Among women, a high dietary GI was significantly associated with an increased risk of mortality from total stroke. The interaction between each dietary factor and sex was not significant in each model, but the term with dietary GI had a relatively small *P* value. Table 3 shows the association between each dietary factor of interest and the risk of mortality from hemorrhagic stroke. Among men, the risk was not significantly associated with any of the dietary variables. Among women, dietary GL and rice intake were significantly associated with the increased risk of hemorrhagic stroke. A positive trend for dietary GI was also observed, but the association failed to reach significance. We found a statistically significant interaction between intake of rice and sex on the risk of hemorrhagic stroke. Table 4 shows the association between each dietary factor and the risk of mortality from ischemic stroke. Among men, the risk or mortality from ischemic stroke was not significantly associated with the dietary GI, GL, carbohydrate intake, or rice intake. Among women, the risk of death from ischemic stroke increased with higher dietary GI. There was no significant interaction between sex and each dietary factor.

To separate the effect of the dietary GI from the effect of rice intake, we roughly estimated GI sourcing from all foods except for rice. The dietary GI not sourcing from rice was not associated with total stroke or hemorrhagic stroke among men and among women, and not associated with ischemic stroke among women. It was inversely associated with the risk of ischemic stroke among men (HR for comparing highest to the lowest quartiles was 0.36 [95% confidence interval, 0.15-0.83]).

Table 5 summarizes the analyses stratified by BMI. Among women with BMI less than 23 kg/m^2, higher dietary GI was significantly associated with an increased risk of mortality from total stroke. However, the interaction term between BMI and dietary GI was not significant. No other associations clearly varied by BMI.

4. Discussion

To our knowledge, the current study is the first prospective cohort study that suggests an association between the dietary GI and the risk of stroke. Among Japanese women in this population, the dietary GI was significantly associated with an increasing risk of mortality from stroke. Such association was not observed among men.

In previous studies, diets high in GI have been linked with an increased risk of diabetes and glucose intolerance [19-22]. The association of the dietary GI to the risk of diabetes may explain the increased risk of stroke observed in the current study. Subjects who reported a history of diabetes were excluded in the current study, but prediabetes or developed diabetes during the follow-up in association with a high dietary GI may have increased the risk of stroke. Many epidemiologic studies suggested that type 2 diabetes mellitus has been an important risk factor for stroke [23-27]. In addition, previous studies showed a significantly greater risk in women with diabetes developing stroke than in men with diabetes [25,27-29], indicating that women are more susceptible to diabetes or glucose intolerance and subsequent

Table 3
Hazard ratio of death from hemorrhagic stroke according to quartiles of dietary GI, energy-adjusted dietary GL, total carbohydrate intake, and rice intake among 12 561 men and 15 301 women in the Takayama study, Japan

	Men					Women				
	Quartile				*P* for trend	Quartile				*P* for trend
	1	2	3	4		1	2	3	4	
GI										
No. of cases	14	9	13	12		6	9	15	16	
Age adjusted	1	0.64 (0.28-1.49)	0.97 (0.46-2.06)	0.90 (0.42-1.94)	.94	1	1.38 (0.49-3.88)	2.15 (0.83-5.57)	2.10 (0.82-5.39)	.08
P interaction with sex[a]										.35
Energy-adjusted GL										
No. of cases	18	8	8	14		6	9	15	16	
Age adjusted	1	0.44 (0.19-1.00)	0.48 (0.21-1.11)	0.86 (0.43-1.73)	.47	1	1.33 (0.47-3.73)	2.08 (0.80-5.37)	2.30 (0.90-5.88)	.05
P interaction with sex[a]										.13
Carbohydrate intake										
No. of cases	17	9	8	14		7	10	11	18	
Age adjusted	1	0.51 (0.23-1.14)	0.47 (0.20-1.08)	0.84 (0.42-1.71)	.46	1	1.22 (0.47-3.22)	1.27 (0.49-3.29)	1.96 (0.82-4.70)	.11
P interaction with sex[a]										.13
Rice intake										
No. of cases	17	13	6	12		6	7	17	16	
Age adjusted	1	0.73 (0.35-1.50)	0.39 (0.15-1.00)	0.71 (0.34-1.49)	.15	1	0.98 (0.33-2.91)	1.81 (0.71-4.66)	2.36 (0.92-6.03)	.02
P interaction with sex[a]										.03

[a] Adjusted for age, sex, and the single dietary factor of the interaction term.

Table 4
Hazard ratio of death from ischemic stroke according to quartiles of dietary GI, energy-adjusted dietary GL, total carbohydrate intake, and rice intake among 12 561 men and 15 301 women in the Takayama study, Japan

	Men					Women				
	Quartile				*P* for trend	Quartile				*P* for trend
	1	2	3	4		1	2	3	4	
GI										
No. of cases	15	16	16	13		6	15	13	32	
Age adjusted	1	1.00 (0.50-2.03)	1.22 (0.60-2.46)	0.91 (0.43-1.92)	.96	1	1.67 (0.64-4.31)	1.18 (0.44-3.12)	2.45 (1.01-5.92)	.03
P interaction with sex[a]										.29
Energy-adjusted GL										
No. of cases	20	13	13	14		8	16	23	19	
Age adjusted	1	0.56 (0.28-1.12)	0.77 (0.38-1.55)	0.92 (0.47-1.83)	.77	1	1.42 (0.61-3.32)	1.63 (0.72-3.66)	1.59 (0.70-3.65)	.27
P interaction with sex[a]										.73
Carbohydrate intake										
No. of cases	16	13	16	15		15	9	20	22	
Age adjusted	1	0.62 (0.30-1.30)	0.90 (0.45-1.80)	0.91 (0.45-1.85)	.97	1	0.43 (0.19-0.98)	0.80 (0.41-1.57)	0.86 (0.44-1.65)	.85
P interaction with sex[a]										.78
Rice intake										
No. of cases	18	21	5	16		7	18	25	16	
Age adjusted	1	0.97 (0.51-1.82)	0.52 (0.19-1.41)	1.21 (0.61-2.37)	.97	1	1.53 (0.64-3.68)	1.14 (0.49-2.67)	1.67 (0.69-4.07)	.39
P interaction with sex[a]										.37

[a] Adjusted for age, sex, and the single dietary factor of the interaction term.

stroke than men. That may also support that a significant risk increase of stroke with high dietary GI was only observed among women in the current study. Previously, the intake of carbohydrates was generally not found to predict the risk of diabetes [20-28]. The studies may support the findings of the current study because no clear association was observed between carbohydrate intake and the risk of total stroke.

Dietary GI may have influence on factors other than diabetes, such as others that lead to the increased risk of stroke. It was reported that low-GI diets increased body fat loss among overweight or obese young adults in an intervention study, and progression of atherosclerosis was accelerated with high carbohydrate intake from high-GI sources among women with coronary heart disease in a 3-year prospective study [30,31]. These results may be supported by the studies that indicated the inflammatory reactions with hyperglycemia [32,33]. In the current study, however, subjects with high dietary GI were likely to consume low level of dietary fat; and the effect of dietary GI on lipid profile, if it existed, could be overridden.

Findings from previous prospective cohort studies implied that dietary GL was positively associated with the risk of stroke [3-5], whereas the association between dietary GL and the risk of total stroke was not clear in the current study. This could be attributed to the fact that the subjects in the current study population were relatively slim. Two of the studies found associations between the dietary GL and stroke among overweight women but not among those who were not overweight [3,4]. Alternatively, our results may indicate that, although large amounts of carbohydrates were regularly consumed among Japanese population, the quality of carbohydrates (represented by dietary GI) is more important than its quantity (partially represented by dietary GL).

