Carotid Intima-Media Thickness and Plaque Characteristics as a Risk Factor for Stroke in Japanese Elderly Men

Akihiko Kitamura, MD; Hiroyasu Iso, MD; Hironori Imano, MD; Tetsuya Ohira, MD; Takeo Okada, MD; Shinichi Sato, MD; Masahiko Kiyama, MD; Takeshi Tanigawa, MD; Kazumasa Yamagishi, MD; Tetsuya Shimamoto, MD

**Background and Purpose**—Few cohort studies have examined the association of carotid intima-media thickness (IMT) and plaque characteristics with the risk of stroke in apparently healthy persons. We examined the relationship of carotid IMT and the surface, morphology, and calcification of carotid plaques with the incidence of stroke among Japanese men.

**Methods**—Carotid IMT and plaque were evaluated bilaterally with ultrasonography in 1289 men aged 60 to 74 years without a previous stroke or coronary heart disease. In this cohort, the subsequent incidence of stroke was investigated.

**Results**—During the 4.5-year follow-up, 34 strokes occurred. The multivariate-adjusted relative risk (95% CI) for the highest versus lowest quartiles of maximum IMT of the common carotid artery (CCA; ≥1.07 versus ≤0.77 mm) was 3.0 (1.1 to 8.3) for stroke. The combination of CCA and internal carotid artery (ICA) wall thickness was a better predictor of the risk of stroke than was CCA wall thickness alone. Men with a plaque, defined as a focal wall thickness of ≥1.5 mm, in the ICA had a 3-fold higher risk of stroke than those without a plaque, and the plaque surface irregularity further increased the stroke risk. A significant excess risk of stroke was confined to men with an uncalcified plaque.

**Conclusions**—Increased IMT of the CCA and an uncalcified plaque in the ICA, as assessed by ultrasonography, are risk factors for stroke in elderly Japanese men. *(Stroke. 2004;35:2788-2794.)*

**Key Words:** atherosclerosis ■ carotid artery ■ epidemiology ■ risk factors ■ stroke

Prospective population-based studies in Europe and the United States have documented that carotid intima-media thickness (IMT) and plaque are positively associated with the subsequent incidence of stroke. Furthermore, 2 prospective studies have investigated the association between echogenicity of plaques or carotid artery lesions and stroke risk in American populations; 1 study indicated that hypochoic plaque was associated with increased risk of ischemic stroke, and the other study implied that acoustic shadowing on carotid artery lesions is predictive of ischemic stroke.

In Asian countries, a previous follow-up study of Japanese patients with cardiovascular diseases or high-risk profiles showed a positive association between the severity of carotid plaque and the risk of ischemic stroke, but no prospective study has been conducted in a general population. The aim of this prospective study was to systematically examine the incidence of stroke in relation to carotid IMT and the surface, morphology, and calcification of carotid plaque in community-dwelling Japanese elderly men.

**Subjects and Methods**

**Study Population**

Subjects comprised 1358 men aged 60 to 74 years who were all participants of the target ages in a cardiovascular risk survey between 1996 and 2000. Subjects lived in 1 urban and 2 rural communities in Japan (Minamitakayasu district in Yao City, an urban community in Osaka Prefecture, 278 miles west of Tokyo, with a total census of 23,552 in 2000; Ikawa town, a rural community in Akita Prefecture, 280 miles northeast of Tokyo, with a total census of 611; and Noichi town, a rural community in Kochi Prefecture, 393 miles southwest of Tokyo, with a total census of 16,595). Participants were recruited from all the residents ≥40 years old in each community for the purpose of primary prevention of cardiovascular diseases, and the number of participants was 420 in the urban community, 435 in the northeast rural community, and 503 in the southwest rural community. The respective participation rate for the census population within the target ages was 31%, 79%, and 45%. Individuals with a history of stroke (n=46) or coronary heart disease (n=23) were excluded, leaving 1289 men for the analysis.

