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Green tea and death from pneumonia in Japan: the Ohsaki cohort study[1–3]

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ABSTRACT

Background: Experimental and animal studies have shown the activities of catechins, the main constituents of green tea, against infectious agents. No data are available on the association between green tea consumption and the risk of pneumonia in humans.

Objective: We examined the association between green tea consumption and death from pneumonia in humans.

Design: We conducted a population-based cohort study, with follow-up from 1995 to 2006. The participants were National Health Insurance beneficiaries in Japan (19,079 men and 21,493 women aged 40–79 y). We excluded participants for whom data on green tea consumption frequency were missing or who had reported a history of cancer, myocardial infarction, stroke, and extreme daily energy intake at baseline. We used Cox proportional hazards regression analysis to calculate hazard ratios (HRs) and their 95% CIs for death from pneumonia according to green tea consumption.

Results: Over 12 y of follow-up, we documented 406 deaths from pneumonia. In women, the multivariate HRs of death from pneumonia that were associated with different frequencies of green tea consumption were 1.00 (reference) for <1 cup/d, 0.59 (95% CI: 0.36, 0.98) for 1–2 cups/d, 0.55 (95% CI: 0.33, 0.91) for 3–4 cups/d, and 0.53 (95% CI: 0.33, 0.83) for ≥5 cups/d, respectively (*P* for trend: 0.008). In men, no significant association was observed.

Conclusion: Green tea consumption was associated with a lower risk of death from pneumonia in Japanese women. *Am J Clin Nutr* 2009;90:672–9.

INTRODUCTION

Pneumonia ranks as the fourth-leading cause of death in Japan, where it is responsible for ≈10% of total deaths, despite the development of effective antimicrobial chemotherapy (1). To prevent the disease, the association between lifestyles, such as fish consumption, fatty acid consumption, smoking, alcohol consumption, or exercise, and pneumonia has been investigated with prospective cohort study design (2–5). These studies showed that smoking was a risk factor for pneumonia, but no definite conclusion was available for other factors.

For thousands of years, plants have played a significant role in maintaining human health and improving the quality of human life (6). Tea catechins, the main constituents of green tea, have received attention because of their possible antiviral and antimicrobial activities (7, 8). Experimental and animal studies have shown the activities of catechins against a variety of infectious agents (9–13). To our knowledge, no epidemiologic data are available on the association between green tea consumption and the risk of pneumonia in humans. If green tea does protect humans against pneumonia, this beverage would be a useful additional agent to ease the threat of the disease.

We therefore designed this prospective study to examine the association between green tea consumption and death from pneumonia within a large population-based cohort in Japan.

SUBJECTS AND METHODS

Study population

The present data were derived from the Ohsaki National Health Insurance (NHI) beneficiaries cohort study. The details of the study project have been described in previous reports (14, 15). In brief, we delivered a self-administered questionnaire between October and December 1994 to all NHI beneficiaries, aged 40–79 y, living in the catchment area of Ohsaki Public Health Center, Miyagi prefecture, northeast Japan. The Ohsaki Public Health Center, a local government agency, provides preventive health services for the residents of 14 municipalities in Miyagi prefecture. Of 54,996 eligible individuals, 52,029 (95%) responded. The study protocol was approved by the Tohoku University School of Medicine Ethics Committee. We considered the return of self-administered questionnaires signed by the study participants to imply their consent to participate.

From 1 January 1995, we started prospective collection of data on the date of death and withdrawal from the NHI, by obtaining NHI withdrawal history files from the local NHI Association. We excluded 776 participants because they had withdrawn from the NHI before collection of the NHI withdrawal history files. Thus, 51,253 participants formed the study cohort.

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[2] Supported by a Health Sciences Research Grant for Health Services (H18-Choju-Ippan-014, H20-Choju-Ippan-001, H20-Junkankitou [Seisyu]-Ippan-013), Ministry of Health, Labour, and Welfare, Japan.

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Received February 6, 2009. Accepted for publication June 24, 2009.
First published online July 22, 2009; doi: 10.3945/ajcn.2009.27599.

Am J Clin Nutr 2009;90:672–9. Printed in USA.

Of these study participants, we excluded those for whom data on green tea consumption frequency were missing (n = 6791) or who reported extreme daily energy intake (n = 440; sex-specific cutoffs for upper 0.5%, 3575.2 kcal/d for men and 2286.6 kcal/d for women; for lower 0.5%, 348.9 kcal/d for men and 200.0 kcal/d for women), because an extreme numerical value might reflect possible misreporting of self-reported data on the frequency of consumption of each food. We also excluded participants who reported a history of cancer (n = 1488), myocardial infarction (n = 1238), or stroke (n = 975) at the baseline, because these diseases could have affected their diet and lifestyle. Consequently, 40,572 participants (19,079 men and 21,493 women) were included in this analysis.

Measurements

The self-administered questionnaire used in the baseline survey included items on dietary intake [40-item food-frequency questionnaire (FFQ)], history of diseases, family history of diseases, drinking habit, smoking habit, job status, education, body weight, height, time spent walking per day, and physical function status. The 40-item FFQ asked about the average frequency of consumption of each food. The frequency of green tea consumption was divided into 5 categories: never, occasional, 1–2 cups/d, 3–4 cups/d, and ≥5 cups/d. Within the study region, the volume of a typical cup of green tea is 100 mL. We had previously conducted a validation study of the FFQ (16). In brief, 113 participants provided four 3-d food records within a period of 1 y and subsequently responded to the FFQ. Spearman's correlation coefficient between the amounts of green tea consumed according to the food records and the amounts consumed according to the FFQ was 0.71 for men and 0.53 for women. We examined the daily consumption of 40 food items, total energy, and nutrients from the FFQ by converting the selected frequency category for each food to a daily intake, using portion sizes based on the median values observed in four 3-d food records.

Body mass index (BMI; in kg/m^2) was calculated from self-reported data. Physical function status was assessed by using the 6-item physical function status measure of the Medical Outcomes Study (MOS) Short-Form General Health Survey. On the basis of their responses, the subjects were classified into 3 groups: those who were able to perform vigorous or moderate activity (MOS score of 5–6), those who were capable of light activity (MOS score of 2–4), and those who were capable only of self-care or unable to do anything unaided (MOS score of 0–1).

Follow-up

The endpoint was death from pneumonia. To follow-up the participants for death and migration, we reviewed the NHI Withdrawal History files for the period from 1 January 1995 to 31 December 2006. When a participant was withdrawn from the NHI system because of death, emigration, or employment, the date of withdrawal and its reason were coded on the files. Because we were unable to obtain subsequent information on the participants who withdrew from the NHI, we discontinued follow-up of participants who withdrew from the NHI system because of emigration or employment.

Data on causes of death were based on the death certificates filed at Ohsaki Public Health Center. Death certificates must be completed by a physician, and from 1995, in Japan, the cause of death has been recorded according to the rules for selecting the underlying cause of death in the *International Statistical Classification of Diseases and Related Health Problems, 10th revision* (ICD-10) (17). All death certificates are submitted to a local government office and forwarded to the Public Health Center in the area of residence. Death certificates are then sent to the Japan Ministry of Health, Labour, and Welfare, and the primary cause of death is reassessed and coded by trained physicians according to the ICD-10. We limited deaths from influenza and pneumonia (J10–J18), and we did not include aspiration pneumonia (J69) because the cause would be largely different from the former (J10–J18). Thus, for deaths from pneumonia identified in this study, pneumonia was the primary cause of death.

Statistical analysis

From 1 January 1995 to 31 December 2006, we prospectively counted the number of person-years of follow-up for each participant from the beginning of follow-up until the date of death, withdrawal from the NHI, or the end of the study period, whichever occurred first. We used Cox proportional hazards regression analysis to calculate the hazard ratios (HRs) and their 95% CIs of death from pneumonia according to green tea consumption categories and to adjust for potentially confounding variables with the SAS version 9.1 statistical software package (SAS Institute Inc, Cary, NC). For all models, the proportional hazards assumptions were tested and met through addition of time-dependent covariates to the models. Dummy variables were created for green tea consumption categories.

We combined the lower 2 categories of green tea consumption into the single category of <1 cup/d because of the small number of participants in each of these categories (7.3% never and 19.0% occasionally). The lowest category of green tea consumption (<1 cup/d) was used as a reference category. Furthermore, we repeated the analysis based on the 5 categories of green tea consumption, without combining the lower 2 categories, using the category of never as a reference. The P values for analysis of linear trends were calculated by scoring the categories, from 1 for the lowest category to 4 for the highest category, and entering the number as a continuous term in the regression model. All reported P values were 2-tailed, and $P <$ 0.05 was considered statistically significant.

