# Higher Stroke Incidence in the Spring Season Regardless of Conventional Risk Factors

## Takashima Stroke Registry, Japan, 1988–2001

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***Background and Purpose***—Seasonal variation in stroke incidence was examined using 14-year stroke registration data in a Japanese population. We also examined if this variation was modified by conventional stroke risk factors hypertension, diabetes mellitus, drinking, and smoking.

***Methods***—Data were obtained from the Takashima Stroke Registry, which covers a stable population of ≈55 000 in Takashima County in central Japan. There were 1665 (men, 893; women, 772) registered first-ever stroke cases during 1988 to 2001. The average age of stroke onset for men and women patients was 69.4 and 74.2 years, respectively. Incidence rates (per 100 000 person-years) and 95% CI were calculated by gender, age, and stroke subtype for winter, spring, summer, and autumn. After stratifying patients by their risk factor history, the OR (with 95% CI) of having a stroke in autumn, winter, and spring were calculated, with summer serving as a reference.

***Results***—Among the seasons, stroke incidence per 100 000 person-years was highest in the spring (231.3; 95% CI, 211.1 to 251.5). Spring incidence was highest in both men (240.8; 95% CI, 211.5 to 270.2) and women (222.1; 95% CI, 194.4 to 249.9), and in subjects younger than 65 years (72.6; 95% CI, 60.0 to 85.3) and 65 years or older (875.9; 95% CI, 787.5 to 964.3). Among stroke subtypes, spring incidence was highest for cerebral infarction (154.7; 95% CI, 138.2 to 171.2) and cerebral hemorrhage (53.7; 95% CI, 44.0 to 63.4). The spring excess in stroke incidence was observed regardless of the presence or absence of the risk factor histories.

***Conclusions***—Stroke incidence appears to be highest in the spring among a Japanese population regardless of conventional risk factor history. Factors that explain this excess need further investigation. (***Stroke*. 2008;39:745-752.**)

**Key Words:** epidemiology ■ incidence ■ risk factor ■ season ■ stroke

A seasonality of stroke incidence has been reported in various parts of the world.[1–13] Studies have reported an increase in stroke incidence, mortality, and stroke hospitalization during the colder months of winter and spring and a decrease during the warmer summer and autumn.[1–11] However, other studies have found no apparent seasonal trend in stroke incidence.[12,13] Although a few studies in Japan have reported a seasonal variation in stroke incidence,[8–10] these studies were primarily hospital-based,[8] of shorter duration,[8,9] or included a small numbers of stroke events.[10] In contrast, a stroke registry of long duration covering an entire population would be most suitable for addressing issues such as a seasonal variation in stroke incidence. A population-based stroke registry also has the potential for generating information on the diverse characteristics of strokes related to geographical, demographical, and environmental influences. Although it is well-established that stroke incidence is affected by risk factors such as hypertension, diabetes mellitus, cigarette smoking, and alcohol intake,[14] the effects of these risk factors on a seasonal variation in stroke incidence have not been clearly addressed. Information about seasonal trends regarding episodes of increased stroke incidence and how these trends are influenced by conventional stroke risk factors might be used as a surrogate to predict stroke onset and might be helpful in preparing awareness messages during periods of increased stroke risk.

In the present study we examined the seasonal variation in stroke incidence using data from the Takashima Stroke Registry that covers a stable population of ≈55 000 individuals in central Japan. We also examined the modification of

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these seasonal variations by history of traditional risk factors. We considered the role of hypertension, diabetes mellitus, cigarette smoking, and alcohol intake in contributing to any excesses in stroke incidence during seasons when stroke risk might be highest.

# Methods

## Takashima Stroke Registry

Takashima Stroke Registry is the integrated part of the Takashima Cardiocerebrovascular Disease Registration System established in 1988 in Takashima County, Shiga, Japan. The objective of this disease registration system for stroke is to measure trends in the incidence and case fatality of stroke and to compare these to sources inside and outside of Japan.[15]

## Topography and Climate of the Registration Area

Takashima County is located in the rural part of Shiga prefecture in the central part of Japan. The largest freshwater lake in Japan, Biwako Lake, popularly known as Lake Biwa, is located to the east of Takashima County stretching from north to south. In addition, the Mount Hira mountainous belt, locally called Hira-san, runs north and south to the west. The weather in Shiga, as with central Japanese weather, follows 4 very distinct seasons: winter, spring, summer, and autumn. There are early spring rains in April, a rainy period between mid June to mid July, autumn rains in September, and typhoons before and after September. There are also snowfalls between December and February. Takashima County is located at ≈35° north and 136° east. The average annual temperature is ≈13.5°C, ranging from 2.5°C in February to 29.5°C in August. The annual precipitation is ≈175 cm, with the highest monthly averages in June (22 cm).

## Population Characteristics of the Registration Area

The population of Takashima County remained stable during the 14-year study period. It is a community with inhabitants mainly classified culturally into a single subgroup and with similar standards of living. With an aging populace, the population included 55 451 inhabitants (men, 49.2%; women, 50.7%) in the year 2000.[16] Among the population, 22.3% were aged 65 or older, which is higher than the all Japan proportion of 17.4%.

## Case Finding and Registration Process

The registered patients included all residents of the Takashima County who were hospitalized with stroke in the county hospitals. Stroke patients who were residents of Takashima County but visited or were referred to 1 of the 3 tertiary hospitals outside the county were also included in the registry. Registered stroke patients were monitored annually by death certification. Original death certificates were seen at the county health center with the permission of the Ministry of Public Management, Home Affaires, Post and Telecommunications, Japan, to establish the cause of death. Patient privacy was protected. Approvals for this study regarding ethical issues were obtained from the Institutional Review Boards of the Shiga University of Medical Science, the participating hospitals, as well as from the administration of Takashima County. Stroke was defined[17,18] as sudden onset of neurological symptoms, which continued for a minimum of 24 hours or resulted in death. Diagnosis of stroke type was based on clinical symptoms as well as neurological imaging by CT or MRI. Stroke was categorized into cerebral infarction, intracerebral hemorrhage, subarachnoid hemorrhage, and unclassified stroke. Items recorded at registration of a stroke were the date and time of stroke onset, the situation and symptoms at the event, the extent of neurological symptoms and clinical observations at the event, history, family history, treatment given, rehabilitation, fatality, cause of death, recurrence in acute stage, neurological imaging observations, and so forth. Details of the case finding, registration process, diagnostic criteria, and items registered have been described elsewhere.[15]

## Statistical Methods

Our analysis included all patients from the Takashima Stroke Registry who experienced their first ever stroke irrespective of outcome. The period of the present study covered the time period from January 1, 1988 to December 31, 2001. During this 14-year period (5114 days, leap years also taken into account), the seasonal variation of stroke incidence was examined by comparing incidence rates within several groups. The year was divided into 4 seasons: winter included December, January, and February; spring included March, April, and May; summer included June, July, and August; and autumn included September, October, and November. To examine the effect of age on the patterns of stroke incidence, patients were stratified into groups younger than 65 and those 65 years or older at the time of stroke onset.

Incidence rates of stroke per 100 000 person-years, including 95% CI,[19] were measured among the 4 seasons by gender, age group and stroke subtype. To calculate the incidence, the total number of stroke events was divided by the person-years of subjects at risk within Takashima County across the 14 years of available data within a season. For example, the person-years for spring was calculated by multiplying the population average in Takashima County by 14 years after weighting by the number of days in the spring season (1288 days). We calculated the population average by averaging the population census for each year for the years 1988 to 2001 for the relevant group. The population demographic data derived from the routine census and vital statistics system are collected annually for the Takashima County for each of the years of the study period. These provide the precise denominator for the calculations of rates.

Stroke incidence was categorized as having occurred in winter, spring, summer, or autumn, based on its day of onset. Using multinomial logistic regression,[20] stroke case across season was modeled as a dependent variable. From such models, 3 regression coefficients were estimated, which provide estimates of the OR of stroke occurring in the winter, spring, and autumn versus the summer as a reference. The OR was calculated as $e^{\beta}$ with 95% CI$=e^{(\beta\pm1.96\times SE)}$. Here, "$\beta$" is the regression coefficient corresponding to winter, spring, or autumn (with summer as a reference), and "SE" is the standard error of "$\beta$." The ORs were calculated separately within gender, age group, risk factor strata (presence or absence of a history of hypertension, diabetes mellitus, and drinking and smoking status), and by stroke subtype. In other analyses, risk factors were modeled as independent variables to further examine the possible effect of interactions between risk factors on the seasonal occurrence of stroke.

Among the risk factors, information on hypertension, diabetes mellitus, cigarette smoking, and alcohol drinking were missing in 13.0%, 14.8%, 25.5%, and 29.8% of the stroke cases, respectively. To determine whether seasonal stroke patterns were different in individuals without information on risk factor histories, ORs (and 95% CIs) were also calculated for those whose risk factor data were missing.

All statistical analyses were performed using SPSS for windows, version 13.0 (SPSS Inc) and SAS version 9.1 (SAS Institute).

# Results

Table 1 shows the characteristics of the registered stroke cases from 1988 to 2001. A total of 1665 stroke cases (men, 893; women, 772) were registered during the study period of 1988 to 2001. The average age of the registered patients at stroke onset was 69.4 years in men and 74.2 years in women. Most of the cases were classified as cerebral infarction (1131; men, 654; women, 486) and cerebral hemorrhage (352; men, 171; women, 181). There were 30 stroke cases (1.8%) with a history of myocardial infarction. The average age at stroke onset did not vary significantly across the seasons.

Table 2 shows the incidence rates of stroke and its subtypes across the seasons. The incidence rate of stroke was highest in the spring (231.3 per 100 000 person-years; 95% CI, 211.1 to

**Table 1. Population and Registered Stroke Patients of Takashima Stroke Registry, Shiga, Japan, 1988–2001**

| Characteristics | Takashima County Population* N (%) | | |
|---|---|---|---|
| Overall | 55 451 | | |
| Men | 27 323 (49.2) | | |
| Women | 28 128 (50.7) | | |
| <65 yr | 43 081 (77.7) | | |
| ≥65 yr | 12 354 (22.3) | | |
| | Registered Stroke Cases | | |
| | Men | Women | All Cases |
| All stroke | | | |
| Total incidence | 893 | 772 | 1665 |
| Average year at onset (yr) | 69.4 | 74.2 | 71.6 |
| SD | 11.9 | 12.0 | 12.2 |
| <65 yr | 280 | 139 | 419 |
| ≥65 yr | 613 | 633 | 1246 |
| Stroke subtype | | | |
| Cerebral infarction | 645 | 486 | 1131 |
| Intracerebral hemorrhage | 171 | 181 | 352 |
| Subarachnoid hemorrhage | 62 | 95 | 157 |
| Unclassified | 15 | 10 | 25 |
| | N (%) | | |
| Presence of risk factor history | | | |
| Hypertension | 876 (52.6) | | |
| Diabetes mellitus | 271 (16.3) | | |
| Drinking | 333 (20.0) | | |
| Smoking | 419 (25.2) | | |
| Myocardial infarction | 30 (1.8) | | |

*Data are based on the population census of Japan for the year 2000 (age reported unknown for 16 persons).

