Estimation of the GFR

Serum creatinine (SCr) was measured in all participants using an enzymatic method. The method used to measure SCr was initially calibrated at the Central Laboratory in Aichi prefecture for all four centers, and their precision and accuracy were authorized by the Japanese Association of Medical Technologists. The GFR of each participant was estimated from the SCr value, using the modified Modification of Diet in Renal Disease (MDRD) equation (adapted for Japanese by the Japanese Society of Nephrology [12]), as follows:

$$\text{Estimated GFR (eGFR) (mL/min/1.73m}^2\text{)} = 194 \times \text{SCr}^{-1.094}\,(\text{mg/dL}) \times \text{age}^{-0.287}\,(\text{years})\ (\times\ 0.739 \text{ if female}).$$

Definition of hyperfiltration and hypofiltration in healthy subjects

The distributions of eGFR in subjects without prediabetes (FPG < 100 mg/dL) and prehypertension (BP < 120/80 mmHg) were divided into 10-year age groups. Subjects being treated for diabetes, hypertension, kidney diseases and cancer and those with proteinuria (urinary protein ≥1+ on dipstick test) were excluded. The number of subjects aged ≥80 years was too small to derive reference values, so they were combined with those aged ≥70 years. Hyperfiltration was defined as eGFR above the age- and sex-specific 95th percentile for healthy subjects, while hypofiltration was defined as eGFR below the 5th percentile.

Prevalence of hyperfiltration and hypofiltration according to the stages of prediabetes and prehypertension

Using the reference values determined as above, all of the participants were divided according to their eGFR as showing hyperfiltration, normal filtration and hypofiltration. The characteristics of the subjects were compared between those with hyperfiltration/hypofiltration and normal filtration. The prevalence of hyperfiltration and hypofiltration was also compared according to the stages of prediabetes and prehypertension [8, 9]. Subjects were categorized as having normal fasting glucose (i.e. no prediabetes; FPG <100 mg/dL), Stage 1 prediabetes (FPG 100–109 mg/dL), Stage 2 prediabetes (FPG 110–125 mg/dL) or diabetes (FPG ≥126 mg/dL or under treatment for diabetes). Subjects were also categorized as having normal BP (i.e. no prehypertension; BP < 120/80 mmHg), Stage 1 prehypertension (BP 120–129/80–84 mmHg), Stage 2 prehypertension (BP 130–139/85–89 mmHg) or hypertension (BP ≥ 140/90 mmHg or under treatment for hypertension).

Statistical analysis

Odds ratios (ORs) and 95% confidence intervals were estimated for hyperfiltration and hypofiltration using unconditional logistic regression analysis adjusted for age and sex (adjusted ORs) and for age, sex, body mass index, high-density lipoprotein cholesterol (HDL-C), lipid-lowering medication use, uric acid and smoking status. The analyses of stages of prediabetes were also adjusted for systolic BP and anti-hypertensive medication use, while analyses of stages of prehypertension were also adjusted for FPG and glucose-lowering medication use as the stages of prediabetes and prehypertension were confounding (fully adjusted ORs). Proteinuria was not adjusted in the analysis because proteinuria is not just a confounder to be adjusted but the outcome (kidney damage) itself. The P-values for trends were calculated using a score variable assigning 0, 1, 2 and 3 for no prediabetes, Stage 1 prediabetes, Stage 2 prediabetes and diabetes (or for no prehypertension, Stage 1 prehypertension, Stage 2 prehypertension and hypertension). P <0.05 was considered statistically significant. All analyses were carried out using STATA version 9 software (StataCorp, College Station, TX).

Results

A total of 99 140 people (54 547 males and 44 593 females) aged 20–89 years participated in this study. The distribution of eGFR and the reference values for hyperfiltration/hypofiltration in subjects without prediabetes or prehypertension ($n = 30\ 426$) for each 10-year age group are shown in Figure 1. Among those aged 50–59 years, the reference values for hyperfiltration and hypofiltration were ~100 and 60 mL/min/1.73m^2, respectively, for both sexes.

The characteristics of subjects according to filtration status are shown in Table 1. We found no clinically important differences between subjects with hyperfiltration and those with normal filtration except for fasting blood glucose level, while more of the subjects with hypofiltration were older males with higher uric acid, dyslipidemia and proteinuria, as compared with subjects with normal filtration.

Table 2 shows the prevalence of hyperfiltration and hypofiltration according to the stages of prediabetes and prehypertension. The prevalence of hyperfiltration increased with increasing stage of prediabetes (ORs: 1.29, 1.58 and 2.47 for Stage 1 prediabetes, Stage 2 prediabetes and diabetes, respectively; P for trend: <0.001) and stage of prehypertension (ORs: 1.10, 1.33 and 1.52 for Stage 1 prehypertension, Stage 2 prehypertension and hypertension, respectively; P for trend: <0.001). We found no association between hypofiltration and prediabetes or prehypertension, as the age- and sex-adjusted ORs were almost 1.00. Furthermore, hypofiltration was only weakly associated with diabetes and hypertension.

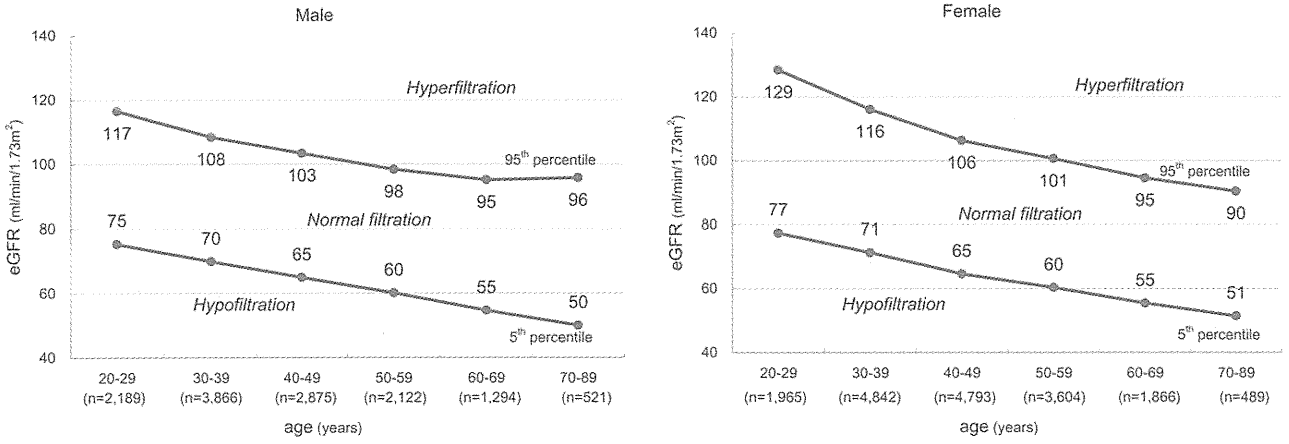

Fig. 1. Distribution of eGFR in subjects without prediabetes or prehypertension by sex and age ($n = 30\ 426$). The 95th and 5th percentiles are shown in 10-year age groups. Subjects with prediabetes (FPG ≥ 100 mg/dL), prehypertension (BP ≥ 120/80 mmHg), confirmed proteinuria (urinary protein ≥1+ on dipstick test) or being treated for diabetes, hypertension, renal diseases or cancer were excluded from this analysis. Hyperfiltration was defined as an eGFR over the age- and sex-specific 95th percentile and hypofiltration was defined as an eGFR below the 5th percentile.

Table 1. Characteristics of subjects with hyperfiltration/hypofiltration compared with subjects with normal filtration ($N = 99\ 140$)

	Normal filtration ($n = 87\ 251$)	Hyperfiltration ($n = 5548$)	Hypofiltration ($n = 6341$)
Age (years)	50.5 ± 15.1	51.4 ± 14.8	55.0 ± 16.0
Female	39 455 (45.2%)	2531 (45.6%)	2607 (41.1%)
Body mass index	22.63 ± 3.28	22.41 ± 3.65	23.28 ± 3.32
FPG (mg/dL)[a]	94.7 ± 15.6	100.9 ± 30.6	95.2 ± 15.1
HbA1c (%)[a]	5.17 ± 0.47	5.30 ± 0.92	5.22 ± 0.44
Glucose-lowering medication	3116 (3.6%)	400 (7.2%)	416 (6.6%)
Systolic BP (mmHg)[b]	122.1 ± 15.9	123.8 ± 16.6	123.2 ± 17.0
Diastolic BP (mmHg)[b]	74.4 ± 10.4	74.5 ± 10.7	75.5 ± 11.0
Anti-hypertensive medication	11 698 (13.4%)	830 (15.0%)	1667 (26.3%)
HDL-C (mg/dL)[c]	67.4 ± 17.8	67.7 ± 17.9	64.8 ± 18.4
Triglycerides (g/dL)[c]	88 (61–129)	87 (61–128)	100 (69–145)
Lipid-lowering medication	5841 (7.7%)	337 (6.6%)	730 (12.7%)
Uric acid (mg/dL)	5.29 ± 1.37	4.77 ± 1.33	6.15 ± 1.53
Proteinuria	3367 (3.9%)	270 (4.9%)	812 (12.9%)
Ever smokers	34 843 (39.9%)	2360 (42.5%)	2354 (37.1%)

[a]Subjects taking glucose-lowering medication are excluded.
[b]Subjects taking anti-hypertensive medication are excluded.
[c]Subjects taking lipid-lowering medication are exclued. Data are mean ± SD, number (%) or median (interquartile range) for triglycerides. Hyperfiltration was defined as an eGFR over the age- and sex-specific 95th percentile and hypofiltration was defined as an eGFR below the 5th percentile as shown in Figure 1.

Discussion

We found that the prevalence of hyperfiltration increased with increasing stages (i.e. worsening) of prediabetes and prehypertension. This suggests that renal function should be monitored in people with prediabetes or prehypertension to identify those with hyperfiltration who might be at increased risk for subsequent kidney damage.

