, there was a trough in low-pressure months, such as August in summer (Figure 4C). There was no evident trend in the relationship between humidity and SAH in Rizhao from 2005 to 2017 (Figure 4D). Table II shows interrelation among meteorological parameters themselves and their correction with SAH frequency. All the meteorological Factors except TCP (r=0.06, p<0.001) were not associated with SAH frequency.

Case-Crossover With Distributed Lag Model Study of TCP and SAH Occurrence

Dispersion was tested for in the Poisson model, and no significant dispersion (Lagrange Multiplier Test: χ^2 = 19.722, df = 12, p = 0.07) was detected. The main results of our study were shown in Figure 5, which reflected the relationship between TCP exposure and SAH risk. The overall cumulative ORs for SAH progressively increased (Figure 5A). With the reference at 0°C, the overall cumulative ORs at extreme high (the 99th percentiles of TCP, 5.1°C) was 0.53 (95% CI: 0.37-0.76), 25th percentiles of TCP (-1.1°C) was 1.14 (95% CI: 1.05-1.23), extreme low (the first percentiles of TCP) (-6.2°C) was 2.11 (95% CI: 1.37-3.25).

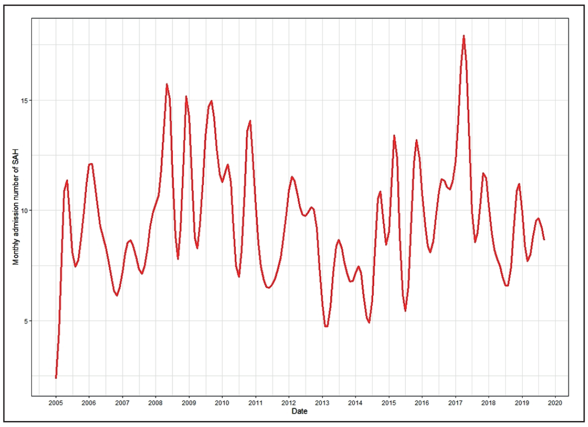

Figure 3. Time series of monthly admissions due to SAH in Rizhao (2005-2019).