251.5) and lowest in the summer (183.1; 95% CI, 165.2 to 201.1). An excess stroke incidence in the spring was observed in both men (240.8; 95% CI, 211.5 to 270.2) and women (222.1; 95% CI, 194.4 to 249.9), and in subjects younger than 65 years (72.6; 95% CI, 60.0 to 85.3) as well as subjects 65 years or older (875.9; 95% CI, 787.5 to 964.3). A spring excess of stroke incidence was observed for both cerebral infarction (154.7; 95% CI, 138.2 to 171.2) and cerebral hemorrhage (53.7; 95% CI, 44.0 to 63.4).

Figure 1 presents the OR of a stroke stratified by stroke subtype, gender, and age for autumn, winter, and spring, with summer as a reference. Among all strokes, the spring excess was significantly higher compared with the summer. In addition, the ratio of stroke risk in the spring compared with the summer for cerebral infarction and cerebral hemorrhage was 1.21 (95% CI, 1.03 to 1.43) and 1.47 (95% CI, 1.09 to 1.97), respectively. For women, the stroke risk was 1.50 (95% CI,1.22 to 1.84) times higher in spring than the summer. Among older stroke victims (65 years or older), stroke risk was 1.27 (95% CI, 1.09 to 1.48) times higher in spring than the summer.

Figure 2 presents the OR of a stroke stratified by the presence or absence of a history of risk factors (hypertension, diabetes mellitus, smoking, and drinking) for autumn, winter, and spring, with summer as a reference. Regardless of the presence or absence of a history of these risk factors, there was an elevated stroke risk in the spring. Although the sample size and statistical power were reduced within each of the risk-factor strata, a significantly elevated stroke risk continued to be observed in the absence of diabetes mellitus and in nondrinkers and nonsmokers. Although among the risk factors the seasonal distributions were not exactly similar, in all instances, the highest risk of stroke still occurred in the spring relative to the other seasons. Whereas sample size and statistical power are limited, we found a similar pattern of seasonal stroke incidence that appeared in those with and without missing data.

Figure 3 presents the OR of a stroke for the seasonal comparisons after adjustment for a history of hypertension, diabetes mellitus, smoking, and drinking status. Differences from Figure 2 are modest. Whereas risk factor interactions were also assessed, none was statistically significant. This latter finding, however, could be a consequence of limited statistical power.

## Discussion

The present study shows a seasonal variation in the incidences of stroke events in both men and women and in younger and older age groups. Stroke incidence was highest

**Table 2. Incidence Rate (per 100 000 person-yr) for Stroke for Seasons by Gender, Age Group, and Subtype in the Takashima Stroke Registry, Shiga, Japan, 1988–2001**

| | Winter (95% CI) | Spring (95% CI) | Summer (95% CI) | Autumn (95% CI) |
|---|---|---|---|---|
| All stroke | 214.8 (195.1–234.4) | 231.3 (211.1–251.5) | 183.1 (165.2–201.1) | 190.7 (172.3–209.2) |
| Gender | | | | |
| Men | 224.6 (195.9–253.2) | 240.8 (211.5–270.2) | 217.5 (189.6–245.4) | 203.9 (176.7–231.0) |
| Women | 205.3 (178.3–232.2) | 222.1 (194.4–249.9) | 149.9 (127.1–172.7) | 178.0 (153.0–203.0) |
| Age group | | | | |
| <64 years | 61.8 (50.0–73.6) | 72.6 (60.0–85.3) | 57.2 (45.9–68.4) | 61.3 (49.6–72.9) |
| ≥65 years | 836.0 (748.8–923.2) | 875.9 (787.5–964.3) | 694.7 (615.9–773.4) | 716.4 (635.9–796.8) |
| Stroke subtype | | | | |
| Cerebral infarction | 149.3 (132.9–165.6) | 154.7 (138.2–171.2) | 127.6 (112.6–142.6) | 120.7 (106.0–135.3) |
| Cerebral hemorrhage | 42.1 (33.4–50.8) | 53.7 (44.0–63.4) | 37.2 (29.1–45.3) | 44.5 (35.6–53.5) |
| Subarachnoid hemorrhage | 21.5 (15.3–27.7) | 18.8 (13.4–24.6) | 16.5 (11.1–21.9) | 21.3 (15.2–27.5) |

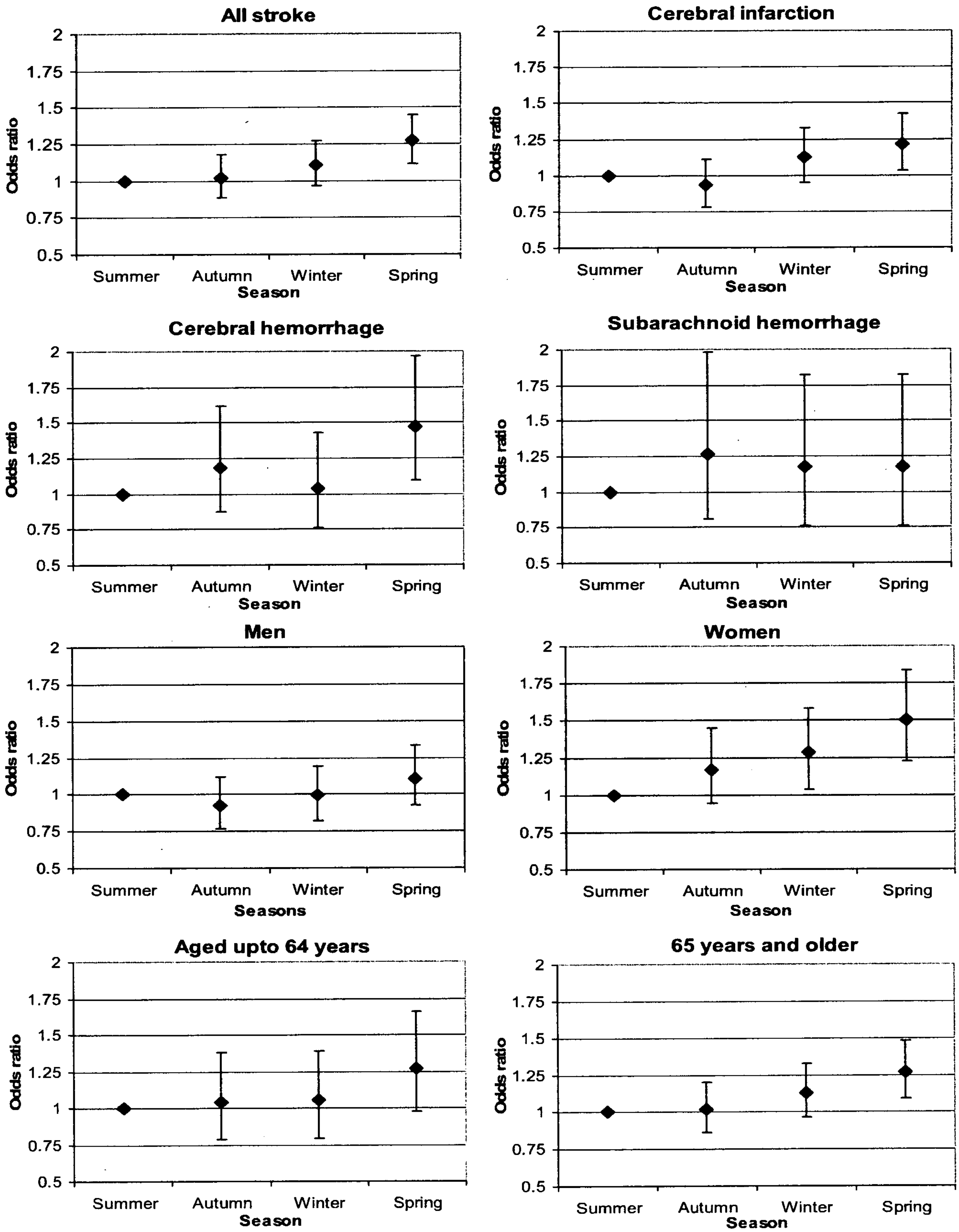


**Figure 1.** The ORs and 95% CIs are shown for the occurrence of stroke stratified by stroke subtype, gender, and age in autumn (September, October, and November), winter (December, January, and February), and spring (March, April, and May) compared with summer (June, July, and August). Takashima Stroke Registry, Shiga, Japan (1988–2001).