Glomerular hyperfiltration is a well-recognized early renal change in subjects with diabetes and hypertension [1, 2], partly because of inappropriate afferent arteriole dilatation in diabetes [13] or elevated glomerular hydraulic pressure in hypertension [5]. GFR was reported to decrease significantly faster in subjects with hyperfiltration [1], and long-standing hyperfiltration may contribute to the development of kidney damage [3, 4]. Kidney failure may occur in people having had hyperfiltration for 30 years [5] because of progressive glomerular sclerosis that occurs as a result of prolonged glomerular hyperfiltration [6]. Preventing glomerular hyperfiltration can reduce glomerular injury [7].

New designations for prediabetes (impaired fasting glucose or impaired glucose tolerance) and prehypertension were recently introduced [8, 9]. Subjects with prediabetes and prehypertension are at increased risk for the development of CKD [14, 15] and ESRD [16, 17]. As a large proportion of the population has prediabetes and prehypertension (20 and 37% in our study), identifying subjects at increased risk for CKD/ESRD among those with prediabetes or prehypertension by finding those with hyperfiltration may represent a beneficial and effective preventative strategy.

We found significant associations between hyperfiltration and prediabetes or prehypertension in a large population of subjects. To our knowledge, the only other study to have shown an association between hyperfiltration and prediabetes contained a small number of subjects with prediabetes ($n = 24$) [18]. On the other hand, we are aware of no studies describing an association between hyperfiltration and prehypertension. Thus, this study is the largest study to date to show associations of hyperfiltration with prediabetes and prehypertension.

Interestingly, we found no association between hypofiltration and prediabetes or prehypertension. It is possible that prediabetes and prehypertension are associated with earlier stages of kidney damage (i.e. glomerular hyperfiltration), while long-term diabetes and hypertension are associated with hypofiltration and CKD. The finding that diabetes and hypertension were significantly associated with hypofiltration, whereas prediabetes and prehypertension were not, supports this hypothesis. Curhan [19] proposed the term 'pre-CKD' for low levels of albuminuria, and we suppose that hyperfiltration could represent pre-CKD, an early and reversible stage of kidney damage. Current guidelines recommend that prehypertension in subjects with CKD should be treated to achieve a target BP of <130/80 mmHg [9]. Treating high BP much earlier may stop the progression of nephropathy [20]. We suggest that hyperglycemia and high BP in people with hyperfiltration should be treated earlier to prevent the progression of renal dysfunction to CKD and ESRD.

There is no generally accepted definition for hyperfiltration [10]. In our study, we determined age- and sex-specific reference values for hyperfiltration and hypofiltration using a large presumably healthy population. We used the upper 95th and lower 5th percentiles rather than the mean ± 2 SD because eGFR is not normally distributed and because hyperfiltration and hypofiltration represent different disease conditions. Although the subjects with hyperfiltration in our study had lower eGFRs (being ~100 mL/min/1.73m^2 for people aged 50–59 years) compared with the subjects in former studies [10, 18], the prevalence of prediabetes and prehypertension was higher in our subjects. Thus, eGFR reference values for each sex and age group should be established for clinical use, particularly for older subjects. Hyperfiltration was prevalent in younger subjects followed by a higher prevalence of hypofiltration at an older age in diabetic subjects (23 and 0% in age 20s, and 7 and 13% in age 70s for prevalence of hyperfiltration and hypofiltration, respectively). This distribution is in accordance with the hyperfiltration hypothesis [5]. The Japanese eGFR equation can be used to identify people with hyperfiltration because the Japanese eGFR equation is more accurate than the MDRD Study equation, particularly for hyperfiltration [12, 21].

One limitation of our study is that we lack information on microalbuminuria and glucose tolerance following an oral glucose challenge. Thus, only impaired fasting glucose, but not impaired glucose tolerance, was used as a criterion for prediabetes. Microalbuminuria is another marker of early

Table 2. Prevalence of hyperfiltration/hypofiltration according to the stages of prediabetes and prehypertension in all the subjects ($N = 99\ 140$)

	Normal filtration ($n = 87\ 251$)	Hyperfiltration ($n = 5548$)				Hypofiltration ($n = 6341$)			
	n	*n* (%)	Adjusted OR[a] (95% CI[a])	Fully adjusted OR[b] (95% CI[b])	P for trend[b]	*n* (%)	Adjusted OR[a] (95% CI[a])	Fully adjusted OR[b] (95% CI[b])	P for trend[b]
Stages of prediabetes					<0.001				0.813
No prediabetes (FPG <100 mg/dL)	64 566	3525 (4.9%)	1 (reference)	1 (reference)		4384 (6.1%)	1 (reference)	1 (reference)	
Stage 1 prediabetes (FPG 100-109 mg/dL)	12 024	787 (5.7%)	1.22 (1.12–1.32)	**1.29** (1.17–1.41)		960 (7.0%)	1.01 (0.94–1.09)	0.89 (0.82–0.97)	
Stage 2 prediabetes (FPG 110-125 mg/dL)	4938	408 (7.1%)	1.53 (1.37–1.71)	**1.58** (1.38–1.80)		388 (6.8%)	0.95 (0.85–1.06)	0.77 (0.68–0.88)	
Diabetes (FPG ≥126 mg/dL or under treatment)	5723	828 (11.6%)	2.81 (2.58–3.06)	**2.47** (2.22–2.75)		609 (8.5%)	1.19 (1.08–1.30)	**1.18** (1.05–1.33)	
Stages of prehypertension					<0.001				0.044
No prehypertension (BP <120/80 mmHg)	32 757	1902 (5.2%)	1 (reference)	1 (reference)		1890 (5.2%)	1 (reference)	1 (reference)	
Stage 1 prehypertension (BP 120-129/80-84 mmHg)	17 542	1036 (5.3%)	1.01 (0.93–1.09)	1.10 (1.00–1.20)		1036 (5.3%)	0.99 (0.91–1.07)	0.90 (0.82–0.98)	
Stage 2 prehypertension (BP 130-139/85-89 mmHg)	14 689	999 (6.0%)	1.16 (1.07–1.26)	**1.33** (1.21–1.47)		975 (5.9%)	1.07 (0.99–1.16)	0.91 (0.83–1.01)	
Hypertension (BP ≥140/90 mmHg or under treatment)	22 263	1611 (6.1%)	1.26 (1.16–1.36)	**1.52** (1.38–1.68)		2440 (9.3%)	1.45 (1.35–1.56)	**1.12** (1.02–1.22)	

[a]Adjusted for age and sex.
[b]Adjusted for age, sex, body mass index, high-density lipoprotein (HDL-C), lipid-lowering medication use, uric acid and smoking status; the analyses of stages of prediabetes were also adjusted for systolic BP and anti-hypertensive medication use, while analyses of stages of prehypertension were also adjusted for FPG and glucose-lowering medication use. Bold style represents ORs which showed significant results in both adjustments. CI, confidence interval. Hyperfiltration was defined as an eGFR over the age- and sex-specific 95th percentile and hypofiltration was defined as an eGFR below the 5th percentile as shown in Figure 1.

kidney damage, although glomerular hyperfiltration precedes the development of microalbuminuria [22]. Another limitation is that among diabetic subjects with normal filtration, subjects with renal damage who have already undergone hyperfiltration stage might be included in accordance with the hyperfiltration hypothesis [5], though this mixture does not affect the association between prediabetes and hyperfiltration. Since these results were obtained in a Japanese population, confirmation in other ethnic groups is needed.

Our findings should be considered descriptive rather than pathogenetic because we lack longitudinal data on GFR and information on microalbuminuria. Though we believe treating hyperglycemia and high BP from an early and reversible stage as hyperfiltration is important to prevent kidney damage, further confirmation by longitudinal studies is needed. Also, whether age-specific reference values reflect the risk of ESRD, cardiovascular disease or mortality should be proved by prospective studies.

In conclusion, we found that the prevalence of hyperfiltration increased with increasing stage (i.e. worsening) of prediabetes and prehypertension. Kidney function should be monitored in subjects with prediabetes or prehypertension. In people with hyperfiltration, we suggest that hyperglycemia and high BP should be treated as early as possible to prevent the development of kidney damage.

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Conflict of interest statement. None declared.

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Prevention of type 2 diabetes in a primary healthcare setting: Three-year results of lifestyle intervention in Japanese subjects with impaired glucose tolerance

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Abstract

Background: A randomized control trial was performed to test whether a lifestyle intervention program, carried out in a primary healthcare setting using existing resources, can reduce the incidence of type 2 diabetes in Japanese with impaired glucose tolerance (IGT). The results of 3 years' intervention are summarized.

Methods: Through health checkups in communities and workplaces, 304 middle-aged IGT subjects with a mean body mass index (BMI) of 24.5 kg/m^2 were recruited and randomized to the intervention group or control group. The lifestyle intervention was carried out for 3 years by public health nurses using the curriculum and educational materials provided by the study group.

Results: After 1 year, the intervention had significantly improved body weight (-1.5 ± 0.7 vs. -0.7 ± 2.5 kg in the control; p = 0.023) and daily non-exercise leisure time energy expenditure (25 ± 113 vs. -3 ± 98 kcal; p = 0.045). Insulin sensitivity assessed by the Matsuda index was improved by the intervention during the 3 years. The 3-year cumulative incidence tended to be lower in the intervention group (14.8% vs.8.2%, log-rank test: p = 0.097). In a sub-analysis for the subjects with a BMI > 22.5 kg/m^2, a significant reduction in the cumulative incidence was found (p = 0.027).

Conclusions: The present lifestyle intervention program using existing healthcare resources is beneficial in preventing diabetes in Japanese with IGT. This has important implications for primary healthcare-based diabetes prevention.

Trial registration number: UMIN000003136

Background

The incidence of type 2 diabetes is increasing in Japan [1]. Although Japanese have a lower prevalence of obesity than Westerners, a tendency to gain weight due to lifestyle changes coupled with an aging of the population seems to be closely related to the rapid expansion of the diabetic population [1]. There is thus an urgent need for effective public health strategies to combat this situation in Japan.

