Cerebral Angiographic and Clinical Differences in Carotid System Transient Ischemic Attacks Between American Caucasian and Japanese Patients

Katsuya Nishimaru, M.D., Lawrence C. McHenry, Jr., M.D.,* and James F. Toole, M.D.*

SUMMARY Cerebral angiographic findings of 32 Japanese patients with carotid system TIA's were compared with those of an equal number of age and sex matched American Caucasians. The end points included irregularity, ulceration, stenosis or occlusion of the carotid artery appropriate to the side of TIA. Atherosclerotic changes were found in 27 patients (84.4%) of the Japanese and 30 patients (93.7%) of the American patients. Mild lesions (49% stenosis and below) were similar in either frequency of topography between both groups; namely 25 intracranial and 17 extracranial lesions in Japanese as well as 29 intracranial and 10 extracranial in Caucasian patients. There was, however, an extra-intracranial difference in severe lesions (50% stenosis and above) between American Caucasian and Japanese patients; 10 of 12 severe lesions in Japanese were located intracranially, while 17 of 20 severe lesions present in the American group occurred in the extracranial portion of the internal or common carotid arteries.

Cerebral angiographic and pathologic studies have shown a difference in the atherosclerotic changes in stroke patients between Japanese and United States populations.* 1, 2 Japanese patients have been shown to have more severe lesions intracranially, whereas American patients have more severe lesions extracranially. In patients with transient ischemic attacks (TIA), the cervical portion of the carotid artery has been the focus of etiological attention in Western nations. In Japan, however, the intracranial portion of the carotid artery or the stem of the middle cerebral artery have been found to be the likely site of severe arterial lesions in patients with TIA.3-5 Therefore this study compares the cerebral angiographic findings in Japanese patients with those of age and sex matched American Caucasian patients.

Material and Methods

The Japanese patient group consisted of 25 men and 7 women. All had carotid system TIA's that consisted of a focal neurologic deficit, ischemic in etiology, that cleared within 24 hours. Four of the patients were admitted to Kyushu University Hospital between 1964 and 1968, and 28 patients were admitted to Fukuoka University Hospital between 1969 and 1982. Each patient had cerebral angiography at the time of investigation of the TIA.

The American Caucasian group were selected from patients with carotid system TIA in the TIA Registry of the Cerebrovascular Research Center, Bowman Gray School of Medicine and who had been admitted to North Carolina Baptist Hospital, Winston-Salem,
North Carolina from 1977 through 1981. The patients were age and sex matched with corresponding Japanese patients. Those patients with a presumed cardiac embolic source of their TIA were excluded from both groups.

All cerebral angiograms in both groups were evaluated by the same individual (K.N.), and all angiograms were restricted to those with well-defined carotid system TIA's. For evaluation of the angiogram the carotid arterial system was divided in four portions: (1) common carotid and extracranial portion of the internal carotid artery; (2) intracranial portion of the internal carotid artery; (3) middle cerebral artery from the origin to the trifurcation and the anterior cerebral artery from the origin to the anterior communicating artery; and (4) cortical branches of the anterior and middle cerebral arteries. Abnormalities evaluated included irregularity, ulceration, stenosis and occlusion of the artery. The degree of stenosis was measured by comparing minimal arterial diameter with a normal segment. The maximum change of the atherosclerotic abnormalities within each arterial portion was chosen as a representative value and grouped into five categories: (1) atherosclerotic changes below 24% stenosis; (2) 25-49% stenosis; (3) 50-74% stenosis; (4) 75-99% stenosis; and (5) 100% occlusion.

The difference in features between both groups, including symptoms of the clinical event, hypertension, heart disease, diabetes mellitus, blood pressure at admission, obesity, serum cholesterol, and serum triglycerides, were evaluated.

**Results**

The age of the Japanese patients at their first TIA was 57.9 ± 9.1 (1 S.D.) years. On the average, the men were 57.2 years, ranging from 43 to 76 years, while the women averaged 60.4 years, ranging from 41 to 71 years. The American patients were 57.3 ± 8.5 years old. The average age of the men were 56.6 years and ranged from 41 to 75 years. The American women averaged 60.0 years, ranging from 46 to 71 years. The age at cerebral angiography was 58.3 ± 9.0 in the Japanese and 57.9 ± 8.3 in the American group.

**Angiographic Findings (Table 1)**

Five (15.6%) of the Japanese patients and two (6.3%) of the American patients showed normal angiograms in all arterial portions.