Differences in the association between dietary GI and stroke subtypes were not clear in the current study. Among women, the risk of mortality from ischemic stroke was increased among the subjects with the highest level of dietary GI; and a similar pattern of risk increase for hemorrhagic stroke was also observed, although the association was not significant. Previous studies consistently reported that diabetes increased the risk of ischemic stroke [23,24,28], whereas the risk of hemorrhagic stroke does not seem to increase among people with diabetes [7,24,34]. However, in the current study, the dietary GL and rice intake significantly increased the risk of hemorrhagic stroke; but the associations were not significant with the risk of ischemic stroke among women in the current study. The large consumption of rice and the dietary GL may have been linked to the Japanese-style diet [35]. It was reported in the Honolulu Heart Program that a Western-type diet, compared with an Oriental-style diet, tended to be inversely associated with thromboembolic and hemorrhagic stroke. However, a recent cohort study in Japan reported that the Japanese dietary pattern was associated with a decreased risk of total stroke mortality [36]. The dietary GI sourcing from food items other than rice was not associated with the risk of total stroke or hemorrhagic stroke in the current study, and the inverse association was observed with the risk of ischemic stroke among men. Nonetheless, there is still a possibility that

Table 5
Hazard ratio of death from stroke according to quartiles of dietary GI, energy-adjusted dietary GL, total carbohydrate intake, and rice intake among 6970 men and 9747 women whose BMI was less than 23 and 4886 men and 4698 women whose BMI was 23 or over in Takayama study, Japan

	Men						Women					
	Quartile				*P* for trend	*P* for interaction with BMI[a]	Quartile				*P* for trend	*P* for interaction with BMI[a]
	1	2	3	4			1	2	3	4		
GI												
BMI <23 kg/m^2												
No. of cases	19	17	20	17			5	19	21	36		
Age-adjusted HR	1	0.84 (0.44-1.62)	1.09 (0.58-2.05)	0.93 (0.49-1.80)	.99		1	2.92 (1.09-7.84)	2.55 (0.96-6.81)	3.86 (1.51-9.90)	.01	
BMI ≥23 kg/m^2												
No. of cases	8	8	4	5			6	7	8	8		
Age-adjusted HR	1	1.21 (0.45-3.23)	0.68 (0.21-2.26)	0.82 (0.27-2.50)	.57		1	1.00 (0.33-2.97)	1.06 (0.36-3.08)	0.94 (0.32-2.76)	.94	
						.94						.21
Energy-adjusted GL												
BMI <23 kg/m^2												
No. of cases	23	17	16	17			9	21	26	25		
Age-adjusted HR	1	0.65 (0.35-1.22)	0.79 (0.42-1.49)	0.90 (0.48-1.69)	.71		1	1.86 (0.85-4.06)	1.87 (0.87-4.01)	1.92 (0.90-4.13)	.15	
BMI ≥23 kg/m^2												
No. of cases	11	3	4	7			6	6	9	8		
Age-adjusted HR	1	0.27 (0.08-0.98)	0.48 (0.15-1.50)	0.85 (0.33-2.20)	.56		1	0.81 (0.26-2.52)	1.17 (0.42-3.31)	1.16 (0.40-3.35)	.64	
						.46						.73
Carbohydrate intake												
BMI <23 kg/m^2												
No. of cases	18	19	17	19			17	14	23	27		
Age-adjusted HR	1	0.96 (0.51-1.84)	0.94 (0.48-1.81)	1.14 (0.60-2.17)	.90		1	0.59 (0.29-1.20)	0.87 (0.46-1.62)	0.88 (0.48-1.62)	.93	
BMI ≥23 kg/m^2												
No. of cases	9	3	4	9			7	6	5	11		
Age-adjusted HR	1	0.27 (0.07-0.99)	0.40 (0.12-1.30)	0.96 (0.38-2.41)	.90		1	0.84 (0.28-2.49)	0.59 (0.19-1.86)	1.27 (0.49-3.28)	.64	
						.70						.65
Rice intake												
BMI <23 kg/m^2												
No. of cases	21	26	10	16			7	24	29	21		
Age-adjusted HR	1	1.09 (0.62-1.94)	0.67 (0.31-1.42)	0.87 (0.45-1.67)	.44		1	2.02 (0.87-4.72)	1.48 (0.64-3.42)	2.10 (0.89-4.94)	.22	
BMI ≥23 kg/m^2												
No. of cases	8	8	2	7			7	5	9	8		
Age-adjusted HR	1	0.91 (0.34-2.44)	0.50 (0.10-2.41)	1.10 (0.40-3.05)	.93		1	0.56 (0.18-1.78)	0.79 (0.29-2.14)	0.98 (0.36-2.73)	.77	
						.45						.87

[a] Adjusted for age, BMI, and the single dietary factor of the interaction term.

nutrients or food items typical in Japanese-style diet could have played a role as confounders in the association between the dietary variables and stroke or its subtypes. Further evaluation of the consumption of rice in relation to risk of stroke and its subtypes in a larger study is warranted.

The dietary GI may have been associated with risk factors of stroke subtypes, other than diabetes. Several studies reported that a low dietary GI was associated with a high concentration of serum high-density lipoprotein cholesterol [37,38]. Low serum cholesterol levels with a condition of high blood pressure are reported risk factors of hemorrhagic stroke [39,40]. If the prevalence of uncontrolled high blood pressure was high in the group with a high dietary GI, GL, or rice consumption, such a condition with a lowered level of high-density lipoprotein cholesterol might explain the increased the risk of hemorrhagic stroke observed among women.

In the current study, stratified analysis by BMI showed that dietary GI and dietary GL were significantly associated with increased risk of death from total stroke among women with BMI less than 23. The interaction terms between BMI and the dietary factors were not significant. The results contradicted previous studies reporting the association between dietary GL and total stroke, or the association between dietary GL and cardiovascular disease among overweight or obese women [3,4]. There were a limited number of events available in the current study, and they may be too few to draw a conclusion after the stratification.

This study has several limitations. The FFQ in this study was not specifically designed to derive dietary GI values, as in many other studies; and thus, no validation data for the estimation of the dietary GI or GL exist. The data we collected for food and nutrient intake and estimated dietary GL may have been overestimated by the FFQ. However, our questionnaire was designed to measure the relative intake of food and nutrients rather than the absolute value. Correlation coefficients between the value from the FFQ and that from the food record for carbohydrate intake were relatively low; and attenuation of association, if the association existed, may have occurred. It was suggested that the correlation needs to be at least 0.3 or 0.4 to detect associations between diet and disease [41], and our FFQ may have minimal validity for the assessment of carbohydrate intake. The diagnoses of outcome were based on death certificates; and the possibility of misdiagnosis, especially for the subtypes of stroke, cannot be ruled out for the findings of the current study. High dissemination of computerized tomography in Japan, however, may warrant sufficient accuracy for the use of death certificate in the current study [42,43]. The information in deaths was not able to be updated after 1999, and the number of deaths from the subtypes of stroke was not enough to control for the potential risk factors. The impact of initial exclusion of the subjects on the study results is unknown; but the fairly high participation rates reduce concern of bias from nonparticipation, and its systematic effect, if it exists, may be minimal. We repeatedly performed statistical tests, so the results should be interpreted with caution.

5. Summary

In conclusion, we found a positive relationship between the dietary GI and risk of mortality from stroke among women in a community-based cohort in Japan, where a high risk of stroke is still observed. The results of the study also suggest that the risk of mortality from ischemic stroke is increased with increased level of the dietary GI among women, and a positive trend is also suggested between dietary GL and mortality from hemorrhagic stroke among women. Conducting further studies that precisely investigate the biomarkers for glucose metabolism in relation to the dietary GI and the risk of stroke would be desirable, and further investigation of the risk factors of stroke subtypes in response to the dietary GI with a specific focus on male-female differences is recommended.

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Consumption of coffee, green tea, oolong tea, black tea, chocolate snacks and the caffeine content in relation to risk of diabetes in Japanese men and women

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Although the inverse association between coffee consumption and risk of diabetes has been reported numerous times, the role of caffeine intake in this association has remained unclear. We evaluated the consumption of coffee and other beverages and food containing caffeine in relation to the incidence of diabetes. The study participants were 5897 men and 7643 women in a community-based cohort in Takayama, Japan. Consumption of coffee, green tea, oolong tea, black tea and chocolate snacks were measured with a semi-quantitative FFQ in 1992. At the follow-up survey in 2002, the development of diabetes and the time of diagnosis were reported. To assess the association, age, smoking status, BMI, physical activity, education in years, alcohol consumption, total energy intake, fat intake and women's menopausal status were adjusted. Among men who consumed one cup per month to six cups per week and among those who consumed one cup per d or more, the associated hazard ratios were 0·69 (95 % CI 0·50, 0·97) and 0·69 (95 % CI 0·49, 0·98) compared with those who drank little to no coffee, with a P value for trend of 0·32. The hazard ratios for women with the same coffee consumption patterns were 1·08 (95 % CI 0·74, 1·60) and 0·70 (95 % CI 0·44, 1·12), with a P value for trend of 0·03. The association between estimated total caffeine intake and risk of diabetes was insignificant both among men and among women. The results imply that coffee consumption decreased the risk of developing diabetes. The protective effect may exist aside from the influence of caffeine intake.

Coffee: Diabetes mellitus: Caffeine: Japanese

The protective effect of heavy consumption of coffee on the development of diabetes has been reported in many epidemiological studies, substantially from European countries and the USA, where coffee is widely consumed[1–8]. Because caffeine is one of the biologically active components in coffee, its role in the association with diabetes has also been investigated as described below. Several clinical studies have shown that oral administration of caffeine increases thermogenesis and metabolism[9–11]. These results may support the protective effect of caffeine intake over the risk of diabetes through reducing the risk of obesity, although the studies have expressed a rather short-term effect. On the other hand, several other studies have shown that caffeine intake causes the reduction of glucose disposal and increases insulin resistance[12–14]. To assess the long-term effects of caffeine intake, observational studies have been conducted to examine the relationship between caffeine intake and the development of diabetes. The results of some of the studies indicated a lowered risk of diabetes with increased caffeine intake[15–19]. On the contrary, several studies showed that decaffeinated coffee also decreased the risk of diabetes[18–20].