There is now substantial evidence that the development of type 2 diabetes can be prevented or delayed in high-risk subjects through lifestyle intervention [2-8]. The Finnish Diabetes Prevention Study (DPS) [4] and the US Diabetes Prevention Program (DPP) [5] have clearly shown that, in obese subjects with impaired glucose tolerance (IGT), lifestyle changes associated with a 5-7% decrease in body weight resulted in a 58% reduction in the development of diabetes. Thus lifestyle modifications

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are considered the most effective means of delaying or preventing the development of type 2 diabetes. There are several examples in the literature about the various levels of effectiveness of lifestyle intervention [9]. In both the DPP [5] and DPS [4], considerable efforts were made by well-trained staff to achieve changes in lifestyle among participants. However, results are not consistent across studies in primary healthcare settings. How to translate the findings of clinical research, such as the DPS and DPP, into real-world practice [10,11] is a key issue to be addressed. In Japan, by law, much of the adult population undergoes a health checkup every year in the workplace or at community centers. The checkups have revealed a huge number of subjects at a high risk for developing type 2 diabetes. These people are usually given simple information and guidance about diabetes and a healthy lifestyle. Despite this approach, the diabetic population has increased at the national level, probably due to a lack of evidence-based methodologies of lifestyle intervention and mechanisms to implement these widely at public health care levels. It is not known to what extent lifestyle intervention in a primary healthcare setting is effective. The present study is a randomized control trial to test the feasibility and effectiveness of a lifestyle intervention program, carried out in a primary healthcare setting using existing resources, in Japanese with IGT. We found that this relatively modest intervention could produce beneficial effects on the incidence of type 2 diabetes over a 3-year period. This has important implications for primary healthcare-based diabetes prevention.

Methods

The study protocol was approved by the Ethics Committee of the National Hospital Organization Kyoto Medical Center, and all subjects gave their written informed consent before the start of the study. Thirty-two community health care institutions and company clinics across the country participated in the study as collaborative centers. In each center, a public health nurse was appointed as a study nurse for recruitment, intervention, laboratory referral, and clinical measurements.

Study design and subjects

Subjects with IGT, aged 30-60 years, were recruited through health checkups conducted at each collaborative center. The recruitment started in March 1999 and was completed in December 2002. A two-step strategy was adopted for identifying subjects with IGT as described previously [12]. Using the data from health checkups, those who met one of the following criteria were extracted: 1) fasting plasma glucose (FPG) concentration ≥5.6 mmol/l but < 7.0 mmol/l, 2) casual plasma glucose (CPG) concentration ≥7.8 mmol/l but <11.1 mmol/l when blood is drawn within 2 hours after a meal, or CPG concentration ≥6.1 mmol/l but <7.8 mmol/l when blood is drawn 2 hours or more after a meal, or 3) IGT as indicated by a previous 75 g oral glucose tolerance test (OGTT). Those with 1) a previous diagnosis of diabetes mellitus other than gestational diabetes, 2) a history of gastrectomy, 3) physical conditions such as ischemic heart disease, heart failure, exercise-induced asthma, and orthopedic problems where exercise was not allowed by a doctor, 4) definitive liver and kidney diseases, 5) autoimmune diseases, and 6) a habit of drinking heavily (69 g or more of ethanol per day) [13] were excluded. Those who had already begun lifestyle modifications, such as routine moderate to vigorous exercise, were also excluded. Thus it should be noted that the findings obtained cannot be generalized to all high-risk people with IGT. It was roughly estimated that there were more than 10,000 people with borderline hyperglycemia at the 32 collaborative centers. Each center recruited study candidates using posters, through fliers, and by word of mouth. Figure 1 shows a flow diagram for recruiting study subjects. Altogether, 1279 subjects who met the criteria and gave written informed consent, underwent a 75 g OGTT. Diabetes and IGT were diagnosed based on the World Health Organization (WHO)'s criteria [14].

Finally, 304 subjects diagnosed with IGT were randomly assigned to either a lifestyle intervention group or a control group by the committee of the study group. Two subjects from the control group and 6 from the intervention group were excluded from the study, since it turned out that they did not meet the eligibility criteria. The result of the randomization was unmasked to the participants, those administering the interventions, and those assessing the data. The average number of participants per center (including both the control and intervention groups) was 9. We planned to follow-up the participants for 6 years regarding the development of diabetes.

According to prospective studies on the Japanese population, the yearly incidence of diabetes among subjects with IGT varies between 1 and 5% [15-17]. Therefore, it was assumed that the 6-year cumulative incidence of diabetes would be 30% in the control group. The present study was designed to detect a 50% reduction in the incidence by the intervention. Thus the sample size required was 313 with a type 1 error of 5%, with 80% power (beta = 20%) at the two-tailed 5% significance level, and allowing for a withdrawal rate of 30%.

Intervention

The follow-up of the participants started in April 1999 and the last case completed a three-year follow-up in January 2006.

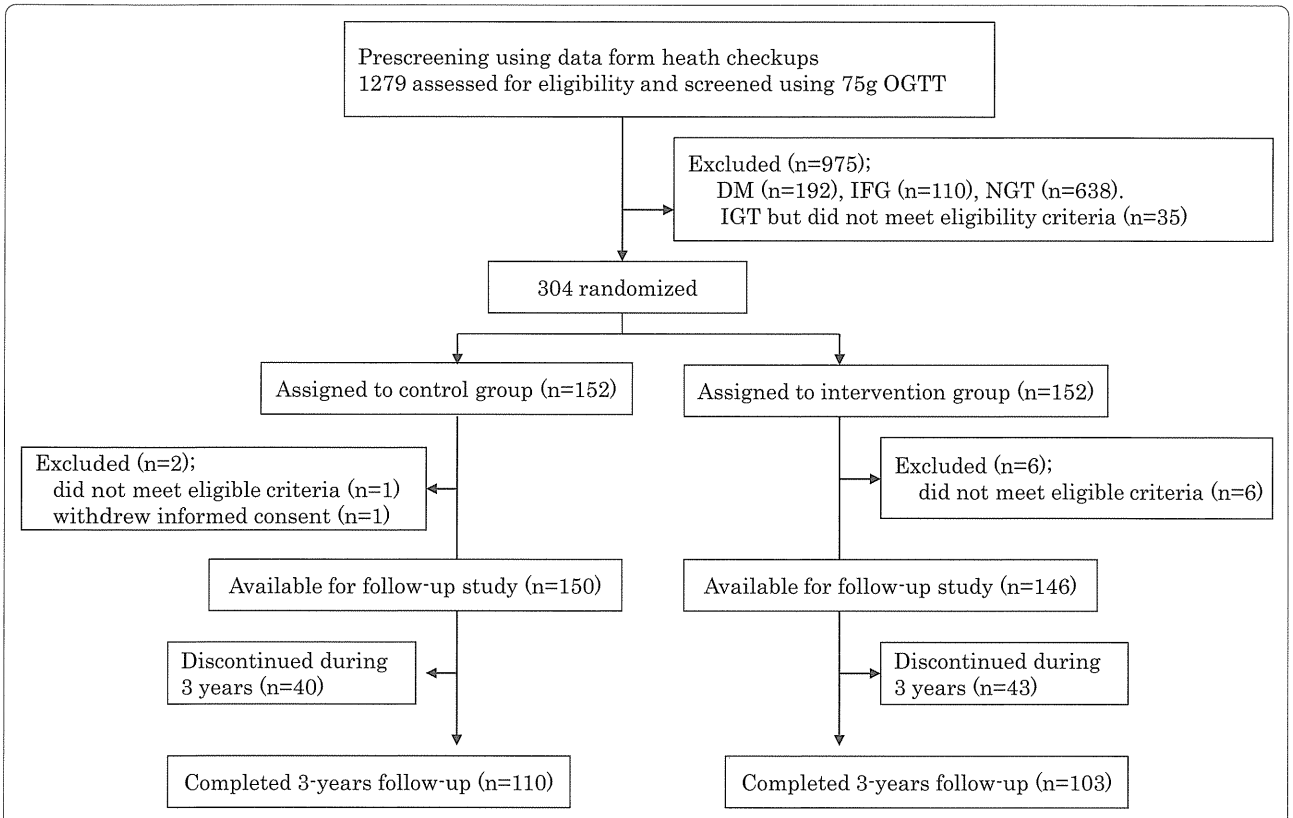


Figure 1 Recruitment, random assignment, and 3 - year follow-up of study subjects. DM: diabetes mellitus, IFG: impaired fasting glucose, NGT: normal glucose tolerance.

The goals of intervention were: 1) to reduce initial body weight by 5% in overweight and obese subjects, and 2) to increase energy expenditure due to leisure time physical activity (LTPA) by 700 kcal per week. The interventions were carried out by the study nurse in each collaborative center in the form of both group and individual sessions, using the guideline, curriculum, and educational materials provided by the committee of the study group. When needed, the study nurse could ask a part-time dietician for diet counseling. A 27-page booklet titled "Change Your Lifestyle to Prevent Diabetes" was given to each participant as a guide. During the initial six months, four group sessions were conducted using slides, videotapes, and a booklet with each session lasting two or three hours. The main subjects in each group session were as follows: (1) What is diabetes?, What is IGT?, How to prevent diabetes?, (2) Healthy diets to prevent diabetes, (3) Exercise tips to prevent sporting injuries, and (4) Let's enjoy exercise. The individual session was conducted biannually during the three years with each session lasting 20 to 40 minutes. Personalized goals, such as a minimum of 20 minutes' moderate walking each day, were set. The session was conducted based on theoretical concepts and techniques for behavioral change, such as self-efficacy, self-monitoring, and the transtheoretical model [18]. After the first year, contact by telephone could replace the individual face to face sessions. The study subjects attended both group and individual sessions by themselves without any support person.

