Dietary patterns and risk of dementia in an elderly Japanese population: the Hisayama Study

Mio Ozawa, Toshiharu Ninomiya, Tomoyuki Ohara, Yasufumi Doi, Kazuhiro Uchida, Tomoko Shirata, Koji Yonemoto, Takanari Kitazono, and Yutaka Kiyohara

ABSTRACT

Background: To our knowledge, there are no previous reports that assessed the association between dietary patterns and risk of dementia in Asian populations.

Objective: We investigated dietary patterns and their potential association with risk of incident dementia in a general Japanese population.

Design: A total of 1006 community-dwelling Japanese subjects without dementia, aged 60–79 y, were followed up for a median of 15 y. The reduced rank regression procedure was used to efficiently determine their dietary patterns. Estimated risk conferred by a particular dietary pattern on the development of dementia was computed by using a Cox proportional hazards model.

Results: Seven dietary patterns were extracted; of these, dietary pattern 1 was correlated with high intakes of soybeans and soybean products, vegetables, algae, and milk and dairy products and a low intake of rice. During the follow-up, 271 subjects developed all-cause dementia. Of these individuals, 144 subjects had Alzheimer disease (AD), and 88 subjects had vascular dementia (VaD). After adjustment for potential confounders, risks of development of all-cause dementia, AD, and VaD were reduced by 0.66 (95% CI: 0.46, 0.95), 0.65 (95% CI: 0.40, 1.06), and 0.45 (95% CI: 0.22, 0.91), respectively, in subjects in the highest quartile of score for dietary pattern 1 compared with subjects in the lowest quartile.

Conclusion: Our findings suggest that a higher adherence to a dietary pattern characterized by a high intake of soybeans and soybean products, vegetables, algae, and milk and dairy products and a low intake of rice is associated with reduced risk of dementia in the general Japanese population. 

INTRODUCTION

The number of patients with dementia is growing rapidly in conjunction with the aging of the world population (1). However, the cause of most types of dementia has not been fully clarified. Consequently, those factors that are known to affect dementia and can be modified, such as dietary factors, have been widely discussed in terms of their potential to prevent the development of the disease (2). Some epidemiologic studies have reported that the intake of certain types of foods, such as fish and vegetables, may protect against all-cause dementia and Alzheimer disease (AD) (3), but these results are still inconsistent (3, 4). In any case, we do not consume foods or nutrients in isolation but, rather, combined as meals. Therefore, a key part of the solution may be to identify the dietary patterns that make the greatest contribution to dementia prevention. In Western countries, there have been several epidemiologic reports that suggested that a Mediterranean dietary pattern is protective against dementia (5–7). However, a Mediterranean diet is very different from a traditional Asian diet, and it is possible that there is another dietary pattern that would be equally or more effective for Asian people. Thus, it is important to determine whether there is a dietary pattern specific to Asian customs that would help to reduce risk of dementia. To clarify this issue, we performed a prospective cohort study to evaluate dietary factors associated with the development of dementia in a general Japanese elderly population. The ultimate goal of this study was to identify a dietary pattern that could contribute to risk of dementia and its subtypes in elderly Japanese.

SURFACE AND METHODS

Study populations

The Hisayama Study is a population-based prospective cohort study ongoing in the town of Hisayama, which is located in 

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4Abbreviations used: AD, Alzheimer disease; DP1, dietary pattern 1; RRR, reduced rank regression; VaD, vascular dementia.

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a suburb of the Fukuoka metropolitan area on Kyushu Island, Japan (8). The study began in 1961 to elucidate the actual conditions of cerebrocardiovascular diseases and their risk factors in Japanese. Data from the national census and nutrition survey has shown that the age and occupational distributions and nutrient intake of the population of Hisayama have been mostly the same as those of Japan as a whole for each year from 1961 until now (9). Comprehensive surveys of cognitive impairment and dementia in the elderly, including neuropsychological tests, have been conducted since 1985 (8). In 1988, a screening examination, including a dietary survey, was performed in 1073 residents aged 60–79 y (participation rate: 89.6%) for the current study. After the exclusion of 15 subjects who already suffered from dementia, one subject with no blood sample, and 51 subjects who did not complete dietary questionnaires at baseline, the remaining 1006 subjects (433 men and 573 women) were enrolled in this study.

