Association of Adiponectin With Cerebrovascular Disease
A Nested Case–Control Study

Masatoshi Matsumoto, MD; Shizukiyo Ishikawa, MD; Eiji Kajii, MD

Background and Purpose—Even though adiponectin is associated with many traditional cardiovascular risk factors, studies assessing the association between adiponectin and cerebrovascular disease (CVD) are scarce. We assessed the odds of CVD at different plasma levels of adiponectin.

Methods—A nested case–control study was conducted involving 5243 subjects, drawn from 12 490 subjects of the Jichi Medical School Cohort Study, whose blood samples had been drawn between 1992 and 1995. Over an average of 9.7 years of follow-up, through 2005, 179 patients with cerebrovascular events were identified, in addition to 630 controls matched for age, sex, and community (total n=809). Odds ratios were estimated relative to the highest quartile of adiponectin level.

Results—There was neither a significant difference in the odds of stroke between the lowest and highest adiponectin quartiles, nor a significant linear trend toward a reduced risk of stroke at higher adiponectin levels. These results did not change after excluding participants with diabetes, impaired glucose metabolism, or metabolic syndrome. The odds of ischemic stroke in the lowest quartile were significantly higher than in the highest quartile, when adjusted for age and sex (OR 2.04 [95% CI, 1.09 to 3.80]). However, the odds failed to achieve statistical significance when adjusted further for other cardiovascular risk factors. Again exclusion of subjects with diabetes, impaired glucose metabolism, or metabolic syndrome did not alter results.

Conclusions—Adiponectin levels are not independently associated with stroke or brain infarction. The use of adiponectin as a cerebrovascular disease predictor may be premature. (Stroke. 2008;39:323-328.)

Key Words: adiponectin □ atherosclerosis □ cerebrovascular disease □ prospective study

Adiponectin, also termed Acrp30, AdipoQ, apM1, and GBP28, is an approximately 30-kDa plasma protein, and the most abundant gene product in adipose tissue. Lower plasma adiponectin levels have been shown to be associated with hypertension, type 2 diabetes, increased insulin resistance, high triglyceride levels, low levels of high-density (HDL) lipoprotein cholesterol, and inflammation. In short, adiponectin is associated with many traditional cardiovascular risk factors; and some role of adiponectin in the development of atherosclerosis, inflammation, and subsequent cardiovascular diseases is highly anticipated.

However, the number of studies evaluating the association between adiponectin and cardiovascular diseases is limited, and results are inconclusive. Some investigators suggest a pathogenic role of hypoadiponectinemia in myocardial infarction, whereas other studies fail to do so. Studies assessing the association between adiponectin and cerebrovascular disease (CVD) are even scarcer. Two case–control studies have been reported, one with a positive and one with a negative result, and no study has prospectively assessed whether adiponectin is associated with ischemic CVD, independent of other cardiovascular risk factors.

Consequently, we conducted a case–control study nested within the Jichi Medical School (JMS) Cohort Study to identify any association between plasma adiponectin concentrations and the risk of CVD over a follow-up period of 9 years.

Methods

Study Population
The JMS Cohort Study began in 1992. Its primary objective was to clarify the relationship between potential risk factors and cardiovascular diseases in 12 rural districts in Japan. The baseline data of this cohort study were obtained between April 1992 and July 1995. If several sets of data were obtained for a single subject during that period, the first set was used as baseline. The baseline data were collected as part of a national mass-screening program. In Japan, mass screening for cardiovascular diseases has been conducted since 1982, in accordance with the Health and Medical Service for the Aged Act of 1981. Local government offices in each community issued invitations to eligible residents for the mass screening, and personal invitations also were sent to all potential subjects by mail. As a result, 12 490 subjects were eligible (4913 males and 7577 females) across all ages (19 to 93 years of age). Among them 112 (0.9%) had a previous history of stroke. The overall response rate among the 12 communities was 65.0%. Written informed consent to participate in the study was obtained individually from all respondents of the mass screening.

