Relations between protein intake and blood pressure in Japanese men and women: the Circulatory Risk in Communities Study (CIRCS)\textsuperscript{1–3}

Mitsumasa Umesawa, Shinichi Sato, Hironori Imano, Akihiko Kitamura, Takashi Shimamoto, Kazumasa Yamagishi, Takeshi Tamigawa, and Hiroyasu Iso

ABSTRACT

Background: An inverse association between protein intake and blood pressure has been reported in Western countries. However, the evidence is limited for Asians, whose protein sources are different from those in Western populations.

Objectives: The objective was to examine the association between protein intake and blood pressure in Japanese adults.

Methods: We conducted a population-based, cross-sectional study of 7585 subjects (3499 men and 4086 women) from 40 to 69 y of age living in 5 communities in Japan. Dietary intakes of total, animal, and plant protein were estimated by a single 24-h dietary recall. We then examined the associations between dietary intake of those proteins and blood pressure after adjustment for age, sex, community, body mass index, antihypertensive medication use, ethanol intake, smoking, and dietary intakes of sodium, potassium, and calcium.

Results: After adjustment for cardiovascular disease risk factors, a 25.5-g/d increment in total protein intake was associated with a decrease in systolic blood pressure of 1.14 mm Hg ($P < 0.001$) and in diastolic blood pressure of 0.65 mm Hg ($P < 0.001$), and a 19.9-g/d increment in animal protein intake was associated with a decrease in systolic blood pressure of 1.09 mm Hg ($P < 0.001$) and in diastolic blood pressure of 0.41 mm Hg ($P = 0.003$). A 13.1-g/d increment in plant protein intake was associated with a decrease in diastolic blood pressure of 0.57 mm Hg ($P < 0.001$). Further adjustment for nutritional factors weakened these associations, but the inverse associations of total protein intake with diastolic blood pressure and of animal protein intake with systolic blood pressure remained statistically significant.


INTRODUCTION

The relation between protein intake and blood pressure has been investigated since the 1980s. Total protein intake, estimated with a 24-h dietary recall (1–3), and measurement of urinary urea nitrogen excretion, a urinary biomarker of protein intake (4, 5), were found to be inversely associated with systolic (1, 3–5) and diastolic (1–5) blood pressure. A recent Japanese study reported that total protein intake, estimated on the basis of urea nitrogen and creatinine concentrations in spot urine, was inversely associated with diastolic blood pressure among men (6).

Animal protein intake, estimated with the 24-h dietary recall method (7) or urinary biomarkers such as the ratio of inorganic sulfate to urea nitrogen in spot urine (8) and the ratio of 3-methylhistididine to creatinine in 24-h urine samples (9), were also found to be inversely associated with blood pressure. Two previous studies reported that plant protein intake was inversely associated with systolic and diastolic blood pressure (10, 11).

These findings suggest that protein intake, especially total and animal protein intake, has a hypotensive effect. However, the evidence is limited to Asian populations whose major sources of protein intake were plants and seafood. The findings of national surveys were that, in 2003, the Japanese obtained 23% of their protein intake from fish and shellfish, 18% from meat and poultry, and 47% from plants (12), whereas the corresponding values for Americans in 1998–1991 were 6%, 36%, and 33%, respectively (13). The aim of the present study was to examine the association between protein intake and blood pressure for Japanese populations with a variety of dietary intakes. We used the data from 24-h dietary recalls and health check-ups for middle-aged residents.
SUBJECTS AND METHODS

Subjects and nutritional surveys

The subjects were 40- to 69-y-old residents in 5 communities in a community-based cohort of the Circulatory Risk in Community Study (CIRCS) (14). They lived in the towns of Ikawa and Ishizawa (15, 16) in Akita Prefecture in northeastern Japan, in Kyowa town (17), Ibaraki Prefecture in eastern Japan, in Minami-Takayasu district (15), Yao City, Osaka Prefecture in central Japan, and in Noichi town (18), Kochi Prefecture in southwestern Japan.

The nutrition surveys were carried out as part of annual cardiovascular disease risk surveys, and the participants who were recruited for the nutrition survey were not informed beforehand that their usual nutritional status would be examined (19).

