Prevalence and Clinicoepidemiological Features of Moyamoya Disease in Japan
Findings From a Nationwide Epidemiological Survey

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Background and Purpose—The objectives of the present study were to estimate an annual number of patients with moyamoya disease in Japan and to describe the clinicoepidemiological features of the disease.

Methods—The study consisted of 2 questionnaire surveys, which were distributed to randomly selected departments of neurosurgery, internal medicine, neurology, cerebrovascular medicine, and pediatrics in hospitals throughout Japan. The first survey inquired about the number of the patients treated in 2003, and the second requested additional detailed clinicoepidemiological information about each patient identified in the first survey.

Results—In 2003, the total number of patients treated in Japan was estimated at 7700 (95% confidence interval, 6300 to 9300). Sex ratio (women to men) of the patients was 1.8. For men, the peak of moyamoya disease was observed in patients aged 10 to 14 years and for women aged 20 to 24 years. Annual rate of newly diagnosed cases in 2003 was 0.54 per 100,000 population. Family history of moyamoya disease was found in 12.1% of the patients. The majority (77.9%) were treated as outpatients.

Conclusions—Although the clinicoepidemiological features of the patients in the present study were almost similar to those obtained in previous ones, the estimated prevalence of moyamoya disease in Japan has almost doubled during the recent decade (3900 in 1994 and 7700 in 2003). The increase could partly be explained by the increase in newly diagnosed cases (0.35 in 1994 and 0.54 in 2003 per 100,000 population). (Stroke. 2008;39:42-47.)

Key Words: epidemiology ■ Japan ■ moyamoya disease ■ prevalence

Moyamoya disease is a unique occlusive disease of the bilateral internal carotid arteries; compensation for occlusion results in rich arterial collaterals at the base of the brain.1 The idiopathic form was first reported in 1957 in Japan,2 where the incidence is believed to be the highest.3 Subsequently, it has been reported worldwide.4–8 A large-scale survey is required to clarify the clinicoepidemiological features of such rare diseases as moyamoya disease. The data, from such research, could provide clues to clarify the pathophysiology and assist in the administrative planning to ensure appropriate health services.

The Ministry of Health, Labour and Welfare of Japan has promoted scientific research on many intractable diseases, and nationwide epidemiological surveys have been conducted in Japan with the financial support from the Ministry.9 For moyamoya disease, 3 nationwide surveys were conducted: in 1986, 1990, and 1995.10,11

To estimate the current annual number of patients treated for moyamoya disease in Japan and to describe the updated clinicoepidemiological features, we again undertook a nationwide epidemiological survey of this disease.

Materials and Methods
We conducted a 2-staged postal survey. The first survey aimed to estimate the number of individuals with moyamoya disease, and the second survey aimed to elucidate the clinicoepidemiological characteristics of moyamoya disease. The criteria prepared by the Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) in Japan12 were used for clinical diagnosis of moyamoya disease. The guidelines for the diagnosis are as follows.

Diagnostic Criteria
A. Cerebral angiography is indispensable for the diagnosis and should present at least the following findings:

1. Stenosis or occlusion at the terminal portion of the internal carotid artery and/or at the proximal portion of the anterior and/or the middle cerebral arteries;

Received April 6, 2007; accepted April 25, 2007.
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Stroke is available at http://stroke.ahajournals.org
DOI: 10.1161/STROKEAHA.107.490714

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2. Abnormal vascular networks in the vicinity of the occlusive or stenotic lesions in the arterial phase; and
3. These findings should present bilaterally.

B. When MRI and magnetic resonance angiography clearly demonstrate all the subsequently described findings, conventional cerebral angiography is not mandatory.

1. Stenosis or occlusion at the terminal portion of the internal carotid artery and at the proximal portion of the anterior and middle cerebral arteries on magnetic resonance angiography; 
2. An abnormal vascular network in the basal ganglia on magnetic resonance angiography. Note that an abnormal vascular network can be diagnosed when more than 2 apparent flow voids are seen in one side of the basal ganglia on MRI; and
3. (1) and (2) are seen bilaterally (refer to the “Image Diagnostic Guidelines by MRI and Magnetic Resonance Angiography”).