An assessment of the dietary intake of each participant was conducted using a semiquantitative food frequency questionnaire (FFQ) [19] with photographs of 122 varieties of dishes and foods. Each item was shown with a real portion size. The subjects were advised to take the proper amount of calories, decrease the mean percent of energy derived from dietary fat to less than 25%, and restrict daily alcohol consumption to less than 160 kcal. They were also advised to eat three meals a day and avoid eating late at night. Self-reported levels of LTPA were assessed using a physical activities questionnaire [20]. To achieve the exercise goal, aerobic exercise such as walking was recommended. Data on dietary intake and physical activities were assessed by the study group and the results were sent back to study nurses at each collaborative center.

To reinforce the intervention, between-visit contact by fax was also made monthly during the initial twelve

months. Simple cartoons were drawn on the fax sheet to give tips for improving lifestyle.

The control group received only one group session on a healthy lifestyle and the prevention of diabetes at the baseline. No individual guidance was given during the study period. However, the control group received anthropometric and blood examinations regularly during the study as did the intervention group.

Measurements

Anthropometric (height, body weight, and waist circumference) and blood pressure measurements were done every three months during the first year and biannually thereafter. Waist circumference was measured at the umbilical level. Biochemical studies, including a 75 g-OGTT, were conducted biannually during the first year and annually thereafter. Total cholesterol, high-density lipoprotein (HDL)-cholesterol, triglyceride, creatinine, uric acid, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), HbA1c, plasma glucose, and insulin levels were measured at a central laboratory (SRL Co. Ltd.,, Tokyo, Japan). For the intervention group, the results of these measurements were given back individually to each subject in the intervention group during individual sessions with the study nurse. For the control group, the results were sent by mail with brief comments. The assessment of dietary intake was conducted annually. Levels of LTPA were assessed biannually during the first year and annually thereafter. Pancreatic β cell function and insulin resistance were assessed using the homeostasis model assessment (HOMA-β and HOMA-IR, respectively) [21]. An insulin sensitivity index (Matsuda index) was also calculated using insulin and glucose data obtained from 75 g OGTTs [22,23]. Body mass Index (BMI) was calculated as weight in kilograms divided by height in meters squared. "Overweight" and "obese" were defined according to the WHO recommendations for Asians [24]. All clinical and diet and exercise data were collected at each collaborative center by the study nurse and sent to the study group for analysis.

Endpoint

The primary endpoint was the development of diabetes, diagnosed and confirmed by two consecutive 75 g-OGTTs. The diagnosis of diabetes was based on the WHO's criteria [14].

Training of the study nurses

The study group organized a one and a half day study meeting for the study nurses in the beginning and annually thereafter. The meeting was designed to 1) standardize the intervention method, 2) improve their skills for eliciting motivation from the participants to achieve the lifestyle goals, and 3) increase their knowledge on diabetes, nutrition, exercise, and behavioral modification. The attendance rate for the nurses was almost 100% in the initial training course and between 70 and 90% for the annual training course after 1 year.

Statistical analysis

All data are presented as the means ± SD. Comparisons of baseline values and mean changes from baseline to year 1 between the groups were made with a two-tailed unpaired t test or the χ^2 test when applicable. A two-tailed paired t-test was used to analyze differences within groups between the baseline and year 1. Survival curves were calculated to estimate the cumulative incidence of diabetes. The difference between the groups in the incidence of diabetes was tested by means of the two-sided log-rank test. A p value less than 0.05 was considered statistically significant. The analyses were done using the SPSS/PC statistical program (version 11.1 for windows; SPSS, Inc., Chicago, IL, USA).

Results

We randomly assigned the 304 subjects with IGT to two groups and analyzed the data for 296 individuals (150 in the control group and 146 in the intervention group) (Figure 1). A total of 83 subjects (28%) withdrew from the study before the 3-year mark (40 in the control group and 43 in the intervention group). The withdrawals were due to personal reasons (moving etc) in 18 cases, medical reasons in 5, and loss of contact in 40. Twenty subjects were not able to continue the study for reasons related to the collaborative centers themselves, such as the closure of a center. The rate of withdrawal was higher among men than women (36.9% vs. 19.0%, $p < 0.01$). No differences were found in age and BMI between those who withdrew from the study before the 3-year mark and those who continued. The baseline characteristics of both the control and intervention groups were similar as regard to age (51 ± 6 and 51 ± 7, respectively) and male to female ratio (76/74 and 74/74, respectively), and proportion of overweight (23.0≤BMI<27.4: 48.5% and 50.0%, respectively) and obese (BMI ≥27.4: 18.6% and 18.8%, respectively) people. There was no difference in exercise LTPA between the groups at the baseline ($p = 0.197$), although non-exercise LTPA (below 3 METs) was significantly greater in the control group ($p = 0.043$). Non-exercise LTPA included gardening, shopping, Sunday carpentering, playing musical instruments, and so on. There were no significant differences in other lifestyle, anthropometric, and biochemical measurements at the baseline between the groups (Table 1). Thus we were able to successfully assign the cohort of subjects to two groups.

Table 1 shows mean changes in lifestyle, anthropometric, and biochemical parameters from the baseline at the 1-year and 3-year marks in both groups. In the intervention group, the mean daily energy intake decreased by 202 kcal and mean daily energy expenditure by LTPA increased by 64 kcal at the 1-year mark. These beneficial lifestyle changes were observed even at the 3-year mark. Body weight, BMI, waist circumference, and systolic and diastolic blood pressure (not shown in the Table 1) decreased significantly from the baseline at the 1-year mark. The changes in body weight and BMI were seen also at the 3-year mark.

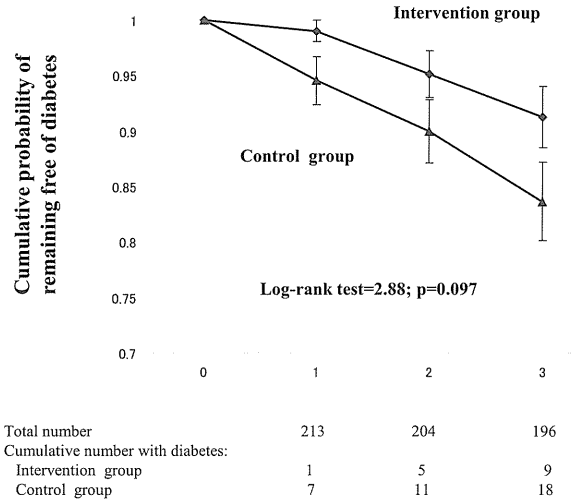
Although fasting and 2 hour plasma glucose decreased, fasting and 2 hour insulin concentrations did not change during the three years. HOMA-IR and HOMA-β did not change either (data not shown). However, Matsuda index, as a marker of whole body insulin sensitivity calculated using plasma glucose and serum insulin levels from 75 g OGTTs, increased from the baseline at both the 1-year and 3-year marks. Serum GGT levels decreased at the 1-year mark. Serum HDL cholesterol levels increased at the 1-and 3-year marks while serum triglyceride and cholesterol levels did not change (data not shown). Beneficial changes were also found in the control group although to a lesser extent. Between the groups, changes in daily energy expenditure due to non-exercise LTPA, body weight and BMI, serum GGT levels, and the Matsuda index were significantly different at the 1-year mark. These differences were not significant at the 3-year mark except for the Matsuda index. The difference in the Matsuda index remained significant even at the 3-year mark.

Diabetes was diagnosed in a total of 27 subjects during the three years; 9 in the intervention group and 18 in the control group. The estimated cumulative incidence of diabetes over the 3-year period was 8.2% in the former and 14.8% in the latter. The relative risk reduction was thus 53% with the intervention [95% confidence interval (CI); 0.25-1.13]. The difference between the groups, however, did not reach a level of statistical significance (log-rank test: p = 0.097) at the 3-year mark (Figure 2). Our study group included both lean and obese subjects with a BMI ranging widely from 16.8 to 39.6 kg/m^2. It may be thus possible that the heterogeneity in BMI in our cohort accounts for the statistically insignificant results. To examine if the effects of lifestyle intervention alter with BMI, the participants were then stratified into quartiles according to the baseline BMI. Diabetes developed in 5 out of 52 in the lowest quartile (2 from the control group and 3 from the intervention group) during the 3 years. Thus the effect of lifestyle intervention was not apparent in this lowest BMI quartile. The sub-analysis for the subjects with a BMI>22.5, however, revealed a significant decrease in the cumulative incidence with the intervention (log-rank test:

Table 1 Baseline and 1-year or 3-year follow-up data in the control and intervention groups