The total number of subjects was 7585 (3499 men and 4086 women): 1304 (621 men and 683 women) in Ikawa, 655 (349 men and 306 women) in Ishizawa, 2130 (961 men and 1169 women) in Kyowa, 1688 (724 men and 964 women) in Yao, and 1808 (844 men and 964 women) in Noichi. For those who were subjects of a nutritional survey twice or more, we used the results of the first survey. The surveys were carried out from 1973 to 1997 in Ikawa and Yao, from 1973 to 1987 in Ishizawa, from 1975 to 1997 in Noichi, and from 1982 to 1997 in Kyowa.

We adopted the 24-h dietary recall method for collecting the dietary data (20). The subjects were interviewed by trained dietitians regarding what they had eaten during the 24 h before the examination. Throughout the surveys, the dietitians carried out the interviews by using our dietary-recall manual and held a meeting to follow up the manual before each survey. We hired the same dietitians for all the surveys to avoid discrepancies in interviewing technique. When new dietitians were employed, training sessions were held for the new dietitians to train with the experienced dietitians.

Food intakes were estimated based on the Standard Tables of Food Composition in Japan (5th revised edition), and the 24-h intakes of nutrients were calculated by multiplying the amount of each food consumed by its nutrient content and totaling the nutrient intakes for all foods.

Population surveys

Measurement of arterial systolic blood pressure and fifth-phase diastolic blood pressure was done by well-trained physicians or nurses using standard mercury sphygmomanometers on the right arm of quietly seated participants after a rest of ≥5 min while seated. A second measurement of blood pressure was performed when participants had high blood pressure (≥140 mm Hg systolic blood pressure or ≥90 mm Hg diastolic blood pressure) at the first measurement for detection and follow-up of hypertensive subjects. The data for the first blood pressure measurement were used for the analyses.

We also measured several potential confounders. Body mass index was calculated by first measuring height in stocking feet and body weight while the subjects were wearing light clothing, and then dividing the weight in kilograms by the height in meters squared. Every participant was interviewed to determine usual weekly alcohol consumption as go, a traditional Japanese unit of volume equal to 180 mL sake (Japanese rice wine), which contains 23 g ethanol. Smokers were also interviewed to determine smoking status and the daily number of cigarettes smoked. Subjects were also interviewed about history of hypertension, use of antihypertensive medication, history of cardiovascular disease, and renal disease.

Statistical analysis

The statistical analyses were based on the data for sex-specific quartiles of total, animal, and plant protein intakes. Age- and sex-adjusted means or proportions of confounding variables, as well as age-, sex-, community-, and multivariable-adjusted means for systolic and diastolic blood pressure were calculated based on these quartiles. Because there was no heterogeneity in the associations between protein intake and blood pressure, the data after adjustment for community were presented. We also calculated the effects of a 1-SD protein intake on blood pressure by using multivariable regression analysis. The confounding variables included age (y), sex, community (4 areas), body mass index (kg/m²), use of antihypertensive medication (yes or no), ethanol intake (g ethanol/d), current smoking (yes or no), and sex-specific quartiles of sodium intake, potassium intake, and calcium intake. We used SAS version 9.13 software (SAS Institute Inc, Cary, NC) for all analyses. P values <0.05 were regarded as statistically significant.

RESULTS

The mean (±SD) systolic blood pressure was 136.5 ± 20.5 mm Hg for men and 134.6 ± 20.6 mm Hg for women and of diastolic blood pressure was 83.3 ± 12.1 and 80.6 ± 11.6 mm Hg, respectively. The mean (±SD) total dietary protein intake was 83.1 ± 27.4 g/d for men and 65.4 ± 20.6 g/d for women, with corresponding intakes of 40.1 ± 22.3 and 30.9 ± 16.4 g/d for animal protein and 43.0 ± 14.0 and 34.5 ± 10.8 g/d for plant protein. Mean (±SD) meat and fish intakes were 51 ± 64 and 120 ± 95 g/d for men and 37 ± 44 and 86 ± 68 g/d for women, respectively.

