

Table 2. Daily intake of melatonin-contained vegetables and other nutrients at the baseline and at the end of study period, in the melatonin intervention and control groups

	Melatonin-contained vegetables supplemented (n = 46)				Control (n = 48)			
	Baseline		End of intervention		Baseline		End of intervention	
	Mean	Standard error of mean (SEM)	Mean	SEM	Mean	SEM	Mean	SEM
From the six vegetables								
Sweet corn (g)	2.5	1.0	65.7	7.1	2.6	0.8	0.4	0.2
Bitter melon (g)	8.7	2.9	84.5	8.6	9.3	4.1	0.3	0.3
Japanese radish sprout (g)	0.3	0.2	39.0	4.8	0.7	0.5	0.1	0.1
Garland chrysanthemum (g)	1.2	0.6	48.3	5.5	0.3	0.3	0.7	0.7
Shimeji mushroom (g)	3.0	0.7	36.7	4.7	3.7	1.0	0.1	0.1
Shiitake mushroom (g)	2.3	0.6	37.4	5.9	2.1	0.7	0.4	0.2
Total six vegetables intake (g)	18.1	3.2	311.6	24.2	18.8	4.6	2.1	0.9
Melatonin intake from the six vegetables (ng)	124.9	38.4	1288.0	118.1	132.8	54.7	5.3	3.8
All vegetable intake (g)	270.4	18.8	412.1	24.8	301.5	22.2	248.8	15.6
Nutrients intake from the total diet								
Energy (kcal)	1878	44	1892	54	1874	64	1846	62
Protein (g)	67.5	1.7	69.2	2.5	67.4	2.3	67.0	2.3
Fat (g)	59.4	2.1	59.9	2.8	57.9	2.9	55.8	2.9
Cholesterol (mg)	284	14	291	21	259	21	310	19
Carbohydrate (g)	257	7	264	7	263	10	259	11
Crude fiber (g)	14.7	0.6	21.1	1.2	16.2	0.8	14.5	0.7
Vitamin A (μ g)	463	30	688	55	609	65	463	31
Vitamin B1 (mg)	1.00	0.06	1.10	0.05	1.10	0.11	1.11	0.13
Vitamin B2 (mg)	1.50	0.15	1.57	0.08	1.48	0.20	1.50	0.16
Vitamin C (mg)	160.5	29.1	213.3	25.9	153.2	22.1	179.5	36.3
Vitamin D (μ g)	8.74	0.97	8.87	1.20	10.13	1.86	6.86	0.94
Vitamin E (mg)	7.4	0.3	12.7	3.3	7.9	0.4	7.2	0.4
Calcium (mg)	576	36	595	32	604	33	522	31
Iron (mg)	8.5	0.4	9.0	0.5	8.9	0.5	8.4	0.4
Folate (μ g)	331.19	16.40	523.67	29.04	338.29	17.83	346.41	17.51
Salt (g)	10.8	0.8	11.3	0.9	10.2	0.5	9.6	0.4
Alcohol (g)	4.2	0.8	3.7	0.8	2.8	0.7	3.1	1.0
Caffeine (g)	0.18	0.02	0.25	0.04	0.18	0.02	0.21	0.02
Mean bedtime before the urine collection days (2 days average)	23:22	0:05	23:28	0:07	23:26	0:06	23:19	0:07
Mean time of urine collection (2 days average)	6:07	0:06	6:25	0:08	5:50	0:05	6:18	0:07
Level of physical activities (metabolic equivalent/wk)	44.7	6.5	52.2	6.5	44.0	5.9	55.1	6.8

Table 3. Change in creatinine-adjusted urinary 6-sulfatoxymelatonin concentration by food intake group

	Melatonin-contained vegetables supplemented group (n = 46)			Control group (n = 48)			Difference in change between the groups
	Initial	Final	P^a	Initial	Final	P^a	P^b
Geometric mean ^c (ng/mg creatinine)	48.1	49.6	0.39	55.5	50.8	0.03	0.03
95% Confidence interval ^c	(40.4, 57.2)	(42.8, 57.3)		(48.7, 63.2)	(44.0, 58.7)		

^aThe paired *t*-test.^bThe two-sample *t*-test.^cObtained by taking antilog of log-transformed values.

Discussion

Increasing the consumption of vegetables that are high in melatonin for more than 2 months raised morning 6-sulfatoxymelatonin concentrations in urine compared with suppressing the intake of such vegetables. The finding

supports the results of our previous cross-sectional study, which implied an association between vegetable intake and melatonin concentrations in humans [23]. Several previous studies administered melatonin orally, in which the amount varied from 0.1 to 80 mg at a time, and reported the increased concentration of serum, plasma, or urinary

melatonin [31–35]. The amount of melatonin from the six vegetables in the current study was quite small compared with the amounts administered in these studies. However, it was reported that infusion of 10 µg of melatonin still increased serum melatonin concentrations about 40 times at 5 min among healthy male volunteers [36]. Had we used edible plants with higher levels of melatonin such as certain medical herbs [37], the results may have been more dramatic. Moreover, Reiter et al. have showed that with rats, blood melatonin levels increased substantially after they were fasted for 24 hr and then given exclusively a high melatonin-contained food [38]. Fasting or restricting vegetables to washout their possible effect before the intervention was not practiced among the participants of the current study. Still, our focus was on consumption of common vegetables for certain period of time in regular diets.

Although we randomly divided the subjects into two study groups, the initial mean value of urinary 6-sulfatoxymelatonin concentrations was somewhat higher among the subjects in the control group than among the subjects in the intervention group. Several baseline factors and characteristics appeared to be distributed unequally by study group, and this might have been associated with the observed difference in 6-sulfatoxymelatonin concentrations at the baseline. Total vegetable consumption was one such factor. At the baseline, it was estimated from the 3-day diet record that the daily consumption of the six vegetables was slightly different between the groups, and the total vegetable intake was larger in the control group than in the intervention group. Therefore, melatonin sourcing from total vegetable consumption may have contributed to the elevated urinary 6-sulfatoxymelatonin concentrations in the control group at the baseline. As information on melatonin contents of many other vegetables was unavailable, we were not able to estimate the degree of the effect of total vegetable intake on the urinary 6-sulfatoxymelatonin concentration.

Other such factors were regular alcohol consumption and parity status. The prevalence of non-alcohol drinkers was about two times higher among the subjects in the control group than that among the subjects in the intervention group. We observed that the baseline 6-sulfatoxymelatonin concentrations were negatively associated with baseline alcohol intake by using the linear regression model ($P = 0.02$). Inverse associations of human urinary melatonin concentrations with both temporal and regular alcohol intake were previously reported in several studies [39–41], but not in all [42, 43]. Likewise the proportion of parous women was significantly higher in the control group than in the intervention group. A few previous studies assessed the relationship between the parity status and melatonin concentration and some of them reported high melatonin concentrations among parous women [16, 44, 45]. Other potential factors [39, 44, 46–49], such as the influence of bedtime, body mass index, smoking status, concentration of physical activity, aspirin use or coffee consumption, on baseline urinary 6-sulfatoxymelatonin concentrations may be eliminated as the values of these characteristics were not significantly different between the study groups at the baseline.

The current study showed that urinary 6-sulfatoxymelatonin concentrations were reduced in the control group. Besides the change in the consumption of the vegetables, seasonal changes during the study period (end of summer to early winter) or changes in the length of the days may have influenced on the 6-sulfatoxymelatonin concentrations in both groups, which may partially explain the decrease in melatonin concentrations at the end of the period. Using raw data from our previous cross-sectional study [23], we observed that each additional hour of daylight was associated with a 16.4% higher 6-sulfatoxymelatonin concentration in morning urine. Also, it was reported in a previously conducted nested case-control study of breast cancer that among 353 female control subjects, concentrations of 6-sulfatoxymelatonin in urine samples collected in winter was 11.4% lower than the concentrations in the samples collected in fall [16].

In summary, the daily consumption of a high amount of selected vegetables increased 6-sulfatoxymelatonin concentrations in first-void morning urine in approximately a 2-month period. To our knowledge, this is the first intervention study of its kind. Although the relationship between urinary melatonin concentrations and the risk for cancer is not yet clearly established in humans, the results of the current study raise the possibility that vegetable intake in the regular diet has an influence on melatonin concentrations, which may lead the beneficial effect in terms of reduction and prevention of cancer and cardiovascular disease.