Parameters	Control group			Intervention group			*P value*[b]	
	Baseline[a] (n = 131)	1-year (n = 131)	3-year (n = 110)	Baseline (n = 123)	1-year (n = 123)	3-year (n = 103)	at 1-year mark	at 3-year mark
Energy intake (kcal)	2455 ± 838	2292 ± 739*	2153 ± 734*	2299 ± 788	2097 ± 895*	2016 ± 677*	0.647	0.794
Fat[c] (%)	27.5 ± 5.2	27.4 ± 5.2	27.8 ± 5.4	26.5 ± 5.6	25.5 ± 5.6*	25.7 ± 5.2	0.088	0.110
Alcohol (g)	21.0 ± 36.1	18.6 ± 29.2	13.7 ± 23.2*	20.1 ± 44.8	24.6 ± 87.7	15.7 ± 29.8	0.171	0.149
Leisure time physical activity (kcal)	136 ± 159	163 ± 172*	181 ± 201*	91 ± 132	155 ± 180*	161 ± 215*	0.078	0.214
Exercise (kcal)	57 ± 79	86 ± 99*	92 ± 105*	43 ± 88	82 ± 122*	74 ± 117*	0.474	0.958
Exercise (minutes per week)	118 ± 160	184 ± 206*	185 ± 229*	91 ± 187	184 ± 262*	160 ± 229*	0.339	0.556
Non-exercise (kcal)[d]	79 ± 139	76 ± 133	90 ± 174	49 ± 85	74 ± 119*	88 ± 186*	0.045	0.148
Weight (kg)	63.9 ± 11.7	63.1 ± 11.7*	62.5 ± 11.2*	64.9 ± 12.9	63.5 ± 12.9*	63.1 ± 12.9*	0.023	0.069
Body mass index (kg/m^2)	24.5 ± 3.2	24.2 ± 3.1*	24.4 ± 3.3*	24.8 ± 3.6	24.2 ± 3.6*	24.3 ± 3.7*	0.022	0.051
Waist circumference (cm)	84.4 ± 9.4	83.3 ± 8.6*	84.2 ± 9.5	85.9 ± 10.9	84.2 ± 10.5*	84.7 ± 11.9	0.309	0.362
Fasting plasma glucose (mmol/l)	6.1 ± 0.5	5.9 ± 0.6	6.0 ± 0.9	5.9 ± 0.5	5.8 ± 0.6*	6.0 ± 0.8	0.698	0.481
2-hplasma glucose (mmol/l)	9.0 ± 0.9	8.3 ± 2.0*	8.5 ± 2.4	9.2 ± 0.9	8.0 ± 2.1*	8.4 ± 2.5*	0.083	0.553
Fasting insulin (pmol/l)	43.8 ± 21.6	44.4 ± 40.8	45.8 ± 23.9	43.2 ± 22.2	44.4 ± 25.2	47.6 ± 36.1	0.861	0.632
2-h insulin (pmol/l)	330.6 ± 211.8	308.4 ± 178.8	377.4 ± 280.7	337.8 ± 199.8	342.0 ± 271.2	390.0 ± 374.2	0.413	0.999
Matsuda index[e]	5.4 ± 3.5	5.6 ± 3.3	5.3 ± 3.2	4.8 ± 2.3	5.9 ± 3.7*	5.5 ± 3.4*	<0.001	<0.001
Aspartate aminotransferase (IU/l)	25 ± 8	25 ± 12	26 ± 15	25 ± 12	23 ± 13	25 ± 17	0.170	0.977
Alanine aminotranseferase (IU/l)	25 ± 16	26 ± 17	27 ± 16	26 ± 18	24 ± 17	25 ± 14	0.212	0.520
Gamma-glutamyltransferase (IU/l)	53 ± 58	59 ± 91	59 ± 97*	48 ± 46	44 ± 47*	43 ± 66	0.041	0.158

Data are means ± SDs. [a]There were no significant differences in any of the baseline variables between the control and intervention groups except for non-exercise physical activity. [b]P values for differences in change between groups. [c]Proportion of energy derived from dietary fat. [d]Non-exercise leisure time physical activity includes gardening, carpentry, shopping, and playing a musical instrument. [e]The Matsuda index is an insulin sensitivity index derived from oral glucose testing. * P value < 0.05 (Baseline vs. 1-year or 3-year).



Total number	213	204	196
Cumulative number with diabetes:			
Intervention group	1	5	9
Control group	7	11	18

Figure 2 Cumulative incidence of diabetes over the three years in all participants. Kaplan-Meier plots. Intervention group (black circle) and Control group (black triangle).

p = 0.027). There was no difference in changes in BMI, waist circumference, and serum lipid levels between the lowest BMI quartile and the upper BMI quartiles in the intervention group. The change in serum ALT was significantly improved in the upper 3 BMI quartiles than the lowest BMI quartile at the 1-year mark (-3 ± 16 IU/l vs. +3.0 ± 9 IU/l; p = 0.010), although there was no difference in the control group (+1 ± 14 IU/l vs. 0 ± 15 IU/l; p = 0.498). The Matsuda index of the upper 3 BMI quartiles in the intervention group was significantly improved than in the control group at the 1-year mark (+1.1 ± 3.0 vs. -0.2 ± 3.6; p = 0.026), although there was no difference in the lowest BMI quartile between groups (+1.3 ± 3.4 vs. +1.0 ± 3.7; p = 0.702).

Discussion

This is the first randomized control trial to test whether a lifestyle intervention, carried out on a community or workplace basis using existing healthcare resources, can prevent or delay the development of type 2 diabetes in middle-aged Japanese with IGT.

The participants were recruited through health check-ups at community health centers and in the workplace. They were all volunteers, who participated in response to posters, fliers, and word of mouth. Therefore it was likely that they were motivated and prepared to alter their lifestyle, at least in the beginning. The rate of withdrawal before the 3-year follow-up was, however, high (28%). About one third of male participants withdrew from the study. This might represent the limitations of intervention carried out in a primary healthcare setting. Generally speaking, middle-aged men in Japan tend to prioritize work over health. Therefore, modifying lifestyle among the middle-aged was a challenge.

Compared with the DPS [4] and DPP [5], the present study had a less intensive intervention. The majority of the public health nurses, reflecting the real world primary healthcare setting, did not have special training in lifestyle modifications. At a feasible level, they carried out the intervention using the protocol and educational materials provided by the study group. As a rule, the same study nurse carried out the interventions on the same participant during the study. But this was not always possible due to a personnel change at the collaborative center.

We found improvements in lifestyle and anthropological and biochemical parameters with the intervention. However, between the intervention and control groups, differences in changes from the baseline were statistically significant only in increases in energy expenditure due to non-exercise LTPA, in weight reduction and, among biochemical parameters, in serum GGT levels and the Matsuda index. The mean body weight reduction was very modest, being 1.5 ± 2.7 kg (2.3%) in the intervention group and 0.7 ± 2.5 kg (1.3%) in the control group at the 1-year mark. At the 3-year mark, the differences between the groups were not statistically significant for any of the parameters except the Matsuda index. Thus it was suggested that the improvement in insulin sensitivity assessed by the Matsuda index was maintained during the three years.

In this study, four group sessions were given to the intervention group during the initial 6 months, while one session was given to the control group about diabetes mellitus and a healthy lifestyle at the baseline. The control group, however, underwent physical and blood examinations regularly during the study as did the intervention group. In addition, as the study subjects were individually randomized at each collaborating center, exchanges of information among participants at the same collaborative centers could have happened. All these factors might lead to difficulties in obtaining statistically significant differences between the groups. Therefore, it would be more appropriate to refer to the groups as a conventional intervention group and an intensive intervention group instead of a control group and an intervention group, respectively.

Most importantly, we found that this relatively modest intervention could produce beneficial effects on the incidence of type 2 diabetes during a 3-year period. The halving (51%) of the relative risk for overall subjects through this intervention is not negligible, even though it did not reach a statistically significant level. Our cohort was heterogeneous in BMI with 30% of the subjects having a normal or lower than normal BMI. Due to the small number of subjects in the present study, a

subgroup analysis was difficult. But we found a significant reduction in cumulative incidence (log-rank test: p = 0.027) for the subjects with a BMI> 22.5. Thus the effects of the intervention for lean subjects might attenuate the impact on the incidence. Regarding this, it would be important to clarify an effective measure for the prevention of diabetes in subjects with a low BMI in future studies, since the Japanese IGT population includes a considerable number of such subjects.

In the DPP, weight reduction was found to be essential for the lifestyle intervention to be beneficial [5]. In an Indian Study [7], however, the benefits seemed independent of weight change. In a hospital-based lifestyle intervention, Kosaka concluded that the benefits of lifestyle intervention could not be solely ascribed to weight reduction [6]. The present study found that minimal weight reduction in the intervention group (less than 3% on average) lowered the relative risk to 53% over 3 years, similar to the risk reduction seen in the DPS and DPP (58%) where the subjects lost 5-7% of body weight on average. Thus it seems that the relationship between body weight and diabetes risk in Asians is not as straightforward as in Western people. Asians have lower BMI but higher body fat levels than do whites [25,26]. Japanese Americans are prone to develop visceral obesity and metabolic syndrome [27,28]. A reasonable explanation for the present findings might be a more profound reduction in specific fat depots, such as visceral fat and liver fat. It has been reported that lifestyle intervention with diet and physical activity is effective at reducing hepatic steatosis in patients with non-alcoholic fatty liver disease [29]. Although there was no difference in daily alcohol consumption between the groups, we found that serum GGT levels decreased in the intervention group, but increased in the control group. These findings are important, since it has been reported that the serum concentrations of GGT and ALT are a predictive marker of type 2 diabetes [30-33], even at concentrations still considered to be within the normal range [34]. Thus, the difference in the changes in GGT levels between the groups is likely to reflect changes in liver fat contents. Further examination including abdominal ultrasonography and computed tomography [35] will be needed.

Conclusions

In conclusion, the present study suggests that lifestyle intervention using existing healthcare resources in communities and workplaces is beneficial in preventing or delaying the development of diabetes in middle aged Japanese with IGT. General improvements in lifestyle including dietary and exercise habits might be meaningful even if the weight reductions achieved are only modest. The findings have important implications for primary healthcare-based diabetes prevention.

List of abbreviations used

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BMI: Body mass index; CPG: Casual plasma glucose; DPP: Diabetes Prevention Program; DPS: Diabetes Prevention Study; FFQ: Food frequency questionnaire; FPG: Fasting plasma glucose; GGT: Gamma-glutamyltransferase; HDL: High-density lipoprotein; HOMA: Homeostasis model assessment; IGT: Impaired glucose tolerance; LTPA: Leisure time physical activity; OGTT: Oral glucose tolerance test.

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Authors' contributions

HK, the project leader, is involved in all aspects of the study. JS, ST, MT, SK, YS, IK, KY, and SS designed the study, and prepared the protocol of intervention. TK contributed to study design and coordination. NS, KK, and KT performed the statistical analysis and prepared the manuscript. TU and YT helped to draft the manuscript participated in the critical revision of the manuscript and the trial management. All authors have read and approved the final version of the manuscript.

Competing interests

The authors declare that they have no competing interests.

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Original Article

Relationship of cigarette smoking status with other unhealthy lifestyle habits in Japanese employees

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Objective: To clarify the relationship of the cigarette smoking status with other unhealthy lifestyle habits in Japanese employees.