Characteristics of the participants per quartile of total, animal, and plant protein intakes are shown in Table 1. Among all subjects, total protein intake was positively associated with intakes of alcohol, sodium, potassium, and calcium and inversely associated with body mass index and use of antihypertensive medication. These associations were similar for both men and women, except for no association with alcohol intake among women. Animal protein intake was also positively associated with intakes of alcohol, sodium, potassium, and calcium and inversely associated with body mass index and use of antihypertensive medication among total subjects. These associations were similar in both men and women, except for no association with body mass index in men. Plant protein intake was positively associated with intakes of sodium, potassium, and calcium among all subjects and in men and women, separately.

Age, sex, community-adjusted, and multivariable-adjusted blood pressure per quartile of total protein intake and the effects of 1-SD increments in total protein intake on blood pressure in men, women, and all subjects are shown in Table 2. Among total subjects, after adjustment for cardiovascular disease risk factors, total protein intake for all subjects was...
### Table 1
Age- and sex-adjusted characteristics of the subjects by quartiles (Q) of protein intake

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total protein</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of subjects</td>
<td>1896</td>
<td>1896</td>
<td>1894</td>
</tr>
<tr>
<td>Age (y)</td>
<td>55</td>
<td>53</td>
<td>52</td>
</tr>
<tr>
<td>Total protein intake (g/d)</td>
<td>46.8 ± 0.3</td>
<td>46.2 ± 0.2</td>
<td>78.3 ± 0.2</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.8 ± 0.1</td>
<td>23.6 ± 0.1</td>
<td>23.5 ± 0.1</td>
</tr>
<tr>
<td>Ethanol intake (g/d)</td>
<td>10.9 ± 0.4</td>
<td>11.4 ± 0.4</td>
<td>13.1 ± 0.4</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>32</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Use of antihypertensive drugs (%)</td>
<td>22</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td><strong>Sodium intake (mmol/d)</strong></td>
<td>157.1 ± 1.7</td>
<td>199.3 ± 1.7</td>
<td>223.2 ± 1.7</td>
</tr>
<tr>
<td><strong>Potassium intake (mmol/d)</strong></td>
<td>48.1 ± 0.5</td>
<td>62.1 ± 0.5</td>
<td>71.7 ± 0.5</td>
</tr>
<tr>
<td><strong>Calcium intake (mmol/d)</strong></td>
<td>8.2 ± 0.1</td>
<td>11.5 ± 0.1</td>
<td>13.9 ± 0.1</td>
</tr>
<tr>
<td><strong>Animal protein</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of subjects</td>
<td>1887</td>
<td>1904</td>
<td>1897</td>
</tr>
<tr>
<td>Age (y)</td>
<td>54</td>
<td>53</td>
<td>52</td>
</tr>
<tr>
<td>Animal protein intake (g/d)</td>
<td>14.3 ± 0.2</td>
<td>27.1 ± 0.2</td>
<td>38.5 ± 0.2</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.9 ± 0.1</td>
<td>23.6 ± 0.1</td>
<td>23.5 ± 0.1</td>
</tr>
<tr>
<td>Ethanol intake (g/d)</td>
<td>10.4 ± 0.4</td>
<td>12.2 ± 0.4</td>
<td>12.4 ± 0.4</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>31</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>Use of antihypertensive drugs (%)</td>
<td>22</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td><strong>Sodium intake (mmol/d)</strong></td>
<td>178.6 ± 1.9</td>
<td>204.6 ± 1.9</td>
<td>218.6 ± 1.9</td>
</tr>
<tr>
<td><strong>Potassium intake (mmol/d)</strong></td>
<td>54.8 ± 0.6</td>
<td>63.6 ± 0.6</td>
<td>71.0 ± 0.6</td>
</tr>
<tr>
<td><strong>Calcium intake (mmol/d)</strong></td>
<td>9.3 ± 0.2</td>
<td>11.7 ± 0.2</td>
<td>13.7 ± 0.2</td>
</tr>
<tr>
<td><strong>Plant protein</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of subjects</td>
<td>1893</td>
<td>1891</td>
<td>1898</td>
</tr>
<tr>
<td>Age (y)</td>
<td>54</td>
<td>53</td>
<td>52</td>
</tr>
<tr>
<td>Plant protein intake (g/d)</td>
<td>24.9 ± 0.1</td>
<td>33.3 ± 0.1</td>
<td>40.5 ± 0.1</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.6 ± 0.1</td>
<td>23.6 ± 0.1</td>
<td>23.6 ± 0.1</td>
</tr>
<tr>
<td>Ethanol intake (g/d)</td>
<td>12.7 ± 0.4</td>
<td>11.8 ± 0.4</td>
<td>11.9 ± 0.4</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>31</td>
<td>30</td>
<td>29</td>
</tr>
</tbody>
</table>