Among the 12 490 subjects, 5243 subjects (42.0%) whose blood samples remained stored in 2007 were extracted as potential study participants because adiponectin measurements were not included in baseline analyses. Among these potential subjects, 252 individuals
with at least one cardiovascular event and 756 matched controls were extracted (a case to control ratio of 1 to 3) for another case–control study. Matching was for sex and community, and within 5 years for age. For our study, within the case sample, individuals with non-stroke events, those who did not sign the agreement to participate in the study, and those who had a past history of stroke were excluded. In the end, 809 subjects (179 cases and 630 controls) remained and were analyzed as study participants.

**Measurement of Baseline Variables**

To synchronize the methods of data collection, we established a central committee, which was composed of the chief medical officers from all of the participating districts. This committee developed a detailed manual for data collection. Body weight was recorded with the subject clothed, and 0.5 kg in summer or 1 kg during the other seasons was subtracted from the recorded weight. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). Systolic blood pressure and diastolic blood pressure were measured with a fully-automated sphygmomanometer, BP203RV-II (Nippon Colin), placed on the right arm of a seated subject who had rested in the sitting position for 5 minutes before measurement. Information about medical history and lifestyle was gathered by means of a written questionnaire.

Blood samples were drawn from the antecubital vein of seated subjects, with minimal tourniquet use. Specimens were collected in siliconised vacuum glass tubes containing a 1/10 volume of 3.8% trisodium citrate for blood glucose, and no additives for lipids. Tubes were centrifuged at 3000g for 15 minutes at room temperature. After separation, the serum samples were stored at 4°C in refrigerated containers if analysis was to be performed within a few days. Otherwise, the samples were frozen until analysis. Plasma samples were frozen as rapidly as possible to −80°C for storage, until laboratory examination could be performed.

Total cholesterol and triglycerides were measured using an enzymatic method (Wako; interassay coefficient of variation [CV]: 1.5% for total cholesterol and 1.7% for triglyceride). HDL cholesterol was measured using the phosphotungstate precipitation method (Wako; interassay CV: 1.9%). Blood glucose was measured via an enzymatic method (Kanto Chemistry; interassay CV: 1.9%). High-sensitivity C-reactive protein (hsCRP) levels were measured using nephelometry, a latex particle-enhanced immunoassay (NA Latex CRP Kit, Dade Behring). The value in the calibrator was assigned from the Certified Reference Material 470 (BMR), an international plasma protein reference manual; its interassay and intraassay CVs were 1.18 and 1.36%, respectively; the assay is sensitive enough to detect 0.03 mg/dL of CRP. Plasma adiponectin concentrations were measured by solid phase enzyme-linked immunosorbent assay (adiponectin ELIZA kit; Otsuka Pharmaceutical Co Ltd) The interassay coefficient of variation was less than 10%. The ideal measurement range was between 0.375 and 12.0 mg/dL. The maximal detectable range was >23.4 pg/mL. Both high-sensitivity CRP and adiponectin were measured in 2007. The other biochemical markers were measured concurrent with sample collection.

In this study, blood samples of 634 (78.4%) subjects were drawn after overnight fasting. “Diabetic subjects” were defined as those with currently-treated diabetes, plasma glucose ≥126 mg/dL, after overnight fasting, or casual blood glucose ≥200 mg/dL. Subjects with “impaired glucose metabolism” were defined as those with currently-treated diabetes, plasma glucose ≥110 mg/dL, after overnight fasting, or casual blood glucose ≥140 mg/dL.

According to the criteria of International Diabetes Federation, subjects with “metabolic syndrome” were defined as those with “obesity” plus any 2 of the following conditions:14

1. Triglyceride level >150 mg/dL or treatment for this lipid abnormality
2. HDL cholesterol <40 mg/dL in males and <50 mg/dL in females or treatment for this lipid abnormality
3. Systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg or treatment of diagnosed hypertension
4. Fasting plasma glucose ≥100 mg/dL or casual blood glucose ≥140 mg/dL or previously diagnosed diabetes.

Because information on waist circumference was not available in most cases, BMI ≥25 kg/m^2 was used for the definition of “obesity.”

**Follow-Up**

Repeat examinations, which also were part of the national mass-screening program, were used to follow most subjects every year. Those examined were asked whether they had experienced a CVD after enrolling. Subjects who did not come to the screening examination were contacted by mail or phone. Public health nurses visited the subjects to obtain pertinent information when necessary. In all, 100% of the subjects were contacted. Those with a history of CVD were asked in which hospital they had been treated and when the disease was ascertained. Medical records at hospitals in the areas also were checked to determine whether these subjects had been treated. If an incident was suspected, forms were filled out and pertinent computer tomography or MRI images were obtained for diagnostic ascertainment of CVD.

