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Maintenance of a low-sodium, high-carotene and -vitamin C diet after a 1-year dietary intervention: The Hiraka Dietary Intervention Follow-up Study

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Abstract

Background. The importance of dietary modification for disease prevention is widely accepted. The difficulty of implementing and sustaining long-term changes is also well documented. Nevertheless, a few studies have attempted to achieve significant dietary change for extended periods.

Methods. The Hiraka Dietary Intervention Study was a community-based randomized cross-over trial designed to develop an effective dietary modification tool and system in an area with high mortality for stomach cancer and stroke in 1998–2000. The main study subjects were 550 healthy volunteers, who were randomized into two groups and given tailored dietary education aimed at decreasing the intake of sodium and increasing that of carotene and vitamin C in either the first or second year. Four (first intervention group) and three (second intervention group) years after the intervention ended, 308 subjects were selected for this follow-up dietary survey.

Results. The low-sodium, high-vitamin C and -carotene diet was maintained with only a small, nonsignificant reversal from post-intervention to follow-up ($P = 0.082$ – 0.824). Significant changes from pre-intervention to follow-up were also maintained ($P < 0.01$).

Conclusion. This dietary intervention program was maintained well over 4 years after the termination of the intervention sessions.
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Keywords: Follow-up studies; Intervention studies; Dietary; Maintenance; Sodium; Carotene; Vitamin C

Introduction

Although the incidence of stomach cancer and stroke is decreasing, they remain major causes of death in Japanese (The Research Group for Population-based Cancer Registration in Japan, 1998; Liu et al., 2001). Primary prevention through lifestyle modification is regarded as an important strategy for reducing these diseases at the population level. The two diseases have common dietary etiologic factors: a high sodium and salted food intake is a probable risk factor for both, and hypertension is the major risk factor for the latter (Report of a joint FAO/WHO Experts Consultation, 2003; Tsugane et al., 2004). A high fruit

and vegetable intake is possibly preventive for both (Report of a joint FAO/WHO Experts Consultation, 2003). Dietary intervention methods able to modify the intake of these nutrients are therefore urgently needed in Japan.

The Hiraka Dietary Intervention Study was a community-based randomized cross-over trial designed to develop an effective dietary modification tool and system in an area with high mortality for stomach cancer and stroke (Takahashi et al., 2003). Just after the intervention, favorable modifications were observed in all targeted nutrients.

The importance of dietary change for disease prevention is widely accepted. The difficulty of implementing and sustaining long-term changes is also often documented. Nevertheless, a few previous studies have attempted to achieve significant dietary modification for extended periods (Bowen and Beresford, 2002). The aim of the present study was to determine the degree

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Table 1
Subject characteristics of Hiraka Dietary Intervention Follow-up Study (Akita, Japan, 1998–2003) at the pre-intervention point

Characteristic	Main study subjects (n = 550)	Follow-up study (n = 308)			P values ^a
		Participants (n = 278)	Non-responders (n = 30)	P values ^b	
Age (years) ^c	56.2 (7.7)	55.3 (7.7)	53.8 (7.8)	0.298	0.064
Sex (%female)	67.0	66.9	51.5	0.087	0.909
Body height (cm) ^c	155.6 (7.9)	156.8 (7.5)	158.5 (7.4)	0.200	0.220
Body weight (kg) ^c	57.3 (9.0)	57.5 (8.5)	60.5 (7.1)	0.092	0.837
Body mass index (kg/m ²) ^c	23.6 (2.8)	23.4 (2.7)	24.1 (3.1)	0.217	0.925
Smoker (%current)	11.5	12.7	8.0	0.334	0.544
Alcohol drinker (%current)	49.0	49.4	56.0	0.080	0.961

^a P values for comparison between follow-up study participants (n = 308) and main study participants (n = 550).

^b P values for comparison between participants (n = 278) and non-responder (n = 30) at follow-up.

^c Values are means (standard deviation).

of maintenance of the diet at 3 and 4 years after completion of the intervention. We also examined the level of maintenance among the nutrients and foods examined.

Methods

Overview of the Hiraka dietary intervention study

The Hiraka Dietary Intervention Study was a community-based randomized cross-over trial held in 1998–2000. Subjects were 550 healthy volunteers (202

men and 348 women, aged 40–69 years) living in two rural villages, Taiyu and Sannai, in Akita Prefecture, Japan. They were randomized into two groups and provided tailored dietary education to encourage a decrease in sodium intake and an increase in vitamin C and carotene intake either in the first year (first intervention group, n = 274) or second year (second intervention group, n = 276).

Members of the intervention group received two individual 15-min dietary counseling sessions from trained dietitians, as well as one group lecture and two newsletters. The face-to-face individual counseling was prepared based on the results of a dietary assessment and health check-up conducted at the initiation of the study. The individual feedback sheets consisted of a summary of dietary habits and nutrient intakes and a check-list of dietary behaviors. Further, four or five leaflets were also tailored to individual dietary intake level and dietary behavior by a computer system. These feedback sheets and leaflets were checked by the trained dietitians and were modified when necessary. In the counseling, each subject was provided with detailed advice in consideration of the individual's dietary habits and preferences. To encourage an increase in carotene and vitamin C intake, subjects were advised to increase their intake of fruit and vegetables based on the individual's dietary intakes and preferences. Similarly, to decrease sodium intake, they were primarily instructed to decrease their intake of salted foods. During the first year, changes differed significantly between the intervention (first intervention group) and control group (second intervention group) for both dietary sodium intake and urinary sodium excretion. Although favorable net changes were also observed in dietary carotene and vitamin C intake, serum level differences were modest. A detailed description of the intervention program and its short-term effects is provided elsewhere (Takahashi et al., 2003). After completion of the intervention, an annual newsletter about the results of the trial was mailed to all subjects to check for changes in address and to disseminate information about the present follow-up study.

Sample collection for the follow-up study

Three hundred and ten subjects living in Taiyu village who completed the main dietary intervention study from 1998 to 2000 were asked to participate in the present study. One subject died and a second moved away from the village before the start of the study, giving 308 subjects (155 first intervention and 153 second intervention group) agreeing to participate. Signed informed consent was obtained from all participants.

Table 2
Reported mean body weight and daily intake of energy and selected nutrients at each point in the Hiraka Dietary Intervention Follow-up Study: Akita, Japan, 1998–2003^{a,b}

	Pre-intervention	Post-intervention	Follow-up	Change from pre- to post-intervention		Change from post-intervention to follow-up		Change from pre-intervention to follow-up		
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	P value	Mean (SD)	P value	Mean (SD)	P value	
Body weight (kg)	57.5 (8.5)	57.5 (8.5)	57.5 (8.8)	0.0 (2.5)	0.584	0.0 (3.0)	0.426	0.0 (2.9)	0.752	
<i>Nutrient intake</i>										
Energy (kcal/day)	2054 (635)	1948 (596)	1982 (605)	-106 (462)	<0.001	34 (447)	0.209	-72 (468)	0.011	
Protein (percent of energy)	15.3 (2.8)	15.3 (2.7)	15.4 (2.7)	0.0 (2.4)	0.990	0.1 (2.6)	0.473	0.1 (2.6)	0.471	
Carbohydrates (percent of energy)	56.7 (7.1)	56.8 (7.1)	56.5 (7.2)	0.0 (6.3)	0.918	-0.3 (7.1)	0.490	-0.3 (7.4)	0.564	
Fat (percent of energy)	23.0 (5.8)	23.4 (5.5)	23.4 (6.0)	0.4 (4.8)	0.171	0.1 (4.9)	0.771	0.5 (5.8)	0.167	
Alcohol (percent of energy)	3.7 (6.2)	3.3 (5.7)	3.4 (5.9)	-0.4 (3.5)	0.046	0.1 (3.6)	0.664	-0.3 (3.7)	0.151	
Dietary fiber (g/1000 kcal)	7.6 (2.4)	8.0 (2.4)	8.3 (2.7)	0.4 (2.1)	0.001	0.2 (2.2)	0.069	0.7 (2.5)	<0.001	
Soluble dietary fiber	1.1 (0.4)	1.2 (0.5)	1.3 (0.5)	0.1 (0.4)	0.001	0.1 (0.5)	0.011	0.2 (0.5)	<0.001	
Insoluble dietary fiber	6.0 (1.8)	6.3 (1.8)	6.4 (1.9)	0.3 (1.6)	0.004	0.1 (1.5)	0.348	0.4 (1.8)	0.001	
Sodium (mg/1000 kcal)	2852 (795)	2651 (660)	2700 (729)	-201 (713)	<0.001	49 (698)	0.243	-152 (753)	0.001	
Potassium (mg/1000 kcal)	1361 (381)	1419 (388)	1401 (389)	58 (310)	0.002	-18 (315)	0.338	40 (326)	<0.001	
Carotene (μg/1000 kcal)	1380 (1008)	1625 (1047)	1672 (1118)	245 (1027)	<0.001	48 (1079)	0.462	292 (1090)	<0.001	
Alpha-carotene (μg/1000 kcal)	156 (141)	205 (170)	187 (142)	49 (163)	<0.001	-18 (176)	0.082	31 (156)	0.001	
Beta-carotene (μg/1000 kcal)	1215 (911)	1410 (925)	1477 (1029)	195 (924)	0.001	67 (978)	0.253	262 (1002)	<0.001	
Vitamin C (mg/1000 kcal)	66 (40)	78 (41)	78 (55)	12 (36)	<0.001	-1 (49)	0.824	11 (52)	<0.001	

^a Values are means (standard deviation, SD).

^b Results with the combined data of first (4 years from the end of the intervention, n = 142) and second intervention group (3 years from the end of the intervention, n = 136).

Table 3
Daily food intake (g/1000 kcal) at each point in the Hiraka Dietary Intervention Follow-up Study: Akita, Japan, 1998–2003^{a,b}

	Pre-intervention	Post-intervention	Follow-up	Change from pre- to post-intervention		Change from post-intervention to follow-up		Change from pre-intervention to follow-up		
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	P value	Mean (SD)	P value	Mean (SD)	P value	
Salted foods										
Miso ^c	13.9 (6.9)	11.7 (6.3)	12.0 (5.7)	-2.3 (7.2)	<0.001	0.4 (6.8)	0.365	-1.9 (7.6)	<0.001	
Salted pickles	29.1 (21.7)	24.4 (18.5)	26.6 (24.0)	-4.8 (21.6)	<0.001	2.2 (22.3)	0.098	-2.5 (26.7)	0.116	
Green and yellow vegetables ^d	5.9 (9.3)	4.3 (6.8)	5.6 (9.6)	-1.6 (9.1)	0.004	1.4 (10.0)	0.022	-0.2 (12.1)	0.762	
Other vegetables	23.3 (17.5)	20.1 (16.7)	21.0 (19.3)	-3.2 (18.2)	0.004	0.8 (18.4)	0.448	-2.3 (20.7)	0.064	
Salted fish	18.6 (14.7)	17.0 (12.8)	17.3 (11.6)	-1.6 (14.1)	0.057	0.3 (13.5)	0.691	-1.3 (15.4)	0.159	
Seasonings	21.4 (22.4)	20.4 (20.7)	21.4 (25.2)	-3.2 (45.9)	0.241	1.5 (46.9)	0.605	-1.8 (59.0)	0.615	
Fruits and vegetables										
Vegetables	149.8 (80.4)	166.7 (94.5)	160.3 (83.0)	16.9 (89.8)	0.002	-6.4 (87.9)	0.227	10.5 (82.1)	0.034	
Green and yellow vegetables ^e	66.8 (51.6)	80.3 (71.3)	78.3 (55.3)	13.5 (71.8)	0.002	-2.0 (70.6)	0.643	11.5 (56.7)	<0.001	
Other vegetables	83.0 (45.7)	86.4 (49.2)	82.0 (43.4)	3.4 (47.7)	0.232	-4.4 (47.8)	0.124	-1.0 (44.3)	0.707	
Fruits	53.8 (41.0)	63.6 (44.9)	54.6 (42.9)	9.8 (41.3)	<0.001	-9.0 (44.1)	<0.001	0.8 (44.9)	0.757	

^a Values are means (standard deviation, SD).