Caffeine is also contained in other dietary items such as tea and chocolate. In contrast to people in several European countries and the USA, tea is commonly consumed in Japan, and, hence, it should also be considered as its source to evaluate caffeine intake among Japanese subjects. Three previous studies among Japanese people evaluated green tea consumption with the risk of diabetes, but the results were inconsistent[15,16,21]. Studies in the USA implied a protective effect of tea consumption on diabetes risk, although the upper 95 % CI was at the null value; the hazard ratio was 0·77 (95 % CI 0·59, 1·00) for a two cups per d increment in intake in one study[17], and it was 0·88 (95 % CI 0·64, 1·23) for four or more *v.* no cups per d in the other study[19]. Another study in the USA failed to show the association between tea consumption and risk of diabetes[18]. Chocolate snacks are relatively common in Japan, although the reported per capita consumption has been found to be lower than that in most Western countries: 23 % of the consumption in the UK, and 37 % of the consumption in the USA[22].

We assessed the association between coffee consumption and risk of developing diabetes in a prospective cohort study among men and women in a general Japanese population. We further evaluated the consumption of beverages and foods containing caffeine. Total caffeine intake was estimated and discussed in relation to the risk of diabetes.

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Materials and methods

Subjects in the present study were from a community-based cohort study conducted in Takayama City (Gifu, Japan). The rationale and design of the Takayama study have been described in detail elsewhere[23–25]. In 1992, 31 152 individuals aged 35 years and over completed a baseline self-administered questionnaire which included a semi-quantitative FFQ for 169 food items consumed in the previous year, and other questions asking about physical and demographic characteristics such as age, height, weight, marital status and length of education. Women's health issues including menopausal status and use of hormone replacement therapy were also asked. The questionnaire also asked about smoking status, previous diagnosis of diabetes and other medical and reproductive histories. To assess the amount of regular physical activity, the average time (in hours) spent for listed physical activities was sought, and the metabolic equivalents were estimated. The list contained vigorous sports (such as jogging, bicycling on hills, tennis, racquet ball, swimming laps, or aerobics), vigorous work requiring muscle strength and endurance (such as moving heavy furniture, loading or unloading trucks, shovelling, or other equivalent manual labour) and moderate sports or work (such as housework, brisk walking, golfing, bowling, bicycling on level ground, or gardening). Further details and the validity information of the physical activity questionnaire have been previously reported[26,27]. The participation rate for the questionnaire administered at baseline was 85·3 %. In the cohort, participants who were younger than 70 years at baseline (*n* 26 546) were followed for the present study. Among them, 1120 participants died and 1058 participants moved out of Takayama between September 1992 and March 2000, as confirmed by the residential registry. For the remainder of the follow-up until July 2002, we did not have access to the residential registry, but we identified an additional 404 deaths using the obituaries issued by Takayama city. After excluding the deaths and relocations, we sent 23 964 participants a follow-up questionnaire in 2002. In response to sending out the questionnaire, we learned that an additional 1460 participants had moved out of Takayama, eighteen had died and fifty-one were physically unable to complete the questionnaire. Of the remaining subjects, 14 975 completed the questionnaire, which yielded the response rate of 66·7 %. Compared with the 14 975 subjects, the 11 571 subjects without follow-up data were slightly younger (aged 50·3 *v.* 52·3 years among men and aged 50·8 *v.* 52·0 years among women), less likely to be educated 12 years or longer (43·9 *v.* 46·9 % among men and 35·5 *v.* 39·4 % among women), more likely to have high caffeine intake (139 *v.* 132 mg among men and 144 *v.* 138 mg among women), but were similar in terms of BMI.

For the present analysis, participants who reported a diagnosis of diabetes (*n* 541), cancer (*n* 274), or either myocardial infarction, angina or stroke (*n* 535) at baseline were excluded. We further excluded participants who were newly identified having diabetes at baseline from the follow-up questionnaire (*n* 85). After these exclusions, 5897 men and 7643 women were included in the present analysis.

The information on baseline consumption of coffee and other beverages and foods among the participants was derived from the FFQ administered at baseline. The validity and reliability of the questionnaire and other detailed information have been described previously[24]. In the present study, we evaluated the following drinks: coffee, decaffeinated coffee, green tea, oolong tea and black tea. We also examined the consumption of chocolate snacks, since chocolate is also a source of caffeine[28,29]. Chocolate truffles and solid chocolate bars are common chocolate snacks in Japan. Since there were separate questions for cookies/biscuits and cake, chocolate cookies, chocolate-covered cookies and chocolate cake were not likely to be classified as chocolate snacks by many participants. The content of caffeine from coffee and tea was estimated by using data from the Standard Tables of Food Composition in Japan, 5th edition, published by the Science and Technology Agency of Japan. In the questionnaire, one serving was defined as 150 g for coffee and decaffeinated coffee, 100 g was defined as one serving for green tea and black tea, and 250 g was defined as one serving for oolong tea. The estimated content of caffeine per serving was 90 mg for coffee, 20 mg for green tea, 30 mg for black tea and 50 mg for oolong tea. The consumption of decaffeinated coffee was asked separately from the consumption of coffee, and, hence, estimated consumption of coffee and that of decaffeinated coffee were mutually exclusive. The caffeine content in chocolate snacks was defined as 12·5 mg per 100 g according to a literature review[28]. We estimated the intake of caffeine from each beverage and chocolate snack by totalling a weight proportional to the frequency of consumption in the questionnaire, and multiplying that total by the above caffeine content. We also estimated the intake of other nutrients based on the FFQ by referring to the same standard table. The intake of each nutrient was adjusted for total energy after log-transformation by using the residual method proposed by Willett[30].

The participants who developed diabetes between the time of the baseline study and at the time of follow-up were identified in the questionnaire. All participants were asked if they had ever been diagnosed with diabetes, and, if so, how old they were at the time of the diagnosis. Using the information on their age at baseline and age at diagnosis, the time from baseline to diagnosis was estimated. Because thirty-one men and ten women who developed diabetes during the follow-up period did not provide the information regarding the time of diagnosis, we assigned median values of length to the diagnosis among participants for men and women separately.

Statistical analysis

Participants were placed into categories based on the frequency of consumption of coffee, tea and chocolate snacks, roughly based on the distribution of consumption of each item in the current population. Three categories for frequency of coffee and oolong tea consumption were created: never or almost never, once per month to six times per week, and once per d or more. Four categories for frequency of green tea consumption were created: never or almost never, once per month to six times per week, once per d, and twice per d or more. For the consumption of decaffeinated coffee and black tea, two categories were created: never or almost never and once per month or more. The amount of chocolate snacks consumed was multiplied by the frequency of consumption, and put into three categories: never or almost never, one piece

per month to two or three pieces per month, and one piece per week or more. Caffeine intake was analysed in tertile groups. Cox proportional hazards models were used to assess the contributions of coffee, tea, chocolate consumption, and caffeine intake respectively, to the subsequent risk of developing diabetes. The age-adjusted model and multivariate model adjusted for potential confounders, age, smoking status, BMI, physical activity, education in years, alcohol consumption, total energy intake, fat intake and women's menopausal status were examined for each beverage and chocolate snacks respectively. To test for linear trends across categories, we modelled the median of each category of coffee, tea and chocolate consumption, and caffeine intake as a continuous variable.

All statistical analyses were performed by using SAS statistical software (version 9.1; SAS Institute, Inc., Cary, NC, USA). Statistical significance was considered to be $P<0{\cdot}05$. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethics Committee at Gifu University Graduate School of Medicine. Written informed consent was obtained from all subjects.

Results

Of the 5897 men and 7643 women participating in the study, 278 men and 175 women reported the development of diabetes during the follow-up. Baseline characteristics of the study participants across sex-specific categories of coffee consumption are presented in Table 1. Higher coffee consumption was associated with younger age, 12 years or more of education, and cigarette smoking. Total energy intake and carbohydrate intake were higher with an increased level of coffee consumption. Consumption of soda was also higher with the increased level. Correlation coefficient analysis between caffeine intake and BMI showed no clear correlation both among men and among women (data not shown).

With the multivariate model, hazard ratios among men showed that participants who consumed coffee once per month to six times per week and who consumed coffee daily had a significantly decreased risk of diabetes compared with those who never or almost never consumed coffee, with no significance in analysis of trend (Table 2). Among women, although hazard ratios did not show a significant association, an analysis for linear trend after multivariate adjustment showed a statistically significant decrease in the development of diabetes (Table 2).

