In Incidence of Stroke in Shibata, Japan: 1976-1978

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SUMMARY A stroke registry was established in Shibata City, Niigata Prefecture, Japan (population 75,000) in 1976. WHO recommendations for criteria were followed. This paper reports stroke incidence for the initial 3 years of the registry: 1976 through 1978. All living patients were examined clinically by a staff physician. Only patients with a diagnosis of first stroke were included in the study. Sensitivity of the referral system was estimated at 85 + %, comparable to that in American studies.

Average annual incidence per 1,000 residents ≥20 years was 2.61 for all strokes (3.42 for males; 1.88 for females), 0.20 for subarachnoid hemorrhage, 0.61 for cerebral hemorrhage, 1.51 for cerebral infarction — rates similar to those reported 10-20 years previously for the United States.

The male-female ratio, 2:1, reflected a high rate among males, low among females. Rates among Shibata males were higher than 1972 U.S. rates reported by the Epidemiologic Study Group; rates among Shibata females were lower than corresponding U.S. rates.

Incidence of all strokes combined increased with age, the age relationship being strongest for cerebral infarction. No subarachnoid hemorrhage was observed in Shibata residents ≥70 years of age.

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STROKE has been the leading cause of death in Japan since 1951. According to international comparisons, Japan has the highest mortality rate from stroke of any developed country. Because mortality rates can be affected by factors such as access to medical care and survival, incidence is a more reliable measure of frequency. There have been few reports, however, on the incidence of stroke in Japan. Incidence rates would be helpful for studying the natural history of the disease and for developing appropriate health care facilities. To meet this need, a stroke registry was developed in Shibata, Niigata Prefecture, Japan, beginning in 1976. This paper presents data from the stroke registry during the initial 3-year period and compares the incidence rate in Shibata with incidence rates recorded from other areas of Japan and from the United States.

Methods

Study Population

Shibata was selected as the city in which to develop a registry because Niigata Prefecture has one of the highest age-adjusted death rates from stroke in Japan. The city of Shibata covers an area of 434 square kilometers and is located in the northern part of the prefecture (fig. 1). Shibata includes a central commercial residential area surrounded by an agricultural rice-producing area. Most of the householders in the commercial residential area are salaried employees. Thirty percent of them are engaged in commerce, 20% in manufacturing, 20% in services, and 10% in construction. The majority of the families in the rice-producing area are farmers who supplement their income with part-time jobs in other occupations.

The population of Shibata was 75,168 persons on July 1, 1977. This represents the midpoint of the observation period from 1976 through 1978 (table 1). The population of Shibata is relatively stable, with the natural increases and decreases balancing one another. More than 10% (10.4%) of the population was 65 years or older compared with 8.4% for Japan as a whole. For the purposes of this paper, only those individuals over the age of 20 are considered to be the population at risk; this included 25,127 males and 27,844 females.

Case Ascertainment

The Shibata stroke registry was established in the Department of Public Health, City of Shibata, January 1, 1976. The methods used for the development of the stroke registry were those outlined by the WHO study.

Because many stroke patients, particularly elderly ones, are traditionally cared for at home in the Shibata area, an extensive system was employed for identifying stroke patients. Suspected patients were referred to the stroke registry by all general practitioners in the Shibata area (29 clinics with beds and 23 clinics without beds) and by the Niigata Prefectural Shibata Hospital (the only general hospital in the city), a private mental hospital, and a nursing home. Patients were also referred by the 12 visiting public health nurses, by a layman's association for stroke control, and by the nearby Kita-Kambara County
Hospital in Suibara. The records of the Division of Emergency Services of the Shibata Fire Department and the social insurance records were also regularly reviewed by a staff physician. Information about fatal strokes was obtained by review of all death certificates, with supplementary clinical data obtained from the certifying physicians. The majority of the middle-aged patients were examined by neurologists from the Niigata Prefectural Shibata Hospital or the Kita-Kambara County Hospital.

Verification of Diagnosis

All patients who were alive at the time of referral to the study were examined by a staff physician, and their clinical histories were reviewed. If the patient was dead at the time of the referral, a member of the study staff collected clinical information from the relatives of the patient and the certifying physician.