**Diagnostic Criteria**

Diagnoses were determined independently, by means of a diagnosis committee, composed of 1 radiologist, 1 neurologist, and 2 cardiologists. A diagnosis of stroke was determined on the basis of the presence of a focal and nonconvulsive neurological deficit, of clear onset, lasting for 24 hours or longer. Stroke subtypes were confirmed based on computer tomography or MRI images in all cases except 2 (1.1%) whose images were unavailable and therefore the diagnosis was based only on medical records in local hospitals.

**Statistical Analysis**

Statistical analyses were carried out using SPSS for Windows, version 11.5 (SPSS Inc., Japan). Continuous variables were compared between cases and controls using unpaired t tests. Categorical variables were compared using chi-squared analysis or the Fisher exact test. Correlations between plasma adiponectin levels and selected cardiovascular risk factors were evaluated by estimating age- and sex-adjusted partial correlation coefficients for continuous variables and performing unpaired t tests for categorical variables.

The associations between adiponectin and stroke and ischemic stroke were examined by means of logistic regression analysis. Goodness of fit was confirmed by the Hosmer and Lemeshow method. For logistic regression analysis, adiponectin levels were categorized into quartiles, using results from all study subjects. Three separate models were generated for regression analysis: Model 1 was adjusted for age and sex; Model 2 was adjusted for age, sex, BMI, HDL cholesterol, and triglyceride; and Model 3 was adjusted for age, sex, BMI, HDL cholesterol, triglyceride, systolic blood pressure, current smoking status, and high-sensitivity CRP.14 Log10-transformed adiponectin level and standard deviation increase in log10 adiponectin were used to test for linear trends across categories. The standard deviation increase in log10 adiponectin was further evaluated excluding diabetes subjects and subjects with impaired glucose metabolism, because of the presumed interaction between these factors and both adiponectin levels and CVD risk.

Levels of adiponectin, triglyceride, and high-sensitivity CRP were not normally distributed; consequently, they were log10-transformed in all analyses. All analyses were 2-tailed. P < 0.05 was considered statistically-significant.

**Results**

The mean follow-up periods was 9.7 years (10.60 years [SD, 2.55] in controls and 6.42 years [SD, 3.35] in cases). Measurements of adiponectin and high-sensitivity CRP were conducted 14.2 years [SD, 1.04] in controls and 14.3 years [SD, 1.00] in cases after initial sample collection.

Comparisons of characteristics between stroke cases and controls are shown in Table 1. The proportion of impaired glucose metabolism was significantly greater in stroke cases than controls (22.9% versus 11.5%; P = 0.017), as were mean
systolic blood pressure (140.46 [SD, 23.33] versus 132.19 [SD, 22.35] mm Hg; \( P < 0.001 \)) and mean diastolic blood pressure (82.02 [SD, 12.74] versus 78.11 [SD, 13.21] mm Hg; \( P < 0.001 \)).

Associations between adiponectin and selected cardiovascular risk factors are shown in Table 2. Within the case group, adiponectin levels were negatively correlated with BMI, systolic blood pressure, diastolic blood pressure, triglyceride, and high-sensitivity CRP; among controls, adiponectin levels were negatively correlated with these same variables, plus total cholesterol. Adiponectin was positively correlated with HDL cholesterol, both in cases and controls. Adiponectin levels were higher in males, current smokers, current drinkers, diabetics, those with impaired glucose metabolism, and those with metabolic syndrome, both in stroke cases and controls.

Table 3 shows multivariable-adjusted odds ratios for stroke, across quartiles of adiponectin level. The odds of stroke in the lowest adiponectin quartile (Quartile 1) were higher than those in the highest quartile (Quartile 4), but the difference was not statistically significant. The difference between the odds ratios for the lowest versus the highest quartile was largest in Model 1, in which there was adjustment for other cardiovascular risk factors; there was no significant linear trend toward a reduced risk of stroke at higher adiponectin levels, when all study participants were considered. Excluding either the subjects with diabetes or those with impaired glucose metabolism or those with metabolic syndrome did not alter this result.

