Incidence of Aneurysmal Subarachnoid Hemorrhage in Shimokita, Japan, From 1989 to 1998

Hiroki Ohkuma, MD; Seiichiroh Fujita, MD; Shigeharu Suzuki, MD

Background and Purpose—The incidence of subarachnoid hemorrhage (SAH) has been investigated in many studies. A recent study in Izumo, Japan, indicates that the incidence of SAH is as high as that in Finland. The purpose of this study was to confirm the high incidence of SAH in Japan.

Methods—The incidence rate of SAH was investigated from 1989 through 1998 in the Shimokita peninsula, which is a clearly defined closed-boundary area in northern Japan with a population of 89 991. The registration was based on the complete referral system of SAH patients. All cases suspected of SAH underwent CT scan, and the images were referred to stroke specialists. The moribund cases and dead-on-arrival cases suspected of SAH also underwent CT scan.

Results—From 1989 through 1998, 198 cases were diagnosed as having aneurysmal SAH. Out of these, 26 cases were moribund or dead when the initial CT scan was performed. The age-adjusted annual incidence of SAH was 21 per 100 000 person-years. The age and sex distribution of the cases indicated that the incidence plateaued after age 45 in men and the incidence increased after age 45 and reached the peak after 75 years in women.

Conclusions—The high incidence of SAH in Japan is confirmed. The incidence of SAH obtained in this study is near to that of the Izumo study, of which the size of the geographic region and denominator and diagnostic criteria were similar to this study. (Stroke. 2002;33:195-199.)

Key Words: cerebral aneurysm ■ epidemiology ■ incidence ■ subarachnoid hemorrhage

The incidence of subarachnoid hemorrhage (SAH) has ranged widely among reports from different regions of the world and at different points in time.1–3 The incidence appears to be especially high in Finland compared with other parts of the world.1,2,4–8 Recent studies also suggest that Japan has a high incidence of SAH that is comparable to Finland.9–12 This study aimed to confirm the high incidence of SAH in Japan.

Because the incidence of SAH is affected by case ascertainment, diagnostic criteria including rate of CT, and the size of the population denominator,1,13–15 we used uniform and standardized methods to compare our data with those from other studies. The most recently published incidence study in Japan was undertaken in Izumo City during 1987 to 1992.12 Izumo City is located in the western part of Japan, and its population is ≈80 000. Our study in Shimokita was conducted in a population size similar to that of Izumo.

Subjects and Methods

The Shimokita area is located in the most northern part of mainland Japan and covers a rural area of 1415 km² (Figure 1). Geographically, Shimokita peninsula is largely a closed-boundary area because it is surrounded by sea on three sides. The emergency transportation system in this area has been established to transfer all of emergency cases including SAH cases to the public hospitals in this district. Therefore, there is very little possibility that any patients would be transferred or referred to a hospital in another district, which was one of the reasons why this area was selected for this study. This area has 4 regional public hospitals equipped with a CT scan, and one of these, Mutsu General Hospital, has a neurosurgical department.

Patients were prospectively registered through the complete referral system of SAH patients in the Shimokita area, which was established in 1989. The access of SAH patients to medical care in this region was divided into three patterns. All emergency cases suspected of SAH were transferred by ambulance to the regional public hospitals equipped with a CT scan, and all of them, including moribund cases and cases dead on arrival, underwent CT scan. All patients who visited the regional public hospitals equipped with a CT scan by themselves, if suspected of SAH, were immediately transferred to the nearest public hospital by ambulance, and a CT scan was performed in all of them.

Medical records and CT scan images of all patients suspected of SAH were referred for interpretation to the neurosurgeons at Mutsu General Hospital and judged by them as to whether SAH on CT scan was due to aneurysmal rupture or not. All of the patients who were diagnosed as having aneurysmal SAH judged to be an indication for aneurysm surgery were transferred to Mutsu General Hospital, followed by cerebral angiography and/or aneurysm surgery. If SAH could not be determined on CT scan in spite of strong suspicion of SAH, based on clinical signs, lumbar puncture was performed. If bloody or xanthochromic cerebrospinal fluid was verified by lumbar puncture, cerebral angiography was performed.