All patient information was entered into a standardized record form which was adapted from the standard WHO form.*• Information collected included identifying information, personal health status prior to stroke, family history, previous medical history, self-care status prior to stroke, early stages of the present attack, clinical state at time of maximal impairment, clinical and laboratory findings at the first medical examination, treatment received prior to the present stroke, physical performance at work, dietary habits, smoking habits, alcohol ingestion, etc. This information and the results of the examination and review of the hospital and general practitioner's records were considered by 3 staff physicians to determine if the patient met the criteria as a stroke case. An attempt was made to diagnose the stroke according to anatomical type (subarachnoid or cerebral hemorrhage, cerebral infarction, or undetermined type).

Definition and Classification of Stroke

All strokes were categorized into the various subtypes primarily by the clinical judgment of the staff physicians according to the criteria of Millikan, the World Health Organization, Okinaka, and the Japanese Association for Cerebro-Cardiovascular Disease Control. For 40.2% of the cases (54.8% of subarachnoid hemorrhages, 48.5% of cerebral hemorrhages, 42.1% of cerebral infarctions, and 4.3% of strokes of undetermined type), laboratory information, including results of computerized axial tomography, angiography, electroencephalography, brain scan, echoencephalography, and lumbar puncture were available. Autopsy data were available only for 9.4% of the 244 fatal cases.

Stroke was defined by the occurrence of rapidly developing clinical signs of focal or global disturbances of cerebral function which lasted more than 24 hours or resulted in death for which there was no apparent cause other than a vascular accident.*•* Transient episodes of cerebral ischemia were excluded by definition.

Stroke was subclassified according to the following criteria:

Subarachnoid Hemorrhage. The sudden onset of very severe headache with only a relatively momentary disturbance of consciousness, signs of meningeal irritation, the absence of focal neurological signs, subhyaloid hemorrhage, and the presence of blood in the cerebrospinal fluid.

Cerebral Hemorrhage. The rapid evolution of focal neurological signs, rapid progression to coma, signs of meningeal irritation, elevated blood pressure, headache, and frequently blood-stained cerebrospinal fluid.

Cerebral Infarction. A slow, gradual development of focal neurological signs lasting more than 24 hours, relative preservation of consciousness, elevated blood pressure, and the absence of blood in the cerebrospinal fluid. This category included cerebral embolus with a sudden onset of focal neurological symptoms and evidence of emboli.

### Table 1 Population by Sex and Age, City of Shibata, Niigata Prefecture, Japan (January 1, 1977)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Sex</th>
<th>≤ 19</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>≥ 80</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>36,621</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11,494</td>
<td>5,711</td>
<td>5,098</td>
<td>5,600</td>
<td>3,939</td>
<td>2,878</td>
<td>1,527</td>
<td>374</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>10,703</td>
<td>5,468</td>
<td>5,072</td>
<td>6,081</td>
<td>4,779</td>
<td>3,620</td>
<td>2,122</td>
<td>702</td>
<td>38,547</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>22,197</td>
<td>11,179</td>
<td>10,170</td>
<td>11,681</td>
<td>8,718</td>
<td>6,498</td>
<td>3,649</td>
<td>1,096</td>
<td>75,168</td>
</tr>
</tbody>
</table>
**Undetermined Type.** A history of onset and residual deficit sufficiently well documented to ensure a high probability that stroke had occurred but incomplete clinical data to further subcategorize the type of stroke.¹⁴

**Results**

From January 1, 1976, through December 31, 1978, a total of 744 individuals were referred to the registry with a suspected stroke. One hundred sixty-eight of these persons had had onset of their stroke before the observation period began. An additional 161 had nonvascular intracranial lesions on further examination. Thus, a total of 415 patients (258 men and 157 women) were identified as having a new stroke during the study period.