We considered the following variables to be potential confounders a priori with clinical significance: age (as a continuous variable); years of education (<10 y of education or ≥10 y of education); BMI (<18.5, 18.5–24.9, or ≥25.0); time spent walking (<1 h/d or ≥1 h/d); physical function status (those who were able to perform vigorous or moderate activity, those who were capable of light activity, those who were capable of only self-care or unable to do anything unaided); history of hypertension (yes or no); history of diabetes mellitus (yes or no); history of gastric ulcer (yes or no); history of tuberculosis (yes or no); smoking status (never, former, currently smoking <20 cigarettes/d, or currently smoking ≥20 cigarettes/d); alcohol consumption (never, former, currently); daily total energy intake (continuous variable); daily consumption of miso (soybean paste) soup (yes or no); daily consumption of soybean products, total fish, and total green or yellow vegetables (for each food, continuous variable); and consumption of coffee (<1 cup/d or

≥1 cup/d). To correct the estimate for socioeconomic status, the models were adjusted for years of education. Time spent walking was used as an indicator of physical activity because it is the most common type of physical activity among middle-aged and older individuals in Japan. The validity and reproducibility of the question on time spent walking has been reported previously (18). Before including the above variables into the multivariate models, interactions between green tea consumption and confounders were tested through the addition of cross-product terms to the multivariate model.

We conducted stratified analyses by age, physical function status, and smoking status. We stratified by age (<70 y or ≥70 y), because death from pneumonia increases with age (19, 20). We also stratified by physical function status, because we considered that the participants with limited physical function (MOS score of 0–1) would be at high risk of aspiration pneumonia. In addition, stratified analysis by smoking status was conducted, because smoking is a risk factor for pneumonia (4, 5). For stroke, our previous study found an inverse association between green tea consumption and death from stroke (15). Therefore, to

TABLE 1
Baseline characteristics of men according to green tea consumption (n = 19,079)

	Green tea consumption				
Characteristics	<1 cup/d (n = 5775)	1–2 cups/d (n = 4313)	3–4 cups/d (n = 3897)	≥5 cups/d (n = 5094)	P value[1]
Age (y)	57.2 ± 10.7[2]	57.3 ± 10.8	59.8 ± 10.3	61.4 ± 9.9	<0.0001
Years of education [n (%)]					<0.0001
<10 y	3460 (62.6)	2356 (56.6)	2206 (58.5)	3041 (61.6)	
≥10 y	2067 (37.4)	1808 (43.4)	1564 (41.5)	1894 (38.4)	
BMI [n (%)]					<0.006
<18.5 kg/m^2	179 (3.3)	138 (3.4)	103 (2.7)	193 (3.9)	
18.5–24.9 kg/m^2	3824 (69.6)	2929 (71.0)	2713 (72.2)	3489 (71.3)	
≥25.0 kg/m^2	1489 (27.1)	1056 (25.6)	942 (25.1)	1215 (24.8)	
Time spent walking [n (%)]					<0.006
<1 h/d	2676 (49.9)	2062 (51.0)	1960 (53.7)	2443 (51.4)	
≥1 h/d	2685 (50.1)	1979 (49.0)	1693 (46.3)	2308 (48.6)	
Physical function status [n (%)]					<0.0001
Able to perform vigorous or moderate activity	4663 (83.0)	3579 (85.2)	3258 (85.6)	4251 (85.3)	
Capable of light activity	627 (11.1)	411 (9.8)	388 (10.2)	527 (10.6)	
Capable of self-care or unable to do anything	329 (5.9)	210 (5.0)	160 (4.2)	203 (4.1)	
History of hypertension [n (%)]					<0.0001
Yes	1238 (21.4)	1003 (23.3)	986 (25.3)	1248 (24.5)	
No	4537 (78.6)	3310 (76.7)	2911 (74.7)	3846 (75.5)	
History of diabetes mellitus [n (%)]					0.09
Yes	386 (6.7)	284 (6.6)	304 (7.8)	371 (7.3)	
No	5389 (93.3)	4029 (93.4)	3593 (92.2)	4723 (92.7)	
History of gastric ulcer [n (%)]					0.002
Yes	1102 (19.1)	848 (19.7)	794 (20.4)	1116 (21.9)	
No	4673 (80.9)	3465 (80.3)	3103 (79.6)	3978 (78.1)	
History of tuberculosis [n (%)]					<0.0001
Yes	205 (3.5)	151 (3.5)	206 (5.3)	307 (6.0)	
No	5570 (96.5)	4162 (96.5)	3691 (94.7)	4787 (94.0)	
Smoking status [n (%)]					<0.0001
Never	1151 (21.7)	804 (20.4)	722 (19.9)	824 (17.5)	
Former	1289 (24.3)	964 (24.4)	1022 (28.2)	1349 (28.6)	
Current, <20 cigarettes/d	930 (17.6)	713 (18.0)	650 (17.9)	898 (19.1)	
Current, ≥20 cigarettes/d	1926 (36.4)	1471 (37.2)	1230 (34.0)	1640 (34.8)	
Alcohol consumption [n (%)]					<0.0001
Never	931 (16.5)	615 (14.6)	563 (14.8)	918 (18.5)	
Former	540 (9.6)	379 (9.0)	372 (9.8)	547 (11.1)	
Current	4161 (73.9)	3214 (76.4)	2865 (75.4)	3490 (70.4)	
Total energy intake (kcal/d)	1783 ± 612.5	1812 ± 603.3	1852 ± 587.7	1901 ± 591.3	<0.0001
Daily dietary consumption					
Miso (soybean paste) soup [n (%)]	4914 (85.1)	3807 (88.3)	3504 (89.9)	4633 (91.0)	<0.0001
Soybean products (g/d)	47 ± 28.7	50 ± 28.3	53 ± 27.7	57 ± 26.9	<0.0001
Total fish (g/d)	55 ± 35.5	58 ± 34.8	61 ± 34.3	67 ± 34.6	<0.0001
Green or yellow vegetables (g/d)	62 ± 42.9	67 ± 43.2	72 ± 43.3	78 ± 45.9	<0.0001
Coffee, ≥1 cup/d [n (%)]	2357 (44.3)	1892 (50.9)	1415 (42.5)	1513 (35.7)	<0.0001

[1] ANOVA or chi-square test.
[2] Mean ± SD (all such values).

distinguish the relation between green tea consumption and pneumonia risk and that between green tea consumption and stroke risk, we conducted a sensitivity analysis with the use of a subset of data that was restricted to participants with a very low risk of stroke, who had no history of hypertension, and had never smoked.

To minimize the possibility that diet or lifestyle factors had changed in response to subclinical disease, we repeated all analyses after excluding participants who had died in the first 3 y of follow-up. To ensure that the estimates were not biased by multicollinearity, the age-adjusted HRs for the green tea consumption categories were also calculated and compared with the multivariate-adjusted HRs.

RESULTS

Baseline characteristics of the participants according to green tea consumption category are shown in **Table 1** and **Table 2**.

TABLE 2
Baseline characteristics of women according to green tea consumption (n = 21,493)

	Green tea consumption				
Characteristics	<1 cup/d (n = 4877)	1–2 cups/d (n = 4458)	3–4 cups/d (n = 4950)	≥5 cups/d (n = 7208)	P value[1]
Age (y)	58.5 ± 10.8[2]	59.6 ± 10.5	61.2 ± 9.7	62.2 ± 9.2	<0.0001
Years of education [n (%)]					<0.0001
<10 y	2683 (58.9)	2288 (54.3)	2545 (54.0)	3980 (58.0)	
≥10 y	1689 (41.1)	1926 (45.7)	2167 (46.0)	2877 (42.0)	
BMI [n (%)]					0.003
<18.5 kg/m^2	209 (4.6)	158 (3.7)	192 (4.1)	252 (3.7)	
18.5–24.9 kg/m^2	2942 (64.3)	2770 (65.3)	3096 (65.5)	4,335 (62.9)	
≥25.0 kg/m^2	1422 (31.1)	1317 (31.0)	1438 (30.4)	2301 (33.4)	
Time spent walking [n (%)]					0.0006
<1 h/d	2444 (55.7)	2295 (56.1)	2670 (59.2)	3836 (58.7)	
≥1 h/d	1941 (44.3)	1794 (43.9)	1843 (40.8)	2703 (41.3)	
Physical function status [n (%)]					<0.0001
Able to perform vigorous or moderate activity	3171 (67.1)	2963 (68.6)	3313 (68.4)	4925 (70.0)	
Capable of light activity	936 (19.8)	859 (19.9)	1039 (21.4)	1482 (21.1)	
Capable of self-care or unable to do anything	621 (13.1)	496 (11.5)	494 (10.2)	624 (8.9)	
History of hypertension [n (%)]					<0.0001
Yes	1203 (24.7)	1212 (27.2)	1413 (28.5)	2157 (29.9)	
No	3674 (75.3)	3246 (72.8)	3537 (71.5)	5051 (70.1)	
History of diabetes mellitus [n (%)]					0.06
Yes	252 (5.2)	204 (4.6)	264 (5.3)	413 (5.7)	
No	4625 (94.8)	4254 (95.4)	4686 (94.7)	6795 (94.3)	
History of gastric ulcer [n (%)]					0.70
Yes	531 (10.9)	510 (11.4)	545 (11.0)	774 (10.7)	
No	4346 (89.1)	3948 (88.6)	4405 (89.0)	6434 (89.3)	
History of tuberculosis [n (%)]					0.0002
Yes	123 (2.5)	102 (2.3)	161 (3.2)	253 (3.5)	
No	4754 (97.5)	4356 (97.7)	4789 (96.8)	6955 (96.5)	
Smoking status [n (%)]					<0.0001
Never	3370 (87.5)	3231 (91.6)	3654 (92.9)	5062 (89.3)	
Former	112 (2.9)	84 (2.4)	91 (2.3)	152 (2.7)	
Current, <20 cigarettes/d	236 (6.1)	138 (3.9)	146 (3.7)	316 (5.6)	
Current, ≥20 cigarettes/d	136 (3.5)	73 (2.1)	44 (1.1)	140 (2.4)	
Alcohol consumption [n (%)]					<0.0001
Never	2883 (70.7)	2697 (73.0)	3092 (74.9)	4341 (72.4)	
Former	220 (5.4)	146 (3.9)	159 (3.9)	248 (4.1)	
Current	977 (23.9)	853 (23.1)	876 (21.2)	1407 (23.5)	
Total energy intake (kcal/d)	1188 ± 365.9	1231 ± 347.9	1268 ± 329.8	1310 ± 330.4	<0.0001
Daily dietary consumption					
Miso (soybean paste) soup [n (%)]	4004 (82.1)	3886 (87.2)	4409 (89.1)	6395 (88.7)	<0.0001
Soybean products (g/d)	43 ± 24.2	47 ± 23.1	50 ± 22.0	51 ± 21.5	<0.0001
Total fish (g/d)	47 ± 30.6	50 ± 30.3	54 ± 29.0	57 ± 29.7	<0.0001
Green or yellow vegetables (g/d)	72 ± 47.0	81 ± 47.4	85 ± 46.6	89 ± 48.4	<0.0001
Coffee, ≥1 cup/d [n (%)]	1829 (42.2)	1783 (47.0)	1599 (39.1)	1715 (29.4)	<0.0001