Corresponding to this system of diagnosis and treatment, the patients with aneurysmal SAH were divided into 3 groups, based on...
CT findings: (1) patients with SAH on CT scan determined to be due to ruptured cerebral aneurysm by cerebral angiography and/or aneurysm surgery; (2) patients with CT findings identical to SAH caused by ruptured cerebral aneurysms but without either cerebral angiography or aneurysm surgery because of poor clinical conditions; (3) patients with SAH determined by lumbar puncture because of ambiguous findings of SAH on CT scan, followed by determination of ruptured aneurysm by cerebral angiography and aneurysm surgery. In addition, the death certificates of residents who died during the study period were reviewed. Furthermore, the cases registered to this study were limited to the patients having their first-ever SAH and living in this area when they had the SAH. This study was approved by the Human Subjects Review Committee of Shimokita Medical Center.

The evaluation period was 10 years, from 1989 to 1998; the population of this area fluctuated between 88,620 and 92,704, and the mean population of the Shimokita area during this period was 89,991. The crude annual incidence was calculated from the number of cases and the population of each year, and the age- and sex-adjusted annual incidences were calculated with the use of the census population data of Japan in 1990 for the first 3 years and in 1995 for the last 7 years. The confidence intervals of the incidence rates were analyzed by means of Poisson regression. The incidence was also estimated with the use of the sex and age distribution of the world populations in 1995 published by the United Nations. Changes in incidence rates were analyzed by means of Poisson regression.

Results

During the 10-year period from 1989 through 1998, 274 cases were suspected of SAH from the clinical signs, and all of them underwent CT scan (Figure 2). CT scan was performed on the day of the ictus in 235 cases, within 1 week except the day of the ictus in 32 cases, and during the second week in 7 cases. SAH was seen on CT scan in 207 cases. Of the 207 cases, cerebral angiography was performed in 174 cases, and cerebral aneurysms were verified as a cause of SAH in 162 cases, which was followed by aneurysm surgery in 134 cases. In 12 cases with SAH on CT scan and without cerebral aneurysms on cerebral angiography, 7 cases corresponded to so-called perimesencephalic SAH. Of 207 cases with positive CT scan findings, neither cerebral angiography nor aneurysm surgery was performed in 33 cases because of poor clinical conditions; however, the CT findings of these patients were identical to aneurysmal SAH. Of these 33 cases, 20 cases were moribund and 6 cases were dead when the initial CT scan was performed. CT scan showed no obvious SAH in 67 cases; however, 14 cases underwent lumbar puncture because of strong suspicion of SAH from the clinical signs. Out of these 14 cases, 4 cases showing bloody cerebrospinal fluid underwent cerebral angiography, and cerebral aneurysms were seen in 3 cases, which were confirmed as the cause of SAH by aneurysm surgery. In total, 198 cases were diagnosed as having aneurysmal SAH. In 64 cases, in which SAH was suspected on the initial diagnosis but was ruled out on CT scan and/or lumbar puncture, 14 cases were moribund or dead when the CT scan was performed. Final diagnoses of these 64 cases were migraine, cluster headache, muscle contraction headache, intracerebral hemorrhage, intraventricular hemorrhage, epilepsy, arrhythmia, or myocardial infarction.

In death certificates during the same period, except for the death cases registered by the above diagnostic procedures, there were 3 cases reported to have SAH as a cause of death. However, they died at home before any examination was performed, and diagnosis was made only from the clinical course by general practitioners. Therefore, these 3 cases were not included in this study.

The crude annual incidence of aneurysmal SAH in male, female, and both sexes combined was 16.6, 27.2, and 22.1 per 100,000 population, respectively (Table 1). The age-adjusted annual incidence by means of the census population of Japan in 1990 and 1995 for male, female, and both sexes combined was 16.1, 25.4, and 21.0 per 100,000 population, respectively. The incidence adjusted to Finland population for male, female, and both sexes combined was 15.8, 24.5, and 20.1 per 100,000 population, respectively.

The annual incidences in each year fluctuated between 17 and 32 (Table 1). The highest incidence was seen in 1996, which was 1.9 times higher compared with 1997; however, no significant trends were observed, with an annual rate ratio of 1.00 (95% CI, 0.96 to 1.06). The age and sex distribution of the patients and the age-specific annual incidences
are shown in Table 2. In men, the incidence plateaued between 45 and 84 years. In women, the incidences increased after 45 years and reached the peak in >75 years.

