Seasonal Variation of Stroke Incidence in Japan for 35631 Stroke Patients in the Japanese Standard Stroke Registry, 1998-2007

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Background: Seasonal variation of stroke incidence has been reported in many countries. The present study was designed to elucidate seasonal and monthly variations in the incidence of subtypes of acute ischemic stroke and hypertensive hemorrhagic stroke using the Japanese Standard Stroke Registry Study (JSSRS) database, which is currently the world's largest hospital-based stroke database, accumulating records from 163 Japanese institutions. *Methods:* Among 47,782 patients with acute stroke registered with JSSRS between 1998 and 2007, we selected 35,631 for analysis (patients with ischemic or hemorrhagic stroke of unknown etiology were excluded). A simple moving average was used to examine monthly variation of stroke incidence. We also examined seasonal variation of ischemic stroke subtypes. *Results and Conclusions:* Monthly variation in incidence of all ischemic stroke was significant ($P < .001$). Noncardioembolic ischemic stroke was more frequent in summer than in winter ($P < .001$). Lacunar stroke showed higher incidence in summer than in winter ($P < .001$), although the increase did not reach significance for atherothrombotic stroke ($P = .057$). In contrast, cardioembolic stroke ($P < .001$) and hemorrhagic stroke ($P < .001$) occurred more frequently in winter than in summer. Hemorrhagic stroke showed a regional difference of incidence between northern and southern Japan. There is a temporal variation of stroke incidence in Japan, with different patterns of variation depending on stroke subtype. These findings may help in developing strategies for preventing stroke. **Key Words:** Atherothrombolic stroke—cardioembolic stroke—hemorrhagic stroke—lacunar stroke—seasonal variation—stroke.

Seasonal differences of hospital- or community-based stroke incidence have been examined in many countries,[1-15] including Japan.[11-15] However, the results show considerable variability. Many studies have concluded that stroke occurs most frequently in winter.[1-3,5,8-13] In Japan, Suzuki et al[11] and Shinkawa et al[12] found the same tendency, but a recent report from Takashima Stroke Registry[14] found that stroke occurs most frequently in spring, followed closely by winter. On the other hand, the Japan Multicenter Stroke Investigators' Collaboration[15] reported that stroke occurs least frequently in spring, followed by winter, fall, and summer. These discrepancies may be partly related to differences in ambient temperature,[2] atmospheric pressure,[16] and platelet aggregation.[17]

Here, we describe seasonal and monthly variations of stroke using the Japanese Standard Stroke Registry Study (JSSRS) database.[18] Between December 1998 and November 2007, JSSRS accumulated 47,782 patients with stroke in 163 institutions (see Appendix A) throughout Japan; as the largest hospital-based stroke registration database in the world at present, it offers a unique opportunity to obtain reliable data on seasonal variations in stroke

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incidence. Further, because stroke subtype is available for most JSSRS-registered patients, we also evaluated seasonal variation in lacunar, atherothrombotic, and cardioembolic stroke. Third, because the Japanese islands extend over 3000 kilometers, we also evaluated the difference of stroke incidence between northern and southern Japan.

Methods

To examine seasonal and monthly variation of stroke, we analyzed data for 47,782 patients diagnosed with cerebral infarction (atherothrombotic, lacunar, cardioembolic stroke, and others), transient ischemic attack, cerebral hemorrhage, subarachnoid hemorrhage, and others who were hospitalized within 7 days after symptom onset who were registered in JSSRS from December 1998 to November 2007.[18] Atherothrombotic, lacunar, or cardioembolic subtype was determined from the patients' neurologic, radiologic, cardiologic, and hematologic profiles, principally according to the classification of cerebrovascular diseases III by the National Institute of Neurological Disorders and Stroke.[19] To clarify the seasonal incidence of each subtype of ischemic stroke or hypertensive hemorrhagic stroke, we excluded ischemic or hemorrhagic stroke of unknown cause or etiology and subarachnoid hemorrhage.

The monthly number of patients was corrected for a standard month of 30 days (for months with 31 days, the actual number was multiplied by 30/31; for February, it was multiplied by a factor of $[30 \times 9]/[\{28 \times 7\} + \{29 \times 2\}]$ to take account of the 2 leap years). A simple moving average, calculated by averaging the number of patients in the month of interest and the previous and following months, was used to smooth random variation. To examine seasonal variation in the incidence of ischemic and nonischemic stroke patients, months were grouped into 4 seasons: spring (March-May), summer (June-August), fall (September-November), and winter (December-February).

To analyze regional difference in noncardioembolic and hypertensive hemorrhagic stroke incidence, we divided Japan into northern and southern regions, taking the Kanto district as the dividing line. Because the numbers of patients in the northern and southern regions differed, we used the moving average of monthly patients calculated as a percentage of total annual incidence of noncardioembolic or hemorrhagic stroke. To examine the relation between environmental temperature and stroke incidence, we obtained regional monthly temperature data for 1998 to 2007 from the Japan Meteorological Agency.

The Chi-square test was used to analyze the seasonal and monthly variations of stroke incidence. SPSS software (version 16; SPSS, Inc, Chicago, IL) was used for statistical analysis, and $P < .05$ was considered statistically significant. Kruskal–Wallis tests were used to evaluate the significance of age in each subgroup.

Results

Table 1 shows the characteristics of registered stroke patients. Among the 47,782 patients registered with JSSRS between 1998 and 2007, we excluded those with ischemic stroke of unknown cause (2426 patients) and hemorrhagic stroke of unknown etiology (1272 patients). We enrolled 35,631 patients (71 ± 12 years of age; 21,302 men and 14,329 women) comprised of 29,238 ischemic stroke patients (72 ± 11 years of age) and 6393 hypertensive hemorrhagic stroke patients (67 ± 13 years of age). Ischemic stroke was classified into 3 subtypes: atherothrombotic (9227 patients; 29.1% of ischemic stroke), lacunar (10,828; 34.2%) and cardioembolic (9183; 29.0%). A significant difference of age was observed among subgroups.

Monthly and Seasonal Variation in All Ischemic Strokes

Fig 1A shows the moving average of monthly incidence of all ischemic strokes. The monthly variation was significant ($P < .001$), and the incidence was highest in May. The seasonal difference in incidence was not statistically significant (Fig 1, *B*; $P = .065$), but the incidence in summer was significantly higher than in winter (incidence ratio 1.035; $P < .05$).

Table 1. *Characteristics of registered stroke patients*

	Type of stroke			
	Lacunar	Atheromatous	Cardioembolic	Hemorrhagic
No. of patients	10828	9227	9183	6393
No. of men	6708	5670	5144	3780
No. of women	4120	3557	4039	2613
Age, y (mean ± SD)	70 ± 11*	72 ± 11*	75 ± 11*	67 ± 13*
<75 y	6893	5322	4136	4494
>75 y	3935	3905	5047	1899

*Significant difference of age among subgroups ($P < .001$; Kruskal–Wallis test).