[1] ANOVA or chi-square test.
[2] Mean ± SD (all such values).

Men and women with higher green tea consumption were significantly older and had a history of hypertension and tuberculosis, but they were less likely to have time spent walking. They were also more likely to have a higher energy intake and to consume individual foods such as miso soup, soybean products, total fish, and total green or yellow vegetables. No apparent associations were observed between green tea consumption categories and years of education and alcohol consumption. Men were more likely to have a history of gastric ulcer, but they were less likely to be obese and to have never smoked. Women were more likely to be obese and to have a history of diabetes mellitus.

Over 12 y of follow-up (406,824 person-years), we documented 406 deaths from pneumonia. A total of 6033 participants were lost to follow-up during the study period because of withdrawal from the NHI system, and the follow-up rate was 85.1%. The association between green tea consumption and the HRs and associated 95% CIs of death from pneumonia are shown in **Table 3**. We found inverse associations between green tea consumption and death from pneumonia in women but not in men. In women, the multivariate HRs of death from pneumonia associated with different frequencies of green tea consumption were 1.00 (reference) for <1 cup/d, 0.59 (95% CI: 0.36, 0.98) for 1–2 cups/d, 0.55 (95% CI: 0.33, 0.91) for 3–4 cups/d, and 0.53 (95% CI: 0.33, 0.83) for ≥5 cups/d (*P* for trend: 0.008). Comparison between the age-adjusted model and the multivariate model suggested that the estimates were not biased by multicollinearity. The multivariate HRs of death from pneumonia according to the 5 categories of green tea consumption, without combining the lower 2 categories, were 1.00 (reference) for never, 0.56 (95% CI: 0.30, 1.02) for occasional, 0.41 (95% CI: 0.22, 0.76) for 1–2 cups/d, 0.38 (95% CI: 0.21, 0.70) for 3–4 cups/d, and 0.36 (95% CI: 0.21, 0.65) for ≥5 cups/d (*P* for trend: 0.002). When we excluded the 47 participants who died within the first 3 y of follow-up, the results did not change substantially.

We also tested the interaction between green tea consumption and confounders through the addition of cross-product terms to the multivariate model. Interaction between green tea consumption and sex was statistically significant ($P = 0.01$), but no interaction between green tea consumption and the other variables was observed.

The multivariate HRs of death from pneumonia according to green tea consumption stratified by age, physical function status, and smoking status in women are shown in **Table 4**. Among participants aged <70 y and participants aged ≥70 y, the point estimates of the HRs for death from pneumonia were below unity. In contrast, in men, no apparent association was observed between green tea consumption and HRs of death from pneumonia among participants aged <70 y and those aged ≥70 y. Although we additionally conducted stratified analyses by age at 65 y and 75 y, the results also did not change substantially. For physical function status, in men, no apparent association was observed between green tea consumption and the HRs of death from pneumonia in all subgroups. In women, in all subgroups, the point estimates of the HRs for death from pneumonia were below unity, although the trend test showed no statistically significant relations. Among never smokers in women, green tea consumption was substantially associated with a low risk of death from pneumonia. Because the number of deaths from pneumonia in former smokers and current smokers was insufficient for separate analysis, we combined the data of the former smokers and current smokers. In contrast, for men, no apparent association was observed between green tea consumption and the HRs of death from pneumonia among the participants in all subgroups.

When analysis was restricted to the 13,735 participants with a low risk of stroke, who had no history of hypertension and had never smoked, the point estimates of the HRs for death from pneumonia were below unity. The multivariate HRs were 1.00

TABLE 3
Hazard ratios (HRs) of death from pneumonia according to green tea consumption in Japan[1]

	Green tea consumption				
	<1 cup/d	1–2 cups/d	3–4 cups/d	≥5 cups/d	*P* for trend
Men (*n* = 19,079)					
Person-years	57,481	42,963	38,830	51,309	
No. of deaths	75	52	55	93	
Age-adjusted HR[2]	1.00 (referent)	0.90 (0.63, 1.28)	0.81 (0.57, 1.15)	0.91 (0.67, 1.23)	0.49
Multivariate HR[2,3]	1.00 (referent)	0.98 (0.69, 1.41)	1.02 (0.71, 1.45)	1.15 (0.83, 1.59)	0.38
Multivariate HR[2–4]	1.00 (referent)	0.97 (0.65, 1.45)	1.07 (0.73, 1.56)	1.21 (0.86, 1.71)	0.24
Women (*n* = 21,493)					
Person-years	47,426	44,411	50,528	73,879	
No. of deaths	43	24	26	38	
Age-adjusted HR[2]	1.00 (referent)	0.54 (0.33, 0.89)	0.48 (0.30, 0.78)	0.44 (0.29, 0.68)	0.0004
Multivariate HR[2,3]	1.00 (referent)	0.59 (0.36, 0.98)	0.55 (0.33, 0.91)	0.53 (0.33, 0.83)	0.008
Multivariate HR[2–4]	1.00 (referent)	0.65 (0.39, 1.09)	0.56 (0.33, 0.94)	0.50 (0.31, 0.81)	0.005

[1] HRs were calculated by Cox proportional hazard regression analysis.
[2] 95% CIs in parentheses.
[3] Adjusted for age (continuous variable); years of education (<10 or ≥10 y); BMI (in kg/m^2; <18.5, 18.5–24.9, or ≥25.0); time spent walking (<1 or ≥1 h/d); physical function status (those able to perform vigorous or moderate activity, those capable of light activity, or those capable of self-care or unable to do anything); history of hypertension (yes or no); history of diabetes mellitus (yes or no); history of gastric ulcer (yes or no); history of tuberculosis (yes or no); smoking status (never, former, currently smoking <20 cigarettes/d, or currently smoking ≥20 cigarettes/d); alcohol consumption (never, former, or currently drinking); daily total energy intake (continuous variables); daily consumption of miso (soybean paste) soup (yes or no); daily consumption of soybean products, total fish, and total green or yellow vegetables (for each food, continuous variable); and daily consumption of coffee (<1 or ≥1 cup).
[4] Participants who died in the first 3 y of follow-up were excluded from this analysis.