**Baseline Examination**

Carotid arteries were evaluated with high-resolution B-mode ultrasonography. We adopted the same ultrasonography protocol used in one of the largest population-based studies of carotid atherosclerosis among elderly Americans [the Cardiovascular Health Study (CHS)]. A single trained physician (A.K.) conducted the ultrasonographic scanning and interpreted the results. The imaging protocol involved obtaining a single longitudinal lateral view of the distal 10 mm of the right and left common carotid arteries (CCAs) and 3 longitudinal views (anterior-oblique, lateral, and posterior-oblique) of each internal carotid artery (ICA). The ICA was defined as including the carotid bulb, identified by loss of the parallel wall.
present in the CCA, and the 10-mm segment of the ICA distal to the

tip of the flow divider that separates the internal and external carotid

arteries. To quantify the degree of thickening of the carotid artery

carotid walls, we assessed the maximum IMT; maximum IMT of the CCA

was defined as the single thickest wall of the near and far right or left

walls of the CCA. Maximum IMT of the ICA was defined in the same

way from the 3 scan views on the right and left ICA. Plaque in the

ICA wall was defined as a focal wall thickness of $\geq 1.5$ mm and

was categorized according to several surface characteristics: smooth-

ness (smooth, mildly irregular, markedly irregular, or ulcerated),

morphology (homogeneous or heterogeneous), and density (hypo-
dense, isodense, hyperdense, or calcified). In cases with multiple

plaques, only the thickest plaque was evaluated. These definitions

were similar to those used in the CHS.5

Cardiovascular risk factors were also measured at baseline exam-

ination, using the same protocol among the 3 communities. Systolic

blood pressure (SBP) and fifth-phase diastolic blood pressure (DBP)

in the right arm were measured by trained nurses using standard

mercury sphygmomanometers in quietly seated participants after a

$\geq 5$-minute rest. When the first SBP was $\geq 140$ mm Hg or the first

DBP was $\geq 90$ mm Hg, the measurement was repeated. The second

reading was used in the analyses; otherwise, the first reading was

used. Physical and biochemical examinations, ECG, assessment of

smoking and drinking habits by interviews, and quality control

procedures have been reported previously.6 Hypertension was de-

fined as an SBP $\geq 140$ mm Hg, DBP $\geq 90$ mm Hg, or use of

antihypertensive medication. ST-T abnormalities and left ventricular

hypertrophy (LVH) on ECG were defined as Minnesota Codes 4-1 to

4-3 or 5-1 to 5-3 and 3-1 plus 5-1 to 5-3, respectively. Diabetes

mellitus was defined as a fasting glucose level of $\geq 126$ mg/dL, or a

nonfasting glucose level of $\geq 200$ mg/dL, or use of medication for
diabetes.

Ascertainment of Incident Cardiovascular Diseases

Subjects were followed to determine the incidence of stroke occur-
ing by the end of 2002. Clinical end points were assessed blinded to

the ultrasound measurements. Follow-up was terminated when

subjects withdrew from the cohort because of nonstroke death

(n=78) or moved out from the communities (n=15). Subjects were

censored from the follow-up analysis at the date of the withdrawal.

Stroke was defined as a constellation of neurological deficits,
sudden or rapid in onset, lasting $\geq 24$ hours, or until death. A
diagnosis of embolic infarction was made when evidence of an
embolic source was reported in the medical records and if imaging
studies and a neurology consult supported the diagnosis. Classifica-
tion of other stroke subtypes (large-artery occlusive infarction,
lacunar infarction, intraparenchymal hemorrhage, and subarachnoid
hemorrhage) was based on imaging studies.9 Nonembolic stroke

cases without imaging studies available were categorized according
to clinical signs and symptoms.9 The study protocol was approved by

the human ethics review committee of Osaka Medical Center for

Health Science and Promotion.

