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Research Report

Acute Effects of Environmental Factors on the Circulatory System: An Epidemiological Approach

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■ABSTRACT■ Epidemiological studies provide useful information on human health issues. We have evaluated the acute effects of meteorological conditions on the circulatory system with an epidemiological approach. Study subjects were the patients who had been transported by ambulance in Nagoya between April 2008 and December 2012 with cardiovascular diseases (e.g., ischemic heart disease, arrhythmia, heart failure and hypertension (20223 cases)) and with cerebrovascular diseases (e.g., cerebral ischemia and intracranial hemorrhage (19509 cases)). To estimate the risk due to meteorological factors, we used a time-stratified case-crossover design adjusting for the effects of air pollutants (nitrogen dioxide, suspended particulate matter and photochemical oxidants). Temperature was the most prominent meteorological factor for both the cardiovascular diseases and the cerebrovascular diseases. The cerebrovascular diseases showed a stronger relationship with meteorological factors than the cardiovascular diseases. Time lags between exposure and occurrence of patients were slightly shorter for the cardiovascular diseases than for the cerebrovascular diseases.

■KEYWORDS■ Epidemiology, Temperature, Cardiovascular Disease, Cerebrovascular Disease

1. Introduction

Epidemiological studies provide direct information on the relationship between environmental and/or genetic factors and diseases in humans. Such information is useful for planning and evaluating programs to prevent, diagnose, and treat diseases as well as programs to promote health. The research object of epidemiology is diseases and their risk factors encountered in daily life. Therefore, concepts of the study (e.g., design, analysis, interpretation of results, and limitations) differ greatly between epidemiological studies and experimental studies.

The aim of epidemiological studies at Toyota Central R&D Labs., Inc. is to gain a better understanding of epidemiology as well as to contribute to health promotion in communities. We have been conducting epidemiological studies in environmental fields such as weather and air pollution.

A substantial number of critical-care patients present with circulatory diseases, such as acute myocardial infarction and stroke. As for the seasonal variation, there is a greater occurrence of patients with circulatory diseases in winter,^(1,2) and a negative correlation is observed between temperature and the

occurrence of patients with these diseases. On the other hand, when we focus on individual diseases, such as subarachnoid hemorrhage, the relationship with temperature is inconsistent.⁽³⁾ Acceptable explanations for the inconsistency include the difference in the sensitivity of individual diseases to meteorological factors, the difference in meteorological conditions in the study area, and the difference in the study design, such as consideration of the time lag from exposure to onset. It is useful to compare various studies on the effects of meteorological factors. Moreover, detailed disease classifications or stratified analyses help to understand the mechanisms of exacerbation due to meteorological factors. The accumulation of such information will make it possible to predict the occurrence of patients with circulatory diseases who are in need of emergency transportation based on the meteorological conditions. Improvement of the life-saving rate is expected by the optimization of the emergency care system based on the prediction. The aim of this study is to provide information on the acute effects of meteorological factors on circulatory diseases in Nagoya, a large metropolis in Japan with a population of approximately 2.2 million.

2. Methods

2.1 Study Subjects

Subjects in this study were the patients with circulatory diseases (infectious diseases and congenital diseases were excluded) who were transported to hospitals by ambulance between April 1, 2008 and December 31, 2012 in Nagoya. To prevent identification of individual patients, the names and the addresses of the patients were deleted from the patient database.

The cardiovascular diseases^{*1} include ischemic heart disease (i.e., myocardial infarction and angina pectoris), arrhythmia, heart failure, and hypertension. The cerebrovascular diseases were divided into cerebral ischemia (i.e., cerebral infarction, transient cerebral ischemia, and cerebral thrombosis) and intracranial hemorrhage (i.e., cerebral hemorrhage, subarachnoid hemorrhage, and subdural hemorrhage). Myocardial infarction, angina pectoris, arrhythmia, heart failure, hypertension, cerebral infarction, and transient cerebral ischemia were analyzed independently because there was a substantial number of patients with these diseases.^{*2}

2.2 Meteorological Factors

Meteorological data measured at the Nagoya Local Meteorological Observatory were obtained from the Japan Meteorological Agency. The data included daily mean temperature, daily maximum temperature, daily minimum temperature, relative humidity, air pressure, hours of sunshine, solar radiation, saturated vapor pressure, rainfall, snowfall, mean cloudiness, and mean wind speed. We also calculated temperature increase (i.e., the difference between maximum temperature and minimum temperature on the same day), temperature decrease (i.e., the difference between minimum temperature of one day and maximum temperature of the previous day), and average temperature difference from the previous day.

