Warm Front Passage on the Previous Day Increased Ischemic Stroke Events

Ryo Shimomura, MD, PhD,*,† Naohisa Hosomi, MD, PhD,*,† Miwako Tsunematsu, PhD,‡ Tomoya Mukai, MD, PhD,*,§ Yoshimasa Sueda, MD, PhD,*,¶ Yutaka Shimoe, MD, PhD,* Tomohiko Ohshita, MD, PhD,|| Tsuyoshi Torii, MD, PhD,** Tomohisa Nezu, MD, PhD,* Shiro Aoki, MD, PhD,* Masayuki Kakehashi, PhD,‡ Masayasu Matsumoto, MD, PhD,* and Hirofumi Maruyama, MD, PhD*, on behalf of the Hiroshima 'Emergency and Weather' Study-stroke collaborators

Background and Purpose: The influence of a weather front passage is rarely evaluated on stroke events. We hypothesized that a weather front passage on the stroke onset day or during the previous days may play an important role in the incidence of stroke. *Methods:* A multicenter retrospective study was conducted to evaluate the frequency of stroke events and their interaction with weather front passages. Consecutive acute stroke patients (n = 3935, 73.5 ± 12.4 years, 1610 females) who were admitted to 7 stroke hospitals in 3 cities from January 2012 to December 2013 were enrolled in this study. Multivariate Poisson regression models involving time lag variables were used to compare the daily rates of stroke events with the day of a weather front passage and the previous 6 days, adjusting for considerable influences of ambient temperature and atmospheric pressure. *Results:* There were a total of 33 cold fronts and 13 warm fronts that passed over the 3 cities during the study period. The frequency of ischemic stroke significantly increased when a warm front passed on the previous day (risk ratio 1.34, 95% confidence interval 1.07-1.69, *P* = .016). *Conclusions:* This study indicated that a weather front passage on the previous days may be associated with the occurrence of stroke.

Key Words: Meteorological conditions—stroke—weather front—epidemiology

Introduction

The effects of weather conditions on the human organism have been examined, especially in cardiovascular or respiratory diseases, by various studies.[1,2] Cardiovascular events have been considered to be at high risk on a cold day.[3,4] Presently, we cannot predict when strokes occur. If

From the *Department of Clinical Neuroscience and Therapeutics, Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan; †Department of Neurology, Brain Attack Center Ota Memorial Hospital, Fukuyama, Japan; ‡Department of Health Informatics, Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan; §Department of Neurology, Hiroshima Prefectural Hospital, Hiroshima, Japan; ¶Department of Neurology, National Hospital Organization Higashihiroshima Medical Center, Higashihiroshima, Japan; ||Department of Neurology, Suiseikai Kajikawa Hospital, Hiroshima, Japan; and **Department of Neurology, National Hospital Organization Kure Medical Center, Kure, Japan.

Received December 28, 2018; revision received March 27, 2019; accepted April 6, 2019.

Sources of Financial Support: This study was supported in part by research grants from JSPS KAKENHI (Grant Numbers 23590598, 15K08615). The funders had no role in the study design, data collection, and analysis, decision to publish, or the preparation of the manuscript.

Address correspondence to Naohisa Hosomi, MD, PhD, Department of Clinical Neuroscience and Therapeutics, Hiroshima University Graduate School of Biomedical Sciences, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan. E-mail: hosomi@hiroshima-u.ac.jp.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.04.011

we can identify high-risk days for the occurrence of stroke, we may be able to take preventive measures.

Thermo-hydrological index (THI) is an established appropriate measure for the evaluation of the effect of air temperature on health outcomes because it takes into account mean air temperature after controlling for the effect of relative humidity.[5] We have reported that ischemic stroke significantly increases with variation in the THI by .99°C or more.[6] Intracerebral hemorrhage frequency significantly increased when the THI cooled by .99°C or more over the 5 to 4 days prior to the event. The THI on the day of the event did not influence ischemic stroke events but did influence intracerebral hemorrhage events. When the THI was 23.8°C or higher, the risk of intracerebral hemorrhage was low.

