

Association Between Meteorological Factors and the Rupture of Intracranial Aneurysms

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Background—Both meteorological factors and morphological factors are important factors to predict intracranial aneurysm rupture. This study investigated the relationship between meteorological factors and aneurysmal subarachnoid hemorrhage (aSAH). Additionally, the morphological differences between ruptured and unruptured aneurysms under these high-risk meteorological conditions were assessed.

Methods and Results—The records of 1751 patients with aSAH with 2124 intracranial aneurysms were retrospectively analyzed. Spearman rank correlation analysis was used to assess the risks of incident aSAH on the basis of daily meteorological data. Morphological parameters were analyzed using 1-way ANOVA tests, and significant parameters (P<0.05) were further examined using a multivariable logistic regression analysis. Daily aSAH incidence had significant negative correlations with daily mean, maximum, and minimum temperature (P<0.001) and a significant positive correlation with daily mean atmospheric pressure (P<0.001). Additionally, 58 patients with multiple aneurysms were assessed to determine morphological differences. There were significant differences in the mean values for aneurysm size, neck width, length, height, width, parent artery diameter, shape of the aneurysm, aspect ratio, size ratio, and bottleneck factor (P<0.05). The multivariable logistic regression analysis showed that aspect ratio (β =1.277, odds ratio=3.585, 95% CI, 1.588–8.090; P=0.002) was an independent risk factor for aneurysm rupture. Receiver operating characteristic curve analysis indicated that the ruptured aneurysm threshold of size was 3.45 mm and aspect ratio was 1.05.

Conclusions—Lower daily mean, maximum, and minimum temperatures and a higher daily mean atmospheric pressure were associated with an increased rate of aSAH. Additionally, under these meteorological conditions, the aneurysm size and aspect ratio thresholds for predicting rupture of an aneurysm may be lower. (*J Am Heart Assoc.* 2019;8:e012205. DOI: 10.1161/JAHA.119. 012205.)

Key Words: cerebral aneurysms • intracranial aneurysms • meteorological factors • morphological features

W ith a prevalence of 1% to 5% in the general population, intracranial aneurysms (IAs) are relatively common.¹ The annual incidence of subarachnoid hemorrhages (SAHs) is \approx 91/100 000 and 85% of SAH cases are caused by rupture of an IA, which is one of the most serious complications

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associated with aneurysms.^{2,3} Morbidity and mortality of aneurysmal subarachnoid hemorrhage (aSAH) remain high. Therefore, it is critical to understand the risk factors associated with this disease.

The mechanisms underlying IA development and the factors associated with IA rupture are not yet fully understood. Previous studies have identified several risk factors for aSAH, including high blood pressure, smoking, female sex, and a family history of IA.⁴⁻⁸ Recently, it was suggested that an additional possible risk factor of aSAH is weather conditions. Although several studies have reported potential correlations between meteorological factors and the incidence of aSAH, the results vary according to geography, climate, and study design. Some studies found that meteorological changes (eg, temperature or pressure) were associated with an increased incidence of aSAH,⁹⁻²¹ whereas others reported no such association.²²⁻²⁷ Therefore, evidence regarding the impact of meteorological factors on the incidence of aSAH remains limited and controversial. Still other studies have investigated morphological differences

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Accompanying Tables S1 through S6 and Figures S1, S2 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.012205

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Clinical Perspective

What Is New?

• This study shows the effect of the combination of meteorological factors and aneurysm morphology on the prediction of aneurysm rupture.

What Are the Clinical Implications?

• Under some meteorological conditions, the aneurysm size and aspect ratio thresholds for predicting rupture of an aneurysm may be lower, which may provide some reference for clinical management of intracranial aneurysms.

between ruptured and unruptured aneurysms in terms of the size, shape, and the neck, height, length, and width of the IA body.^{28–35} However, the effect of the combination of meteorological factors and aneurysm morphology on the prediction of aneurysm rupture has not been accurately evaluated.

This study investigated the association between meteorological factors and aSAH. Additionally, the morphological differences between ruptured and unruptured aneurysms under these high-risk meteorological conditions were assessed.

Materials and Methods

We will make the data, methods used in the analysis, and materials used to conduct the research available to any researcher for purposes of reproducing the results or replicating the procedure.

Target Area

JiangXi Province in central China is located within the Tropic of Cancer (N 24°29'14" to 30°04'41", E 113°34'36" to 118°28'58"). It has a subtropical humid climate, and its topography consists primarily of basins. This province has \approx 46.2 million inhabitants and covers an area of 166 900 square kilometers.