C. Because the etiology of this disease is unknown, cerebrovascular disease with the following basic diseases or conditions should thus be eliminated:

1. Arteriosclerosis; 
2. Autoimmune disease; 
3. Meningitis; 
4. Brain neoplasm; 
5. Down syndrome; 
6. Recklinghausen’s disease; 
7. Head trauma; 
8. Irradiation to the head; and

D. Instructive pathological findings:

1. Intimal thickening and the resulting stenosis or occlusion of the lumen is observed in and around the terminal portion of the internal carotid artery usually on both sides. Lipid deposits are occasionally seen in the proliferating intima; 
2. Arteries constituting the circle of Willis such as the anterior and middle cerebral and the posterior communicating arteries often show stenosis of various degrees or occlusion

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### Table 1. Number of the Total, Surveyed, Responded Departments and Number of the Reported Patients With Moyamoya Disease

<table>
<thead>
<tr>
<th>Strata</th>
<th>Total No. of Departments</th>
<th>No. of Surveyed Departments</th>
<th>Sampling Rate (%)</th>
<th>No. of Responded Departments</th>
<th>Response Rate (%)</th>
<th>No. of Reported Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurosurgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University hospitals</td>
<td>101</td>
<td>101</td>
<td>100.0</td>
<td>71</td>
<td>70.3</td>
<td>507</td>
</tr>
<tr>
<td>Selected hospitals</td>
<td>39</td>
<td>39</td>
<td>100.0</td>
<td>34</td>
<td>87.2</td>
<td>906</td>
</tr>
<tr>
<td>General hospitals with ≥500 beds</td>
<td>202</td>
<td>202</td>
<td>100.0</td>
<td>129</td>
<td>63.9</td>
<td>600</td>
</tr>
<tr>
<td>General hospitals with 400–499 beds</td>
<td>157</td>
<td>126</td>
<td>80.3</td>
<td>71</td>
<td>56.3</td>
<td>176</td>
</tr>
<tr>
<td>General hospitals with 300–399 beds</td>
<td>293</td>
<td>117</td>
<td>39.9</td>
<td>66</td>
<td>56.4</td>
<td>134</td>
</tr>
<tr>
<td>General hospitals with 200–299 beds</td>
<td>310</td>
<td>62</td>
<td>20.0</td>
<td>36</td>
<td>58.1</td>
<td>56</td>
</tr>
<tr>
<td>General hospitals with 100–199 beds</td>
<td>517</td>
<td>53</td>
<td>10.3</td>
<td>24</td>
<td>45.3</td>
<td>39</td>
</tr>
<tr>
<td>General hospitals with ≤99 beds</td>
<td>588</td>
<td>54</td>
<td>9.2</td>
<td>23</td>
<td>42.6</td>
<td>22</td>
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<tr>
<td><strong>Subtotal</strong></td>
<td>2207</td>
<td>754</td>
<td>34.2</td>
<td>454</td>
<td>60.2</td>
<td>2440</td>
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<td><strong>Neurology</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University hospitals</td>
<td>314</td>
<td>314</td>
<td>100.0</td>
<td>214</td>
<td>68.2</td>
<td>52</td>
</tr>
<tr>
<td>Selected hospitals</td>
<td>2</td>
<td>2</td>
<td>100.0</td>
<td>2</td>
<td>100.0</td>
<td>6</td>
</tr>
<tr>
<td>General hospitals with ≥500 beds</td>
<td>244</td>
<td>244</td>
<td>100.0</td>
<td>96</td>
<td>39.3</td>
<td>16</td>
</tr>
<tr>
<td>General hospitals with 400–499 beds</td>
<td>206</td>
<td>182</td>
<td>88.3</td>
<td>82</td>
<td>45.1</td>
<td>8</td>
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<tr>
<td>General hospitals with 300–399 beds</td>
<td>405</td>
<td>220</td>
<td>54.3</td>
<td>88</td>
<td>40.0</td>
<td>21</td>
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<tr>
<td>General hospitals with 200–299 beds</td>
<td>623</td>
<td>194</td>
<td>31.1</td>
<td>87</td>
<td>44.8</td>
<td>24</td>
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<tr>
<td>General hospitals with 100–199 beds</td>
<td>1543</td>
<td>226</td>
<td>14.6</td>
<td>113</td>
<td>50.0</td>
<td>25</td>
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<tr>
<td>General hospitals with ≤99 beds</td>
<td>3274</td>
<td>214</td>
<td>6.5</td>
<td>99</td>
<td>46.3</td>
<td>31</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td>6611</td>
<td>1596</td>
<td>24.1</td>
<td>781</td>
<td>48.9</td>
<td>183</td>
</tr>
<tr>
<td><strong>Pediatrics</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University hospitals</td>
<td>128</td>
<td>128</td>
<td>100.0</td>
<td>100</td>
<td>78.1</td>
<td>68</td>
</tr>
<tr>
<td>Selected hospitals</td>
<td>1</td>
<td>1</td>
<td>100.0</td>
<td>1</td>
<td>100.0</td>
<td>8</td>
</tr>
<tr>
<td>General hospitals with ≥500 beds</td>
<td>221</td>
<td>221</td>
<td>100.0</td>
<td>149</td>
<td>67.4</td>
<td>42</td>
</tr>
<tr>
<td>General hospitals with 400–499 beds</td>
<td>185</td>
<td>149</td>
<td>80.5</td>
<td>100</td>
<td>67.1</td>
<td>19</td>
</tr>
<tr>
<td>General hospitals with 300–399 beds</td>
<td>353</td>
<td>146</td>
<td>41.4</td>
<td>113</td>
<td>77.4</td>
<td>14</td>
</tr>
<tr>
<td>General hospitals with 200–299 beds</td>
<td>451</td>
<td>103</td>
<td>22.8</td>
<td>63</td>
<td>61.2</td>
<td>7</td>
</tr>
<tr>
<td>General hospitals with 100–199 beds</td>
<td>753</td>
<td>91</td>
<td>12.1</td>
<td>53</td>
<td>58.2</td>
<td>12</td>
</tr>
<tr>
<td>General hospitals with ≤99 beds</td>
<td>1166</td>
<td>65</td>
<td>5.6</td>
<td>34</td>
<td>52.3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td>3258</td>
<td>904</td>
<td>27.7</td>
<td>613</td>
<td>67.8</td>
<td>174</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12 076</td>
<td>3254</td>
<td>26.9</td>
<td>1848</td>
<td>56.8</td>
<td>2797</td>
</tr>
</tbody>
</table>