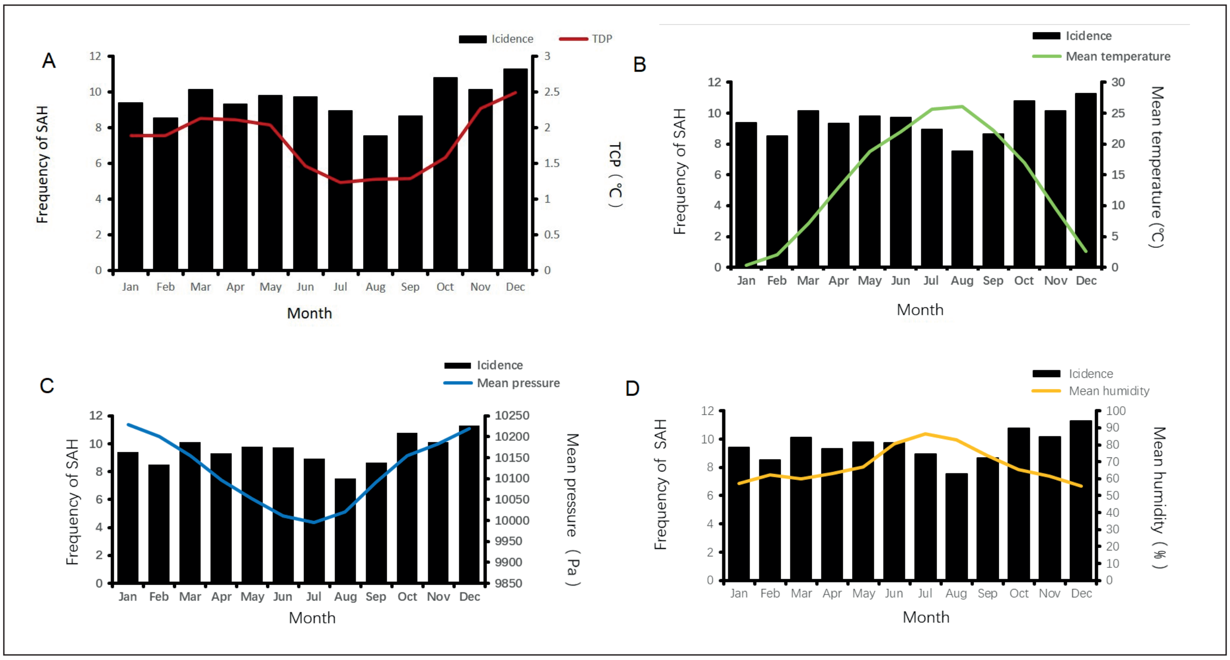

Figure 4. The relationships between meteorological parameters and subarachnoid hemorrhage (SAH) in Rizhao (2005-2019). **A,** Relationship between monthly mean temperature decline from the previous day (TDP) and SAH. **B,** Relationship between monthly mean temperature and SAH. **C**, Relationship between monthly mean atmospheric pressure and SAH. **D,** Relationship between monthly mean humidity and SAH.

The delayed effects plotted in Figure 5B indicated a decreasing risk of SAH in association with exposure to ambient temperature decline (TCP=-6.2°C) between lag 0 to lag 4. The ORs decreased gradually from 1.34 (95% CI: 1.19-1.52) for day 0 TCP (TCP on the day of SAH onset) to 1.00 (95% CI: 0.88-1.13) for day 4 of TCP. The lowest value of TCP was associated with much largest ORs, showed the strong and immediate effect. While, high TCP had a negative connection with SAH.

Analyses

Results of sensitivity analyses including all patients with female, age ≤65, aneurismal subarachnoid hemorrhage patients and extending the maximum lag length from 4 to 6d all produced similar results (Table III). A multivariable conditional Poisson regression model was built, and TDP remained a significant trigger of SAH after adjustment for daily mean temperature, barometric pressure, and humidity (Table IV). Daily mean temperature and barometric pressure were not included in the analysis simultaneously to avoid multicollinearity in multivariate analysis.

In DLNM, the plots (Figure 6) showed the estimated effects of TCP on SAH were non-linear. For TCP, an immediate and strong effect was observed with the lowest value of TCP at a lag of 0 days and then declined sharply as the lag days increased. DLNM showed that temperature increase was not significantly correlated with SAH onset as DLM did.

Table II. Spearman's correlation coefficients between meteorological factors and daily SAH cases.

Variables	Temperature	Change in temperature	Pressure	Humidity	Daily number of SAH
Temperature	1				
Change in temperature	0.07*	1			
Pressure	-0.84*	-0.07*	1		
Humidity	0.47*	-0.07*	0.52*	1	
Daily number of SAH	-0.02	-0.05*	0.01	-0.007	1

*$p < 0.05$.

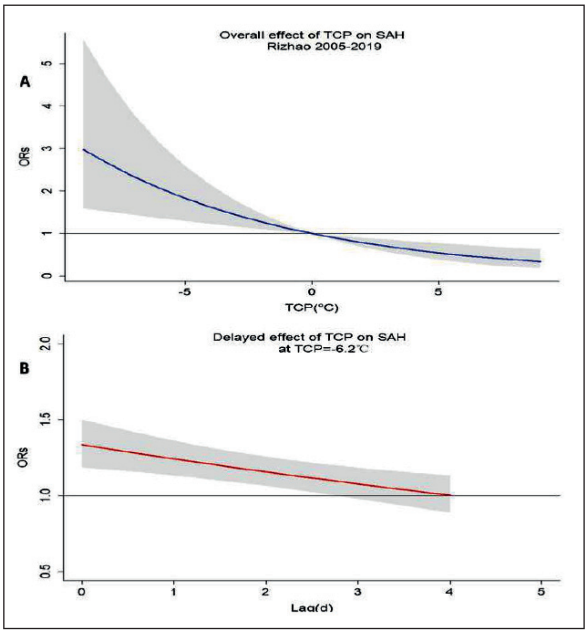

Figure 5. The linear relationship of TCP on subarachnoid hemorrhage (SAH). **A,** The overall cumulative odds ratios (ORs) of SAH by temperature change from the previous day (TCP) for total cases. The ORs are shown as a blue line and the 95% confidence interval is shown in the gray regions. The mean value of TCP (0°C) is as a reference level. **B,** The estimated effect at the first percentiles of TCP (-6°C) at different lag days on SAH cases. The mean value of TCP (0°C) is as a reference level. The red line is the odds ratios (ORs) and the gray region is 95% CI.