On the other hand, there are other weather conditions, for example, weather front passages, that should be considered. A weather front is a boundary between 2 air masses whose properties are contrasting. At the boundary, there are differences in temperature, wind shift, humidity, and atmospheric pressure. The conceptual model of a cold front is the leading edge of a colder air. Cooler air tilts forward under the prefrontal warmer air, and the passage of the surface cold front is indicated by a sharp temperature decrease and an atmospheric pressure increase.[7] A warm front belongs to the zone of low atmospheric pressure, which also contains a cold front. The conceptual model is a warm front tilting forward over the prefrontal cold air and extending from the surface to the midtroposphere, and the passage of the surface warm front is indicated by a coincident temperature increase, a cyclonic wind shift, and a decrease in surface pressure.[8] Warm fronts are generally weaker and have less dramatic weather changes than cold fronts. An occluded front is formed when a cold front catches a preceding warm front. When an occluded front passes, weather change can be a wide variety because of combination of a warm front and a cold front. The influence of weather front passages on stroke events is rarely evaluated. In the present study, we evaluated the association between weather front passages and the frequency of stroke events in Japanese patients.

Methods

Patients

This study was performed as a part of the Hiroshima 'Emergency and Weather' Study—stroke [6]. The study protocol was approved by the Institutional Review Board of Hiroshima University. Then, the local ethical committee in each participating institute approved the protocol. All clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki. No informed consent was given because the data were analyzed anonymously. Consecutive acute stroke patients who were admitted to 1 of 7 emergency hospitals within 7 days of stroke onset in the Hiroshima prefecture, which included the cities of Hiroshima (4 hospitals), Kure (2 hospitals), and Fukuyama (1 hospital), from January 2012 to December 2013 were retrospectively enrolled. These 3 cities contained the official meteorological observatories that were used as the source of meteorological data. The onset date and subtype of acute strokes were recorded for each patient. Ischemic stroke subtypes were classified using the Trial of Org 10172 in Acute Stroke Treatment criteria.[9]

Hemorrhagic infarction and trauma-induced hemorrhage were excluded from intracerebral hemorrhage. The primary diseases of nonhypertensive intracerebral hemorrhage included tumor, arteriovenous malformation, moyamoya disease, and cerebral amyloid angiopathy. Stroke subtype diagnoses were determined before discharge using brain computed tomography or magnetic resonance imaging. Expert neurologists assigned the diagnoses for all patients.

Study Area

Japan is located in a temperature climate zone that has 4 distinct seasons: spring, summer, autumn, and winter. The Hiroshima prefecture is located in the western part of Japan (north latitude 34-35° and east longitude 132-133°) in a Cfa zone (warm temperature, moist, hot summer), based on the Köppen-Geiger climate classification.[10]

Meteorological Date

The day of passage of the weather front (such as a cold front or a warm front) was obtained based on the local meteorological observatories (Japan Meteorological Agency, Ministry of Land, Infrastructure, Transport and Tourism). The meteorological data used in this study included the daily mean ambient temperature (Ta,°C), the daily mean atmospheric pressure (hPa), and the daily mean relative humidity (RH, %) of the 24-hour calendar day period (0:00 AM-11:59 PM). The THI (°C) was calculated using the formula $THI = Ta - .55 \times (1 - .01 \times RH) \times (Ta - 14.5)$, as reported previously.[5,11] The distance from each hospital to the local meteorological observatory ranged from .2 km to 12.8 km (average distance = 5.3 km). All meteorological data were obtained from the website of each local meteorological observatory.

Statistical Analysis

The data are expressed as the mean ± standard deviation for continuous variables and as frequencies and percentages for discrete variables. We first investigated basic trends of the changes in THI and atmospheric pressure on the day of each front passage from 6 days before to 6 days after its passage day.

We then used a multivariable Poisson regression model involving time lag variables instead of a common multiple regression model to analyze the incidence of stroke

because the response variables were count data or non-negative integers.[6,12] The risk ratio and the 95% confidence interval of stroke in accordance with each front passage for the previous 6 days were adjusted for ambient temperature, atmospheric pressure, and their changes, which we had previously reported as a potent influence factors on the risk of stroke events ($P < .20$) in addition to the location of the hospitals, using the Poisson regression model.[6] For ischemic stroke, the selected factors were ambient temperature and atmospheric pressure on the day of interest and the changes in ambient temperature from the previous day to the day of interest and from 2 days prior to the previous day. For intracerebral hemorrhage, the selected factors were ambient temperature and atmospheric pressure on the day of interest and the changes in ambient temperature from 2 days prior to the previous day, from 5 days prior to 4 days prior, and from 7 days prior to 6 days prior, and the changes in atmospheric pressure from 6 days prior to 5 days prior to the day of interest.

Statistical analysis was performed using the SPSS software package (IBM SPSS Statistics for Windows, version 22.0, IBM Corp., Armonk, New York). A 2-tailed *P*value <.05 was regarded as statistically significant.