*Departments of internal medicine, neurology, and cerebrovascular medicine were integrated into one category.*
associated with fibrocellular thickening of the intima, a waving of the internal elastic lamina, and an attenuation of the media; 3. Numerous small vascular channels (perforators and anastomotic branches) are observed around the circle of Willis; and 4. Reticular conglomerates of small vessels are often seen in the pia mater.

**Diagnosis**

As mentioned previously, the diagnostic criteria are classified as follows: Autopsy cases not undergoing cerebral angiography should be investigated separately while referring to (D).

1. **Definite case:** one that fulfills either (A) or (B) and (C). In children, however, a case that fulfills (A) (1) and (2) or (B) (1) and (2) on one side and with remarkable stenosis at the terminal portion of the internal carotid artery on the opposite side is also included; and

2. **Probable case:** one that fulfills (A) (1) and (2) or (B) (1) and (2) and (C) (unilateral involvement).

Both definite and probable cases, defined by the criteria, were included in the present study. This study protocol was approved by the Ethics Committee of the Tohoku University Graduate School of Medicine.

**First-Stage Survey**

**Selection of Target Health Institutions and Departments**

All departments of neurosurgery, internal medicine, neurology, cerebrovascular medicine, and pediatrics departments from all hospitals in Japan were listed. These hospitals were categorized according to the institution type (ie, university hospitals/general hospitals) and the number of hospital beds. Hospitals were then randomly selected from within these categories. The sampling rates used were based on the results of a previous study that evaluated the optimal sampling rate in nationwide epidemiological surveys to minimize the standard errors in estimating the number of patients. The number of patients treated in 2003 was estimated based on the assumption that the response from departments was independent of the frequency of patients. The formulae to compute the number of patients and the 95% CI is as follows. The number of patients in stratum \( k \) was estimated as

\[
\hat{N}_k = \frac{1}{SRT_k RRT_k} \sum_{i} i N_{ki},
\]

\[
= \frac{1}{NS_k N_i} \sum_{i} i N_{ki},
\]