1. **Extracranial Portion of the Carotid Artery**

In the Japanese normal extracranial angiograms were present in 13 cases (40.6%). An irregularity or ulceration of the arterial wall or 24% stenosis or less occurred in 15 cases in the Japanese; stenosis of 25-49% was present in two cases; and two Japanese patients had 50-74% stenosis. On the contrary, 5 (25.6%) American patients had normal angiograms in the extracranial portion of the carotid artery. Minimal lesions with 24% or less occurred in 8 cases; 25-49% stenosis was present in 2 cases; 50-74% stenosis occurred in 8 American cases; and stenosis of 75-99% was present in 5 cases. Occlusion of the carotid artery occurred in 4 cases of American patients. Carotid stenosis of over 50% was noticed in only 2 (6.3%) of the Japanese cases, whereas 17 (53.1%) of the American cases showed severe stenosis.

2. **Intracranial Portion of the Carotid System**

The frequency of irregularity, ulceration or mild stenosis below 49% was similar in both patient groups, namely 25 lesions in the Japanese and 29 lesions in American cases. Severe stenosis over 50% at the intracranial portion of the internal carotid was evident in 6 (18.8%) of the Japanese patients and in 2 (6.3%) of the American patients. Three (9.4%) Japanese cases and 1 (3.1%) American cases had at least 50% stenosis at the stem of the anterior or middle cerebral arteries, and 1 (3.1%) of the Japanese patients had cortical branch stenosis of 50% or more.

**Clinical and Laboratory Profile (Table 2)**

The clinical symptoms, duration and number of TIA's, risk factors and laboratory data are shown in Table 2. Clinically, motor disturbance was more frequent in Japanese patients. Sensory disturbance and amaurosis fugax was less common in the Japanese group than in the American group. The duration and number of episodes were similar in both groups. Heart disease was more common in the American patients.

### Table 1: Angiographic Findings in Carotid System TIA Patients

<table>
<thead>
<tr>
<th></th>
<th>Extracranial carotid</th>
<th>Intracranial carotid</th>
<th>Stem of ACA &amp; MCA</th>
<th>Cortical branch</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Japan</td>
<td>USA</td>
<td>Japan</td>
<td>USA</td>
</tr>
<tr>
<td>Irregular, ulcer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-24% stenosis</td>
<td>15</td>
<td>8</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>25-49% stenosis</td>
<td>2</td>
<td>2</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>50-74% stenosis</td>
<td>2</td>
<td>8</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>75-99% stenosis</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>100% occlusion</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

ACA: anterior cerebral artery.
MCA: middle cerebral artery.
but the frequency of diabetes mellitus was greater in the Japanese patients. There was no difference between both groups in blood pressure on admission, hypercholesterolemia or hypertriglyceridemia.

Clinical Features of Patients with Severe Stenosis

Clinical feature in the Japanese cases with severe stenosis were compared to a similar group of American Caucasian patients in an attempt to correlate any etiological difference between them. Four (26.7%) of 15 Japanese patients 60 years old and above had stenosis over 50%, while 12 (80.0%) of 15 American patients 60 years old and above had stenosis over 50%. Ten (52.6%) of 15 American patients with severe stenosis were obese. This was higher than the frequency of obesity (2 cases, 15.4%) in 13 American patients with only mild stenosis or normal angiograms. Japanese, however, had no difference in obesity between cases with and without severe stenosis. There was no other characteristic indicator correlating the difference between Japanese and American patients with 50% arterial stenosis and above.

Discussion

In American Caucasians with TIA, arterial changes occur most frequently in the cervical portion of the carotid artery. On the contrary, arterial stenotic lesions occur most frequently intracranially in Japanese. This study has compared atherosclerotic changes demonstrated by cerebral angiography in carotid system TIA patients of both countries, including minimal lesions, as well as marked stenosis, and has disclosed the similar frequency of angiographic atherosclerosis in both patient groups. Although there is a different tendency in the distribution of arterial stenotic lesions by their severity stenotic changes were seen in 27 cases (84.4%) of Japanese and 30 American patients (93.7%). With regard to mild lesions, namely 49% stenosis or less, Japanese patients had 42 lesions (25 intracranially and 17 extracranially), while the American group had 39 lesions (29 intracranially and 10 extracranially) as shown in figure 1. In contrast, the severe stenotic lesion of 50 to 100% stenosis were demonstrated more often in the Ameri-

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Clinical and Laboratory Profile of Carotid System TIA Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Japan</td>
</tr>
<tr>
<td>Clinical Features</td>
<td></td>
</tr>
<tr>
<td>Symptom</td>
<td></td>
</tr>
<tr>
<td>motor weakness</td>
<td>25</td>
</tr>
<tr>
<td>sensory disturbance</td>
<td>5</td>
</tr>
<tr>
<td>speech disturbance</td>
<td>10</td>
</tr>
<tr>
<td>amaurosis fugax</td>
<td>4</td>
</tr>
<tr>
<td>Duration</td>
<td></td>
</tr>
<tr>
<td>-10 min.</td>
<td>17</td>
</tr>
<tr>
<td>11-60 min.</td>
<td>11</td>
</tr>
<tr>
<td>1-24 hrs.</td>
<td>4</td>
</tr>
<tr>
<td>Number</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>2-9</td>
<td>15</td>
</tr>
<tr>
<td>10-</td>
<td>6</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>40-59 yrs.</td>
<td></td>
</tr>
<tr>
<td>-49% stenosis</td>
<td>11</td>
</tr>
<tr>
<td>50-100% stenosis</td>
<td>6</td>
</tr>
<tr>
<td>total occlusion</td>
<td>17</td>
</tr>
<tr>
<td>60-79 yrs.</td>
<td></td>
</tr>
<tr>
<td>-49% stenosis</td>
<td>11</td>
</tr>
<tr>
<td>50-100% stenosis</td>
<td>4</td>
</tr>
<tr>
<td>total occlusion</td>
<td>15</td>
</tr>
</tbody>
</table>