^b Results with the combined data of first (4 years from the end of the intervention, $n = 142$) and second intervention group (3 years from the end of the intervention, $n = 136$).

^c Fermented and salted soy-bean paste.

^d Includes salted pickles made of dark-green leafy vegetables or carrots.

^e Include dark-green leafy vegetables, carrots, pumpkin, tomatoes, broccoli, sweet peppers, tomato juice, and vegetable juice.

Data collection

Data for the follow-up study were collected from April to July 2003 using the same procedures as in the main study. A validated self-administered diet history questionnaire (DHQ) was used to estimate average nutrient intakes. The DHQ surveyed dietary habits for the previous 1 month, with questions on the semi-quantitative frequency and quantity for 127 selected food items, dietary behavior, major cooking methods for vegetables, fish and meats, and open-ended questions (Sasaki et al., 1998a,b, 2000). Nutrient and food intake were calculated using a specially developed computer program. The DHQ was completed just before the annual health check-up by all subjects. Medical history, smoking status and

anthropometric data were also collected at the health check-up. Body mass index (BMI) was calculated as self-reported weight (kg) divided by height (m) squared.

Statistical analysis

A total of 93% (144 of 155 subjects) of the first intervention group subjects and 90% (138 of 153) of the second completed the follow-up questionnaire. The remaining subjects were lost to follow-up for various reasons, including death, serious illness, nursing of family members and work demands. Subjects were excluded from analysis if their estimated energy intake was less than 50% of that

Table 4
Daily fruit and vegetable intake (g/1000 kcal) at each point in the Hiraka Dietary Intervention Follow-up Study: Akita, Japan, 1998–2003^{a,b}

	Pre-intervention	Post-intervention	Follow-up	Change from pre- to post-intervention		Change from post-intervention to follow-up		Change from pre-intervention to follow-up		
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	P value	Mean (SD)	P value	Mean (SD)	P value	
Vegetables										
Broccoli	3.9 (5.6)	4.8 (6.6)	5.2 (11.0)	0.8 (6.5)	0.033	0.4 (11.4)	0.585	1.2 (11.3)	0.073	
Dark-green leafy vegetable	21.1 (24.5)	24.0 (24.8)	30.1 (31.0)	2.9 (25.4)	0.059	6.1 (30.3)	<0.001	9.0 (30.2)	<0.001	
Carrot	6.1 (6.0)	7.9 (6.9)	7.4 (6.1)	1.9 (6.7)	<0.001	-0.5 (7.5)	0.271	1.4 (6.7)	<0.001	
Squash	3.0 (6.4)	4.5 (6.4)	3.6 (4.9)	1.5 (8.1)	0.002	-0.9 (7.1)	0.028	0.6 (6.5)	0.143	
Tomato	13.7 (23.1)	13.1 (16.2)	13.3 (20.6)	-0.6 (19.2)	0.576	0.2 (20.0)	0.878	-0.5 (24.9)	0.757	
Sweet pepper	4.1 (6.2)	4.5 (5.0)	3.8 (5.8)	0.4 (5.5)	0.200	-0.6 (6.0)	0.079	-0.2 (6.6)	0.591	
Salted pickles ^c	5.8 (9.3)	4.3 (6.8)	5.7 (9.7)	-1.6 (9.1)	0.005	1.5 (10.0)	0.016	-0.1 (12.2)	0.885	
Tomato/Vegetable juice	9.1 (21.3)	17.2 (58.6)	9.2 (24.6)	8.1 (60.6)	0.026	-8.0 (59.4)	0.025	0.1 (26.3)	0.951	
Fruits										
Citrus fruits	9.1 (13.6)	11.9 (14.5)	13.1 (17.8)	2.8 (15.3)	0.002	1.2 (18.3)	0.271	4.0 (18.4)	<0.001	
Banana	9.5 (12.3)	12.8 (14.4)	11.1 (13.0)	3.2 (13.3)	<0.001	-1.7 (15.1)	0.060	1.5 (14.8)	0.086	
Apple	10.5 (23.3)	12.5 (24.2)	10.3 (20.5)	2.0 (23.6)	0.157	-2.2 (22.1)	0.093	-0.2 (23.2)	0.869	
Strawberry	5.7 (15.0)	7.2 (13.7)	7.5 (15.7)	1.5 (15.0)	0.090	0.3 (19.3)	0.796	1.8 (20.7)	0.140	
Other fruits	19.0 (16.9)	19.2 (17.2)	12.6 (10.5)	0.1 (16.5)	0.891	-6.6 (15.7)	<0.001	-6.4 (15.0)	<0.001	

^a Values are means (standard deviation, SD).

^b Results with the combined data of the first (4 years from the end of the intervention, $n = 142$) and second intervention group (3 years from the end of the intervention, $n = 136$).

^c Includes salted pickles made of dark-green leafy vegetables or carrots.

required for a sedentary lifestyle or greater than 150% of that required for a vigorous lifestyle. A total of 92% (142 of 155 subjects) of the first intervention group subjects and 89% (136 of 153) of the second were included in this analysis.

Subjects were divided into two groups by time of intervention, namely the first intervention group at 4 years from the end of the intervention and the second at 3 years. Mean daily intake of selected nutrients and foods pre- and post-intervention (1 year from pre-intervention) and at follow-up was calculated by group. As maintenance of the diet between the groups was similar, the results are given as a combination of data for the first and second intervention groups. For vegetable intake, the intakes of carotene- and vitamin C-rich vegetables (green and yellow vegetables) and of others (other vegetables) were calculated separately. The definitions used referred to the guidelines proposed by the Ministry of Health and Welfare, Japan, 1993, with "green and yellow vegetables" including dark-green leafy vegetables, carrots, squash, broccoli, tomatoes, sweet peppers and tomato/vegetable juice. Intake of major salted foods such as miso (fermented and salted soy-bean paste), salted fish, salted vegetable pickles and seasonings were also calculated, and the mean values at follow-up were compared with pre- and post-intervention values using the paired *t* test.

Results

Table 1 shows the demographic characteristics of the follow-up study and the main study subjects at baseline. There were no statistically significant differences in subject characteristics between the main study and follow-up study participants. In the follow-up study, the non-responders were younger and had higher BMI and higher male-to-female ratio than the participants, although these differences did not reach statistical significance.

Table 2 shows nutrient intake at each point and their net changes. Body weight did not remarkably change throughout the trial or follow-up period. Energy intake decreased significantly after intervention (-106 kcal/day, $P < 0.001$). The only difference between the post-intervention and follow-up points was a slight increase in sodium intake ($+49 \pm 698$ mg/1000 kcal, $P = 0.243$). However, differences between the pre-intervention and follow-up points remained significant (-152 ± 753 mg/1000 kcal, $P < 0.001$). Carotene and vitamin C intake significantly increased after intervention and this change remained at the follow-up point. Differences between the pre-intervention and follow-up points were significant ($+292 \pm 1090$ μ g/1000 kcal, $P < 0.001$ for carotene and $+11 \pm 52$ mg/1000 kcal, $P < 0.001$ for vitamin C). Dietary fiber intake increased significantly at the post-intervention point, and this was well-sustained at the follow-up point. Intake of the other nutrients did not change between the trial and follow-up points.

The intake of salted foods, fruits and vegetables at each point is shown in Table 3. Miso intake decreased significantly after intervention, and this change remained at follow-up point. Salted pickles intake decreased after intervention, but increased thereafter at the follow-up point (difference between the post-intervention and the follow-up points: $+2.2$ g/1000 kcal, $P = 0.098$), although not to the pre-intervention level (difference between the pre-intervention and the follow-up points: -2.5 g/1000 kcal, $P = 0.116$). Although vegetable and fruit intake significantly increased at the end of the intervention, fruit intake subsequently returned to the values at the pre-intervention point.

Table 4 presents the intake of individual fruit and green and yellow vegetable items. Dark-green leafy vegetables significant-

ly increased between the post-intervention and the follow-up points ($+6.1$ g/1000 kcal, $P < 0.001$). Although the intake of squash, sweet pepper and tomato/vegetables juice was significantly increased just after the intervention, it decreased thereafter to close to the pre-intervention values.

Discussion

The Hiraka Dietary Intervention Study was successful in bringing about substantial changes in all targeted nutrients shortly after the intervention (Takahashi et al., 2003). Moreover, the present follow-up study results show that the effects of the intervention were maintained well for 4 years after the termination of intervention. Additional modifications were difficult to achieve, but those which were obtained were mostly maintained until follow-up. Although our intervention scheme was computerized to the greatest extent possible, the greater part of the program's success in maintaining long-term dietary modification may have actually owed to the dietitian's personal instructions, made in consideration of the individual characteristics of each subject.

A few previous studies with large sample sizes have attempted to achieve dietary modifications for long periods of time. These targeted dietary fat intake, and used intensive interventions (Gorder et al., 1997; Women's Health Initiative Study Group, 2004). The present study is unique, however, in that it investigated the long-term effect of a moderate intensity dietary intervention in healthy free-living subjects that targeted sodium, vitamin C and carotene.

Maintenance of low-sodium diet

In the intervention trial, subjects were primarily instructed to decrease their intake of miso, salted vegetable pickles, salted fish and seasonings, which were their main sources of dietary sodium. Consumption of all foods except seasonings decreased at the end of the intervention, of which only that for miso was maintained until follow-up. Because salted pickles vegetables and salted fish are 'traditional and familiar staple foods' in the study area, their avoidance may be difficult to maintain, notwithstanding that intake decreased temporarily just after intervention. They are highly salted foods, with salt contents of 5–15% by weight in salted fish, for example, and of 1–10% in salted pickled vegetables. From the viewpoint of stomach cancer prevention, because not only salt per se but also these highly salted foods are probable risk factors of stomach cancer (Tsugane et al., 2004), the achievement of any long-term modification may require the adoption of continuous reinforcement.

Maintenance of a high-carotene and vitamin C (fruit and vegetable) diet

Although the consumption of fruit and vegetables decreased at the follow-up point, that of dark-green leafy vegetables, broccoli, citrus fruits and strawberry actually increased at this time. These foods are relatively rich in carotene and vitamin C compared to other fruits and vegetables. As a consequence of

these changes, carotene and vitamin C intake were sustained until follow-up.

