Seasonal Variation in Stroke Incidence in Hisayama, Japan

Atsushi Shinkawa, MD, Kazuo Ueda, MD, Yutaka Hasuo, MD, Yutaka Kiyohara, MD, and Masatoshi Fujishima, MD

We investigated seasonal variation in the incidence of cerebral stroke among the general population aged ≥40 years in November of 1961 in Hisayama, Japan. During the 24-year follow-up period, 311 cases of cerebrovascular diseases occurred. The date or month of onset was determined in 308 cases, of which 51 were classified as intracerebral hemorrhage, 223 as cerebral infarction, and 27 as subarachnoid hemorrhage. We observed a significant seasonality in the incidence of all stroke (p<0.01), of intracerebral hemorrhage (p<0.05), and of cerebral infarction (p<0.01), whereas subarachnoid hemorrhage had no significant seasonal pattern. Subjects <64 years of age showed a significant seasonal variation in the incidence of both intracerebral hemorrhage (p<0.05) and cerebral infarction (p<0.01). A significant seasonal pattern for the incidence of intracerebral hemorrhage was also noted among persons with hypertension (p<0.05) or a high serum cholesterol level (p<0.05), whereas such a pattern for cerebral infarction was documented among normotensive persons (p<0.05) and those with a low serum cholesterol level (p<0.01). In addition, the incidences of intracerebral hemorrhage and cerebral infarction were negatively correlated with mean ambient temperature (p<0.01 and p<0.05, respectively), and all stroke and intracerebral hemorrhage in men were significantly related to intradiurnal temperature change (p<0.05 and p<0.01, respectively). The significance of the seasonal occurrence of stroke is discussed in relation to relevant risk factors.

The aim of our study is to elucidate in a long-term prospective population survey conducted in Hisayama, Japan, the seasonal variation in the incidence of stroke and the influence of traditional risk factors for cerebrovascular diseases and environmental factors on the seasonality of the onset of cerebrovascular diseases. We selected sex, age at onset, blood pressure, and serum cholesterol concentration as the traditional risk factors and mean ambient temperature and mean intradiurnal temperature change (the difference between the daily maximum and minimum temperatures) in each month as the environmental factors.

Subjects and Methods

Hisayama Town is a rural area adjacent to Fukuoka City on Kyushu Island, in the southern part of Japan. As Hisayama and Fukuoka are situated on the same plain, the climates of these two areas are almost identical. Although located at approximately 33° north, almost the latitude of Los Angeles or Casablanca, Hisayama is quite cold during the winter. Mean ambient temperature during January is 5.7°C in Fukuoka, while that in Los Angeles and Casablanca is approximately 13° C. The population of Hisayama Town is approximately 7,000 and has
scarcely changed for 30 years. Sex and age distributions in Hisayama are similar to those in the whole of Japan.

A prospective population study has been carried out in this area since 1961 to elucidate the incidence of cardiovascular disease in a general population sample and to explore its risk factors. In November 1961, 1,621 men and women aged ≥40 years (approximately 90% of all residents in this age group) were recruited from Hisayama residents as the cohort. This cohort has been followed since then. A communication system was established between the study center at the university and local physicians or the town office. Through this network, newly occurring cardiovascular diseases among the cohort were sequentially detected and examined by the study physicians. In addition, >80% of the deceased among the cohort were autopsied, and the causes of death were examined. The clinical diagnosis of stroke (including its type) was determined by detailed histories, neurologic examination, and ancillary diagnostic procedures (such as lumbar puncture, cerebral angiography, and computed tomography) and confirmed at autopsy. As for those in the cohort who moved out of Hisayama, we kept annual contact with their families or attending physicians by letter or telephone and detected their death or illness. Follow-up has been reasonably complete, with only two cohort subjects (0.1%) lost. Details of the methods of examination and follow-up have been described.

The cumulative number of cases of cerebrovascular disease by month during the 24 years of follow-up (from November 1961 to October 1985) was the basic data from which we calculated the rates associated with seasonal variation in the occurrence of type-specific cerebral stroke. As a mathematical model of seasonal variation, we chose the cosine function, which is a simple curve of cyclic periodicity. Significance of the seasonal variation was examined using Roger's method, which is sensitive to cyclic trends based on the cosine function. We calculated the estimated monthly occurrence of cerebrovascular disease (based on the cumulative number for the 24 years of follow-up), the amplitude of the seasonality, and the peak month of occurrence. Detailed procedures for the mathematics are given in Appendix 1. Analysis focused on the seasonal incidence of all stroke, intracerebral hemorrhage, cerebral infarction, and subarachnoid hemorrhage. We included both thrombosis and embolism in the category of cerebral infarction because of the difficulty in differentiating between the two in some cases.