Statistical Analysis

Differences in mean values and prevalence of baseline characteris-
tics between men who developed stroke and men who remained free

of stroke were tested by the t test and $\chi^2$ test, respectively. Incidence

dates per 1000 person years for stroke were calculated by quartiles of

maximum IMT of the CCA, maximum IMT of the ICA, and the

combination of maximum IMT of the CCA and the ICA, each split

at the fourth quartile. Kaplan–Meier method was used to examine

cumulative stroke-free rates according to quartiles of carotid artery

IMT, and differences in cumulative stroke-free rates by quartiles

were tested using log-rank test. The Cox proportional-hazards

regression model was used to estimate the relative risk of stroke

relative to the lowest quartile of maximum IMT or relative to men

having no plaque in the ICA, adjusting for age and other potential

confounding factors. The potential confounding factors included age

(years), SBP (mm Hg), antihypertensive medication use (yes or no),

ST-T abnormalities (yes or no), body mass index (kg/m2), and

community (dummy variables). All analyses were performed using a

standard statistical package (SPSS/PC, version 11.0; SPSS Inc.).

Results

During the mean follow-up period of 4.5 years, we identified

34 strokes. Twenty-five stroke cases were confirmed by

imaging studies comprising 9 intraparenchymal hemorrhages,

10 lacunar infarctions, 4 large-artery occlusive infarctions,

and 2 embolic infarctions. Nine stroke cases without imaging

studies consisted of 6 probable lacunar infarctions with minor

motor and sensory symptoms, 1 probable large-artery occlusive

infarction with cortical signs, and 2 unclassified strokes.

Table 1 shows the baseline risk characteristics of incident

stroke and those who remained free of stroke. The mean age,

SBP and DBP levels, prevalence of hypertension, the mean

maximum IMT of the CCA, and prevalence of plaque were

significantly higher in men who developed stroke than in men

who remained free of stroke. Prevalence of antihypertensive

medication use, ST-T abnormalities and LVH on ECG, and the

mean body mass index tended to be higher in men with

incident stroke than in men without stroke, although the
differences were not statistically significant. Adjustment for

age did not alter these findings (data not shown).

Figure 1 shows the incidence rates per 1000 person years of

stroke according to quartiles of maximum CCA or ICA IMT.

Compared with men with the lowest quartile of CCA wall

thickness, the incidence of stroke tended to be higher in men

in the second or third quartile and was $\geq 4$-fold higher in men

in the highest quartile. The gradient of increased risk of stroke

was less pronounced for ICA than for CCA wall thickness. The

combined categories of wall thickness of the CCA and the

ICA showed a more prominent risk gradient than each

measure alone. The cumulative stroke-free rate declined more

for the fourth quartile of CCA IMT than for the other 3

quartiles of CCA (Figure 2). A similar but weaker trend was

observed for ICA IMT. The divergence of the stroke-free rate

according to the combined categories was most evident.

Table 2 provides the relative risks of stroke by quartiles of

maximum CCA or ICA wall thickness. The age-adjusted

relative risk among men in the highest versus lowest quartiles

of maximum CCA wall thickness was 3.5 for total stroke and

3.8 for ischemic stroke. Further adjustment for potential

cardiovascular factors attenuated these associations slightly,

but relative risk remained statistically significant for total

stroke. In contrast, there was no significant association

between the degree of maximum ICA IMT and the incidence

of total or ischemic stroke. The combined category of

maximum CCA and ICA wall thickness was a better predictor

than was maximum CCA wall thickness alone.

The age-adjusted relative risks (95% CI) in men with a

plaque (n=535) in the ICA compared with men without

plaque (n=754) was 3.3 (1.5 to 7.1) for total stroke and 4.4

(1.6 to 12.2) for ischemic stroke. The respective multivariate

relative risk was 3.2 (1.4 to 7.1) and 4.2 (1.5 to 11.8; not

shown in the table).

The relative risks of stroke according to plaque character-

istics in the ICA are shown in Table 3. Age-adjusted and

multivariate-adjusted relative risks of total and ischemic

stroke were higher with increasing surface irregularity. These
excess risks were similar among men with homogeneous plaque and those with heterogeneous plaque. The excess risks were higher among men with an uncalcified plaque than among men with a calcified plaque.