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Vegetable consumption and urinary melatonin concentration

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Original Article

Rationality/Anti-emotionality Personality and Dietary Habits in a Community Population in Japan

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ABSTRACT

Background: There are no strong and consistent predictors of dietary habits although some associations have been shown with psychological factors. The purpose of the present study was to examine the relationships between the rationality and anti-emotionality (R/A) personality and dietary consumption in a Japanese community.

Methods: The Takayama study is a community-based cohort study on diet and cancer in Gifu, Japan, and was initiated on September 1, 1992. Cross-sectional analyses were conducted on dietary and lifestyle data. The consumption of 169 food and beverage items was measured along with portion size by using a food frequency questionnaire. Questions regarding the R/A-personality scale and lifestyle habits were included in the questionnaire. The participants were 28077 adults (13082 males and 14995 females) aged 35 years and over.

Results: Both males and females with high R/A-personality scores (i.e., high degree of rational thought and emotional repression) consumed more soy products, green and yellow vegetables, other vegetables, and seaweed than the other participants. Males with high R/A-personality scores drank fewer alcoholic beverages, and females with high scores were found to snack less on sweet and salty foods than the other participants. Males with high R/A-personality scores showed higher consumption of meat and dairy products, and females with high scores showed higher consumption of fish, shellfish, and eggs than those with low R/A-personality scores.

Conclusion: The R/A-personality scale may differentiate dietary habits in males and females in a Japanese community.

Key words: Personality, Rationality, Repressed Emotion, Dietary Habits, Lifestyle

INTRODUCTION

Dietary habits are related to nutritional intake and are the predictors of several diseases and health conditions, such as obesity, cardiovascular disease, cancer, and osteoporosis.¹⁻³ Research on the relationship between diet and disease has frequently yielded inconclusive results due to small sample sizes and the corresponding lack of diversity with regard to previous diet and lifestyle data.⁴ Nevertheless, some general relationships between diet and disease are currently known, including those between selenium, carotenoids, and cancer; vitamin E, ω -3 fatty acids, and coronary heart disease; dietary fat and obesity; dietary sodium and hypertension; and alcohol intake and stroke.⁵⁻¹¹ To prevent these chronic diseases, modification of dietary habits is often required, but this may be hindered by an individual's food preferences, health consciousness, and other psychological factors.¹² There are

no strong and consistent predictors of dietary habits although factors such as sex, age, ethnicity, weight, mental stress, and personality characteristics show associations with dietary habits.¹³⁻¹⁶

The rationality and anti-emotionality (R/A) personality (blocked emotion and conscious suppression of emotion during interpersonal communication) is considered a cancer-prone personality.¹⁷⁻²¹ In contrast, results from Japanese studies have demonstrated an inverse association with chronic diseases, indicating that higher scores on the R/A-personality scale were associated with lower prevalence of stroke in males and females and lower prevalence of diabetes in males²² and with a lower risk of death from all causes in females.²³ Thus, conflicting data exist regarding the relationship between personality traits and mortality in Western and Japanese societies. In addition, several Western and Japanese studies have reported that such personality traits

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are not associated with cancer risk.²⁴⁻²⁷ Thus, not only are the findings regarding the relationships between personality traits and chronic diseases inconsistent, but there are only a few studies that have examined whether personality traits are related to dietary habits, which are believed to be one of the risk factors for chronic diseases.

The purpose of the present study was to examine the relationships between R/A personality and diet consumption in the residents of a Japanese community. It was predicted that individuals who scored high on the R/A-personality scale would have more health-oriented dietary habits than those who scored low on this scale. For example, it was predicted that individuals with high scores would show higher consumption of vegetables and fruits and lower consumption of alcoholic beverages than those who had low scores.

METHODS

Participants

The Takayama study is a community-based cohort study on diet and cancer in Gifu, Japan, and was initiated on September 1, 1992. Questionnaires were distributed to all the 36990 residents of Takayama City, Gifu, Japan who were aged 35 years and over. The final response rate was 90.3% (33399/36990). After eliminating participants for whom data regarding sex, age, R/A-personality scale, medical history, and/or smoking habits were missing, questionnaires from 13082 males and 14995 females (mean ages: 54.2 and 55.1 years, respectively) were obtained. The participants classified according to their individual medical histories are as follows: 163 males and 463 females with cancer, 802 males and 758 females with cardiovascular diseases, 2679 males and 2775 females with hypertension, 824 males and 441 females with diabetes mellitus, 3149 males and 2059 females with internal diseases, and 910 males and 1427 females with allergies.

The participants were divided into 3 groups based on the R/A-personality score tertile that was used in a study by Hirokawa et al.²³ The 0-5 group (33.7% males and 26.6% females) comprised the lower level; the 6-8 group (37.7% males and 39.2% females) comprised the middle level; and the 9-11 group (28.6% males and 34.2% females) comprised the higher level. The distribution of age, body mass index (BMI), weight, physical activity, marital status, years of education, smoking habits, and medical history by sex and the R/A-personality scores are shown in Table 1.

Questionnaires

The R/A-personality scale consists of 11 items (Appendix). The scale was developed by Grossarth-Maticek et al.^{19,20} to assess characteristics such as rational thought and emotional repression. Participants were asked to answer either "1" for yes or "0" for no. A high score indicated a tendency for thinking rationally and repressing emotion, while a low score

indicated a tendency for thinking less rationally and expressing emotion. The questions were translated into Japanese by Mizunuma et al.²⁸ The internal consistency of the R/A-personality scale was tested in preceding studies.^{22,23} Cronbach's alpha coefficients for the present study were 0.71 for both males and females.

In this cohort study, dietary consumption was assessed using a food frequency questionnaire (FFQ), and the validity and reproducibility of the FFQ have been reported.²⁹ In the FFQ, 169 food and beverage items commonly used in Japan for FFQs were included along with information on portion size. The frequencies of most items were assessed using 8 response categories, ranging from never or hardly ever to 2 or more times a day over the past year. The quantities of dietary consumption were estimated in g/d for 12 arbitrarily selected food categories, which were the typical food groups consumed regularly by Japanese residents. Among the food categories, soy products were included because they are known to be associated with a reduced risk of certain cancers and cardiovascular diseases.³⁰⁻³² For alcoholic beverages, frequencies were assessed using 9 categories, and the range was extended to 4 or more times a day over the past year. The consumption of 4 alcoholic beverages was estimated in terms of the amount (g) of pure ethanol/d. Participants who answered "never or hardly ever consume alcohol" were considered to consume 0 g pure ethanol/d. The FFQ, like all methods of dietary assessment, is subject to measurement error. However, in the present study, the questionnaire had been validated by comparison with 12 daily diet records maintained over 1 year. Spearman's correlation coefficients between the questionnaire and the 12 daily diet records maintained over a 1-year period for grains and potatoes, soy products, fish and shellfish, meat and meat products, eggs, milk and dairy products, green and yellow vegetables, other vegetables, fruit, snacks (sweet and salty), seaweed, and alcohol were 0.20, 0.75, 0.61, 0.18, 0.23, 0.90, 0.47, 0.66, 0.38, 0.57, 0.31, and 0.87 in males, respectively. The corresponding values in females were 0.49, 0.62, 0.33, 0.62, 0.51, 0.77, 0.53, 0.23, 0.48, 0.74, 0.53, and 0.78 respectively.³³⁻³⁵ The nutritional values of the items were obtained from the Standard Tables of Food Composition in Japan, 4th edition.³⁶

In a self-administered questionnaire, age, height, weight, current marital status ("married" categorized as 1 or "without partner" categorized as 0), years of education, and major medical history (cancer, cardiovascular diseases, internal diseases, diabetes mellitus, hypertension, and allergy) were polled. Physical activity based on metabolic equivalents (METs), which measure daily energy expenditure, was assessed using the questionnaire.^{37,38} Information concerning current smoking habits was also sought. Participants were asked if they currently smoked, had stopped smoking, or had never smoked. If they reported to have ever smoked, they were asked the number of cigarettes they smoked per day.

Table 1. Characteristics of participants by sex and the rationality/anti-emotionality personality group.