^{*1} Generally, cardiovascular diseases include coronary heart diseases and vascular diseases (including cerebrovascular diseases). In this study, to distinguish the effects on the heart and brain, coronary heart diseases and vascular diseases except cerebrovascular diseases were classified as cardiovascular diseases.

^{*2} Although stroke included ca. 1800 patients, it was classified only as a cerebrovascular disease because we could not distinguish whether it was caused by infarction or hemorrhage.

2.3 Air Pollutants

The observation values of air pollutants (nitrogen dioxide (NO₂), suspended particulate matter (SPM), and photochemical oxidants (O_x)) at 16 general ambient air monitoring stations in Nagoya were obtained from the Environment Division of Aichi Prefecture. Daily average concentrations of NO₂ and SPM for the city were calculated based on the daily average concentration obtained at each monitoring station. The maximum values of 8-hour moving averages of the O_x concentration for the city were calculated based on 1-hour average values obtained from all monitoring stations.

2.4 Statistical Analyses

For the cluster analysis, we standardized each meteorological factor and conducted an analysis according to the Ward method with IBM SPSS Statistics ver. 22. To evaluate the risks due to meteorological factors, we used a time-stratified case-crossover design. We defined case periods as the day of emergency transportation. Control periods were the corresponding days of the week within the same calendar month of the same year. A conditional logistic regression model was used to evaluate the association between meteorological factors and the occurrence of emergency transportation adjusting for air pollutants as the confounders. Odds ratios (ORs) were estimated for a unit change in each meteorological factor. To examine the possibility that the effects of the meteorological factors might appear after several days, we examined various time lags from lag day 0 (i.e., the same day) to lag day 5. Stratified analyses were performed by season (spring: March–May, summer: June–August, autumn: September–November, winter: December–February). STATA ver. 12 was used for the conditional logistic regression analyses.

3. Results

3.1 Aggregate Calculation of Patients

Table 1 shows the number of patients classified by diseases and season. Approximately 20000 patients were identified for both the cardiovascular diseases and the cerebrovascular diseases in the study period. The occurrence of patients was greater in winter, which suggests the effects of low temperature.

3.2 Selection of Meteorological Factors

We considered 12 meteorological factors. Since these factors might have correlations with each other, it is inadequate to put such factors into a statistical model at one time. We, therefore, conducted a cluster analysis to select factors to be evaluated. The 12 meteorological factors were classified into four clusters (i.e., daily mean temperature; daily maximum temperature; daily minimum temperature; saturated vapor pressure, relative humidity; mean cloudiness; rainfall, hours of sunshine; solar radiation; temperature increase; average temperature difference, and temperature decrease; air pressure; snowfall; mean wind speed, **Fig. 1**). The representative factor was selected from each cluster in consideration of a simple correlation with the occurrence of patients, generality, and data distribution. Daily mean temperature, solar radiation, relative humidity, and air pressure were selected as the representatives of each cluster. **Table 2** shows the summary statistics of these selected factors. There was a large difference between the minimum and maximum daily mean temperature in spring and autumn. Solar radiation was low in autumn and winter. Air pressure was slightly low in summer. These are common weather conditions on the Pacific side of Japan.

3.3 Risk Estimation of Meteorological Factors with Case-crossover Analyses

Figures 2 and 3 show the results of the case-crossover analyses of daily mean temperature, air pressure, relative humidity, and solar radiation for the cardiovascular diseases and the cerebrovascular diseases stratified by season. The ORs and 95% confidence intervals for all diseases that were statistically significant ($p < 0.05$) are summarized in **Tables 3 and 4**. When ORs were statistically significant for more than one time lag (days), the OR of a day that showed the largest value was selected. Since a decrease in daily mean temperature showed an increased risk for most diseases in each season, ORs were shown as the values per 1°C decrease. Daily mean temperature showed the most definitive risk for both the cardiovascular diseases and the cerebrovascular diseases. ORs for the temperature were generally larger for the cerebrovascular diseases than for the cardiovascular diseases. The cardiovascular diseases showed a slightly shorter time lag than the cerebrovascular diseases. The time lag with the most definitive OR was, in most cases, 0 to 1 day for cardiovascular diseases and 1 to 2 days for cerebrovascular diseases.

Table 1 Summary of study subjects.

	Spring (429 days)	Summer (460 days)	Autumn (455 days)	Winter (392 days)	Total (1736 days)
All cardiovascular diseases	5056	4745	5232	5214	20247
Ischemic heart disease*	1416	1529	1586	1425	5956
Myocardial infarction	711	734	793	763	3001
Angina pectoris	705	795	791	661	2952
Arrhythmia	824	853	938	807	3422
Heart failure	1789	1411	1593	2038	6831
Hypertension	1012	944	1090	933	3979
All cerebrovascular diseases	4929	4331	5012	5237	19509
Cerebral ischemia	2716	2357	2689	2969	10731
Cerebral infarction	1663	1597	1631	1615	6506
Transient cerebral ischemia	685	515	658	862	2720
Intracranial hemorrhage†	1086	929	1104	1039	4158

* Ischemic heart disease includes myocardial infarction, angina pectoris, and coronary embolism.