Methods: A cross-sectional questionnaire survey was conducted in 4009 males and 1620 females. Multivariate logistic regression analysis was performed to evaluate the relationship between the cigarette smoking status and each survey item of the lifestyle habits after adjusting for potential confounding factors. Multivariate regression analysis was performed to evaluate the relationship of the duration of smoking cessation with other lifestyle habits.

Results: In both genders, compared to nonsmokers, current smokers drank more sugar-sweetened beverages (odds ratio 2.01 in males, 1.93 in females), preferred strong flavors (OR 2.23 in males, 1.64 in females), added soy sauce to cooked meals (OR 3.02 in males, 1.92 in females), skipped breakfast (OR 2.54 in males, 5.42 in females), and drank more alcohol (OR 2.28 in males, 3.24 in females). The current smokers ate snacks, fruit, soy beans and milk products less frequently. Particularly in males, current smokers took less regular exercise, had less physical activity and more sleep problems. The duration of smoking cessation in males was significantly and positively related with physical activity ($\beta = 0.052$, $p < 0.01$) and was inversely related with the score for undesirable eating habits ($\beta = -0.160$, $p < 0.01$) and alcohol consumption ($\beta = -0.089$, $p < 0.01$, adjusted $R^2 = 0.124$).

Conclusion: Current smokers had multiple unhealthy lifestyle habits compared to nonsmokers in both genders. In addition, the duration of smoking cessation in males appeared to be significantly related to a change in unhealthy lifestyle habits.

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Key Words: smoking, lifestyle, cross-sectional study, employee, Japan

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Introduction

Cigarette smoking is an important risk factor for cardiovascular disease, cancer, and other diseases[1], and an aggravating factor for metabolic syndrome[1,2]. As compared with nonsmokers, current smokers have been reported to exercise less regularly, to skip breakfast more often, to eat more quickly, and to eat a greater amount of salty foods, fewer vegetables, less fruit, fewer soy bean products[3,4], and to have higher alcohol consumption[4,5]. Thus, smokers accumulate unhealthy lifestyle habits other than smoking[3-5]; therefore, some investigators[6] claim that the clustering of unhealthy lifestyle habits in an individual has multiple effects on the risk of cardiovascular disease, cancer, and other diseases.

Concerning the relationship of smoking with eating habits, daily drinkers have been reported to consume a greater amount of salty food, instant food, and more salted dried fish[4]; however, few studies have examined the relationship of smoking with eating habits by adjusting for the effects of alcohol consumption on eating habits[3,4]. Among ex-smokers, the duration of smoking cessation was found to be related with a decrease in the ingestion of an unbalanced diet and alcohol intake[7,8]; however, little information is available about the impact of smoking cessation on the improvement of lifestyle habits, such as a decrease in alcoholic consumption. In addition, previous studies have not comprehensively examined the relationship of smoking with physical activity, eating habits, alcohol consumption, sleep problems, global health status and the psychological health status. It is important to comprehensively explore the smoking status-related unhealthy lifestyle habits. Such findings would benefit both smokers and their healthcare professionals for better and more effective health counseling.

The aim of this study was therefore to clarify the relationship of the cigarette smoking status with other unhealthy lifestyle habits.

Methods

Study participants

We conducted a cross-sectional study of 6,264 employees (4,504 males and 1,760 females) who underwent annual health check-ups from April 2009 to March 2010 either at Osaka Medical Center for Health Science and Promotion in Japan or on-site at each affiliate company. All employees of 11 companies which had a contract for annual health check-ups with our Medical Center participated in the present study without exception. The participants worked in various categories, such as finance, broadcasting, manufacturing, transportation and others. Each participant had company health insurance. The occupational groups of participants were office clerks (37.3%), sales (18.2%), technical specialists (17.5%), managerial and supervisory (16.2%), manufacturing (4.2%), and others (6.6%). We excluded participants who were younger than 20 years old (n=13), and who had errors in check-up items (n=622). Information from 5,629 (4,009 males and 1,620 females) participants was analyzed; however, 4,004 (2,702 males and 1,302 females) participants who underwent an annual health checkup at Osaka Medical Center were asked to answer a follow-up health questionnaire on their global health status and sleep problems.

The study protocol was approved by the Ethics Committee of Osaka Medical Center for Health Science and Promotion in Japan.

Health questionnaire

Lifestyle habits were determined by a structured interview or by a self-administered health questionnaire. The health questionnaire was distributed to the participants three to four weeks prior to the day of the health check-up.

Cigarette smoking status: We asked the participants if they had smoked ≥1 cigarette every day (current smoker) or they had previously smoked ≥1 cigarette every day and had not smoked until they filled in the health questionnaire (ex-smoker) or they had never smoked in the past (non-smoker). We asked the ex-smokers about their age when they started to smoke and when they had stopped. We assumed that the ex-smokers had stopped smoking they received the health questionnaire and filled it in, which usually occurred about 3 weeks before the health check-up. Current and ex-smokers were asked about the average number of cigarettes smoked per day. We classified the number of cigarettes smoked per day in current smokers into 3 categories: 1-10 (light smokers), 11-20 (middle smokers), and ≥21 cigarettes per day (heavy smokers). We classified the years since cessation in ex-smokers into 3 categories: <3 (short duration), 3-4 (intermediate duration), and ≥5 years (long duration).

Physical activity[9]: We asked the participants if they performed regular exercise and activities of daily living. If the answer was "yes," we asked about the type of physical activities, such as walking and those related with daily household chores, and their frequency. A respondent was regarded as a regular exerciser if they exercised more than 4 metabolic equivalent-hours per week (MET-hours/week), or if they performed physical activity for more than 23 MET-hours/week as the sum of exercise and activities of daily living.

Eating habits[10]: We asked 20 questions about eating habits, such as, "Did you often skip breakfast during the last month?" The answer choices were yes or no. The eating habit questionnaire was composed of 4 categories: overeating (5 items), fat consumption (4 items), salt consumption (6 items), and nutritional balance (5 items).

Alcohol consumption: We asked the participants about alcohol consumption (current drinking or nondrinking). Current drinkers were then asked about their weekly frequency of alcohol consumption and the usual amount consumed daily. The categorization was based on *go*, a unit of measurement that equals 180 ml and is the traditional unit for Japanese *sake*, which contains 13% alcohol (equivalent to approximately 23 grams of ethanol).

Global health status: We asked the participants to rate their own current health as excellent, very good, fair or poor. A respondent was regarded as having a poor global health status if the answer was fair or poor.

Psychological health status[11-13]: Concerning perceived stress[11], we asked the participants if they suffered very often, often, seldom or never. A respondent was regarded as perceiving stress if the answer was very often[11]. To measure depressive symptoms, we extracted 2 items for depressive symptoms from the Primary Care Evaluation of Mental-Disorders

(PRIME-MD)[12], i.e., "little interest or pleasure in doing things" and "feeling down, depressed, or hopeless". These questions were originally answered by yes or no and therefore we used these questions similarly in this study. A respondent was regarded as depressed if they answered "yes" to both of the components[13] or were currently being treated for mental illness. The validation of these questions on the psychological health status was confirmed in our previous study[11] in which we reported a significant relationship between stress and depression and current smoking in females after adjusting for age.

Sleep problems: Concerning sleep problems, participants responded for the 3 months before the health check-up and we asked them about their average sleep time per day. A respondent was regarded as having sleep problems if they slept less than 6 hours per day[11]. Information on snoring (more than once a week) and sleep apnea (yes or no) was obtained from a family member, if any. 'Family member' referred to any cohabiter, regardless of kinship. If the family member was not able to answer these questions or the participant was living alone, we excluded those participants from the analysis. A total of 387 males and 353 females were excluded because of the absence of information on snoring. Concerning sleep apnea, 737 males and 402 females were excluded for the same reason.

Socioeconomic status

We categorized the participants based on occupation and their position in society according to a previous study[8]: professional, administrative or not, because the cigarette smoking status is related to social class[7]; therefore, we used this category for social class adjustment.

Anthropometric measurements

We calculated the body mass index as weight divided by the square of height in meters. Clinical laboratory staff measured waist circumference at the umbilical level in unclothed, standing participants after normal expiration.

Statistical analysis

We estimated the magnitude of the relationship between the cigarette smoking status and each of the unhealthy behaviors using logistic regression analysis. Odds ratios and 95% confidence intervals (CIs) were calculated by multivariate adjustment, which included age (continuous), socioeconomic status (professional, administrative or not), score for undesirable eating habits (one point was given for each undesirable habit; continuous), regular physical activity (yes or no; dichotomous) and alcohol consumption status (current drinking or nondrinking; dichotomous).

Multivariate regression analysis was performed to evaluate the relationship of the duration of smoking cessation with other lifestyle habits, excluding non-smokers, who underwent an annual health checkup at Osaka Medical Center. The duration of smoking cessation was assumed to be 0 for current smokers. Independent variables in this analysis were as follows: the amount of physical activity (MET-hours/week), score for undesirable eating habits, alcohol consumption (grams of ethanol per week), perceived stress, depressive symptoms, poor global health status, and sleep problems (snoring and/or sleep apnea). These variables were analyzed after adjustment for age and socioeconomic status. Data were analyzed using the SPSS/PC statistical

package (15.0 J for Windows). $P<0.05$ was regarded as significant.

Results

Table 1 shows the characteristics of the participants by the cigarette smoking status among males and females. The prevalence of current smokers, ex-smokers and non-smokers was 33.6% (n=1,348), 32.6% (n=1,306) and 33.8% (n=1,355) in males, and 10.9% (n=177), 8.1% (n=131) and 81.0% (n=1,312) in females, respectively. The mean age and standard deviation (SD) of the enrolled participants was 46.1 (SD10.6) years in males and 40.4 (SD11.6) years in females. Particularly in males, significant differences were observed between current/ex-smokers and non-smokers.