Patient Selection

This study was a multicenter (3 hospitals) retrospective investigation of patients hospitalized for IAs. Patients from northern JiangXi Province were recruited mainly from the First Affiliated Hospital of Nanchang University in Nanchang City, while those from southern JiangXi Province were recruited mainly from Ganzhou People's Hospital and Ganzhou Central Hospital in Ganzhou City. The medical records of all patients presenting with aSAH at these 3 hospitals were identified and those with a radiologically confirmed diagnosis of aSAH, on computed tomographic angiography, magnetic resonance angiography, or digital subtraction angiography (DSA), between January 1, 2015, and December 31, 2017, were included in the study analyses. Cases of trauma and/or any other cause of secondary SAH were excluded during the chart review. Additionally, patients for whom the day and time of symptom onset (not the admission day) were unknown, and those who were transferred in from outside the local area were excluded from the analyses.

Meteorological Data

Climate data were obtained from the JiangXi Meteorologic Bureau (http://weather.org.cn/), which includes 94 weather stations located across the province. The location and time of onset for each patient were recorded, and then the meteorological data from the local weather stations were assessed. The following meteorological parameters, on the day of and the day before aSAH onset, were recorded: daily maximum, minimum, and mean ambient temperatures (°C), daily mean relative humidity (%), daily mean atmospheric pressure (hPa), 24-hour precipitation (mm), and daily sunshine duration (hours). Changes in these meteorological parameters were calculated as differences between the day of and day before the onset of aSAH. All data were checked for accuracy using 2 different sources.

Morphological Parameters of the IAs

In patients with multiple IAs, the morphological characteristics were assessed using the aneurysm measurement method described by Skodvin et al³⁶ (Figure 1A). The 1-dimensional parameters of the aneurysms included: size, which was defined as maximum aneurysm diameter; neck width (Wn), which was the largest diameter of the neck plane; length, which was the maximum distance between any point on the aneurysm dome and the neck plane center; height, which was the maximum vertical distance between the neck plane center and the aneurysm dome; width, which was the maximum distance perpendicular to the length; parent artery diameter (D), which was based on Dhar's³⁷ definitions of aneurysm morphology research (for sidewall aneurysms, D was the average between D_1 [artery diameter near the neck] and D_2 [artery diameter that had a distance of $1.5 \times D_1$ near the neck], Figure 1B; for bifurcation aneurysms, D was the average between the D and the diameters of the blood vessel branches; Figure 1C); and shape of the aneurysm (regular shape was defined as a simple saccular aneurysm, and irregular shape was defined with additional blebs). The 2dimensional parameters included aspect ratio (AR), which was the ratio between height and Wn; size ratio (SR), which was the ratio between length and D; the height-to-width ratio; and



Figure 1. Definitions of 1-dimensional morphology parameters and method of measurement. A, definitions of aneurysm size (S), neck width (Wn), length (L), height (H), width (W); B and C, definitions of parent artery diameter (D).

the bottleneck factor (BN), which was the ratio between width and Wn. $^{\rm 38,39}$

Study Design and Statistical Analysis

First, the seasons were defined based on local climatology, as follows: winter (December to February), spring (March to May), summer (June to August), and autumn (September to November). Additionally, the circadian rhythm was analyzed according to the time of aSAH onset on the basis of six 4-hour periods: morning (04:00–07:59), forenoon (08:00–11:59), midday (12:00–15:59), afternoon (16:00–19:59), evening (20:00–23:59), and night (00:00–03:59). A chi-square goodness-of-fit test was used to analyze these differences.

Next, the correlations between the meteorological parameters and the occurrence of aSAH were analyzed. The daily weather data and number of aSAH cases were first standardized using an annual standardization approach²³ to facilitate comparisons among the weather stations. For the annual standardization, the means and SDs were calculated for each year at each weather station, and daily values were transformed to a standard scale by subtracting the mean and then dividing by the SD. All statistical tests were performed using the standardized data. Spearman rank correlation analyses were conducted to assess the significance of the associations between meteorological parameters and the incidence of aSAH.

Ultimately, it was hypothesized that 1 or more indices or abrupt daily changes in the meteorological parameter(s) would be related to the onset of aSAH. Under the high-risk environments, patients with multiple aneurysms were selected to analyze morphological differences between ruptured and unruptured aneurysms. Chi-square and 1-way ANOVA tests were used to compare morphological differences between the 2 groups and a receiver operating characteristic (ROC) curve analysis of each morphological parameter was conducted. A multivariable logistic regression (backward elimination) was performed to evaluate the value of each morphological parameter for predicting aneurysm rupture.

All statistical analyses were performed with SPSS software (version 24.0; IBM Corp., Armonk, NY). For the demographic and morphological data, a P<0.05 was considered to indicate statistical significance. When assessing interactions between the meteorological data and the number of aSAH cases, Bonferroni-corrected statistical thresholds were used to adjust for multiple tests. The study was approved by the Jiangxi Medical Ethics Committee, which decided the study to be exempt from patient consent.

Results

Study Population

Between January 1, 2015, and December 31, 2017, a total of 1751 patients (1062 females and 689 males) were included in the present analysis. The characteristics of these aSAH patients are summarized in Table. The mean age (\pm SD) of all patients was 57.3 \pm 10.9 years; the highest incidence of aneurysms was in the posterior communicating artery (553/ 1751, *P*<0.001).