*Note: Values are means ± standard error. P for trend values are calculated from analysis of variance.*
TABLE 1 (Continued)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Men (continued)</th>
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<tbody>
<tr>
<td></td>
<td>Total Men</td>
</tr>
<tr>
<td></td>
<td>Q1 (low)</td>
</tr>
<tr>
<td></td>
<td>P for trend</td>
</tr>
<tr>
<td>Use of antihypertensives (%)</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>0.078</td>
</tr>
<tr>
<td>Sodium intake (mmol/d)</td>
<td>163.0 ± 6.2</td>
</tr>
<tr>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Potassium intake (mmol/d)</td>
<td>51.3 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Calcium intake (mmol/d)</td>
<td>9.8 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>0.001</td>
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</table>

*Values are means ± SD. Calculated by regression analysis.
2 Mean ± SE (all such values).

inverseely associated with both systolic and diastolic blood pressure ($P$ for 1-SD change $<0.001$ for both). However, after further adjustment for nutritional variables such as sodium, potassium, and calcium intakes, the total protein intake showed an inverse association with diastolic blood pressure ($P = 0.028$), but not with systolic blood pressure ($P = 0.360$). In men and women separately, these associations were statistically significant after adjustment for cardiovascular disease risk factors in both sexes, but, after further adjustment for nutritional variables, the association remained significant only in women ($P = 0.022$). Similar associations were found among men and women who did not use antihypertensive medication; for example, a 25.5-g/d increment in total protein intake was associated with a decrease in systolic blood pressure of 1.08 mm Hg and in diastolic blood pressure of 0.66 mm Hg ($P < 0.001$ for both) after adjustment for cardiovascular disease risk factors.

Data per quartile of animal protein intake and 1-SD increments in animal protein intake are shown in Table 3. Among total subjects, after adjustment for cardiovascular disease risk factors, animal protein intake was inversely associated with both systolic and diastolic blood pressure ($P$ for 1-SD change $<0.001$ and $P = 0.003$, respectively). After further adjustment for nutritional variables, animal protein intake showed an inverse association with systolic blood pressure ($P = 0.028$), but not with diastolic blood pressure ($P = 0.256$). In men and women separately, the association with systolic blood pressure was statistically significant for both sexes ($P = 0.003$ for men and $P < 0.001$ for women) after adjustment for cardiovascular disease risk factors, but the association remained significant only among women ($P = 0.019$) after further adjustment for nutritional variables. These associations were similar among men and women who did not use antihypertensive medication; for example, a 19.9-g/d increment in animal protein intake was associated with a decrease in systolic blood pressure of 0.97 mm Hg and in diastolic blood pressure of 0.39 mm Hg ($P < 0.001$ and $P = 0.007$, respectively) after adjustment for cardiovascular disease risk factors.

Because animal protein comes from 2 major sources, ie, fish and meat, we examined the associations of these food intakes with blood pressure. A 1-SD increment in meat intake (54.5 g/d) was associated with a decrease in systolic blood pressure of 0.72 mm Hg ($P = 0.001$) and in diastolic blood pressure of 0.35 mm Hg ($P = 0.007$) after adjustment for cardiovascular disease risk factors. A 1-SD increment in fish intake (83.5 g/d) was associated with a decrease of 0.44 mm Hg ($P = 0.044$) and of 0.14 mm Hg ($P = 0.298$), respectively.