**Discussion**

The present study showed a positive association between carotid IMT, a measure of carotid and generalized atherosclerosis, and the incidence of stroke in Japanese male residents aged 60 to 74 years. Maximum IMT of the CCA and plaque in the ICA are strong predictors for risk of stroke. The combination of CCA and ICA wall thickness provided a better prediction for stroke than did either IMT variable alone.

Three population-based prospective studies in the United States and Netherlands reported a positive association between intima-media thickening in the CCA and the incidence of stroke. The CHS reported that the multivariate relative risk of stroke for the highest versus lowest quintiles of maximum IMT in the CCA (≥1.18 mm versus <0.87 mm) was 2.13 (95% CI, 1.38 to 3.28). The Atherosclerosis Risk in Communities (ARIC) Study showed that the multivariate relative risk of ischemic stroke for the highest versus lowest tertiles of mean IMT of the far wall of the CCA (≥0.70 mm versus <0.59 mm) was 2.69 (95% CI, 1.49 to 4.87) in men and 1.65 (95% CI, 0.85 to 3.19) in women. In the Rotterdam Study, the multivariate relative risk of total stroke for the highest tertile versus lowest tertile of mean IMT in the CCA

**Table 1. Baseline Characteristics of Men Developing Stroke and Remaining Free of Stroke**

<table>
<thead>
<tr>
<th></th>
<th>Incident Stroke (n=34)</th>
<th>Free of Stroke (n=1255)</th>
<th>Difference (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68 (3)</td>
<td>66 (4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>146 (19)</td>
<td>138 (18)</td>
<td>0.007</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>87 (9)</td>
<td>83 (11)</td>
<td>0.018</td>
</tr>
<tr>
<td>Antihypertensive medication use, %</td>
<td>35 25</td>
<td>25</td>
<td>0.16</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>77 53</td>
<td>53</td>
<td>0.008</td>
</tr>
<tr>
<td>ST-T abnormalities, %</td>
<td>15 6</td>
<td>6</td>
<td>0.06</td>
</tr>
<tr>
<td>ECG-LVH, %</td>
<td>9 3</td>
<td>3</td>
<td>0.06</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>24.1 (2.8)</td>
<td>23.2 (2.8)</td>
<td>0.07</td>
</tr>
<tr>
<td>Ethanol intake, g per day</td>
<td>23.6 (20.4)</td>
<td>25.4 (25.7)</td>
<td>0.69</td>
</tr>
<tr>
<td>Serum total cholesterol, mmol/L</td>
<td>5.31 (0.91)</td>
<td>5.10 (0.90)</td>
<td>0.20</td>
</tr>
<tr>
<td>High-density lipoprotein-cholesterol, mmol/L</td>
<td>1.35 (0.32)</td>
<td>1.43 (0.39)</td>
<td>0.24</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>12 11</td>
<td>11</td>
<td>0.78</td>
</tr>
<tr>
<td>Current smokers, %</td>
<td>50 39</td>
<td>39</td>
<td>0.21</td>
</tr>
<tr>
<td>Maximum CCA IMT, mm</td>
<td>1.11 (0.28)</td>
<td>1.03 (0.43)</td>
<td>0.27</td>
</tr>
<tr>
<td>Maximum ICA IMT, mm</td>
<td>1.97 (0.93)</td>
<td>1.57 (0.76)</td>
<td>0.002</td>
</tr>
<tr>
<td>Plaque, %</td>
<td>71 41</td>
<td>41</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are unadjusted means (SD) or proportions.