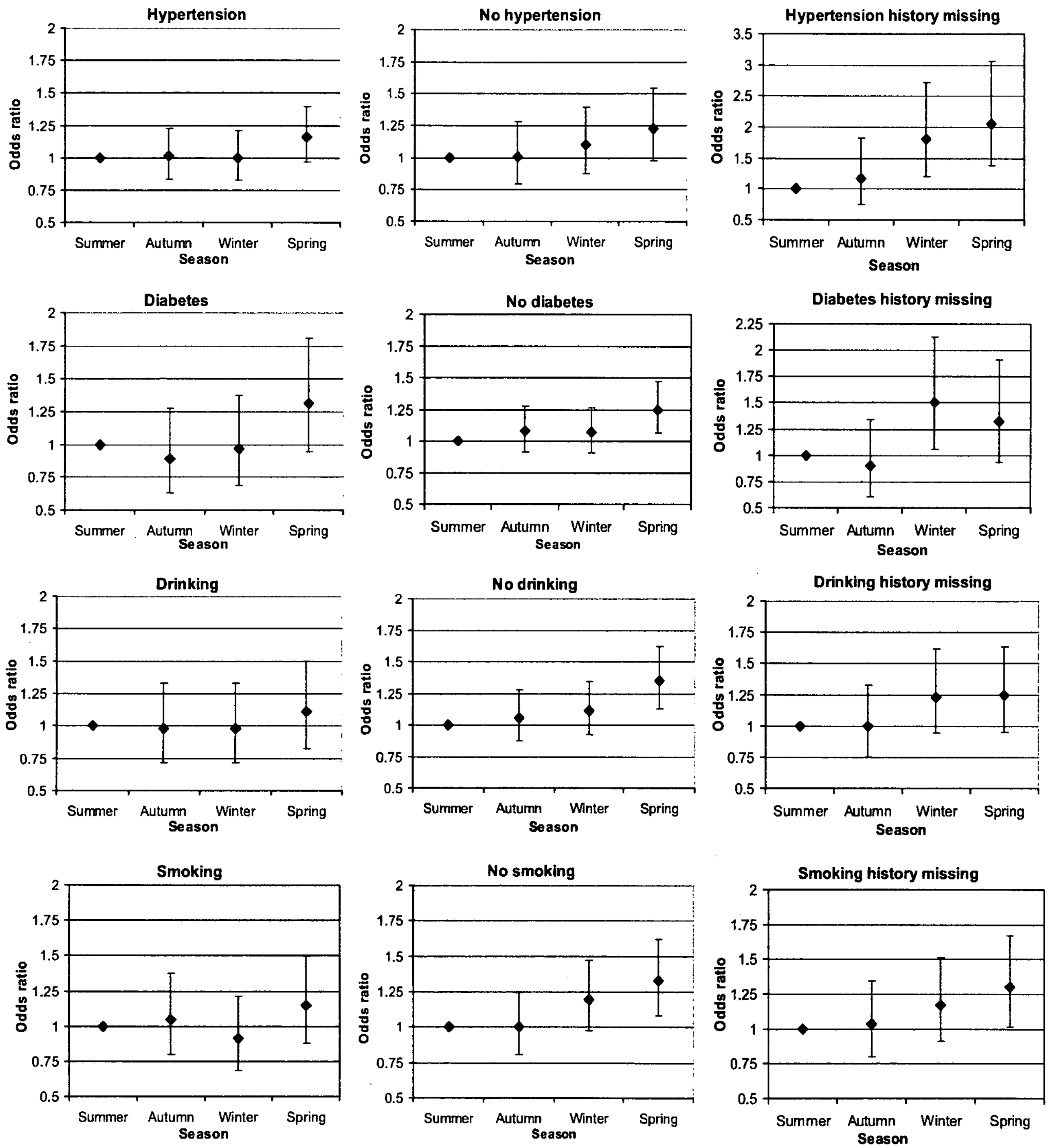


**Figure 2.** The ORs and 95% CIs are shown for the occurrence of stroke stratified by the presence and absence of a history of hypertension, diabetes mellitus, drinking, and smoking status in autumn (September, October, and November), winter (December, January, and February), and spring (March, April, and May) compared with summer (June, July, and August). Takashima Stroke Registry, Shiga, Japan (1988–2001). ORs are also given for those with missing data.

in the spring, followed closely by the winter. A similar seasonal pattern was observed for both cerebral infarction and cerebral hemorrhage. This pattern seems to hold regardless of the presence and absence of a history of risk factor histories, including hypertension, diabetes mellitus, smoking, and drinking.

Our findings are similar to other studies in Japan, where stroke incidence was found to be higher during the winter and spring.[8–10] Among reports from studies outside of Japan,[1–7] there also is evidence that the incidence of stroke peaks in the winter and spring, with a trough in the summer and autumn seasons. Similar to the findings of others,[2,6,8,10] we did not observe any seasonal pattern for subarachnoid hemorrhage, although this in part could have been attributable to the small numbers of these events. Although Shinkawa et al[10] describe seasonality according to months within a year, their findings

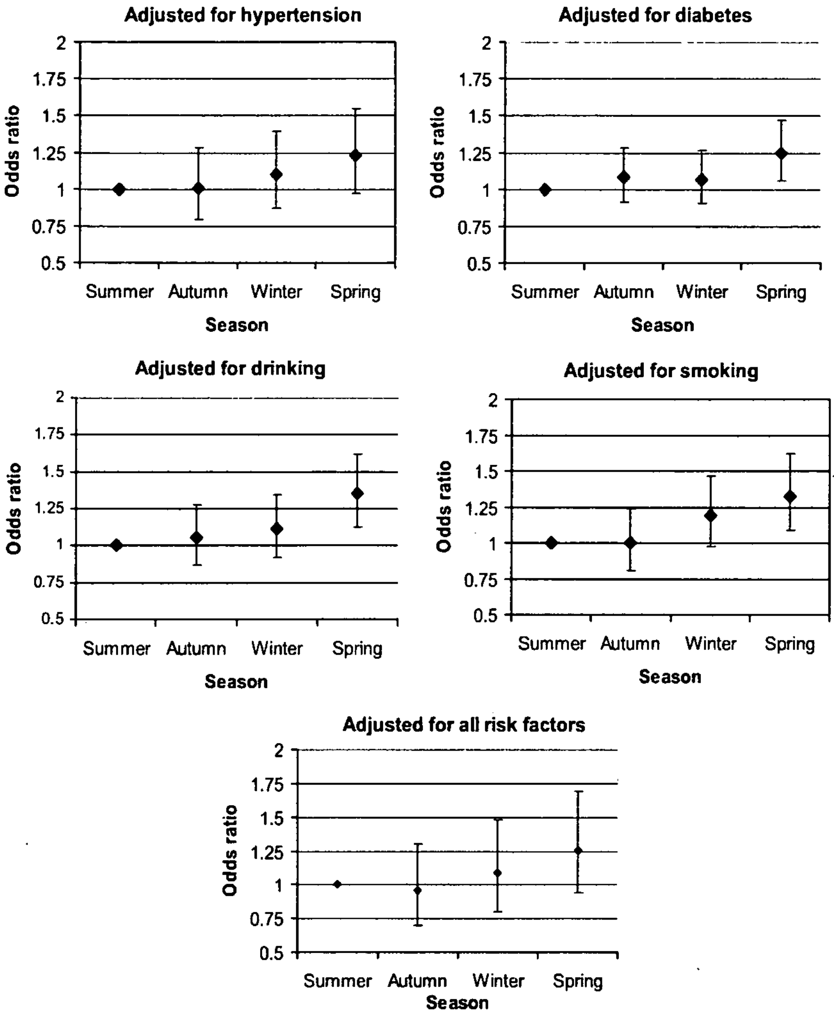


**Figure 3.** The ORs and 95% CIs are shown for the occurrence of stroke adjusted for a history of hypertension, diabetes mellitus, drinking, and smoking in autumn (September, October, and November), winter (December, January, and February), and spring (March, April, and May) compared with summer (June, July, and August). Takashima Stroke Registry, Shiga, Japan (1988–2001).

are comparable and in agreement with the current report. In our study, however, the spring excess in stroke incidence appeared to be present regardless of the presence or absence of history of hypertension, diabetes mellitus, drinking, and smoking. This pattern seems to hold after adjusting for risk factor histories as independent variables. All stroke seasonal distribution showed significant distribution across seasons, but after stratifying for risk factor status significant excess continued to be observed in the absence of diabetes mellitus and in nondrinkers and nonsmokers. In instances of the other risk factor status significance was no longer present; however, findings could in part be attributed to a large reduction in sample size because of missing data and a loss of statistical power. It was also observed that the proportion of the presence or absence within the risk factors did not vary across the seasons. Hence the prevalence of risk factors for stroke was quite similar among the 4 seasons, indicating that the spring peak pattern of the stroke incidence holds irrespective of the risk factor histories.

This present study is based on a registry data, thus a community-based surveillance system data, which do not assist in exploring the mechanisms or causes related to the seasonal variation of stroke. Now identifying the seasonal trend, an interesting area for investigation will be the relationship of variations in physical activity and environmental factors and stroke occurrence among seasons using longitudinal data.

The mechanisms underlying seasonal variation of strokes are not fully understood. The weather component factors could serve as a set-off factor for stroke. The physiological processes related to these weather components may trigger the acute stroke event. Among seasons, variation in temperature has been considered to be the most likely reason to influence the stroke incidence.[21] Probable explanations for seasonal variation in stroke incidence include seasonal variation of biological factors such as blood pressure, serum lipids, some blood components, and hypercoagulable state (plasma fibrinogen concentration and viscosity).[1,10,22] Seasonal pattern of influenza epidemic, air pollution, and other respiratory tract infections[1,10,22] also are presumed to influence the seasonality of the stroke and cardiovascular incidence.

The seasonal fluctuation in blood pressure is very similar to that for stroke with blood pressure having an elevation in colder weather and a trough in warmer conditions.[23–25] Sustained higher level of blood pressure during the colder weather might be associated with increased risk of stroke occurrence.[26] Furthermore, serum cholesterol,[27] C-reactive protein, factor VII activity,[28] red blood cells, and platelet count[29] are all higher in colder weather. Elevation of these parameters may contribute to an increased tendency toward arterial thrombosis and a higher incidence of cardio-cerebrovascular disease.[22,30] Plasma fibrinogen concentration and viscosity show considerable seasonal variations, at least in elderly individuals,[28] and it has been reported that fibrinogen is a significant stroke predictor.[31] Infection, particularly influenza epidemics and other respiratory tract infections,[32,33] may also play a role. Influenza may cause some complications in atherosclerotic disease and induce hypercoagulation.[34] In Japan, peak influenza activity in the winter and early spring coincides with peak stroke incidence.

Psychological stress is reported to be a significant risk for stroke and coronary artery disease, even after adjustment for other established risk factors in middle-aged men.[35,36] Regarding cardiovascular and cerebrovascular sudden death, it has been reported that in Japanese working population it occurred more frequently in April, when the new business year starts, compared to other months.[37] It was hypothesized that younger people in Japan might have to face greater occupational stress at the end of the old financial year and the beginning of the new year coinciding with winter and spring.[10,37]

The quality of our registration system was assured by its completeness. Our registry system was planned to capture all the cases in the study area by covering all the hospitals of the county. It has been estimated that >98% of all hospital admissions of Takashima County are seen in these institutions.[15] To ensure that eligible patients hospitalized outside the county were not left out, registration procedures were also conducted at 3 high-level medical facilities outside the county.

In Japan almost 100% of the residents are covered by health insurance under the control of Ministry of Health and Welfare.[15,38] People with mild stroke who visited general physicians in the community are almost always referred to secondary or tertiary level hospitals for extensive investigations. In addition to that, 24-hour emergency ambulance service is available for residents without any charge. The usual practice in Japan is to take patients with any acute disease conditions to the emergency facilities. Thus, we believe that extremely few patients would be left out of our registration system.

Japan has the most MRI units (35 units per million population) and CT scanners (93 units per million population) per capita among the developed countries.[39] In our registered stroke cases, the diagnoses were verified by neurological imaging in 93.3% cases. Of these cases, 58.8% had CT alone, 37.2% had both CT and MRI, and 4.2% had MRI alone. Therefore, in our registration system, identification of stroke cases among the study area was almost complete and stroke categorization was highly accurate.