Influences of Season, Month, and Circadian Rhythms on aSAH

The total aSAH incidence according to time of onset is shown in Table S1. The peak incidence of aSAH was in the morning (04:00–07:59; 394/1751), followed by the afternoon (16:00–19:59; 357/1751), whereas the trough was at night (00:00–03:59; 135/1751; P<0.001). The monthly and seasonal

Table.Characteristics of the Patients With aSAH in ThisAnalysis

Summary Statistic	No. of Patients (%)	P Value
Total no. of patients	1751 (100)	
Sex	- ()	
Female	1062 (60.7)	<0.001*
Male	689 (39.3)	
Age (mean±SD)	57.3±10.9	
Female	59.1±10.8	<0.001 [†]
Male	54.6±10.3	
Hypertension	925 (52.8)	0.018 [‡]
Diabetes mellitus	80 (4.6)	<0.001 [‡]
Smoking history	388 (22.2)	<0.001‡
Alcohol history	278 (15.9)	<0.001‡
Location of ruptured IA		<0.001*
ICA	131 (7.5)	
MCA	335 (19.1)	
ACA	60 (3.4)	
PCA	16 (0.9)	
ACoA	539 (30.8)	
PCoA	553 (31.6)	
VBA	61 (3.5)	
Others	56 (3.2)	

ACA indicates anterior cerebral artery; ACoA, anterior communicating artery; aSAH, aneurysmal subarachnoid hemorrhage; IA, intracranial aneurysm; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; PCoA, posterior communicating artery; VBA, vertebrobasilar artery.

*Chi-square goodness-of-fit test.

[†]Student *t* test.

[‡]Nonparametric chi-square test.

incidence rates are shown in Figures 2 and 3. The peak monthly incidence was in January (173/1751) and February (170/1751), and the trough monthly incidence was in July (110/1751, P=0.001). The seasonal incidence peaked in winter (December to February, 507/1751) and exhibited a trough in summer (June to August, 364/1751; P<0.001).

Correlations Between Meteorological Parameters and the Occurrence of aSAH

Figure S1 depicts the approximate relationship between the standardized number of aSAH and the mean standardized meteorological data. Table S2 shows the results of Spearman rank correlation analysis. The daily mean temperature (R=-0.043, P<0.001), daily maximum temperature (R=-0.041, P<0.001), and daily minimum temperature (R=-0.042, P<0.001) had significant negative correlations with daily aSAH incidence, whereas the daily mean atmospheric

pressure had a significant positive correlation with daily aSAH incidence (R=0.043, P<0.001). However, 24-hour precipitation, daily sunshine duration, and daily mean relative humidity were not significantly correlated with aSAH incidence.

Next, the daily fluctuations in temperature (daily maximum temperature minus daily minimum temperature) and fluctuations on the day of and the day before onset were analyzed (Table S3), there were no significant relationships between the incidence of aSAH and daily fluctuations in all factors.

The delayed effects of meteorological fluctuations on the number of hospital admissions for aSAH within 48 and 72 hours were also considered using Spearman rank correlation analysis (Table S4). There were no significant correlations between them.

Morphological Differences Between Ruptured and Unruptured Aneurysms

ROC curve analysis was performed using daily average temperature and daily average pressure in Nanchang City (Figure S2). Of the 1097 days during the study period, 299 had a daily average temperature lower than 12.5°C or a daily average pressure higher than 1016.65 hPa. On these days, 137 patients suffered an aSAH, and 58 of these patients had multiple aneurysms (58 ruptured aneurysms and 83 unruptured aneurysms). The location, morphological parameters of the aneurysms, and the statistical results are shown in Table S5.

The most common rupture location was in the anterior communicating artery (20/58, 34.5%), followed by the middle cerebral artery (MCA, 14/58, 24.1%), these differences were statistically significant (χ^2 =16.419, *P*=0.019). The rupture rates for aneurysm sizes <3, 3 to 7, and >7 mm were 19.4% (12/62), 56.3% (27/48), and 61.3% (19/31), respectively, which indicates that larger aneurysms were more likely to rupture (χ^2 =21.876, *P*<0.001). For aneurysm shape, the rate of aneurysms with 1 or more bleb(s) among the 58 ruptured aneurysms was 58.6% (34/58) and the rate of aneurysms with 1 or more bleb(s) among the 83 unruptured aneurysms was 38.6% (32/83, χ^2 =5.522, *P*=0.019). The ANOVA and ROC curve analyses revealed that the size, Wn, height, length, width, AR, SR, and BN values of the 2 groups were significantly different (P<0.05; Table S5). To determine the morphological parameters that are independently correlated with aneurysm rupture, the parameters of Wn, height, length, width, AR, SR, and BN with statistically significant in ANOVA were used for the multivariable logistic regression analysis with stepwise elimination. After 6 steps, length, SR, BN, width, and height were excluded successively, and finally Wn and AR were retained; however, for Wn, there was no statistical significance with P=0.57, and only AR was independently with aneurysm rupture (β =1.277, odds associated



Figure 2. Monthly incidence of aSAH from 2015 to 2017 (chi-square goodness-of-fit contingency table: χ^2 =32.10, *P*=0.001). aSAH indicates aneurysmal subarachnoid hemorrhage.

ratio=3.585, 95% Cl, 1.588–8.090; *P*=0.002), which indicates that for every additional unit in AR value, the risk of aneurysm rupture was 3.585 times higher.