Follow-up survey

Subjects were followed up from December 1988 to November 2005. The median follow-up time was 15 y. During this time, health examinations were performed every 1–2 y (10). For subjects who did not have examinations or who had moved out of town, the postal service or telephone was used to collect their health information (11). We also established a daily monitoring system in the study team and local physicians or members of the Health and Welfare Office of the town to identify new events, including stroke, cognitive impairment, and dementia. Follow-up screening surveys of cognitive function, including neuropsychological tests, the Hasegawa Dementia Scale (12), the Hasegawa Dementia Scale-Revised (13), or the Mini-Mental State Examination (14), were conducted in 1992, 1998, and 2005. When a subject was suspected to have new neurologic symptoms, including cognitive impairment, the subject was carefully evaluated by the study physician and psychiatrist, who conducted comprehensive investigations including interviews of the family or attending physician, physical and neurologic examinations, and a review of the clinical records. Furthermore, when a subject died, we reviewed all available clinical information, interviewed the attending physician and the family of the deceased subject, and tried to obtain permission for an autopsy from the family. During follow-up, 446 subjects died; of those, 326 (73.1%) underwent a brain examination at autopsy. No subjects were lost to follow-up.

Diagnosis of dementia

The guidelines of the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition, were used for defining the diagnosis of dementia (15). The criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s disease and Related Disorders Association were used to define subjects with AD (16), and the criteria of the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l’Enseignement en Neurosciences were used to determine the diagnoses of vascular dementia (VaD) (17). Clinical information, including neuroimaging, was used to diagnose possible and probable dementia subtypes. Definite dementia subtypes were also determined on the basis of clinical and neuropathologic information in dementia subjects who underwent autopsy. The diagnostic procedure for autopsy cases has been reported previously (18). Definite VaD cases were confirmed with a causative stroke or cerebrovascular change and no neuropathologic evidence of other forms of dementia. Each case of dementia was adjudicated by expert stroke physicians and psychiatrists.

During the follow-up period, 271 incident cases of dementia were shown. Of these cases, 128 subjects (47.2%) underwent an autopsy, and 114 subjects were examined by using brain imaging, such as computed tomography and MRI. Therefore, 242 subjects in all (89.3%) underwent some kind of morphologic examination. The remaining 29 subjects were examined by using clinical features. In all dementia cases, 19 AD cases and 15 VaD cases had other subtypes of dementia; of those, 11 cases were a mixed type of AD and VaD. These cases were counted as events in the analyses for each subtype. Finally, 144 subjects experienced AD, 88 subjects experienced VaD, and 50 subjects experienced other subtypes of dementia.

Nutritional survey

At the baseline screening examination in 1988, a dietary survey was conducted by using a 70-item semiquantitative food-frequency questionnaire concerning food intake (19). The validity of this questionnaire has been reported previously (20). The questionnaire was completed by each participant in advance and was checked by a trained dietitian or a nutritionist in the screening examination. The average food intake per day was calculated from the weekly frequency of intake of various foods and the amount (quantity) of each food portion. The nutritional intake was calculated by using the fourth revision of the Standard Tables of Food Composition in Japan (21). Each nutritional element was adjusted for energy intake by using the nutrient density method (22).

Risk-factor measurements

At baseline, each subject completed a self-administered questionnaire that covered medical history, antidiabetic and antihypertensive treatments, educational status, smoking habits, and physical activity. A history of stroke was defined as a pre-existing sudden onset of nonconvulsive and focal neurologic deficit that persisted ≥24 h on the basis of all available clinical data. Educational levels were divided into 3 categories as follows: low (<7 y of education), intermediate (7–12 y of education), and high (≥13 y of education). Smoking habits were categorized as either current use or no current use. Physical activity during leisure time was defined as 4 categories as follows: always sedentary, walking, exercise or sports 1–2 d/wk, and exercise or sports ≥3 d/wk. Blood pressure was measured 3 times by using a standard mercury sphygmomanometer in the sitting position after rest for ≥5 min. The mean of 3 measurements was used for the analysis. Hypertension was defined as blood pressure ≥140/90 mm Hg or current use of antihypertensive drugs. Body height and weight were measured in light clothing without shoes, and BMI (in kg/m²) was calculated. Diabetes was defined as a fasting plasma glucose concentration ≥7.0 mmol/L, 2-h postload glucose concentrations or postprandial
glucose concentrations ≥11.1 mmol/L, or the current use of insulin or oral medication for diabetes.