Consumption of decaffeinated coffee tended to be associated with a decreasing risk of diabetes among women, but the association was not statistically significant (Table 2). Green tea consumption and black tea consumption were not significantly associated with a risk of diabetes either. Consumption of oolong tea was insignificantly positively associated with a risk of diabetes among men, and the trend analysis showed the risk increased significantly with higher consumption among women (Table 2). Although the association with consumption of oolong tea was attenuated after multivariate adjustment among men, it remained significant after the adjustment among women. We observed a weak but significant inverse association between the consumption of chocolate snacks and the risk of diabetes among men in the trend analysis. The lowered risk was also observed among women, although not all the decreases in hazard ratios were statistically significant, and no significance was observed in the trend analysis (Table 2).

The association between coffee consumption and risk of diabetes remained in an analysis which included the categorical variables of coffee consumption and caffeine intake simultaneously in the multivariate model. The hazard ratios for diabetes according to coffee consumption categories of never or almost never, once per month to six times per week, and once per d or more were 1·00, 0·70 (95 % CI 0·50, 0·99) and 0·66 (95 % CI 0·43, 1·03), and the P value for trend was 0·33 among men. The corresponding hazard ratios for women were 1·00, 1·00 (95 % CI 0·67, 1·49) and 0·60 (95 % CI 0·36, 1·01), with the P value for trend of 0·02. In the same model, no significant association between caffeine intake and risk of diabetes was observed (data not shown).

To minimise a potential effect of subclinical disease, we conducted additional analyses by excluding thirty-eight men and nineteen women who reported the diagnosis of diabetes during the first 2 years of the follow-up period. The results did not alter our original findings. Because we needed to assign the median length of follow-up to forty-one participants who developed diabetes, we conducted a separate analysis using logistic regression, but these results also did not alter our findings; the multivariate OR for diabetes according to the coffee consumption categories of never or almost never, once per month to six times per week, and once per d or more were 1·00, 0·70 (95 % CI 0·50, 0·98) and 0·69 (95 % CI 0·48, 0·99), and the P value for trend was 0·31 among men. Among women, the same results were 1·00, 1·00 (95 % CI 0·67, 1·48) and 0·60 (95 % CI 0·37, 0·96), with a P value for trend of 0·01.

Discussion

Higher coffee consumption modestly decreased the risk of development of diabetes both among men and women even though consumption of coffee is relatively low in the current Japanese population compared with that in Western countries. In contrast, caffeine intake estimated from coffee, green tea and other caffeinated beverages and chocolate snacks was not associated with risk. The results suggest that a beneficial effect of coffee consumption exists aside from its caffeine content. Studies conducted in the USA showed that a higher caffeine intake significantly lowered the risk of diabetes, but in some of the studies, the association between caffeine intake and risk of diabetes was diminished after further adjustment for coffee consumption[17–19]. In the same studies, it was reported that the consumption of decaffeinated coffee was also inversely associated with the risk of diabetes[17–19]. The consumption of coffee may increase the intake of antioxidants other than caffeine. It has been reported that chlorogenic acid, a polyphenol abundant in coffee, is probably responsible for the substantial part of antioxidants[31–33].

The present study failed to observe any association between decaffeinated coffee and diabetes risk, which may have been caused by a lack of power since a very small number of the participants, less than one-tenth of them, reported consumption of decaffeinated coffee in some frequency. The significant

Table 1. Baseline characteristics of the study population according to level of coffee consumption
(Mean values and standard deviations or percentages)

	Men (*n* 5897)						Women (*n* 7643)					
	Never or almost never (*n* 931)		Once/month to six times/week (*n* 2402)		Once/d or more (*n* 2564)		Never or almost never (*n* 1398)		Once/month to six times/week (*n* 3312)		Once/d or more (*n* 2933)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	56·7	8·0	53·1	8·7	48·9	8·6	56·4	8·7	52·5	8·9	48·0	8·1
BMI (kg/m^2)*	22·3	2·6	22·7	2·6	22·6	2·7	21·9	2·9	22·3	2·7	22·0	2·7
Smoking status (%)†												
Never	23·4		21·9		11·7		79·8		84·4		76·1	
Current	39·0		44·0		65·5		5·9		5·3		15·5	
Past	34·8		32·7		21·4		2·4		3·1		3·7	
Currently married (%)	95·0		93·9		94·5		81·9		86·8		85·9	
Education 12 years or longer (%)	30·9		44·9		57·3		24·2		37·7		51·1	
Physical activity (metabolic equivalents/h per week)	26·6	39·8	31·1	43·3	28·0	42·1	18·0	26·8	22·6	33·1	22·0	30·4
Postmenopausal (%)							74·3		58·5		38·4	
Current use of hormone replacement therapy (%)							2·2		1·7		1·4	
Daily dietary intake												
Total energy (kJ)	10 820	3438	11 059	3375	11 408	3640	8570	3160	9154	3058	9391	3232
Fat (g)	56·9	28·0	60·2	26·5	63·7	29·2	51·5	25·5	57·5	25·9	60·7	26·6
Carbohydrate (g)	349	105	366	107	388	118	304	108	321	102	327	111
Dietary fibre (g)	16·1	9·0	16·0	7·9	16·4	8·9	16·7	9·5	17·2	8·5	17·1	8·5
Mg (mg)	400	171	401	154	415	166	360	163	374	146	383	152
Caffeine (mg)	42	48	79	57	218	100	60	56	97	66	226	103
Alcohol (g)	50·7	44·1	44·5	40·5	41·0	39·1	6·2	13·9	6·8	14·1	9·5	17·5
Soda (servings)	0·08	0·21	0·15	0·28	0·22	0·39	0·08	0·24	0·10	0·23	0·13	0·28
Coffee, tea and chocolate consumption per d (servings)												
Coffee	0·0	0·0	0·3	0·3	1·8	0·9	0·0	0·0	0·3	0·2	1·6	0·8
Decaffeinated coffee	0·01	0·1	0·02	0·1	0·06	0·3	0·02	0·2	0·02	0·1	0·07	0·4
Green tea	1·2	1·4	1·3	1·4	1·3	1·3	1·7	1·4	1·8	1·4	1·6	1·3
Black tea	0·03	0·2	0·06	0·2	0·06	0·2	0·04	0·2	0·07	0·2	0·08	0·3
Oolong tea	0·2	0·6	0·3	0·6	0·3	0·7	0·3	0·8	0·4	0·8	0·5	0·9
Chocolate snack pieces	0·05	0·2	0·10	0·2	0·12	0·3	0·08	0·2	0·15	0·3	0·19	0·4

* For men, *n* 5677; for women, *n* 7416.
† Values do not add to 100 % because of missing data.

Table 2. Risk of diabetes incidence according to consumption of coffee and tea, and caffeine intake
(Hazard ratios (HR) and 95 % confidence intervals)

	Men						Women					
	Subjects (*n*)	Cases (*n*)	HR (adjusted for age)	95 % CI	HR (multivariate adjustment)*	95 % CI	Subjects (*n*)	Cases (*n*)	HR (adjusted for age)	95 % CI	HR (multivariate adjustment)*	95 % CI
Coffee												
Never or almost never	931	56	1·00	–	1·00	–	1398	39	1·00	–	1·00	–
Once/month to six times/week	2402	107	0·74	0·53, 1·03	0·69	0·50, 0·97	3312	92	1·10	0·75, 1·60	1·08	0·74, 1·60
Once/d or more	2564	115	0·73	0·52, 1·03	0·69	0·49, 0·98	2933	44	0·73	0·46, 1·15	0·70	0·44, 1·12
P value for trend			0·35		0·32				0·04		0·03	
Caffeine intake												
1st tertile	1966	98	1·00	–	1·00	–	2553	58	1·00	–	1·00	–
2nd tertile	1967	81	0·81	0·60, 1·09	0·81	0·60, 1·10	2547	66	1·35	0·94, 1·94	1·26	0·88, 1·82
3rd tertile	1964	99	1·00	0·75, 1·35	0·95	0·69, 1·30	2543	51	1·18	0·79, 1·75	0·95	0·63, 1·43
P value for trend			0·77		0·94				0·55		0·53	
Green tea												
Never or almost never	2131	104	1·00	–	1·00	–	1539	32	1·00	–	1·00	–
Once/month to six times/week	801	48	1·30	0·92, 1·84	1·23	0·87, 1·76	1075	24	0·92	0·54, 1·58	0·90	0·52, 1·54
Once/d	616	28	0·94	0·61, 1·43	0·97	0·63, 1·49	778	14	0·94	0·50, 1·77	1·00	0·53, 1·89
Twice/d or more	2349	98	0·91	0·69, 1·20	0·94	0·71, 1·26	4251	105	1·07	0·72, 1·60	1·03	0·69, 1·55
P value for trend			0·20		0·38				0·51		0·64	
Oolong tea												
Never or almost never	2245	95	1·00	–	1·00	–	2702	52	1·00	–	1·00	–
Once/month to six times/week	2997	142	1·17	0·90, 1·52	1·05	0·80, 1·37	3696	77	1·05	0·74, 1·51	0·89	0·62, 1·28
Once/d or more	655	41	1·39	0·96, 2·02	1·12	0·77, 1·64	1245	46	2·00	1·34, 3·00	1·37	0·90, 2·07
P value for trend			0·12		0·58				0·0001		0·03	
Decaffeinated coffee												
Never or almost never	5394	249	1·00	–	1·00	–	6931		1·00	–	1·00	–
Once/month or more	503	29	1·21	0·82, 1·78	1·09	0·73, 1·61	712	164	0·74	0·40, 1·36	0·66	0·36, 1·23
P value for trend			0·34		0·69			11	0·33		0·19	
Black tea												
Never or almost never	4225	205	1·00		1·00		4586	98	1·00		1·00	
Once/month or more	1672	73	0·91	0·70, 1·19	0·88	0·67, 1·16	3057	77	1·29	0·96, 1·74	1·30	0·95, 1·77
P value for trend			0·48		0·37				0·10		0·11	
Chocolate snack pieces												
Never or almost never	2825	149	1·00	–	1·00	–	2494	74	1·00	–	1·00	–
Once/month to less than once/week	2199	98	0·83	0·64,1·07	0·84	0·65, 1·09	3546	67	0·68	0·49, 0·94	0·70	0·50, 0·98
Once/week or more	873	31	0·68	0·46, 1·00	0·65	0·43, 0·97	1603	34	0·79	0·53, 1·19	0·73	0·48, 1·13
P value for trend			0·06		0·04				0·53		0·32	