TABLE 4
Stratified analysis of the association between green tea and death from pneumonia in women[1]

	Green tea consumption					
	<1 cup/d	1–2 cups/d	3–4 cups/d	≥5 cups/d	*P* for trend	*P* for interaction
Age						0.15
<70 y (*n* = 17,235)						
Person-years	39,752	36,582	40,865	58,538		
No. of deaths	11	7	5	8		
Multivariate HR[2,3]	1.00 (referent)	0.69 (0.26, 1.82)	0.38 (0.13, 1.13)	0.42 (0.16, 1.10)	0.05	
≥70 y (*n* = 4258)						
Person-years	7673	7829	9662	15,341		
No. of deaths	32	17	21	30		
Multivariate HR[2]	1.00 (referent)	0.56 (0.31, 1.02)	0.61 (0.35, 1.08)	0.57 (0.34, 0.96)	0.06	
Physical function status						0.32
Able to perform vigorous or moderate activity (*n* = 14,372)						
Person-years	31,638	30,038	34,326	51,240		
No. of deaths	11	4	9	12		
Multivariate HR[3,4]	1.00 (referent)	0.33 (0.10, 1.05)	0.52 (0.20, 1.31)	0.46 (0.20, 1.11)	0.18	
Capable of light activity (*n* = 4316)						
Person-years	8976	8499	10,603	15,049		
No. of deaths	11	12	3	12		
Multivariate HR[3,4]	1.00 (referent)	1.00 (0.43, 2.35)	0.23 (0.06, 0.84)	0.58 (0.24, 1.36)	0.07	
Capable of self-care or unable to do anything (*n* = 2235)						
Person-years	5350	4564	4634	5844		
No. of deaths	21	7	13	12		
Multivariate HR[3,4]	1.00 (referent)	0.38 (0.16, 0.92)	0.62 (0.30, 1.30)	0.45 (0.22, 0.95)	0.07	
Smoking status						0.31
Never (*n* = 15,317)						
Person-years	32,973	32,321	37,575	52,132		
No. of deaths	26	21	21	25		
Multivariate HR[3,5]	1.00 (referent)	0.81 (0.45, 1.46)	0.67 (0.37, 1.21)	0.56 (0.32, 0.99)	0.04	
Former (*n* = 439) or current (*n* = 1229)						
Person-years	4682	2880	2751	6124		
No. of deaths	7	1	0	3		
Multivariate HR[3,5]	1.00 (referent)	0.11 (0.01, 1.09)	—	0.13 (0.02, 0.67)	0.01	

[1] Hazard ratios (HRs) were calculated by Cox proportional hazard regression analysis and were adjusted for age (continuous variable); years of education (<10 or ≥10 y); BMI (in kg/m^2; <18.5, 18.5–24.9, or ≥25.0); time spent walking (<1 or ≥1 h/d); history of hypertension (yes or no); history of diabetes mellitus (yes or no); history of gastric ulcer (yes or no); history of tuberculosis (yes or no); alcohol consumption (never, former, or currently drinking); daily total energy intake (continuous variables); daily consumption of miso (soybean paste) soup (yes or no); daily consumption of soybean products, total fish, and total green or yellow vegetables (for each food, continuous variable); and daily consumption of coffee (<1 or ≥1 cup).

[2] Additionally adjusted for physical function status (those able to perform vigorous or moderate activity, those capable of light activity, or those capable of self-care or unable to do anything) and smoking status (never, former, currently smoking <20 cigarettes/d, or currently smoking ≥20 cigarettes/d).

[3] 95% CIs in parentheses.

[4] Additionally adjusted for smoking status (never, former, currently smoking <20 cigarettes/d, or currently smoking ≥20 cigarettes/d).

[5] Additonally adjusted for physical function status (those able to perform vigorous or moderate activity, those capable of light activity, or those capable of self-care or unable to do anything).

(reference) for <1 cup/d, 0.65 (95% CI: 0.30, 1.40) for 1–2 cups/d, 0.80 (95% CI: 0.41, 1.57) for 3–4 cups/d, and 0.77 (95% CI: 0.41, 1.43) for ≥5 cups/d (*P* for trend: 0.52).

DISCUSSION

This is the first prospective cohort study to have investigated the association between green tea consumption and death from pneumonia. Our study showed an inverse association between green tea consumption and death from pneumonia in women. This finding was consistent with in vitro and animal studies that have shown activities of catechins against a variety of infectious agents (9–13).

Our study showed a discrepancy between men and women for the association between green tea consumption and risk of death from pneumonia. We first considered that this discrepancy might be attributable to the effect of cigarette smoking, because the smoking rate was higher in men than in women. However, inverse associations were observed among never smokers in women (Table 4), and no apparent associations were observed for any smoking status among men. In addition, no interaction between green tea consumption and smoking status was observed. We therefore secondly considered that catechin activities might differ between men and women. It has been reported that tea catechins may have estrogenic activity, which might partly account for the discrepancy between men and women

(21). However, the reasons for the discrepancy remain largely uncertain.

Our previous study also indicated an inverse association between green tea consumption and death as a result of cardiovascular disease, and this inverse association was stronger in women (15). Therefore, the present results could be interpreted as not only an effect of green tea in preventing pneumonia, but also as an effect of green tea in preventing other diseases that are associated with pneumonia risk, such as stroke. We did not follow the incidence of stroke that had occurred after the baseline survey. However, the results of sensitivity analysis of participants with a low risk of stroke, who had no history of hypertension and had never smoked, showed an inverse association between green tea consumption and risk of death from pneumonia. In Japan, primary cause of death has been determined according to the rules for selecting the underlying cause of death in the ICD-10. Therefore, death from pneumonia associated with previous stroke was classified as stroke, and pneumonia unrelated to previous stroke was classified as pneumonia. The present results might therefore be interpreted as an effect of green tea against infection.

The observed inverse associations between green tea consumption and death from pneumonia might be mediated by health and comorbidities that lead to aspiration pneumonia. However, we limited deaths from influenza and pneumonia (J10–J18), and we did not include aspiration pneumonia (J69). We also statistically controlled for a variety of potential confounding factors in the multivariate-adjusted model and conducted analyses after excluding participants who had died in the first 3 y of follow-up. In addition, we conducted a stratified analysis by age, because death from pneumonia increases with age (19, 20). The inverse association between green tea consumption and risk of death from pneumonia was consistently observed in women, irrespective of whether they were aged <70 y or aged ≥ 70 y. We also conducted a stratified analysis by physical function status, because we considered that participants with limited physical function would be at higher risk of aspiration pneumonia. The inverse association between green tea consumption and risk of death from pneumonia was consistently observed, irrespective of whether participants were able to perform vigorous or moderate activity, light activity, or merely self-care or unable to do anything unaided. The finding that their 95% CIs were not significant might have been due to lack of statistical power. Therefore, the observed inverse associations between green tea consumption and death from pneumonia might not be mediated by health and comorbidities that lead to aspiration pneumonia.

Our finding of an inverse association between green tea consumption and death from pneumonia appeared to be a threshold effect. In women, the multivariate HRs of death from pneumonia compared with <1 cup/d were 0.59 for 1–2 cups/d, 0.55 for 3–4 cups/d, and 0.53 for ≥ 5 cups/d. The results of analysis according to the 5 categories, without combining the lower 2 categories of green tea consumption, also showed a threshold effect. In other words, persons consuming ≥ 1 cup/d might receive the benefit from the beverage. There may be differences in dietary intake and health characteristics besides green tea consumption between the lowest fourth and the highest three-fourths of the distribution. However, in our models we adjusted for various potential confounders, and the estimates did not change substantially from the age-adjusted estimates. Furthermore, a previous study showed that higher intakes of fruit and vegetables were associated with lower risk of death from all causes, cancer, and cardiovascular disease, and that the association appeared to be a threshold effect (22). Taken together, the results might indicate that polyphenols, contained in fruit and vegetables as well as green tea, might operate through a threshold effect.

Our study had several limitations. First, we collected the information on green tea consumption only once before the follow-up period. Therefore, measurement error caused by changes in green tea consumption over time among the subjects could have distorted our results. However, this misclassification may be nondifferential and would tend to result in underestimation of the effect of green tea consumption. Second, we had no information about the cause of pneumonia. Of 406 deaths from pneumonia, 96% were classified as organism unspecified (J18) because such information was not provided on the death certificates. However, the causative agent responsible for pneumonia is rarely identified, even in rigorous epidemiologic studies of pneumonia (23, 24). Third, although we statistically controlled for a variety of potential confounding factors in the multivariate-adjusted model, conducted analyses after excluding participants who had died in the first 3 y of follow-up, and conducted a stratified analysis by age and physical function status, we were unable to eliminate residual confounding. In addition, we were unable to fully exclude the possibility that the death from pneumonia might have included pneumonia associated with previous stroke, although the primary cause of death was determined according to the rules for selecting the underlying cause of death in the ICD-10. Aspiration pneumonia also might have been coded as death from pneumonia, although we limited deaths from pneumonia (J10–J18), and we did not include aspiration pneumonia (J69). Therefore, clinical trials are ultimately necessary to confirm the protective effect of green tea on death from pneumonia.

In conclusion, this prospective cohort study has shown an inverse association between green tea consumption and death from pneumonia among Japanese women. Our data showed the effect of green tea consumption against pneumonia and support the possibility that green tea components exert antiviral and antimicrobial activities against a variety of infectious agents.

The authors' responsibilities were as follows—IW: designed the study, analyzed and interpreted the data, and prepared the manuscript; SK: designed the study, acquired the data, analyzed and interpreted the data, prepared the manuscript, and supervised the study; MK, TS, KOM, NK, and AH: acquired data and analyzed and interpreted the data; and IT: designed the study, acquired and interpreted the data, obtained funding, and supervised the study. None of the authors had a conflict of interest.