	Males			Females			P for trend
	Lower (0-5)	Middle (6-8)	Higher (9-11)	Lower (0-5)	Middle (6-8)	Higher (9-11)	
n	4419	4950	3713	4017	5939	5039	
Age (y)	51.7	53.8	57.7	51.9	53.8	59.3	<0.01
Body mass index (kg/m ²)	22.6	22.5	22.3	22	22	21.9	0.60
Physical activity (METs)	27.5	26.3	23.7	16.8	18.5	17	0.97
Marital status (%)							
Without partner	9.8	8.7	8.4	24.8	23	29.2	<0.01
Married	90.2	91.3	91.6	75.2	77	70.8	
Years of education (%)							
<5	1.1	0.4	0.7	2.8	1.1	1.6	<0.01
6-8	16.8	20.9	26.2	17.6	21.5	32.7	
9-11	38.1	33.5	32.6	37.1	41.1	39.3	
12-14	33.1	32.6	28.5	35.9	31.5	23.1	
>15	10.9	12.6	12	6.5	4.8	3.4	
Smoking* (%)							
Non-smoker**	15.4	17.1	19	78.7	83.2	86.4	<0.01
<10 cigarettes/d	13.1	15.3	17.8	10.9	9	7.8	
11-20 cigarettes/d	36.4	35.7	38.5	8.1	6.2	4.7	
>21 cigarettes/d	35.1	31.9	24.7	2.3	1.6	1.1	
Medical history (%)							
Cancer	1.1	1.2	1.6	2.7	2.7	3.8	<0.01
Cardiovascular diseases	5.9	5.7	7.1	4.5	4.7	5.9	<0.01
Internal diseases	22.9	24.2	25.3	13	13.7	14.4	0.06
Diabetes mellitus	6.7	5.8	6.5	2.7	2.4	3.7	<0.01
Hypertension	19.4	19.9	22.5	16.2	17.5	21.6	<0.01
Allergy	7.5	7.1	6.2	10.7	9.4	8.8	<0.01

P for trend shows the associations between the rationality/anti-emotionality personality group and demographic variables.
 *: The number of cigarettes smoked per day was inquired among current smokers and ex-smokers.
 **: Individuals who had never smoked.

Statistical Analysis

Age, smoking, and total energy intake were selected as confounders based on a previous study.³⁹ Medical history, which was considered to be associated with R/A personality,²² was also selected as a confounder. In addition, the following correlations were determined based on Spearman's correlation coefficients (for men and women respectively) for each food consumed. BMI was significantly correlated with many food groups, for example, soy products ($r = 0.03$ and 0.05), green and yellow vegetables ($r = 0.02$ and 0.06), and other vegetables ($r = 0.08$ and 0.09). Physical activity was significantly correlated with soy products and green and yellow vegetables ($r = 0.10$ and 0.07) and other vegetables ($r = 0.14$ and 0.12). Years of education was also significantly correlated with soy products ($r = -0.05$ and -0.02) and seaweed ($r = -0.05$ and 0.02). These parameters were selected as confounders. To examine differences between the 3 groups classified according to the R/A-personality scores (i.e., higher, middle, and lower levels), analysis of covariance (ANCOVA) was performed, controlling for age, BMI, the number of cigarettes smoked per day, physical activity (METs), years of education, medical history, and total energy intake as covariates. Multiple comparisons using the Dunnett-Hsu test were also conducted as post hoc analyses. A P value less than 0.05 was used to indicate statistical significance of the results of ANCOVA. All statistical analyses were performed using the computer program PC-SAS[®], version 6.12.⁴⁰

RESULTS

Table 1 shows that R/A personality was linearly associated with age, marital status, years of education, smoking, cardiovascular diseases, hypertension, and allergy in the case of both males and females. Participants in the higher level of the R/A-personality scale were older and were more likely to be non-smokers, suffer from cardiovascular diseases and hypertension, and have fewer allergies than those in the lower level. A high percentage of males in the higher level of the R/A-personality scale were married, whereas a low percentage of females in the higher level of the R/A-personality scale were married. The R/A-personality scale was also linearly associated with BMI, physical activity, and internal diseases in the case of males and with cancer and diabetes mellitus in the case of females. Males in the higher level of the R/A-personality scale had a lower level of physical activity and lower BMI and a higher percentage of internal diseases. The percentage of cancer and diabetes mellitus was higher in females in the higher level of the R/A-personality scale than in those in the lower level.

Table 2 shows the adjusted means of food consumption. Both males and females in the higher level of the R/A-

personality scale showed higher consumption of soy products, green and yellow vegetables, other vegetables, and seaweed than that shown by participants in other levels of the R/A-personality scale. Males in the higher level of the R/A-personality scale consumed 6.2-13.4% more of these vegetables and seaweed than males in the lower level did, and females in the higher level consumed 7.0-10.7% more of these foods than females in the lower level did. Males in the higher level of the R/A-personality scale consumed 4.0% more meat and meat products and 6.8% more milk and dairy products than that consumed by males in the lower level. Males in the middle level of the R/A-personality scale consumed 1.5% more grain and potatoes than that consumed by males in the lower level. Females in the higher level of the R/A-personality scale consumed 4.2% more fish and shellfish and 2.9% more eggs than those in the lower level did and consumed 10.2% fewer sweet snacks and 9.0% fewer salty snacks than those in the lower level did.

With regard to nutrient intake, as compared to participants in the lower level, both males and females in the higher level of the R/A-personality scale consumed more of the following foods (values in the parentheses are adjusted means in the case of males and females, respectively): protein (96 and 84 g), calcium (736 and 735 mg), iron (14 and 13 mg), carotene (3925 and 4204 μg), vitamin E (9 and 8 mg), vitamin C (121 and 125 mg), and dietary fiber (16 and 16 g). The corresponding nutrient values for males and females in the lower level of the R/A-personality scale were: 93 and 81 g, 696 and 700 mg, 13 and 12 mg, 3558 and 3771 μg , 8 and 8 mg, 109 and 116 mg, and 14 and 15 g, respectively ($P < 0.01$). Participants in the higher level of the R/A-personality scale consumed 2.8-11.5% more of the abovementioned nutrients than that consumed by participants in the lower level. Furthermore, both males and females in the higher level of the R/A-personality scale consumed more fat (62 and 56 g) and cholesterol (358 and 311 mg) than that consumed by participants in the lower level. The corresponding nutrient values for those in the lower level of the R/A-personality scale were: 60 and 56 g and 350 and 302 mg, respectively ($P < 0.05$). No difference in the consumption of salt was found among the 3 R/A-personality groups.

Table 3 shows the adjusted means of alcohol consumption. Males in the lower level of the R/A-personality scale drank 10.8% more alcoholic beverages, including sake, beer, and whisky, than those in the higher level did.

DISCUSSION

Both males and females with high R/A-personality scores showed higher vegetable consumption, including that of soy products and seaweed, than that shown by participants with low R/A-personality scores. Females with high R/A-personality scores showed higher fish and shellfish

Table 2. Adjusted mean (95% confidence interval [CI]) of food consumption (g/d) by the rationality/anti-emotionality personality group.

Item	Males				Females				P*	
	Lower (0-5)	(95% CI)	Middle (6-8)	Higher (9-11)	Lower (0-5)	(95% CI)	Middle (6-8)	Higher (9-11)		
Grains and potatoes	388	(385-390)	b	393	(391-396)	a	389	(387-392)	b	<0.01
Soy products	98	(96-100)	b	100	(98-102)	b	104	(102-106)	a	<0.01
Fish and shellfish	103	(101-104)		104	(102-105)		106	(104-108)		0.05
Meat and meat products	75	(73-76)	b	75	(74-76)	b	77	(76-79)	a	<0.01
Eggs	48	(47-49)		49	(48-50)		49	(48-50)		0.23
Milk and dairy products	189	(183-196)	b	199	(192-205)	b	202	(195-210)	a	0.03
Green and yellow vegetables	126	(123-129)	c	133	(130-136)	b	143	(140-147)	a	<0.01
Other vegetables	225	(222-229)	c	234	(230-237)	b	243	(238-247)	a	<0.01
Seaweed	23	(22-23)	b	24	(23-24)		24	(24-25)	a	<0.01
Fruit	118	(114-121)		121	(118-125)		124	(120-128)		0.06
Sweet snacks	31	(29-32)		31	(30-32)		31	(30-33)		0.74
Salty snacks	6.2	(6.0-6.4)		6.4	(6.2-6.6)		6.5	(6.1-6.9)		0.40

* : P value was computed based on F value for the main effect of the rationality and anti-emotionality personality group. a, b, and c indicate a significant difference between values (i.e., a > b > c, P < 0.05), according to the post hoc test. Consumption was adjusted for age, body mass index, physical activity, years of education, smoking habits, medical history, and total energy intake.