Hypertension

-49% stenosis | 10 (46%) | 6 (46%)
50-100% stenosis | 7 (70%) | 11 (58%)
total occlusion | 17 | 17

Heart disease

-49% stenosis | 4 (18%) | 3 (23%)
50-100% stenosis | 2 (20%) | 8 (42%)
total occlusion | 6 | 11

Diabetes mellitus

-49% stenosis | 5/22 (23%) | 2/13 (15%)
50-100% stenosis | 3/10 (30%) | 1/19 (5%)
total occlusion | 8 | 3

Obesity

-49% stenosis | 7/22 (32%) | 2/13 (15%)
50-100% stenosis | 3/10 (30%) | 10/19 (53%)
total occlusion | 10 | 12

Blood pressure

Normal (below 140/90)

-49% stenosis | 12 | 5
50-100% stenosis | 3 | 6
total occlusion | 15 | 11

Borderline

-49% stenosis | 5 | 6
50-100% stenosis | 2 | 10
total occlusion | 7 | 16

Hypertension (SP ≥ 160
and/or DP ≥ 95)

-49% stenosis | 5 | 2
50-100% stenosis | 5 | 3
total occlusion | 10 | 5

Hypercholesterolemia

(≥ 300 mg/dl)

-49% stenosis | 1/22 (5%) | 0/11
50-100% stenosis | 0/8 | 1/11 (9%)
total occlusion | 1 | 1

Hypertriglyceridemia

(≥ 150 mg/dl)

-49% stenosis | 9/22 (41%) | 2/9 (22%)
50-100% stenosis | 4/8 (50%) | 4/10 (40%)
total occlusion | 13 | 6

Downloaded from http://stroke.ahajournals.org/ by guest on August 14, 2017
RACIAL DIFFERENCE IN TIA/Nishimaru et al

Figure 1. Angiographic extra-intracranial difference of severe stenosis.

RACIAL DIFFERENCE IN TIA/Nishimaru et al

can than in the Japanese patients, that is, 20 lesions and 12 lesions respectively. In addition, the distribution of severe lesions were also different between both groups, namely 17 of 20 lesions in American group were located in the extracranial carotid artery, while only 2 of 12 lesions in Japanese group were in the same location. This extra-intracranial shift of the severe arterial stenosis has been emphasized in the previous reports.

The analysis of the clinical features failed to disclose any specific risk factors for the extra-intracranial difference shift. Hypertension, heart disease, diabetes mellitus, blood pressure, serum cholesterol and triglycerides all showed a similarity in frequency in both groups. American Caucasians with severe stenosis were more obese than those without such stenosis, whereas the Japanese had no such tendency. The possibility of a metabolic or genetic cause of the extra-intracranial difference shift may exist.

The Honolulu Heart Study reported an incidence of TIA among Japanese Hawaiian cases similar to the incidence among Caucasians, and somewhat greater than the figures reported in Japan. That report suggested that TIA is a disease from Westernization of the Japanese Hawaiians. Another report showed certain biochemical risk factors, such as serum cholesterol, glucose, uric acid and triglycerides as being lower for Japanese men than those in Hawaii and California. The intra-extracranial differentiation, however, exists still between Hawaiian-born Japanese and Caucasians.

Other racial differences have also been reported. Russo found Blacks have much less of an abnormality in the cervical portion of the carotid arteries than Caucasians. He suspected the existence of some inherent racial difference in postangiodine and/or platelet aggregation. More extensive investigative efforts are needed to determine the etiology of the extra-intracranial differences in the progression of cerebral vascular disease in various population groups.

Acknowledgment

The contributions of Ms. Jan Frye, Ms. Kathy Elledge and Ms. Donna Hunt are gratefully acknowledged.

References

Cerebral angiographic and clinical differences in carotid system transient ischemic attacks between American Caucasian and Japanese patients.

K Nishimaru, L C McHenry, Jr and J F Toole

Stroke. 1984;15:56-59
doi: 10.1161/01.STR.15.1.56

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/15/1/56

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org/subscriptions/