Table 2 shows the relationship between current/ex-smokers and each of the survey items of lifestyle habits in males. Compared to non-smokers, current smokers were found to have several characteristics: they more often went to bed within 1-2 hours after dinner (odds ratio, 1.26, 95% confidence interval: 1.07-1.47; they drank more sugar-sweetened beverages (2.01: 1.71-2.36), ate quickly (1.25: 1.07-1.46), preferred strong flavors (2.23: 1.89-2.63), drank almost all noodle soup (1.35: 1.14-1.59), added soy sauce to cooked meals (3.02: 2.52-3.61), ate pickles (1.59: 1.18-2.14), skipped breakfast (2.54: 2.11-3.05), drank more alcohol (2.28: 1.87-2.77). They also snored more frequently (1.34: 1.08-1.67) and had more sleep apnea (1.44: 1.09-1.91). Moreover, they took regular exercise, and performed physical activity less frequently. Finally, by multivariate adjustment, they ate until full, eat snacks, seafood, vegetables, fruit, soy bean products and milk products less frequently. Among current smokers, the daily cigarette consumption was significantly related with eating snacks, drinking sugar-sweetened beverages, eating quickly, eating fatty meat, preferring strong flavors, adding soy sauce to cooked meals, skipping breakfast and eating less fruit and milk products ($P<0.05$ for trend, respectively). Ex-smokers who had quit for ≥5 years still ate quickly, preferred strong flavors, added soy sauce to cooked meals, drank more alcohol and had sleep problems.

Table 3 shows the relationship between current/ex-smokers and each of the survey items of lifestyle habits in females. Compared to non-smokers current smokers drank more sugar-sweetened beverages (odds ratio 1.93, 95% confidence interval: 1.39-2.68), preferred strong flavors (1.64: 1.17-2.28), added soy sauce to cooked meals (1.92: 1.20-3.06), skipped breakfast (5.42: 3.79-7.73), and drank more alcohol (3.24: 2.23-4.71). Moreover, they ate snacks, eggs, fruit, soy beans and milk products less frequently.

Table 4 shows the results of multivariate regression analysis, which was performed to evaluate the relationship of the duration of smoking cessation with other lifestyle habits. The duration of smoking cessation in males was significantly and positively associated with physical activity ($\beta=0.052$, $p<0.01$) and was inversely related with the score for undesirable eating habits ($\beta=-0.160$, $p<0.01$) and alcohol consumption ($\beta=-0.089$, $p<0.01$, adjusted $R^2=0.124$). On the other hand, in females, the relationship of the duration of smoking cessation with these variables was not statistically significant.

Table 1 Characteristics of the subjects by cigarette smoking status among males and females

	Males				Females			
	Current smoker (N=1,348)	Ex-smoker (N=1,306)	Nonsmoker (N=1,355)	P-value	Current smoker (N=177)	Ex-smoker (N=131)	Nonsmoker (N=1,312)	P-value
Age, Anthropometric measurements								
Age (years)	46.2 (SD10.4)	49.6 (SD 9.6)	42.8 (SD10.8)	<0.001	42.8 (SD10.4)	42.9 (SD10.4)	39.8 (SD11.8)	<0.001
Waist circumference (cm)	84.1 (SD 9.0)	84.9 (SD 8.0)	83.0 (SD 9.2)	<0.001	74.7 (SD 8.6)	75.8 (SD 9.4)	74.0 (SD 9.0)	0.079
Weight (kg)	69.2 (SD10.9)	69.7 (SD 9.7)	68.8 (SD10.7)	0.110	53.2 (SD 8.5)	54.0 (SD 8.8)	52.7 (SD 8.3)	0.230
Body mass index (kg/m^2)	23.7 (SD 3.4)	24.0 (SD 3.0)	23.6 (SD 3.4)	0.020	21.2 (SD 3.0)	21.5 (SD 3.3)	21.0 (SD 3.2)	0.184
Socioeconomic status								
professional	308 (22.8)	395 (30.2)	203 (15.0)	<0.001	2 (1.1)	2 (1.5)	6 (0.5)	0.669
administrative	260 (19.3)	282 (21.6)	340 (25.1)		10 (5.7)	9 (6.9)	86 (6.6)	
other	780 (57.9)	629 (48.2)	812 (59.9)		165 (93.2)	120 (91.6)	1,220 (92.9)	
Physical activity								
Little regular exercise	1,004 (74.5)	779 (59.6)	910 (67.2)	<0.001	150 (84.7)	110 (84.0)	1,069 (81.5)	0.475
Amount of exercise (MET-hours/week)	17.2 (SD14.7)	16.7 (SD15.2)	17.4 (SD14.3)	0.777	13.4 (SD 8.8)	14.3 (SD10.9)	14.7 (SD13.9)	0.884
Little regular physical activity	1,219 (90.4)	1,109 (84.9)	1,172 (86.5)	<0.001	168 (94.9)	125 (95.4)	1,247 (95.0)	0.978
Amount of physical activity (MET-hours/week)	40.3 (SD19.0)	37.7 (SD18.4)	35.7 (SD15.3)	0.080	39.1 (SD27.3)	37.6 (SD12.5)	37.1 (SD16.9)	0.951
Eating habits								
Overeating								
Go to bed within 1-2 hours after dinner	605 (44.9)	530 (40.6)	524 (38.7)	0.004	34 (19.2)	34 (26.0)	264 (20.1)	0.261
Frequently eat until full	767 (56.9)	845 (64.7)	862 (63.6)	<0.001	109 (61.6)	92 (70.2)	848 (64.6)	0.285
Eat snack (almost every day)	191 (14.2)	218 (16.7)	289 (21.3)	<0.001	56 (31.6)	59 (45.0)	579 (44.1)	0.006
Drink sugar-sweetened beverage (almost every day)	646 (47.9)	350 (26.8)	459 (33.9)	<0.001	74 (41.8)	46 (35.1)	375 (28.6)	0.001
Frequently eat quickly	833 (61.8)	857 (65.6)	785 (57.9)	<0.001	89 (50.3)	71 (54.2)	593 (45.2)	0.106
Fat consumption								
Eat fried food (almost every day)	418 (31.0)	350 (26.8)	450 (33.2)	0.001	40 (22.6)	35 (26.7)	317 (24.2)	0.704
Eat eggs (almost every day)	479 (35.5)	465 (35.6)	506 (37.3)	0.542	49 (27.7)	41 (31.3)	508 (38.7)	0.006
Eat fatty meat (≥3 days/week)	598 (44.4)	502 (38.4)	636 (46.9)	<0.001	58 (32.8)	50 (38.2)	515 (39.3)	0.250
Eat seafood (<3 days/week)	725 (53.8)	583 (44.6)	671 (49.5)	<0.001	106 (59.9)	80 (61.1)	770 (58.7)	0.843
Salt consumption								
Frequently prefer strong flavors	584 (43.3)	459 (35.1)	344 (25.4)	<0.001	66 (37.3)	27 (20.6)	345 (26.3)	0.001
Eat miso or other soup (≥2 times/day)	172 (12.8)	202 (15.5)	213 (15.7)	0.055	13 (7.3)	10 (7.6)	107 (8.2)	0.919
Drink almost all noodle soup	456 (33.8)	421 (32.2)	375 (27.7)	0.002	26 (14.7)	15 (11.5)	169 (12.9)	0.690
Eat salty foods (≥3 days/week)	138 (10.2)	158 (12.1)	107 (7.9)	0.001	10 (5.6)	9 (6.9)	108 (8.2)	0.444
Add soy sauce to cooked meal	541 (40.1)	380 (29.1)	235 (17.3)	<0.001	26 (14.7)	17 (13.0)	105 (8.0)	0.004
Eat pickles (≥2 times/day)	130 (9.6)	121 (9.3)	77 (5.7)	<0.001	18 (10.2)	7 (5.3)	72 (5.5)	0.046
Nutritional balance								
Frequently skip breakfast	460 (34.1)	193 (14.8)	280 (20.7)	<0.001	74 (41.8)	36 (27.5)	174 (13.3)	<0.001
Eat vegetables (<3 times/day)	1,011 (75.0)	903 (69.1)	954 (70.4)	0.002	125 (70.6)	97 (74.0)	898 (68.4)	0.376
Eat fruit (<7 days/week)	1083 (80.3)	886 (67.8)	900 (66.4)	<0.001	143 (80.8)	90 (68.7)	816 (62.2)	<0.001
Eat soy products (<7 days/week)	1,035 (76.8)	808 (61.9)	858 (63.3)	<0.001	125 (70.6)	90 (68.7)	830 (63.3)	0.091
Eat milk products (<7 days/week)	843 (62.5)	689 (52.8)	636 (46.9)	<0.001	86 (48.6)	61 (46.6)	518 (39.5)	0.028
Alcohol consumption								
Current drinker	1,036 (76.9)	1,047 (80.2)	905 (66.8)	<0.001	95 (53.7)	76 (58.0)	484 (36.9)	<0.001
Daily alcohol consumption (grams/day)	41.4 (SD29.9)	36.8 (SD32.2)	19.9 (SD23.0)	<0.001	27.6 (SD18.4)	25.3 (SD18.4)	10.7 (SD16.1)	0.001
Psychological health status								
Stressed	193 (14.3)	165 (12.6)	184 (13.6)	0.446	24 (13.6)	12 (9.2)	148 (11.3)	0.475
Depressed	81 (6.0)	56 (4.3)	81 (6.0)	0.083	13 (7.3)	6 (4.6)	51 (3.9)	0.104
Global health status								
Poor current health	137 (15.7)	142 (15.5)	126 (13.8)	0.455	19 (13.8)	20 (20.6)	155 (14.5)	0.252
Sleep problems								
Sleeping time (<6 hours/day)	232 (26.5)	201 (22.0)	288 (31.5)	<0.001	37 (26.8)	28 (28.9)	290 (27.2)	0.931
Snoring	488 (64.0)	536 (65.8)	376 (51.0)	<0.001	36 (35.3)	26 (37.7)	200 (25.7)	0.019
Sleep apnea	199 (30.0)	205 (30.4)	110 (17.6)	<0.001	4 (4.3)	3 (5.0)	18 (2.4)	0.329

Age, waist circumference, weight, body mass index, regular exercise, regular physical activity and alcohol consumption are expressed as the mean plus standard deviation; other data are expressed as n (%).
Global health status and sleeping time: Number of current smokers, ex-smokers and non-smokers were 874, 914 and 914 in males, and 138, 97 and 1,067 in females, respectively.
Snoring: Number of current smokers, ex-smokers and non-smokers were 763, 815 and 737 in males, and 102, 69 and 778 in females, respectively.
Sleep apnea: Number of current smokers, ex-smokers and non-smokers were 664, 675 and 626 in males, and 94, 60 and 746 in females, respectively.