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J Epidemiol 2009;19(6):294-302
doi:10.2188/jea.JE20080076

Original Article

Factors Associated With Psychological Distress in a Community-Dwelling Japanese Population: The Ohsaki Cohort 2006 Study

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Received August 8, 2008; accepted May 13, 2009; released online September 12, 2009

ABSTRACT

Background: In Asia, there has been no population-based epidemiological study using the K6, a 6-item instrument that assesses nonspecific psychological distress.

Methods: Using cross-sectional data from 2006, we studied 43 716 (20 168 men and 23 548 women) community-dwelling people aged 40 years or older living in Japan. We examined the association between psychological distress and demographic, medical, lifestyle, and social factors by using the K6, with psychological distress defined as 13 or more points out of a total of 24 points.

Results: The following variables were significantly associated with psychological distress among the population: female sex, young and old age, a history of serious disease (hypertension, diabetes mellitus, stroke, myocardial infarction, or cancer), current smoking, former alcohol drinking, low body mass index, shorter daily walking time, lack of social support (4 of 5 components), and lack of participation in community activities (4 of 5 components). Among men aged 40 to 64 years, only "lack of social support for consultation when in trouble" and a history of diabetes mellitus remained significant on multivariate analysis. Among men aged 65 years or older, age was not significantly associated with psychological distress, and the significant association with current smoking disappeared on multivariate analysis. Among women aged 40 to 64 years, a history of stroke was not associated with psychological distress. Among women aged 65 years or older, the significant association with current smoking disappeared on multivariate analysis.

Conclusions: A number of factors were significantly associated with psychological distress, as assessed by the K6. These factors differed between men and women, and also between middle-aged and elderly people.

Key words: cross-sectional; K6; population-based; psychological distress

INTRODUCTION

Mental health is an important component of overall well-being. About 14% of the global disease burden has been attributed to mental illness, mostly due to the chronically disabling nature of depression and other common mental disorders.[1,2] Although numerous studies have produced systematic evidence regarding the risk factors for physical health, the understanding of factors related to mental health, particularly in Asian countries, is still limited.[2]

In 2002, in an attempt to devise a method to easily assess mental health in general population surveys, Kessler and colleagues developed a scale of nonspecific psychological distress—the K6—that comprises only 6 questions.[3] The K6 was originally developed to identify persons with a high likelihood of developing mental conditions, such as depression and mood or anxiety disorders.[4] However, the K6 and the K10 (the K6 plus 4 additional questions related to symptoms of distress) have also been used to estimate the prevalence of nonspecific psychological distress in general population surveys,[5] and as part of the World Health Organization's World Mental Health Surveys.[6] Although it is brief enough to be added to lengthy general health questionnaires, a major limitation of the K6 is that it does not

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provide information on the particular psychiatric diagnosis or diagnoses a respondent may have. Nevertheless, researchers have begun to use the K6 for studies in clinical settings,[7] as well as in epidemiological studies[8,9] and large, nationally representative surveys. Despite the frequent use of the K6, no population-based epidemiological study has used this scale to clarify the factors associated with mental health in Asian countries.

The objective of the present study was to use the K6 to identify factors associated with psychological distress in a community-dwelling Japanese population. We also briefly describe the overall design of the study, as this is the first report from a new prospective cohort study, the Ohsaki Cohort 2006 Study.

METHODS

Study design, setting, and participants

The Ohsaki Cohort 2006 Study is a prospective cohort study, from which we analyzed cross-sectional data from a baseline survey. The source population for the baseline survey comprised community-dwelling individuals aged 40 years or older who were included in the Residential Registry for Ohsaki City, Miyagi Prefecture, northeastern Japan, as of December 1, 2006. The Residential Registry identified 78 101 persons (36 397 men; 41 704 women) living in the area.

The baseline survey was conducted from December 1 to December 15, 2006. A questionnaire was distributed by the heads of individual administrative districts to individual households, and returned by mail. Of the 78 101 persons, 866 were ineligible due to death, move-out, or hospitalization, yielding an eligible population of 77 235. The baseline questionnaires (described below) were collected from 50 210 persons, and valid responses were received from 49 855 (22 547 men and 27 308 women), who ultimately formed the study population of cohort participants. Among the study population, 26 512 persons (53.2%) were aged 40 to 64 years, and 23 343 (46.8%) were aged 65 years or older. The response rate was calculated by dividing the study population by the total eligible population, yielding 64.5%. The corresponding response rates, with respect to sex and age categories, were 54.9% and 60.4% among men and women aged 40 to 64 years, respectively, and 77.1% and 73.2% among men and women aged 65 years or older, respectively.

When analyzing the prevalence of psychological distress and its associations with demographic, medical, lifestyle, and social factors, we excluded participants for whom K6 data were missing ($n = 6139$). Consequently, the analyzed population comprised 43 716 participants (20 168 men and 23 548 women; 56.6% of the eligible population).

Baseline survey

The baseline questionnaires for persons aged 40 to 64 years consisted of the following details in sequence: (1) history of diseases, (2) family history of diseases, (3) health status during the preceding year, (4) smoking status, (5) alcohol drinking status, (6) dietary habits,[10] (7) job status and educational status, (8) present and past body weight and height, (9) health status in general, (10) sports and exercise,[11,12] (11) psychological distress (K6),[3,4] (12) social support,[13] (13) participation in community activities, (14) dental status, and (15) reproductive factors (among women).

The baseline questionnaires for persons aged 65 years or older consisted of the following details in sequence: (1) a frailty checklist (the Kihon checklist),[14] (2) history of diseases, (3) health status during the preceding year, (4) smoking status, (5) alcohol drinking status, (6) dietary habits,[10] (7) past body weight and height, (8) health status in general, (9) pain, (10) daily activities, (11) sports and exercise,[11,12] (12) psychological distress (K6),[3,4] (13) social support,[13] (14) participation in community activities, and (15) dental status.

Questionnaire items for persons aged 65 years or older were identical to those for persons aged 40 to 64 years, except that the former excluded family history of diseases, job status and educational status, present and past body weight and height, and reproductive factors in women, and included the frailty checklist, past body weight and height, pain, and daily activities.

Measurement of psychological distress

The K6 was used as an indicator of psychological distress.[3,4] The 6 questions were as follows: "Over the last month, how often did you feel: (1) nervous, (2) hopeless, (3) restless or fidgety, (4) so sad that nothing could cheer you up, (5) that everything was an effort, (6) worthless?" Participants were asked to respond by choosing "all of the time" (4 points), "most of the time" (3 points), "some of the time" (2 points), "a little of the time" (1 point), and "none of the time" (0 points). Total point score therefore ranged from 0 to 24. The K6 has been developed using modern psychometric theory and has been shown to be superior to some existing scales in brevity and psychometric properties.[3,4,15] The Japanese version of the K6 has been recently developed, using the standard back-translation method, and has been validated.[16] As suggested by Kessler and colleagues,[15] we classified participants with scores of 13 points or more as having psychological distress.

Measurement of other variables

The degree of social support available to each person was assessed by asking the following questions[13]: (1) Do you have someone with whom you can consult when you are in trouble?, (2) Do you have someone with whom you can consult when your physical condition is bad?, (3) Do you have someone who can help you with your daily housework?, (4) Do you have someone who can take you to a hospital when you do not feel well?, and (5) Do you have someone

who can take care of you when you are ill in bed? This social support questionnaire consisted of 5 questions, each requiring an answer of yes or no. This questionnaire was only available in Japanese, and its validity and reliability were not evaluated.

The frailty checklist is a tool developed by the Japanese Ministry of Health, Labour, and Welfare to screen for frail persons and is designed to measure actual task performance.[14] Researchers have also begun to use this tool in epidemiological surveys.[14]

Ethical issues

The return of questionnaires completed by the participants was regarded as consent to participate in the study, which involved cross-sectional analysis of the baseline survey data and the longitudinal study of subsequent mortality and immigration. The study protocol was reviewed and approved by the Ethics Committee of Tohoku University Graduate School of Medicine.

Statistical analysis

We used univariate and multivariate logistic regression analysis to calculate the odds ratios (ORs) for psychological distress (a K6 total score of ≥13 points) relative to demographic, medical, lifestyle, and social factors. In these analyses, we investigated the following factors: sex, age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, ≥85 years), history of hypertension (yes, no), history of diabetes mellitus (yes, no), history of stroke (yes, no), history of myocardial infarction (yes, no), history of cancer (yes, no), smoking status (never, former, current), alcohol drinking (never, former, current), body mass index (kg/m^2) calculated with self-reported weight and height; <18.5, 18.5–24.9, ≥25.0), daily walking time (<30 min/day, 30 min–1 hour/day, ≥1 hour/day), social support (yes, none), participation in community activities (yes, none). In the multivariate models, the above variables were all adjusted for each other. Analyses were repeated by stratifying the population by sex and age categories (40–64 years, 65 years or older). When analyzing the data for men and women aged 40 to 64 years, we further added current employment status (yes, no) and duration of education (≤12 years, >12 years) as covariates. All statistical analyses were performed with SAS version 9.1 (SAS Inc., Cary, NC, USA), and all statistical tests were 2-sided. A P value less than 0.05 was considered to indicate statistical significance.