We also examined seasonality in relation to the traditional risk factors for stroke, including sex, age at onset, blood pressure, and serum cholesterol concentration. Blood pressure (for all subjects) and serum cholesterol concentration (when available) were obtained from data recorded at the initial examination in 1961.

Mean ambient temperature and mean intradiurnal temperature change by month were taken from the official meteorologic data of Fukuoka City for the years 1951–1980. We examined whether the number of newly-occurring cases of cerebrovascular disease is correlated with either environmental factor. We calculated the correlation coefficient between each environmental factor and monthly stroke incidence separately, and we used stepwise multivariate analysis to see whether both environmental factors influenced the incidence of stroke simultaneously.

### Results

The demographic and clinical characteristics of the cohort subjects by stroke type are presented in Table 1. During the 24 years of follow-up, 311 cases of cerebrovascular disease were observed. Date of the initial episodes was clarified for 308 cases, of which 51 were intracerebral hemorrhage, 223 were cerebral

### Table 1. Demographic and Clinical Characteristics of Cohort Subjects, Hisayama, Japan

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All stroke (n=308)</th>
<th>Intracerebral hemorrhage (n=51)</th>
<th>Cerebral infarction (n=223)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>156</td>
<td>35</td>
<td>113</td>
</tr>
<tr>
<td>Female</td>
<td>152</td>
<td>16</td>
<td>110</td>
</tr>
<tr>
<td>Age at onset (yr)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–64</td>
<td>66</td>
<td>21</td>
<td>37</td>
</tr>
<tr>
<td>65–75</td>
<td>111</td>
<td>13</td>
<td>82</td>
</tr>
<tr>
<td>75+</td>
<td>131</td>
<td>17</td>
<td>104</td>
</tr>
<tr>
<td>Overall</td>
<td>72.5±10.0</td>
<td>68.0±10.8</td>
<td>74.0±9.5</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>155.0±29.9</td>
<td>155.1±26.6</td>
<td>155.1±30.0</td>
</tr>
<tr>
<td>Diastolic</td>
<td>86.9±15.6</td>
<td>91.4±15.9</td>
<td>86.2±15.5</td>
</tr>
<tr>
<td>Serum cholesterol (mg/dl)</td>
<td></td>
<td>154.9±44.5</td>
<td>159.1±37.2</td>
</tr>
</tbody>
</table>

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infarction, 27 were subarachnoid hemorrhage, and seven were of an undifferentiated type.

Seasonal variation in incidence with 1-year periodicity was apparent for all stroke (Figure 1, \( p<0.01 \)), intracerebral hemorrhage (Figure 2, top; \( p<0.05 \)), and cerebral infarction (Figure 2, bottom; \( p<0.01 \)). There was no significant seasonal variation in the incidence of subarachnoid hemorrhage or undifferentiated stroke type (Table 2).

The influence of traditional risk factors for cerebrovascular disease on the seasonality of stroke incidence is shown in Table 3. For all stroke seasonal variation was significant in both sexes, in those aged <64 and those aged >75 years, in those with hypertension, and in those with a low serum cholesterol concentration. For intracerebral hemorrhage, a significant seasonal pattern was found in subjects aged <64 years, in those with hypertension, and in those with a high serum cholesterol concentration. For cerebral infarction, a significant seasonal pattern was observed in men, in subjects aged <64 years, in those without hypertension, and in those with a low serum cholesterol concentration.

Figure 3 shows the monthly mean ambient temperature and the monthly mean intradiurnal temperature change in Fukuoka City, adjacent to Hisayama. Monthly mean ambient temperature had a variation of one cycle/yr. Although its range of variation was small compared with that of monthly mean ambient temperature, monthly mean intradiurnal temperature change had a variation of two cycles/yr (high in March–May and October–November and low in June–August and December–January). Correlation coefficients between the monthly number of stroke onsets by type and ambient temperature or intradiurnal temperature change are presented in Table 4. When both sexes were combined, a significant negative correlation was found between ambient temperature and the onset of all stroke, intracerebral hemorrhage, and cerebral infarction. Significant correlations with ambient temperature are shown in Table 4.

### Table 2. Seasonal Variation in Incidence of Stroke by Type, Hisayama, Japan

<table>
<thead>
<tr>
<th>Stroke type</th>
<th>( n )</th>
<th>Monthly mean</th>
<th>Amplitude</th>
<th>Peak/trough ratio</th>
<th>Peak month</th>
<th>( R^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke</td>
<td>308</td>
<td>25.7</td>
<td>7.6*</td>
<td>1.35</td>
<td>February</td>
<td>0.655</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td>51</td>
<td>4.3</td>
<td>2.4†</td>
<td>1.77</td>
<td>January</td>
<td>0.696</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>223</td>
<td>18.6</td>
<td>5.6*</td>
<td>1.35</td>
<td>March</td>
<td>0.530</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>27</td>
<td>2.3</td>
<td>0.1</td>
<td>-</td>
<td>-</td>
<td>0.001</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>7</td>
<td>0.6</td>
<td>0.5</td>
<td>-</td>
<td>-</td>
<td>0.253</td>
</tr>
</tbody>
</table>

Amplitude, difference between peak and trough of estimated cosine curve function. —, Not calculated because Amplitude (seasonal variation) is not significant.