It has been suggested that the increase in stroke events during the colder weather might be an artifact of the registration process attributable to referral bias.[12] However, the health care system in Japan covers and ensures treatment availability for all the residents and the round-the-clock free of charge emergency ambulance service ensures all hospital transfers. Also, the standard practice in Japan is to take patients with any acute disease conditions to the emergency facilities. Thus, these unique characteristics of the Japanese health care system minimized the influence of referral bias in our registry.

The main limitation of our study is the missing information for a number of registered patients regarding their history of risk factors such as hypertension, diabetes mellitus, smoking, and drinking. Even after examining individuals with missing risk factor information, there was a similar pattern of seasonal stroke incidence that appeared in those without missing data. We also could not determine the disease duration for hypertension and diabetes mellitus or quantify the amount of alcohol or cigarette smoking, both in cases of habitual quantity or just before the stroke onset. Rather, we used information reported about presence or absence of the risk factor history. An additional limitation is that the Takashima Stroke Registry covers a rural and semi-urban population in Japan that may be different from the metropolitan population.

In conclusion, we found that there was increased stroke incidence during the spring, followed by winter. This was observed in both young and old subjects and in both men and women. This spring excess of stroke incidence was observed for both in the presence and absence of conventional risk factors. Thus, our analysis points toward an influence of internal or external stroke-triggering factors in the time preceding acute onset of stroke. The identity of these triggering factors, which may be of significant use in stroke prevention strategies, requires further investigation.

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## Disclosures

None.

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# Registration and Surveillance of Acute Myocardial Infarction in Japan: Monitoring an Entire Community by the Takashima AMI Registry
## — System and Design —

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**Background** The purpose of this registration is to follow incidence and case fatality trend of acute myocardial infarction (AMI) in Japan, using a whole community population disease registry that surveys the most up-to-date information. Since the 1970s, mortality from coronary heart disease has followed a declining trend in Japan, which has been attributed to a decrease in the incidence of AMI and some evidence suggests that incidence has leveled off during the past couple of decades. These reported decreasing or stable trends in AMI have been observed despite recent worsening of the cardiovascular risk factor situation in Japan (Japanese paradox). Therefore, monitoring the disease course of AMI is of immense importance.
**Methods and Results** The Takashima AMI Registry established in 1988 covers a stable population of approximately 55,000 in Takashima County in central Japan. Registered patients included all Takashima County residents who have been diagnosed with AMI. The criteria of AMI are in accord with those of the World Health Organization's Monitoring of Trends and Determinants in Cardiovascular Disease (WHO-MONICA) project.
**Conclusion** Comprehensive disease registry data is especially appropriate for determining the incidence as well as the trend of diseases such as AMI. This registration study covering an entire community will enable researchers to follow trends in AMI incidence with a high degree of precision. (*Circ J* 2007; **71:** 1617–1621)

**Key Words:** Acute myocardial infarction; Community; Registration; Surveillance

Most previous studies in Japan have examined cardiovascular disease trends by comparing prevalence or incidence rates of hospitalized cases among different time periods,[1,2] dividing a long-term cohort follow-up period into several parts within cohort studies,[3,4] performing multiple cross-sectional surveys of a population on separate occasions,[5] or following multiple cohorts at different starting points.[6] All these methods, however, can be potentially biased because of not being able to follow an entire community population.[7,8] Disease registries for chronic diseases, such as acute myocardial infarction (AMI), are indispensable in determining the incidence and trends in a particular population and a disease registry that covered a whole community population continuously for a long period of time would enable the incidence, as well as the trend, of any disease, especially AMI, within that population to be determined precisely. A disease registry complements cross-sectional studies of the differences in disease rates by

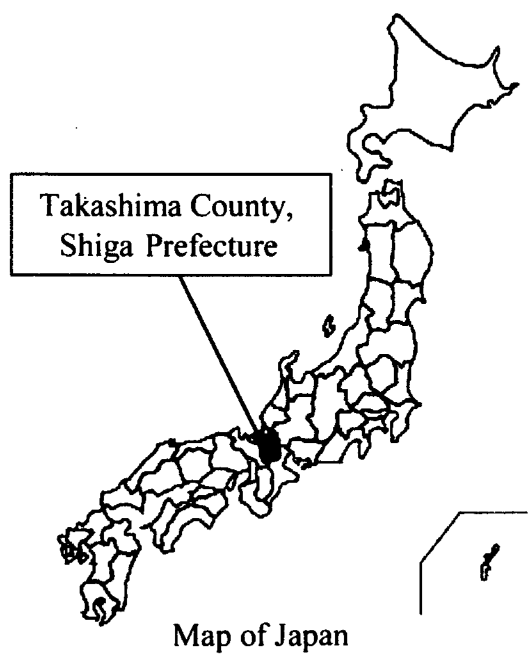


Fig 1. Takashima County, Shiga prefecture on the map of Japan.

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**Table 1 Population Characteristics in the Takashima Registration Area, Takashima County, Shiga, Japan***

| *Characteristics* | *Takashima County* | | |
|---|---|---|---|
| *Population* | *N* | | *%* |
| *Total* | *55,451* | | – |
| *Gender* | | | |
| *Men* | *27,323* | | *49.2* |
| *Women* | *28,128* | | *50.7* |
| *Age group* | | | |
| *≤14 years* | *8,720* | | *15.7* |
| *14–64 years* | *34,360* | | *62.0* |
| *>65 years* | *12,354* | | *22.3* |
| *Sex ratio (males per 100 females)* | | *94.9* | |
| *Households* | | | |
| *Total number* | | *16,540* | |
| *Mean no. family members per household* | | *3.36* | |
| *Population density* | | | |
| *Total land area (km²)* | | *511* | |
| *No. people per km² (total land area)* | | *108* | |
| *No. people per km² (total residential area)* | | *470* | |
| *Industrial population* | | | |
| *Primary†* | *1,871* | | *6.8* |
| *Secondary‡* | *10,470* | | *38.1* |
| *Tertiary§* | *15,145* | | *55.1* |

**Data are based on the 2000 population census of Japan (age unknown 16).*
*†Primary: agriculture, fishing, forestry, etc; ‡Secondary: industrial sector; §Tertiary: service sector.*

longitudinal investigation. Simultaneous monitoring of the incidence, mortality, morbidity, case fatality, risk factor levels, social and behavioral tendency within a defined community over a period of years will help in clarify the interrelationships among these variables in terms of the dynamics of change in the natural history of a disease. Information about AMI incidence and the risk factors in the population is essential[9–11] and disease surveillance provides this essential information that can be used for designing effective prevention strategies, appropriate allocation of health resource, assessment of effectiveness of the health programs etc.

## Takashima AMI Registry in Japan

*Takashima AMI Registry*

Takashima AMI Registry is an integrated part of the Takashima Cardio-cerebrovascular Disease Registration System established in Japan in 1988. The objective of this disease registration system is to measure trends in the incidence and case-fatality of AMI and to compare the trend with those in other populations within Japan and in other countries. The registry information also can be used to asses the extent to which these trends are related to changes in known risk factors, daily living habits, health care, or major socioeconomic features of the Japanese population.

*Topography of the Registration Area*

Fig 1 shows Takashima County, which is located in the rural area of Shiga prefecture in the center of Japan. Much of it is mountainous rural areas with only 1 primary road running through the area and movement is therefore restricted to this extent. The largest freshwater lake in Japan, Biwako Lake, popularly known as Lake Biwa, is located to the east of Takashima County, stretching from north to south, and the Mount Hira mountainous belt, locally called Hira-san, runs north-south to the west. Weather in Shiga, as with central Japanese weather, follows 4 very distinct seasons: winter, spring, summer and autumn.

*Population Characteristics of Registration Area*

Table 1 shows the characteristics of the residents of Takashima County. It is a rural community with similar cultural values and standards of living throughout the region. More than 90% of the industrial population is engaged in the secondary and tertiary sectors, but many are also part-time farmers engaging in agriculture and farming-related activities on some holidays or weekends only. The population has remained fairly stable during the 16-year study period. In the year 2000 the population was 55,451 (49.2% males, 50.7% females) and 22.3% is aged 65 years or more, which is higher than the all-Japan proportion of 17.4%.[12]

The population demographic data derived from routine census and vital statistics for Takashima County are collected annually for each year of the study period and provide the precise denominator for calculations of different rates.

*Case Finding and Registration Process*

The basic information for the registry is investigation of medically recognized cardiovascular events, fatal and nonfatal, using medical, medico-administrative and medico-legal sources. Takashima County has 2 community hospitals: Takashima General Hospital, a public facility with 261 beds located in the south of the county, and Makino Hospital, a private facility with 72 beds located in the north. Additionally, there is a geriatric hospital, Imazu Hospital, which is the only dedicated facility for elderly people in the county. Nearly all hospital admissions are at these community hospitals. Any other patients requiring advanced treatment are generally seen at 1 of 3 tertiary-care hospitals located outside the county but within Shiga prefecture: Shiga University of Medical Science Hospital and Otsu Red Cross hospital in Otsu City, and Shiga Medical Center for Adults in Moriyama City. Although percutaneous catheter interventional (PCI) therapy for AMI began in public hospitals in 1998, prior to that almost all cases of AMI were transferred to the tertiary hospitals, but all of the patients in the county were taken to a local hospital before transfer.

Fig 2 is the flow chart of the case finding and registration process of the Takashima AMI Registration System. Registered patients include all residents of the county who are hospitalized with AMI. Events in non-residents occurring in the study area or admitted to hospital in the study area do not qualify for the registry. Also included are AMI patients who are residents of Takashima County but visited or were referred to the tertiary hospitals. Events in residents occurring out of the study area do qualify. Internist and specialist investigative personnel trained by cardiologists and epidemiologists carry out both the case finding and registration of patients who meet the criteria. The trained staff visit each hospital once every 3 months and review the medical records to identify possible cases. We register all cases that meet the inclusion criteria[13,14] on the basis of the medical records from all the relevant hospitals inside and outside the county, the county ambulance records and the county death records. The local registration teams periodically send their data to the coordinating centre at Shiga University of Medical Science where the data are checked for logical errors. Registered AMI patients are monitored annually by death certificates. Original death certificates are reviewed at the county health center in order to establish cause of death. Before the final decision about inclusion in the registry, physicians and epidemiologists cross-check the records for absolute verification for eligibility for inclusion in the register. Patient privacy is protected. Approval for this study regarding ethics issues was obtained from the Institutional Review Board of the Shiga University of Medical Science, the participating hospital authorities, as well as from the administration of Takashima County.