Statistical analysis

Dietary patterns associated with risk of dementia were assessed by using a reduced rank regression (RRR) analysis (23). Usually, a dietary pattern analysis is conducted by using either a hypothesis-oriented approach that requires a known ideal dietary pattern (eg, the Mediterranean diet) or a principal components analysis that determines dietary patterns specific to the target population. In contrast with these analyses, RRR does not require any known dietary pattern and can allow for previous information about the pathway from the diet to relevant disease. RRR identifies linear functions of food groups (ie, the dietary pattern) that explain as much of the variation of nutrients selected as risk or preventive factors for the relevant disease as possible. Consequently, the score for dietary pattern computed by this method is likely to be associated with risk of the relevant disease. RRR could be the most appropriate method to estimate the ideal dietary pattern for the prevention of dementia. We selected the following 7 nutrients as risk or preventive factors for dementia: SFA (24, 25), MUFA (25), PUFA (25, 26), vitamin C (27), potassium (28), calcium (28), and magnesium (28). These nutrients were known or suspected to confer risk of or protection against dementia and were variables with \( P < 0.2 \) in the univariate analyses regarding their intakes and risk of the development for dementia. Dietary patterns related to the intakes of these 7 nutrients were derived on the basis of 19 food groups. Pearson’s correlation coefficients in nutrients, food groups, and scores for the extracted dietary pattern were calculated. Scores for the dietary pattern were categorized in quartiles. Trends in mean values or frequencies of risk factors across scores for the dietary pattern were tested by using the general linear model or logistic regression analysis, respectively. The age- and sex-adjusted multiple-linear regression analysis revealed that a higher score for DP1 was associated with an increased intake for that food group. Food groups with a factor loading ≥0.2 were soybeans and soybean products, green vegetables, other vegetables, algae, and milk and dairy products, whereas the food with a factor loading less than −0.2 was rice.

Clinical characteristics of study subjects according to the quartile of scores for DP1 at baseline are shown in Table 3. Subjects with higher scores for DP1 were likely to be women and more likely to have diabetes and smoking habits. Mean values of serum total cholesterol and BMI increased with higher scores for DP1.

We estimated HRs and 95% CIs for the development of dementia and its subtypes according to the quartile of scores for DP1 (Table 4). Risk of all-cause dementia decreased by two-thirds in subjects with the highest quartile of scores for DP1 compared with subject with the lowest quartile; the age- and sex-adjusted HR (95% CI) was 0.66 (0.47, 0.94). This relation remained unchanged even after adjustment for education, diabetes, hypertension, total cholesterol, history of stroke, BMI, smoking habits, and the intake of energy. With regard to subtypes of dementia, subjects with the highest quartile of scores for DP1 had a significant lower risk of either AD or VaD after adjustment for the aforementioned confounding factors; the HR (95% CI) was 0.65 (0.40, 1.06) for AD and 0.45 (0.22, 0.91) for VaD (Table 5). There was a significant linear relation between scores for DP1 levels and risk of VaD (P-trend = 0.02) but not for AD (P-trend = 0.17). As a reference, there was no evidence of a significant relation between dietary patterns 2–7 and dementia.

Finally, we conducted sensitivity analyses stratified by diabetic status because subjects with diabetes were likely to modify their dietary patterns.

### Ethical considerations

This study was conducted with the approval of the Kyushu University Institutional Review Board for Clinical Research. Written informed consent was obtained from participants.

### RESULTS

The mean age of the overall study population was 68 y, and the proportion of women was 57%. The prevalence of diabetes and hypertension was 15.0% and 51.7%, respectively. In total subjects, 23.7% of subjects had smoking habits, and 70.5% of subjects were sedentary during leisure time.

In our subjects, 7 dietary patterns were extracted by using RRR. These dietary patterns explained 87.1% of the total variation of intakes of the following 7 nutrients selected as responsible variables: SFA, MUFA, PUFA, vitamin C, potassium, calcium, and magnesium. Scores for dietary pattern 1 (DP1) accounted for 54.3% of the total variation of all responsible variables, and scores for dietary patterns 2–7 explained very few variations (see Table 1 under “Supplemental data” in the online issue). Therefore, we selected scores for DP1 as a target dietary pattern in this study. Scores for DP1 were highly correlated with intakes of each nutrient (all Pearson’s correlation coefficients >0.50) (Table 1).