† Intracranial hemorrhage includes cerebral hemorrhage, subarachnoid hemorrhage, and subdural hemorrhage.

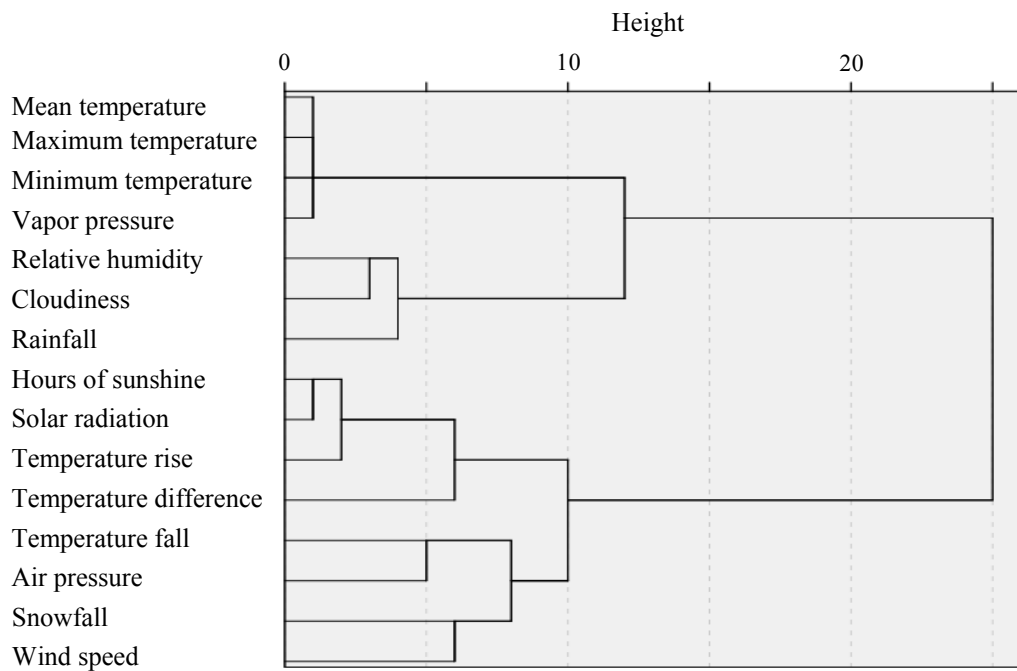


Fig. 1 Dendrogram for hierarchical clustering of the meteorological factors.

Table 2 Summary statistics of the meteorological factors.

Season (Days of observation)		Mean temperature (°C)	Air pressure (hPa)	Relative humidity (%)	Solar radiation (MJ/m ²)
Through (1736)	Average	16.8	1007.6	64.7	14.3
	Minimum	-1.5	984	24	1
	Maximum	32.1	1024	98	30
	SD	8.55	6.17	12.18	7.14
Spring (429)	Average	14.4	1007.6	59.3	17.3
	Minimum	2.8	988	24	1
	Maximum	24.2	1023	98	30
	SD	5.04	6.10	14.45	8.09
Summer (460)	Average	26.3	1003.3	69.5	17.2
	Minimum	15.5	984	40	2
	Maximum	32.1	1014	96	30
	SD	3.15	4.56	10.00	6.89
Autumn (455)	Average	18.8	1009.1	65.7	12.4
	Minimum	5.8	985	43	1
	Maximum	31.8	1024	97	24
	SD	5.82	5.74	10.56	5.85
Winter (392)	Average	5.9	1011.0	63.6	9.9
	Minimum	-1.5	992	37	1
	Maximum	15.3	1023	95	19
	SD	3.03	5.50	10.98	3.96