Results

The baseline characteristics of the study population and meteorological conditions of the evaluated days were presented in the previous report.[6] Briefly, during the 2-year observation period (731 days in 3 cities) of this study, a total of 3935 patients (1610 females and 2325 males) with stroke were enrolled. The mean age of the study participants was 73.5 ± 12.4 years (median 75 years; range 11-101 years). The subjects consisted of 3197 ischemic stroke patients and 738 intracerebral hemorrhage patients. The average annual THI of the 3 cities was 16.0 ± 7.3°C. The average annual atmospheric pressure in the study area was 1012.6 ± 7.1 hPa. The annual THI and atmospheric pressure were not significantly different among the 3 cities.

Table 1 shows the number of passages of each type of front during the 2-year observation period (731 days) of this study. There were a total of 33 cold fronts and 13 warm fronts that passed over the 3 cities on the same day.

The THI was 15.2 ± 4.1°C on the days of a warm front passage and 13.8 ± 4.8°C on the days of a cold front passage. The mean atmospheric pressure was 1006.6 ± 4.4 hPa on the days of a warm front passage and 1009.1 ± 5.3 hPa on the days of a cold front passage. Changes in the mean THI and the mean atmospheric pressure are presented for the previous 6 days before each front passage and the following 6 days after each front passage in Figures 1 and 2.

Table 1. *Total number of days of weather front passages*

	731 days for 3 cities
Weather front passage	
Warm front, n (%)	13 (1.8)
Cold front, n (%)	33 (4.5)

For ischemic stroke, a warm front passage on the previous day was significantly associated with a high frequency of events using the multivariate Poisson regression models involving time lag variables (risk ratio 1.34, 95% confidence interval 1.07-1.69, $P = .01$; Fig 3). No significant association was detected for the frequency of ischemic stroke with cold front passages.

No significant association was detected with cold or warm front passages (Fig 4).

Discussion

This study revealed that a warm front passage on the previous day was significantly associated with an increase in ischemic stroke events.

Currently, the influence of the temperature on the day of a stroke event on the human physical condition becomes difficult to detect with the prevalence of indoor air conditioning. The fluctuations in temperature and atmospheric pressure may also influence the human physical condition. Previously, we have reported that changes in ambient temperature from the previous day to the day of interest increases the occurrence of ischemic stroke events. In addition, the decrease in ambient temperature from 5 to 4 days prior increases the occurrence of intracerebral hemorrhage events.[6]

In this study, we have evaluated the influence of weather front passages on ischemic stroke and intracerebral hemorrhage events adjusted for those factors, which may show considerable influences.[6] A warm front passage on the previous day was significantly associated with an increase in the occurrence of ischemic stroke events. This phenomenon might be caused by the difference in the properties of the front. A warm front proceeds a cold front, thus most cold fronts also pass over a city on the same day as a warm front passage (12/13 days in 3 cities in this study). In addition, the length of a warm front is generally shorter than that of a cold front. Therefore, a zone of low atmospheric pressure may be closer to cities during a warm front passage than on the days of only a cold front passage. Zaninovic has reported that after a cold front passage, the coagulability of blood tended to increase in stroke patients.[13]

The association of weather fronts and cardiovascular disease has been reported. Frequencies of acute myocardial infarction events increase during the 7-12 hours after a warm front passage.[14] Cardiovascular disease-related mortality including stroke increase on the day of warm front passage and 1 day after warm front passage.[15] These results suggest the considerable impact of