Factor loadings of the 19 food groups associated with scores for DP1 and correlation coefficients between food groups and 7 response variables are shown in Table 2. Factor loadings represent the magnitude and direction of each food group’s contribution to scores for DP1. A positive value of a factor loading indicated that a higher score for DP1 was associated with an increased intake for that food group. Food groups with a factor loading ≥0.2 were soybeans and soybean products, green vegetables, other vegetables, algae, and milk and dairy products, whereas the food with a factor loading less than −0.2 was rice.

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dietary customs because of the medical treatment. As a consequence, multivariable-adjusted HRs of all-cause dementia and its subtypes increased linearly with higher scores for DP1 in subjects without diabetes (all \(P\)-trend < 0.01) but not in subjects with diabetes.

**DISCUSSION**

The current study identified a dietary pattern that was associated with lower risk of dementia in a general Japanese elderly population. This dietary pattern was characterized by high intakes of soybeans and soybean products, green vegetables, other vegetables, algae, and milk and dairy products and a low intake of rice, which roughly corresponded to a customary Japanese diet. The findings from this study are expected to provide valuable information for the establishment of preventive strategies against dementia through lifestyle modification in the general Japanese population.

Several studies have assessed the relation between a dietary pattern and risk of dementia (29). Most studies addressed effects of the Mediterranean dietary pattern on risk of dementia and showed that higher intakes of vegetables, fruits, and fish were linked to lower risk of dementia. However, it would not be desirable to apply a Mediterranean dietary pattern to Asian populations because it is not a common dietary pattern for Asian people. For a similar reason, Gu et al (30) have assessed the relations between dietary patterns and risk of dementia in subjects with a greater adherence to this dietary pattern had lower risk of dementia. Similar findings were also observed in our analysis. This consistency was observed despite the clear difference in dietary customs between the 2 study populations, which underscores the reliability of our results.

In the current study, intakes of potassium, calcium, and magnesium were included in the RRR analysis as preventive factors for dementia on the basis of our previous findings (28). These minerals are abundantly present in milk and dairy products. As a consequence, a greater milk and dairy intake was positively correlated with higher scores for DP1, which linked to lower risk of dementia. Some cross-sectional studies have shown that the lower intake of dairy products was related to poor cognitive function (31, 32). These findings may support our results. We also showed that scores for DP1 were positively correlated with the intake of SFA. Even though the favorable effects of \(\omega-3\) PUFA on dementia have been well established in several epidemiologic studies (33, 26), effects of SFA remain inconclusive (34). The Chicago Health and Aging Project showed a positive association between SFA intake and risk of AD (24), whereas the Rotterdam study indicated no association between saturated fat and risk of dementia (35). Despite this fact, DP1, which suggested a protective effect on dementia, showed a positive correlation with SFA. Our findings could be attributable to the abundance of SFA in milk and dairy products, which also contain a lot of favorable minerals such as calcium and magnesium.

We showed a negative correlation between rice intake and DP1. Rice constitutes a large part of the Japanese daily diet. This association may arise from an imbalance in food intake (ie, a high

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**TABLE 2**

Factor loadings of food groups associated with dietary pattern 1 and correlation coefficients between food groups and nutrients (response variable)\(^1\)