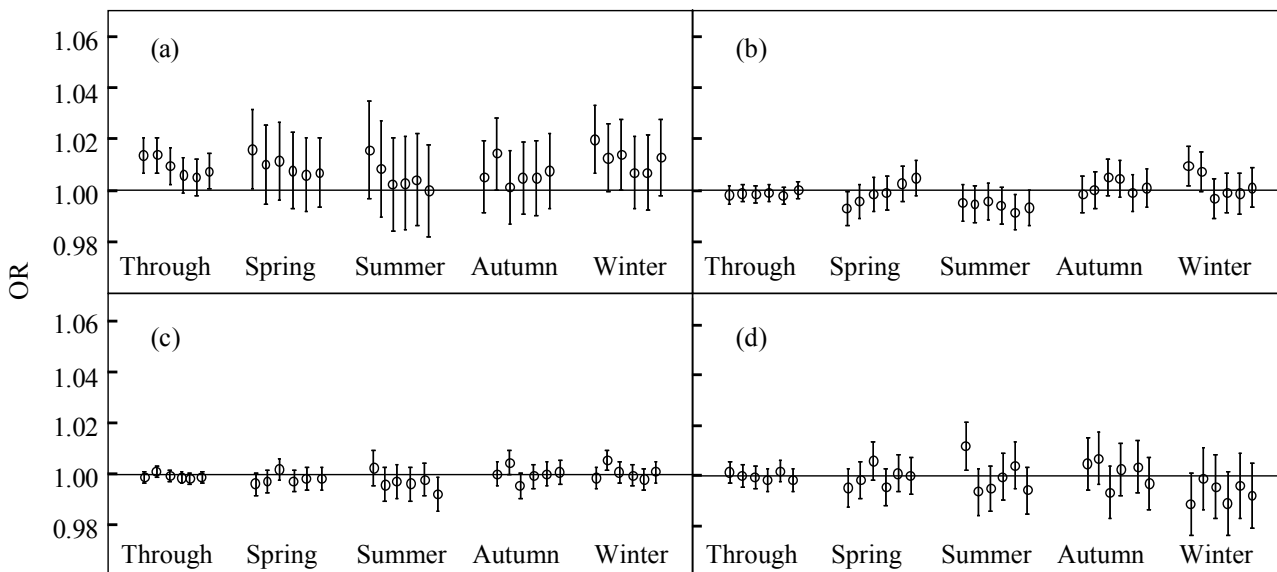


Fig. 2 ORs (point estimates and 95% confidence intervals) for emergency transport of patients with cardiovascular diseases per unit change in the meteorological factors. (a): mean temperature (per 1°C decrease), (b): air pressure (per 1 hPa increase), (c): relative humidity (per 1% increase), (d): solar radiation (per 1 MJ/m² increase). Data points represent, from left to right, lag 0, lag 1, lag 2, lag 3, lag 4, and lag 5 (days).

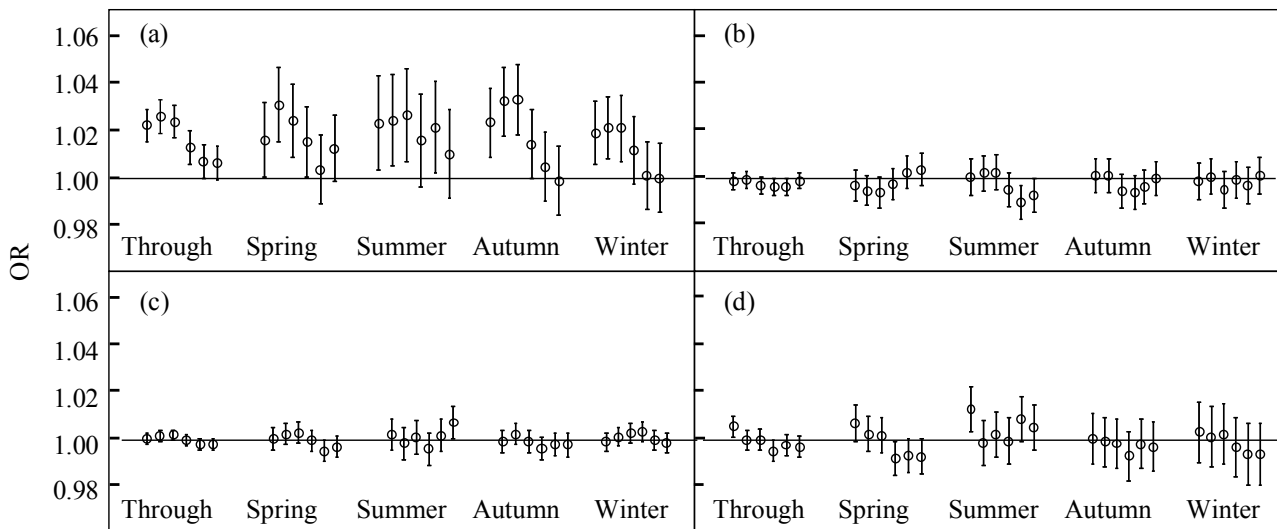


Fig. 3 ORs (point estimates and 95% confidence intervals) for emergency transport of patients with cardiovascular diseases per unit change in the meteorological factors. (a): mean temperature (per 1°C decrease), (b): air pressure (per 1 hPa increase), (c): relative humidity (per 1% increase), (d): solar radiation (per 1 MJ/m² increase). Data points represent, from left to right, lag 0, lag 1, lag 2, lag 3, lag 4, and lag 5 (days).