* Adjusted for age, smoking status, BMI, physical activity, length of education in years, alcohol consumption, total energy intake, fat intake and women's menopausal status to examine beverage and chocolate snacks, respectively.

association between coffee consumption and risk of diabetes was present even after controlling for caffeine intake in the present study.

Green tea consumption was not associated with the risk of diabetes in the present study. A prospective study in Japan reported a significant inverse association between green tea consumption and diabetes risk, primarily among women[15]. Two other studies in Japan failed to find an association between green tea consumption and risk of diabetes[16,21], although these studies were cross-sectionally conducted. In the present study, a higher consumption of oolong tea raised the risk of diabetes among women. In our data, an especially high incidence of diabetes was observed among women who reported consuming oolong tea twice per d or more. We speculated that participants who were at risk for diabetes may have chosen to drink oolong tea because of its reputed ability to cleanse the body of extra fat, although an additional analysis showed that the association between oolong tea consumption and risk of diabetes among women remained after the exclusion of participants who developed diabetes within the first 2 years during the follow-up. A previously conducted clinical trial reported that oolong tea consumption decreased the plasma glucose level among patients with type 2 diabetes[34]. More observational studies are needed to evaluate the association of consumption of oolong tea with the risk of diabetes.

The consumption of chocolate snacks was inversely associated with a risk of diabetes among men, and the association was also implied among women. Several previous studies included chocolate snacks to estimate total caffeine intake and assessed it with the risk of diabetes[17–19], but to our knowledge, no previous observational study has shown an association between chocolate snacks alone and risk of diabetes. The finding must be, however, interpreted with caution and any benefit derived from a possible reduction in the risk might be outweighed by the increased health risks, such as obesity, caused by the regular consumption of the high-energy snacks. The finding still leaves room for further evaluation of their components such as polyphenols for possible protective effects, although the possible effect of caffeine content cannot be completely eliminated. A clinical trial testing the insulin response to an oral glucose tolerance test indicated that polyphenol-rich dark chocolate improved insulin sensitivity in healthy subjects, which may support our finding[35].

The use of self-reported status of diabetes may be one of the limitations of the present study. A previous study conducted in Japan reported a substantial agreement between diabetes reported in a questionnaire and its diagnosis; 82 % of cases of self-reported diabetes were confirmed by medical records[36]. Even so, we were not able to determine the proportion of the participants who had diabetes and did not report it. Those subjects have been classified as not having diabetes, and this may attenuate the true association, if it exists. There is a possibility that subjects whose socio-economic status was high and who were health conscious were more likely to respond to the follow-up questionnaire, having the fact that the respondents were more likely to have high education levels than non-respondents. Furthermore, other dietary items might have contributed to the caffeine intake. The present study did not discuss caffeine intake from the consumption of sodas, since the FFQ did not allow us to distinguish sodas with caffeine from those without caffeine. The consumption of sodas was relatively low in the current population, and it slightly increased with the level of coffee consumption, and hence it would not have much impact on the results. There still exists a possibility that the study results are influenced by some residual confounders, such as family history of diabetes, on which information is not available, which prevents us from making a definitive conclusion.

The present study has several advantages. First, it was a community-based study, and the participants were men and women from a general Japanese population. The risk of diabetes in relation to the consumption of coffee and tea was prospectively evaluated after controlling for potential confounders in a multivariate model. The values of nutrient intake and physical activity included in the model were measured with a validated questionnaire. We evaluated the association not only with coffee but also with other kinds of tea and foods containing caffeine, including green tea, which is commonly consumed in Japan. Caffeine intake was estimated from coffee, tea and chocolate snacks and was evaluated separately from coffee consumption.

In summary, a modest inverse association between coffee consumption and risk of development of diabetes was observed among men and women in a community-based cohort from the general Japanese population. Green tea consumption and total caffeine intake appeared to have no relationship with the risk of diabetes. It was suggested that the association of coffee consumption with risk of diabetes was separate from the influence of caffeine intake on the risk. Further studies may be needed to investigate which substances in coffee play a role in the beneficial effect on the risk of diabetes, as well as the association of tea and chocolate snack consumption with the risk.

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H. S. and C. N. designed the study and directed the study implementation. C. N., H. S. and N. T. supervised the field activities and collected data. S. O. conducted the statistical analysis and all authors interpreted the analysis results. S. O. and C. N. initially drafted all the sections of the text, and K. N., K. F., T. K., N. T. and H. S. were responsible for critical revision of the manuscript. All authors contributed to and approved the final version of the manuscript.

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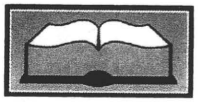

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Diet Based on the Japanese Food Guide Spinning Top and Subsequent Mortality among Men and Women in a General Japanese Population

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ABSTRACT

Background The Japanese Food Guide Spinning Top was developed by the Japanese Ministry of Health, Labor, and Welfare and the Ministry of Agriculture, Forestry, and Fishery to promote healthful diets.

Objective Adherence to the Japanese Food Guide Spinning Top was evaluated in terms of future mortality in a prospective cohort study.

Design A prospective cohort study among men and women in a general Japanese population.

Subjects/setting The cohort consisted of 13,355 men and 15,724 women residing in Takayama, Japan, in 1992. At baseline, a food frequency questionnaire was administered, and adherence to the food guide was measured based on consuming the recommended number of servings of grains, vegetables, fish and meat, milk, and fruits, as well as total daily energy intake and energy from snacks and alcoholic beverages. Higher scores indicated better adherence to the recommendations on a scale of 0 to 70. Based on data obtained from the Office of the National Vital Statistics, deaths occurring among members of the cohort were prospectively noted from 1992 to 1999.

Statistical analyses performed To assess the magnitude of association of adherence scores with subsequent mortality, a Cox proportional hazard model was applied to estimate hazard ratios (HRs) with 95% confidence intervals (CIs).

Results Among women, the adherence score was significantly associated with a lower risk of mortality from all causes (comparing highest and lowest quartiles of the score, HR 0.78, 95% CI 0.65 to 0.94, *P* for trend 0.01) in a multivariate analysis; noncardiovascular, noncancer causes (HR 0.69, 95% CI 0.50 to 0.96, *P* for trend 0.04) and cardiovascular disease (HR 0.76, 95% CI 0.56 to 1.04, *P* for trend 0.05). No statistically significant association was observed between the adherence score and mortality among men.

Conclusions The results suggest that diets based on the food guide have the benefit of reducing future mortality in women.