Discussion

To our knowledge, this is the first study to have investigated increased risk of subarachnoid hemorrhage (SAH) in response to temperature decline under zone of the continental monsoon climate and further, no studies have used a case-crossover design to examine linear and distributed lag effects of meteorological variables on ictus of SAH. We observed noticeable clusters of in hospitalized patients with SAH after sudden decreases in temperature during cold seasons such as fall, winter, and spring. The sudden temperature decline which happens after

Table III. Univariate conditional Poisson regression analyses of TCP that trigger SAH onset.

Variable	ORs (95% CI)*
Lag 4 days	
All SAH	1.14 (1.05-1.23)
Aneurysmal SAH	1.16 (1.06-1.26)
Female	1.13 (1.02-1.25)
Age ≤ 65	1.13 (1.04-1.24)
Lag 6 days	
All SAH	1.12 (1.02-1.24)
Aneurysmal SAH	1.15 (1.03-1.28)
Female	1.12 (0.99-1.28)
Age < 65	1.13 (1.00-1.26)

ORs, overall cumulative odds ratios; CI, 95% confidence intervals. *The overall cumulative odds ratios (ORs) at 25th percentiles of TCP (-1.1°C).

Table IV. Association between TDP and SAH onset, after adjustment for other environmental factors*.

Covariates	ORs (95% CI)†
Daily mean temperature, adjusted	1.11 (1.00-1.23)
Daily mean temperature + humidity, adjusted	1.11 (1.00-1.23)
Daily barometric pressure, adjusted	1.14 (1.05-1.24)
Daily mean temperature + barometric pressure + humidity, adjusted	1.14 (1.05-1.24)

ORs, overall cumulative odds ratios; CI, 95% confidence intervals. *Multivariable conditional Poisson regression analyses was used to adjust other environmental factors. †The overall cumulative odds ratios (ORs) at 25th percentiles of TCP (-1.1°C).

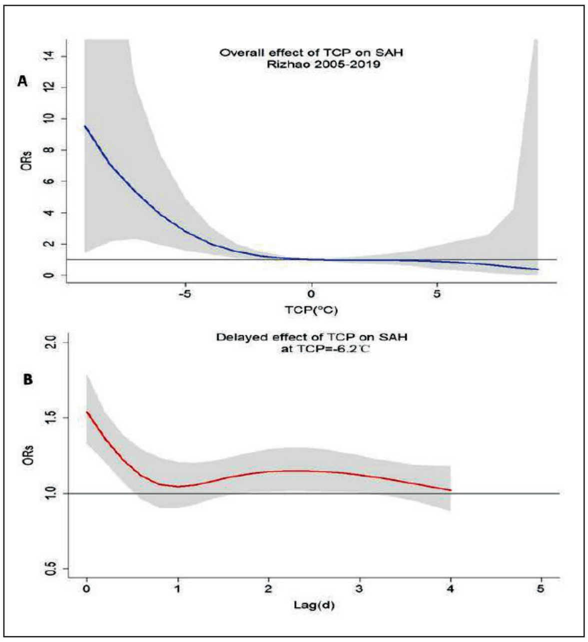

Figure 6. The non-linear relationship TCP on subarachnoid hemorrhage (SAH). A smooth red line and 95% CI shown in the gray region demonstrated the non-linear relationship between temperature change from the previous day (TCP) and SAH. **A,** The overall cumulative odds ratios (ORs) of SAH by TCP. **B,** The estimated effect at the first percentiles of TCP (-6.20°C) at different lag days on SAH cases.

a change in temperature from seasonably cold weather to unseasonably warm weather is common in the Rizhao area and appears to be much more dramatic associated with an increase in a SAH incidence. Lejeune et al[7] found that aneurysmal bleeding was associated with humidity and atmospheric pressure. We found that humidity (r=-0.007, p>0.05), atmospheric pressure (r=0.01, p>0.05) were not associated with SAH frequency, as correlation analysis showed in Table II. The failure to show any associations may due to the characteristics of population and climates. However, the relation between temperature decline and SAH (r=0.06, p<0.001) is found in our research and temperature may be risk factor for SAH in our area. A higher incidence rate of SAH during the winter, spring months has been reported[2,13], whereas our research found an increase in the incidence rate of SAH during the autumn month. This inconsistency may be due to drastic temperature changes in our area.