Table 3 ORs and 95% confidence intervals (CIs) for emergency transport of patients with cardiovascular diseases per unit change in each meteorological factor.

	Temperature (per 1°C decrease)			Air pressure (per 1 hPa increase)			Humidity (per 1% increase)			Solar radiation (per 1 MJ/m ² increase)								
	Lag (day)	OR	P	Lag (day)	OR	P	Lag (day)	OR	P	Lag (day)	OR	P	95% CI Lower	95% CI Upper				
All cardiovascular diseases																		
Through	1	1.014	0.000	-	-	-	-	-	-	-	-	-	-	-				
Spring	0	1.016	0.040	0	0.993	0.036	0.987	1.000	-	-	-	-	-	-				
Summer	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
Autumn	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
Winter	0	1.020	0.003	0	1.010	0.016	1.002	1.017	1	1.006	0.005	1.002	1.010	-				
Ischemic heart disease																		
Through	1	1.018	0.007	-	-	-	-	-	-	-	-	-	0.991	0.031	0.983	0.999		
Spring	-	-	-	-	-	-	-	-	-	-	-	-	2	1.016	0.033	1.001	1.030	
Summer	-	-	-	-	-	-	-	-	-	-	-	-	0	1.022	0.009	1.006	1.039	
Autumn	1	1.031	0.019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Winter	-	-	-	-	-	-	-	-	1	1.009	0.023	1.001	1.017	-	-	-	-	
Myocardial infarction																		
Through	1	1.024	0.008	-	-	-	-	-	1	1.007	0.030	1.001	1.013	-	-	-	-	
Spring	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Summer	-	-	-	5	0.977	0.014	0.959	0.995	5	0.982	0.037	0.965	0.999	-	-	-	-	
Autumn	1	1.050	0.009	-	-	-	-	-	0	1.014	0.024	1.002	1.027	-	-	-	-	
Winter	-	-	-	-	-	-	-	-	1	1.013	0.019	1.002	1.024	-	-	-	-	
Angina pectoris																		
Through	-	-	-	5	1.011	0.019	1.002	1.020	-	-	-	-	5	0.986	0.012	0.974	0.997	
Spring	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Summer	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Autumn	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Winter	-	-	-	-	-	-	-	-	-	-	-	-	0	0.940	0.001	0.907	0.974	
Arrhythmia																		
Through	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Spring	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Summer	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Autumn	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Winter	0	1.037	0.035	-	-	-	-	-	-	-	-	-	3	1.037	0.005	1.011	1.064	
Heart failure																		
Through	0	1.021	0.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Spring	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Summer	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Autumn	-	-	-	2	1.015	0.035	1.001	1.028	-	-	-	-	-	-	-	-	-	
Winter	0	1.035	0.001	0	1.014	0.032	1.001	1.026	-	-	-	-	5	0.978	0.043	0.957	0.999	
Hypertension																		
Through	-	-	-	-	-	-	-	-	0	0.995	0.038	0.990	1.000	-	-	-	-	
Spring	-	-	-	-	-	-	-	-	1	0.986	0.007	0.977	0.996	-	-	-	-	
Summer	-	-	-	-	-	-	-	-	0	1.023	0.005	1.007	1.038	0	1.031	0.005	1.009	1.053
Autumn	-	-	-	-	-	-	-	-	0	0.985	0.004	0.976	0.995	-	-	-	-	
Winter	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

-*: not statistically significant (p > 0.05)

Table 4 ORs and 95% confidence intervals (CIs) of emergency transport of patients with cerebrovascular diseases per unit change in each meteorological factor.