The pattern of change differed between fruits and vegetables. Consumption of dark-green leafy vegetables further increased at follow-up, whereas that of squash, sweet pepper and tomato/vegetable juice returned to near pre-intervention values. Although it is unclear why, foods whose intake returned to the pre-intervention point seemed to be unpopular among the subjects. The average intake of these foods at the pre-intervention point was relatively lower than that of the other fruits and vegetables, i.e., 3.0, 4.1, 9.1 g/1000 kcal for squash, sweet pepper and tomato/vegetable juice, respectively. On the contrary, that of dark-green leafy vegetables at pre-intervention was relatively higher than that of the other vegetables, i.e., 21.1 g/1000 kcal. In Japan, many kinds of dark-green leafy vegetable prepared by various cooking methods are eaten throughout the year. The adoption of unpopular foods such as tomato/vegetable juice, sweet pepper and squash may require strong accustomization to the new taste and the knowledge of cooking method and recipes. The choice of culturally acceptable alternatives to unpopular foods in a target population therefore seems important to achieving the long-term maintenance of dietary modification. The example in this study was a large variety of green-leafy vegetables. Nevertheless, the reason for the marked increase in dark-green leafy vegetable consumption at follow-up study is unclear. Food choices are the result of complex interplays among sociodemographic, psychosocial, environmental, cultural, taste preference and economic factors (Nestle et al., 1998; Gedrich, 2003). Fruit and vegetable intake are related to taste preference, cost and availability (Brug et al., 1995; Treiman et al., 1996; Keim et al., 1997; Glanz and Yaroch, 2004; Glanz and Hoelscher, 2004). These factors may have influenced the long-term maintenance of dietary modification.

Study limitations

The primary limitation of this study is the use of self-reported dietary data, which may be biased as a result of greater social desirability and intervention-associated bias (Hebert et al., 1995; Kristal et al., 1998). In our main study, the effects of dietary intervention were assessed not only from responses to a self-administered questionnaire but also with the corresponding biomarkers, such as serum concentrations of ascorbic acid and carotenoids and urinary excretion of sodium. We did not use these biomarkers in the follow-up study, however, because blood sampling and urinary collection were found to be a serious burden on free-living healthy participants. Further, our main study results showed that serum concentrations of vitamin C and carotene were insufficiently sensitive for the detection of small dietary changes in a moderate intensity dietary intervention. We asked the subjects to answer the dietary assessment questionnaire as honestly as possible because the individualized results would be feedback into the system and used in subsequent dietary counseling. This was done partly to reduce the impact of social desirability on the answers. However, the real impact is unknown.

Other limitations to the interpretation of our results are related to the study design. The main study was conducted as a ran-

domized cross-over trial. The short-term intervention effects were examined using data of the first half of the trial; in other words, the group receiving dietary intervention in the first year was used as the intervention group, while the other group was used as the control group. In the absence of a control group, the results of this follow-up study might have been affected by unknown factors, and should therefore be interpreted with caution.

Conclusion

The effects of this dietary intervention program on targeted nutrient intake were maintained well at 4 years after the termination of the intervention. The results are generally encouraging for the feasibility of future dietary intervention trials. However, it is unknown whether the same or similar results can be achieved in other populations with other targeted nutrients. Further studies are required.

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Dietary patterns associated with bone mineral density in premenopausal Japanese farmwomen¹⁻³

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ABSTRACT

Background: Because several nutrients are known to affect bone mineral density (BMD), the analysis of dietary patterns or combinations of foods may provide insights into the influence of diet on bone health.

Objective: We evaluated associations between dietary patterns and BMD in Japanese farmwomen.

Design: The study included 291 premenopausal farmwomen (aged 40–55 y) who participated in the Japanese Multi-centered Environmental Toxicant Study (JMETS; $n = 1407$). Forearm BMD was measured by using dual-energy X-ray absorptiometry. Diet was assessed by using a validated self-administered diet history questionnaire comprising 147 food items, from which 30 food groups were created and entered into a factor analysis.

Results: Four dietary patterns were identified. The “Healthy” pattern, characterized by high intakes of green and dark yellow vegetables, mushrooms, fish and shellfish, fruit, and processed fish, was positively correlated with BMD after adjustment for several confounding factors ($P = 0.048$). In contrast, the “Western” pattern, characterized by high intakes of fats and oils, meat, and processed meat, tended to be inversely associated with BMD; however, the association was not significant ($P = 0.08$).

Conclusion: A dietary pattern with high intakes of fish, fruit, and vegetables and low intakes of meat and processed meat may have a beneficial effect on BMD in premenopausal women. *Am J Clin Nutr* 2006;83:1185–92.

KEY WORDS Bone mineral density, dietary pattern, diets, fruit and vegetables, Japanese farmwomen

INTRODUCTION

Osteoporosis and related fractures among senior citizens are well recognized as a major public health problem in developed nations. They are the second-leading cause in Japan for patients to become bedridden, preceded only by cerebrovascular diseases in Japan. The prevalence of osteoporosis and related fractures appears to be increasing (1). In addition, osteoporosis and related fractures impose high health care costs in long-term nursing home care. The prevention of bone loss is thus desirable for both medical and economic reasons.

With regard to nutritional approaches to bone metabolism, a great deal of attention has been focused on the benefits of calcium and vitamin D. Other nutrients and dietary components, such as potassium, magnesium, vitamin K, and fruit and vegetables, have

also shown beneficial effects (2–6), although a clear relation with bone metabolism has not been established. Moreover, beneficial effects have been hypothesized for protein, saturated fat, phosphorus, vitamin C, sodium, and dietary isoflavone (7–12). With regard to diet, however, the most common approach, that of examining single nutrients or foods, may not adequately account for complicated interactions and cumulative effects. Because people consume diets consisting of a variety of foods with complex combinations of nutrients, rather than isolated nutrients, the examination of only single nutrients or foods could result in the identification of erroneous associations between dietary factors and disease.

To overcome these limitations, the dietary pattern approach—namely, the measurement of overall diet—has been widely used to elucidate the relations between diet and disease (13, 14). This approach allows the development of appropriate recommendations for overall dietary habits to prevent undesirable conditions and diseases. Tucker et al (15) used the dietary pattern approach with cluster analysis to show that a diet rich in fruit and vegetables is associated with a greater bone mineral density (BMD) in elderly men. In Japan, only one study (16) examined the relation between diet and the results of an ultrasound bone density meter (USBDM) among elderly men and women. The results showed that the factor 2 score (ie, that for a diet with a high intake of breads instead of rice and a frequent intake of dairy products, called a bread-style diet) was significantly lower among elderly women in the USBDM-measured low bone density group (16). In the current study, we attempted to identify dietary patterns by using factor analysis. In addition, we examined the relations between dietary patterns and BMD in Japanese farmwomen aged

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40–55 y who live in rural communities and have maintained more traditional dietary habits than do typical residents of large cities.

SUBJECTS AND METHODS

Study population

The Japanese Multi-centered Environmental Toxicant Study (JMETS) was a nationwide, community-based study of farm-women sampled between 2000 and 2003. The study was conducted in 5 districts—1 district is on the north end of Kyushu Island (the southernmost Japanese island), and the other 4 districts are located at the north end of Honshu Island (the largest Japanese island)—where the rice produced and consumed by the farmers has a low-to-moderate cadmium contamination. Study recruitment and enrollment were described in detail elsewhere (17, 18). Before the study, orientation sessions were held to explain the purposes and protocol of the study to the participants. At the same time, participants were instructed in completing 2 kinds of questionnaires and were asked to bring the questionnaires to the examination. A total of 1407 women aged 20–78 y who agreed to participate in the study completed the questionnaires, and their BMD was measured.

All subjects provided written informed consent. The study protocol was approved by the Committee on Medical Ethics of the Jichi Medical School.

Dietary assessment and food grouping

We used a previously validated 16-page self-administered diet history questionnaire (DHQ) to assess dietary habits in the previous month (19, 20). The DHQ consists of 7 sections: general dietary behaviors; most frequent cooking methods; frequency and amount of consumption of 6 alcoholic beverages; consumption frequency and semiquantitative portion size of 121 selected food and nonalcoholic beverages; dietary supplements; frequency and amount of consumption of 19 staple foods (ie, rice, bread, noodles, and other wheat foods) and miso soup (fermented soybean paste soup); and open-ended items for foods consumed regularly (≥ 1 time/wk) but not appearing in the DHQ. The food and beverage items and portion sizes in the DHQ were derived primarily from data in the National Nutrition Survey of Japan and several cookbooks for Japanese dishes (19). Measures of dietary intakes of 147 food and beverage items and energy were calculated by using an ad hoc computer algorithm for the DHQ, which was based on the Standard Tables of Food Composition in Japan (21). Information on dietary supplements and data from the open-ended questionnaire items were not used in the calculation of dietary intakes. More detailed descriptions of the questionnaire, the methods of calculating nutrients, and the validity of the questionnaire are given elsewhere (19, 20).

To reduce the complexity of the data, food items were categorized into groups (Table 1). In general, the food grouping was based on the principles of similarity of nutrient profiles or culinary usage of the foods, mainly according to the Standard Tables of Food Composition in Japan (21), and the classification of food groups used by the National Nutrition Survey of Japan (22). Finally, 30 separate food groups were established and used in our analyses to identify dietary patterns.

Measurement of bone mineral density

BMD (g/cm^2) and bone mineral mass [(BMM) g] were measured by using dual-energy X-ray absorptiometry (DXA) of each participant's nondominant forearm by using an osteometer (DTX-200; Osteometer MediTech Inc, Hawthorne, CA). DXA scanned at the distal sites of the radius and ulna. Subjects' BMD and bone mineral content [(BMC) g] were calculated in the area of the bones between the distal site of an 8-mm gap between the 2 bones and the proximal site 24 mm from the gap. The CVs of forearm BMD measurements were all within 1.0%.

Measurement of confounding factors

In addition to diet, we measured the following factors that may be related to BMD: body weight, body height, physical activity level, smoking habit, history of bone fracture, supplement use, menopausal status, current use of hormone replacement therapy, parity, and age at menarche. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, while subjects were wearing light clothing but no shoes. Body mass index (BMI) was calculated as body weight (kg) divided by body height squared (m^2). The maximum grasping power value of a participant's nondominant hand was measured 3 times by using a hand dynamometer. Grasping power was used in our analyses as an indicator of physical activity.

Age (in y, continuous), current smoking (yes or no), frequency of bone fracture (times, continuous), current use of hormone replacement therapy (yes or no), parity (times, continuous), and age at menarche (in y, continuous) were obtained from an 8-page questionnaire. Alcohol consumption (g/d) and use of calcium or multivitamin supplements (yes or no) were assessed from the DHQ.

Statistical analysis

In the statistical analysis, the dietary environmental cadmium exposure of the subjects did not show any significant effects on renal tubular functions (17) or BMD (18) after adjustment for possible confounders. However, to avoid unknown long-term effects of cadmium exposure, we restricted the cohort of the current study to the 339 women aged 40–55 y who were still menstruating at the time of entry. Of these 339 women, 48 were excluded for collagen disease ($n = 1$), hyperthyroidism ($n = 1$), a reported daily energy intake < 2.7 or > 14.4 MJ (650–3450 kcal) ($n = 9$; 23), and a reported change in dietary habits within the previous 3 y ($n = 38$). The remaining subjects had no history of taking medications that may affect bone or calcium metabolism and no history of any condition that affects bone metabolism. Thus, data from 291 women were included in the final analysis.