Table 3. Adjusted mean (95% confidence interval [CI]) of alcohol consumption (grams of pure ethanol per day) by the rationality/anti-emotionality personality group.

Item	Males				Females				P*	
	Lower (0-5)	(95% CI)	Middle (6-8)	Higher (9-11)	Lower (0-5)	(95% CI)	Middle (6-8)	Higher (9-11)		
Sake (Japanese rice alcohol)	14.852	(14.2-15.5)	a	14.141	(13.7-14.6)		13.509	(12.9-14.1)	b	<0.01
Beer	11.771	(11.5-12.1)	a	10.665	(10.4-11.0)	b	10.428	(10.1-10.7)	b	<0.01
Wine	0.395	(0.3-0.4)		0.316	(0.3-0.4)		0.395	(0.3-0.4)		0.27
Whisky	2.449	(2.3-2.6)	a	1.975	(1.8-2.1)	b	1.975	(1.8-2.1)	b	<0.01
Total alcohol consumption	34.918	(34.0-35.8)	a	31.521	(30.6-32.5)	b	30.81	(29.7-31.9)	b	<0.01

* : P value was computed based on the F value for the main effect of the rationality/anti-emotionality personality group. a and b indicate a significant difference between values (i.e., a > b, P < 0.05), according to the post hoc test. Consumption was adjusted for age, body mass index, physical activity, years of education, smoking habits, medical history, and total energy intake. A total of 9.0% male participants and 33.5% female participants did not consume alcoholic beverages (participants who answered "not at all consume alcohol").

consumption than that shown by females with low R/A-personality scores. Males with high R/A-personality scores showed lower alcohol consumption than that of males with low R/A-personality scores. Snacking on sweet and salty foods was also reduced in females with high R/A-personality scores compared with that in females with low R/A-personality scores. Accordingly, males and females with high R/A-personality scores showed higher consumption of a variety of nutrients, including protein, calcium, iron, carotene, vitamin E, vitamin C, and dietary fiber than that in participants with low R/A-personality scores.

These results support previous Japanese studies,^{22,23} which suggested that individuals who show high degrees of emotional repression and rational thought are at reduced risk for disease. It appears that in Japan at least, an individual with a rational and unemotional personality may not be cancer-prone. For instance, soy products are reputed to be associated with a lower risk for certain cancers, cardiovascular diseases, and other adverse health outcomes,³⁰⁻³² and they are also reported to prevent hot flashes and other menopausal symptoms in Japanese females.^{41,42} High consumption of green, yellow, and other vegetables is also associated with reduced risks of cardiovascular diseases and many cancers.⁴³⁻⁴⁷ Seaweed consumption, being particular to Japanese culture, appears to be linked to the prevention of cancers, including breast cancer,^{48,49} and cardiovascular diseases.⁵⁰ Fish consumption has been demonstrated to have a protective effect on mortality from cardiovascular diseases⁵¹ and colorectal cancer, which is predominantly seen in females.⁵² Alcohol consumption, on the other hand, is reportedly associated with a higher risk for certain cancers and cardiovascular diseases.⁵³⁻⁵⁵

In the present study, males in the higher level of the R/A-personality scale consumed more meat and meat products and milk and dairy products, and females in the higher level of the R/A-personality scale consumed more eggs than that consumed by participants in the lower level of the R/A-personality scale. Participants in the higher level of the R/A-personality scale showed higher cholesterol and fat intake than those in the lower level of the R/A-personality scale did. To our knowledge, no study has found an association between egg consumption and coronary heart disease, even though egg consumption increases total serum cholesterol concentrations.⁵⁶ Although meat and dairy products are considered risk factors for cancer and cardiovascular diseases, the results obtained are inconsistent.⁵⁷⁻⁵⁹ Further studies on personality characteristics and their relationship to dietary habits are required to confirm these findings.

Japanese culture is characterized by a strong emphasis on harmony and the suppression of individual emotion.⁶⁰ In Japanese culture, there are negative connotations associated with the expression of emotion and lack of empathy. The expression of emotions focused on internal attributes such as anger and frustration is reinforced more in Western

societies.⁶¹ Personality traits may be a reflection of cultural differences, which may influence social behavior, emotion, and health. Maladaptation to a cultural environment may undermine health-oriented dietary habits, and the expression of anger and hostility in interpersonal communication may cause mental distress, possibly resulting in an increase in alcohol intake, especially in males. In this study, mental distress and other psychological factors were not measured, and the existence of a mechanism linking personality characteristics and dietary habits could not be confirmed.

The limitations of this study were as follows: First, because tools for the measurement of personality had not been sufficiently validated when the present study was conducted, there was no standard available against which the R/A personality scale could be measured. In addition, although a certain degree of measurement error might have occurred while calculating the R/A personality score in our cohort, the factorial validity of this scale was confirmed in a previous study.²³ In this study, the R/A-personality score was positively correlated with age. A Japanese study reported that anger expression decreased with increasing age.⁶² A tendency toward repressing emotion may be related to aging, and repressed emotion among the older population does not seem to be an exclusive characteristic of the Takayama cohort. It remains unclear whether the R/A-personality score changes with age, or whether generational differences are responsible for the variances in the scores. Second, the present study was conducted in 1992, and the dietary habits of Japanese people may have changed since that time. Nevertheless, according to the National Nutrition Survey by the Ministry of Health, Labour and Welfare,⁶³ the trends in Japanese nutritional intake during the past decade have not dramatically changed. Third, even though the data in the current study were obtained from a large community sample, and the reliability and validity of food consumption has been well studied,²⁹ due to the fact that the R/A-personality score was positively correlated with age, lapses in time should not be ignored. In addition, there could be a recall bias regarding food consumption that may have affected the R/A-personality score. For example, participants in the higher level of the R/A-personality scale tended to remember what they ate during the past year; therefore, their responses showed a higher consumption of a variety of foods than that observed in the case of participants in the lower levels of the R/A-personality scale. However, male consumption of alcoholic beverages and female consumption of sweet and salty snacks were higher in participants in the lower level of the R/A-personality scale than in the other groups.

The results of the present study suggest that psychological personality traits are related to dietary habits. Both males and females in the higher level of the R/A-personality scale consumed more soy products, green and yellow vegetables, other vegetables, and seaweed. Males in the higher level consumed more meat and dairy products and fewer alcoholic

beverages, and females consumed more fish, shellfish, and eggs and fewer sweet and salty snacks than those in the lower level of the R/A-personality scale did. Whether psychosocial factors play a role in the prevention of diseases is an issue that should be explored in future studies.

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Appendix. Rationality/anti-emotionality personality questions.

1. Do you always try to do things reasonably?
2. Do you always try to understand other people?
3. Do you try to behave rationally in the arena of human relationships?
4. Do you try not to express emotions in the arena of human relationships?
5. Do you try not to blame, criticize, or get angry at someone who condemns you?
6. Can you always get on with relationships by repressing your emotion?
7. Do you try to understand someone whose behavior is contradictory to your wishes?
8. Does your behavior often change on an impulse? *
9. Do you often condemn others for being emotional? *
10. Do you try to understand someone whom you do not like?
11. Do you think rationally and try not to criticize others whom you think are mean?

Participants were instructed to answer either "yes" (score 1) or "no" (score 0).

* : Reversed item. If the participants answered "yes," then they scored 0, and if they answered "no," they scored 1.