The age-sex distribution and average annual incidence by decade of age is given in table 2. The incidence of stroke was higher among men in each age group for each of the major types. Although the incidence of cerebral infarction increased with age, the rate of cerebral hemorrhage declined slightly in the oldest age group. The incidence of subarachnoid hemorrhage increased with age until age 69, and that of cerebral hemorrhage until age 79 years. No subarachnoid hemorrhage was observed in residents above 69 years of age.

Seven and one-half percent of all strokes met the criteria for subarachnoid hemorrhage, 23.4% for cerebral hemorrhage, 57.8% for cerebral infarction, and in 11.3% anatomic type could not be determined. The corresponding rates were 0.20 per 1,000 population ≥20 years of age for subarachnoid hemorrhage, 0.61 per 1,000 for cerebral hemorrhage, and 1.51 per 1,000 for cerebral infarction.

Fifty-three percent of the male patients and 68.2% of the females died during the study period. The case fatality during the study period was 54.8% for subarachnoid hemorrhage, 72.2% for cerebral hemorrhage, 53.8% for cerebral infarction, and 59.6% for stroke of undetermined type.

To determine the proportion of cases of all strokes in the community that were being reported to the registry, 2 substudies were made: 1) an intensive survey of 2 subdivisions of Shibata and 2) a case-control study.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Number of Cases and Average Annual Incidence of Stroke Subtype per 1,000 Population Aged 20 Years and Older, Shibata, 1976-1978</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subtype</strong></td>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>Total</td>
<td>No.</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>Total</td>
<td>No.</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>Total</td>
<td>No.</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>Stroke of undetermined type</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>Total</td>
<td>No.</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>All strokes</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
<tr>
<td>Total</td>
<td>No.</td>
</tr>
<tr>
<td></td>
<td>Rate</td>
</tr>
</tbody>
</table>
comparison of the accuracy of clinical diagnosis of patients admitted to a special hospital for stroke in Osaka, Japan.

A survey was carried out in 2 of the 9 governmental subdivisions of the City of Shibata in 1976. The 2 divisions selected had a combined population of 4,027 residents ≥20 years of age. In these 2 subdivisions 84.2% of the men and 92.8% of the women underwent the screening examination. A member of the staff visited the homes of the non-respondents to detect missing patients. Thirteen stroke cases were identified in these 2 subdivisions. Of these, 11 had been included in the registry. The 2 additional patients found on the survey had developed slight neurological signs lasting a few days. Both had been seen only by a general practitioner. A special screening examination and a follow-up neurological examination, which included computerized axial tomography, revealed a small cerebral infarction in both individuals. Thus, the estimated proportion of living cases identified by the registry was 85% (11 of 13). All deaths were identified by physician reports plus review of death certificates, so that the sensitivity of the referral system for all strokes was probably considerably higher than 85%.

The second technique for estimating the sensitivity and specificity of clinical diagnosis — which was the basis of the reporting system for the registry — was to carry out a special case-control study on 143 stroke patients and 48 non-stroke patients admitted to a special hospital for stroke in Osaka, Japan. The subjects were assigned a diagnosis on the basis of clinical information only. This diagnosis was then compared to the diagnosis of the same individual following completion of computerized axial tomography, lumbar puncture, angiography, electroencephalography, brain scan, and echocardiography. Ninety-seven percent of the patients were confirmed as having stroke by laboratory studies and 98% of those confirmed as not having had a stroke had been so designated by clinical diagnosis. Of the 19 subarachnoid hemorrhages, 68.4% were diagnosed correctly using clinical judgment alone, as were 86.0% of the 50 cerebral hemmorhages and 82.4% of the 74 cerebral infarctions.

These 2 studies suggest that the referral system for the registry identified most cases and that the clinical judgment of physicians was adequate to identify stroke cases although the original sub-classification of stroke type by the referring physician may not have been accurate.

Discussion

There has been considerable discussion in the literature about the accuracy of the determination of stroke frequency in Japan. Goldberg and Kurland have raised questions as to the diagnostic accuracy of stroke in Japan, and Kurtzke has suggested that high mortality may be an artifact due to differences in assignment of cases to diagnostic categories. Consequently, the authors in this study have estimated the incidence of stroke by subtype in a well-defined population in Japan, using the methods advocated by the World Health Organization.