Several studies[7-11,15,20,30] reported potential correlations between low ambient temperature and SAH onset. Conversely, such an association was not found to be significant in studies from the US[24,26]. These reports compared the ambient temperature with the SAH prevalence in univariate and multivariate models without taking delayed effect into consideration, which may have been subject to statistic defects. Associations between the SAH incidence and trends of specific meteorological variables thus far investigated in existing studies have lacked controls, adequately adjusting for potential confounder such as seasonality, long-term trend, weekly confounding, different environmental factors[9,15,16,18,20,44]. Our case-crossover design with within-subject controls combining a DLM enabled the study of the relationships and delayed effects of meteorological variables on the risk of an acute event, such as SAH[45-48]. Using distributed lag linear model fitted to a case-crossover model involving 1682 SAH patients, we found that the incidence of SAH increased when temperature declined from the previous day to the event day. In our cohort of patients with SAH, we noted a statistically significant increase in SAH within the day of exposure. Lee et al[11] observed that low temperature over periods of 2-3 days before onset is a risk factor for SAH. Mukai et al[29] found intracerebral hemorrhage increased when temperature got extremely cooler in 4 days prior. Because triggers of SAH onset are multifactorial, human behavior and psychology may result in the difference. Mechanisms underlying the increased SAH risk in colder climate have not been resolved but exposure to low daily mean temperature has been shown to influence the incidence of SAH through systemic blood pressure elevation[49-51]. Yet, because daily mean temperature fluctuates according to the season, it is associated with chronic changes in systemic blood pressure and allows physiological adaptation[52]. And thus, this may not be drastic enough to trigger SAH[51,53]. Seasonal variability in SAH is considered to be multifactorial and the risk factors of hypertension, genetic, malformations unhealthy living habits are supported by evidence[4-6]. But meteorological factors could also play an important role. Associations between meteorological variables and their changes and the occurrences and characteristics of SAH have been largely investigated. This has been strongly supported by evidence of pooled data[12] analysis. It suggests that in a population at high risk for SAH, variation in certain lifestyle and meteorological factors could act as a synchronizer to SAH. In addition several of the factors including caffeine intake, straining for defecation, sexual intercourse, vigorous to extreme physical exercise known to cause a short-lasting and sudden increase in blood pressure have been reported to trigger SAH[54,55]. Likewise, meteorological variation in the shorter hazard period would be able to trigger SAH. Thus, decreasing TCP which signals temperature decline from the previous day could be a trigger of SAH. Previous articles[11,20] showed that one-day maximum temperatures changes and changes of temperature over thresholds in mild climate regions were associated with changes in SAH incidences, suggesting that SAH ictus is correlated with vigorous temperature variation.

In our study, temperature decline showed the strong and immediate effect towards increasing risk of SAH, and previously, Fukuda et al[30] indicated decrease of temperature on the day of SAH onset was significantly associated with SAH incidence days while no significantly association was found 1 to 4 days after exposure. Other researches[56,57] have showed a temperature effect for up to 14 days for the occurrence of myocardial infarction. The differences in these risk time periods may be attributable to the distinctions in pathological mechanisms of onset for myocardial infarction (being plaque rupture from atherothrombosis) and SAH (being mainly due to the rupture of intracerebral vessels).

This hospital-based study has several limitations. First, given that some patients died of cardiopulmonary arrest due to SAH before admission, this may cause selection bias. Therefore, community-based studies on a general SAH population are necessary to validate our findings. Second, we could not include individual information regarding true environmental status (indoor and outdoor), socioeconomic background at onset. Finally, with events recorded on only 23.8% of days the DLNM (Figure 5) showed unreliability at both the lower and the upper extremes of the TCP range with wide confidence intervals, reflecting the limited number of events, which occurred on these extreme TCP days. The AICs of DLNM and DLM are 8634 and 8628 respectively, therefore, we used DLM to analyze our cohort of SAH. Besides, DLNM showed that temperature increase was not significantly correlated with SAH onset as DLM did. It is mainly because of sample shortage so we could not give conclusion that high TCP had a protective effect towards SAH. Further multi-center investigation including the large sample of a wide range of patients would be warranted to demonstrate the non-liner association between TCP and SAH prevalence.

Conclusions

Taken together these data indicate that the temperature decline from the previous day was correlated with the prevalence of SAH. It showed the strong and immediate effect on the day of exposure.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

Shandong Natural Science Foundation (ZR2016HB64); Funding of Applied Research Project for postdoctoral researchers in Qingdao (40518060079).