Data per quartile of plant protein intake and 1-SD increments in plant protein intake are shown in Table 4. Among total subjects, after adjustment for cardiovascular disease risk factors, plant protein intake for all subjects tended to be inversely associated with systolic blood pressure ($P$ for 1-SD change $<0.001$ and $P = 0.034$) but tended to be inversely associated with diastolic blood pressure ($P = 0.063$). Among men and women, separately, plant protein intake was inversely associated with diastolic blood pressure after adjustment for cardiovascular disease risk.
factors ($P = 0.001$ and $P = 0.002$, respectively), but after further adjustment for nutritional variables, the inverse association remained statistically significant only among women ($P = 0.048$). The positive association between plant protein intake and systolic blood pressure was not statistically significant in either sex. Similar associations were found in men and women without antihypertensive medication; for example, a 13.1-g/d increment in plant protein intake was associated with a decrease in systolic blood pressure of 0.48 mm Hg and in diastolic blood pressure of 0.61 mm Hg ($P = 0.047$ and $P < 0.001$, respectively) after adjustment for cardiovascular disease risk factors.

**DISCUSSION**

In this large cross-sectional study of 7585 Japanese men and women, we identified inverse associations between total protein intake and diastolic blood pressure and between animal protein intake and systolic blood pressure after adjustment for cardiovascular disease risk and nutritional factors.

Several previous studies reported an inverse association of total protein intake with systolic and/or diastolic blood pressure (1–6, 8). In the present study, total protein intake was inversely associated with both systolic and diastolic blood pressure; after further adjustment for nutritional factors, the association with diastolic blood pressure remained statistically significant. As for animal protein intake, some studies reported the inverse association with systolic and/or diastolic blood pressure (7–9), whereas other studies showed no association (10, 11). In the present study, animal protein intake was inversely associated with systolic and diastolic blood pressure; after adjustment for nutritional factors, the association with systolic blood pressure remained statistically significant. As for plant protein intake, 2 studies reported the inverse association with both systolic and diastolic blood pressure (10, 11), whereas one study showed no association (3). In the present study, plant protein intake was inversely associated with diastolic blood pressure; after further adjustment for nutritional factors, the association was no longer statistically significant. However, plant protein intake was positively associated with systolic blood pressure.

The reason for the positive association between plant protein intake and systolic blood pressure in the present study, in contrast with the inverse association in previous studies, is unknown (10, 11). Dietary sodium intake or urinary sodium was generally higher in Japanese than in other races. For example, urinary sodium excretion was 213 mmol/d in our study of 100% in Japanese, whereas it was 181 mmol/d in the previous study of 58% in whites, 18% in Chinese, and 24% in Japanese (11). Furthermore, the Japanese usually eat plant foods with salty
TABLE 3
Age-, sex-, community-, and multivariable-adjusted mean blood pressure values by quartile (Q) of animal protein intake