We calculated the ratio of energy intake (EI) to basal metabolic rate (BMR) to evaluate the relative accuracy of the reported energy intake. To compare the relative degree of underreporting and overreporting, we temporarily used EI:BMR as defined by FAO/WHO/UNU: ratios of 1.27 for the minimum survival level, 1.56 for the sedentary level for women and 2.0–2.4 for the maximum sustainable lifestyle level (24).

Analyses were conducted by using FACTOR PROCEDURE software (version 8.2; SAS Inc, Cary, NC; 25). Factor analysis was used to derive the dietary patterns on the basis of the 30 food groups from the DHQ. Intake of these food groups was adjusted for total energy intake by using the residual method (26). To



TABLE 1
The 30 food groupings used in the dietary pattern analysis¹

Food group	Foods in the group
Rice	Well-milled rice, rice with barley (70% rice and 30% barley), rice with embryo, half-milled rice, 70%-milled rice, brown rice
Noodles	Japanese noodles (buckwheat or Japanese wheat noodles), instant noodles, Chinese noodles, pasta, spaghetti
Breads	White bread, butter roll, croissant, pizza, okonomiyaki (Japanese pancake fried with various ingredients), takoyaki (small ball of wheat flour with bits of octopus)
Miso soup	Miso (fermented soybean paste) soup
Dairy products	Whole milk, low-fat milk, skim milk, yogurt, cheese, cottage cheese, lactic acid bacteria beverages, ice cream, coffee cream
Meats	Beef, pork, ground beef or pork, chicken, liver (beef, pork, or chicken)
Processed meats	Ham, sausage, bacon, salami
Fish and shellfish	Eel, white-meat fish (sea bream, flatfish, codfish, and others), blue-back fish (mackerel, sardine, herring, and others), red-meat fish (tuna, salmon, and skipjack), shrimp, squid, octopus, oysters, other shellfish
Processed fish	Dried fish, small fish with bones, canned tuna, fish eggs, boiled fish in soy sauce, salted gut (fish, squid, or shellfish), surimi (ground fish meat) products
Eggs	Eggs
Nuts	Peanuts, other types of nuts
Soy products	Tofu (soybean curd), tofu products such as atsuage (deep-fried tofu cutlet), ganmodoki (deep-fried tofu burger), aburaage (deep-fried tofu pouch), natto (fermented soybeans), cooked beans, miso as seasoning
Green and dark yellow vegetables	Carrots, pumpkins, tomatoes, green pepper, broccoli, lettuce, green leafy vegetables such as spinach
White vegetables	Cabbage, cucumber, Chinese cabbage, bean sprouts, Japanese radish, onion, cauliflower, eggplant, burdock, lotus root
Pickled vegetables	Salted pickles, umeboshi (pickled and dried plum), kimchi (Korean pickles)
Fruit and vegetable juices	Vegetable juice, tomato juice, 100% fruit juice, sweetened fruit drinks (50% fruit)
Fruit	Oranges, grapefruits, bananas, apples, strawberries, grapes, peaches, pears, kiwi fruit, persimmons, melons, watermelon, raisins, canned fruit
Sugary foods	Sugar for coffee and tea, sugar for cooking, jam, marmalade
Mushrooms	Shiitake, shimeji, enoki
Seaweeds	Wakame seaweed, purple laver, brown algae
Potatoes	White potatoes, French fries, sweet potatoes, taros, konnyaku (devil's tongue jelly)
Sweets	Japanese sweetened bun, pancake, potato chips, senbei and arare (rice snacks), crackers, salted snacks, Japanese sweets with or without azuki beans, cakes, soft cookies, hard cookies, chocolates, candies, caramels, chewing gums, jellies, doughnut
Butter	Butter
Fats and oils	Margarine, vegetable oil, salad dressing with oil
Alcohol	Beer, sake (rice wine), shochu (distilled spirits), chuhai (shochu highball), whiskey, wine
Tea	Green tea, oolong tea, black tea
Coffee	Coffee, cocoa
Soft drinks	Cola, nonfruit juices, soft drinks without sugar, such as sports beverages
Seasonings	All condiments (eg, ketchup), mayonnaise, table salt, salt and salt-rich seasonings used during cooking, soy sauce, oil-free dressings, curry or stew roux, spices
Soup	Corn soup, Chinese soup

¹ Foods listed in the table were from the self-administered diet history questionnaire.

identify the number of factors to be retained, we used the criterion of eigenvalues > 1.0 , the most widely used criterion in factor analysis, as a first step. However, this procedure created 12 independent factors, a number too large for further analyses. The screen plots dropped substantially (from 1.81 to 1.59) after the third factor and remained closer (1.54 for the fifth factor and 1.50 for the sixth factor) after the fifth factor, which suggested that the retention of 3 or 4 factors would be optimal. Finally, we decided to retain 4 factors for further analyses. The factors were rotated by orthogonal transformation (VARIMAX rotation function in SAS) to achieve a simpler structure with greater interpretability. After Varimax rotation, factor scores for each subject were saved from the principal component analysis. Factor loadings represent correlation coefficients between individual food groups and dietary patterns. The proportion of variance explained by each factor was calculated by dividing the sum of the squares of the respective factor loadings by the number of variables. The factor

scores for each pattern and for each individual were determined by summing the intakes of each food group weighted by the factor loading (27). All data presented here are from the Varimax rotation. The scores were used for comparison with nutrient intake and other lifestyle factors and to estimate associations with BMD.

Factors were divided into quintiles, and sample means and frequencies were calculated. Partial correlation coefficients (adjusted for age) were calculated between each factor and forearm BMD and between each factor and energy-adjusted nutrient intake. We compared the adjusted mean (\pm SE) for each quintile of each dietary pattern using 3 models. In model 1, we adjusted for age and lifestyle variables, such as BMI, grasping power, and current smoking, as confounding factors. In model 2, we further adjusted for a history of bone fracture and female hormone-related factors, such as the use of hormone replacement therapy, age at menarche, and parity. In model 3, we also adjusted for



TABLE 2
Characteristics of study subjects¹

	Premenopausal women
Age (y)	46.4 ± 3.7 ²
Body height (cm)	156.1 ± 5.2
Body weight (kg)	57.8 ± 8.4
BMI (kg/m ²)	23.7 ± 3.3
Grasping power (kg)	29.1 ± 4.5
Forearm bone mineral density (g/cm ²)	0.489 ± 0.053
Forearm bone mineral mass (g)	3.20 ± 0.45
Smoking status [n (%)]	
Current	11 (4)
Former	4 (1)
Never	276 (95)
History of fracture [n (%)]	26 (9)
Hormone replacement therapy [n (%)]	2 (1)
Age at menarche (y)	13.0 ± 1.2
Parity (n)	2.5 ± 0.9
Calcium supplement use [n (%)]	13 (4)
Multivitamin supplement use [n (%)]	14 (5)
EI:BMR ³	1.41 ± 0.32
< 1.27	100 (34)
> 2.4	1 (1)
Nutrient intakes	
Total energy (MJ/d)	7.9 ± 1.7
Protein (% of energy)	13.6 ± 2.1
Fat (% of energy)	26.5 ± 5.6
Carbohydrate (% of energy)	57.8 ± 7.0
Potassium (mg/d)	2322 ± 713
Magnesium (mg/d)	251 ± 73
Calcium (mg/d)	498 ± 185
Phosphorus (mg/d)	969 ± 282
Vitamin C (mg/d)	109 ± 55
Vitamin D (μg/d)	7.8 ± 4.4
Vitamin K (μg/d)	322 ± 181
Isoflavon (mg/d)	36.4 ± 21.8
Alcohol (g/d)	2.6 ± 6.1

¹ n = 291. EI:BMR, the ratio of energy intake to basal metabolic rate.

² $\bar{x} \pm SD$ (all such values).

³ Subjects who had an EI:BMR < 1.27 were defined as severe under-reporters and those with an EI:BMR > 2.4 were defined as over-reporters according to the FAO/WHO/UNU (24).

dietary variables, such as the use of calcium or multivitamin supplements. *P* values to test for linear trends were calculated by using dietary pattern scores as a continuous variable after control for possible confounding factors.

All statistical analyses were performed by using SAS software (version 8.2). A *P* value of < 0.05 was considered significant, except during the analysis of correlations between dietary patterns and nutrient intake, because those correlations were not necessarily independent of each other. In those instances, a partial correlation coefficient of > 0.2 or < -0.2 was considered significant.

RESULTS

Mean (\pm SD) values for forearm BMD, nutrient intake, and continuous potential confounders used in the present analysis are shown in **Table 2**. Proportional distributions are presented for categorical variables. The following activities were rare among participants in the current study: current smoking (4%) and the use of calcium supplement (4%), multivitamin supplement (5%),

and hormone replacement therapy (1%). The mean value of EI:BMR as an indicator of reporting accuracy was 1.41 ± 0.32 . Thirty-four percent of the subjects had an EI:BMR below the minimum survival value of 1.27, and 1% had an EI:BMR higher than the maximum value of 2.4 for a sustainable lifestyle.

The factor-loading matrices are shown in **Table 3**. The high positive loadings indicate strong associations between given food groups and patterns, whereas negative loadings indicate negative associations with the patterns. The patterns were labeled according to the food groups with high loadings. Factor 1, which loaded heavily on green and white vegetables, mushrooms, fish and shellfish, fruit, processed fish, seaweed, and soy products, was labeled the "Healthy" pattern. Factor 2, with high loadings for rice, miso soup and soy products, was labeled the "Japanese traditional" pattern. Factor 3 with high loadings for fats and oils, meat, processed meats, and seasoning was labeled the "Western" pattern. Factor 4, with high loadings for coffee, soft drinks, dairy products, sugary foods, and meats, was labeled the "beverage and meats" pattern. Overall, the 4 dietary patterns accounted for 29.7% of the variance in food intakes.

The subjects were divided into quintiles by the factor score of each dietary pattern. Sample means and frequencies were calculated across quintiles. Sample characteristics of premenopausal women in the lowest and highest quintiles of each food pattern (Q1 and Q5, respectively) are shown in **Table 4**. Participants in the highest quintile of the Healthy pattern were older (47.3 ± 3.7 y), whereas those in the highest quintile of the Western pattern were younger (45.6 ± 3.3 y). The greatest incidence of calcium supplement use (10.3%) was observed in the highest quintile of the Western pattern, whereas the smallest incidence of multivitamin supplement use (3.5%) was observed in the highest quintile of the Japanese traditional pattern.