References

1) de Rooij NK, Linn FH, van der Plas JA, Algra A, Rinkel GJ. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry 2008; 78: 1365-1372.
2) Feigin VL, Lawes CM, Bennett DA, Anderson CS. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurol 2003; 2: 43-53.
3. Hackett M, Anderson C, Group F. Health outcomes 1 year after subarachnoid hemorrhage: an international population-based study. Neurology 2000; 55: 658-662.
4) Qureshi A, Suri MF, Yahia A. From GWAS to the clinic: risk factors for subarachnoid hemorrhage. Neurosurgery 2001; 49: 607-612.
5) Saksen J, Egge A, Waterloo K. Risk factors for aneurysmal subarachnoid hemorrhage: the Tromso study. J Neurol Neurosurg Psychiatry 2002; 73: 185-187.
6) Sandvei MS, Romundstad PR, Müller TB, Vatten L, Vik A. risk factors for aneurysmal subarachnoid hemorrhage in a prospective population study the HUNT study in Norway. Stroke 2009; 40: 1958-1962.
7) Lejeune JP, Vinchon M, Amouyel P, Escartin T, Escartin D, Christiaens JL. Association of occurrence of aneurysmal bleeding with meteorologic variations in the North of France. Stroke 1994; 25: 338-341.
8) Abe T, Ohde S, Ishimatsu S, Ogata H, Hasegawa T, Nakamura T, Tokuda Y. Effects of meteorological factors on the onset of subarachnoid hemorrhage: a time-series analysis. J Clin Neurosci 2008; 15: 1005-1010.
9) Huang Q1, Lin SW, Hu WP, Li HY, Yao PS, Sun Y, Zeng YL, Huang QY, Kang DZ, Wu SY. Meteorological variation is a predisposing factor for aneurismal subarachnoid hemorrhage: a 5-year multicenter study in Fuzhou, China. World Neurosurg 2019; 132: e687-e695.
10) Backes D, Rinkel GJ, Algra A, Vaartjes I, Donker GA, Vergouwen MD. Increased incidence of subarachnoid hemorrhage during cold temperatures and influenza epidemics. J Neurosurg 2016; 125: 737-745.
11) Lee S, Guth M. Associations between temperature and hospital admissions for subarachnoid hemorrhage in Korea. Int J Environ Res Public Health 2017; 14: E449.
12) Feigin VL, Anderson CS, Anderson NE, Broad JB, Pledger MJ, Bonita R. is there a temporal pattern in the occurrence of subarachnoid hemorrhage in the southern hemisphere? pooled data from 3 large, population-based incidence studies in Australasia, 1981 to 1997. Stroke 2001; 32: 613-619.
13) Inagawa T. Seasonal variation in the incidence of aneurysmal subarachnoid hemorrhage in hospital- and community-based studies. J Neurosurg 2002; 96: 497-509.
14) Fischer T, Johnsen SP, Pedersen L, Gaist D, Sørensen HT, Rothman KJ. Seasonal variation in hospitalization and case fatality of subarachnoid hemorrhage - a nationwide Danish study on 9,367 patients. Neuroepidemiology 2005; 24: 32-37.

15) Chyatte D, Chen TL, Bronstein K, Brass LM. Seasonal fluctuation in the incidence of intracranial aneurysm rupture and its relationship to changing climatic conditions. J Neurosurg 1994; 81: 525-530.

16) Jehle D, Moscati R, Frye J, Reich N. The incidence of spontaneous subarachnoid hemorrhage with change in barometric pressure. Am J Emerg Med 1994; 12: 90-91.

17) Buxton N, Liu C, Dasic D, Moody P, Hope DT. Relationship of aneurysmal subarachnoid hemorrhage to changes in atmospheric pressure: results of a prospective study. J Neurosurg 2001; 95: 391-392.

18) Setzer M, Beck J, Hermann E, Raabe A, Seifert V, Vatter H, Marquardt G. The influence of barometric pressure changes and standard meteorological variables on the occurrence and clinical features of subarachnoid hemorrhage. Surg Neurol 2007; 67: 264-272; discussion 272.

19) Law HY, Wong GK, Chan DT, Wong L, Poon WS. Meteorological factors and aneurysmal subarachnoid haemorrhage in Hong Kong. Hong Kong Med J 2009; 15: 85-89.

20) Gill RS, Hambridge HL, Schneider EB, Hanff T, Tamargo RJ, Nyquist P. Falling temperature and colder weather are associated with an increased risk of aneurysmal subarachnod hemorrhage. World Neurosurg 2013; 79: 136-142.