Figure 3. Seasonal incidence of aSAH from 2015 to 2017 (chi-square goodness-of-fit contingency table: χ^2 =25.23, *P*<0.001). aSAH indicates aneurysmal subarachnoid hemorrhage.

We make a relative weight analysis of all factors (Table S6). The results show that size, height, length, width, AR, SR, and BN have high relative weights, while for the location of aneurysms, the relative weight is negative, but the value is small. We may think that the location of aneurysms has little effect on the rupture of aneurysms, but the results of statistics should be combined with clinical practice; we only found more ruptured anterior communicating aneurysms in 58 patients with multiple aneurysms, which may be related to the size of our samples.

Discussion

The influences of seasonal and meteorological changes on IA rupture remain a matter of debate because of the inconsistent findings of studies evaluating the relationship between different weather conditions and aSAH. In our study, the incidence of aSAH was the highest in winter (January and February); lowest in summer (July); and significantly higher in 2 periods, from 04:00 to 07:59 and 16:00 to 19:59, than at other times of day. Additionally, lower daily mean, maximum, and minimum temperatures and higher atmospheric pressure were associated with lower rates of hospital admission for ruptured IAs.

Some previous studies have reported that low temperature or changes in temperature might increase the risk of aSAH.^{9,10,13-15,18-21,40} Rivera-Lara et al²⁰ and Gill et al¹³ suggested that peripheral vasoconstriction during cold weather could lead to increased blood and pulse pressure, which would increase pressure on IA walls, especially under conditions with abrupt temperature changes. Unstable blood pressure may also occur because of decompensation and thus contribute to IA rupture. Furthermore, cold weather typically results in behavioral changes such as smoking indoors, increased heavy drinking, and strenuous exercise by those resistant to cold, which are all risk factors for IA rupture. Previous findings regarding the correlation between atmospheric pressure and the incidence of aSAH remain controversial. A study conducted in Nantes, France, found that the incidence of aSAH significantly increased when the atmospheric pressure was >10 hPa.¹⁶ Changes in atmospheric pressure may also affect blood pressure and indirectly influence IA rupture. Herbowski⁴¹ found a positive correlation between intracranial pressure and atmospheric pressure, which may increase stress on IA walls and thus also the risk of rupture.

Previous studies have shown that hemodynamic changes play a crucial role in the occurrence, development, and rupture of aneurysms, which in turn may cause morphological changes in aneurysms and the parent arteries.^{42–45} Backes et al³² suggested that an AR >1.3 and an irregular shape are associated with rupture of aneurysm. Bhogal et al³³ reported that complex aneurysm morphology was the strongest risk factor for rupture (odds ratio=29.27, 95% Cl, 14.33–59.78; *P*<0.001) in aneurysms with a size <7 mm (odds ratio=17.74, 95% Cl, 4.07–77.35; *P*<0.001). However, the effect of the combination of meteorological factors and aneurysm morphology on the prediction of aneurysm rupture has not been accurately evaluated. Thus, this study analyzed the morphological differences between ruptured and unruptured aneurysms in patients with multiple aneurysms living in high-risk climate conditions.

Aneurysm size is thought to be an important risk factor for the prediction of aneurysm rupture.^{32–34,46,47} Investigators from the International Study of Unruptured Intracranial Aneurysms reported that aneurysms with a size ≤ 10 mm have a low risk of rupture (annual rate of rupture=0.05%), whereas aneurysms with a size >10 mm have a 1% annual rate of rupture.⁴⁶ International Study of Unruptured Intracranial Aneurysms II investigators recommended 7 mm as the size threshold for predicting aneurysm rupture.⁴⁷ However, a recent study found that the size of a ruptured aneurysm can be <7 mm.³³ Our study found that rupture occurred more often in small aneurysms (aneurysm size <5 mm) in high-risk weather conditions, and ROC curve analysis showed that the optimal threshold was 3.45 mm. Thus, aneurysms with a size >3.45 mm have a higher risk of rupture.