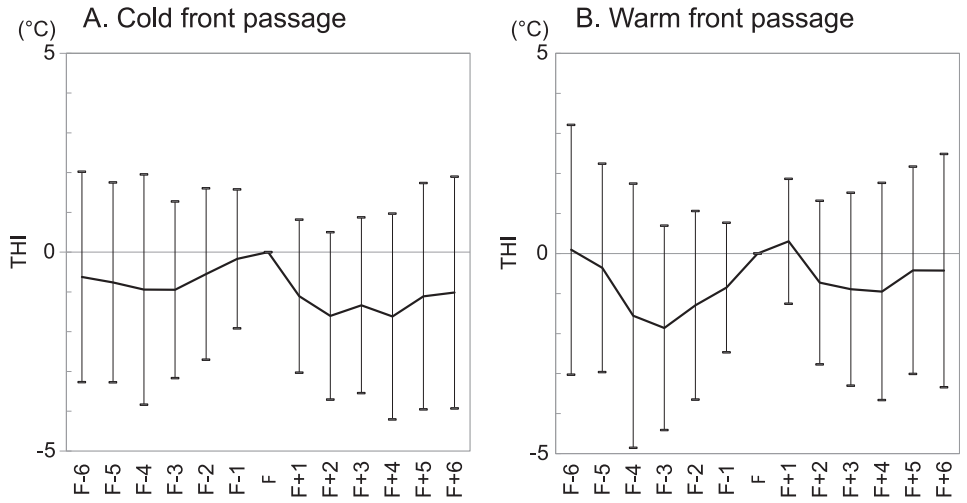

Figure 1. *Changes in THI with weather front passages. The difference in THI during the previous 6 days and the following 6 days of cold front passages (A) and warm front passages (B) in comparison to the day of each weather front passage are presented. Abbreviations: F, the day of the weather front passage; THI, thermo-hydrological index.*

a warm front for our physical condition arise a day after the front passage supporting our results. However, actual definition of influences of warm front passage on frequencies of cerebro- and cardiovascular diseases has not been made. Generally, as shown in our results, ambient temperature gradually increases for several days until warm front passage. In our previous study, we have reported that when ambient temperature varied from a previous day, the frequency of ischemic stroke increases.[6] Therefore, influences of warm front passage on frequencies of ischemic stroke may depend on changes of ambient temperature, although changes of ambient temperature from a previous day were also included as a factor of multivariate analysis in this study. Our present study suggested that the occurrence of stroke events was increased after warm front passages, indicating that front passage may influence the human physical condition.

The influence was largest on 1 day after warm front passages.

This study has several limitations. First, this is a retrospective study of 3 cities in the Hiroshima prefecture in Japan. However, this study and prior epidemiological studies are similar with respect to patient demographics,[16] such as stroke subtype and age; as a result, our findings may be applicable to other cities. Second, this study is based on patients admitted to hospitals. We cannot exclude the possibility that patients experiencing the onset

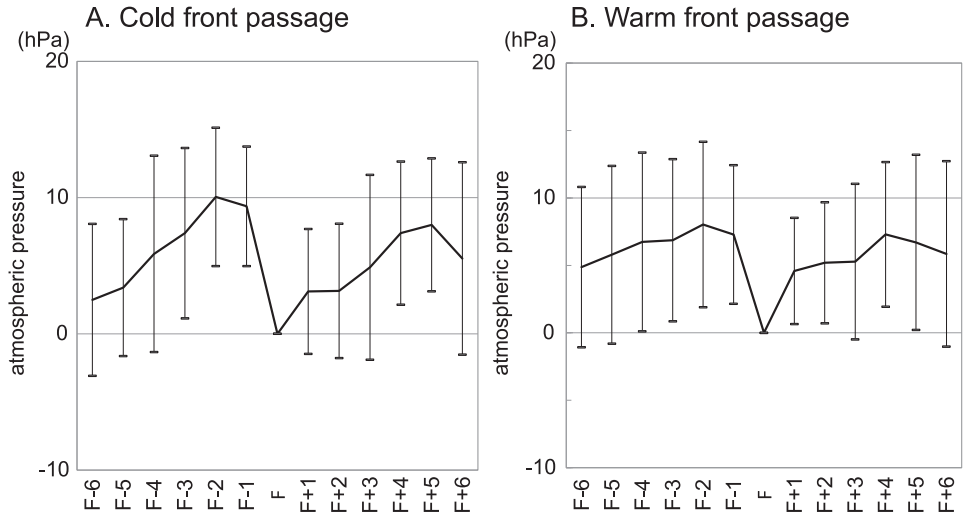

Figure 2. *Changes in atmospheric pressure with weather front passages. The differences in atmospheric pressure during the previous 6 days and the following 6 days of cold front passages (A) and warm front passages (B) in comparison to the day of each weather front passage are presented. Abbreviation: F, the day of the weather front passage.*