According to a survey of epidemiologic studies of stroke conducted by the American Heart Association, the majority of epidemiologic studies in the United States have ascertained cases from hospital records, reports of attending physicians or patients, and death certificates, and have also included an examination by the study physician. We have included these sources of case ascertainment and have, in addition, examined all living patients within 3 weeks of occurrence of stroke. Further, we have included the results of computerized axial tomography. Very few of the American studies were successful in examining their patients within 3 weeks of occurrence and in including diagnostic procedures, such as cerebrospinal puncture, electroencephalography, and angiography. We used the same definition and classification of stroke as those employed by the American studies, but many of these studies also identified cases with transient ischemic attacks.

The completeness of ascertainment rested primarily on the cooperation of general practitioners and hospital physicians in Shibata and the surrounding areas. Fortunately, these individuals were very helpful in working with us throughout the study period. For example, 226 of the 238 individuals referred to the registry as having had a suspected stroke in 1976 were identified by these physicians, although in many cases duplicate referrals of these same patients were made by other sources. None of the physicians in the area refused to cooperate in the study. The sensitivity of the referral system for living patients was estimated to be at least 85%.

In epidemiologic studies, the antemortem diagnosis of stroke rests primarily on evaluation of signs and symptoms rather than on the results of laboratory examination. Sixty percent of the stroke cases seen in our study were diagnosed primarily on the basis of clinical judgment. Because autopsies are very difficult to obtain in Japan, a comparison of the clinical judgment was made with the results of computerized axial tomography. The sensitivity and specificity of clinical judgment for stroke estimated from the sub-study in Osaka was high (97%, 98%, respectively). The rates of agreement by type of stroke were also acceptable. It should be noted, however, that computerized axial tomography remains normal in the majority of individuals with cerebral infarction for as long as 8 to 24 hours after occurrence, and that it does not distinguish well between cerebral hemorrhage and cerebral infarction in their later stages.

Results of a study comparing clinical judgment to autopsy diagnosis in Japan indicated a correct diagnosis in 80% of 15 subarachnoid hemorrhages, 71% of 73 cerebral hemorrhages, and 83% of 47 cerebral infarctions. Katsuki, in a similar study, reported that the clinical diagnosis was in agreement with results of autopsies for 86% of subarachnoid hemorrhages, 70% of cerebral hemorrhages, and 85% of cerebral infarctions. No comparable epidemiologic studies have been reported for the United States.

Thus, the cooperation of the medical community, the case ascertainment, and the close agreement
between clinical diagnosis and diagnosis of stroke made by computerized axial tomography suggest that our study was at least as sensitive and specific as similar American studies.

Many investigators continue to use mortality data to make comparisons of stroke rates between countries. Death is a reasonable surrogate for incidence, however, only when the interval between occurrence and death is short and the disease has a high case fatality rate. Ascertainment of the one-year survival rate for stroke from the Middlesex study, the middle-Missouri study, the Rochester study, and our own preliminary study indicate that the one-year survival rate is relatively high and the case fatality rate low. Thus, stroke does not meet the major criteria for substitution of death rate for incidence.

We have attempted to compare the incidence derived from our study in Shibata with incidence rates for other communities. There are often differences, however, in the method of the ascertainment, definition and classification of stroke, and in the reporting of age-specific incidences. We have compared the results of the Shibata study with those of 2 studies in Japan which used comparable methodology. Koijima, in cooperation with Komachi et al., determined the incidence of stroke in 3 rural communities in Akita Prefecture from 1964 to 1969 and in 2 urban areas of Osaka Prefecture from 1963 to 1968. The age-, sex-adjusted incidence of stroke in individuals ≥30 years of age, using the census population of the United States in 1970, was estimated to be 8.09 per 1,000 for Akita, 4.30 for Osaka, and 3.80 for Shibata. Although this would suggest that the rate in Shibata is the lowest of the 3, a decreasing trend in incidence of all stroke has been reported for several Japanese communities from which reliable data have been recorded. The age-adjusted death rate has been noted to have decreased by 40% in Akita Prefecture, by 35% in Niigata Prefecture in which Shibata is located, and by 25% in Osaka Prefecture. Thus, the rate noted in Shibata for 1976–1978 may be comparable to the rates for Akita and Osaka for the current time period.