RESULTS

Prevalence proportion, and univariate and multivariate analysis of psychological distress among the total population

The crude prevalence proportion of psychological distress in the analyzed population was 6.7% (2921/43 716; 95% confidence interval [CI], 6.5 to 6.9). Univariate analysis showed that the following were significantly associated with a higher prevalence of psychological distress: female sex, young and old age, a history of serious disease, a current smoking habit, a former alcohol drinking habit, low BMI, shorter daily walking time, lack of social support, and lack of participation in community activities.

After mutual adjustment for the variables shown in Table 1, women had approximately 1.6 times the odds of psychological distress, relative to men. There was a U-shaped association between age category (5-year categories from 40–44 to ≥85 years) and the prevalence of psychological distress, with a nadir for those aged 65 to 69 years.

History of hypertension, diabetes mellitus, stroke, myocardial infarction, or cancer were all associated with a significantly higher prevalence of psychological distress in the multivariate models (Table 1). Among these diseases, a history of stroke was most strongly associated with psychological distress, and had more than 2 times the odds of psychological distress, relative to those who had no history of stroke.

A current smoking habit (vs never smoker), former smoking habit (vs never smoker), former alcohol drinking habit (vs never drinker), low BMI (vs normal BMI), and less daily walking time (vs time spent walking ≥1 hr) were associated with a higher odds for psychological distress, even in multivariate analysis (Table 1). In contrast, a moderate daily walking time (vs time spent walking ≥1 hr) was associated with a significantly lower odds.

Among the variables studied, lack of social support for consultation when in trouble was most strongly associated with a high prevalence of psychological distress in the multivariate models, although the association between other components of lack of social support and psychological distress was substantially attenuated in multivariate analysis (Table 1). The multivariate-adjusted OR (95% CI) for psychological distress associated with lack of social support for consultation when in trouble was 2.24 (1.97 to 2.56). The association of lack of participation in community activities with psychological distress was also attenuated, but lack of participation in neighborhood association activities, sports or exercise, volunteering, and community social gatherings were all associated with a higher prevalence of psychological distress, even in multivariate analysis.

Stratified analysis by sex and age categories (40 to 64 years, 65 years or older)

Stratified analysis by sex and age categories (40 to 64 years, 65 years or older) yielded results similar to those for the participants as a whole (Table 1), but the statistically significant associations that had been observed between several factors and psychological distress disappeared in each stratum.

Table 1. Univariate and multivariate analysis of the associations between psychological distress and demographic, medical, lifestyle, and social factors among the total study population[a]

Variables	No. of persons with psychological distress /No. of participants	Univariate OR (95% CI)	Multivariate OR (95% CI)[b]
Sex			
Male	1146/20 168	1.00 (referent)	1.00 (referent)
Female	1775/23 548	1.35 (1.25–1.46)	1.58 (1.41–1.76)
Age group (years)			
40–44	316/3702	1.00 (referent)	1.00 (referent)
45–49	380/4739	0.93 (0.80–1.09)	0.93 (0.79–1.09)
50–54	390/5712	0.79 (0.67–0.92)	0.79 (0.67–0.93)
55–59	398/6734	0.67 (0.58–0.79)	0.65 (0.56–0.77)
60–64	226/4461	0.57 (0.48–0.68)	0.54 (0.45–0.65)
65–69	240/5091	0.53 (0.45–0.63)	0.52 (0.43–0.63)
70–74	296/5242	0.64 (0.54–0.76)	0.57 (0.47–0.68)
75–79	281/4167	0.78 (0.66–0.92)	0.60 (0.50–0.72)
80–84	214/2347	1.08 (0.90–1.29)	0.74 (0.60–0.91)
≥85	180/1521	1.44 (1.19–1.75)	0.87 (0.69–1.08)
History of diseases			
Hypertension	907/12 658	1.11 (1.03–1.21)	1.17 (1.07–1.28)
Diabetes mellitus	319/3819	1.31 (1.16–1.48)	1.26 (1.11–1.44)
Stroke	156/1012	2.63 (2.21–3.14)	2.12 (1.76–2.57)
Myocardial infarction	122/1147	1.69 (1.40–2.05)	1.51 (1.23–1.86)
Cancer	225/2432	1.46 (1.27–1.68)	1.48 (1.28–1.73)
Smoking status			
Never	1443/22 219	1.00 (referent)	1.00 (referent)
Former	553/9030	0.94 (0.85–1.04)	1.15 (1.01–1.31)
Current	701/9699	1.12 (1.02–1.23)	1.32 (1.17–1.49)
Alcohol drinking status			
Never	1187/17 041	1.00 (referent)	1.00 (referent)
Former	407/3633	1.69 (1.50–1.90)	1.49 (1.31–1.70)
Current	1156/20 840	0.78 (0.72–0.85)	0.94 (0.84–1.04)
Body-mass index			
<18.5 kg/m^2	226/1803	2.12 (1.82–2.45)	1.59 (1.36–1.86)
18.5–24.9 kg/m^2	1689/26 610	1.00 (referent)	1.00 (referent)
≥25.0 kg/m^2	752/12 231	0.97 (0.89–1.06)	0.96 (0.87–1.05)
Time spent walking per day			
<30 min	1426/16 476	1.64 (1.49–1.80)	1.26 (1.14–1.40)
30 min–1 hr	710/14 190	0.91 (0.82–1.02)	0.89 (0.79–0.99)
≥1 hr	658/12 024	1.00 (referent)	1.00 (referent)
Lack of social support:			
(i) to consult when you are in trouble	873/5354	3.46 (3.18–3.77)	2.24 (1.97–2.56)
(ii) to consult when you are in bad physical condition	698/4167	3.39 (3.09–3.72)	1.24 (1.08–1.44)
(iii) to help with your daily housework	852/6701	2.47 (2.27–2.69)	1.12 (0.99–1.27)
(iv) to take you to a hospital	579/3834	2.86 (2.60–3.16)	1.27 (1.10–1.46)
(v) to take care of you	769/5563	2.71 (2.48–2.96)	1.42 (1.25–1.61)
No participation in community activities			
(i) Activities of neighborhood association	1952/22 109	2.26 (2.08–2.46)	1.27 (1.15–1.41)
(ii) Sports or exercise	2090/23 258	2.70 (2.47–2.95)	1.63 (1.47–1.81)
(iii) Volunteering	2307/28 871	2.48 (2.23–2.75)	1.17 (1.03–1.32)
(iv) Social gatherings	2016/22 568	2.48 (2.27–2.71)	1.31 (1.18–1.46)

Abbreviations: OR, odds ratio; CI, confidence interval.
[a]The K6 was used as an indicator of psychological distress,[3,4] with a cut-off point of ≥13 out of 24 points.[15]
[b]In the multivariate models, all variables shown in Table 1 were adjusted for each other.

The statistically significant association between history of hypertension and psychological distress disappeared in all strata. Among men aged 40 to 64 years, there was loss of significant associations with a history of myocardial infarction, history of cancer, being a former smoker, spending less than 30 min per day walking, lacking social support for consultation when in a bad physical condition, lacking social support for transport to a hospital, lacking social support for receiving care, lack of participation in community activities in a neighborhood association, and lack of participation in

Table 2. Multivariate analysis of the association between psychological distress and demographic, medical, lifestyle, and social factors among men aged 40 to 64 years[a]

Variables	No. of persons with psychological distress /No. of participants	Multivariate OR (95% CI)[b]
Age group (years)		
40–44	128/1802	1.00 (referent)
45–49	169/2299	0.99 (0.77–1.27)
50–54	173/2781	0.85 (0.67–1.09)
55–59	168/3269	0.65 (0.50–0.83)
60–64	98/2108	0.55 (0.41–0.73)
History of diseases		
Hypertension	164/2529	1.17 (0.96–1.42)
Diabetes mellitus	98/1030	1.65 (1.30–2.10)
Stroke	24/170	2.42 (1.51–3.89)
Myocardial infarction	18/173	1.62 (0.94–2.76)
Cancer	23/307	1.26 (0.80–1.99)
Smoking status		
Never	97/2099	1.00 (referent)
Former	218/3940	1.19 (0.92–1.54)
Current	405/6087	1.38 (1.09–1.75)
Alcohol drinking status		
Never	107/1622	1.00 (referent)
Former	89/775	1.52 (1.11–2.07)
Current	531/9746	0.89 (0.71–1.11)
Body-mass index		
<18.5 kg/m^2	39/266	2.20 (1.51–3.21)
18.5–24.9 kg/m^2	457/7749	1.00 (referent)
≥25.0 kg/m^2	235/4135	0.94 (0.79–1.12)
Time spent walking per day		
<30 min	330/4418	1.13 (0.94–1.37)
30 min–1 hr	177/3807	0.80 (0.64–0.98)
≥1 hr	217/3847	1.00 (referent)
Lack of social support:		
(i) to consult when you are in trouble	339/2269	2.87 (2.30–3.58)
(ii) to consult when you are in bad physical condition	258/1777	1.11 (0.87–1.41)
(iii) to help with your daily housework	274/2205	1.23 (0.98–1.53)
(iv) to take you to a hospital	185/1340	1.14 (0.86–1.50)
(v) to take care of you	176/1261	1.28 (0.97–1.69)
No participation in community activities		
(i) Activities of neighborhood association	425/5549	1.00 (0.83–1.21)
(ii) Sports or exercise	480/6078	1.35 (1.12–1.63)
(iii) Volunteering	545/7508	1.19 (0.95–1.48)
(iv) Social gatherings	476/5964	1.23 (1.02–1.50)

Abbreviations: OR, odds ratio; CI, confidence interval.
[a]The K6 was used as an indicator of psychological distress,[3,4] with a cut-off point of ≥13 out of 24 points.[15]
[b]In the multivariate models, all variables shown in Table 2 were adjusted for each other.