<table>
<thead>
<tr>
<th>Food groups</th>
<th>Factor loadings (dietary pattern 1)</th>
<th>SFA</th>
<th>MUFA</th>
<th>PUFA</th>
<th>Vitamin C</th>
<th>Potassium</th>
<th>Calcium</th>
<th>Magnesium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rice</td>
<td>-0.45</td>
<td>-0.48²</td>
<td>-0.49²</td>
<td>-0.53²</td>
<td>-0.07</td>
<td>-0.37²</td>
<td>-0.57²</td>
<td>-0.40²</td>
</tr>
<tr>
<td>Breads</td>
<td>0.10</td>
<td>0.29²</td>
<td>0.12</td>
<td>0.13²</td>
<td>-0.04</td>
<td>0.01</td>
<td>0.16²</td>
<td>0.06</td>
</tr>
<tr>
<td>Noodles and other cereals</td>
<td>0.01</td>
<td>-0.03</td>
<td>-0.03</td>
<td>0.02</td>
<td>-0.03</td>
<td>-0.001</td>
<td>0.02</td>
<td>0.09</td>
</tr>
<tr>
<td>Potatoes</td>
<td>0.16</td>
<td>0.01</td>
<td>0.1</td>
<td>0.05</td>
<td>0.22²</td>
<td>0.33²</td>
<td>0.08</td>
<td>0.23²</td>
</tr>
<tr>
<td>Soybeans and soybean products</td>
<td>0.37</td>
<td>0.07</td>
<td>0.28²</td>
<td>0.72²</td>
<td>0.02</td>
<td>0.34³</td>
<td>0.46²</td>
<td>0.42</td>
</tr>
<tr>
<td>Miso</td>
<td>0.01</td>
<td>-0.006</td>
<td>0.09</td>
<td>0.02</td>
<td>0.03</td>
<td>0.03</td>
<td>0.02</td>
<td>0.21</td>
</tr>
<tr>
<td>Pickles</td>
<td>0.04</td>
<td>-0.08</td>
<td>-0.09</td>
<td>-0.11</td>
<td>0.30²</td>
<td>0.31³</td>
<td>-0.02</td>
<td>-0.07</td>
</tr>
<tr>
<td>Green vegetables</td>
<td>0.40</td>
<td>-0.004</td>
<td>0.06</td>
<td>0.1</td>
<td>0.72²</td>
<td>0.70²</td>
<td>0.28²</td>
<td>0.63²</td>
</tr>
<tr>
<td>Other vegetables</td>
<td>0.36</td>
<td>-0.009</td>
<td>0.03</td>
<td>0.04</td>
<td>0.74²</td>
<td>0.67²</td>
<td>0.22²</td>
<td>0.57²</td>
</tr>
<tr>
<td>Fruits and fruit juices</td>
<td>0.19</td>
<td>-0.007</td>
<td>-0.01</td>
<td>-0.03</td>
<td>0.56²</td>
<td>0.32²</td>
<td>0.07</td>
<td>0.30²</td>
</tr>
<tr>
<td>Algae</td>
<td>0.24</td>
<td>0.04</td>
<td>0.17²</td>
<td>0.21²</td>
<td>0.22²</td>
<td>0.37²</td>
<td>0.22²</td>
<td>0.28²</td>
</tr>
<tr>
<td>Fish</td>
<td>0.17</td>
<td>-0.07</td>
<td>0.16²</td>
<td>0.21²</td>
<td>-0.05</td>
<td>0.12²</td>
<td>0.46²</td>
<td>0.13²</td>
</tr>
<tr>
<td>Meat</td>
<td>0</td>
<td>0.34²</td>
<td>0.1</td>
<td>-0.14²</td>
<td>0.02</td>
<td>-0.01</td>
<td>-0.11</td>
<td>-0.05</td>
</tr>
<tr>
<td>Egg</td>
<td>0.15</td>
<td>0.29²</td>
<td>0.36²</td>
<td>0.07</td>
<td>0.03</td>
<td>0.1</td>
<td>0.14</td>
<td>0.08</td>
</tr>
<tr>
<td>Milk and dairy products</td>
<td>0.37</td>
<td>0.63²</td>
<td>0.27²</td>
<td>0.06</td>
<td>-0.03</td>
<td>0.26²</td>
<td>0.64²</td>
<td>0.50²</td>
</tr>
<tr>
<td>Fats and oils</td>
<td>0.12</td>
<td>0.41²</td>
<td>0.61²</td>
<td>0.23²</td>
<td>0.07</td>
<td>-0.04</td>
<td>-0.07</td>
<td>-0.01</td>
</tr>
<tr>
<td>Sugar and confectioneries</td>
<td>-0.1</td>
<td>0.01</td>
<td>-0.06</td>
<td>-0.12²</td>
<td>-0.006</td>
<td>-0.11</td>
<td>-0.12</td>
<td>-0.19²</td>
</tr>
<tr>
<td>Alcoholic drinks</td>
<td>-0.17</td>
<td>-0.14²</td>
<td>-0.23²</td>
<td>-0.17²</td>
<td>-0.19²</td>
<td>-0.19²</td>
<td>-0.09</td>
<td>-0.14²</td>
</tr>
<tr>
<td>Salt</td>
<td>-0.008</td>
<td>-0.05</td>
<td>-0.008</td>
<td>-0.13²</td>
<td>0.24²</td>
<td>0.15³</td>
<td>-0.08</td>
<td>-0.14³</td>
</tr>
</tbody>
</table>