\[
= \frac{n_k}{N_k} \sum_{i} i N_{ki},
\]

where \( SRT_k \), \( RRT_k \), \( NS_k \), \( n_k \), \( N_k \), and \( N_0 \) denote the sampling rate, response rate, the number of sampling departments, the total number of departments, the number of responding departments, and the number of departments with \( i \) patients in stratum \( k \), respectively. The 95% CI of \( \hat{N}_k \) was

\[
(\hat{N}_k - 1.96 s_k, \hat{N}_k + 1.96 s_k)
\]

\[
s_k = \sqrt{\frac{1}{N_k} \sum_{i} i^2 N_{ki} - \left( \frac{1}{N_k} \sum_{i} i N_{ki} \right)^2} \left( \frac{1}{N_k} \frac{1}{n_k} \right)^{1/2}
\]

where \( s_k \) is the estimated standard error of \( \hat{N}_k \).

**Survey Method**

The survey was mailed out to the hospitals. In January 2004, letters of request for participation, diagnostic criteria, and survey slips were sent to the target departments of health institutions as well as requests for reports of number of patients with moyamoya disease seeking treatment between January 1, 2003, and December 31, 2003. In March 2004, a second request was sent to all departments that had not responded by the deadline (end of February 2004). After the first-stage survey, acknowledgement letters were sent to departments that responded that they had not seen any patients with moyamoya disease during 2003.

**Estimation of Prevalence**

The number of patients treated in 2003 was estimated based on the assumption that the response from departments was independent of the frequency of patients. The formulae to compute the number of patients and the 95% CI is as follows. The number of patients in stratum \( k \) was estimated as

\[
\hat{N}_k = \frac{1}{SRT_k RRT_k} \sum_{i} i N_{ki},
\]

\[
= \frac{1}{NS_k N_i} \sum_{i} i N_{ki},
\]

\[
= \frac{n_k}{N_k} \sum_{i} i N_{ki},
\]

where \( SRT_k \), \( RRT_k \), \( NS_k \), \( n_k \), \( N_k \), and \( N_0 \) denote the sampling rate, response rate, the number of sampling departments, the total number of departments, the number of responding departments, and the number of departments with \( i \) patients in stratum \( k \), respectively. The 95% CI of \( \hat{N}_k \) was

\[
(\hat{N}_k - 1.96 s_k, \hat{N}_k + 1.96 s_k)
\]

\[
s_k = \sqrt{\frac{1}{N_k} \sum_{i} i^2 N_{ki} - \left( \frac{1}{N_k} \sum_{i} i N_{ki} \right)^2} \left( \frac{1}{N_k} \frac{1}{n_k} \right)^{1/2}
\]

where \( s_k \) is the estimated standard error of \( \hat{N}_k \).
Table 4. Medical Care Status in the Last Year Among the Patients With Moyamoya Disease by Sex

<table>
<thead>
<tr>
<th>Medical Care</th>
<th>Treated Mainly as Inpatients</th>
<th>Treated Mainly as Outpatients</th>
<th>Treated as In- and Outpatients</th>
<th>Moved to Other Hospitals/Clinics</th>
<th>Others</th>
<th>Subtotal</th>
<th>Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>5</td>
<td>250</td>
<td>45</td>
<td>18</td>
<td>6</td>
<td>324</td>
<td>112</td>
<td>436</td>
</tr>
<tr>
<td>Percent</td>
<td>1.5</td>
<td>77.2</td>
<td>13.9</td>
<td>5.6</td>
<td>1.9</td>
<td>100.0</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Women</td>
<td>20</td>
<td>476</td>
<td>86</td>
<td>19</td>
<td>7</td>
<td>608</td>
<td>196</td>
<td>804</td>
</tr>
<tr>
<td>Percent</td>
<td>3.3</td>
<td>78.3</td>
<td>14.1</td>
<td>3.1</td>
<td>1.2</td>
<td>100.0</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>932</td>
<td>1240</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The total number of patients, \( \hat{\alpha} \), was computed as follows:

\[
\hat{\alpha} = \sum_{k} \delta_{k}
\]

and the 95% CI was

\[
(\hat{\alpha} - 1.96s, \hat{\alpha} + 1.96s), \quad s = \sqrt{\sum_{k} s_{k}^{2}}
\]

where \( s \) is the estimated standard error of \( \hat{\alpha} \).