Table 3. Multivariate analysis of the association between psychological distress and demographic, medical, lifestyle, and social factors among women aged 40 to 64 years[a]

Variables	No. of persons with psychological distress /No. of participants	Multivariate OR (95% CI)[b]
Age group (years)		
40–44	188/1900	1.00 (referent)
45–49	211/2440	0.87 (0.70–1.08)
50–54	217/2931	0.75 (0.60–0.93)
55–59	230/3465	0.65 (0.52–0.81)
60–64	128/2353	0.51 (0.39–0.66)
History of diseases		
Hypertension	162/2225	1.10 (0.90–1.33)
Diabetes mellitus	49/567	1.19 (0.86–1.64)
Stroke	9/61	1.84 (0.87–3.91)
Myocardial infarction	8/48	3.00 (1.34–6.73)
Cancer	55/564	1.58 (1.17–2.13)
Smoking status		
Never	649/10 120	1.00 (referent)
Former	79/819	1.32 (1.02–1.71)
Current	181/1467	1.48 (1.22–1.79)
Alcohol drinking status		
Never	440/6637	1.00 (referent)
Former	104/800	1.55 (1.21–1.98)
Current	391/5197	1.04 (0.89–1.22)
Body-mass index		
<18.5 kg/m^2	79/641	1.49 (1.14–1.93)
18.5–24.9 kg/m^2	636/8876	1.00 (referent)
≥25.0 kg/m^2	248/3423	0.98 (0.84–1.16)
Time spent walking per day		
<30 min	389/5036	0.93 (0.79–1.10)
30 min–1 hr	277/4147	0.91 (0.76–1.09)
≥1 hr	275/3623	1.00 (referent)
Lack of social support:		
(i) to consult when you are in trouble	279/1349	2.20 (1.73–2.79)
(ii) to consult when you are in bad physical condition	256/1254	1.38 (1.07–1.78)
(iii) to help with your daily housework	310/2016	1.15 (0.93–1.42)
(iv) to take you to a hospital	218/1232	1.33 (1.05–1.67)
(v) to take care of you	305/2031	1.40 (1.13–1.74)
No participation in community activities		
(i) Activities of neighborhood association	618/6833	1.26 (1.07–1.48)
(ii) Sports or exercise	702/7344	1.70 (1.43–2.02)
(iii) Volunteering	763/9303	0.97 (0.79–1.19)
(iv) Social gatherings	664/7327	1.20 (1.02–1.42)

Abbreviations: OR, odds ratio; CI, confidence interval.
[a]The K6 was used as an indicator of psychological distress,[3,4] with a cut-off point of ≥13 out of 24 points.[15]
[b]In the multivariate models, all variables shown in Table 3 were adjusted for each other.

community volunteer activities (Table 2). Among women aged 40 to 64 years, there was loss of the significant associations with a history of diabetes mellitus, history of stroke, spending less than 30 min per day walking, and lack of participation in community volunteer activities (Table 3).

Among men aged 65 years or older, there was a loss of the significant associations with age, a history of diabetes mellitus, history of myocardial infarction, being a former smoker, being a current smoker, lacking social support for consultation when in bad physical condition, and lack of participation in community sports or exercise activities (Table 4). Among women aged 65 years or older, there was a loss of the significant associations with a history of diabetes mellitus, being a former smoker, being a current

Table 4. Multivariate analysis of the association between psychological distress and demographic, medical, lifestyle, and social factors among men aged 65 years or older[a]

Variables	No. of persons with psychological distress /No. of participants	Multivariate OR (95% CI)[b]
Age group (years)		
65–69	95/2323	1.00 (referent)
70–74	114/2379	1.01 (0.75–1.35)
75–79	105/1833	0.98 (0.72–1.33)
80–84	65/925	1.01 (0.71–1.43)
≥85	31/449	0.78 (0.49–1.22)
History of diseases		
Hypertension	194/3295	1.23 (0.99–1.53)
Diabetes mellitus	77/1128	1.25 (0.95–1.64)
Stroke	61/445	1.91 (1.39–2.62)
Myocardial infarction	44/544	1.33 (0.94–1.88)
Cancer	63/860	1.39 (1.03–1.87)
Smoking status		
Never	77/1862	1.00 (referent)
Former	222/3925	1.06 (0.80–1.40)
Current	90/1855	1.05 (0.76–1.47)
Alcohol drinking status		
Never	92/1646	1.00 (referent)
Former	149/1524	1.37 (1.03–1.83)
Current	154/4573	0.75 (0.57–1.00)
Body-mass index		
<18.5 kg/m^2	35/343	1.56 (1.04–2.34)
18.5–24.9 kg/m^2	209/4597	1.00 (referent)
≥25.0 kg/m^2	91/1878	1.13 (0.86–1.47)
Time spent walking per day		
<30 min	234/2687	2.14 (1.58–2.88)
30 min–1 hr	80/2767	0.95 (0.67–1.34)
≥1 hr	63/2255	1.00 (referent)
Lack of social support:		
(i) to consult when you are in trouble	112/1039	1.87 (1.35–2.58)
(ii) to consult when you are in bad physical condition	68/614	0.90 (0.59–1.36)
(iii) to help with your daily housework	100/1198	0.92 (0.66–1.28)
(iv) to take you to a hospital	70/572	1.77 (1.18–2.67)
(v) to take care of you	81/682	1.68 (1.16–2.43)
No participation in community activities		
(i) Activities of neighborhood association	299/3693	1.82 (1.32–2.51)
(ii) Sports or exercise	285/3886	1.23 (0.92–1.64)
(iii) Volunteering	326/4641	1.64 (1.11–2.41)
(iv) Social gatherings	278/3477	1.35 (1.00–1.82)

Abbreviations: OR, odds ratio; CI, confidence interval.
[a]The K6 was used as an indicator of psychological distress,[3,4] with a cut-off point of ≥13 out of 24 points.[15]
[b]In the multivariate models, all variables shown in Table 4 were adjusted for each other.

Table 5. Multivariate analysis of the association between psychological distress and demographic, medical, lifestyle, and social factors among women aged 65 years or older[a]

Variables	No. of persons with psychological distress /No. of participants	Multivariate OR (95% CI)[b]
Age group (years)		
65–69	145/2768	1.00 (referent)
70–74	182/2863	1.06 (0.84–1.34)
75–79	176/2334	1.08 (0.84–1.37)
80–84	149/1422	1.31 (1.01–1.69)
≥85	149/1072	1.49 (1.14–1.96)
History of diseases		
Hypertension	387/4609	1.14 (0.98–1.33)
Diabetes mellitus	95/1094	1.01 (0.80–1.28)
Stroke	62/336	1.86 (1.37–2.51)
Myocardial infarction	52/382	1.46 (1.06–2.00)
Cancer	84/701	1.61 (1.25–2.08)
Smoking status		
Never	620/8138	1.00 (referent)
Former	34/346	0.94 (0.64–1.39)
Current	25/290	0.92 (0.59–1.43)
Alcohol drinking status		
Never	548/7136	1.00 (referent)
Former	65/534	1.42 (1.06–1.91)
Current	80/1324	1.01 (0.78–1.31)
Body-mass index		
<18.5 kg/m^2	73/553	1.38 (1.04–1.83)
18.5–24.9 kg/m^2	387/5388	1.00 (referent)
≥25.0 kg/m^2	178/2795	0.84 (0.70–1.02)
Time spent walking per day		
<30 min	473/4335	1.73 (1.37–2.18)
30 min–1 hr	176/3469	1.05 (0.81–1.35)
≥1 hr	103/2299	1.00 (referent)
Lack of social support:		
(i) to consult when you are in trouble	143/697	1.75 (1.29–2.37)
(ii) to consult when you are in bad physical condition	116/522	1.63 (1.14–2.31)
(iii) to help with your daily housework	168/1282	1.13 (0.86–1.48)
(iv) to take you to a hospital	106/690	1.20 (0.88–1.63)
(v) to take care of you	207/1589	1.50 (1.18–1.90)
No participation in community activities		
(i) Activities of neighborhood association	610/6034	1.38 (1.09–1.75)
(ii) Sports or exercise	623/5950	2.22 (1.72–2.85)
(iii) Volunteering	673/7419	1.69 (1.18–2.43)
(iv) Social gatherings	598/5800	1.57 (1.24–1.99)

Abbreviations: OR, odds ratio; CI, confidence interval.
[a]The K6 was used as an indicator of psychological distress,[3,4] with a cut-off point of ≥13 out of 24 points.[15]
[b]In the multivariate models, all variables shown in Table 5 were adjusted for each other.

smoker, and lacking social support for help with daily housework (Table 5).