In our study, multivariable logistic regression analysis revealed that AR was an independent risk factor for predicting

rupture. AR is defined as the ratio of height to Wn and is currently a widely used index for the analysis of aneurysm ruptures. It is possible that an aneurysm with a small neck but a high AR may decrease blood flow to the aneurysm body and cause reconstruction of the aneurysm wall, which would then increase the risk of rupture.^{39,48} It is also possible that a high-AR aneurysm is associated with low wall shear stress and larger areas of low wall shear stress within an aneurysm.⁴⁹ Ujiie⁵⁰ performed an ROC curve analysis and found that an AR >1.6 was the optimal threshold for predicting aneurysm rupture; Dhar et al³⁷ reported that aneurysms with an AR >1.2 ruptured more easily. However, the present ROC analysis showed that the optimal threshold for AR was 1.05, which implies that some aneurysms with relatively wide necks rupture in high-risk weather conditions.

The other morphological parameters (Wn, height, length, width, D, SR, height-to-width ratio, and BN) assessed in the present study were not independent risk factors of rupture; however, future studies from our research group will include more patients to analyze these effects. The present results indicate that some aneurysms that were not considered likely to rupture may rupture more easily in high-risk meteorological environments.

Limitations

This study had several limitations that should be considered. First, this was a retrospective study with inherent limitations. Second, the meteorological data assessed in this study were also limited. For meteorological factors other than temperature, only daily average values could be obtained, and this may have weakened assessments of the complexity of weather changes. Future studies with large samples and abundant meteorological data will be necessary to overcome these limitations. Finally, it is extremely difficult to avoid mistakes when measuring the morphological parameters of aneurysms, particularly when making judgments about ruptures in patients with multiple aneurysms. Thus, clinicians and radiologists with abundant experience are necessary.

Conclusions

Lower daily mean, maximum, and minimum temperatures and a higher daily mean atmospheric pressure were associated with an increased rate of aSAH. Additionally, under these meteorological conditions, the aneurysm size and aspect ratio thresholds for predicting rupture of an aneurysm may be lower.

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Disclosures

None.

References

- Thompson BG, Brown RJ, Amin-Hanjani S, Broderick JP, Cockroft KM, Connolly EJ, Duckwiler GR, Harris CC, Howard VJ, Johnston SC, Meyers PM, Molyneux A, Ogilvy CS, Ringer AJ, Torner J. Guidelines for the management of patients with unruptured intracranial aneurysms: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46:2368–2400.
- 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. 2007;78:1365–1372.
- Macdonald RL, Schweizer TA. Spontaneous subarachnoid haemorrhage. Lancet. 2017;389:655–666.
- Broderick JP, Viscoli CM, Brott T, Kernan WN, Brass LM, Feldmann E, Morgenstern LB, Wilterdink JL, Horwitz RI. Major risk factors for aneurysmal subarachnoid hemorrhage in the young are modifiable. *Stroke*. 2003;34:1375– 1381.
- Qureshi Al, Suri MF, Yahia AM, Suarez JI, Guterman LR, Hopkins LN, Tamargo RJ. Risk factors for subarachnoid hemorrhage. *Neurosurgery*. 2001;49:607– 613.
- Teunissen LL, Rinkel GJ, Algra A, van Gijn J. Risk factors for subarachnoid hemorrhage: a systematic review. *Stroke*. 1996;27:544–549.
- Sandvei MS, Mathiesen EB, Vatten LJ, Muller TB, Lindekleiv H, Ingebrigtsen T, Njolstad I, Wilsgaard T, Lochen ML, Vik A, Romundstad PR. Incidence and mortality of aneurysmal subarachnoid hemorrhage in two Norwegian cohorts, 1984–2007. *Neurology*. 2011;77:1833–1839.
- Sandvei MS, Romundstad PR, Muller 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.
- Lee S, Guth M. Associations between temperature and hospital admissions for subarachnoid hemorrhage in Korea. Int J Environ Res Public Health. 2017;14: E449.
- Tarnoki AD, Turker A, Tarnoki DL, Iyisoy MS, Szilagyi BK, Duong H, Miskolczi L. Relationship between weather conditions and admissions for ischemic stroke and subarachnoid hemorrhage. *Croat Med J.* 2017;58:56–62.
- Lai PM, Dasenbrock H, Du R. The association between meteorological parameters and aneurysmal subarachnoid hemorrhage: a nationwide analysis. *PLoS One*. 2014;9:e112961.
- Jeong TS, Park CW, Yoo CJ, Kim EY, Kim YB, Kim WK. Association between the daily temperature range and occurrence of spontaneous intracerebral hemorrhage. J Cerebrovasc Endovasc Neurosurg. 2013;15:152–157.
- 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 subarachnoid hemorrhage. *World Neurosurg.* 2013;79:136–142.
- Neidert MC, Sprenger M, Wernli H, Burkhardt JK, Krayenbuhl N, Bozinov O, Regli L, Woernle CM. Meteorological influences on the incidence of aneurysmal subarachnoid hemorrhage—a single center study of 511 patients. *PLoS One*. 2013;8:e81621.
- Miranpuri AS, Akture E, Baggott CD, Miranpuri A, Uluc K, Gunes VE, Lin Y, Niemann DB, Baskaya MK. Demographic, circadian, and climatic factors in non-aneurysmal versus aneursymal subarachnoid hemorrhage. *Clin Neurol Neurosurg.* 2013;115:298–303.
- Patrice T, Rozec B, Desal H, Blanloeil Y. Oceanic meteorological conditions influence incidence of aneurysmal subarachnoid hemorrhage. J Stroke Cerebrovasc Dis. 2017;26:1573–1581.
- de Steenhuijsen PW, Algra A, van den Broek MF, Dorhout MS, Rinkel GJ. Seasonal and meteorological determinants of aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. *J Neurol.* 2013;260:614–619.
- 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.
- 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.
- Rivera-Lara L, Kowalski RG, Schneider EB, Tamargo RJ, Nyquist P. Elevated relative risk of aneurysmal subarachnoid hemorrhage with colder weather in the mid-Atlantic region. *J Clin Neurosci.* 2015;22:1582–1587.