*†\( p<0.01, 0.05, \) respectively, different from 0.
were also seen for the onset of all stroke and cerebral infarction for women. Intradiurnal temperature change was significantly correlated with the occurrence of all stroke and intracerebral hemorrhage for men. Ambient temperature was estimated together with intradiurnal temperature change to take their interaction into account. The results of stepwise multivariate analysis revealed the same tendency; both ambient temperature and intradiurnal temperature change were related to the incidence of all stroke for men and intracerebral hemorrhage for both sexes (Table 5).

Discussion

We demonstrate seasonal variation in the incidence of all stroke, intracerebral hemorrhage, and cerebral infarction but not subarachnoid hemorrhage. Previous reports about the seasonality of cerebral stroke had been based on hospital admission or mortality statistics and were hardly concerned about the relation between risk factors for stroke and seasonality. As far as we know, ours is the first study that is based on the general population and elucidates the relation between traditional risk factors and stroke seasonality.

![Figure 3](image-url)  
**Figure 3.** Graph of mean ambient temperature (—) and intradiurnal temperature change (— - -) by month in Fukuoka City, Japan.
Seasonality was found in the younger (those aged ≤64 years at onset) rather than in the older age group. The elderly seem to be more sensitive to environmental changes, but younger people may be more frequently exposed to such changes. That is, the influence of environmental exposure may be stronger for the younger group than for the older. In contrast, different results have been reported by other investigators, who have found strong seasonality in the older age group than in the younger one.

For intracerebral hemorrhage, significant seasonal variation was observed in those with hypertension and those with a high serum cholesterol level. On the other hand, seasonal variation in cerebral infarction and all stroke were found to be significant in those without hypertension and those with a low serum cholesterol concentration. The seasonal variation in blood pressure is well known, blood pressure being higher in winter. Elevated blood pressure during the winter may play an important role as a trigger for intracerebral hemorrhage. Seasonal variation in serum cholesterol concentration has been reported, but its relation with the seasonality of intracerebral hemorrhage or cerebral infarction has not been explained.

The seasonal patterns for all stroke, intracerebral hemorrhage, and cerebral infarction were negatively correlated with ambient temperature. Temperature and other environmental factors related to it may produce cerebral stroke through changing internal conditions such as blood pressure, blood viscosity, and blood coagulability. Platelet and erythrocyte counts, blood viscosity, and catecholamine secretion increase with decreasing temperatures. Concentrations of clotting factor VII, antithrombin III, and cholesterol decrease while fibrinolytic activity increases with decreasing temperatures.

In addition to ambient temperature, a positive correlation was observed between intradiurnal temperature change and the incidence of all stroke and intracerebral hemorrhage for men. One-year periodicity with one peak and one trough a year might not be the only pattern of seasonal change. If there is 6-month periodicity (two peaks a year), intradiurnal temperature change may be related to it. Intradiurnal temperature change may affect blood pressure or the balance of the autonomic nervous system within a day, and if a large intradiurnal temperature change induced a large hemodynamic change, it may trigger cerebral stroke. Recently, ambulatory blood pressure monitoring has made it easier to investigate the diurnal pattern of blood pressure. Studying the daily pattern of blood pressure in association with diurnal or seasonal changes in temperature will help to clarify the diurnal or seasonal pattern in the occurrence of cardiovascular disease.

**Appendix 1.**

The cosine function was fitted to the 1-year periodicity with one peak and one trough a year using the monthly cumulative number of incident cases. The estimated cosine function is $Y = m + a \cos(2\pi t/12)$ ($t-\phi$), where $Y$ is the estimated number of monthly occurrences of cerebrovascular disease (based on the cumulative number for the 24 years of follow-up), $t$ represents the month (1=January, 2=February, . . ., 12=December), $M$ is the mesor (mean monthly number of cases), $A$ is amplitude (difference between the estimated number of cases in the peak and the trough), and $\phi$ is the acrophase of the seasonal variation, indicating the peak month (if $0<\phi<1$, then the peak month is January, if $1<\phi<2$, then the peak month is February, and so on). When the actual monthly number of cases were given, the estimated cosine curve function can be determined using the least-squares method (technical detail is omitted).

**References**

17. Katsuki S: Epidemiological and clinicopathological study on cerebrovascular disease in Japan. Prog Brain Res 1966;21B:64–89

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