\(^1\) Factor loadings represent the magnitude and direction of the contribution of each food group to a dietary pattern 1 score. A positive value of factor loading indicated an increased intake of the food group. A negative value of loading indicated less intake of the food group. Patterns were derived by using a reduced rank regression with 7 nutrients (ie, SFA, MUFA, PUFA, vitamin C, potassium, calcium, and magnesium) as response variables and 19 foods and food groups as independent variables.

\(^2\) \(P < 0.001\).
intake of rice may result in lower intake of foods favorable for the prevention of dementia) rather than any harmful effects of rice itself. Therefore, these findings cannot be taken to mean that cessation of rice consumption per se will have any benefit against dementia; rather, they findings may simply underscore that a well-balanced meal with many nutritional foods is recommended for a reduction in risk of dementia.

In the current study, diabetes was associated with a greater adherence to DP1. This may be because subjects with diabetes tend to adopt a more favorable pattern of diet in response to diet therapy. Because diabetes has been considered a risk factor for dementia (36), this reclassification of the dietary pattern is likely to weaken the relation between the dietary pattern and risk of dementia, especially AD, in subjects with diabetes. In support of this idea, the analysis stratified by diabetic status revealed significant linear relationships between the dietary pattern and risk of all-cause dementia and its subtypes in subjects without diabetes. In contrast, there was no significant relation between DP1 and dementia in subjects with diabetes.

### TABLE 4

<table>
<thead>
<tr>
<th>Variables</th>
<th>Quartile 1 (n = 251)</th>
<th>Quartile 2 (n = 252)</th>
<th>Quartile 3 (n = 252)</th>
<th>Quartile 4 (n = 251)</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scarcity of dietary pattern 1^1</td>
<td>1.5</td>
<td>0.0</td>
<td>0.4</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (y)</td>
<td>68 ± 5.5^1</td>
<td>69 ± 5.6</td>
<td>68 ± 5.4</td>
<td>69 ± 5.6</td>
<td>0.63</td>
</tr>
<tr>
<td>Women (%)</td>
<td>42.7</td>
<td>53.2</td>
<td>57.1</td>
<td>74.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education (%)</td>
<td>11.9</td>
<td>11.9</td>
<td>12.3</td>
<td>7.6</td>
<td>0.15</td>
</tr>
<tr>
<td>≤13 y</td>
<td>5.2</td>
<td>7.5</td>
<td>9.1</td>
<td>11.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>140 ± 24</td>
<td>136 ± 22</td>
<td>138 ± 23</td>
<td>138 ± 20</td>
<td>0.36</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>77 ± 11</td>
<td>75 ± 10</td>
<td>76 ± 10</td>
<td>76 ± 11</td>
<td>0.47</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>55.0</td>
<td>50.0</td>
<td>51.6</td>
<td>50.6</td>
<td>0.46</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>10.0</td>
<td>13.1</td>
<td>13.5</td>
<td>23.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum total cholesterol (mg/dL)</td>
<td>199 ± 43</td>
<td>207 ± 46</td>
<td>214 ± 42</td>
<td>217 ± 40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>22 ± 3</td>
<td>22.3 ± 3</td>
<td>22.5 ± 3</td>
<td>22.8 ± 3</td>
<td>0.01</td>
</tr>
<tr>
<td>History of stroke (%)</td>
<td>4.4</td>
<td>4.8</td>
<td>4.0</td>
<td>4.4</td>
<td>0.89</td>
</tr>
<tr>
<td>Smoking habits (%)</td>
<td>33.5</td>
<td>24.6</td>
<td>25.8</td>
<td>10.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical activity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always sedentary</td>
<td>75.3</td>
<td>71.0</td>
<td>69.9</td>
<td>65.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Walking</td>
<td>6.0</td>
<td>9.5</td>
<td>8.7</td>
<td>12.0</td>
<td>0.04</td>
</tr>
<tr>
<td>Exercise or sport 1–2 d/wk</td>
<td>5.2</td>
<td>6.0</td>
<td>7.1</td>
<td>5.6</td>
<td>0.72</td>
</tr>
<tr>
<td>Exercise or sport ≥3 d/wk</td>
<td>13.5</td>
<td>13.5</td>
<td>14.3</td>
<td>16.7</td>
<td>0.30</td>
</tr>
<tr>
<td>Energy intake (kcal/d)</td>
<td>1721 ± 469</td>
<td>1605 ± 392</td>
<td>1620 ± 374</td>
<td>1649 ± 358</td>
<td>0.08</td>
</tr>
</tbody>
</table>