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Japanese diets have attracted considerable attention in Western countries because of the low rate of coronary heart disease and the long life expectancy in Japan (1-3). The Japanese Food Guide Spinning Top was introduced in 2005 by the Japanese Ministry of Health, Labor, and Welfare and the Ministry of Agriculture, Forestry, and Fishery (see the Figure). This pictorial food guide is based on the *Dietary Guidelines for Japanese*, which was drawn up in 2000 by the former Ministry of Education, the former Ministry of Health and Welfare, and the Ministry of Agriculture, Forestry and Fishery. The aim of the Japanese Food Guide Spinning Top is to provide recommended food choices and quantities for a healthful diet that can be easily adopted by the Japanese public (4,5). The food guide may be developed based on a common Japanese meal consisting of rice (*gohan-mono*),

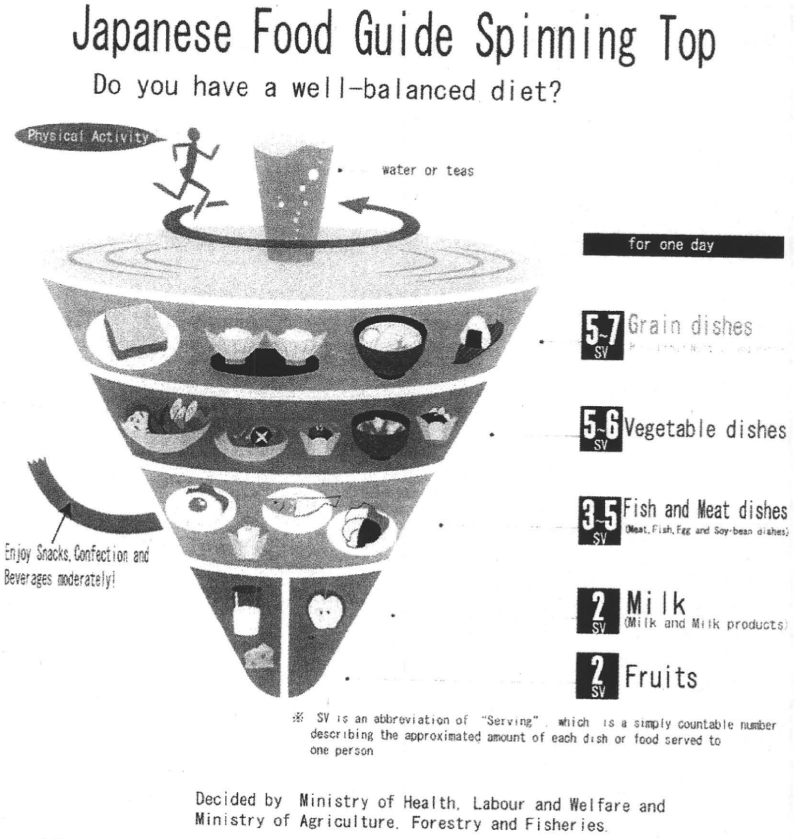

Figure. Graphic representation of the Japanese Food Guide Spinning Top. (Source: Japanese Ministry of Health, Labour and Welfare and Ministry of Agriculture, Forestry and Fisheries [4].) NOTE: This figure is available online at www.adajournal.org as part of a PowerPoint presentation.

soup (such as *miso* or *sumashi*), a main dish (*okazu*), and side dishes (*tsukeawase*). Although the guide was developed to promote healthful diets for Japanese people, the health benefits of following this guide have not been examined. The aim of our study was to evaluate whether diets based on the Japanese Food Guide Spinning Top are associated with reduced total mortality and mortality from cardiovascular disease, cancer, and noncardiovascular, noncancer causes in a prospective cohort study among men and women in a general Japanese population.

METHODS

Study Participants

The data were obtained from the Takayama Study in Japan, the details of which have been described elsewhere (6-8). Briefly, the study population was men and women residing in Takayama city who were aged 35 years or older in 1992. At the baseline, a self-administered questionnaire was distributed to 36,990 residents. Among them, subjects who left four out of nine two-page spreads or more all blank, who answered only 16 items or fewer out of 173 food items, who were regarded to be responded by the other person, who selected the food frequency category of "Never" for all food items, or who selected the food frequency category of "Once a day" or "Two or more times a day" for continuous 40 food items or over were excluded from the study (7). Furthermore, subjects who reported to have staple food (any kind of rice, bread, flour, or noodles) five times or more, meat seven times or more, fish seven times or more, or ethanol 400 mL or more per day were excluded (7). After the exclusion, the fixed cohort consisted of 31,552 subjects, 14,427 men and 17,125 women, yielding a response rate of 85.3%. Physician diagnoses of major diseases were reported in the questionnaire. For this study, those who reported cancer, myocardial infarction, angina, or stroke were excluded from the cohort, and the final cohort for the study consisted of 29,079 subjects, including 13,355 men and 15,724 women.

Definition of Scores and Data Collection

The Japanese Food Guide Spinning Top consists of five basic food group categories: grain dishes (including rice, bread, and noodles), vegetable dishes (including vegetables, mushrooms, potatoes, and seaweed), fish and meat dishes (including meat, fish, eggs, and soybeans), milk (milk and milk products), and fruits (fruits and 100% fruit juice counted as half the weight) (Figure). The amount of a particular type of food that counts as a serving is estimated in the food guide. One serving of grain dish is composed of about 40 g carbohydrates. In one serving of a vegetable dish, the main ingredient

Table 1. The recommended serving number and caloric intake per day for adults in the Japanese Food Guide Spinning Top

Age and Level of Physical Activity		Grain dishes	Vegetable dishes	Fish and meat dishes	Milk	Fruits	Total energy	Snacks and alcoholic beverages
Men	Women	← (serving) →					← (kcal) →	
70 y or older	70 y or older or 18-69 y with low physical activity	4-5	5-6	3-4	2	2	1,800±200	0-200
18-69 y with low physical activity	18-69 y with moderate or higher physical activity	5-7	5-6	3-5	2	2	2,200±200	0-200
18-69 y with moderate or higher physical activity	—	7-8	6-7	4-6	2-3	2-3	2,600±200	0-200

weighs about 70 g. One serving of a fish or meat dish contains about 6 g protein, and one serving of milk contains about 100 mg calcium. In one serving of fruits, the main ingredient weighs about 100 g (9). The recommended number of servings by food group and the recommended total energy intake are specified according to sex, age, and two levels of physical activity (Table 1). For this study, low physical activity was defined as a metabolic equivalents (METs)-hours per week level of less than 1.5 per week. About 25% of participants fell under this category, and all such participants had 0 METs-hours per week. Also in the food guide, the recommended number of kilocalories from snacks and alcoholic beverages together is set at 200 kcal/day for all people.

Based on the above recommended number of servings of the five food groups and two additional groups (energy from total diet and energy from snacks or alcoholic beverages), the scores measuring adherence to this food guide were retrospectively calculated from the information in food frequency questionnaire (FFQ). A person who consumed the recommended number of servings from any of five food groups or the recommended energy from either of the two additional groups received a score of 10 for that group. For a person who exceeded or fell short of the recommended servings or energy, the score was calculated proportionately between 0 and 10. For example, if a person consumed three of the recommended five to six servings of vegetables, the score was calculated as $(10\times3/5=6)$. Likewise, if a person consumed eight servings of fish and meat when the recommendation was three to five servings, the score was $(10-10\times[8-5]/5=4)$. When the calculation produced a negative score because of excess servings or energy, the score was converted to 0.

The FFQ was administered at the baseline of the cohort study in 1992. It was in a semiquantitative format measuring 169 food items, and validated for intake of major foods and nutrients (6). From the FFQ, total daily energy intake and intake of each nutrient and food item were estimated according to the Japanese Standard Tables of Food Composition, 5th edition, published by the Science and Technology Agency of Japan. Detailed information on the FFQ, including its validity and reproducibility, is described elsewhere (6-8). In a previous comparison of the outcomes of this FFQ with those of a 3-day food record, overestimates (meat, eggs, milk, vegetables, soy, as well as alcohol for men and women, and snacks for men), and underestimates (fish for men and snacks for women) of intake were observed. Such overestimations or underestimations were adjusted in the current data. Although the FFQ was administered at the baseline, the estimation of the score was conducted retrospectively because the food guide was issued after the cohort study was planned.

Information on baseline characteristics of the study cohort, such as age, height, weight, cigarette smoking, use of medication, and education level, was reported in the questionnaire at the baseline. For women, information about menopausal status was requested in the questionnaire. The level of regular physical activity was estimated based on the average hours per week spent performing various kinds of activities during the past year as reported in the questionnaire, and the number was translated into the METs-hours per week (10).

Ascertainment of Mortality

Deaths in the cohort were recorded between September 1992 and December 1999. After obtaining permission to review the death data from the Ministry of Internal Affairs and Communication, causes and dates of death were confirmed based on data from the Office of the National Vital Statistics. The Statistics and Information Department of the Japanese Ministry of Health and Welfare obtained all the causes of deaths, which were coded according to the International Classification of Diseases, 10th Revision. Those already coded according to the International Classification of Diseases, 9th Revision (1992-1994) were converted into International Classification of Diseases, 10th Revision. The major endpoint of this study was mortality from all causes, cardiovascular disease (I00 through I99 and Q25 through Q28), cancer (C00 through C97), and mortality from noncardiovascular, noncancer causes. This study was approved by the Ethics Committee at Gifu University Graduate School of Medicine.