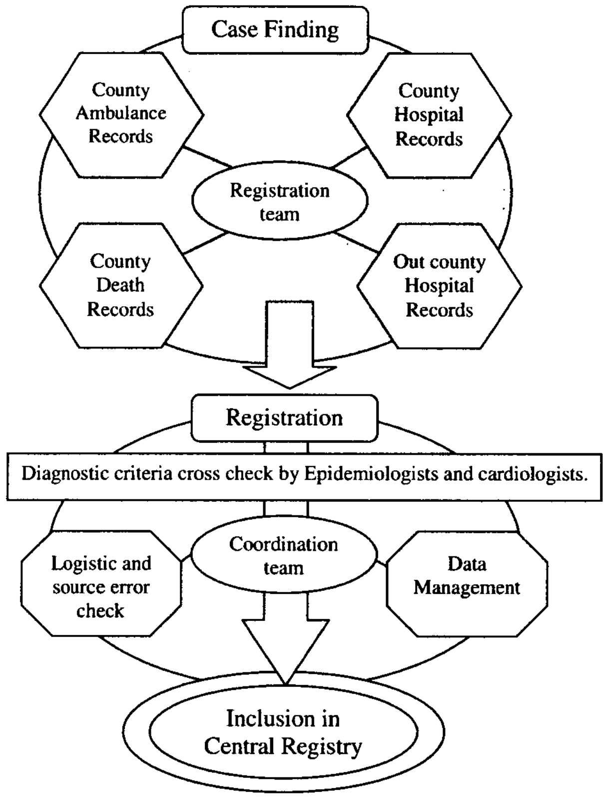


Fig 2. Flow chart of the case finding and registration process of the Takashima Acute Myocardial Infarction Registration System.

*Diagnostic Criteria*

The AMI diagnostic criteria used in this study are those established for the Monitoring System for Cardiovascular Disease commissioned by the Ministry of Health and Welfare, Japan.[13] These criteria are in accord with the World Health Organization's Monitoring of Trends and Determinants in Cardiovascular Disease (WHO-MONICA) project.[14] In order to define the diagnostic category of a suspect event, information about the symptoms, electrocardiogram (ECG), cardiac enzymes and necropsy findings were considered. Definite AMI is defined as cases with (a) definite ECG findings, (b) cases with typical or atypical or inadequately described symptoms, together with probable ECG and abnormal enzymes, (c) cases with typical symptoms and abnormal enzymes with ischemic or non-codable ECG or ECG not available, or (d) fatal cases, whether sudden or not, with gross appearance of fresh myocardial infarction (MI) and/or recent coronary occlusion found at necropsy. Possible AMI cases are defined as (a) living patients with typical symptoms whose ECG and enzyme results do not place them in a definite category and in whom there was not good evidence for another diagnosis; (b) fatal cases, whether sudden or not, where there was not good clinical or autopsy evidence for another cause of death and the symptoms were typical or atypical or inadequately described; (c) fatal cases, whether sudden or not, where there was not good clinical or autopsy evidence for another cause of death and without typical or atypical or inadequately described symptoms but with evidence of chronic coronary occlusion or stenosis or old myocardial scarring at necropsy; (d) fatal cases, whether sudden or not, where there was not good clinical or autopsy evidence for another cause of death but with a good history of chronic ischemic heart disease such as definite or possible MI, or (e) coronary insufficiency or angina pectoris in the absence of significant valvular disease or cardiomyopathy. Every coronary event must have its apparent onset within the study period and more than 28 days from any preceding recorded coronary event in the individual. Second, the event must be detected and diagnosed within 28 days of onset. Unrecognized (silent) MI is found to constitute a proportion of all infarctions in a population, but this cannot be covered fully for obvious reasons and is a problem shared by most studies of this kind. In cases of silent MI diagnosed subsequently, the onset dates are taken as the oldest possible date of documentation. The starting point for calculating the 28-day survival period is the onset of the first findings of a suspect coronary event (symptoms, ECG, enzymes). If there are recurrences during the next 28 days they belong to the same event. Case fatality is defined as death within 28 days after onset. The day of onset=day zero and the difference in calendar days is calculated by subtracting the date of onset from the date of death. In our study the methods of case ascertainment and the diagnostic criteria of AMI are consistent.

*Items Recorded*

Items recorded at registration of an AMI event are the date and time of onset, age, sex, location and activity at the time of onset, time of admission, signs and symptoms of the event, ECG findings, region of infarction, Q wave or non-Q wave infarction, coronary risk factors, personal and family medical history, including history of hypertension, diabetes mellitus, cardiac diseases, dyslipidemia, stroke,

**Table 2 Acute Myocardial Infarction Cases in the Takashima Registration System Area, Takashima County, Shiga, Japan (1988–2003)**

| | *AMI cases* |
|---|---|
| *Total* | *404* |
| *Men* | *260 (64.4%)* |
| *Women* | *144 (35.6%)* |
| *Average age (years)* | |
| *Men* | *68.6 (SD:12.9)* |
| *Women* | *75.8 (SD:10.4)* |
| *≤64 years* | *114 (28.2%)* |
| *>65 years* | *290 (71.8%)* |
| *Total fatal cases within 28 days* | *147* |
| *Men* | *84 (57.1%)* |
| *Women* | *63 (42.9%)* |
| *Average age of fatal cases within 28 days (years)* | |
| *Men* | *72.9 (SD:14.3)* |
| *Women* | *78.2 (SD:10.3)* |

*AMI, acute myocardial infarction; SD, standard deviation.*

kidney diseases, obesity, drinking and smoking. We record the immediate history of the current event, blood serological findings including creatine kinase (CK), the myocardial band fraction of CK (CK-MB), and coronary angiography findings, which are categorized as (a) no stenosis, (b) 1-vessel disease, (c) 2-vessel disease, (c) 3-vessel disease or (e) left main trunk disease. Acute therapy, both pharmacological and interventional, is recorded. The pharmacological treatment record includes information about intracoronary and intravenous thrombolysis. The interventional and surgical record included information about PCI, plain optimal balloon angioplasty, and coronary artery bypass grafting. We also record information about complications in the acute stage of the AMI event, Killip's classification, death within 28 days, assessment at discharge, New York Heart Association functional classification at discharge, early rehabilitation information, autopsy information in cases of death, death certificate details, and follow-up information on cause of death.

*Quality Assurance*

To ensure that the data collection process is complete and accurate we have a local data checking procedure that uses a processing check-list. All data are verified to reduce keying errors as much as possible. The data are checked for (a) completeness (ie, contains all the records it should contain) and (b) correctness and consistency (ie, does not contain illegal or erroneous values). All suspect data items are checked against the original documents from which the data were collected. To ensure the quality of event registration, personnel with medical and nosological training and medical or record review experience have been recruited for case investigation and validation. They have explicit rules and instructions for how to investigate the records. Initially, 2 processes are undertaken to ensure the reliability and comparability of the records, by (1) re-reviewing previously reviewed cases and (2) a standard set being reviewed by multiple personnel. Furthermore, during the surveys the investigators continuously follow the inter- and intra-observer variations to detect possible problems and take early corrective measures. Because we are using an abstracting technique for the collection of incidence data from multiple hospitals, they have been given a uniform guideline regarding data of suspect coronary events. Because of the skill required in applying the diagnostic criteria, that is done by the reviewers (physicians and epidemiologists), not the persons abstracting the data from the clinical records. Periodically, a number of selected suspect cases are studied in detail by the investigators. Data collected and entered into the computer are reported regularly and these tabulations are reviewed at the central database for possible out-of-range or unusual values, and efforts are taken to identify and correct entry errors.

*Registered Events*

The Takashima Stroke Registry is an ongoing disease registry that has been compiling AMI cases since 1988 and as of 2003, a total of 404 cases have been recorded (Table 2).

*Comprehensiveness*

The comprehensiveness of a registration system for cardio-cerebrovascular diseases such as AMI is essential if the incidence and trends in a particular area are to be determined with any accuracy. The reliability of the procedures monitoring the coronary event registration depends on 2 components: (i) coverage (ie, completeness of case finding procedure) and (ii) accuracy (ie, correctness of applying the given diagnostic criteria to identified cases). A system to capture all patients in the study area, together with accurate diagnosis, is required to ensure the comprehensiveness and reliability of the registration. Registration systems cannot be effective if the medical care system is disorganized, fragmented and inefficient. Factors that reduce the comprehensiveness of a register include missing cases or cases lacking a confirmed diagnosis, patients being admitted to hospitals outside the registration area, and non-registration.

The quality of our registration system is assured by its completeness. In Japan, generally all non-fatal diagnosed cases of AMI are treated in a hospital. Our registry system was planned to capture all cases in the study area by covering all the hospitals of the county, and these hospitals cover nearly all the hospital admissions of Takashima County. Even cases that are referred to higher treatment facilities are generally first taken to a local hospital in Takashima County and then transferred to the designated facility. Thus, patients transferred within a short period after admission to a Takashima hospital will be included in the hospital records as well as in the ambulance records. Furthermore, to ensure that eligible patients hospitalized outside the county were not omitted, registration procedures were also conducted at the 3 high-level medical facilities outside the county. Because we have been using multiple sources for case identification, there are multiple records for some cases and these are identified using cross-matching of name, gender, birth date, address and onset date. Therefore, we believe that there is very little possibility of double registration in our registry.

In Japan almost 100% of residents are covered by health insurance under the control of the Ministry of Health and Welfare![5] Health insurance is not expensive and the policies cover all diseases, except road traffic accident injury, which is covered by a separate mandatory automobile insurance system. Therefore, the usual practice in Japan is that people with health problem visit a general physician in the community, who, if AMI is suspected from the symptoms and signs, would almost always refer the patient to a secondary or tertiary level hospital for extensive investigations. In addition, 24-h emergency ambulance service is available for residents. The ambulance service in Japan is also publicly funded and users are transported free of charge to hospital. The common practice in Japan is to take patients with any acute disease condition to an emergency facility. Thus, we believe that extremely few patients will be left out of our registration system.

The registration study population is persons with their chief current residence in the study area, which is defined geographically to correspond with administrative and census boundaries. Instability of the population followed is among certain factors that can, in general, influence the detection of events and calculation of the event rates, in terms of temporary or permanent migration in and out of the study area. However, in our registry coverage area, the Takashima County, the population has remained reasonably stable during the study period.

With regard to the possibility of a limitation of our data collection related to cases of non-fatal AMI managed outside the main medical facilities; we estimate that there will be very few patients who would go to hospitals that were not participating in our registration system. It has been estimated that approximately 98% of all hospital admissions are seen at the main medical facilities under registry coverage. We registered cases of out-of-hospital cardiac death, but because the ECG findings and concentrations of cardiac enzymes are often not available in such cases, we had to base registration on the patients' location and symptoms at onset and their history. We tried to register only cases of definite or possible AMI death in accordance with the registry's definition.