Partial correlation coefficients between each of the 4 dietary patterns and forearm BMD and energy-adjusted nutrient intakes are shown in **Table 5**. BMD was not correlated with any dietary pattern after adjustment for age only. For energy-adjusted nutrient intakes, the Healthy pattern was correlated with protein ($r = 0.65$), potassium ($r = 0.82$), magnesium ($r = 0.69$), calcium ($r = 0.51$), phosphorus ($r = 0.70$), vitamin C ($r = 0.51$), vitamin D ($r = 0.53$), vitamin K ($r = 0.48$), and alcohol ($r = 0.22$). The Western pattern was positively correlated with fat ($r = 0.54$) and negatively correlated with carbohydrate ($r = -0.55$). In contrast, the Japanese traditional pattern showed a strong positive correlation with isoflavone ($r = 0.49$) and a negative correlation with fat ($r = -0.22$).

The multivariate-adjusted mean BMD across quintiles of all 4 dietary patterns is shown in **Table 6**. The highest quintile of the Healthy pattern had a significantly higher BMD than did the lowest quintile after adjustment for nondietary factors and dietary supplements (0.498 ± 0.006 and 0.476 ± 0.006 g/cm² for Q5 and Q1, respectively; $P = 0.014$). The highest quintile of the Western pattern had a significantly lower BMD than did the lowest quintile (0.480 ± 0.006 and 0.500 ± 0.006 g/cm² for Q5 and 1, respectively; $P = 0.043$). To test for linear trend, modeling of factor scores as continuous variables showed a positive and significant association in the Healthy pattern ($P = 0.048$), whereas a negative, but nonsignificant, association was observed in the Western pattern for premenopausal women ($P = 0.08$). No association with BMD was seen for any other dietary pattern.



TABLE 3

Factor-loading matrix for the 4 dietary patterns identified among 291 premenopausal Japanese farmwomen who participated in the Japanese Multi-centered Environmental Toxicant Study¹

	Factor 1: Healthy	Factor 2: Japanese traditional	Factor 3: Western	Factor 4: Beverage and meats
Green and dark yellow vegetables	0.61	—	—	—
Mushrooms	0.57	—	—	—
Fish and shellfish	0.57	—	—	—
Fruit	0.49	—	—	—
Processed fish	0.44	—	—	-0.35
White vegetables	0.40	0.35	0.33	—
Eggs	—	—	—	—
Alcohol	—	—	—	—
Rice	-0.50	0.64	-0.28	—
Miso soup	—	0.61	—	—
Soy products	0.26	0.54	—	—
Seaweeds	0.36	0.39	—	—
Nuts	—	—	—	—
Noodles	—	-0.33	—	-0.25
Sweets	—	-0.53	-0.42	—
Breads	—	-0.63	—	—
Fats and oils	—	—	0.62	—
Meats	—	—	0.59	0.30
Processed meats	—	—	0.54	—
Butter	—	—	0.41	—
Seasonings	—	—	0.37	—
Soup	—	—	0.30	—
Salted vegetables	0.30	—	-0.37	—
Coffee	—	—	—	0.65
Sugary foods	—	—	—	0.50
Soft drinks	—	—	—	0.35
Dairy products	—	—	—	0.35
Fruit and vegetable juices	—	—	—	—
Potatoes	—	0.30	—	-0.37
Tea	—	—	—	-0.45
Percentage of variance (%)	8.3	8.1	7.0	6.3

¹ Data for 291 subjects from the self-administered diet history questionnaire. Absolute values < 0.25 were excluded from the table for simplicity.

DISCUSSION

Using factor analysis, an approach that considers overall eating patterns, we identified 4 dietary patterns in premenopausal women aged 40–55 y and found associations between dietary patterns and BMD. The Healthy pattern showed a positive correlation with BMD, whereas the Western pattern showed a negative association.

To our knowledge, no previous study examined the relation between dietary patterns by using factor analysis and BMD as measured by DXA. Although only one cross-sectional study has examined the relation between dietary patterns and BMD in Japanese elderly men and women, BMD in that study was measured by using USBDM (16). Uchida et al (16) reported that the factor 2 score (ie, a bread-style diet) was significantly lower in the low USBDM-measured group than in the mean and high USBDM-measured groups of elderly women. A second study, by Tucker et al (15), examined the association between BMD and dietary patterns derived from cluster analysis. That study, a case-control study from the Framingham Osteoporosis Study, found that the cluster for a diet high in fruit, vegetables, and cereals had significantly greater BMD at all 3 hip sites and in the radius in elderly men but not in elderly women, whereas a cluster high in candy had significantly lower BMD in both men and women. Direct comparison between the results of our study and these

other studies is difficult because they are derived by using different analytic methods (ie, factor or cluster analysis) and in populations with different age ranges and genetic and cultural make-ups, who may have the specific (customary) dietary and lifestyle patterns of Western and Asian countries. Therefore, the results should be interpreted with caution.

Diets high in animal meat intakes and low in fruit and vegetable intakes—typical diets in industrialized countries—have a negative effect on bone health by increasing calcium excretion and bone resorption (28). In addition, acidosis may inhibit osteoblast function and increase osteoclast activity, which limits bone formation and increasing bone loss (29). However, high intakes of dietary potassium and magnesium, along with other nutrients associated with intakes of fruit and vegetables, have been suggested to promote an alkaline environment by reducing the potential renal acid load and net endogenous acid production (30, 31). In a previous study, New et al (4) and Macdonald et al (7) found that the intakes of several nutrients related to fruit and vegetables were positively correlated with BMD and negatively correlated with bone loss in premenopausal women (4, 7). In addition, a previous cross-sectional study showed a correlation between high intakes of magnesium, potassium, and fruit and vegetables (per serving) and BMD in both elderly men and



TABLE 4

Sample characteristics for the lowest and highest quintiles (Q) of 4 dietary patterns identified for 219 premenopausal women participating in the Japanese Multi-centered Environmental Toxicant Study¹

	Healthy		Japanese traditional		Western		Beverage and meats	
	Q1	Q5	Q1	Q5	Q1	Q5	Q1	Q5
Age (y)	45.3 ± 3.7 ²	47.3 ± 3.7 ²	45.8 ± 4.2	46.2 ± 3.6	47.2 ± 4.0	45.6 ± 3.3 ⁴	47.2 ± 3.8	45.8 ± 3.7
Grasping power (kg)	29.5 ± 4.0	27.5 ± 4.0 ⁴	30.0 ± 5.0	28.8 ± 5.0	28.5 ± 4.4	28.9 ± 4.1	29.4 ± 5.0	28.8 ± 4.5
Forearm bone mineral density (g/cm ²)	0.482 ± 0.054	0.495 ± 0.052	0.496 ± 0.058	0.495 ± 0.048	0.499 ± 0.055	0.482 ± 0.059	0.479 ± 0.061	0.496 ± 0.051
Forearm bone mineral mass (g)	3.19 ± 0.51	3.28 ± 0.44	3.29 ± 0.48	3.18 ± 0.50	3.34 ± 0.48	3.17 ± 0.46	3.13 ± 0.48	3.29 ± 0.45
Age at menarche (y)	12.9 ± 1.3	13.1 ± 1.2	13.0 ± 1.2	13.2 ± 1.3	12.8 ± 1.1	13.0 ± 1.2	13.2 ± 1.3	12.9 ± 1.2
Parity (n)	2.5 ± 1.0	2.4 ± 0.8	2.4 ± 0.7	2.7 ± 0.9	2.4 ± 0.9	2.5 ± 0.8	2.5 ± 1.1	2.5 ± 0.9
BMI (kg/m ²)	24.6 ± 3.6	24.0 ± 3.3	24.3 ± 3.4	23.7 ± 3.1	23.8 ± 4.1	24.0 ± 3.5	23.9 ± 3.6	24.5 ± 3.0
< 18.5 [n (%)]	2 (3.5)	2 (3.5)	1 (1.7)	2 (3.5)	1 (1.7)	2 (3.5)	3 (5.2)	0 (0)
18.5–24.9 [n (%)]	33 (56.9)	34 (58.6)	37 (63.8)	39 (67.2)	37 (63.8)	36 (62.1)	36 (62.1)	33 (56.9)
≥ 25.0 [n (%)]	23 (39.7)	22 (37.9)	20 (34.5)	17 (29.3)	20 (34.5)	20 (34.5)	19 (32.8)	25 (43.1)
Smoking status [n (%)]								
Current	1 (1.7)	3 (5.2)	2 (3.5)	2 (3.5)	3 (5.2)	2 (3.5)	1 (1.7)	4 (6.9)
Former	2 (3.5)	0 (0)	1 (1.7)	0 (0)	1 (1.7)	1 (1.7)	1 (1.7)	2 (3.5)
Never	55 (94.8)	55 (94.8)	55 (94.8)	56 (96.7)	54 (93.1)	55 (94.8)	56 (96.6)	52 (89.7)
Calcium supplement use [n (%)]	2 (3.5)	4 (6.9)	2 (3.5)	4 (6.9)	1 (1.7)	6 (10.3) ⁵	3 (5.2)	3 (5.2)
Multivitamin supplement use [n (%)]	3 (5.2)	4 (6.9)	5 (8.6)	2 (3.5) ⁵	3 (5.2)	4 (6.9)	2 (3.5)	2 (3.5)
History of fracture [n (%)]	8 (13.8)	3 (5.3)	8 (14.0)	4 (6.9)	3 (5.2)	7 (12.3)	7 (12.1)	4 (6.9)
Hormone replacement therapy [n (%)]	0 (0)	1 (1.7)	0 (0)	0 (0)	1 (1.7)	0 (0)	1 (1.7)	0 (0)

¹ The factors were standardized continuous variables, and each subject had a score for each factor. $n = 58$ in Q1, Q2, Q4, and Q5 and 59 in Q3.

² $\bar{x} \pm SD$ (all such values).

^{3,4} Test for linearity across quintiles of factors: ³ $P < 0.001$, ⁴ $P < 0.05$.

⁵ Significant difference between quintiles in all categories, $P < 0.01$ (chi-square test).

women (3). In accordance with these previous findings, the Western pattern identified in the current study is negatively associated with BMD; however, the association was not significant ($\beta = -0.005$, $P = 0.08$). In contrast, the Healthy pattern, which was highly and positively correlated with potassium, magnesium, calcium, vitamin C, vitamin D, and vitamin K, also was positively correlated with BMD ($\beta = 0.006$, $P = 0.048$).

The current study has several limitations. First, the DHQ assessed dietary habits only in the previous month, which was too short a time for the examination of a nutrient–bone mass association. Therefore, as in our previous report, we included only those subjects who had maintained stable dietary habits for ≥ 3 y

(6). Second, the classification of menopausal status was self-reported according to 3 categories (regular, irregular, or no menstrual cycle). We did not ask the irregularly menstruating or nonmenstruating women about the length of time since their last menses. Therefore, given its clear effect on bone metabolism, we also considered age in the definition of menstrual status. Moreover, because the BMD of the perimenopausal women showed no decrease and did not differ significantly from that of the premenopausal women (0.492 and 0.486 g/cm², respectively; $P = 0.14$), we evaluated women with regular and irregular cycles together as premenopausal women. Third, 4 of the 5 selected districts were cadmium-polluted areas, in which low-to-moderate cadmium contamination of rice has been detected.