Table 2. Baseline characteristics of 13,355 men and 15,724 women by quartile of the score on adherence to the Japanese Food Guide Spinning Top in Takayama Study, Japan

	Quartile of the Score				
	1	2	3	4	*P* value[a]
Men					
Median score	29.5	37.0	42.8	49.8	
	← *mean± standard deviation* →				
Age (y)	53.1±12.2	53.1±11.8	54.1±12.1	55.7±12.2	<0.01
Body mass index	22.7±2.9	22.6±2.7	22.4±2.7	22.3±2.8	<0.01
Physical activity (metabolic equivalents-h/wk)	31.2±46.4	27.2±41.0	25.4±40.1	24.4±37.8	<0.01
	← % →				
Currently married[b]	91.1	90.4	91.3	93.0	<0.01
Education 12 years or longer[b]	39.2	43.0	44.2	45.1	<0.01
Cigarette smoking status[b]					<0.01
Never smoker	12.3	15.0	18.0	22.0	
Current smoker	62.8	59.2	53.2	44.9	
Former smoker	25.0	25.8	28.9	33.2	
Aspirin use within half year	5.0	3.8	3.8	3.7	0.02
Hypertension	20.5	19.4	17.7	18.0	0.01
Diabetes	5.0	5.1	5.9	7.8	<0.01
Women					
Median score	33.0	41.8	47.4	53.6	
	← *mean± standard deviation* →				
Age (y)	54.5±13.0	54.7±13.3	55.2±13.0	56.1±12.7	<0.01
Body mass index	22.1±3.0	21.9±2.9	22.0±2.9	21.8±2.9	<0.01
Physical activity (metabolic equivalents-h/wk)	18.1±30.1	18.0±28.8	19.3±29.3	19.9±30.3	<0.01
	← % →				
Currently married[b]	74.4	75.9	75.4	75.1	0.51
Education 12 years or longer[b]	67.4	66.2	66.0	65.1	0.20
Cigarette smoking status[b]					<0.01
Never smoker	78.6	80.9	84.0	86.6	
Current smoker	17.1	14.3	11.5	9.5	
Former smoker	4.29	4.8	4.4	3.9	
Aspirin use within half year	8.8	6.9	6.4	4.9	<0.01
Hypertension	16.1	17.7	18.0	17.5	0.12
Diabetes	2.0	2.5	2.8	3.5	<0.01
Postmenopausal	55.7	56.5	59.9	63.4	<0.01

[a]One-way analysis of variance for continuous variables and χ^2 test for categorical variables.
[b]Only individuals whose information is available are included. Currently married: n=13,226 for men and n=15,469 for women, education in years: n=13,194 for men and n=15,477 for women, and current cigarette smokers: n=12,969 for men and n=14,090 for women.

Statistical Analysis

The scores on the food guide were analyzed by quartile. The intake of each nutrient was logarithmically transformed to approximately normalize the distribution and was adjusted for total energy intake using the regression analysis proposed by Willett (11) to minimize the effect of an association between total energy intake and mortality. While controlling for age, the partial correlation coefficients between the intake of each nutrient and the adherence score was calculated. The back-transformed (geometric) mean for each nutrient intake was obtained to determine differences in scores among quartiles.

To assess the magnitude of association of adherence scores with subsequent mortality, a Cox proportional hazard model was applied to estimate hazard ratios with 95% confidence intervals. To evaluate the linear trend with mortality, the adherence score was entered in regression models as a continuous variable. Both an age-adjusted model and a multivariate model adjusting for possible confounders: age, body mass index (in kilograms/meters^2, classified into quintile groups or a group of missing value), smoking status (current, past, never smoked, or status missing), physical activity, education (12 years or longer, or not), reported history of hypertension and diabetes, and women's menopausal status was considered. All the statistical analyses were performed with SAS software (version 9.1, 2004, SAS Institute Inc, Cary, NC).

Table 3. Daily nutrients intake by quartile of the score on adherence to the Japanese Food Guide Spinning Top in Takayama Study, Japan

	Men (n=13,355)					Women (n=15,724)				
	Geometric Mean[a]					Geometric Mean[a]				
	Quartile of the Score					Quartile of the Score				
	1	2	3	4	ρ^b	1	2	3	4	ρ^b
Total energy (kcal)[c]	3,182	2,598	2,370	2,294	−0.44	2,782	1,993	1,895	1,829	−0.58
Carbohydrate (g)	331	341	352	364	0.25	297	296	295	295	−0.03
Total fat intake (g)	51.0	52.7	55.3	58.7	0.19	46.8	49.1	50.9	51.9	0.17
Saturated fat (g)	13.5	14.2	15.3	16.8	0.27	12.9	13.4	14.1	14.7	0.17
Monounsaturated fat (g)	17.7	18.2	18.8	19.6	0.14	15.9	16.6	17.0	17.2	0.13
Polyunsaturated fat (g)	14.3	14.5	14.9	15.4	0.10	13.1	13.5	13.8	14.0	0.10
Salt (g)	12.8	12.6	13.0	13.6	0.06	11.6	11.7	12.1	12.6	0.10
Cholesterol (mg)	350	350	359	371	0.05	286	304	317	326	0.14
Protein (g)	84.7	84.7	87.2	90.4	0.12	73.4	74.8	76.8	77.9	0.13
Dietary fiber (g)	13.2	13.6	14.7	16.9	0.26	14.1	14.0	15.1	16.8	0.17
Calcium (mg)	568	595	666	776	0.33	581	601	663	725	0.22
Vitamin A (IU)	828	859	949	1,118	0.24	857	887	977	1,122	0.21
Vitamin C (mg)	110	118	129	151	0.25	118	120	130	147	0.17
Vitamin E (mg)	9.3	9.4	9.9	10.7	0.17	9.2	9.3	9.6	10.1	0.12
Folate (μg)	393	397	420	469	0.19	387	386	414	456	0.16

[a]Values for nutrient intake are energy adjusted.
[b]Correlation with the score on the food guide, partially controlling for age. Each nutrient intake was log transformed and adjusted for total energy intake.
[c]Arithmetic means of raw values.

RESULTS

The mean scores for adherence to the food guide were 39.6 among men and 43.6 among women. Baseline characteristics of the study participants across quartile categories for the adherence score on the food guide are presented in Table 2. Participants with high scores were less likely to smoke, more likely to have 12 or more years of education, and more likely to be diagnosed with diabetes. The adherence score on the food guide was significantly associated with age, and older participants were more likely to obtain a higher score. Daily servings of meat and fish were likely to exceed the recommended number (72% of men and 62% of women with exceeding the recommended number), whereas milk intake was less likely to reach the recommended serving number (79% of men and 64% of women with below the recommended serving number). Individuals with high physical activity levels have high total energy intake, especially among men (correlation coefficients between total energy intake and METs-hours per week were 0.16 among men and 0.08 among women). Table 3 presents the geometric mean of energy-adjusted nutrient intake for each quartile of the adherence score, and the correlation between nutrient intake and adherence score.

The relation of the adherence score to subsequent mortality is presented in Table 4. Among women, the risks of mortality from all causes, and noncardiovascular, noncancer causes were significantly lower for women in the highest quartile compared to those in the lowest quartile of the adherence score, and the analysis of linear trend also showed inverse associations. A significant association between the risk of mortality from cardiovascular diseases and the adherence score was also observed in the trend analysis among women. Such associations observed in the age-adjusted model were even stronger in the multivariate model. Among men, no significant association was observed between the adherence score and later mortality.

DISCUSSION

The results of this prospective study among a general Japanese population imply that diets based on the Japanese Food Guide Spinning Top have a beneficial influence on future mortality among women. With higher adherence scores among women, reductions in mortality from all causes and noncardiovascular, noncancer related causes were observed, and a weak reduction in mortality from cardiovascular disease was also observed. No relation to mortality from cancer was observed among men or women.