In a community-based registry of chronic disease there are always chances of referral bias, which may lead to trend results with artifacts. However, the healthcare system in Japan covers and ensures treatment availability for all residents and the 24-h free emergency ambulance service ensures all hospital transfers. Furthermore, the standard practice in Japan is to take patients with any acute disease condition to an emergency facility. Thus, these unique characteristics of the Japanese healthcare system minimize the influence of referral bias in our registry.

*Representation*

The Takashima AMI Registry covers a rural and semi-urban community in Japan that is likely to be different from the metropolitan population in Japan. On the other hand, a previous report of a mainly hospital-based study of AMI cases in 7 areas in Japan, including Takashima County, showed that the age-adjusted first AMI incidence rates per 100,000 for all ages in Takashima was in the median of the 7 regions studied.[16] Therefore, we believe that Takashima AMI registry is representative of similar population in Japan.

*Significance*

We are following the incidence of AMI in Takashima County in Japan and compiling information from the disease registration covering the entire county. Natural history of a chronic disease is related to a change in disease incidence, or change in case fatality, or both. Our registry system makes it possible to explore and assess the AMI incidence and case fatality trend in Japan using a population-based disease registry that includes the most up-to-date information on AMI in a Japanese population.

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Original Paper

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# Increase of Stroke Incidence after Weekend Regardless of Traditional Risk Factors: Takashima Stroke Registry, Japan; 1988–2003

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**Key Words**
Epidemiology · Stroke incidence, weekday · Variation, stroke incidence

**Abstract**
***Background and Purpose:*** The study purpose was to identify patterns of variation in stroke incidence among days of the week and examine if it is modified by conventional stroke risk factors: hypertension, diabetes, drinking and smoking. ***Methods:*** Data were obtained from the Takashima Stroke Registry, which covers a stable population of roughly 55,000 residents of Takashima County in central Japan. A total of 1,773 stroke cases (men: 943 and women: 830) occurred between 1988 and 2003. We divided the days into 3 groups: 'weekend', 'after weekend' and 'rest of the week', and calculated stroke incidence rates and incidence rate ratios. To identify the effect of conventional risk factors on the variation, proportion of differences between observed and expected stroke incidences were considered. ***Results:*** The stroke incidence for the after weekend group (250.1 per 100,000 person years, 95% CI: 222.0–278.3) was higher than for the other day groups among men. The after weekend increase was observed mainly among older men aged 65 years or more. Among the stroke subtypes, the incidence for cerebral infarction was highest in the after weekend group (857.2, 95% CI: 730.6–983.8) and was 1.37 times (95% CI: 1.12–1.68) higher than in the rest of the week group. Tendency of after weekend increase was observed regardless of the presence or absence of risk factor history. ***Conclusions:*** Week day variation for stroke was observed predominantly among older men regardless of presence and absence of risk factor history. Information about the weekly trend regarding episode of increased stroke incidence can be used as a surrogate predictor for stroke onset and would be helpful in designing more effective insights for preventive strategies.



## Introduction

In the investigation of variation in stroke incidence between days of the week, Monday increase of stroke has been reported in some studies [1–5]. There are also reports of an increased stroke incidence on weekends [6, 7], although other studies found no apparent trend in stroke incidence over the days of the week [8–10]. A study examining the influence of the day of the week of admission on the length of hospital stay in stroke patients reported that patients with ischemic stroke admitted on Tuesdays

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or Wednesdays had the longest length of hospital stay [11]. The immediate circumstances preceding the stroke onset are not that clearly identified. Information about weekly trends of increased stroke incidence can be used as a surrogate predictor of stroke onset and might be helpful in designing more effective prevention strategies.

It is well established that stroke incidence is affected by risk factors such as having hypertension, diabetes or having the habit of smoking or drinking [12–14]. But the relationship of the acute stroke onset to the risk factor history has not been that clearly recognized. Insinuation regarding the influence of risk factors on the available trend may help in identifying people more vulnerable to the week day scenario, thus help in developing specific preventive measures.

In the present study we examined variation in incidence of stroke onset among the days of the week using data from the cardio-cerebrovascular disease registration system. The study also examined the modification of these variations by risk factor histories. We hypothesized that stroke incidence would vary among the days of the week.

## Population and Methods

*Takashima Cardio-Cerebrovascular Disease Registry*

The Takashima Cardio-Cerebrovascular Disease Registry is a disease registration system for stroke and acute myocardial infarction which was established in Takashima County, Shiga, Japan, in 1988. The objective of the registration is to measure trends in the incidence and case fatality of stroke and acute myocardial infarction and to compare these trends both inside and outside of Japan [15, 16].

*Population Characteristics of Registration Area*

Takashima County is located in the rural part of Shiga prefecture in the central part of Japan. The population of Takashima County remained stable over the 16-year study period. It is a farming community with inhabitants mainly classified culturally into the same subgroup with similar standards of living. With an aging populace, the population was 55,451 (men 49.2% and women 50.7%) in the year 2000 [17], with 22.3% of the population aged 65 years or above.

*Case Finding and Registration Process*

Takashima County contains 2 community hospitals and a geriatric hospital. It has been estimated that approximately 98% of all hospital admissions are at these hospitals [15]. The remaining patients are generally seen at 3 tertiary hospitals outside the county but in the same prefecture, which have more sophisticated facilities for advanced treatment. The registered patients included all the residents of the Takashima County who were hospitalized with stroke in the county hospitals. Also included were stroke patients who were residents of Takashima County but visited or were referred to the 3 tertiary hospitals outside the county. We registered all cases that met the inclusion criteria [15, 18] on the basis of the medical records from all the relevant hospitals inside and outside the county and the county ambulance records. Registered stroke patients were monitored annually by death certifications. Original death certificates were examined at the county health center in order to establish the cause of death. Patients' privacy was protected.

*Diagnostic Criteria and Items Registered*

Stroke was defined [15, 18, 19] as sudden onset of neurological symptoms, which continue for a minimum of 24 h or result in death. Early case fatality was defined as patients who died within 28 days of the onset of the stroke event. Diagnosis of stroke type was based on clinical symptoms as well as computed tomography (CT) scans and/or magnetic resonance imaging (MRI). Stroke was classified as cerebral infarction, intracerebral hemorrhage and subarachnoid hemorrhage. For patients who satisfied clinical symptoms of acute stroke but whose type of stroke could not be determined from clinical signs and/or CT scan, MRI was categorized as unclassified stroke. Among the study cases in our registry, 92.9% had CT or MRI performed.

Items recorded at registration of a stroke were the date and the time of the stroke event, the situation and symptoms at the time of the event, the extent of neurological symptoms at the time of the event, clinical observations at the event (blood pressure, presence of atrial fibrillation, level of consciousness, impairment of neurological function), history, family history, smoking history, drinking history, rehabilitation, fatality (within 28 days), cause of death, recurrence in the acute stage, and CT scan or MRI observations. Items investigated in CT scan were the size of regions of low-density absorption in association with cerebral infarction and the size of regions of high-density absorption in association with cerebral hemorrhage.

*Analysis*

Our analysis included all patients from the Takashima registry who suffered their first stroke irrespective of outcome. The present study covered the period from January 1, 1988, to December 31, 2003. Throughout those 16 years (5,844 days, with leap years also taken into account) the daily variation of stroke incidence was examined by comparing the incidence rates among several groups. Days of the week were divided into 3 groups; 'weekend' group (Saturday and Sunday), 'after weekend' group (Monday and Tuesday) and 'rest of the week' group (Wednesday, Thursday and Friday). To examine the age-specific pattern of variation, stroke onset age was categorized into 2 groups; a younger group (up to 64 years) and an older group (65 years and over).

*Statistical Methods*

The incidence rates for stroke and its subtypes were calculated separately for men and women. The incidence rate for stroke per 100,000 person years was analyzed among the 3 groups by gender and age group. To calculate the incidence rate, the total number of stroke events in the relevant fraction was taken as the numerator and person time of each population at risk was taken as the denominator. For example, the stroke incidence rate in the after weekend group was calculated by dividing the total number of stroke events for that group by the person time for that group. Person time of the after weekend group was constructed by multiplying the 16-year population average in Takashima County by the total numbers of Mondays and Tuesdays (1,670 days) in the study period. We determined the 16-year population average by taking the population record of each year for the years 1988–2003 in the relevant group and calculating the average. The result was then multiplied by 100,000 and 365.25 to get the incidence rate of stroke per 100,000 persons per year (person year). Random distribution of stroke events among days of the week and among day groups was analyzed by $\chi^2$ test.

The incidence rate ratio for the groups was calculated using the rest of the week group as the reference group. For example, the incidence rate ratio for the after weekend group was calculated by dividing the incidence rate of the after weekend group by the incidence rate of the rest of the week group.

For all the incidence rates and incidence rate ratios, we calculated 95% confidence intervals (CI) [20].

Day of the week variation of stroke incidence among risk factors (history of hypertension, diabetes, drinking and smoking) was also examined in this study. To study variation by risk factors, the proportion of difference between observed and expected stroke incidence was expressed in percent to identify deviations from the expected average frequencies among the day groups. The proportion (percent) of increase or decrease for stroke events from the weekly average by day group was measured. Among the stroke risk factors in older men, the proportion of missing information was 12.8% for hypertension, 14.8% for diabetes, 26% for drinking and 32.4% for smoking. There was no 'pattern of missing' for this information that could be identified. Thus, the variation of incidence cases among different risk factors was analyzed after excluding the cases with missing information.

All statistical analysis was performed using SPSS version 13.0 (SPSS, Chicago, Ill., USA).

**Table 1.** Characteristics of the stroke cases in the Takashima Disease Registration System, Takashima County, Shiga, Japan, 1988–2003

| Characteristics | Stroke cases | |
|---|---|---|
| | number | percentage |
| Total | 1,773 | |
| Gender | | |
| Men | 943 | 53.2 |
| Women | 830 | 46.8 |
| Age group | | |
| Up to 64 years | 439 | 24.8 |
| 65 years and older | 1,334 | 75.2 |
| Subtype of stroke | | |
| Cerebral infarction | 1,194 | 67.3 |
| Cerebral hemorrhage | 384 | 21.7 |
| Subarachnoid hemorrhage | 169 | 9.5 |
| Unclassified | 26 | 1.5 |
| Presence of risk factor history | | |
| Hypertension | 946 | 53.4 |
| Diabetes | 291 | 16.4 |
| Drinking | 340 | 19.2 |
| Smoking | 436 | 24.6 |

Subtype of stroke: diagnosis based on clinical symptoms as well as CT scans and/or MRI. Presence of risk factor history: based on medical records of the patients for the history of risk factors.