TABLE 5

Partial Pearson correlation coefficients between each of 4 dietary patterns and bone mineral density and daily nutrient intakes for 291 premenopausal Japanese farmwomen who participated in the Japanese Multi-centered Environmental Toxicant Study¹

	Factor 1: Healthy	Factor 2: Japanese traditional	Factor 3: Western	Factor 4: Beverage and meats
Forearm bone mineral density (g/cm ²)	0.05	0.01	-0.08	0.08
Nutrient intakes				
Carbohydrate (% of energy)	-0.39	0.20	-0.55	0.06
Protein (% of energy)	0.65	-0.01	0.18	-0.10
Fat (% of energy)	0.25	-0.22	0.54	-0.03
Potassium (mg/d)	0.82	0.14	0.05	0.19
Magnesium (mg/d)	0.69	0.22	0.00	0.02
Calcium (mg/d)	0.51	0.07	-0.07	0.12
Phosphorus (mg/d)	0.70	0.09	0.10	0.06
Vitamin C (mg/d)	0.51	0.11	-0.07	-0.03
Vitamin D (μ g/d)	0.53	-0.01	-0.02	-0.26
Vitamin K (μ g/d)	0.48	0.31	-0.03	-0.04
Isoflavone (mg/d)	0.28	0.49	-0.08	-0.21
Alcohol (g/d)	0.22	-0.15	0.19	-0.01

¹ All nutrients were energy-adjusted by using the residual method. All partial correlation coefficients were adjusted for age. A partial correlation coefficient of >0.2 or <-0.2 was considered significant.



TABLE 6

Multivariate-adjusted bone mineral density by quintile (Q) of 4 dietary patterns among 291 premenopausal women participating in the Japanese Multi-centered Environmental Toxicant Study¹

Dietary pattern	Q1 (n = 58)	Q2 (n = 58)	Q3 (n = 59)	Q4 (n = 58)	Q5 (n = 58)	P for trend
Factor 1: Healthy						
Model 1	0.476 ± 0.006 ²	0.480 ± 0.006	0.504 ± 0.006	0.491 ± 0.006	0.497 ± 0.006	0.11
Model 2	0.476 ± 0.006	0.479 ± 0.006	0.503 ± 0.006 ¹	0.492 ± 0.006	0.498 ± 0.006 ⁴	<0.05
Model 3	0.476 ± 0.006	0.479 ± 0.006	0.504 ± 0.006 ³	0.492 ± 0.006	0.498 ± 0.006 ⁴	<0.05
Factor 2: Japanese traditional						
Model 1	0.491 ± 0.006	0.490 ± 0.006	0.483 ± 0.006	0.488 ± 0.006	0.495 ± 0.006	0.58
Model 2	0.493 ± 0.007	0.490 ± 0.006	0.485 ± 0.006	0.486 ± 0.006	0.495 ± 0.006	0.95
Model 3	0.493 ± 0.007	0.490 ± 0.006	0.485 ± 0.006	0.486 ± 0.007	0.495 ± 0.007	0.92
Factor 3: Western						
Model 1	0.500 ± 0.006	0.484 ± 0.006	0.492 ± 0.006	0.490 ± 0.006	0.480 ± 0.006	0.06
Model 2	0.501 ± 0.006	0.484 ± 0.006	0.492 ± 0.006	0.491 ± 0.006	0.482 ± 0.006	0.08
Model 3	0.501 ± 0.006	0.484 ± 0.006	0.492 ± 0.006	0.491 ± 0.006	0.482 ± 0.007	0.08
Factor 4: Beverage and meats						
Model 1	0.477 ± 0.006	0.494 ± 0.006	0.483 ± 0.006	0.501 ± 0.006	0.492 ± 0.006	0.31
Model 2	0.478 ± 0.006	0.495 ± 0.006	0.484 ± 0.006	0.501 ± 0.006	0.492 ± 0.006	0.35
Model 3	0.478 ± 0.006	0.495 ± 0.006	0.484 ± 0.006	0.501 ± 0.006	0.492 ± 0.006	0.34

¹ Model 1: multivariate models were adjusted for age, BMI (kg/m²), grasping power, and current smoking. Model 2: further adjusted for fracture history, the use of hormone replacement therapy, age at menarche, and parity. Model 3: further adjusted for the use of calcium and multivitamin supplements.


² $\bar{x} \pm SE$ (all such values).

^{3,4} Significantly different from Q1: ³P < 0.01, ⁴P < 0.05.

However, BMD was not related to urinary cadmium excretion in these subjects ($r = 0.02$, $P = 0.72$), and we previously reported that dietary cadmium exposure did not affect BMD in the premenopausal (41–48 y), perimenopausal (49–55 y), and even postmenopausal (56–75 y) women after adjustment for possible confounders (18). Fourth, the validity and reproducibility of the dietary patterns identified in the current study are unknown. Methodologic studies that examine the validity and reproducibility of the dietary factor analysis used in the current study and that establish the appropriate statistical procedures may have improved the current results. Undoubtedly, such studies may be conducted in the future to find more appropriate dietary factors to represent the current diversity of Japanese diets. In fact, the identified dietary factors in the current study accounted for only 29.7% of the variance in food intake in Japan. Finally, our sample size was comparatively small, which may have attenuated our ability to detect significant differences in BMD.

The principal components method itself also has limitations that stem from several subjective or arbitrary decisions that investigators must make. These decisions may have some effect on both the results and their interpretation (32). Therefore, the current study attempted to replicate dietary patterns reported in other epidemiologic studies by using similar steps in the subjective decision-making process. Moreover, we repeated the same analyses with varied numbers of factors and randomly divided the sample into 2 groups to examine whether these subjective choices affected the reproducibility of our findings. The results showed closely similar dietary patterns (data not shown). Our decision to retain 4 factors was based on eigenvalues, scree plots, and interpretability; however, it should be noted that >2 meaningful dietary patterns must exist in nature, as proposed by Newby (33). In addition, the dietary patterns defined in the current study were not established a priori but were based on actual data. The Western pattern in our study was similar to patterns labeled "Western" among Japanese (34), US (11, 35) and Swedish (36) populations. The Healthy pattern was also somewhat

similar to the Healthy and Prudent (13, 35) patterns observed across different populations. Even though we observed similar patterns, it should be noted that the results of dietary pattern analysis depend on the population and may differ according to the geographic area, race, and culture of the population. In the current study, we identified a Japanese traditional pattern, characterized by high consumption of rice, miso soup, and soy products, that was quite different from the Western pattern. This pattern was comparable to the rice/snack and traditional pattern seen in a previous Japanese study (34, 37).

In conclusion, among Japanese premenopausal women, dietary patterns were associated with BMD. A diet with high intakes of green vegetables, fruits, fish and shellfish and low intakes of meat and processed meat may contribute to the maintenance of BMD. Our data suggest dietary recommendations for preventing bone loss in premenopausal women; however, further studies in various populations following different dietary patterns are required to confirm these results. 

HO carried out the data analysis and wrote the manuscript. SS was involved in the design of the dietary study and assisted in manuscript preparation. HH and EO were responsible for the study design, data collection, and data management. KM and YH were involved in data collection. KMK provided statistical programming support. FK was responsible for the study design, data collection, and the overall management. All the authors provided suggestions during the preparation of the manuscript and approved the final version submitted for publication. None of the authors had any personal or financial conflict of interest.

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Dietary glycemic index and load in relation to metabolic risk factors in Japanese female farmers with traditional dietary habits¹⁻³

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ABSTRACT

Background: Little is known about the relation of dietary glycemic index (GI) and glycemic load (GL) to metabolic risk factors, particularly in non-Western populations.

Objective: We examined the cross-sectional associations between dietary GI and GL and several metabolic risk factors in healthy Japanese women with traditional dietary habits.

Design: The subjects were 1354 Japanese female farmers aged 20–78 y from 5 regions of Japan. Dietary GI and GL were assessed with a self-administered diet-history questionnaire. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Fasting blood samples were collected for biochemical measurements.

Results: The mean dietary GI was 67, and the mean dietary GL (/1000 kcal) was 88 (GI for glucose = 100). White rice (GI = 77) was the major contributor to dietary GI and GL (58.5%). After adjustment for potential dietary and nondietary confounding factors, dietary GI was positively correlated with BMI ($n = 1354$; P for trend = 0.017), fasting triacylglycerol ($n = 1349$; P for trend = 0.001), fasting glucose ($n = 764$; P for trend = 0.022), and glycated hemoglobin ($n = 845$; P for trend = 0.038). Dietary GL was independently negatively correlated with HDL cholesterol ($n = 1354$; P for trend = 0.004) and positively correlated with fasting triacylglycerol (P for trend = 0.047) and fasting glucose (P for trend = 0.012).

Conclusions: Both dietary GI and GL are independently correlated with several metabolic risk factors in subjects whose dietary GI and GL were primarily determined on the basis of the GI of white rice. *Am J Clin Nutr* 2006;83:1161–9.

KEY WORDS Glycemic index, glycemic load, white rice, body mass index, triacylglycerol, glucose, glycated hemoglobin, HDL cholesterol, Japanese women, epidemiology, Japanese Multi-centered Environmental Toxicants Study, JMETS

INTRODUCTION

Dietary carbohydrates are typically categorized into simple sugars and complex carbohydrates on the basis of their degree of polymerization. Their effects on health, however, may be better categorized according to their physiologic effects, specifically their ability to raise blood glucose (1), because the blood glucose response varies substantially among different carbohydrate-containing foods and cannot be predicted by their chemical composition (2). This varied glycemic response is quantified according to the glycemic index (GI), which is a measure of how much

each carbohydrate-containing food raises blood glucose compared with a standard food of either glucose or white bread (per 50 g available carbohydrate) (3). In consideration of the amounts of carbohydrate-containing foods and total dietary carbohydrate, the concept of glycemic load (GL: GI \times available carbohydrate content) has also been proposed (4, 5).

Recent results from a limited number of observational studies have suggested that diets with a low GI, a low GL, or both have a beneficial effect on several metabolic risk factors for cardiovascular disease and type 2 diabetes, such as body mass index (BMI; in kg/m^2) (6), HDL cholesterol (7–11), triacylglycerol (9, 10, 12), and glycated hemoglobin (Hb A_{1c}) (12, 13). However, almost all studies of dietary GI or dietary GL and metabolic risk factors have been conducted in Western countries, whereas, to our knowledge, only one small study (10) was carried out in Asian countries, including Japan.

For Japanese people, rice is the food that contributes most to total carbohydrate and energy intake (43% and 29%, respectively), which is a characteristic seldom observed in Western people (14). Therefore, a different correlation of dietary GI or dietary GL and metabolic risk factors may exist between Western and Japanese populations. Additionally, whereas cardiovascular disease is the second leading cause of all death in Japan (15), the number of Japanese people with type 2 diabetes is estimated to be no fewer than 6.8 million (16); thus, as is the case in Western people, these are serious health problems in Japan. Consequently, we examined the cross-sectional associations between dietary GI and GL and several metabolic risk factors for cardiovascular disease and type 2 diabetes, including BMI, fasting

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serum triacylglycerol, fasting plasma glucose, Hb A_{1c}, and serum total, HDL, and LDL cholesterol in a group of apparently healthy Japanese women.