In the data analysis, (1) departments of internal medicine, neurology, and cerebrovascular medicine were integrated into one category; (2) responses from departments not falling into these departments were excluded; (3) if the target departments responded (in their report) with a different department name compared with the original, we used the latter name; and (4) if any institution sent a correction to the original number of patients reported, we used the corrected figure.

The patients who died before 2002 or those who had first visited the hospitals in 2004 or after were excluded from the study as “inappropriate cases.” The calculated total annual number of patients was corrected using the proportion of “inappropriate cases” among the patients reported in the second-stage survey (described subsequently; i.e., the number was multiplied by \( 1 - A \)). The population of Japan in 2003 (n = 127,619,000) was used to calculate the prevalence rate and annual rate of newly diagnosed cases in 2003. The effect of restricting analyses to departments that reported the number of patients was assessed in a sensitivity analysis.

Second-Stage Survey

Requests for all individual patients’ details were sent to those departments responding that they had seen less than 20 patients with moyamoya disease in the first-stage survey. For departments that reported 20 or more patients, information was requested for patients with odd-numbered birth months. The epidemiological items included sociodemographic factors such as sex, date of birth, the time of onset, family history, and status of medical care.

Results

Estimated Annual Number of Patients and Prevalence Rate

Of 3254 departments, 1848 responded to the questionnaire in the first-stage survey (response rate: 56.8%) and 2797 patients were identified (Table 1). Eighty-seven percent of the patients were treated in neurosurgery departments.

In response to the questionnaire in the second-stage survey, we collected detailed clinicoepidemiological information on 1269 patients (45.4%) who were identified by the first questionnaire. Four cases were excluded because gender was not indicated. Among these, 29 (2.3%) cases were found to be “inappropriate” cases. These patients were excluded, leaving 1240 eligible patients with moyamoya disease. More than 94% of these patients (1170 of 1240) were definite cases.

Taking the proportion of “inappropriate” cases into account, the total annual number of patients with moyamoya disease, who were treated in 2003 throughout Japan, was estimated as 7700 (95% CI, 6300 to 9300). The crude prevalence rate was calculated as 6.03 per 100,000 population.

When analyses were restricted to departments that reported the number of patients, the total annual number of patients with moyamoya disease was estimated to be 4700 (95% CI, 3200 to 6200).

Clinicoepidemiological Features of Patients

Table 2 shows the age–sex distribution of moyamoya disease in Japan; a ratio of 1:1.8 (95% CI, 1.7 to 2.1) men to women was noted. In men, there was a major peak among patients aged 10 to 14 years as well as smaller peaks among those aged 35 to 39 years and 55 to 59 years, whereas in women, 2 peaks were seen in patients aged 20 to 24 years and 50 to 54 years. The percentage of patients younger than 10 years and that of patients older than 50 years was 11.9% and 25.5%, respectively.

The distribution pattern regarding year of disease onset is shown in Table 3. Nearly one third of the cases had onset of disease more than 10 years previously, whereas more than one third experienced disease onset during the past 5 years. Table 3 also shows that 9.0% (112 of 1240) of the patients were newly diagnosed with the disease in 2003. This figure yielded the annual rate of newly diagnosed cases in 2003 as 0.54 per 100,000 population.

Family history of moyamoya disease was found in 12.1% (150 of 1240) of the patients. The proportion of the patients
with family history was 12.4% (54 of 436) and 11.9% (96 of 804) for men and women, respectively.

Table 4 presents the status of medical care for the previous year among patients with moyamoya disease. Approximately three fourths were treated mainly as outpatients; however, when those treated mainly as inpatients were combined with those who received inpatient and outpatient care, the results showed that 16.7% of patients had experienced hospital admission. Five patients were reported to have died in 2003.