Multivariable-adjusted odds ratios for brain infarction among subjects in the lowest quartile were significantly higher than among those in the highest quartile (OR 2.04 [95% CI, 1.09 to 3.80]). However, this odds ratio lost its significance in Model 2 (1.94 [0.96 to 3.91]), and, to an even greater degree, in Model 3 (1.60 [0.78 to 3.31]). Adiponectin levels had no linear association with the risk of brain infarction, when they were entered into logistic regression models as continuous variables (\( P \) for trend = 0.23 in Model 1, 0.50 in Model 2, and 0.90 in Model 3). Exclusion of either the subjects with diabetes or those with impaired glucose metabolism or those with metabolic syndrome did not change the results.

**Discussion**

To our knowledge, this is the first prospective study which has assessed for any independent association between serum adiponectin levels and brain infarction. In this study, adiponectin concentrations were associated with most cardiovascular risk factors. However, low adiponectin levels were neither associated with stroke nor with brain infarction, when adjusted for other cardiovascular risk factors. Exclusion of diabetes, prediabetic conditions, and metabolic syndrome did not influence the results.

Two studies have examined for any association between adiponectin levels and CVD. Soderberg et al conducted a nested case–control study in which no difference in adiponectin levels was identified between stroke cases and matched controls.\(^\text{12}\) This finding is in line with our results. However, their study did not analyze the risk of brain infarction separate from that of stroke. In addition, it did not show the risk of stroke in low-adiponectin groups, when adjusted for other cardiovascular risk factors;
consequently, whether adiponectin has an independent association with stroke or not was not revealed. The other was a case–control study, conducted by Chen et al.11 This hospital-based retrospective study with 228 ischemic CVD cases and 306 controls demonstrated a remarkably strong association between hypoadiponectinemia and ischemic CVD. The odds ratio of brain infarction in the lowest versus the highest quartile of adiponectin level was 130.8, which increased to 739.3 when diabetes subjects were excluded. Our study also showed that hypoadiponectinemia is associated with brain infarction, when adjusted for age and sex, with an odds ratio of just over 2.0. However, clearly, the association in our study was much weaker than that reported by Chen, and the statistical significance of any association disappeared when the model was adjusted for risk factors beyond age and sex. There are possible explanations for the discrepancy between our results and those by Chen et al. First, our study entailed adiponectin levels measured in samples collected before incident cerebrovascular events; conversely, Chen used postevent samples. Moreover, the average adiponectin level among the nondiabetic controls in Chen’s study was much higher than among those in our study (21.8 versus 9.8 mg/L, respectively). This indicates that the target populations in the 2 studies were substantially different, which makes any comparison difficult.

Adiponectin is noted for its direct causal link to liver insulin sensitivity and for its antiinflammatory properties.15,16

Table 2. Associations Between Plasma Adiponectin Level and Selected Cardiovascular Risk Factors in Stroke Cases and Controls*

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Cases (n=179)</th>
<th>Controls (n=630)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Correlation</td>
<td>P Value</td>
</tr>
<tr>
<td>Body mass index</td>
<td>−0.21</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>−0.22</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>−0.17</td>
<td>0.03</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>0.03</td>
<td>0.67</td>
</tr>
<tr>
<td>High density lipoprotein cholesterol</td>
<td>0.25</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Triglyceride†</td>
<td>−0.22</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>High-sensitivity C-reactive protein†</td>
<td>−0.26</td>
<td>&lt;0.01</td>
</tr>
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</table>