Figure 1. Incidence of stroke according to quartiles and combined categories of carotid artery IMT. *Quartile cut points are 0.78, 0.96, and 1.07 mm for maximum CCA IMT. †Quartile cut points are 1.06, 1.35, and 1.93 mm for maximum ICA IMT. ‡Combined category was as follows: (1) maximum CCA IMT <1.07 mm and maximum ICA IMT <1.93 mm. These values were the respective cut points of fourth quartile; (2) maximum CCA IMT <1.07 mm and maximum ICA IMT ≥1.93 mm; (3) maximum CCA IMT ≥1.07 mm and maximum ICA IMT <1.93 mm; and (4) maximum CCA IMT ≥1.07 mm and maximum ICA IMT ≥1.93 mm.
Because we used the same protocols for carotid ultrasonography as those used in the CHS, our findings could be compared with data from the CHS. The excess risk of stroke with CCA intima-media thickening tended to be greater in elderly Japanese than in elderly American counterparts; however, the differences in the range of age, gender, cut-off values of IMT, and probably distributions of stroke subtypes must be taken into consideration. Although the CHS did not describe the distribution of stroke subtypes, on the basis of results from previous population-based studies in the United States, 11,12 we inferred that their strokes comprised a higher proportion of large-artery occlusive infarctions than lacunar infarctions and intraparenchymal hemorrhage. In contrast, our stroke cases comprised a higher proportion of definite or probable lacunar infarctions (47%) and intraparenchymal hemorrhage (26%) compared with large-artery occlusive infarctions (15%). Increased carotid IMT may be a strong marker for arteriosclerotic lesions in intracranial small-vessel arteries. Our findings are supported by the results of the Rotterdam Study, which showed that carotid plaques were associated with the risk of lacunar infarction.4

To our knowledge, this is the first prospective study for general populations to demonstrate significant associations of plaque surface irregularity with the subsequent risk of stroke, although the Medical Research Council (MRC) European Carotid Surgery Trial showed that patients with irregular plaque had a higher risk of stroke than did those with smooth plaque.13 We speculate that plaque irregularity in a carotid artery may be a marker of the severity of arteriosclerosis in intracranial small vessels as well as a source of carotid artery-to-brain artery embolism. This speculation is supported by the results of the CHS, which showed a positive association between carotid plaque surface irregularity and the prevalent lacunar infarction detected by MRI.14

Evidence on calcified plaque of the carotid artery and risk of stroke is sparse. A cross-sectional study of Finnish elderly men reported a lack of the association between carotid mineralizations and clinical cardiovascular disease.15 We did not have a significant excess risk of total or ischemic stroke associated with calcified plaque. The CHS also reported a nonsignificant relative risk of 6.93 (95% CI, 0.8 to 60.2) for incident stroke with calcified plaque.5 Plaque accompanied by calcification may be stable and therefore not increase the stroke risk so much. However, it is also possible that the statistical insignificance of the association was attributable to only low stroke incidence. On the other hand, there was a significant excess risk of total and ischemic strokes among men with a plaque free of calcification compared with men with no plaque. The ARIC study showed that carotid artery lesions without acoustic shadowing, after adjustment for several risk factors, were predictive of ischemic stroke in men,6 which supported our findings.

We did not evaluate the risk of stroke for echolucent uncalcified plaques, which have been reported to increase risk for stroke in clinical and epidemiological studies;5,16 the proportion of hypoechoic plaques in our sample was too low (1.2%). Another limitation of the present study is we did not

Figure 2. Cumulative stroke-free rates according to quartiles and combined categories of carotid artery IMT. Cut points for quartile and combined categories were the same as shown in Figure 1. Difference in cumulative stroke-free rates by 4 categories is P<0.001 for all 3 variables.
examine the associations between carotid IMT and risks of stroke subtypes because of the small numbers of cases. A large follow-up study is necessary to clarify these relationships.

We conclude that wall thickening of the CCA and uncalcified plaque formation in the ICA, as assessed by ultrasonography, are positively associated with an increased risk of stroke in elderly Japanese men.