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Fruit and Vegetable Intake and Mortality from Cardiovascular Disease Are Inversely Associated in Japanese Women but Not in Men^{1,2}

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Abstract

Some epidemiological studies undertaken in Western countries have demonstrated that high intake of fruit and vegetables results in decreased risk of cardiovascular disease (CVD). The objective of this study was to examine the hypothesis that high intake of fruit and vegetables lowers CVD mortality in a population-based cohort of Japanese subjects. In 1992, fruit and vegetable intake was assessed in 13,355 men and 15,724 women in Takayama, Gifu, Japan using a validated FFQ. During the follow-up (1992–99), 200 men and 184 women died from CVD. For women, the highest quartile of vegetable intake compared with the lowest was marginally significant and inversely associated with CVD mortality after adjusting for total energy, age, and nondietary and dietary covariates [hazard ratio (HR) = 0.62; 95% CI, 0.36–1.08; *P*-trend = 0.007]. An inverse trend with borderline significance was also observed in fruit intake, excluding CVD deaths in the first 2 y of this study, after adjusting for the above-mentioned covariates (HR = 0.83; 95% CI, 0.51–1.34; *P*-trend = 0.10). In men, CVD death was not associated with fruit (HR = 1.16; 95% CI, 0.77–1.74; *P*-trend = 0.61) and vegetable (HR = 0.81, 95% CI: 0.49–1.34; *P*-trend = 0.47) intake. These data suggest that higher intake of vegetables is associated with reduced risk of death from CVD for women. *J. Nutr.* 138: 1129–1134, 2008.

Introduction

Cardiovascular disease (CVD)⁶ is the main cause of death in Western countries and in the Asia-Pacific region, including Japan (1). In many epidemiological and clinical studies, it has been suggested that the risk factors for CVD, including hypertension, obesity, insulin-resistance diabetes, and hypercholesterolemia, are essentially influenced by diet (2–10). Because dietary habits are correctable, it is possible for individuals to adopt healthy eating habits that have a protective effect against CVD. Several laboratory studies have shown that compounds in fruit and vegetables, which have an antioxidant effect, provide beneficial effects on atherosclerosis and CVD (11–16). On the other hand, a diet high in fruit and vegetables has another advantage, namely, that of lowering the dietary glycemic load and energy density (17).

In some epidemiological studies, the direct association between fruit and vegetable intake and the risk of CVD has been studied

extensively and the results have shown a relationship between high fruit and vegetable intake and reduced risk of stroke and ischemic heart disease (18–25). However, most of these studies have been conducted in Western countries. To our knowledge, there have been only 2 prospective cohort studies that examined the relationship between the estimates of fruit and vegetable intake and CVD in Asian countries, both conducted in Japan (24,25). One study demonstrated that the risk of CVD was inversely associated with fruit, but not vegetable, intake. In the other study, CVD mortality was inversely associated with leafy vegetable intake. A prospective study that was conducted using dietary patterns in China examined the association between vegetable intake pattern and CVD mortality (26). However, vegetable intake was not assessed in the study. Studies on the relationship between fruit and vegetable intake and CVD in Asian countries are too few to compare the findings with those of studies conducted in Western countries. We examined the association between fruit and vegetable consumption and mortality from CVD in a cohort of men and women in a community in Japan (Takayama Study).

Materials and Methods

Study population. Subjects were cohort members from the Takayama Study, which was a population-based cohort study conducted in Takayama, Gifu, Japan in September of 1992. A detailed description has been reported elsewhere (27). Eligible participants were nonhospitalized residents of

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⁶ Abbreviations used: CVD, cardiovascular disease; HR, hazard ratio; ICD10, International Classification of Diseases, Tenth Revision; MET, metabolic equivalent.

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Takayama aged ≥ 35 y. At baseline, a self-administered questionnaire designed to obtain information on demographic characteristics, smoking and drinking habits, diet, exercise, and reproductive and medical histories was distributed to 36,990 residents. Subjects who left pages blank and/or inappropriately completed the questionnaire were excluded from the cohort [criteria shown in (27)]. The final number of subjects in the Takayama Study was 31,152 (14,427 men and 17,125 women). The participation rate was 85.3%.

Assessment of diet and exercise. Dietary history was assessed using a semiquantitative FFQ that included 169 food items. Participants reported average consumption frequency and usual serving size for each food in the previous year. The individual intake of food and nutrients was estimated from the frequency of intake and portion size using the Standard Tables of Food Composition in Japan (28). Fourteen items for vegetables (cucumber, tomato, lettuce, celery, broccoli, cauliflower, cabbage, green vegetables (including spinach and pepper), carrot, pumpkin, mountain plant, Japanese radish, legumes, and other vegetables (including eggplant and onion)), 12 items for fruits (orange, grapefruit, melon, banana, kiwi, mandarin orange, peach, watermelon, apple, pear, Japanese persimmon, and strawberry), and other foods including fruits and vegetables as ingredients were taken into account to estimate the individual intake. Soy products were not included as vegetables. The validity and reproducibility of the FFQ were demonstrated by comparing it with other dietary assessment methods, including 3-d food records, 4 24-h diet recalls, and 12 1-d diet records over 1 y (29). The Spearman correlation coefficients between the questionnaire and the 12 1-d diet records over 1 y for the intake of fruit and vegetables were 0.57 ($P < 0.05$) and 0.51 ($P < 0.05$) in men and 0.74 ($P < 0.001$) and 0.41 ($P = 0.069$) in women, respectively. Our questionnaire was designed to measure an individual's relative intake of food and nutrients rather than absolute values. The estimates calculated for fruit and vegetables may have been overestimated by our questionnaire, because these estimates were ~ 5 –12% higher for fruit and 44–45% higher for vegetables on the FFQ than the those based on the diet records.

Exercise was assessed by asking study participants to specify the average number of hours per week that they had spent performing various kinds of activities during the previous year. The reported time spent at each activity weekly was multiplied by its typical energy expenditure requirements, expressed as a metabolic equivalent (MET) and added to yield a MET h/wk score. The details are described elsewhere (30).

Follow-up and outcomes. All deaths in Takayama and their causes during the follow-up period (1992–99) were ascertained using data from the office of National Vital Statistics. The Statistics and Information Department of the Japanese Ministry of Health and Welfare obtains information on death and codes the causes of death using the International Classification of Diseases, Tenth Revision (ICD10). Permission to inspect the data regarding dates and causes of death was received from the Ministry of Internal Affairs and Communications, Japan. Information on subjects who had moved away from Takayama during the study period was obtained from the residential registers of the city. During the follow-up period, 640 (4.5%) men and 506 (3.0%) women moved out of Takayama. This study was approved by the ethics board of the Gifu University School of Medicine.

The primary endpoint for our analysis was CVD mortality. For the category of CVD-related atherosclerosis, we selected ischemic heart disease (ICD10 codes I20, I21, I24, and I25) and cerebrovascular disease (ICD10 codes I60–64, I67, and I69). For this analysis, we excluded subjects who had reported on the baseline questionnaire that they had a past history of cancer (186 men and 540 women), stroke (253 men and 154 women), or ischemic heart disease (633 men and 707 women). Thus, the final analytic population at the baseline consisted of 29,079 subjects (13,355 men and 15,724 women).

Statistical analysis methods. To evaluate the association of the intake of fruit and vegetables with death from CVD, we computed the hazard ratios (HR) and their 95% CI of death from CVD during the period of our study using Cox proportional hazard models. For each subject, person-years of follow-up were accumulated from the beginning of the

study (September 1, 1992) until the date of death from CVD or any other cause, the date when an individual moved out of Takayama, or the final date of the study (December 31, 1999), whichever came first. Estimates of food and nutrients were adjusted for individual total energy by using the residual method proposed by Willett (31). The energy-adjusted intake of fruit and vegetables was categorized by the quartiles on the basis of their distribution among the total study population at the baseline. The HR and their 95% CI for CVD mortality in the 2nd, 3rd, and highest category of intake of fruit and vegetables were computed compared with the lowest one.

To identify any potential confounders, we adopted not only the variables that changed the risk estimate of CVD mortality in the univariate analysis but also those that have the obvious and well-known effect of fruit and vegetables on CVD. In the multivariate analysis of model 2, the associations of fruit and vegetable intake with CVD mortality were examined by adjusting for age, total energy, and nondietary factors, including marital status, years of education, BMI, smoking status, alcohol consumption, exercise (MET-h/wk), menopausal age, and history of diabetes and hypertension. Saturated fat was a potential confounder in previous studies (32,33). In our cohort, sodium intake was significantly and positively associated with deaths from stroke (34) and protein intake was marginally and inversely associated with the rate of CVD in the present analysis. Therefore, in the analysis of model 3, total protein, saturated fat, and sodium intakes were further included in the model as covariates. Statistical testing for linear trends was performed on continuous variables of intake. All statistical analyses were performed using SAS programs (version 9.1.3.; SAS Institute). Because latent CVD might have contributed to changes in dietary habits, we further repeated the analysis after excluding the subjects who had died from CVD (66 men and 70 women) during the first 2 y of follow-up.