SUBJECTS AND METHODS

Subjects

The subjects in the present study were participants in the Japanese Multi-centered Environmental Toxicants Study (JMETS), the main purpose of which was to identify the threshold concentration in the dose-response relation of cadmium renal dysfunction (17, 18). For this purpose, the JMETS was conducted in female farmers in 4 moderately cadmium-polluted areas and 1 non-cadmium-polluted area in Japan; however, no difference in the effects of environmental exposure to cadmium was observed between the 4 polluted areas and 1 nonpolluted area, at least regarding renal function and bone density (17, 18). Thus, the study did not identify evidence that environmental exposure to cadmium, at the level found in the 4 polluted areas, has an adverse affect on health. The 5 areas surveyed consist of rural agricultural communities with inhabitants who remain in the community even after marriage. Thus, most of the farmers in these areas are assumed to have maintained traditional Japanese dietary patterns, consuming their own crops, including rice, for decades. During the winters of 2000 and 2001, female farmers in each area were recruited through the local Agricultural Cooperative to participate in a medical examination organized for the JMETS. One week before the examination, group orientations were held for the study participants, at which the study purpose and protocol were explained and written informed consent was obtained from each participant. In addition, participants were instructed on how to complete questionnaires regarding diet and other lifestyle factors and were asked to bring them to the examination. The protocol of the JMETS was approved by the ethical committee of Jichi Medical University. Additional details about the JMETS were reported elsewhere (17, 18).

A total of 1407 women aged 20–78 y completed both a medical examination and the lifestyle-related questionnaires. Subjects excluded from the present study were those with previously diagnosed diabetes ($n = 15$) or cardiovascular disease ($n = 18$), those with extremely low or high energy intakes (<600 or >4000 kcal/d; $n = 10$), and those with missing covariate information ($n = 4$). Furthermore, subjects with missing information regarding dependent variables, were excluded from the analysis of LDL cholesterol ($n = 6$), glucose ($n = 609$), and Hb A_{1c} ($n = 527$), and subjects who ate breakfast before blood was drawn were excluded from the analysis of fasting triacylglycerol and glucose ($n = 5$). Thus, the final sample was 1354 for BMI and serum total and HDL cholesterol, 1348 for serum LDL cholesterol, 1349 for fasting serum triacylglycerol, 764 for fasting plasma glucose, and 845 for Hb A_{1c}; however, some subjects were included in more than one exclusion category. Further exclusion of subjects with a diagnosis of hyperglycemia, dyslipidemia, hypercholesterolemia, or a combination thereof ($n = 24$ for BMI, cholesterol, and triacylglycerol and $n = 17$ for glucose and Hb A_{1c}) did not alter the findings of the present study; therefore, these subjects were included in the analyses.

Metabolic risk factors

At the medical examination site, each subject's weight (measured while wearing light clothes and no shoes) was measured

with a set of balance scales calibrated to 0.01 kg. Body height was also measured at the site. The BMI of each subject was calculated as weight (kg) divided by the square of height (m). Peripheral blood samples were obtained from subjects after an overnight fast. Blood was collected in evacuated tubes containing no additives, allowed to clot, and centrifuged at $3000 \times g$ for 10 min at room temperature to separate the serum. Blood samples for blood sugar measurement were collected in hydrogen fluoride-containing tubes. All of the following biochemical variables of the samples were assayed at Mitsubishi Kagaku Bio-Clinical Laboratories Inc (Itabashi, Tokyo, Japan) within 3 d of collection to avoid significant degradation. Total cholesterol, HDL cholesterol, and triacylglycerol were measured by enzymatic assay methods. Serum LDL-cholesterol concentrations were calculated by using the Friedewald equation (19) for subjects with fasting serum triacylglycerol concentrations <400 mg/dL. Hb A_{1c} was measured by latex agglutination-turbidimetric immunoassay. In-house quality-control procedures for all of the abovementioned assays were fulfilled at Mitsubishi Kagaku Bio-Clinical Laboratories Inc.

Dietary assessment

Dietary habits during the past month were assessed with a self-administered diet-history questionnaire (DHQ) (20–22), which was completed by each subject at home and was checked by ≥ 2 dietitians during the medical examination. The DHQ is a 16-page structured questionnaire that consists of the following 7 sections: general dietary behaviors, major cooking methods, consumption frequency and portion size of 6 alcoholic beverages, semiquantitative frequency of intake of 121 selected food and nonalcoholic beverage items, dietary supplements, consumption frequency and amount of 19 staple foods (rice, bread, noodles, and other wheat foods) and *miso* (fermented soybean paste) soup, and open-ended items for foods consumed regularly (≥ 1 time/wk) but not appearing in the DHQ. The food and beverage items and portion sizes in the DHQ were derived primarily from data in the National Nutrition Survey of Japan and several recipe books for Japanese dishes (20). Measures of dietary intake for 147 food and beverage items, energy, fat, total carbohydrate, alcohol, and dietary fiber were calculated by using an ad hoc computer algorithm developed for the DHQ, which was based on the Standard Tables of Food Composition in Japan (23). Information on dietary supplements and data from the open-ended questionnaire items were not used in the calculation of dietary intake. Detailed descriptions of the methods used for calculating dietary intake and the validity of the DHQ were published elsewhere (20–22). Pearson's correlation coefficients between the DHQ and 3-d dietary records were 0.48 for energy, 0.55 for fat, and 0.48 for total carbohydrate in 47 women (20). In addition, Pearson's correlation coefficients between the DHQ and 16-d dietary records were 0.79 for alcohol and 0.69 for dietary fiber in 92 women (S Sasaki, unpublished observations, 2004).

Calculation of dietary GI and GL

The GI of a food is defined as the 2-h incremental area under the blood glucose response curve after consumption of a food portion containing a specific amount (usually 50 g) of available carbohydrate, divided by the corresponding area after consumption of a portion of a reference food (usually glucose or white



bread) containing the same amount of available carbohydrate, and multiplied by 100 to be expressed as a percentage (24). We calculated dietary GI by multiplying the percentage contribution of each individual food to daily available carbohydrate intake by the food's GI value and summed these products. Available carbohydrate was calculated as total carbohydrate minus dietary fiber (24). We also calculated dietary GL by multiplying the dietary GI by the total amount of daily available carbohydrate intake (divided by 100).

To determine the GI value of each food for these calculations, each food item on the DHQ was directly matched to foods in the international table of GI (24), in several publications about the GI of Japanese foods (25–27), and in a recent article about the GI of potatoes (28). Glucose was used as the reference (GI for glucose = 100). The white bread–based GI values were transformed into glucose-based GI values by multiplying the white bread–based GI by 0.7, as in Western studies (24, 28), or by 0.73 [= 100/137 (white bread–based GI value of white bread/white bread–based GI value of glucose)] as in Japanese studies (27). The white rice–based GI values were transformed into glucose-based GI values by multiplying white rice–based GI by 0.82 [= 100/122 (white rice–based GI of white rice/white rice–based GI of glucose)] (25, 26). When more than one GI value was available, the mean GI values was used. Ten foods for which a GI value had not been determined were assigned a value according to the nearest comparable food, as follows: Chinese noodles were assigned the GI of instant noodles, Japanese-style pancakes were assigned the GI of pizza, jellies were assigned the GI of pudding, lotus roots were assigned the GI of carrots, vegetable juice was assigned the GI of tomato juice, curry and roux in stew were assigned the GI of white rice with curry, nutritional-supplement drinks were assigned the GI of sports drinks, nutritional supplement bars were assigned the GI of a sports bar, and ground fish-meat products and boiled-fish, shellfish, and seaweed in soy sauce were assigned the GI of fish fingers. Although alcoholic beverages contain little carbohydrate, large quantities of several alcoholic beverages, such as beer and sake, may raise glucose concentrations slightly; however, by definition, the GI is based on 50 g available carbohydrate. Thus, we ignored alcoholic beverages during the calculation of dietary GI and GL. Furthermore, foods with a very low available carbohydrate content were excluded because their GI values cannot be tested. The cutoff for exclusion of foods was set at 3.5 g available carbohydrate per serving (6). Of the total 147 food and beverage items included in the DHQ, 6 (4.1%) are alcoholic beverages, 8 (5.4%) contain no available carbohydrate, and 63 (42.9%) contain <3.5 g available carbohydrate per serving. The calculation of dietary GI and GL was thus based on the remaining 70 items with GI values ranging from 16 to 91. The GI value of each item is presented in **Table 1**. In the present study, the available carbohydrate content of these 70 items contributed to $94.0 \pm 2.5\%$ ($\bar{x} \pm \text{SD}$) of total available carbohydrate intake, which is comparable with previous studies (6, 10).

Other variables

Smoking status, menopausal status, dietary supplement use during the previous month, and rate of eating were self-reported in questionnaires. Body weight at age 20 y was also self-reported, and BMI at age 20 y was computed by dividing self-reported weight (kg) at age 20 y by the square of current measured height (m). In addition, the subjects reported the average times per week

spent on 13 activities such as sleeping, household-related activities, leisure-time sporting activities, and leisure-time sedentary activities. The reported number of hours spent on each activity (per week) was divided by 7 to obtain the mean number of hours per day. For subjects whose recorded total hours per day were < or >24 h, the total number of hours spent daily were proportionately increased or decreased to equal 24. Each activity was assigned a metabolic equivalent (MET) value from a previously published table (29, 30). The mean number of hours spent per day on each activity was multiplied by the MET value of that activity, and all MET-hour products were summed to give a total MET-hour score for the day. Total energy expenditure was calculated by multiplying the total MET-hour score by body weight. Physical activity level was calculated by dividing total energy expenditure by basal metabolic rate, which was estimated as standard values of basal metabolic rate for Japanese women multiplied by body weight (31).

Statistical analysis

Dietary GI and GL were examined in relation to the 7 metabolic risk factors: BMI; serum total, HDL, and LDL cholesterol; fasting serum triacylglycerol; fasting plasma glucose; and Hb A_{1c}. We used crude values for dietary GI and energy-adjusted values for dietary GL (/1000 kcal) because, by definition, dietary GI is a measure of carbohydrate quality, not quantity, whereas dietary GL is a measure of the combination of carbohydrate quality and quantity. The mean ($\pm \text{SE}$) values for these metabolic factors were calculated according to quintiles of dietary GI and GL after multivariate adjustment for potential confounding variables. Confounding variables included residential area (5 categories), age (≤ 39 , 40–49, 50–59, 60–69, and ≥ 70 y), menopausal status (premenopausal or postmenopausal), current smoking (no or yes), dietary supplement use (no or yes), rate of eating (fast, medium, or slow), physical activity level (quintiles), energy intake (quintiles), percentage of energy as fat (quintiles), alcohol intake (nondrinkers, >0 to <1% of energy, or $\geq 1\%$ of energy), and energy-adjusted intake (g/1000 kcal) of dietary fiber (quintiles). In the analyses, except for the analysis of BMI, current BMI (quintiles) and BMI at age 20 y (quintiles) were also included as confounding variables. Linear trends with increasing levels of dietary GI and GL were tested by assigning each participant the median value for the category and modeling this value as a continuous variable. All statistical analyses were carried out by using SAS statistical software (version 8.2; SAS Institute Inc, Cary, NC). All reported *P* values are 2-tailed, and a *P* value <0.05 was considered statistically significant.