Geographic Mean

<table>
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<tr>
<th>Sex</th>
<th>Geographic Mean</th>
<th>Geographic Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>6.73 (4.60–9.80)</td>
<td>6.73 (4.45–10.05)</td>
</tr>
<tr>
<td>Female</td>
<td>9.43 (7.30–14.20)</td>
<td>10.09 (12.80–7.00)</td>
</tr>
<tr>
<td>Treated hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7.98 (6.05–12.50)</td>
<td>8.27 (4.45–12.75)</td>
</tr>
<tr>
<td>No</td>
<td>8.05 (5.60–12.45)</td>
<td>8.26 (5.40–11.65)</td>
</tr>
<tr>
<td>Treated hyperlipidemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>8.42 (4.58–11.96)</td>
<td>8.02 (7.80–9.10)</td>
</tr>
<tr>
<td>No</td>
<td>8.07 (5.60–12.40)</td>
<td>8.12 (5.30–12.05)</td>
</tr>
<tr>
<td>Current smoker</td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>6.31 (4.20–9.80)</td>
<td>6.62 (3.95–10.20)</td>
</tr>
<tr>
<td>No</td>
<td>8.88 (6.08–13.00)</td>
<td>8.70 (6.00–12.30)</td>
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<tr>
<td>Current drinker</td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6.92 (4.90–10.10)</td>
<td>6.94 (4.50–10.20)</td>
</tr>
<tr>
<td>No</td>
<td>8.97 (6.83–13.30)</td>
<td>9.41 (6.20–12.65)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6.03 (4.80–8.40)</td>
<td>6.23 (4.08–8.43)</td>
</tr>
<tr>
<td>No</td>
<td>8.33 (3.96–12.60)</td>
<td>8.44 (5.40–12.30)</td>
</tr>
<tr>
<td>Impaired glucose metabolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5.84 (5.20–10.10)</td>
<td>6.94 (4.15–8.20)</td>
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<tr>
<td>No</td>
<td>8.83 (5.90–12.90)</td>
<td>8.52 (6.25–12.70)</td>
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<tr>
<td>Metabolic syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6.47 (4.20–9.50)</td>
<td>6.35 (4.20–9.50)</td>
</tr>
<tr>
<td>No</td>
<td>8.38 (5.40–12.40)</td>
<td>8.34 (5.80–12.6)</td>
</tr>
</tbody>
</table>

*Values shown are age- and sex-adjusted partial correlation coefficients for continuous variables, and geographic means (interquartile ranges) for categorical variables.
†Adiponectin, triglyceride, and high-sensitivity CRP were log_{10}-transformed for analysis.
Clinically there is evidence that adiponectin is associated with obesity, type 2 diabetes, metabolic syndrome, dyslipidemia, and hypertension. Taking the evidence into account, that hypoadiponectinemia has no or only a minimal association with CVD is surprising. Two reasons for the discrepancy can be considered. As our study indicates, the association of adiponectin with CVD disappears when other biochemical markers are considered as potential confounders. That any association between adiponectin and CVD appears to be dependent on other risk variables, suggests that the effect of adiponectin on vascular events is not direct, but largely acts through mediators of insulin sensitivity and inflammation. Past studies investigating the link of adiponectin to myocardial infarction also have demonstrated that any association disappears when adjustment is made for lipid profiles and certain other markers. This evidence suggests that adiponectin does not have a direct causal link with cardiovascular diseases. Rather, it is a marker of conditions that predispose to cardiovascular conditions.

Another possible explanation pertains to the degree of effect that dyslipidemias have on CVD. Investigators in the West have reported that hypercholesterolemia is an independent risk factor for stroke, particularly for ischemic stroke, although the results also indicate that the degree to which

| Table 3. Multivariable-Adjusted Odds Ratios for Stroke, Relative to Adiponectin Level (179 Cases and 630 Controls) |
|---------------------------------|----------------|----------------|----------------|----------------|----------------|
| Quartile 1                      | OR 95% CI      | P Value        | OR 95% CI      | P Value        | OR 95% CI      | P Value        |
| Range, mg/L                     | Cases Controls |                |                |                |                |                |
| <5.6                            | 52 146         | 1.49 0.90–2.47  | 0.12           | 1.39 0.79–2.42 | 0.25           | 1.15 0.65–2.06 | 0.63 |
| 5.6–8.3                         | 145 156        | 1.11 0.68–1.82  | 0.68           | 0.96 0.56–1.64 | 0.89           | 0.85 0.49–1.48 | 0.57 |
| 8.4–12.3                        | 166 162        | 1.00 0.62–1.63  | 0.99           | 0.94 0.56–1.57 | 0.80           | 0.89 0.52–1.50 | 0.65 |
| 12.4<                           | 162 162        | 1.00            |                | 1.00            |                | 1.00            |                |

P for trend 0.78 0.91 0.59
Per standard-deviation increase in log
Excluding diabetes§ 0.94 0.78–1.12 0.48
Excluding impaired glucose metabolism 0.95 0.79–1.15 0.59
Excluding metabolic syndrome¶ 0.96 0.79–1.16 0.65