21) Stienen MN, Smoll NR, Battaglia M, Schatlo B, Woernle CM, Fung C, Roethlisberger M, Daniel RT, Fathi AR, Fandino J, Hildebrandt G, Schaller K, Bijlenga P. Intracranial aneurysm rupture is predicted by measures of solar activity. World Neurosurg 2014; 83: 588-595.

22) Jakovljević D, Salomaa V, Sivenius J, Tamminen M, Sarti C, Salmi K, Kaarsalo E, Narva V, Immonen-Räihä P, Torppa J, Tuomilehto J. Seasonal variation in the occurrence of stroke in a Finnish adult population: The FINMONICA Stroke Register. Stroke 1996; 27: 1774-1779.

23) Beseoglu K, Hänggi D, Stummer W, Steiger HJ. Dependence of subarachnoid hemorrhage on climate conditions: a systematic meteorological analysis from the Düsseldorf metropolitan area. Neurosurgery 2008; 62: 1033-1038.

24) Cowperthwaite M, Burnett M. The association between weather and spontaneous subarachnoid hemorrhage: an analysis of 155 US hospitals. Neurosurgery 2011; 68: 132-138.

25) Vuleković P, Nikolic-Djoric E, Kojadinovic Z, PapiĐ V, Karan M, Dóczi T. A temporal pattern in the occurrence of aneurysmal subarachnoid hemorrhage in the province of Vojvodina, Serbia. Acta Neurochir (Wien) 2011; 153: 1313-1319.

26) McDonald RJ, McDonald JS, Bida JP, Kallmes DF, Cloft HJ. Subarachnoid hemorrhage incidence in the United States does not vary with season or temperature. AJNR Am J Neuroradiol 2012; 33: 1663-1668.

27) Rønning P, Langmoen I. Aneurysm rupture-does the weather matter? World Neurosurg 2013; 79: 62-63.

28) Ku JC, Alotaibi NM, Wang J, Ibrahim GM, Schweizer TA, Macdonald RL. Internet search volumes in brain aneurysms and subarachnoid hemorrhage: is there evidence of seasonality? Clin Neurol Neurosurg 2017; 158: 1-4.

29) Mukai T, Hosomi N, Tsunematsu M, Sueda Y, Shimoe Y, Ohshita T, Torii T, Aoki S, Nezu T, Maruyama H, Kakehashi M, Matsumoto M. Various meteorological conditions exhibit both immediate and delayed influences on the risk of stroke events: The HEWS-stroke study. PLoS One 2017; 12: e0178223.

30) Fukuda H, Ninomiya H, Ueba Y, Ohta T, Kaneko T, Kadota T, Hamada F, Fukui N, Nonaka M, Watari Y, Nishimoto S, Fukuda M, Hayashi S, Izumidani T, Nishimura H, Moriki A, Lo B, Ueba T. Impact of temperature decline from the previous day as a trigger of spontaneous subarachnoid hemorrhage: case-crossover study of prefectural stroke database. J Neurosurg 2019; 5: 1-9.

31) Breusch TS, Pagan AR. The lagrange multiplier test and its applications to model specification in econometrics. Rev Economic Studies 1980; 47: 239-253.

32) Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. Am J Epidemiol 1991; 133: 144-153.

33) Whitaker H, Hocine MN, Farrington C. On case-crossover methods for environmental time series data. Environmetrics 2007; 18:1-26.

34) Janes H, Sheppard L, Lumley T. Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. Epidemiology 2005; 16: 717-726.

35) Landers AT, Narotam PK, Govender ST, van Dellen JR. The effect of changes in barometric pressure on the risk of rupture of intracranial aneurysms. Br J Neurosurg 1997; 11: 191-195.

36) Hong YC, Rha JH, Lee JT, Ha EH, Kwon HJ, Kim H. Ischemic stroke associated with decrease in temperature. Epidemiology 2003; 14: 473-478.

37) Levy D, Lumley T, Sheppard L, Kaufman J, Checkoway H. Referent selection in case-crossover analyses of acute health effects of air pollution. Epidemiology 2001; 12: 186-192.

38) Nuvolone D, Balzi D, Chini M, Scala D, Giovannini F, Barchielli A. Short-term association between ambient air pollution and risk of hospitalization for acute myocardial infarction: results of the cardiovascular risk and air pollution in Tuscany (RISCAT) study. Am J Epidemiol 2011; 174: 63-71.