RESULTS

Basic characteristics of the 1354 subjects are shown in **Table 2**. The mean intakes of protein, fat, and carbohydrate were 14.0%, 25.3%, and 59.0% of energy, respectively. The mean dietary GI was 66.7 and the mean dietary GL was 88.0 (/1000 kcal; crude mean = 167.7). White rice was the major contributor to dietary GI and GL (58.5%), followed by confectioneries (10.6%), fruit (6.7%), sugars (5.5%), bread (4.3%), noodles (3.4%), other rice (3.2%), and potatoes (2.6%). Potential confounding variables of the 1354 subjects are shown in **Table 3** according to quintiles of dietary GI and GL. Fewer women in the higher quintiles of dietary GI used dietary supplements and more were nondrinkers of alcohol. Women in the higher quintiles of



TABLE 1

Glycemic index (GI) value of each food and beverage item used in the present study¹

Food and beverage item	GI
White rice	77
White rice with barley	67
White rice with germs	66
50% Polished rice	66
70% Polished rice	70
Brown rice	55
Soba (buckwheat noodles) and udon (Japanese wheat noodles)	47
Instant noodles	47
Chinese noodles	47
Spaghetti	46
White bread	74
Cake bread	62
Butter roll	59
Croissant	67
Pizza	51
Japanese-style pancake	51
Pancake	67
Cornflakes	81
Potato chips	54
French fries	70
Other potatoes	78
Sweet potatoes, yams, and taros	51
Jam and marmalade	51
Sugar for coffee and tea	68
Sugar used during cooking	68
Rice crackers	91
Snacks made from wheat flour	63
Japanese sweets with azuki beans	49
Japanese sweets without azuki beans	68
Cakes	46
Cookies and biscuits	59
Chocolates	43
Candies, caramels, and chewing gum	74
Jellies	44
Doughnuts	76
Boiled beans	16
Raisins	64
Canned fruits	49
Fruit juice (100%)	47
Other fruit juice	47
Tomato juice	38
Oranges	39
Bananas	51
Apples	37
Strawberries	40
Grapes	50
Peaches	42
Pears	38
Persimmons	50
Kiwi fruit	53
Melons	42
Watermelons	58
Pumpkins	75
Lotus roots	47
Vegetable juice	38
Curry and roux in stew	67
Cocoa	51
Lactic acid bacteria beverages	42
Soft drinks	61
Nutritional supplement drinks	66

(Continued)

TABLE 1 (Continued)

Food and beverage item	GI
Ground fish meat products	38
Boiled fish, shellfish, and seaweed in soy sauce	38
Full-fat milk	27
Low-fat milk	30
Skim milk	32
Yogurt (sweetened)	24
Yogurt (nonsweetened)	36
Yogurt (moderately sweetened)	30
Ice cream	61
Nutritional supplement bars	48

¹ GI of glucose = 100. These 70 food and beverage items from the 147 items in the diet-history questionnaire were used for the calculation of GI. The remaining 77 items not used consisted of 6 alcoholic beverages (beer, sake, shochu, shochu highball, whiskey, and wine), 8 items containing no available carbohydrate (oils used during cooking, table salt, salt used during cooking, sugarless soft drinks, chicken, Chinese soup, noodle soup, and water), and 63 items containing <3.5 g available carbohydrate per serving [peanuts, other nuts, konnyaku, butter, margarine, mayonnaise, salad dressing, tofu, tofu products, natto, miso as seasoning, miso in miso soup, carrots, tomatoes, green peppers, broccoli, green leafy vegetables, salted pickled plums (umeboshi), other salted pickles, cabbage, cucumbers, lettuce, Chinese cabbage, bean sprouts, radishes, onions, cauliflower, eggplants, burdocks, mushrooms, wakame seaweed, laver, ketchup, nonoil salad dressing, soy sauce, green tea and oolong tea, tea, coffee, dried fish, small fish with bones, canned tuna, eel, white meat fish, blue-back fish, red meat fish, shrimp, squid and octopus, oysters, other shellfish, fish eggs, salted fish intestines, ground beef and pork, pork, beef, liver, ham and sausages, bacon, eggs (heno and quail), cheese, cottage cheese, coffee cream, corn soup, and artificial sweeteners].

dietary GI had lower mean energy, fat, and dietary fiber intakes. In addition, women in the higher quintiles of dietary GL had higher mean values for age and physical activity level and lower mean energy, fat, and dietary fiber intakes. Fewer women in the higher quintiles of dietary GL were premenopausal, current smokers, and dietary supplement users and more were nondrinkers of alcohol. Similar patterns were observed for potential confounding variables according to quintiles of dietary GI and GL among the subjects included in the analyses of serum LDL cholesterol ($n = 1348$), fasting serum triacylglycerol ($n = 1349$), fasting plasma glucose ($n = 764$), and Hb A_{1c} ($n = 845$) (data not shown).

Multivariate-adjusted mean values for metabolic risk factors across quintile categories of dietary GI and GL are shown in Table 4. After adjustment for potential confounding variables, dietary GI was significantly positively correlated with BMI (mean difference between the lowest and highest quintiles = 0.7; P for trend = 0.017), fasting serum triacylglycerol (mean difference = 16.0 mg/dL; P for trend = 0.001), fasting plasma glucose (mean difference = 6.4 mg/dL; P for trend = 0.022), and Hb A_{1c} (mean difference = 0.2%; P for trend = 0.038). No correlation was observed between dietary GI and serum concentrations of total, HDL, and LDL cholesterol.

In contrast, after control for potential confounding variables, dietary GL was significantly negatively correlated with serum HDL cholesterol (mean difference = -6.4 mg/dL; P for trend = 0.004) and positively correlated with fasting serum triacylglycerol (mean difference = 14.4 mg/dL; P for trend = 0.047) and fasting plasma glucose (mean difference = 12.5 mg/dL; P for trend = 0.012). Other metabolic risk factors examined, including



TABLE 2
Basic characteristics of the 1354 Japanese women

	Value
Age (y)	55.3 ± 10.3 ¹
≤39 y	69 (5.1) ²
40–49 y	319 (23.6)
50–59 y	446 (32.9)
60–69 y	440 (32.5)
≥70 y	80 (5.9)
Body height (cm)	152.9 ± 5.9
Body weight (kg)	56.1 ± 8.3
Current BMI (kg/m ²)	24.0 ± 3.3
BMI at age 20 y (kg/m ²)	21.7 ± 2.6
Menopausal status	
Premenopausal	427 (31.5)
Postmenopausal	927 (68.5)
Current smoking	
No	1309 (96.7)
Yes	45 (3.3)
Dietary supplement use	
No	954 (70.5)
Yes	400 (29.5)
Rate of eating	
Fast	480 (35.5)
Medium	644 (47.6)
Slow	230 (17.0)
Physical activity level	1.84 ± 0.28
Energy intake (kcal/d)	1944 ± 497
Protein intake (% of energy)	14.0 ± 2.2
Fat intake (% of energy)	25.3 ± 5.8
Carbohydrate intake (% of energy)	59.0 ± 7.1
Alcohol intake (% of energy)	0.8 ± 2.3
Nondrinkers	836 (61.7)
>0% to < 1% of energy	271 (20.0)
≥1% of energy	247 (18.2)
Dietary fiber intake (g/1000 kcal)	7.6 ± 2.1
Dietary glycemic index ³	66.7 ± 4.0
Dietary glycemic load (/1000 kcal) ³	88.0 ± 15.1

¹ \bar{x} ± SD (all such values).

² n; percentage in parentheses (all such values).

³ Glycemic index for glucose = 100.

BMI, serum concentrations of total and LDL cholesterol, and Hb A_{1c} were not significantly correlated with dietary GL. Adjustment for the percentage of energy from carbohydrate instead of the percentage of energy from fat did not change the results materially, which suggests that the observed correlations between dietary GI and GL and metabolic risk factors are independent of carbohydrate intake (data not shown).

DISCUSSION

Because only limited evidence is available regarding associations between dietary GI and GL and metabolic risk factors, particularly in Asian populations, we investigated these associations in the present cross-sectional study of healthy Japanese female farmers with traditional dietary habits. We found that dietary GI was positively associated with BMI, fasting serum triacylglycerol, fasting plasma glucose, and Hb A_{1c} after control for potentially confounding lifestyle and dietary factors. We also found that dietary GL was independently negatively associated with serum HDL cholesterol and positively associated with serum triacylglycerol and fasting plasma glucose.

Concerns have been expressed regarding the utility of the GI for mixed meals (32, 33). However, many researchers have shown that the GI of a mixed meal can be predicted consistently as the mean of the GI values of each of the component foods, weighted according to their relative contribution to carbohydrate intake (34–36). In reality, studies using standardized techniques have observed high correlation coefficients between observed and calculated GI values, ranging from 0.84 to 0.99 (34–36). Dietary GI and GL values in the present study were similar when compared with those in a previous Japanese study (67 compared with 64 for GI and 168 compared with 150 for GL) (10). However, the dietary GI and GL values observed in the present and previous (10) Japanese studies were considerably higher than the corresponding values in Western countries (48–60 for GI and 84–120 for GL) (4–6, 7–9, 37–40). This may have resulted from the differences in the major food contributors. Dietary GIs and GLs in Western populations are determined by a variety of food items, including potatoes (7–8%), breakfast cereals (4–7%), bread (5%), and rice (5%) (41–43). However, white rice (GI = 77) was the major contributor in the present and previous (10) Japanese studies, accounting for 59% of dietary GI and GL in the present study.

All self-reported dietary assessment methods are subject to measurement error and selective underestimation or overestimation of dietary intake (44). In the present study, however, we used a previously validated DHQ (20–22) to minimize data inaccuracy. Additionally, dietary GI and GL values calculated in the present study are believed to be relatively accurate because the major determinant of dietary GI and GL in the present study, rice (62%), is more accurately reported than are other foods on the DHQ because it is consumed regularly in relatively fixed amounts. Moreover, the same tendency was observed in a repeated analysis of subjects with a physiologically plausible energy intake, ie, subjects with a ratio of energy intake to basal metabolic rate of 1.2–2.5 (45)—≈78% of the subjects included in the main analysis (data not shown). Thus, we considered that the correlations observed in the present study reflect true associations, not spurious associations resulting from inaccurate dietary data.

In the present study, dietary GI was positively correlated with BMI. A 5-wk crossover, randomized, controlled trial conducted in overweight nondiabetic men with ad libitum dietary intakes also showed a significantly lower fat mass and a tendency for a higher fat-free mass, but not a lower body weight, after a low-GI diet than after a high-GI diet (46). In contrast, other ad libitum trials conducted in subjects with type 2 diabetes showed no significant differences in body weight change between high-GI and low-GI diets (47–49). However, in a 10-wk ad libitum, randomized, controlled trial conducted in healthy overweight women, decreases in body weight and fat mass were larger in a low-GI diet group than in a high-GI diet group, although these differences were not statistically significant (50). Moreover, as was shown in this study, a recent observational study also showed a positive association between dietary GI and BMI and no association between dietary GL and BMI (6).

Dietary GL has consistently been shown to be inversely correlated with HDL cholesterol in cross-sectional studies (8–11). In contrast, the correlation between dietary GI and HDL cholesterol is not consistent. An inverse correlation has been reported