- Steiner T, Juvela S, Unterberg A, Jung C, Forsting M, Rinkel G. European Stroke Organization guidelines for the management of intracranial aneurysms and subarachnoid haemorrhage. *Cerebrovasc Dis.* 2013;35:93–112.
- 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.
- Cowperthwaite MC, Burnett MG. The association between weather and spontaneous subarachnoid hemorrhage: an analysis of 155 US hospitals. *Neurosurgery*. 2011;68:132–139.
- 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.
- Han MH, Yi HJ, Ko Y, Kim YS, Lee YJ. Association between hemorrhagic stroke occurrence and meteorological factors and pollutants. *BMC Neurol.* 2016;16:59.
- Ishikawa K, Niwa M, Tanaka T. Difference of intensity and disparity in impact of climate on several vascular diseases. *Heart Vessels*. 2012;27:1–9.
- Beseoglu K, Hanggi D, Stummer W, Steiger HJ. Dependence of subarachnoid hemorrhage on climate conditions: a systematic meteorological analysis from the Dusseldorf metropolitan area. *Neurosurgery*. 2008;62:1033–1039.
- Zanaty M, Chalouhi N, Tjoumakaris SI, Fernando GL, Rosenwasser RH, Jabbour PM. Aneurysm geometry in predicting the risk of rupture. A review of the literature. *Neurol Res.* 2014;36:308–313.
- 29. Weir B. Unruptured intracranial aneurysms: a review. J Neurosurg. 2002;96:3–42.
- Joo SW, Lee SI, Noh SJ, Jeong YG, Kim MS, Jeong YT. What is the significance of a large number of ruptured aneurysms smaller than 7 mm in diameter? J Korean Neurosurg Soc. 2009;45:85–89.
- Forget TJ, Benitez R, Veznedaroglu E, Sharan A, Mitchell W, Silva M, Rosenwasser RH. A review of size and location of ruptured intracranial aneurysms. *Neurosurgery*. 2001;49:1322–1326.
- Backes D, Vergouwen MD, Velthuis BK, van der Schaaf IC, Bor AS, Algra A, Rinkel GJ. Difference in aneurysm characteristics between ruptured and unruptured aneurysms in patients with multiple intracranial aneurysms. *Stroke*. 2014;45:1299–1303.
- Bhogal P, AlMatter M, Hellstern V, Ganslandt O, Bazner H, Henkes H, Perez MA. Difference in aneurysm characteristics between ruptured and unruptured aneurysms in patients with multiple intracranial aneurysms. *Surg Neurol Int.* 2018;9:1.
- Ishibashi T, Murayama Y, Urashima M, Saguchi T, Ebara M, Arakawa H, Irie K, Takao H, Abe T. Unruptured intracranial aneurysms: incidence of rupture and risk factors. *Stroke*. 2009;40:313–316.
- Juvela S, Porras M, Poussa K. Natural history of unruptured intracranial aneurysms: probability of and risk factors for aneurysm rupture. *J Neurosurg*. 2000;93:379–387.
- Skodvin TO, Johnsen LH, Gjertsen O, Isaksen JG, Sorteberg A. Cerebral aneurysm morphology before and after rupture: nationwide case series of 29 aneurysms. *Stroke.* 2017;48:880–886.
- Dhar S, Tremmel M, Mocco J, Kim M, Yamamoto J, Siddiqui AH, Hopkins LN, Meng H. Morphology parameters for intracranial aneurysm rupture risk assessment. *Neurosurgery*. 2008;63:185–197.
- Hoh BL, Sistrom CL, Firment CS, Fautheree GL, Velat GJ, Whiting JH, Reavey-Cantwell JF, Lewis SB. Bottleneck factor and height-width ratio: association with ruptured aneurysms in patients with multiple cerebral aneurysms. *Neurosurgery*. 2007;61:716–723.
- Nader-Sepahi A, Casimiro M, Sen J, Kitchen ND. Is aspect ratio a reliable predictor of intracranial aneurysm rupture? *Neurosurgery*. 2004;54:1343– 1348.
- Kawai K, Nonaka K, Suzuki H, Kirino T, Tamura A. Differential effects of activity and climate on onset of subarachnoid hemorrhage. *Neurol Med Chir (Tokyo)*. 2001;41:229–237.
- Herbowski L. The major influence of the atmosphere on intracranial pressure: an observational study. *Int J Biometeorol*. 2017;61:181–188.
- 42. Jamous MA, Nagahiro S, Kitazato KT, Tamura T, Aziz HA, Shono M, Satoh K. Endothelial injury and inflammatory response induced by hemodynamic changes preceding intracranial aneurysm formation: experimental study in rats. J Neurosurg. 2007;107:405–411.
- Xiang J, Natarajan SK, Tremmel M, Ma D, Mocco J, Hopkins LN, Siddiqui AH, Levy EI, Meng H. Hemodynamic-morphologic discriminants for intracranial aneurysm rupture. *Stroke*. 2011;42:144–152.
- 44. Cebral JR, Castro MA, Appanaboyina S, Putman CM, Millan D, Frangi AF. Efficient pipeline for image-based patient-specific analysis of cerebral