**Discussion**

It has been emphasized that the same definitions and methods should be used to compare stroke incidence in different parts of the world and at different points in time. However, geographical and secular trends in the incidence of SAH have been less well studied compared with the incidence of stroke in general, largely based on varying diagnostic criteria and case ascertainment. It is important that such studies achieve a high rate of CT because the diagnosis of SAH is unreliable when based solely on clinical symptoms and signs. Typically, only a small number of cases are registered in studies because of the relatively few incidence of SAH, with confidence intervals around rates consequently being wide. Of the 19 studies listed in a recent systematic review of the incidence of SAH, only 3 studies obtained over 100 cases. One strategy to obtain an adequate number of cases is to enlarge the population base and widen the area of case ascertainment. However, this may lead to error and underestimation of rates caused by problems of registering cases who have received medical attention in outlying areas or who die outside of the study area. There are also problems with involving doctors in the diagnosis of SAH who are not well trained. For example, showed that a study performed at the prefecture level showed a lower incidence of SAH compared with a study in a defined small area. Another strategy is to extend the period of case ascertainment in a small population that is able to achieve a high diagnostic rate and complete case ascertainment. However, a period of several years is often necessary to accumulate an adequate number of cases and overcome random variability between years. By extending the study period, both our study and the Izumo study could collect more than 100 cases in spite of a defined area.

In our study, diagnosis of SAH was based on CT, as recommended by others. Linn et al suggested that the apparent decline in the incidence of SAH in recent years was an artifact, explained entirely by the increase use of CT. Of 274 cases with suspected SAH on the basis of typical clinical features in our study, 53 cases (19%) were excluded because of the results of CT. The rate of diagnosis of SAH by CT has ranged widely in previous reports. Even in the WHO MONICA study, where uniform criteria for case ascertainment and diagnosis were used, the rate of CT was not clearly stated. CT is particularly useful for the diagnosis of SAH in severe cases, such as sudden death or death on arrival, of which the number of such cases is substantial for this illness. It is well recognized that the diagnosis of SAH based only on clinical signs or features is unreliable and not adequate for studies of SAH incidence. To some extent, the diagnostic rate can be improved by undertaking autopsies in relevant situations, but the rate of this procedure varies across counties as the result of health care and cultural and other factors. We included a combination of CT and autopsy in our patients who died.

**TABLE 1. Annual Incidence of Aneurysmal SAH per 100 000 Population in the Shimokita Area From 1989 to 1998**

<table>
<thead>
<tr>
<th>Crude Incidence in Each Year</th>
<th>Total (1989–1998)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of SAH Cases</td>
</tr>
<tr>
<td></td>
<td>Crude Incidence (95% CI)</td>
</tr>
<tr>
<td>1989</td>
<td>20</td>
</tr>
<tr>
<td>1990</td>
<td>25</td>
</tr>
<tr>
<td>1991</td>
<td>23</td>
</tr>
</tbody>
</table>

*Age-adjusted annual incidences were calculated with the use of 1990 and 1995 Japan census data.

**TABLE 2. Age-Specific Annual Incidence of Aneurysmal SAH per 100 000 Population in the Shimokita Area From 1989 to 1998**

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–24</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25–34</td>
<td>1</td>
<td>2 (0–11)</td>
<td>1</td>
<td>2 (0–11)</td>
<td>2</td>
</tr>
<tr>
<td>35–44</td>
<td>14</td>
<td>21 (11–35)</td>
<td>12</td>
<td>17 (9–30)</td>
<td>26</td>
</tr>
<tr>
<td>45–54</td>
<td>23</td>
<td>37 (24–56)</td>
<td>21</td>
<td>32 (20–50)</td>
<td>44</td>
</tr>
<tr>
<td>55–64</td>
<td>17</td>
<td>32 (19–52)</td>
<td>38</td>
<td>62 (44–86)</td>
<td>55</td>
</tr>
<tr>
<td>65–74</td>
<td>12</td>
<td>34 (18–60)</td>
<td>28</td>
<td>56 (37–81)</td>
<td>40</td>
</tr>
<tr>
<td>75–84</td>
<td>5</td>
<td>30 (10–71)</td>
<td>21</td>
<td>79 (49–121)</td>
<td>26</td>
</tr>
<tr>
<td>≥85</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>68 (22–158)</td>
<td>5</td>
</tr>
</tbody>
</table>
Our study population was similar in geographical spread to that of Izumo. In obtaining a high number of cases over several years and 100% use of CT, we have shown that the incidence of SAH is similar to that in Izumo (Table 3). The incidence of SAH in Shimokita of 21 per 100,000, which is similar to the pooled incidence in 3 Finnish studies,4,6,8 was 21.4 per 100,000 population.1 The other Japanese studies performed in a prefecture level, the Yamaguchi study, 9 and the Shimane study,9 showed rather lower incidence than our study. The Akita study,10 which was performed in a prefecture level, showed a high incidence because it was performed in people 25 to 74 years of age, and, interestingly, the incidence was similar to the Finnish study8 performed in people of the same age. These findings clearly indicate that the incidence of SAH in Japan is as high as that in Finland.