**Acknowledgments**

This study was supported by grants-in-aid research B (11877069 in 1998 to 1999 and 12470992 in 2000 to 2001) from the Ministry of Health, Welfare and Labor, Japan. We thank Professor Aaron R. Folsom, University of Minnesota, Minneapolis, for the valuable comments. We also thank Professor Daniel H. O’Leary from Tufts University School of Medicine, Boston, Mass, for providing training sessions for scanning and reading the carotid ultrasound.

**TABLE 2. Relative Risk (RR) of Stroke According to Quartiles (or Combination Categories) of Carotid Artery IMT**

<table>
<thead>
<tr>
<th>Maximum CCA IMT</th>
<th>≤0.77 mm</th>
<th>0.78–0.95 mm</th>
<th>0.96–1.06 mm</th>
<th>≥1.07 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at risk</td>
<td>361</td>
<td>273</td>
<td>339</td>
<td>316</td>
</tr>
<tr>
<td>Person years of follow-up</td>
<td>1613</td>
<td>1246</td>
<td>1569</td>
<td>1404</td>
</tr>
</tbody>
</table>

Total stroke

| Age-adjusted RR | 1.0 | 0.9 (0.2–3.4) | 1.1 (0.3–3.6) | 3.5 (1.3–9.5)* |
| Age-adjusted RR | 1.0 | 0.9 (0.2–3.4) | 1.0 (0.3–3.2) | 3.0 (1.1–8.3)* |

Ischemic stroke

| No. of cases | 5 | 5 | 6 | 18 |
| Age-adjusted RR | 1.0 | 1.6 (0.3–7.0) | 1.3 (0.3–5.6) | 3.8 (1.0–13.6)* |
| Multivariate RR§ | 1.0 | 1.7 (0.4–7.6) | 1.1 (0.3–5.1) | 3.3 (0.9–12.2) |

**Maximum ICA IMT**

| ≤1.05 mm | 1.06–1.34 mm | 1.35–1.92 mm | ≥1.93 mm |
| No. at risk | 317 | 309 | 343 | 318 |
| Person years of follow-up | 1437 | 1407 | 1583 | 1396 |

Total stroke

| Age-adjusted RR | 1.0 | 0.9 (0.3–2.4) | 1.6 (0.7–3.9) |
| Multivariate RR§ | 1.0 | 0.9 (0.3–2.3) | 1.4 (0.6–3.5) |

Ischemic stroke

| No. of cases | 6 | 0 | 6 | 11 |
| Age-adjusted RR | 1.0 | 1.0 (0.3–3.4) | 2.0 (0.7–6.0) |
| Multivariate RR§ | 1.0 | 1.0 (0.3–3.2) | 1.7 (0.6–5.2) |

**Maximum CCA and ICA IMT**

| CCA IMT<1.07 mm and ICA IMT<1.93 mm | CCA IMT<1.07 mm and ICA IMT ≥1.93 mm | CCA IMT≥1.07 mm and ICA IMT<1.93 mm | CCA IMT≥1.07 mm and ICA IMT≥1.93 mm |
| No. at risk | 779 | 192 | 190 | 126 |
| Person years of follow-up | 3557 | 861 | 870 | 535 |

Total stroke

| Age-adjusted RR | 1.0 | 1.9 (0.6–5.5) | 3.1 (1.2–8.0)* | 5.5 (2.2–13.5)‡ |
| Multivariate RR§ | 1.0 | 1.6 (0.5–4.8) | 2.8 (1.1–7.2)* | 4.8 (1.9–12.0)† |

Ischemic stroke

| No. of cases | 9 | 3 | 3 | 8 |
| Age-adjusted RR | 1.0 | 1.5 (0.4–5.6) | 1.5 (0.4–5.7) | 6.0 (2.2–16.5)† |
| Multivariate RR§ | 1.0 | 1.2 (0.3–4.6) | 1.3 (0.4–5.1) | 5.2 (1.8–14.6)† |