39) O'Donnell MJ, Fang J, Mittleman MA, Kapral MK, Wellenius GA. Fine particulate air pollution (PM2.5) and the risk of acute ischemic stroke. Epidemiology 2011; 22: 422-431.

40) Wellenius G, Schwartz J, Mittleman M. Air pollution and hospital admissions for ischemic and hemorrhagic stroke among medicare beneficiaries. Stroke 2006; 36: 2549-2553.

41) Mittleman M. Optimal referent selection strategies in case-crossover studies: a settled issue. Epidemiology 2005; 16: 715-716.

42) Gasparrini A. Distributed lag linear and non-linear models in R: the package dlnm. J Stat Softw 2011; 43: 1-20.

43) Armstrong BG, Gasparrini A, Tobias A. Conditional poisson models: a flexible alternative to conditional logistic case cross-over analysis. BMC Med Res Methodol 2014; 14: 122.

44) Hughes MA, Grover PJ, Butler CR, Elwell VA, Mendoza ND. A 5-year retrospective study assessing the association between seasonal and meteorological change and incidence of aneurysmal subarachnoid haemorrhage. Br J Neurosurg 2010; 24: 396-400.

45) Xu M, Yu W, Tong S, Jia L, Liang F, Pan X. Non-linear association between exposure to ambient temperature and children's hand-foot-and-mouth disease in Beijing, China. PLoS One 2015; 10: e0126171.

46) Taj T, Jakobsson K, Stroh E, Oudin A. Air pollution is associated with primary health care visits for asthma in Sweden: a case-crossover design with a distributed lag non-linear model. Spat Spatiotemporal Epidemiol 2016; 17: 37-44

47) Guo Y, Barnett AG, Pan X, Yu W, Tong S. The impact of temperature on mortality in Tianjin, China: a case-crossover design with a distributed lag nonlinear model. Environ Health Perspect 2011; 119: 1719-1725.

48) Zheng D, Arima H, Sato S, Gasparrini A, Heeley E, Delcourt C, Lo S, Huang Y, Wang J, Stapf C, Robinson T, Lavados P, Chalmers J, Anderson CS; INTERACT2 investigators. Low ambient temperature and intracerebral hemorrhage: the INTERACT2 study. PLoS One 2016; 11: e0149040.

49) Modesti PA, Morabito M, Bertolozzi I, Massetti L, Panci G, Lumachi C, Giglio A, Bilo G, Caldara G, Lonati L, Orlandini S, Maracchi G, Mancia G, Gensini GF, Parati G. Weather-related changes in 24-hour blood pressure profile effects of age and implications for hypertension management. Hypertension 2006; 47: 155-161.

50) Jehn M, Appel LJ, Sacks FM, Miller ER 3rd; DASH Collaborative Research Group. The effect of ambient temperature and barometric pressure on ambulatory blood pressure variability. Am J Hypertens 2002; 15: 941-945.

51) Giaconi S, Ghione S, Palombo C, Genovesi-Ebert A, Marabotti C, Fommei E, Donato L. Seasonal influences on blood pressure in high normal to mild hypertensive range. Hypertension 1989; 14: 22-27.

52) Castellani J, Young A. Human physiological responses to cold exposure: Acute responses and acclimatization to prolonged exposure. Auton Neurosci 2016; 196: 63-74.

53) Rose G. Seasonal variation in blood pressure in man. Nature 1961; 189: 235.

54) Vlak MH, Rinkel GJ, Greebe P, van der Bom JG, Algra A. Trigger factors and their attributable risk for rupture of intracranial aneurysms a case-crossover study. Stroke 2011; 42: 1878-1882.

55) Fann JR, Kukull WA, Katon WJ, Longstreth WT Jr. Physical activity and subarachnoid haemorrhage: a population based case-control study. J Neurol Neurosurg Psychiatry 2001; 69: 768-772.

56) Schwartz J, Samet J, Patz J. Hospital admissions for heart disease: the effects of temperature and humidity. Epidemiology 2004; 15: 755-761.

57) Bhaskaran K, Hajat S, Haines A, Herrett E, Wilkinson P, Smeeth L. Short term effects of temperature on risk of myocardial infarction in England and Wales: time series regression analysis of the myocardial ischaemia national audit project (MINAP) registry. BMJ 2010; 341: c3823.