<table>
<thead>
<tr>
<th>No. of subjects</th>
<th>Animal protein intake</th>
<th>Age-, sex-, community-adjusted</th>
<th>Multivariable-adjusted</th>
<th>Age-, sex-, community-adjusted</th>
<th>Multivariable-adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>g/d</td>
<td>mm Hg</td>
<td></td>
<td>g/d</td>
<td>mm Hg</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>1887</td>
<td>14.3 ± 0.2</td>
<td>137.6 ± 0.46</td>
<td>137.1 ± 0.43</td>
<td>136.5 ± 0.46</td>
</tr>
<tr>
<td>Q2</td>
<td>1904</td>
<td>27.1 ± 0.2</td>
<td>136.3 ± 0.45</td>
<td>136.2 ± 0.42</td>
<td>136.0 ± 0.43</td>
</tr>
<tr>
<td>Q3</td>
<td>1897</td>
<td>38.5 ± 0.2</td>
<td>134.1 ± 0.45</td>
<td>134.6 ± 0.43</td>
<td>134.8 ± 0.43</td>
</tr>
<tr>
<td>Q4 (high)</td>
<td>1897</td>
<td>60.7 ± 0.2</td>
<td>133.9 ± 0.46</td>
<td>134.0 ± 0.43</td>
<td>134.7 ± 0.46</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.005</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 SD</td>
<td>19.9</td>
<td>-1.17 ± 0.24</td>
<td>-1.09 ± 0.23</td>
<td>-0.56 ± 0.25</td>
<td>-0.38 ± 0.14</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>874</td>
<td>16.3 ± 0.3</td>
<td>137.7 ± 0.67</td>
<td>138.1 ± 0.64</td>
<td>137.3 ± 0.67</td>
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<tr>
<td>Q2</td>
<td>872</td>
<td>30.5 ± 0.3</td>
<td>137.3 ± 0.67</td>
<td>137.0 ± 0.63</td>
<td>137.0 ± 0.63</td>
</tr>
<tr>
<td>Q3</td>
<td>898</td>
<td>43.6 ± 0.3</td>
<td>135.4 ± 0.67</td>
<td>135.8 ± 0.63</td>
<td>136.0 ± 0.63</td>
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<tr>
<td>Q4 (high)</td>
<td>875</td>
<td>70.0 ± 0.3</td>
<td>135.7 ± 0.68</td>
<td>135.0 ± 0.64</td>
<td>135.9 ± 0.68</td>
</tr>
<tr>
<td>P for trend</td>
<td>0.018</td>
<td>&lt;0.001</td>
<td>0.121</td>
<td>0.248</td>
<td>0.005</td>
</tr>
<tr>
<td>1 SD</td>
<td>22.3</td>
<td>-0.60 ± 0.34</td>
<td>-0.97 ± 0.32</td>
<td>-0.29 ± 0.37</td>
<td>-0.12 ± 0.21</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (low)</td>
<td>1013</td>
<td>12.7 ± 0.2</td>
<td>137.5 ± 0.62</td>
<td>136.3 ± 0.59</td>
<td>135.8 ± 0.63</td>
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<td>Q2</td>
<td>1032</td>
<td>24.1 ± 0.2</td>
<td>135.4 ± 0.61</td>
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<td>135.2 ± 0.58</td>
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<tr>
<td>Q3</td>
<td>1019</td>
<td>34.1 ± 0.2</td>
<td>133.1 ± 0.61</td>
<td>133.7 ± 0.58</td>
<td>133.8 ± 0.58</td>
</tr>
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<td>Q4 (high)</td>
<td>1022</td>
<td>52.8 ± 0.2</td>
<td>132.4 ± 0.62</td>
<td>133.1 ± 0.58</td>
<td>133.6 ± 0.62</td>
</tr>
<tr>
<td>P for trend</td>
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<td>&lt;0.001</td>
<td>0.014</td>
<td>&lt;0.001</td>
<td>0.014</td>
</tr>
<tr>
<td>1 SD</td>
<td>16.4</td>
<td>-1.81 ± 0.35</td>
<td>-1.19 ± 0.30</td>
<td>-0.80 ± 0.34</td>
<td>-0.75 ± 0.18</td>
</tr>
</tbody>
</table>

1 Adjusted for age (y), sex, BMI (kg/m²), current use of antihypertensive medication (yes or no), ethanol intake (g ethanol/d), and current smoking (yes or no).
2 Adjusted for the factors listed in footnote 1 and for sex-specific quartiles of sodium, potassium, and calcium intakes.
3 Mean ± SE (all such values).
4–6 Significantly different from Q1 (ANOVA): 4 P < 0.05, 5 P < 0.001, 6 P < 0.01.
7 Calculated by regression analysis. Represents the 1-SD difference in increment in protein intake.

seasonings, such as soy sauce and soy bean paste. In the present study, sodium intake was associated with plant protein intake (Pearson’s correlation coefficient: r = 0.54) more strongly than with animal protein intake (r = 0.37). Therefore, sodium intake by plant protein foods may weaken a hypotensive effect of plant foods in Japanese.

Several mechanisms may account for the inverse association between animal protein intake and blood pressure. First, specific amino acids such as arginine and taurine that are rich in animal proteins (21) have an important role in the regulation of vasoreactivity (22, 23). t-Arginine is the substrate for nitric oxide, which functions as a vasodilator because t-arginine infusion was found to produce an immediate reduction in systolic and diastolic blood pressure in a human experiment (22). Supplementation with taurine at 6 g/d for 7 d lowered systolic blood pressure by 9.0 mm Hg and diastolic blood pressure by 4.1 mm Hg in borderline hypertensive patients (23). This hypotensive effect may have originated in the central nervous system, because taurine infusion into brain ventricles lowers blood pressure (24), and taurine was found to modulate the release of arginine vasopressin from hypothalamic neurons (24). Specific amino acids such as tryptophan and tyrosine that are rich in animal proteins (21) also showed an antihypertensive effect in rats due to serotonin formation in the central nervous system (25, 26). In addition to the effects of these specific amino acids, nonspecific amino acids have also been reported to have a diuretic effect, which may reduce the plasma volume in the vascular system and lower blood pressure (27).