	Temperature (per 1°C decrease)			Air pressure (per 1 hPa increase)			Humidity (per 1% increase)			Solar radiation (per 1 MJ/m ² increase)				
	Lag (day)	OR	p	Lag (day)	OR	p	Lag (day)	OR	p	Lag (day)	OR	p	Lower	Upper
All cerebrovascular diseases														
Through	1	1.026	0.000	4	0.995	0.008	4	0.997	0.028	4	0.995	0.021	0.990	0.999
Spring	1	1.030	0.000	2	0.993	0.039	4	0.995	0.042	3	0.990	0.012	0.983	0.998
Summer	1	1.026	0.013	4	0.990	0.012	4	0.995	0.042	0	1.012	0.012	1.003	1.022
Autumn	1	1.033	0.000		-	-		-	-		-	-	-	-
Winter	2	1.023	0.002		-	-		-	-		-	-	-	-
Cerebral ischemia														
Through	1	1.028	0.000	4	0.994	0.020	4	0.995	0.002	4	0.993	0.019	0.987	0.999
Spring	1	1.035	0.001	1	0.989	0.019	5	0.993	0.021	3	0.988	0.023	0.978	0.998
Summer		-	-		-	-		-	-		-	-	-	-
Autumn	1	1.043	0.000	4	0.988	0.017	1	1.007	0.046	1	1.000	1.013	-	-
Winter	2	1.037	0.000		-	-		-	-		-	-	-	-
Cerebral infarction														
Through		-	-		-	-	0	0.995	0.022		0.991	0.999	-	-
Spring		-	-	1	0.988	0.035		0.976	0.999		-	-	-	-
Summer		-	-		-	-	3	0.986	0.019		0.975	0.998	1.003	1.037
Autumn	1	1.032	0.016	4	0.986	0.027		0.973	0.998		-	-	-	-
Winter	2	1.029	0.026	5	0.984	0.033	0	0.991	0.019	0	0.984	0.999	-	-
Transient cerebral ischemia														
Through	1	1.055	0.000		-	-	4	0.993	0.037		0.987	1.000	1.002	1.027
Spring	1	1.104	0.000		-	-	5	0.983	0.008		0.971	0.996	0.952	0.993
Summer		-	-	2	1.026	0.022		1.004	1.050		-	-	-	-
Autumn	1	1.054	0.009		-	-		-	-		-	-	-	-
Winter	1	1.058	0.001		-	-		-	-		0	1.031	1.001	1.062
Intracranial hemorrhage														
Through	1	1.015	0.043		-	-		-	-		1	0.988	0.012	0.979
Spring		-	-		-	-		-	-		1	0.982	0.027	0.966
Summer	4	1.070	0.005	5	0.981	0.027		0.965	0.998		-	-	-	-
Autumn		-	-	3	1.019	0.025		1.002	1.035		-	-	-	-
Winter		-	-	5	1.021	0.028		1.002	1.041		5	0.969	0.042	0.940

-: not statistically significant (p > 0.05)

As for the individual diseases, myocardial infarction increased with low temperature, except in summer (statistical significance was observed only in autumn). On the other hand, angina pectoris showed an increasing tendency only in summer (not statistically significant). Arrhythmia and heart failure increased only in winter (statistically significant). The risk for hypertension due to temperature was not apparent.

For the other meteorological factors, the relationships were generally more prominent for the cerebrovascular diseases than for the cardiovascular diseases. However, there were some cases for which similar trends were not observed for the subsequent days or the previous days (e.g., effect of solar radiation on the cardiovascular diseases on lag day 0 in summer (Fig. 2(d)). It is possible that statistical significance was observed by chance in such cases, especially when p values were relatively large.

3.4 Further Analysis of the Risk Due to Temperature

We examined daily mean temperature based on the results of the cluster analysis. However, daily minimum temperature might show a more prominent relationship because the risk, in most cases, was associated with a decrease in temperature. In addition, Honda et al.⁽⁴⁾ reported that daily maximum temperature showed a better correlation with mortality rate for all causes than daily mean temperature. Furthermore, average temperatures over multiple days have been examined⁽⁵⁾ because slight damage to the circulatory system induced by the low temperature of the first day might be exacerbated by low temperatures of the successive days. In the above context, we also evaluated daily maximum temperature, daily minimum temperature, and two-day average temperature instead of daily mean temperature (Fig. 4). There were little differences in the results from the overall analyses for the cardiovascular diseases, the cerebrovascular diseases, or over the entire the year (Figs. 4(a) and (b)). However, there were some cases when a temperature