*P<0.05.
†P<0.01.
‡P<0.001.
§Adjusted further for SBP (mm Hg), antihypertensive medication use (yes or no), ST-T abnormalities (yes or no), body mass index (kg/m²), and community (dummy values).
||Two data of maximum ICA IMT were missing values.
TABLE 3. Relative Risk (RR) of Stroke According to Characteristics of Plaque in the ICA

<table>
<thead>
<tr>
<th>Surface</th>
<th>Smooth or Mildly Irregular Plaque (+)</th>
<th>Markedly Irregular or Ulcerated Plaque (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at risk</td>
<td>752</td>
<td>467</td>
</tr>
<tr>
<td>Person years of follow-up</td>
<td>3417</td>
<td>2094</td>
</tr>
<tr>
<td>Total stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td>1.0</td>
<td>3.1 (1.4–6.9)†</td>
</tr>
<tr>
<td>Multivariate RR‡</td>
<td>1.0</td>
<td>3.0 (1.3–6.9)†</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td>1.0</td>
<td>4.0 (1.4–11.4)†</td>
</tr>
<tr>
<td>Multivariate RR‡</td>
<td>1.0</td>
<td>3.9 (1.4–11.3)*</td>
</tr>
</tbody>
</table>

| Morphology                                   |                                      |                                            |                                            |
| Plaque (−)                                   | 752                                  | 293                                        | 242                                        |
| Person years of follow-up                    | 3417                                 | 1314                                       | 1092                                       |
| Total stroke                                 |                                      |                                            |                                            |
| No. of cases                                 | 10                                   | 13                                         | 11                                         |
| Age-adjusted RR                              | 1.0                                  | 3.4 (1.4–8.0)†                             | 3.2 (1.3–7.8)*                             |
| Multivariate RR‡                             | 1.0                                  | 3.3 (1.4–7.9)†                             | 3.1 (1.2–7.7)*                             |
| Ischemic stroke                              |                                      |                                            |                                            |
| No. of cases                                 | 6                                    | 9                                          | 8                                          |
| Age-adjusted RR                              | 1.0                                  | 4.5 (1.5–13.4)†                            | 4.5 (1.4–14.0)*                            |
| Multivariate RR‡                             | 1.0                                  | 4.3 (1.4–13.0)*                            | 4.3 (1.3–13.7)*                            |

| Calcification                                |                                      |                                            |                                            |
| Plaque (−)                                   | 752                                  | 407                                        | 128                                        |
| Person years of follow-up                    | 3417                                 | 1820                                       | 586                                        |
| Total stroke                                 |                                      |                                            |                                            |
| No. of cases                                 | 10                                   | 19                                         | 5                                          |
| Age-adjusted RR                              | 1.0                                  | 3.5 (1.6–7.9)†                            | 2.5 (0.8–7.8)†                            |
| Multivariate RR‡                             | 1.0                                  | 3.4 (1.5–7.7)†                            | 2.6 (0.8–8.1)†                            |
| Ischemic stroke                              |                                      |                                            |                                            |
| No. of cases                                 | 6                                    | 14                                         | 3                                          |
| Age-adjusted RR                              | 1.0                                  | 4.9 (1.8–13.9)†                            | 3.0 (0.7–12.9)†                            |
| Multivariate RR‡                             | 1.0                                  | 4.7 (1.6–13.4)†                            | 2.8 (0.6–12.5)†                            |

*P<0.05. †P<0.01. ‡Adjusted for the same variables listed in Table 2.

References
Carotid Intima-Media Thickness and Plaque Characteristics as a Risk Factor for Stroke in Japanese Elderly Men

Akihiko Kitamura, Hiroyasu Iso, Hironori Imano, Tetsuya Ohira, Takeo Okada, Shinichi Sato, Masahiko Kiyama, Takeshi Tanigawa, Kazumasa Yamagishi and Takashi Shimamoto

Stroke. 2004;35:2788-2794; originally published online November 4, 2004; doi: 10.1161/01.STR.0000147723.52033.9e

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
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:
http://stroke.ahajournals.org/content/35/12/2788

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/