Discussion

Although the clinicoepidemiological features of the present sample were similar to those obtained in previous surveys, the present survey revealed a substantial increase in the number of patients with a total of 7700 (95% CI, 6300 to 9300) individuals estimated to be affected. This is based on the comparison of the past 3 nationwide surveys on moyamoya disease conducted in Japan, in 1986, 1990, and in 1995, with respective estimates of 1900, 3300, and 3900 affected individuals (Figure).10,11 Although we cannot compare these prevalence rates directly because of the study design in which the data could not be age-standardized, if we had conducted an age-standardized comparison, we would have expected a much greater increase in the number of patients because moyamoya disease is common among pediatric population, and Japan is rapidly becoming an aging society with a low birth rate.

Prevalence is approximately equal to the product of the incidence rate and the mean duration of disease.17 The annual rate of newly diagnosed cases of moyamoya disease in 1994 was reported to be 0.35 per 100,000 population,11 whereas the present survey found 0.54 per 100,000 population. The observed substantial increase in the number of patients could partly be explained by the one and a half times increase of newly diagnosed cases, although whether the increase was due to better ascertainment18–20 or truly increased incidence was unclear. Nevertheless, the increase of newly diagnosed cases might partly be due to the increase of asymptomatic moyamoya disease cases. After induction of noninvasive diagnostic tools, asymptomatic moyamoya disease is occasionally being diagnosed,21 which may contribute to the increase of newly diagnosed cases. If asymptomatic moyamoya disease is more prevalent than recognized before, substantial increase of the patients would be inevitable in the near future. Furthermore, the possible improvement of the patients' prognoses due to careful and long-term neurological and radiological follow-up and appropriate management,3,22–24 which could induce longer mean duration of disease, might also contribute to the increased prevalence of the disease.

Because the 1990 survey only targeted hospitals with more than 200 beds, the 3300 affected patients could have been an underestimate10; however, because the 1986 and 1995 investigations included all hospitals, this difference among target hospitals may not explain the substantial increased prevalence observed in our study.10,11

During the estimation of the number of patients receiving treatment, the rate of duplication was not considered. This was because we did not include patients' names in the second survey. Hence, the issue of overestimation in the results cannot be excluded. However, considering the 1995 survey, which documented a 3.5% duplication rate,11 the effect of this is unlikely to seriously damage our findings.

We estimated the number of patients under the assumption that the response from departments was independent of the frequency of patients.14–16 This assumption has to be vali-
dated because the response rate of 56.8% might not be sufficiently high (Table 1). Hashimoto et al\textsuperscript{25} compared the mean numbers of the patients with an intractable disease who were financially subsidized for treatment from responding departments with those from nonresponding departments; the ratio of the former to the latter was 1.0:1.1. This figure suggests that the assumption might be sufficiently valid for the nationwide epidemiological surveys of intractable diseases in Japan. Nevertheless, to further evaluate the effects of nonresponse, in future surveys, we plan to send a second round of surveys to the subset of individuals who did not respond to the first survey to grasp the difference between those who responded initially and those who did not.

We compared our survey with previous research on the clinicopepidemiological features of moyamoya disease in Japan (Table 5). The sex ratios and rate of patients younger than 10 years were very similar to findings from previous surveys. In contrast, the patterns of age distribution, rates of patients older than 50 years, rates of patients with a family history of the disease, and the status of medical care in the past year were somewhat different. The pattern of age distribution has changed from 2 peaks to 3 peaks in men. The rate of patients older than 50 years increased, suggesting aging of the patients (16.8% in 1989,\textsuperscript{10} 19.0% in 1994,\textsuperscript{11} to 25.5% in 2003). The rate of patients with a family history of the disease and the rate of patients treated mainly as outpatients has also slightly increased.

In conclusion, the present study has shown that the number of patients with moyamoya disease receiving treatment in Japan is substantially rising. The increase could partly be explained by the recent increase in newly diagnosed cases, suggesting the more careful consideration of the disease from the viewpoint of pathophysiology as well as the administrative planning.

Acknowledgments

We are greatly indebted to the many doctors who, despite their busy daily schedules, devoted their time to this investigation. We also thank Ms Hidemi Hattori, Nagoya University Graduate School of Medicine, for her technical assistance.

Source of Funding

This study was supported by a Grant-in-Aid for Research Committee on Epidemiology of Intractable Diseases and the Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) from the Ministry of Health, Labour and Welfare of Japan.

Disclosures

None.

References

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Stroke. 2008;39:42-47; originally published online November 29, 2007;
doi: 10.1161/STROKEAHA.107.490714
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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