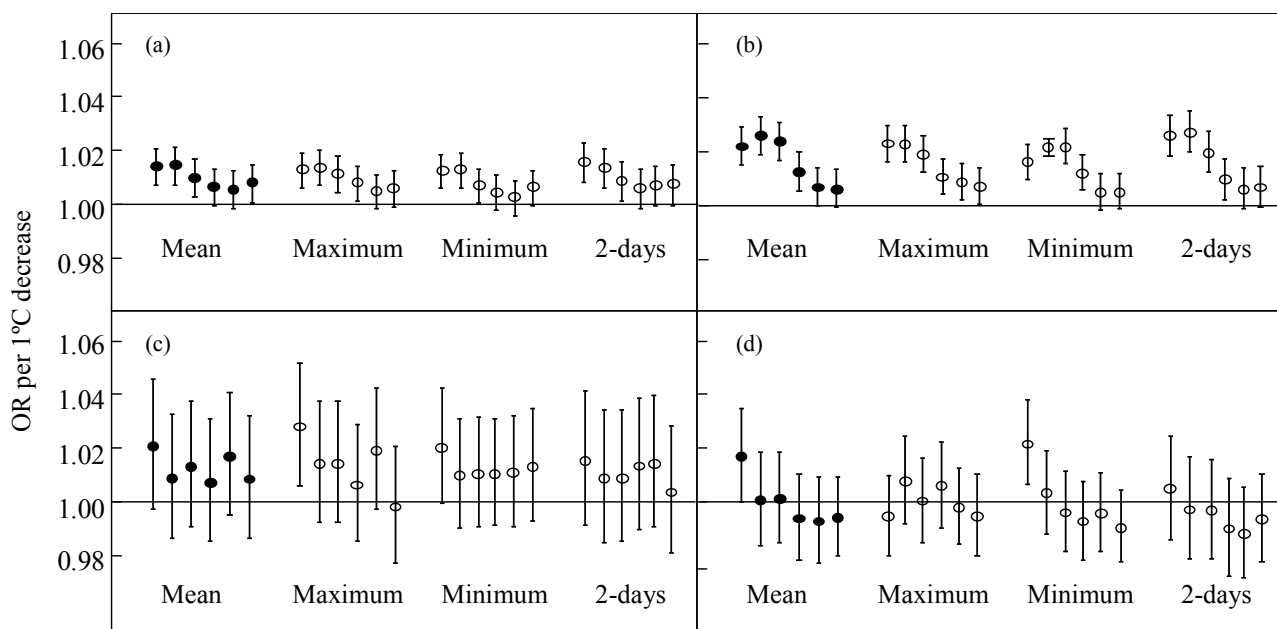


Fig. 4 ORs (point estimates and 95% confidence intervals) for the emergency transport per 1°C decrease in various temperature indices.

(a): all the cardiovascular diseases (through the year), (b): all the cerebrovascular diseases (over the entire year), (c): arrhythmia (summer), panel (d): hypertension (spring). Data points represent, from left to right, lag 0, lag 1, lag 2, lag 3, lag 4, and lag 5 (days).

index other than daily mean temperature showed a better correlation when diseases were specified and/or seasons were limited (Figs. 4(c) and (d)).

4. Discussion

After exposure to low temperature, the cardiovascular diseases seemed to occur more promptly than the cerebrovascular diseases because the time lags that gave the largest ORs were, generally, 0 to 1 day for the cardiovascular diseases and 1 to 2 days for the cerebrovascular diseases. A low temperature induces vascular constriction, which increases blood pressure. In addition, vascular constriction decreases blood flow, which increases the risk of blood coagulation.⁽⁶⁾ These vascular effects are applicable to both the cardiovascular diseases and the cerebrovascular diseases. In addition to the vascular effects, some neurological effects are included in the cardiovascular diseases, such as arrhythmia. Neurological effects can appear more rapidly than vascular effects. This is one of the possible reasons why the cardiovascular diseases showed shorter time lags than the cerebrovascular diseases.

Generally, circulatory diseases are more prevalent in winter than in summer.^(1,2) In our analysis, a low temperature in winter was prominent in many cases. As for the cerebrovascular diseases, however, a significant risk due to low temperature was not observed in winter but in summer. Based on a survey of monthly mortality rates for cerebrovascular diseases in all prefectures of Japan at intervals of 10 years since 1963, Sekimoto et al.⁽⁷⁾ reported that seasonal variation had been gradually decreasing in most prefectures, and that almost no seasonal variation was observed in Tokyo, Osaka, and Hokkaido. They also observed that the variation is relatively small in Aichi Prefecture, where Nagoya is located. In addition, they also observed that the mortality rate for cerebrovascular diseases decreased with the increase in kerosene use. Based on these findings, they speculated that the prevalence of room heating was related to the decrease in the risk for circulatory diseases, especially cerebrovascular diseases. Furthermore, an urban heat-island effect would be an additional reason for the temperature increase in winter. All these factors might have masked the effects of low temperature in winter. On the other hand, the reason why a low temperature in summer was significant is unclear. A low temperature

in summer could increase outdoor activities, which could contribute to the risk for intracranial hemorrhage.