When we further added current employment status and the duration of education as covariates in the multivariate models, as shown in Table 2 and Table 3, the multivariate-adjusted OR (95% CI) for psychological distress associated with being currently employed was 1.65 (1.30 to 2.09) among men and 1.10 (0.84 to 1.28) among women, respectively, and 0.82 (0.68 to 0.98) among men and 0.93 (0.80 to 1.09) among women for longer duration of education.

In addition, we analyzed the data using different cut-off points (≥9/24, ≥11/24, and ≥15/24), but the results did not substantially change in an analysis of all participants or in stratified analyses (data not shown).

DISCUSSION

The use of general population surveys to measure the extent of mental illness presents many challenges because the diagnostic tools employed tend to be lengthy and cumbersome.[17,18] The results of the present study suggest that use of the K6 scale as a proxy indicator of mental health impairments contributes to the investigation of factors associated with mental health at the population level.

On the basis of baseline cross-sectional data from a new, large, population-based, prospective cohort study, we found that female sex, young and old age, history of hypertension, history of diabetes mellitus, history of stroke, history of myocardial infarction, history of cancer, current smoking, former alcohol drinking, low BMI, shorter daily walking time, lack of social support, and lack of participation in community activities were all associated with psychological distress, even in multivariate analysis. Nevertheless, stratified analysis by sex and age categories (40 to 64 years, 65 years or older) revealed some differences among strata. The present findings indicate that factors associated with psychological distress differ between men and women, and also between middle-aged and elderly people.

We found that, as compared to men, women were more likely to have psychological distress, even in multivariate analysis, which was consistent with 2 previous US studies that used the K6.[5,8] Several studies have also shown that women have a higher risk of anxiety and mood disorders, suggesting that many factors, such as female hormones, personality, coping skills, and sociocultural roles, play a direct role in anxiety and mood disorders, as do socioeconomic status and comorbid conditions.[19–21]

The association of advanced age with psychological distress was substantially attenuated in multivariate analysis, suggesting that the high OR in the univariate model might be due to other variables shown in Table 1. Nevertheless, there was still a U-shaped association between age category (5-year categories from 40 to 44 years to ≥85 years) and the prevalence of psychological distress, with a nadir for those aged 65 to 69 years. This pattern of association is consistent with that of a previous study.[5] In contrast, stratified analysis revealed no apparent association between age and psychological distress among men aged 65 years or older, which suggests that age alone was not associated with psychological distress among men in this age category.

The associations of psychological distress with a history of serious disease were as unsurprising. Similar associations were also reported in a survey conducted in the United States.[5] The strong association between a history of stroke and psychological distress may be due to post-stroke depression.[22] Nevertheless, stratified analyses revealed some differences among sex and age categories. A history of hypertension was not significantly associated with psychological distress in any stratum. Although not significant, point estimates for history of hypertension were all above unity, which is suggestive of relatively small differences among strata. A history of diabetes mellitus was significantly associated with psychological distress only among men aged 40 to 64 years, indicating the potential burden of this disease among middle-aged men. A history of stroke was not significantly associated with psychological distress among women aged 40 to 64 years, but the point estimate was similar to that among women aged 65 years or older, suggesting that the disease burden was similar for women in these 2 age groups. The significant association between a history of myocardial infarction and psychological distress disappeared among men aged 40 to 64 years and 65 years or older, suggesting a potential sex difference in disease burden. A history of cancer was not significantly associated with psychological distress among men aged 40 to 64 years, although the reason for this was unclear.

We also found that former smoking, current smoking, former alcohol drinking, being underweight, and shorter daily walking time were associated with a higher prevalence of psychological distress. In contrast, we observed a lower prevalence among participants with a moderate daily walking time. The results for former smoking,[8] current smoking,[5,8] and being underweight[5] were consistent with previous studies. Stratified analyses yielded reduced point estimates for current smoking among men aged 65 years or older and women aged 65 years or older, suggesting that the smoking habit itself, as well as related factors, was not strongly associated with psychological distress among persons aged 65 years or older, in contrast to those aged 40 to 64 years.

Among the variables studied, lack of social support was most strongly associated with a high prevalence of psychological distress, even in multivariate analysis. Although this is the first large population-based epidemiological study using the K6 in an Asian country, previous studies[23,24] have used other mental health scales, such as the Geriatric Depression Scale (GDS)[25] among Japanese populations. Koizumi et al reported that negative responses to the questions "Do you have someone with whom you can consult when you are in trouble?" and "Do you have someone who can take care of you when you are ill in bed?" were significantly associated with an increase in the risk of depression.[23,24] The finding is consistent with, and supports, the present results for persons aged 65 years or older. The depressive symptoms detected by the GDS and the psychological distress detected by the K6 reflect common underlying factors.

Although lack of social support was strongly associated with a high prevalence of psychological distress, the significant association that had been found with 3 components of deficient social support disappeared on multivariate analysis among men aged 40 to 64 years (Table 2). However, lack of social support for consultation when in trouble remained strongly associated with psychological distress. These results appear to underline the importance of such support among men aged 40 to 64 years.

The association of lack of participation in community activities with psychological distress was substantially attenuated in multivariate analysis, indicating that the high OR in the univariate models could be largely explained by other variables shown in Table 1. Nevertheless, the significant increases in OR in the multivariate model indicate that lack of participation in community activities may also be associated with mental health. Stratified analysis revealed that the significant association between lack of participation in community activities in a neighborhood association disappeared among men aged 40 to 64 years, indicating the relatively low influence of neighborhood community on middle-aged men. Also, the significant association with lack of participation in volunteer activities disappeared among men and women aged 40 to 64 years, but the point estimate among men was similar to that among the total population. However, the lower point estimate on multivariate analysis suggests a relatively weak association with participation in volunteer activities among women aged 40 to 64 years.

Our data showed that being currently employed was associated with a high odds of psychological distress, and that a longer duration of education was associated with a lower odds of psychological distress, among men aged 40 to 64 years. Although the reason is unclear, our data suggest that some socioeconomic factors, such as employment and education, are important among men aged 40 to 64 years.

Our study did have some limitations. First, because of the cross-sectional design, the direction of causation for the associations observed in this report cannot be inferred from the data. Prospective studies that measure the K6 in respondents at baseline, follow the respondents over time, and measure the K6 at the end of follow-up, are needed to clarify these causal relationships.

Second, because the response rate was not high (64.5%), the respondents may not be a representative sample of the source population of Ohsaki City residents. The response rates among men and women aged 40 to 64 years were lower (54.9% and 60.4%, respectively) than those among men and women aged 65 years or older (77.1% and 73.2%, respectively). These relatively low response rates, especially among participants aged 40 to 64 years, should be kept in mind when interpreting the results from prospective, as well as cross-sectional, analyses.

Third, because the K6 does not provide information about the specific psychiatric conditions of respondents, it is difficult to identify what is being measured. However, the particular symptoms included in the K6 make it likely that severe, disabling, mood and anxiety disorders are being identified.[3,4,15,16] Although the K6 focuses on nonspecific psychological distress, the majority of cases detected by this instrument would meet the criteria for certain mental health disorders specified in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.[3,15]

Finally, no scales, including the present one, have been adequately validated for use as social support questionnaires in the Japanese population. Also, the first question in the questionnaire, "Do you have someone with whom you can consult when you are in trouble?", might be construed to include the participant's family, which may not qualify as social support.

In conclusion, the findings of this cross-sectional study demonstrate that the factors associated with psychological distress differ between men and women, and also between middle-aged and elderly people. These findings underline the importance of considering sex and age categories when attempting to minimize psychological distress in community-dwelling populations. To our knowledge, this is the first large population-based epidemiological study to use the K6 in an Asian country.

ACKNOWLEDGEMENTS

This study was supported by Health Sciences Research Grants (H19-Seisaku-Ippan-026, H18-Choju-Ippan-014) from the Ministry of Health, Labour and Welfare, Japan, and a Grant-in-Aid for Scientific Research (B) (18390191) from the Japan Society for the Promotion of Science.

The authors thank Professor Toshiaki Furukawa and Dr Atsurou Yamada, Department of Psychiatry and Cognitive-Behavioral Medicine, Nagoya City University Graduate School of Medical Sciences, for their valuable comments on the content of the manuscript. The authors also thank Yoshiko Nakata, Mika Wagatsuma, Naoko Sato, and Yuki Takeda for their technical assistance.

No conflicts of interest are declared.

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