Results

At baseline, participants with the highest consumption of fruits and vegetables tended to be older and were less likely to be tobacco and alcohol users and more likely to be married and educated and to have hypertension and diabetes (Table 1). During 201,156 person-years of follow-up over 7 y (median follow-up period of 7.33 y), 384 deaths (200 men and 184 women) occurred due to CVD, i.e. 269 cases of cerebrovascular disease (137 men and 132 women) and 115 cases of ischemic heart disease (63 men and 52 women). In Table 1, we show the servings per day for the consumption of fruit and vegetables. The serving size was determined as 77 g for vegetables and 80 g for fruits (35).

In model 1, after adjustment for age and total energy, mortality from CVD was not associated with total fruit or vegetable intake for men (Table 2). In a multivariate analysis after controlling for nondietary factors (model 2) or after additional controlling for dietary factors (model 3), the results were not substantially altered.

In women, HR decreased for the highest compared with the lowest quartile of total vegetable intake (HR = 0.68; 95% CI, 0.44–1.07) in model 2. Although the estimate was not significant ($P = 0.09$), the linear trend for vegetable intake and the risk of death from CVD was significant (P -trend = 0.02). In the analysis after exclusion of the subjects who had died due to CVD within the first 2 y of this study, the association of vegetable intake with CVD death was somewhat attenuated, but the linear trend was still significant (P -trend = 0.04).

In the stratified analysis according to tobacco use, vegetable intake was somewhat more inversely associated with CVD mortality in men who had never smoked; the HR and 95% CI of CVD deaths in men with the lowest intake were 0.48 (95% CI, 0.13–1.73), 0.91 (95% CI, 0.32–2.65), and 1.19 (95% CI, 0.62–3.59) for the 2nd to the highest quartiles of vegetable intake, respectively, after excluding CVD deaths during the first 2 y of follow-up. On the other hand, in smokers, the corresponding

TABLE 1 Baseline characteristics of study subjects according to quartile of fruit and vegetable intake¹

Group (fourth):	Men					Women				
	Fourths of intake				P for heterogeneity	Fourths of intake				P for heterogeneity
	1	2	3	4		1	2	3	4	
Fruit										
Median intake, g/d	24.1	62.2	110.6	211.7		35.7	77.0	122.5	213.6	
Servings, ² n/d	0.3	0.7	1.3	2.6		0.4	0.9	1.5	2.7	
n	3339	3339	3339	3338		3931	3931	3931	3931	
Age, y	53.8	54.1	53.8	54.2	0.38	55.5	54.8	54.7	55.5	0.003
BMI, kg/m ²	22.4	22.4	22.5	22.6	0.04	21.8	21.9	22.0	22.1	<0.0001
Alcohol intake, g/d	57.1	43.5	37.9	29.4	<0.0001	10.6	7.7	6.7	5.9	<0.0001
Exercise, MET h/wk	27.2	26.5	27.6	27.0	0.80	17.5	18.8	20.2	18.7	0.0009
Married, %	90.4	90.9	92.1	92.4	0.01	73.8	76.9	76.9	73.2	<0.0001
Education ≥15 y, %	8.9	10.9	13.5	13.5	<0.0001	3.8	5.1	5.0	4.6	<0.0001
Current smoker, %	61.9	54.3	49.1	48.4	<0.0001	16.7	10.7	9.9	9.8	<0.0001
Former smoker, %	24.0	26.8	29.7	29.1	<0.0001	3.9	4.1	4.1	3.5	0.5
History of hypertension, %	20.3	19.3	18.5	17.6	0.04	17.0	17.4	16.9	18.1	0.54
History of diabetes, %	5.7	5.6	6.2	6.4	0.44	2.6	2.5	2.7	3.0	0.53
Postmenopausal, %	-	-	-	-		58.5	57.3	57.7	61.5	0.001
Total energy, ³ kcal/d	2586	2609	2650	2600	0.02	2101	2143	2166	2088	<0.0001
Total protein, g/d	89.5	93.5	96.5	93.7	<0.0001	80.0	83.5	84.6	79.8	<0.0001
Saturated fat, g/d	15.1	16.5	17.5	17.3	<0.0001	14.7	15.7	16.0	15.3	<0.0001
Sodium, g/d	5.4	5.6	5.9	5.8	<0.0001	5.0	5.3	5.4	5.2	<0.0001
Vegetable										
Median intake, g/d	176.4	263.7	360.1	553.6		195.5	281.1	375.6	573.9	
Servings, ² n/d	2.2	3.4	4.6	7.1		2.5	3.6	4.8	7.4	
n	3339	3339	3339	3338		3931	3931	3931	3931	
Age, y	50.8	52.3	54.4	58.4	<0.0001	52.8	53.8	55.6	58.4	<0.0001
BMI, kg/m ²	22.6	22.5	22.5	22.5	0.37	21.8	22.0	21.9	22.1	<0.0001
Alcohol intake, g/d	52.3	42.4	39.5	33.6	<0.0001	9.9	8.0	7.5	5.7	<0.0001
Exercise MET, h/wk	27.0	26.7	27.8	26.7	0.69	17.7	19.4	19.0	19.2	0.05
Married, %	88.1	91.0	92.6	94.2	<0.0001	75.2	76.9	75.4	73.3	0.004
Education ≥15 y, %	10.4	12.8	12.2	11.4	<0.0001	4.2	5.8	4.5	4.0	<0.0001
Current smoker, %	62.0	56.0	51.3	44.3	<0.0001	15.7	12.5	10.7	8.2	<0.0001
Former smoker, %	23.0	26.1	28.2	32.3	<0.0001	4.2	3.9	4.0	3.5	0.39
History of hypertension, %	18.2	17.5	18.7	21.3	0.0005	14.7	16.8	17.4	20.6	<0.0001
History of diabetes, %	4.5	5.0	6.1	8.2	<0.0001	1.5	2.2	2.4	4.7	<0.0001
Postmenopausal, %	-	-	-	-		50.3	53.6	61.0	70.5	<0.0001
Total energy, ³ kcal/d	2604	2589	2632	2620	0.22	2142	2098	2118	2141	0.03
Total protein, g/d	83.2	90.7	96.9	102.2	<0.0001	75.8	80.2	83.9	87.7	<0.0001
Saturated fat, g/d	15.3	16.5	17.3	17.3	<0.0001	15.1	15.4	15.7	15.5	0.009
Sodium, g/d	4.5	5.3	5.9	7.0	<0.0001	4.2	4.9	5.4	6.3	<0.0001

¹ Values are means, n, or %.

² 1 Serving: 77 g for vegetable or 80 g for fruit.

³ 1 kcal = 4.184 kJ.

HR were 0.89 (95% CI, 0.48–1.63), 1.14 (95% CI, 0.65–2.00), and 1.24 (95% CI, 0.73–2.11), respectively. However, the interaction between smoking and vegetable intake for the risk of death from CVD was not significant ($P = 0.53$).

We repeated the analysis between premenopausal and postmenopausal women. The HR of CVD death for the top quartile of fruit and vegetable consumption compared with the lowest was 0.60 (0.15–2.67) and 0.88 (0.15–5.30) in premenopausal women and 0.90 (0.57–1.43) and 0.70 (0.43–1.13) in postmenopausal women, respectively.

We also conducted a subgroup analysis in younger (<60 y) and older (≥60 y) subjects, because there were relatively few older people who ate few vegetables and relatively many who ate more vegetables. In men, the HR (95% CI) of the risk of CVD with the highest compared with the lowest quartile of vegetable

intake were 0.45 (0.16–1.23) and 1.16 (0.74–1.83) in younger and older subjects, respectively. In women, the HR (95% CI) of CVD with the highest compared with the lowest quartile of vegetable intake were 0.34 (0.06–1.55) and 0.65 (0.40–1.05) in younger and older subjects, respectively.