In this study, a low temperature was the most obvious risk factor for the diseases. Morimoto applied a hidden Markov model to the same dataset and found that temperature increase from the previous day together with a decrease in sea level pressure and a shift from a high pressure state to a low pressure state were risky patterns for both the cardiovascular diseases and the cerebrovascular diseases.⁽⁸⁻¹⁰⁾ The direction of temperature risk differed between the case-crossover analysis in this study and Morimoto's hidden Markov model. A hidden Markov model hypothesizes that there are some special patterns of changes in the meteorological factors that are related with the exacerbation of the circulatory diseases, and the occurrence of patients is simulated based on the changes in the meteorological factors as the hidden states. Then the meteorological patterns are extrapolated using time-series data in which the number of patients and meteorological factors change simultaneously. Morimoto found that temperature increase was included as the constituent of the pattern. On the other hand, in a case-crossover analysis, the meteorological condition of a day when a subject was transported is paired with that when the patient was not transported. Then the paired dataset of all the subjects is used for a regression analysis, and the magnitude and direction of the risk due to every meteorological factor is estimated. After the effects of confounding factors were excluded, we found the risk due to temperature tended toward a decrease in temperature. A case-crossover analysis evaluates the magnitude and the direction of the risks due to individual meteorological factors; a hidden Markov model investigates the patterns to predict the occurrence of patients. This difference in the principle of the analysis might have resulted in the difference in the direction of the effect of temperature.

This study was conducted in Nagoya, a metropolis of Japan, so we could investigate a substantial number of patients in a specific area. In addition, the representativeness of observational data at the Nagoya Local Meteorological Observatory as the surrogate of individual exposure to the meteorological factors was relatively good.

One of the most crucial limitations is the accuracy of the diagnosis. Emergency medical care is the highest priority for patients transported to hospitals

by ambulance. Therefore, the diagnosis for such patients is less accurate than that for usual patients, which increases the possibility of misclassification. This is especially true for patients with mild symptoms who were discharged without hospitalization. We adopted all the corresponding days of the week within the same calendar month of the same year as the control day because we thought that the number of the patients might be quite different between weekdays and weekends. However, we did not consider national holidays or long vacations during summer or at the end of the year. Further, even in the same city, the temperature would be different between suburban and downtown areas because of road traffic and air conditioning equipment, which are both major sources of heat. There are many office buildings and condominiums with air conditioning in the downtown area; the correlation of meteorological conditions between indoors and outdoors in these buildings would be different from that of the houses that are dominant in the suburban area.

5. Conclusion

The relationship between meteorological factors and the occurrence of patients with circulatory diseases who were transported to hospitals by ambulance in Nagoya was evaluated using case-crossover analysis. Temperature was the most prominent factor for both the cardiovascular diseases and the cerebrovascular diseases; the cerebrovascular diseases showed a stronger relationship with meteorological factors than the cardiovascular diseases. Time lags between exposure and occurrence of patients were slightly shorter for the cardiovascular diseases than for the cerebrovascular diseases.

Acknowledgements

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References

- (1) Boari, B. et al., "Temporal Variation of Heart Failure Hospitalization: Does It Exist?", *Rev. Cardiovasc. Med.*, Vol. 12, No. 4 (2011), pp. 211-218.
- (2) Jakovljevic, D. et al., "Seasonal Variation in the Occurrence of Stroke in a Finnish Adult Population. The FINMONICA Stroke Register. Finnish Monitoring Trend and Determinants in Cardiovascular Disease", *Stroke*, Vol. 27, No. 10 (1996), pp. 1774-1779.
- (3) Zang, M., "A Study on the Relationship between Weather Conditions and the Occurrence of Subarachnoid Hemorrhage", *Jpn. J. Biometeor.*, Vol. 44, No. 4 (2007), pp. 97-104.
- (4) Honda, Y. et al., "Determination of Optimum Daily Maximum Temperature Using Climate Data", *Environ. Health Prev. Med.*, Vol. 12, No. 5 (2007), pp. 209-216.
- (5) Atsumi, A. et al., "Relationship between Cold Temperature and Cardiovascular Mortality, with Assessment of Effect Modification by Individual Characteristics", *Circ. J.*, Vol. 77, No. 7 (2013), pp. 1854-1861.
- (6) McArthur, K. et al., "What is It with the Weather and Stroke?", *Expert Rev. Neurother.*, Vol. 10, No. 2 (2010), pp. 243-249.
- (7) Sekimoto, H. et al., "Seasonal Stroke Death in Japan during the Past 20 years", *Jpn. J. Stroke*, Vol. 9 (1987), pp. 207-217.
- (8) Morimoto, H., "Association Analysis Identifies Risk of Ischemic Heart Disease When Temperature Increases", *Int. J. Soc. Sci. Studies*, Vol. 4, No. 7 (2016), pp. 55-62.
- (9) Morimoto, H., "Patterns in Stroke Occurrence on Warm Days in Winter by Associations Analysis", *Open J. Appl. Sci.*, Vol. 5 (2015), pp. 776-782.
- (10) Morimoto, H., "Hidden Markov Models to Estimate the Lagged Effects of Weather on Stroke and Ischemic Heart Disease", *Appl. Math.*, Vol. 7 (2016), pp. 1415-1425.

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