The strength of the present study was that we used a large community-based and free-living population, whose sources of dietary protein intake were different from those of Western populations. Compared with previous Japanese and Chinese studies (6, 8, 9), we had a large number of subjects and conducted a more thorough adjustment for confounding variables, including alcohol intake.

Some limitations of the present study warrant discussion. First, we used a single 24-h dietary recall for nutrient intakes of individuals. However, the large number of subjects made the variations in nutrient intakes and blood pressure across populations. Compared with previous Japanese and Chinese studies (6, 8, 9), we had a large number of subjects and conducted a more thorough adjustment for confounding variables, including alcohol intake.
## TABLE 4
Age-, sex-, and multivariable-adjusted mean blood pressure values by quartile of plant protein intake

<table>
<thead>
<tr>
<th>Plant protein intake (g/d)</th>
<th>Systolic blood pressure</th>
<th>Diastolic blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>g/d</td>
<td>mm Hg</td>
<td>mm Hg</td>
</tr>
<tr>
<td>Age-, sex-, community-adjusted (SE)</td>
<td>Multivariable-adjusted¹</td>
<td>Multivariable-adjusted²</td>
</tr>
</tbody>
</table>

### Men

<table>
<thead>
<tr>
<th>No. of subjects</th>
<th>1 (low)</th>
<th>2</th>
<th>3</th>
<th>4 (high)</th>
<th>P for trend</th>
<th>1 SD²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1893</td>
<td>1891</td>
<td>1898</td>
<td>1903</td>
<td>0.048</td>
<td>13.1</td>
</tr>
<tr>
<td>1 (low)</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>4 (high)</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>P for trend</td>
<td>0.048</td>
<td>0.064</td>
<td>0.053</td>
<td>0.048</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 SD²</td>
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<td>0.24</td>
<td>−0.41</td>
<td>0.23</td>
<td>0.59</td>
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<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>community-</td>
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<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>adjusted (SE)</td>
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<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Multivariable-</td>
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<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
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<tr>
<td>adjusted²</td>
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<td>1.0</td>
<td>1.0</td>
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<td>1.0</td>
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</tr>
</tbody>
</table>

### Women

<table>
<thead>
<tr>
<th>No. of subjects</th>
<th>1 (low)</th>
<th>2</th>
<th>3</th>
<th>4 (high)</th>
<th>P for trend</th>
<th>1 SD²</th>
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<tbody>
<tr>
<td>Total</td>
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<td>1875</td>
<td>1872</td>
<td>1877</td>
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<td>1.08</td>
</tr>
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<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
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<td>1.0</td>
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<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>4 (high)</td>
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<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
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<td>P for trend</td>
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<td>0.108</td>
<td>0.153</td>
<td>0.002</td>
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<td>0.194</td>
</tr>
<tr>
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<td>1.08</td>
<td>−0.57</td>
<td>0.34</td>
<td>−0.49</td>
<td>0.32</td>
<td>0.64</td>
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<td>Age-, sex-</td>
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<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>community-</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
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<tr>
<td>adjusted (SE)</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Multivariable-</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>adjusted²</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

¹ Adjusted for age (y), sex, BMI (kg/m²), current use of antihypertensive medication (yes or no), ethanol intake (g ethanol/d), and current smoking (yes or no).

² Mean ± SE (all such values).

4, 5, 6 Significantly different from Q1 (ANOVA); ⁴P < 0.05, ⁵P < 0.001, ⁶P < 0.01.

6 Calculated by regression analysis. Represents the 1-SD difference in increment in protein intake.

The authors’ responsibilities were as follows—MU, KY, and HI: developed the study hypothesis; MU: conducted the analysis and drafted the manuscript; and SS, HI, AK, TS, KY, TT, and HI: critically revised the manuscript. None of the authors had an personal or financial conflict of interest.

## REFERENCES