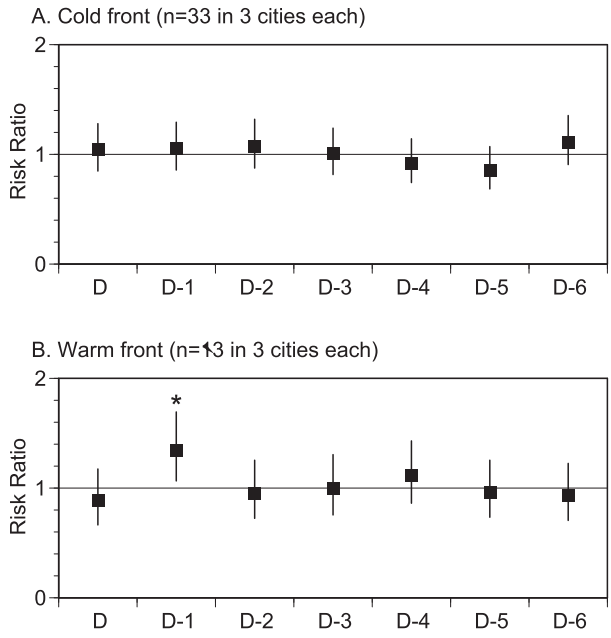

Figure 3. *Relative risks of ischemic stroke and the interaction of weather front passages. (A) Cold front and (B) warm front. Abbreviation: D, the day of interest.*

of mild stroke are not hospitalized. This limitation may also exist in population-based studies. However, in Japan, when a mild stroke patient visits a hospital for acute diagnosis, he or she is essentially admitted and can receive treatment. Therefore, the possibility that mild stroke patients were excluded from this study may be limited.

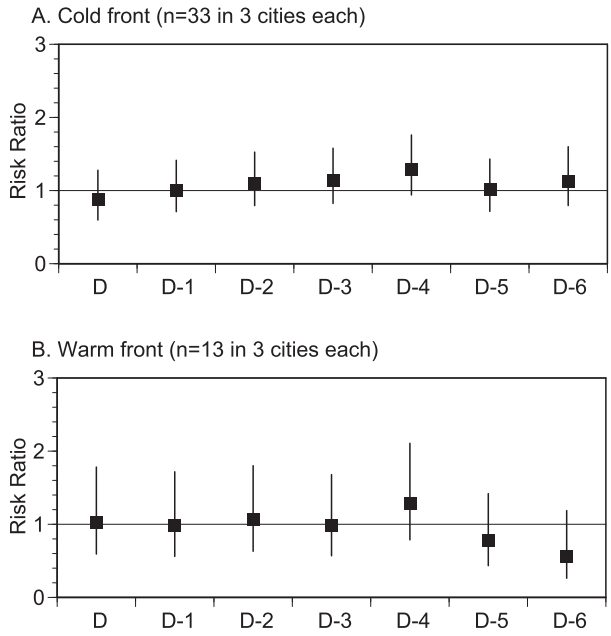

Figure 4. *Relative risks of intracerebral hemorrhage and the interaction of weather front passages. (A) Cold front and (B) warm front. Abbreviation: D, the day of interest.*

Third, it was impossible to include individual information on the true environmental conditions (indoor and outdoor), socioeconomic background, or dietary habits at stroke onset. Fourth, this study was conducted in Japan, and most of the inpatients were Japanese. Asians suffer more hemorrhagic events than Caucasians,[16] and ethnic differences exist in a person's tolerance to environmental change. For example, Hispanics are more likely to be affected by temperature.[17] Further investigations should be undertaken to identify ethnic differences in response to environmental changes.

Conclusions

This study indicated that the passage of a warm front increased ischemic stroke events when adjusted for considerable influences of ambient temperature and atmospheric pressure.

Acknowledgments

We would like to show our appreciation to the participants in the HEWS-stroke collaboration and Mr. Ryuichi Nakata for his expertise on the mechanism of weather fronts.

Author Contributions

Dr. Matsumoto was the principal investigator. Drs. Shimomura, Hosomi, Mukai, Sueda, Matsumoto, and Maruyama were responsible for the study conception and design. Ms. Tsunematsu and Mr. Kakehashi performed the statistical analysis. Drs. Hosomi, Mukai, Sueda, Shimoe, Ohshita, Torii, Nezu, and Aoki interpreted the data. Drs. Shimomura and Hosomi designed the figures. Drs. Shimomura, Hosomi, Matsumoto, and Maruyama contributed to drafting the report. All authors participated in the finalization of the report.