aneurysm hemodynamics: technique and sensitivity. *IEEE Trans Med Imaging*. 2005;24:457–467.

- 45. Tremmel M, Dhar S, Levy El, Mocco J, Meng H. Influence of intracranial aneurysm-to-parent vessel size ratio on hemodynamics and implication for rupture: results from a virtual experimental study. *Neurosurgery*. 2009;64:622–631.
- Unruptured intracranial aneurysms—risk of rupture and risks of surgical intervention. N Engl J Med. 1998;339:1725–1733.
- Wiebers DO, Whisnant JP, Huston JR, Meissner I, Brown RJ, Piepgras DG, Forbes GS, Thielen K, Nichols D, O'Fallon WM, Peacock J, Jaeger L, Kassell NF, Kongable-Beckman GL, Torner JC. Unruptured intracranial aneurysms: natural

history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet.* 2003;362:103–110.

- Tateshima S, Chien A, Sayre J, Cebral J, Vinuela F. The effect of aneurysm geometry on the intra-aneurysmal flow condition. *Neuroradiology*. 2010;52:1135–1141.
- Feigin VL, Anderson CS, Rodgers A, Bennett DA. Subarachnoid haemorrhage occurrence exhibits a temporal pattern—evidence from meta-analysis. *Eur J Neurol.* 2002;9:511–516.
- Ujiie H, Tamano Y, Sasaki K, Hori T. Is the aspect ratio a reliable index for predicting the rupture of a saccular aneurysm? *Neurosurgery*. 2001;48:495– 503.

Supplemental Material

Time period	No. (%) of patients				
Totle (00:00-23:59)	1751(100%)				
Morning (04:00-07:59)	394(22.5%)				
Forenoon (08:00-11:59)	310(17.7%)				
Midday (12:00-15:59)	263(15.0%)				
Afternoon (16:00-19:59)	357(20.4%)				
Evening (20:00-23:59)	292(16.7%)				
Night (00:00-03:59)	135(7.7%)				

Table S1. Number of patients with aSAH with reference to the six time periods.

Chi-square goodness of fit test was used to compare the differences between groups (χ^2 =138.58, p<0.001)

Table S2. Results of Spearman rank correlation analysis of aSAH admission andmeteorological variables.

Spearman										
rank correlation analysis	variables		incidence of aSAH	2	daily maximum temperature	daily minimum temperature	24 hours of precipitation	daily sunshine duration	daily mean relative humidity	daily mean air pressure
anarysis			01 aSAI1	-			precipitation	duration	indificality	-
	incidence of aSAH	R	1.000	043**	041**	042**	020	.016	.007	.043**
		Р		<.001	<.001	<.001	.076	.161	.558	<.001
	daily mean temperature	R		1.000	.975**	.976**	035	.300**	128**	884**
	<u>-</u>	Р		•	<.001	<.001	.002	<.001	<.001	<.001
	daily max temperature	R			1.000	.913**	101**	.405**	274**	849**
	temperature -	Р				<.001	<.001	<.001	<.001	<.001
	daily min temperature	R				1.000	.048**	.181**	.037**	879**
		Р					<.001	<.001	.001	<.001
	24 hours of precipitation	R					1.000	333**	.524**	088**
	precipitation	Р						<.001	<.001	<.001
	daily sunshine	R						1.000	607**	184**
	duration	Р							<.001	<.001
	daily mean	R							1.000	016
	relative humidity	Р								.168
	2	R								1.000
air pressure		Р								

Table S3. Results of Spearman rank correlation analysis of aSAH admission andmeteorological fluctuation variables.

Fluctuation variables	correlation coefficient(R)	P-value
daily fluctuations in temperature	016	.169
Change in mean temperature*	006	.592
Change in max temperature*	001	.957
Change in min temperature*	001	.921
Change in 24 hours of precipitation*	013	.241
Change in sunshine duration*	003	.790
Change in mean relative humidity*	002	.860
Change in mean air pressure*	.010	.370

* change in meteorological data means the value on the day of onset minus the value on the day before.