The Healthy Eating Index (HEI) is an index of overall diet quality, developed in the United States based on 1990 US Dietary Guidelines and the 1992 US Department of Agriculture Food Guide Pyramid (12). Half components of HEI were calculated based on conformity to the recommended serving of five food groups: grains, vegetables, fruits, milk, and meat. These food groups showed a resemblance to the components of the Japanese Food Guide Spinning Top. Although MyPyramid food guide was released later in United States, its similarity with the Japanese Food Guide Spinning Top was still noted (13). HEI was associated with a small reduction in cardiovascular disease risk among men but was not associated with cancer risk among either men or women (14,15). HEI score was updated later as a nine-component Alternate Healthy Eating Index (AHEI) and better predicted chronic disease risk than the HEI (16). AHEI

Table 4. Hazard ratio (HR) of mortality by quartile of the scores on adherence to the Japanese Food Guide Spinning Top among 13,355 men and 15,724 women in the Takayama Study, Japan

	Quartile of Score Based on the Food Guide				
Mortality	**1**	**2**	**3**	**4**	***P* for trend[a]**
Men					
All causes					
No. of deaths	287	257	274	345	
Age-adjusted HR (95% confidence interval)	1	0.91 (0.77-1.08)	0.88 (0.75-1.04)	1.00 (0.85-1.17)	0.98
Multivariate HR (95% confidence interval)[b]	1	0.90 (0.76-1.06)	0.87 (0.73-1.02)	1.01 (0.86-1.19)	0.91
Cardiovascular disease					
No. of deaths	75	66	72	95	
Age-adjusted HR (95% confidence interval)	1	0.90 (0.64-1.25)	0.89 (0.64-1.22)	1.05 (0.77-1.42)	0.75
Multivariate HR (95% confidence interval)[b]	1	0.90 (0.64-1.25)	0.86 (0.62-1.20)	1.06 (0.78-1.45)	0.70
Cancer					
No. of deaths	95	93	97	115	
Age-adjusted HR (95% confidence interval)	1	0.99 (0.74-1.32)	0.95 (0.72-1.26)	1.02 (0.78-1.34)	0.94
Multivariate HR (95% confidence interval)[b]	1	0.98 (0.73-1.30)	0.95 (0.71-1.26)	1.05 (0.80-1.39)	0.76
Other (noncardiovascular, noncancer)					
No. of deaths	117	98	105	135	
Age-adjusted HR (95% confidence interval)	1	0.85 (0.65-1.11)	0.83 (0.64-1.08)	0.95 (0.74-1.22)	0.71
Multivariate HR (95% confidence interval)[b]	1	0.83 (0.63-1.08)	0.80 (0.61-1.04)	0.94 (0.73-1.21)	0.24
Women					
All causes					
No. of deaths	240	227	221	211	
Age-adjusted HR (95% confidence interval)	1	0.91 (0.76-1.09)	0.86 (0.72-1.03)	0.79 (0.66-0.95)	0.01
Multivariate HR (95% confidence interval)[b]	1	0.87 (0.73-1.05)	0.86 (0.72-1.04)	0.78 (0.65-0.94)	0.01
Cardiovascular disease					
No. of deaths	88	92	73	74	
Age-adjusted HR (95% confidence interval)	1	0.99 (0.74-1.33)	0.77 (0.57-1.06)	0.77 (0.56-1.04)	0.04
Multivariate HR (95% confidence interval)[b]	1	0.95 (0.71-1.28)	0.79 (0.58-1.08)	0.76 (0.56-1.04)	0.05
Cancer					
No. of deaths	69	49	66	70	
Age-adjusted HR (95% confidence interval)	1	0.69 (0.48-0.99)	0.90 (0.64-1.26)	0.92 (0.66-1.28)	0.82
Multivariate HR (95% confidence interval)[b]	1	0.68 (0.47-0.98)	0.89 (0.64-1.26)	0.92 (0.66-1.29)	0.84
Other (noncardiovascular, noncancer)					
No. of deaths	83	86	83	67	
Age-adjusted HR (95% confidence interval)	1	0.99 (0.73-1.34)	0.93 (0.69-1.26)	0.73 (0.53-1.00)	0.06
Multivariate HR (95% confidence interval)[b]	1	0.94 (0.69-1.27)	0.93 (0.68-1.26)	0.69 (0.50-0.96)	0.04

[a]To test for the linear trend with mortality, the median value of the score based on the food guide per quartile was used.

[b]Adjusted for age, body mass index, smoking status (current, past, never smoker, or status missing), physical activity (metabolic equivalents-h/wk), education (12 years or longer or not), history of hypertension and diabetes, and women's menopausal status.

NOTE: Information from this table is available online at www.adajournal.org as part of a PowerPoint presentation.

added several new components. One such component is that if appropriate serving of alcohol consumption was maintained, which was similarly considered in the Japanese Food Guide Spinning Top. In a prospective cohort study among women in the United States (age range 40 to 93 years, 87% white), the association of the risk of mortality with a Recommended Food Score based on dietary guidelines was evaluated, and the Recommended Food Score was inversely associated with all causes of mortality (17). The National Health Interview Surveys in the United States (18) showed that the recommended Foods and Behavior score, which reflects the recommended foods and dietary behaviors, modestly reduced the risk of future mortality among men and women. In the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study in the United States, dietary diversity based on five food groups similar to those in our study was measured, and its inverse association with all-cause mortality (19) and with mortality from cardiovascular disease, cancer (except in women), and noncardiovascular, noncancer causes (20) were reported. Considering the similarity in some of the patterns of recommended food groups, the results of our study were comparable to these studies. The measures used in these studies did not thoroughly consider the overconsumption of each component of a food group. The results of our study suggest that, to reduce the risk of mortality, the appropriate consumption of food in each category is important. One previous study using a healthful diet indicator defined by the World Health Organization dietary guidelines analyzed overconsumption by defining an indicator for a healthful diet as consumption of each nutri-

ent or food group within the recommended range. The results showed that the indicator was inversely associated with mortality (21).

The results of our study indicate that diets based on the food guide are not associated with a risk of mortality from cancer. It was previously reported that diets in accordance with the food guidelines or food patterns based on recommended consumption from food groups were associated with a lowered risk of esophageal cancer (22,23) and estrogen receptor-negative breast cancer (24). Similarly, in terms of cancer risk, the benefit of diets based on the Japanese Food Guide Spinning Top might be limited to cancer at specific sites. Using some of the diet recommendations published by the American Institute for Cancer Research, the authors of one study suggested that adherence to the recommendations reduced the risk of cancer incidence but reduced the risk of cancer mortality to a lesser degree (25). Likewise, the benefit in terms of cancer risk of diets based on the Japanese food guide may be limited to the incidence of cancer. A further assessment of this issue was not conducted due to the unavailability of data on the incidence of cancer in all sites.

No benefit of dietary adherence was observed among men in our study considering that the overall mean adherence score was lower among men than that among women. The scores might not have been high enough to derive benefits from diets based on the food guide among men in our study. Alternatively, men with high levels of physical activity may need a higher allowance of energy intake than that recommended in the food guide. The level of physical activity was higher among men than among women and was positively associated with an increased amount of total energy intake. Such an excess intake of energy lowered the adherence score. Two levels of physical activity (low level and moderate or higher level) were defined in the food guide in association with the levels of energy intake, but additional categories for people with higher levels of physical activity may be needed. Moreover, the score on the food guide was positively correlated with the consumption of saturated fat, and the association was stronger among men than among women. In the Japanese Food Guide Spinning Top, there is no recommendation for restricting dietary fat, whereas the HEI and AHEI based on US guidelines considers fat intake. The intake of saturated fat is a major risk factor for cardiovascular disease (26,27), which could explain the less-pronounced association between the adherence score and mortality in our study. Nevertheless, fat is one of the major sources of energy (11), and the consideration of total energy intake in the Japanese food guide might substitute for the need to consider fat intake to a certain degree. Further reasons for the observed differences between men and women may be biological or sex-based in regard to some uncontrolled confounders.

The adherence scores in this study were positively correlated with the intake of some micronutrients estimated from the FFQ after adjustment for total energy intake. Therefore, diets based on the food guide are likely to meet micronutrients requirements, which could explain the reduced mortality found in our study. As in this study, a study based on the third National Health and Nutrition Examination Survey showed that HEI scores were positively correlated with a wide range of blood nutrients that were biomarkers of fruit and vegetable intake, such as serum folate, vitamins C and E, and carotenoids (28).

Limitations of this study include the fact that the FFQ was not specifically designed to measure adherence to this specific food guide. Although the FFQ was validated for major food and nutrient intakes, it is uncertain whether using the FFQ to measure adherence to the food guide was appropriate. The Japanese Food Guide Spinning Top was originally developed for easy use in the actual diets of the general Japanese public (5), not for academic research. The score on the food guide was retrospectively assigned after the follow-up of the study. However, this may not give the prominent influence to the study result because each component of the score was derived from the information in the FFQ, administered at the baseline of the study with using the provided definitions. In addition, the information in deaths occurred was not updated after 1999, and the data may have limited power to detect the association with the mortality.

CONCLUSIONS

This study examined the quality and quantity of total dietary intake and its relationship to health by measuring adherence to the Japanese Food Guide Spinning Top. The results are suggestive of a reduced risk of mortality from cardiovascular disease, noncardiovascular, noncancer causes, and all causes among women. The associations for men and the effects on the risk of cancer for men or women remain unclear. A further assessment of the benefit of the diets based on the food guide in relation to biomarkers or risk factors in major chronic disease would be interesting.

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