Dr. Matsumoto obtained grants from Daiichi Sankyo Co. Ltd. and has received honoraria from Sanofi K.K., Bayer Yakuhin Ltd., Takeda Pharmaceutical Co. Ltd., Otsuka Pharmaceutical Co. Ltd., Nippon Boehringer Ingelheim Co. Ltd., Sumitomo Dainippon Pharma Co. Ltd., Novartis Pharma K. K., Bristol-Myers Squibb, Mochida Pharmaceutical Co. Ltd., Kyowa Hakko Kirin Co. Ltd., Nihon Medi-Physics Co. Ltd., MSD K.K., Pfizer Japan Inc., Shionogi & Co. Ltd., Mitsubishi Tanabe Pharma Co., and Eisai Co. Ltd. outside of the submitted work. Dr. Maruyama has received speaker fees from Daiichi Sankyo, Otsuka Pharmaceutical, Eisai, Nihon Pharmaceutical, Takeda Pharmaceutical, Boehringer Ingelheim, Sumitomo Dainippon Pharma, Mitsubishi Tanabe Pharma, Pfizer, Sanofi, Bayer, Kyowa Hakko Kirin, and Fuji Film; along with JSPS Grants-in-Aid for Scientific Research (JP26293211); and research support from Eisai, Pfizer, Takeda Pharmaceutical, Otsuka Pharmaceutical, Nihon Pharmaceutical, Shionogi, Teijin Pharma, Fuji Film, Boehringer Ingelheim, Nihon Medi-Physics, Bayer, MSD, Daiichi Sankyo, Kyowa Hakko Kirin, Novartis, and Mitsubishi Tanabe Pharma.

Description of Conflict of Interest

The other authors declare that they have no conflicts of interest.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2019.04.011.

References

1. Analitis A, Katsouyanni K, Biggeri A, et al. Effects of cold weather on mortality: results from 15 European cities within the PHEWE project. Am J Epidemiol 2008;168:1397-1408.
2. Lin H, Zhang Y, Xu Y, et al. Temperature changes between neighboring days and mortality in summer: a distributed lag non-linear time series analysis. PLoS One 2013;8:e66403.
3. Danet S, Richard F, Montaye M, et al. Unhealthy effects of atmospheric temperature and pressure on the occurrence of myocardial infarction and coronary deaths. A 10-year survey: the Lille-World Health Organization MONICA project (Monitoring trends and determinants in cardiovascular disease). Circulation 1999;100:E1-E7.
4. Ravljen M, Bilban M, Kajfez-Bogataj L, et al. Influence of daily individual meteorological parameters on the incidence of acute coronary syndrome. Int J Environ Res Public Health 2014;11:11616-11626.
5. Panagiotakos DB, Chrysohoou C, Pitsavos C, et al. Climatological variations in daily hospital admissions for acute coronary syndromes. Int J Cardiol 2004;94:229-233.
6. Mukai T, Hosomi N, Tsunematsu M, et al. Various meteorological conditions exhibit both immediate and delayed influences on the risk of stroke events: The HEWS-stroke study. PLoS One 2017;12:e0178223.
7. Schultz DM. Review of cold fronts with prefrontal troughs and wind shifts. Mon Weather Rev 2005;133:2449-2472.
8. Kemppi ML, Sinclair VA. Structure of a warm front: Helsinki testbed observations and model simulation. Mon Weather Rev 2011;139:2876-2900.
9. Adams Jr. HP, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 1993;24:35-41.
10. Peel MC, Finlayson BL, Mcmahon TA. Updated world map of the K öppen-Geiger climate classification. Hydrology and Earth System Sciences Discussions. Eur Geosci Union 2007;11:1633-1644.
11. Sueda Y, Hosomi N, Tsunematsu M, et al. Effects of meteorological conditions on the risk of ischemic stroke events in patients treated with alteplase−HEWS-tPA. J Stroke Cerebrovasc Dis 2015;24:1500-1505.
12. Bhaskaran K, Gasparrini A, Hajat S, et al. Time series regression studies in environmental epidemiology. Int J Epidemiol 2013;42:1187-1195.
13. Zaninović K, Plesko N, Poljakovic Z, et al. Changes in coagulability of blood in patients with cerebrovascular disease in various meteorological situations. Acta Med Croatica 1992;46:85-89.
14. Kveton V. Weather fronts and acute myocardial infarction. Int J Biometeorol 1991;35:10-17.
15. Lee CC. A systematic evaluation of the lagged effects of spatiotemporally relative surface weather types on wintertime cardiovascular-related mortality across 19 US cities. Int J Biometeorol 2015;59:1633-1645.
16. van Asch CJ, Luitse MJ, Rinkel GJ, et al. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. Lancet Neurol 2010;9:167-176.
17. Basu R, Pearson D, Malig B, et al. The effect of high ambient temperature on emergency room visits. Epidemiology 2012;23:813-820.