^1 General linear model was used to test trends in mean values of risk factors across scores for the dietary pattern. Logistic regression analysis was used to test trends in frequencies of risk factors across scores for the dietary pattern.

^2 All values are medians.

^3 Mean ± SD (all such values).

^4 Cox proportional hazards model was used to estimate the age- and sex-adjusted or multivariate-adjusted HRs (95% CIs).

^5 Adjusted for age, sex, education, diabetes, hypertension, total cholesterol, history of stroke, BMI, smoking habits, exercise, and energy intake.
subjects with diabetes, probably because of the limited sample size and existence of confounders caused by diet therapy. Additional investigations will be needed to elucidate this issue.

Some potential limitations of this study should be noted. Information regarding the intake of dietary nutrients derived from a semiquantitative food-frequency questionnaire may not be fully valid. In addition, the dietary assessment was performed only once at baseline. These limitations were likely to lead to some extent of misclassification of food intake. Such misclassifications would have weakened the association shown in the current study and biased the results toward the null hypothesis. In addition, there is a possibility of reverse causation (ie, our subjects might have already changed their dietary custom because of underlining dementia and other diseases in older age). However, after the sensitivity analysis in which cases who were diagnosed with dementia in the first 3 y after the baseline survey were excluded and did not make any material differences in the findings. Finally, we may not have been able to completely exclude the influence of residual confounding on the relation between the identified dietary pattern and dementia risk.

In conclusion, to our knowledge, this is the first report to suggest a dietary pattern that protects against dementia in a general Japanese population. Subjects with this dietary pattern had an inverse relation with risk of all-cause dementia, AD, and VaD. These results could help to motivate changes in the dietary behavior of the general population in Japan and, thereby, lower risk of the development of dementia.

We thank the staff of the Division of Health and Welfare of Hisayama for their cooperation in this study.

The authors’ responsibilities were as follows—MO: contributed to the writing of the manuscript; TN: contributed to the data collection, endpoint adjudication, interpretation of data, statistical analysis, and writing of the manuscript; TO: contributed to the data collection, endpoint adjudication, and interpretation of data; YH and YD: contributed to the data collection and interpretation of data; and YK: is a study coordinator and contributed to the obtainment of study funds, the study concept, endpoint adjudication, interpretation of data, and writing of the manuscript. None of the authors had a conflict of interest.

### TABLE 5

<table>
<thead>
<tr>
<th>Score for dietary pattern 1</th>
<th>All-cause dementia</th>
<th>Alzheimer disease</th>
<th>Vascular dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without diabetes</td>
<td>With diabetes</td>
<td>Without diabetes</td>
</tr>
<tr>
<td></td>
<td>Events/pat at risk (n)</td>
<td>Age and sex adjusted</td>
<td>Events/pat at risk (n)</td>
</tr>
<tr>
<td>All-cause dementia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without diabetes</td>
<td>64/226</td>
<td>1.0 (95% 0.57, 1.16)</td>
<td>5/25</td>
</tr>
<tr>
<td>With diabetes</td>
<td>62/219</td>
<td>0.81 (95% 0.48, 0.99)</td>
<td>10/33</td>
</tr>
<tr>
<td>Age and sex adjusted</td>
<td>55/218</td>
<td>0.69 (95% 0.35, 0.78)</td>
<td>8/34</td>
</tr>
<tr>
<td>Age and sex adjusted</td>
<td>42/192</td>
<td></td>
<td>25/59</td>
</tr>
</tbody>
</table>

1 Cox proportional hazards model was used to estimate the age- and sex-adjusted HRs (95% CIs).

### REFERENCES