In the United States, the studies by Matsumoto, Alter, Eisenberg, Eckstrom, and their respective colleagues found that the rates, when age-sex-adjusted to the population of the United States in 1970 were 4.40 per 1,000 population ≥35 years of age in Rochester, Minnesota, for the period 1955–1967; 6.34 per 1,000 in Fargo, North Dakota, and Moorhead, Minnesota, for the period 1965–1966; 5.07 per 1,000 in Middlesex, Connecticut, for the period 1957–1958; and 4.10 per 1,000 in 3 mid-Missouri counties for the period 1964–1965. Although these rates appear to be similar to the rate (4.22 per 1,000) reported for Shibata in 1976–1978, a decline over the last several decades has been noted in both incidence and mortality rates for all strokes in the United States.

The Epidemiology Study Group of the Joint Committee for Stroke Facilities (Chairman: R. A. Stallones), in 1972, estimated the minimum, midpoint, and maximum age-specific incidences for stroke in the United States. These rates are compared with the age-specific incidences for Shibata in figure 2. The age-specific rates are highest among males in Shibata, but the rates for females in Shibata were lower than those reported for U.S. females by the Epidemiology Study Group.

Kagan et al. have reported that the mortality, incidence, and prevalence rates for stroke are higher in Japan than in the United States, even when the comparison is restricted to individuals of Japanese ancestry. Owada et al. have reported the same conclusion in comparison with the European countries and the United States. A WHO study has indicated that Japan and Finland have the highest age-specific incidences.

Few data are available as to the incidence of stroke by subtype. The percent distribution of stroke by subtype has been compared among Shibata, Rochester, Fargo-Moorhead, and the reports of Kurtzke and the Epidemiology Study Group which used data from several community-based studies in the United States. The proportion of cerebral hemorrhage was higher in Shibata than in the United States. A WHO study also reported a higher proportion of cerebral hemorrhage in Japan than in other countries. Some investigators have reported that cerebral hemorrhage may be overdiagnosed at the expense of cerebral infarction, particularly in Japan. The comparison of our clinical judgments and the results of computerized axial tomography diagnosis, however, indicated that cerebral hemorrhage was incorrectly diagnosed as cerebral infarction in 10.0% of cases, whereas the reverse occurred in 10.8% of cases.

The age-specific incidence for stroke rose with age. The incidence was greatest for cerebral infarction and least for subarachnoid hemorrhage. These findings are consistent with those of other investigators. In the absence of birth cohort analysis, stroke has been considered a concomitant of aging and thus preventable only to the extent that we can reverse the aging process. Results of the recent High Blood Pressure Detection and Follow-up Program in the United States have, however, suggested that the age-specific attack rates of stroke can be decreased by intensive treatment of hypertension.

The age-adjusted incidence ratio of males to females was 2.1 among persons ≥35 years of age in Shibata as compared to 1.6 for the Rochester study, 1.1 for the Middlesex study, 1.3 for whites in mid-Missouri, and 1.1 for the Fargo-Moorhead study. Although all these studies have identified a higher incidence among males, the reason for the markedly higher ratio in Shibata is unknown.

The age-sex-adjusted incidence of stroke in Shibata between 1976 and 1978 is similar to the rates for several American communities 10 to 20 years earlier, although higher rates are observed among males in Shibata compared to the rates estimated for U.S. males. Mortality rates in both countries have declined, suggesting that the incidence of stroke may be declining in both countries. In fact, a decreasing
Figure 2. Comparison of stroke incidence in Shibata, 1976–1978, with estimated rates in U.S.A.

Trend in incidence of stroke has been observed in a few communities from both countries. Further studies will be required to determine whether the absolute magnitude of the difference in incidence between Japan and the United States is continuing at the same level or changing.

Acknowledgment

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