*Adjusted for age and sex.
†Model 1: HDL cholesterol, triglyceride, and BMI.
‡Model 2: current smoking, systolic blood pressure, high-sensitivity CRP.
§45 controls and 20 cases were excluded.
¶95 controls and 41 cases were excluded.
¶¶75 controls and 27 cases were excluded.

| Table 4. Multivariable-Adjusted Odds Ratios for Brain Infarction, Relative to Adiponectin Level (116 Cases and 630 Controls) |
|---------------------------------|----------------|----------------|----------------|----------------|----------------|
| Quartile 1                      | OR 95% CI      | P Value        | OR 95% CI      | P Value        | OR 95% CI      | P Value        |
| Range, mg/liter                 | Cases Controls |                |                |                |                |                |
| <5.6                            | 39 146         | 2.04 1.09–3.80  | 0.03           | 1.94 0.96–3.91 | 0.06           | 1.60 0.78–3.31 | 0.20 |
| 5.6–8.3                         | 156 156        | 1.50 0.81–2.78  | 0.20           | 1.25 0.63–2.49 | 0.52           | 1.10 0.54–2.33 | 0.80 |
| 8.4–12.3                        | 166 162        | 1.20 0.64–2.23  | 0.57           | 1.08 0.55–2.12 | 0.83           | 1.00 0.50–2.00 | 1.00 |
| 12.4<                           | 162 162        | 1.00            |                | 1.00            |                | 1.00            |                |

P for trend 0.23 0.50 0.90
Per standard-deviation increase in log
Excluding diabetes§ 0.88 0.71–1.09 0.23
Excluding impaired glucose metabolism 0.91 0.72–1.14 0.39
Excluding metabolic syndrome¶ 0.90 0.71–1.13 0.35

*Adjusted for age and sex.
†Model 1: HDL cholesterol, triglyceride, and BMI.
‡Model 2: current smoking, systolic blood pressure, high-sensitivity CRP.
§45 controls and 17 cases were excluded.
¶95 controls and 34 cases were excluded.
¶¶75 controls and 18 cases were excluded.
cholesterol levels influence the incidence of stroke or ischemic stroke is much smaller than that of coronary artery disease.\textsuperscript{17,18} In the Japanese population, in particular, the link between lipids and CVD is weak; no significant association has been reported between cholesterol or triglyceride levels and either stroke or ischemic stroke.\textsuperscript{19–23} In our study, as well, total cholesterol, triglycerides, and HDL cholesterol were not associated with stroke. Adiponectin is an adipokine which influences systemic lipid metabolism. The small role which lipid abnormalities play in the development of CVD, particularly among Japanese, may obscure the relationship between adiponectin and CVD.

This study is not without limitations. The prolonged interval between blood collection and measurement might have affected the measurement results. However, past studies in which plasma adiponectin levels have been measured shortly after plasma collection have shown that mean levels of adiponectin in healthy Japanese populations range between 7.9 and 11.4,\textsuperscript{2,22–24} a range which is in line with the mean adiponectin level detected among the controls in our study (8.26 [interquartile range, 5.7 to 12.4]), suggesting adequate stability of adiponectin levels in frozen, stored samples over time. Another limitation is that our study did not further classify brain infarction to analyze subcategories of brain infarction separately, because of the limited number of cases with CVD. Past investigators have reported that each of the subcategories of brain infarction have different associations with lipids.\textsuperscript{25} Therefore, each of the subclasses of brain infarction may have a different link to adiponectin.

Plasma adiponectin concentration is considered one of the major indicators of systemic atherosclerosis and inflammation. However, our study did not show any independent association of adiponectin with CVD. Further studies are needed to confirm the usefulness of adiponectin concentration as a predictor of CVD.

Sources of Funding
This study was supported in part by Scientific Research Grant from the Ministry of Education, Culture, Sports, Science and Technology, Tokyo, Japan, and in part by grants from the Foundation for the Development of the Community, Tochigi, Japan.

Disclosures
None.

References
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Stroke. 2008;39:323-328; originally published online December 20, 2007;
doi: 10.1161/STROKEAHA.107.497552
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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