Discussion

In this population-based prospective cohort study, we observed a significant trend between vegetable intake and risk of death due to CVD in women but not in men. Compared with women who consumed the lowest amount of vegetables, those women who consumed the highest were at a lower risk of CVD mortality. The inverse association between fruit and death from CVD in women

TABLE 2 HR and 95% CI of mortality from CVD according to fruit and vegetable intake

Fourth	Median intake	CVD deaths	Person-years	HR (95% CI)			
				Model 1 ³	Model 2 ⁴	Model 3 ⁵	Model 3 ^{5,6}
Men							
Total fruit	<i>servings/d</i>	<i>n</i>	<i>n</i>				
1 (low)	0.3	45	22,872	1.00	1.00	1.00	1.00
2	0.7	54	22,829	1.09 (0.73–1.62)	1.11 (0.75–1.65)	1.09 (0.73–1.62)	1.10 (0.70–1.74)
3	1.3	42	22,820	0.85 (0.56–1.29)	0.90 (0.59–1.39)	0.90 (0.58–1.38)	0.93 (0.57–1.52)
4 (high)	2.6	59	22,515	1.16 (0.78–1.71)	1.20 (0.80–1.79)	1.16 (0.77–1.74)	1.27 (0.81–2.01)
<i>P</i> -trend ^{1,2}				0.61	0.49	0.61	0.53
Total vegetable							
1 (low)	2.2	38	23,063	1.00	1.00	1.00	1.00
2	3.4	33	22,860	0.68 (0.43–1.08)	0.70 (0.44–1.11)	0.68 (0.42–1.09)	0.81 (0.46–1.43)
3	4.6	53	22,809	0.87 (0.57–1.32)	0.89 (0.58–1.36)	0.83 (0.52–1.32)	1.08 (0.63–1.85)
4 (high)	7.1	76	22,304	0.84 (0.56–1.25)	0.91 (0.60–1.36)	0.81 (0.49–1.34)	1.02 (0.57–1.82)
<i>P</i> -trend ^{1,2}				0.60	0.93	0.47	0.99
Women							
Total fruit							
1 (low)	0.4	52	27,456	1.00	1.00	1.00	1.00
2	0.9	46	27,638	0.97 (0.65–1.45)	0.98 (0.64–1.48)	0.99 (0.65–1.50)	0.95 (0.59–1.52)
3	1.5	35	27,569	0.75 (0.49–1.14)	0.74 (0.47–1.17)	0.74 (0.47–1.18)	0.71 (0.42–1.18)
4 (high)	2.7	51	27,460	1.05 (0.71–1.55)	1.01 (0.67–1.53)	0.99 (0.66–1.50)	0.83 (0.51–1.34)
<i>P</i> -trend ^{1,2}				0.48	0.52	0.48	0.11
Total vegetable							
1 (low)	2.5	43	27,496	1.00	1.00	1.00	1.00
2	3.6	47	27,621	0.89 (0.59–1.35)	0.84 (0.54–1.31)	0.80 (0.50–1.28)	0.84 (0.49–1.45)
3	4.8	49	27,480	0.82 (0.54–1.23)	0.82 (0.53–1.26)	0.76 (0.47–1.25)	0.83 (0.47–1.47)
4 (high)	7.4	45	27,524	0.66 (0.44–1.01)	0.68 (0.44–1.07)	0.62 (0.36–1.08)	0.77 (0.41–1.46)
<i>P</i> -trend ^{1,2}				0.01	0.02	0.007	0.04

¹ Highest vs. lowest quartile.² Using continuous variables.³ Adjusted for age and total energy.⁴ Adjusted for age, total energy, marital status, years of education, BMI, smoking status (never, former, current), alcohol intake, exercise, history of hypertension or diabetes mellitus (nondietary factors), and menopausal status.⁵ Adjusted for the above nondietary confounders and dietary confounders (total protein, saturated fat, and sodium intake).⁶ Excluded CVD deaths in the first 2 y of the study.

was not significant (P -trend = 0.11). In men, fruit or vegetable consumption was not associated with CVD mortality, even after excluding the cases in which individuals died from CVD in the first 2 y of follow-up.

To our knowledge, there have been 6 prospective cohort studies of dietary fruit and vegetable consumption in relation to the risk of CVD in Western countries. In Japan, we found 2 prospective cohort studies in which the relationship between dietary fruit and vegetable intake and CVD was assessed (24,25). In 1 study conducted between 1980 and 1998, the daily consumption of green-yellow vegetables and fruit was associated with a lower risk of stroke mortality in atomic bomb survivors. However, the estimates of fruit and vegetable intake were based on a limited number of foods listed in the questionnaire (24). Another study conducted between 1995 and 2002 indicated that high consumption of fruit, but not vegetables, was associated with lower risk of CVD (25). In that study, as well as ours, a validated questionnaire using various kinds and items as foods was used.

Three of the 6 studies conducted in Western countries indicated that the intake of fruit and vegetables was significantly and inversely associated with CVD mortality (19,21,23). In these reports, the HR (95% CI) were 0.54 (0.34–0.86), 0.73 (0.58–0.92), and 0.70 (0.55–0.89). The other 3 found that there tended to be an inverse association between fruit and vegetable intake

and the risk of CVD ($P = 0.09$ – 0.15) (18,20,22). These findings suggested a modest inverse association between fruit and vegetable intake and the risk of CVD. In our study, in which fruit and vegetable intake were treated separately, there were modest inverse associations with death of CVD in women, which are consistent with the results from these previous studies. In men, we did not find a significant association between mortality from CVD and fruit intake; however, vegetable intake reduced the risk of CVD. Considering the modest strength of the associations previously reported, our results of vegetable intake in men were not contradictory with those from previous studies.

The difference in the results between men and women may involve an interaction with cigarette smoking. In a previous study (18), inverse associations between fruit and vegetable intake and CVD mortality was stronger in individuals who had never smoked; therefore, there might be an interaction between the fruit and vegetable consumption and smoking status in the present analysis. Because in our cohort, the proportion of smokers in men was larger than in women, this difference might be responsible for the lack of significant differences in the former. The interaction of smoking and serum carotenoid concentrations with the development of diabetes has also been reported by Hozawa et al. (36). They suggested that cigarette smoking modified carotenoid metabolism and may have influenced the risk of diabetes. Another possibility is that the significant inverse trend of

association between fruit and vegetable consumption and the risk of CVD in women might be influenced by an interaction with a sex hormone. Premenopausal women, who produce ovarian hormones in abundance, are protected from CVD and the rates of CVD for men exceeded those for women at all ages (37). In our study, the HR of CVD deaths for fruit and vegetable intake in premenopausal women were lower than those in postmenopausal women.

We also considered the possibility that men had lower fruit and vegetable intakes or reported their diet less accurately than women. However, the intake of fruits as well as vegetables did not differ greatly between men and women. As reported in "Materials and Methods," the results from the validity study of our FFQ were similar for men and women.

Our current study has several methodological advantages. The participants of our study were residents in a community in Japan. In addition, the study was prospective. Thus, we were able to reduce the likelihood of a recall bias and avoid a selection bias. Small loss of this cohort during the follow-up period (3.9%), and high participation rate (85.3%) at the baseline were also an advantage of our study.

On the other hand, our study had several limitations: for example, the use of mortality data rather than incidence data. We could not determine whether fruit and vegetable intake was related to incidence, survival, or both. Although our main interest in this study was CVD mortality, it was desirable to examine which type of CVD was related to dietary fruit and vegetable intake. If this present study had been large enough, we could have conducted a worthwhile analysis of fruit and vegetable intake and the mortality from ischemic stroke, cerebral hemorrhage, and ischemic heart disease separately.

The duration of follow-up may have been too short to assess the relationship between diet and death from CVD. The FFQ, like all methods of dietary assessment, is subject to measurement error. In addition, the dietary assessment was conducted only at baseline. Although we reported the analysis after excluding the individuals who had died from CVD during the first 2 y of follow-up, the change in diet during the follow-up may have affected the results.


In conclusion, our results suggest that high fruit and vegetable intake is associated with a modest reduction in CVD in Japanese women. To more accurately assess the association of fruit and vegetable consumption with death from CVD, larger studies that can include more intake categories are needed.