## Results

Table 1 shows the characteristics of the registered stroke cases from 1988 to 2003. A total of 1,773 stroke cases (men: 943, women: 830) occurred during the study period. The average age of the registered patients was 69.4 years in men and 74.5 years in women. There were 1,194 stroke cases (67.3%) classified as cerebral infarction (men: 671, women: 523) and 384 (21.7%) as cerebral hemorrhage (men: 188, women: 196). There were 33 stroke cases (1.9%) that had a history of myocardial infarction.

Table 2 presents the number of stroke incidences for each day of the week by age group, gender and stroke subtype. Analysis by age group showed that men aged 65 years or older had a significant variation of strokes among the days of the week (p = 0.034). In this age group, the highest stroke incidence was observed on Tuesday (117 cases), followed by Monday (109 cases). Analysis of stroke subtype in older men showed a significant variation for cerebral infarction events among the days of the week (p = 0.047). For cerebral infarction, the highest stroke incidence (88 cases) was observed on both Monday and Tuesday.

Table 3 shows the incidence rates of stroke and its subtypes among the day groups. The incidence rate of stroke in the after weekend group (212.4 per 100,000 person years, 95% CI: 194.2–230.6) was higher than in the other 2 day groups. Among men, the incidence rate of stroke was highest in the after weekend group (250.1, 95% CI: 222.0–278.3). Analysis by age group showed significant variation of stroke events among day groups (p = 0.002) for older men. In the older men, a higher incidence rate in the after weekend group (1,100.7, 95% CI: 957.2–1,244.2) was observed in comparison to the other 2 groups. Analysis of stroke subtype among older men showed significant variation for cerebral infarction events among day groups (p = 0.006). For cerebral infarction a higher incidence rate was observed for the after weekend group (857.2, 95% CI: 730.6–983.8) among older men. In women aged 65 years or more, a higher incidence of cerebral infarction was seen in the rest of the week group (487.8, 95% CI: 421.4–554.3) in comparison to the after weekend group (462.9, 95% CI: 383.6–542.2) and the weekend group (413.4, 95% CI: 338.5–488.3).

**Table 2.** Number of strokes on each day of the week by age group, gender and subtype of stroke in the Takashima Registration System (1988–2003), Shiga, Japan

| Gender and type of stroke | Weekdays | | | | | | | Total | p value |
|---|---|---|---|---|---|---|---|---|---|
| | Saturday | Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | | |
| *Up to 64 years* | | | | | | | | | |
| Men | | | | | | | | | |
| All stroke | 37 | 48 | 39 | 39 | 43 | 47 | 38 | 291 | 0.82 |
| CI | 18 | 32 | 22 | 25 | 27 | 25 | 19 | 168 | 0.44 |
| CH | 9 | 11 | 13 | 9 | 12 | 16 | 11 | 81 | 0.79 |
| SAH | 9 | 5 | 4 | 3 | 4 | 6 | 7 | 38 | 0.57 |
| Unclassified | 1 | – | – | 2 | – | – | 1 | 4 | – |
| Women | | | | | | | | | |
| All stroke | 26 | 24 | 15 | 17 | 22 | 19 | 25 | 148 | 0.53 |
| CI | 14 | 10 | 5 | 6 | 13 | 10 | 10 | 68 | 0.34 |
| CH | 5 | 8 | 7 | 9 | 6 | 5 | 10 | 50 | 0.78 |
| SAH | 6 | 6 | 3 | 2 | 3 | 4 | 5 | 29 | 0.73 |
| Unclassified | 1 | – | – | – | – | – | – | 1 | – |
| *65 years and older* | | | | | | | | | |
| Men | | | | | | | | | |
| All stroke | 83 | 83 | 109 | 117 | 90 | 92 | 78 | 652 | 0.03 |
| CI | 66 | 69 | 88 | 88 | 72 | 66 | 54 | 503 | 0.04 |
| CH | 14 | 11 | 11 | 18 | 13 | 21 | 19 | 107 | 0.38 |
| SAH | 2 | 2 | 6 | 9 | 4 | 3 | 4 | 30 | 0.18 |
| Unclassified | 1 | 1 | 4 | 2 | 1 | 2 | 1 | 12 | – |
| Women | | | | | | | | | |
| All stroke | 92 | 98 | 102 | 87 | 90 | 104 | 109 | 682 | 0.67 |
| CI | 52 | 65 | 74 | 57 | 64 | 67 | 76 | 455 | 0.34 |
| CH | 28 | 21 | 16 | 16 | 18 | 31 | 16 | 146 | 0.08 |
| SAH | 11 | 8 | 11 | 14 | 8 | 5 | 15 | 72 | 0.29 |
| Unclassified | 1 | 4 | 1 | – | – | 1 | 2 | 9 | – |

CI = Cerebral infarction; CH = cerebral hemorrhage; SAH = subarachnoid hemorrhage. p value: random distribution of stroke incidence among the days of the week was tested by $\chi^2$ analysis.

Table 4 illustrates the incidence rate ratios for stroke and its subtypes among the day groups. Men had a stroke incidence rate ratio of 1.17 (95% CI: 1.01–1.37) for the after weekend group in comparison to the rest of the week group. For cerebral hemorrhage the incidence rate ratio between the after weekend and rest of the week groups was 1.27 (95% CI: 1.06–1.51). The incidence rate ratios for cerebral infarction among men aged 65 years or more for the after weekend group was 1.37 times (95% CI: 1.12–1.68) higher than for the rest of the week group. For women aged 65 years or more and for younger men and women no significant difference was observed among day groups. For stroke due to cerebral hemorrhage and subarachnoid hemorrhage, no apparent trend was observed among day groups.

Figure 1 shows the proportion of difference between observed and expected number of stroke among the day of the week groups for older men in the absence of risk factor history; hypertension, diabetes mellitus, drinking and smoking. Figure 2 illustrates the proportion of difference in the presence of the risk factor histories. Regardless of the presence or absence of the risk factor history an apparent trend of increased stroke incidence in the after weekend group was observed. Among women and subjects in the younger age category no apparent trend was found.

## Discussion

The present study examined the day of the week variation of stroke incidence from registration data. After weekend, increase in incidence of cerebral infarction was observed among subjects aged 65 years or more, espe-

**Table 3.** Incidence rate per 100,000 person years based on 1,773 registered stroke cases in the day of the week groups by subtype, age group and gender in the Takashima Registration System 1988–2003, Shiga, Japan

| Age | Gender | Weekend | 95% CI | After weekend | 95% CI | Rest of the week | 95% CI |
|---|---|---|---|---|---|---|---|
| *All stroke* | | | | | | | |
| All ages | men | 206.5 | 181.0–232.1 | 250.1 | 222.0–278.3 | 212.9 | 191.7–234.1 |
| | women | 191.0 | 166.9–215.2 | 175.9 | 152.7–199.1 | 195.9 | 175.9–215.9 |
| | all | 198.6 | 181.1–216.2 | 212.4 | 194.2–230.6 | 204.3 | 189.7–218.8 |
| Up to 64 years | men | 84.2 | 66.3–102.0 | 77.2 | 60.1–94.4 | 84.5 | 69.9–99.2 |
| | women | 51.4 | 37.1–65.6 | 32.9 | 21.5–44.3 | 45.2 | 34.3–56.1 |
| | all | 68.1 | 56.6–79.5 | 55.5 | 45.1–68.8 | 65.2 | 56.1–74.4 |
| 65 years and older | men | 808.5 | 685.5–931.5 | 1,100.7 | 957.2–1,244.2 | 844.5 | 741.9–947.2 |
| | women | 671.4 | 575.9–766.8 | 667.8 | 572.6–763.1 | 714.1 | 633.7–794.5 |
| | all | 729.0 | 653.3–804.8 | 849.9 | 768.1–931.6 | 768.9 | 705.4–832.4 |
| *Cerebral infarction* | | | | | | | |
| All ages | men | 152.2 | 130.3–174.2 | 183.5 | 159.4–207.6 | 144.3 | 126.9–161.8 |
| | women | 112.2 | 93.7–130.8 | 113.0 | 94.4–131.6 | 127.4 | 111.3–143.5 |
| | all | 131.9 | 117.6–146.2 | 147.7 | 132.5–162.8 | 135.7 | 123.9–147.6 |
| Up to 64 years | men | 49.5 | 35.8–63.2 | 46.5 | 33.2–59.8 | 46.9 | 36.0–57.8 |
| | women | 24.7 | 14.8–34.5 | 11.3 | 4.6–18.0 | 22.6 | 14.9–30.3 |
| | all | 37.3 | 28.8–45.8 | 29.2 | 21.7–36.8 | 35.0 | 28.2–41.7 |
| 65 years and older | men | 657.5 | 546.6–768.4 | 857.2 | 730.6–983.8 | 623.7 | 535.4–711.9 |
| | women | 413.4 | 338.5–488.3 | 462.9 | 383.6–542.2 | 487.8 | 421.4–554.3 |
| | all | 516.1 | 452.3–579.8 | 628.7 | 558.4–699.0 | 544.9 | 491.5–598.4 |
| *Cerebral hemorrhage* | | | | | | | |
| All ages | men | 37.0 | 26.2–47.8 | 42.0 | 30.4–53.5 | 50.5 | 40.2–60.8 |
| | women | 49.3 | 37.1–61.6 | 38.2 | 27.4–49.0 | 45.7 | 36.0–55.3 |
| | all | 43.3 | 35.1–51.5 | 40.1 | 32.2–47.9 | 48.0 | 41.0–55.1 |
| Up to 64 years | men | 19.8 | 11.1–28.5 | 21.8 | 12.7–30.9 | 25.8 | 17.7–33.3 |
| | women | 13.4 | 6.1–20.6 | 16.4 | 8.4–24.5 | 14.4 | 8.2–20.5 |
| | all | 16.6 | 11.0–22.3 | 19.2 | 13.1–25.3 | 20.2 | 15.1–25.3 |
| 65 years and older | men | 121.8 | 74.0–169.5 | 141.2 | 89.8–192.6 | 172.2 | 125.8–218.6 |
| | women | 173.1 | 124.7–221.6 | 113.1 | 73.9–152.3 | 153.2 | 115.9–190.4 |
| | all | 151.5 | 117.0–186.1 | 124.9 | 93.6–156.3 | 161.2 | 132.1–190.2 |
| *Subarachnoid hemorrhage* | | | | | | | |
| All ages | men | 14.8 | 8.0–21.7 | 18.1 | 10.5–26.7 | 15.4 | 9.7–21.1 |
| | women | 24.7 | 16.0–33.4 | 23.9 | 15.3–32.4 | 21.2 | 14.7–27.8 |
| | all | 19.8 | 14.3–25.4 | 21.0 | 15.3–26.8 | 18.3 | 14.0–22.7 |
| Up to 64 years | men | 13.9 | 6.6–21.1 | 6.9 | 1.8–12.1 | 11.2 | 5.9–16.6 |
| | women | 12.3 | 5.4–19.3 | 5.1 | 0.6–9.6 | 8.2 | 3.5–12.9 |
| | all | 13.1 | 8.1–18.1 | 6.1 | 2.6–9.5 | 9.8 | 6.2–13.3 |
| 65 years and older | men | 19.5 | 0.39–38.6 | 73.1 | 36.1–110.0 | 35.7 | 14.6–56.8 |
| | women | 67.1 | 36.9–97.3 | 88.3 | 53.7–123.0 | 66.0 | 41.5–90.4 |
| | all | 47.1 | 27.9–66.3 | 81.9 | 56.5–107.3 | 53.3 | 36.5–70.0 |

Weekend: Saturday and Sunday; after weekend: Monday and Tuesday; rest of the week: Wednesday, Thursday and Friday.

cially in men. This pattern seemed to hold regardless of presence and absence of traditional risk factors: hypertension, diabetes, smoking and drinking.