Fluctuation variables	Within 48 hours		Within 72 hours			
	correlation coefficient(R)	P-value*	correlation coefficient(R)	P-value*		
Change in mean temperature	010	.364	008	.489		
Change in max temperature	007	.565	004	.745		
Change in min temperature	012	.275	009	.452		
Change in 24 hours of precipitation	0.009	.441	0.002	.887		
Change in sunshine duration	001	.897	016	.162		
Change in mean relative humidity	.000	.966	.002	.889		
Change in mean air pressure	.009	.411	.013	.245		

Table S4. Results of Spearman rank correlation analysis of aSAH admission anddelayed meteorological fluctuation variables.

parameters	Ruptured	Unruptured	P-value	95%CI	AUC	Optimal thresholds
	IAs (n=58)	IAs (n=83)				(sensitivity, specificity)
Location (n, %)						
МСА	14 (24.1%)	26 (31.3%)	$0.019^{a}(\chi^{2}=16.419)$			
ACA	0 (0%)	1 (1.2%)				
PCA	0 (0%)	1 (1.2%)				
ICA C4	1 (1.7%)	3 (3.6%)				
ICA C5	7 (12.1%)	16 (19.3%)				
ICA C6	2 (3.4%)	6 (7.2%)				
ACoA	20 (34.5%)	7 (8.4%)				
РСоА	12 (20.7%)	21 (25.3%)				
VB	2 (3.4%)	2 (2.4%)				
S (n, %)						
<3mm	12 (20.7%)	50 (60.2%)	$<0.001^{a}(\chi^{2}=21.876)$			
3-7mm	27 (46.6%)	21 (25.3%)				
>7mm	19 (32.7%)	12 (14.5%)				
S (M±SD)	5.81±2.69	4.18±2.84	0.001 ^b	(0.46, 2.8)	0.72	3.45 (77.6%, 62.7%)
Wn (M±SD)	3.16±1.43	2.64 ± 1.50	0.038 ^b	(-0.1, 1.14)	0.64	2.25 (74.1%, 49.5%)
H (M±SD)	4.00±2.11	2.87±2.41	0.005 ^b	(0.26, 2.2)	0.70	2.15 (77.6%, 63.9%)
$L(M\pm SD)$	4.89±2.34	3.65±2.69	0.006 ^b	(0.15, 2.33)	0.69	2.55 (79.3%, 60.2%)
W (M±SD)	3.49±1.90	2.46±2.03	0.003 ^b	(0.2, 1.86)	0.68	2.00 (74.1%, 67.5%)
D (M±SD)	2.93 ± 0.73	2.91 ± 0.84	0.854 ^b	(-0.32, 0.36)	0.58	2.65 (67.2 %, 39.8%)
AR (M±SD)	1.27 ± 0.46	1.02 ± 0.43	0.001 ^b	(0.07, 0.82)	0.66	1.05 (79.3%, 57.8%)

Table S5. The location, morphological parameters of aneurysms and thestatistical analysis results.

SR (M±SD)	1.74 ± 0.93	1.34 ± 1.04	0.020 ^b	(-0.02, 0.82)	0.67	1.05 (67.2 %, 60.2%)
HWR (M \pm SD)	1.18 ± 0.15	1.18 ± 0.24	0.962 ^b	(-0.08, 0.08)	0.51	1.15 (50.0%, 48.2%)
BN (M \pm SD)	1.10 ± 0.41	0.89 ± 0.35	0.001 ^b	(0.05, 0.37)	0.66	0.95 (72.4%, 61.4%)
Shape (n,%)						
regular	24 (41.4%)	51 (61.4%)	$0.019^{a}(\chi^{2}=5.522)$			
bleb(s)	34 (58.6%)	32 (38.6%)				

a, Chi-square test was used; b, one-way analysis of variance was used.

Table S6. Results of relative weight analysis of all factors.

factors	weight coefficient
S	0.143
Wn	0.088
Н	0.144
L	0.144
W	0.143
Dv	-0.05
AR	0.111
SR	0.149
HWR	-0.029
BN	0.116
Location	-0.001
Bleb(s)	0.043

Figure S1. A line trend which we can roughly observed the relationship between standardized numbers of aSAH and mean standardized meteorological data.



Daily aSAH incidence was negatively correlated with the daily mean, maximum, and minimum temperatures but positively correlated with the daily mean atmospheric pressure.

Figure S2. The results of receiver operating characteristic (ROC) curve analysis with the daily average temperature and the daily average pressure in Nanchang city.



The AUC values were 54.2% and 53.3%, P<0.05), respectively, and the optimal thresholds were 12.5° (sensitivity:73.2%, specificity:34.6%) and 1,016.65hPa(sensitivity:55.4%, specificity: 54%), respectively.