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Diabetes/Metabolism Research and Reviews

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Research Article

Higher arterial stiffness, greater peripheral vascular resistance and lower blood flow in lower-leg arteries are associated with long-term hyperglycaemia in type 2 diabetic patients with normal ankle-brachial index

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KEYWORDS

glycaemic control · arterial stiffness · peripheral vascular resistance · blood flow · magnetic resonance imaging · type 2 diabetes

ABSTRACT



Background

Higher arterial stiffness and greater peripheral vascular resistance reduce blood flow in lower-leg arteries and contribute to the development of ischaemic limb in diabetic patients even without peripheral artery occlusive disease. The aim of this study was to clarify whether these vascular parameters are associated with long-term hyperglycaemia in diabetic patients.

Methods

We examined 45 type 2 diabetic patients and 38 age-matched nondiabetic subjects without peripheral artery occlusive disease assessed by ankle-brachial index consecutively admitted to our hospital, and followed them over a 3-year period (3.7 ± 0.7 years) with no vasodilative medication. Blood flow and resistive index, a measure of peripheral vascular resistance, at the popliteal artery were evaluated using gated two-dimensional cine-mode phase-contrast magnetic resonance imaging. Brachial-ankle pulse wave velocity was measured to assess arterial stiffness.

Results

At baseline, consistent with our previous report, diabetic patients showed higher brachial-ankle pulse wave velocity ($p < 0.0001$) and resistive index ($p < 0.0001$) and lower flow volume ($p = 0.0044$) than those of nondiabetic subjects. Stepwise multiple regression analysis revealed that duration of diabetes, mean HbA_{1c} during the study, use of renin-angiotensin system inhibitors and change per year in resistive index were identified as significant independent variables predicting change per year in blood flow ($r^2 = 0.733$, $p < 0.0001$) in diabetic patients. Mean HbA_{1c} during the study was positively correlated with changes per year in brachial-ankle pulse wave velocity ($p = 0.00007$) and resistive index ($p = 0.0014$) and was negatively correlated with that in blood flow ($p < 0.0001$) in diabetic patients.

Conclusions

Long-term hyperglycaemia is a major cause of impaired peripheral circulation in lower-leg arteries in diabetic patients without peripheral artery occlusive disease. Copyright © 2009 John Wiley & Sons, Ltd.

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ARTICLE TEXT

Introduction



Lower extremity arterial disease is an important cause of ischaemic limb, delayed wound healing and lower extremity amputation in diabetic patients [1]. It is essential to ameliorate reduced blood flow in lower-leg arteries in diabetic patients before the onset of limb ischaemia. Diabetic patients have two major types of insufficient arterial blood flow to the lower limbs associated with changes in vessel wall properties. The diabetic condition increases atherosclerotic plaque formation in the vessel wall, which promotes peripheral artery occlusive disease (PAOD) in the lower extremities, resulting in reduced blood supply to the lower limbs during exercise or at rest [2]. To identify high-risk patients with PAOD, the ankle-brachial index (ABI) is generally used [3]. The diabetic condition also causes higher arterial stiffness and greater peripheral vascular resistance, resulting in reduced blood supply in the lower-leg arteries even though the individual has no PAOD [4]. Endothelial dysfunction [5], gradual accumulation of advanced glycation end products in the vessel wall [6], increased intima-media thickness [7][8], and vascular calcification [9][10] are responsible for the development of arterial rigidity in diabetic patients. Biopsy specimen from subcutaneous fat demonstrates that diabetic patients have greater peripheral vascular resistance due to endothelial dysfunction [11] or structural alteration [12] in small resistance arteries. Previous studies found that endothelial dysfunction, increased intima-media thickness and arterial stiffness are retarded or reversed by improvement of glycaemic control in diabetic patients [13][14]. However, the impact of long-term hyperglycaemia on peripheral circulation in lower-leg arteries in diabetic patients without PAOD has not been fully elucidated.

The present study was designed to clarify whether arterial stiffness, peripheral vascular resistance, and blood flow in lower-leg arteries are associated with long-term hyperglycaemia in type 2 diabetic patients even without PAOD by using gated two-dimensional cine-mode phase-contrast magnetic resonance imaging (2D-cine-PC MRI).

Subjects and methods



We examined 45 type 2 diabetic patients and 38 age-matched nondiabetic subjects ranging in age from 44 to 72 years who had been consecutively admitted to our hospital between September 1997 and September 2002. All patients were admitted for strict glycaemic control or assessment of long-term complications of diabetes including eye, renal, neurological, and circulatory disorders. No patients had alcohol abuse, malignant neoplasm, acute illness or urinary tract infections. Presence of pyuria or hematuria was diagnosed by microscopic examination and counting of the number of white blood cells or red blood cells per high-power field in a random spot urine collection. Patients with history of cardiovascular disease or foot oedema caused by heart failure, liver cirrhosis, or nephropathy (serum creatinine $>133 \mu\text{mol/L}$) were excluded from the study. Patients were considered to have cerebrovascular disease if they had a history of sudden focal neurologic deficit. Diagnosis of coronary heart disease was made if the patients had a history of angina pectoris or myocardial infarction or showed abnormal electrocardiographic findings. PAOD was diagnosed by observation of low ABI <0.9 [3]. At study entry, all diabetic patients showed no symptoms of cardiovascular disease, and were then followed for 3.0 to 6.3 (mean 3.7 ± 0.7) years with no vasodilative medications. The endpoint of the study in these diabetic patients was the occurrence of ischaemic limb symptoms such as sensations of foot coldness, numbness or rest pain, or lower-extremity pain, discomfort or weakness produced by walking [15]. Hydroxymethylglutaryl coenzyme A reductase inhibitors (statins) were used for the treatment of dyslipidemia (total cholesterol $>6.21 \text{ mmol/L}$) in diabetic patients and this medication can improve endothelial function [16]. All diabetic patients with hypertension ($>140/90 \text{ mmHg}$) received angiotensin converting enzyme inhibitor (ACE) or angiotensin II receptor blocker (ARB) for the management of high blood pressure and administration of these renin-angiotensin system (RAS) inhibitors can also improve endothelial function [17][18]. The study was approved by the ethics committee of our institution, and informed consent was obtained from all patients before examinations, which were done during their stay in our hospital.

Clinical data at entry were collected during the stay in our hospital. After discharge, all of the diabetic patients regularly visited the outpatient clinic in our hospital every 1-2 months during the study and clinical data were collected at every visit. Systolic (sBP) and diastolic (dBP) blood pressures were measured three times using a sphygmomanometer on the right arm after a 5-min rest in the sitting position, and the mean of the last two measurements was used. Blood samples were taken from the cubital vein after overnight fast. Diabetic patients taking insulin or oral hypoglycaemic drugs were allowed to have a snack or drink containing sugar at any time to raise the blood glucose level as quickly as possible if hypoglycaemic symptoms appeared. Hemoglobin A1c (HbA_{1c}), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) levels were measured in our hospital laboratory. Total number of data to calculate the mean values of sBP, dBP, HbA_{1c} , TC and HDL-C during the study were ranged from 20 to 57 (mean 39 ± 6). An automatic device (BP-203RPE; Colin, Komaki, Japan) was used to measure both ABI and brachial-ankle pulse wave velocity (baPWV), as an index of arterial stiffness [19]. A trained ophthalmologist carried out fundus ophthalmoscopies and classified diabetic patients as without retinopathy or as having simple, preproliferative, or proliferative retinopathy. During the stay in our hospital, diabetic patients were classified by urinary albumin excretion in 24-h urine collection as having normoalbuminuria, microalbuminuria, or macroalbuminuria when at least two of three specimens showed less than the diagnostic thresholds of less than 30, 30-300, or greater than 300 mg/24 h, respectively [20]. After discharge, the diabetic patients were classified by measurement of albumin-to-creatinine ratio in random spot urine collections at our outpatient clinic within a 3- to 6-month period as having normoalbuminuria, microalbuminuria, or macroalbuminuria when at least two of three specimens exhibited diagnostic thresholds less than 30, 30-300 or greater than 300 $\mu\text{g/mg}$ creatinine, respectively [20]. Diabetic patients were screened for distal symmetric polyneuropathy using a 128-Hz tuning fork applied to the bony prominence at the dorsal surface of both great toes, just proximal to the nail bed [21]. If the patient required $>10 \text{ s}$ to detect vibration when the tuning fork was placed