No apparent trend in stroke variation among the days of the week was observed in men in the younger age category. However, younger men should have external triggering factors similar to those in the older men. Absence of any apparent trend in younger men may be attributed to 2 possible reasons. First, the smaller number of cases in the younger-age group may account for the failure to

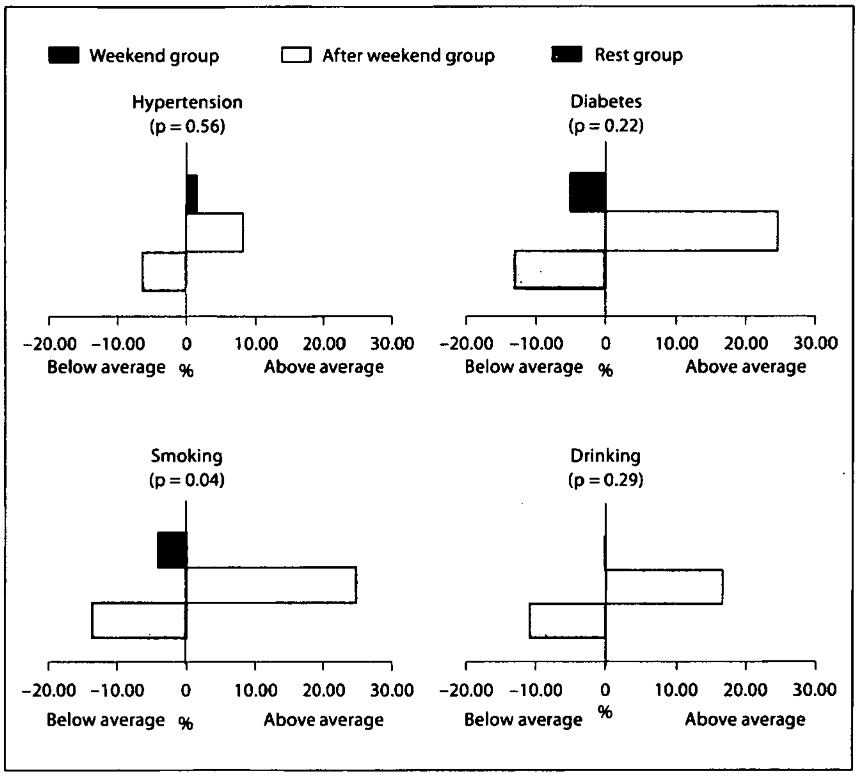


**Fig. 1.** Four separate figures are presented for the proportion of difference (percent) between the observed stroke incidence and the expected incidence stratified by the absence of history of hypertension, diabetes, smoking and drinking (men 65 years or older). The $\chi^2$ p values are for the distribution of stroke events among the day groups. Takashima Disease Registration System, Takashima County, Shiga, Japan, 1988–2003.

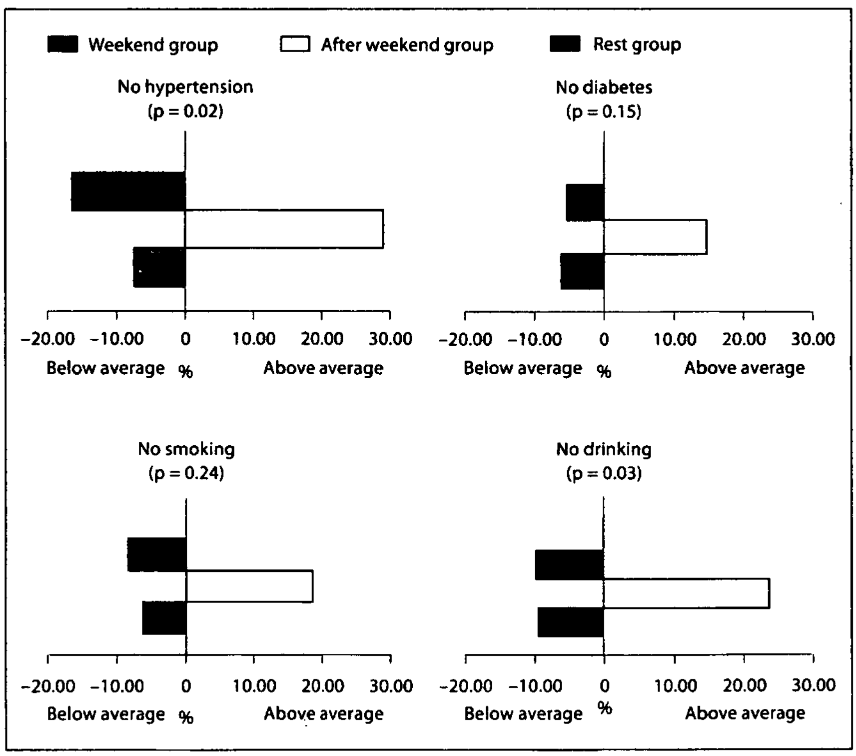


**Fig. 2.** Four separate figures are presented for the proportion of difference (percent) between the observed stroke incidence and the expected incidence stratified by the presence of history of hypertension, diabetes, smoking and drinking (men 65 years or older). The $\chi^2$ p values are for the distribution of stroke events among the day groups. Takashima Disease Registration System, Takashima County, Shiga, Japan, 1988–2003.

**Table 4.** Incidence rate ratios of stroke in the after weekend and weekend groups compared with the rest of the week group by stroke subtype, age group and gender in the Takashima Registration System 1988–2003, Shiga, Japan

| Age | Gender | Incidence rate ratio | | | | |
|---|---|---|---|---|---|---|
| | | weekend | 95% CI | after weekend | 95% CI | rest of the week |
| *All stroke* | | | | | | |
| All ages | men | 0.97 | 0.83–1.14 | 1.17 | 1.01–1.37 | 1 |
| | women | 0.98 | 0.83–1.15 | 0.90 | 0.76–1.06 | 1 |
| | all | 0.97 | 0.87–1.09 | 1.04 | 0.93–1.16 | 1 |
| Up to 64 years | men | 0.99 | 0.65–1.52 | 0.91 | 0.59–1.41 | 1 |
| | women | 1.14 | 0.64–2.01 | 0.73 | 0.38–1.38 | 1 |
| | all | 1.04 | 0.83–1.30 | 0.85 | 0.67–1.07 | 1 |
| 65 years and older | men | 0.96 | 0.71–1.29 | 1.30 | 0.99–1.72 | 1 |
| | women | 0.94 | 0.71–1.24 | 0.94 | 0.71–1.24 | 1 |
| | all | 0.95 | 0.83–1.08 | 1.11 | 0.97–1.25 | 1 |
| *Cerebral infarction* | | | | | | |
| All ages | men | 1.05 | 0.87–1.27 | 1.27 | 1.06–1.51 | 1 |
| | women | 0.88 | 0.71–1.08 | 0.89 | 0.72–1.09 | 1 |
| | all | 0.97 | 0.85–1.12 | 1.09 | 0.95–1.25 | 1 |
| Up to 64 years | men | 1.06 | 0.73–1.52 | 0.99 | 0.69–1.43 | 1 |
| | women | 1.09 | 0.64–1.84 | 0.49 | 0.25–0.99 | 1 |
| | all | 1.06 | 0.79–1.44 | 0.84 | 0.61–1.15 | 1 |
| 65 years and older | men | 1.05 | 0.85–1.31 | 1.37 | 1.12–1.68 | 1 |
| | women | 0.84 | 0.68–1.06 | 0.95 | 0.76–1.18 | 1 |
| | all | 0.95 | 0.81–1.11 | 1.15 | 0.99–1.34 | 1 |
| *Cerebral hemorrhage* | | | | | | |
| All ages | men | 0.73 | 0.51–1. 04 | 0.83 | 0.59–1.17 | 1 |
| | women | 1.08 | 0.78–1.50 | 0.84 | 0.59–1.19 | 1 |
| | all | 0.90 | 0.70–1.15 | 0.83 | 0.65–1.06 | 1 |
| Up to 64 years | men | 0.77 | 0.45–1.32 | 0.85 | 0.50–1.43 | 1 |
| | women | 0.93 | 0.46–1.85 | 1.14 | 0.60–2.19 | 1 |
| | all | 0.82 | 0.53–1.26 | 0.95 | 0.63–1.43 | 1 |
| 65 years and older | men | 0.71 | 0.44–1.14 | 0.82 | 0.52–1.29 | 1 |
| | women | 1.13 | 0.78–1.64 | 0.74 | 0.48–1.13 | 1 |
| | all | 0.94 | 0.70–1.26 | 0.78 | 0.57–1.06 | 1 |
| *Subarachnoid hemorrhage* | | | | | | |
| All ages | men | 0.96 | 0.53–1.74 | 1.18 | 0.67–2.06 | 1 |
| | women | 1.16 | 0.73–1.86 | 1.12 | 0.70–1.81 | 1 |
| | all | 1.08 | 0.75–1.56 | 1.15 | 0.80–1.65 | 1 |
| Up to 64 years | men | 1.23 | 0.61–2.50 | 0.62 | 0.26–1.49 | 1 |
| | women | 1.50 | 0.67–3.34 | 0.62 | 0.22–1.77 | 1 |
| | all | 1.34 | 0.79–2.28 | 0.62 | 0.32–1.22 | 1 |
| 65 years and older | men | 0.55 | 0.17–1.71 | 2.04 | 0.94–4.45 | 1 |
| | women | 1.02 | 0.57–1.82 | 1.34 | 0.78–2.30 | 1 |
| | all | 0.88 | 0.53–1.48 | 1.54 | 0.99–2.39 | 1 |

Weekend: Saturday and Sunday; after weekend: Monday and Tuesday; rest of the week: Wednesday, Thursday and Friday.