The reasons why Japan and Finland have the higher incidence of SAH have not yet been determined and should be investigated in future. Because smoking and hypertension are known to be risk factors for SAH,22 the prevalence of these risk factors might be high in these countries. Because the risk of SAH is in part genetically determined,23 a high prevalence in Japan and Finland of genes linked to aneurysm formation may also play a role in the high incidence of SAH in these areas.

We were unable to determine reliably the influence of age and sex on the incidence of SAH in our population. However, by pooling our data with that from other studies with a high number of cases and a large population denominator, we were able to show that rates are higher in women (Figure 3).5,8,9,12,21 In men, the annual incidence of SAH ranged from 34.5 and 51.3 per 100,000 population over the age of 40 years. Conversely, in women, the annual incidence increased with age and reached peaks between 58.0 and 66.9 per 100,000 population after the age of 60 years. In both sexes, the incidence of SAH increased with age. The high rates in women, especially after the menopause, suggest that aneurysm formation and its rupture might be affected by hormonal factors.24

### Table 3. Incidence of SAH in Finland and Japan

<table>
<thead>
<tr>
<th>Study</th>
<th>Period</th>
<th>Population</th>
<th>No. of Person-Years</th>
<th>Method</th>
<th>Rate of CT Scan Use</th>
<th>Age, y</th>
<th>No. of SAH Cases</th>
<th>Incidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Espoo-Kauniainen4</td>
<td>1972</td>
<td>107 673</td>
<td>107 673</td>
<td>Pp, Pro</td>
<td>0</td>
<td>All ages</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>Central Finland6</td>
<td>1976–1978</td>
<td>241 000</td>
<td>723 000</td>
<td>Hp, Retro</td>
<td>0</td>
<td>All ages</td>
<td>146</td>
<td>20</td>
</tr>
<tr>
<td>Kuopio6</td>
<td>1978–1980</td>
<td>95 420</td>
<td>159 033</td>
<td>Pp, Pro</td>
<td>8</td>
<td>All ages</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>Central Finland7</td>
<td>1980–1987</td>
<td>246 000</td>
<td>1 968 000</td>
<td>Hp, Retro</td>
<td>51</td>
<td>All ages</td>
<td>351</td>
<td>16</td>
</tr>
<tr>
<td>Three areas8</td>
<td>1983–1985</td>
<td>385 011</td>
<td>1 155 033</td>
<td>Pp, Pro</td>
<td>41</td>
<td>25–74</td>
<td>411</td>
<td>30</td>
</tr>
<tr>
<td>Japan</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Izumo9</td>
<td>1980–1984</td>
<td>79 026</td>
<td>395 130</td>
<td>Hp, Retro</td>
<td>95</td>
<td>All ages</td>
<td>83</td>
<td>21 (18)</td>
</tr>
<tr>
<td>Shimane9</td>
<td>1980–1984</td>
<td>789 712</td>
<td>3 948 560</td>
<td>Hp, Retro</td>
<td>94</td>
<td>All ages</td>
<td>548</td>
<td>14 (11)</td>
</tr>
<tr>
<td>Akita10</td>
<td>1983–1985</td>
<td>808 871</td>
<td>2 426 613</td>
<td>Hp, Pro</td>
<td>100</td>
<td>25–74</td>
<td>720</td>
<td>28</td>
</tr>
<tr>
<td>Yamaguchi11</td>
<td>1985–1995</td>
<td>1 500 000</td>
<td>15 000 000</td>
<td>Pp, Pro</td>
<td>100</td>
<td>All ages</td>
<td>3 100</td>
<td>17 (14)</td>
</tr>
<tr>
<td>Izumo12</td>
<td>1987–1992</td>
<td>82 679</td>
<td>496 074</td>
<td>Hp, Pro</td>
<td>100</td>
<td>All ages</td>
<td>123</td>
<td>25 (23)</td>
</tr>
</tbody>
</table>

Pp indicates population-based study; Hp, hospital-based study; Pro, prospective study; and Retro, retrospective study.

*Age-adjusted incidences are set in parentheses.
References

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