Table 2　Adjusted odds ratios of current smokers and ex-smokers versus nonsmokers in males

	Current smoker/ Nonsmoker (N=1,348/1,355)	Ex-smoker/ Nonsmoker (N=1,306/1,355)	Current smoker/Nonsmoker				Ex-smoker/Nonsmoker				P-value for trend[c]
			1-10 cigarettes/day (N=257/1,355)	11-20 cigarettes/day (N=747/1,355)	≥21 cigarettes/day (N=344/1,355)	P-value for trend[a]	<3 years since cessation of smoking (N=249/1,366)	3-4 years since cessation of smoking (N=168/1,355)	≥5 years since cessation of smoking (N=889/1,355)	P-value for trend[b]	
Physical activity											
Little regular exercise	1.34(1.13-1.60)**	0.76(0.64-0.90)**	1.44(1.06-1.96)*	1.36(1.10-1.67)**	1.41(1.06-1.86)*	0.642	0.77(0.58-1.03)	0.80(0.57-1.12)	0.77(0.63-0.92)**	0.753	<0.001
Little regular physical activity	1.54(1.20-1.98)**	1.07(0.85-1.35)	1.72(1.07-2.77)*	1.61(1.19-2.18)**	1.44(0.97-2.13)	0.528	1.40(0.90-2.18)	0.85(0.54-1.34)	1.02(0.79-1.32)	0.255	0.001
Eating habits											
Overeating											
Go to bed within 1-2 hours after dinner	1.26(1.07-1.47)**	1.07(0.91-1.27)	1.14(0.87-1.50)	1.16(0.97-1.40)	1.50(1.18-1.92)**	0.064	0.99(0.74-1.30)	1.34(0.96-1.85)	1.08(0.90-1.31)	0.506	0.126
Frequently eat until full	0.83(0.71-0.97)*	1.31(1.10-1.55)**	0.75(0.56-0.98)	0.80(0.67-0.97)	0.92(0.72-1.18)	0.102	1.29(0.96-1.73)	1.62(1.13-2.32)**	1.20(0.99-1.46)	0.625	<0.001
Eat snack (almost every day)	0.70(0.57-0.85)**	0.94(0.77-1.16)	0.48(0.31-0.72)***	0.65(0.50-0.83)**	1.01(0.74-1.37)	<0.001	1.07(0.76-1.51)	0.76(0.49-1.20)	0.88(0.69-1.12)	0.540	0.008
Drink sugar-sweetened beverage (almost every day)	2.01(1.71-2.36)***	0.87(0.73-1.04)	1.45(1.10-1.92)**	2.13(1.76-2.57)***	2.50(1.95-3.21)***	0.005	1.21(0.90-1.61)	1.13(0.80-1.59)	0.71(0.58-0.88)**	<0.001	<0.001
Frequently eat quickly	1.25(1.07-1.46)**	1.52(1.29-1.80)***	1.06(0.81-1.39)	1.19(0.99-1.43)	1.62(1.26-2.09)***	0.003	1.38(1.04-1.83)*	2.00(1.39-2.86)***	1.41(1.17-1.71)***	0.949	0.012
Fat consumption											
Eat fried food (almost every day)	1.00(0.85-1.18)	0.92(0.77-1.10)	0.76(0.56-1.02)	1.06(0.87-1.29)	0.99(0.76-1.30)	0.115	1.11(0.83-1.49)	0.89(0.62-1.28)	0.88(0.71-1.08)	0.465	0.267
Eat eggs (almost every day)	0.99(0.84-1.16)	1.06(0.90-1.25)	0.83(0.63-1.11)	1.03(0.85-1.25)	1.07(0.83-1.37)	0.175	0.98(0.74-1.31)	1.07(0.76-1.50)	1.06(0.88-1.29)	0.588	0.088
Eat fatty meat (≥3 days/week)	1.07(0.91-1.26)	1.01(0.85-1.19)	0.77(0.58-1.02)*	1.08(0.89-1.31)	1.24(0.96-1.59)	0.004	1.00(0.75-1.34)	1.48(1.06-2.07)*	0.91(0.75-1.11)	0.524	0.399
Eat seafood (<3 days/week)	1.40(1.19-1.63)***	1.10(0.94-1.30)	1.31(0.99-1.72)	1.37(1.14-1.65)**	1.51(1.18-1.93)**	0.381	1.22(0.92-1.61)	0.86(0.62-1.20)	1.12(0.93-1.35)	0.919	0.007
Salt consumption											
Frequently prefer strong flavors	2.23(1.89-2.63)***	1.58(1.33-1.88)***	1.50(1.12-2.00)**	2.40(1.98-2.91)***	2.70(2.11-3.47)***	0.001	2.17(1.64-2.88)***	1.85(1.32-2.60)***	1.40(1.15-1.72)**	0.001	<0.001
Eat miso or other soup (≥2 times/day)	0.82(0.66-1.02)	1.04(0.84-1.30)	0.76(0.51-1.14)	0.82(0.63-1.07)	0.86(0.60-1.22)	0.530	0.95(0.65-1.39)	1.37(0.90-2.06)	1.01(0.79-1.30)	0.902	0.076
Drink almost all noodle soup	1.35(1.14-1.59)***	1.28(1.07-1.52)**	1.09(0.81-1.46)	1.42(1.17-1.73)***	1.40(1.08-1.81)*	0.115	1.55(1.17-2.07)**	2.02(1.45-2.81)***	1.05(0.86-1.29)	0.004	0.108
Eat salty foods (≥3 days/week)	1.18(0.91-1.55)	1.28(0.98-1.68)	1.03(0.62-1.70)	1.30(0.96-1.78)	1.18(0.78-1.76)	0.695	1.21(0.77-1.90)	1.67(1.03-2.70)*	1.14(0.84-1.54)	0.517	0.696
Add soy sauce to cooked meal	3.02(2.52-3.61)***	1.76(1.45-2.13)***	2.11(1.56-2.86)***	3.10(2.52-3.81)***	3.97(3.06-5.14)***	0.001	2.22(1.64-3.00)***	2.61(1.84-3.69)***	1.47(1.18-1.84)**	0.001	<0.001
Eat pickles (≥2 times/day)	1.59(1.18-2.14)**	1.35(0.99-1.83)	2.11(1.33-3.34)***	1.35(0.95-1.93)	2.00(1.33-3.00)**	0.888	1.54(0.94-2.50)	1.28(0.70-2.34)	1.24(0.88-1.74)	0.282	0.129
Nutritional balance											
Frequently skip breakfast	2.54(2.11-3.05)***	0.98(0.79-1.22)	1.45(1.06-2.00)*	2.59(2.09-3.22)***	3.96(3.01-5.21)***	<0.001	1.35(0.96-1.91)	0.87(0.55-1.38)	0.98(0.75-1.27)	0.089	<0.001
Eat vegetables (<3 times/day)	1.36(1.14-1.62)**	1.12(0.94-1.33)	1.04(0.77-1.41)	1.36(1.11-1.68)**	1.58(1.19-2.09)**	0.058	1.21(0.89-1.65)	1.35(0.93-1.94)	1.11(0.91-1.35)	0.476	0.014
Eat fruit (<7 days/week)	2.28(1.90-2.74)***	1.32(1.11-1.57)**	1.73(1.24-2.40)***	2.20(1.76-2.73)***	2.88(2.11-3.94)***	0.028	1.77(1.29-2.44)***	1.76(1.20-2.56)**	1.20(0.99-1.46)	0.008	<0.001
Eat soy products (<7 days/week)	2.03(1.71-2.41)***	1.07(0.90-1.26)	1.76(1.29-2.39)***	2.12(1.72-2.61)***	2.15(1.63-2.85)***	0.347	1.28(0.96-1.71)	0.79(0.57-1.09)	1.05(0.87-1.27)	0.427	<0.001
Eat milk products (<7 days/week)	1.89(1.62-2.21)***	1.30(1.11-1.53)**	1.34(1.02-1.75)*	2.04(1.69-2.47)***	2.06(1.60-2.64)***	0.030	1.58(1.20-2.09)**	1.86(1.34-2.60)***	1.18(0.98-1.41)	0.011	<0.001
Alcohol consumption											
Daily alcohol consumption (≥46 grams/day)	2.28(1.87-2.77)***	1.67(1.36-2.04)***	2.24(1.64-3.07)***	2.21(1.76-2.77)***	2.76(2.08-3.66)***	0.162	2.17(1.58-2.97)***	1.57(1.06-2.32)*	1.51(1.20-1.90)***	0.032	<0.001
Psychological health status											
Stressed	1.00(0.80-1.25)	0.95(0.75-1.20)	0.70(0.46-1.09)	0.96(0.73-1.25)	1.05(0.75-1.48)	0.066	0.93(0.62-1.40)	0.95(0.59-1.54)	0.97(0.74-1.28)	0.580	0.997
Depressed	0.89(0.64-1.24)	0.72(0.50-1.05)	0.69(0.36-1.31)	0.90(0.60-1.33)	1.01(0.62-1.65)	0.234	1.02(0.58-1.80)	0.87(0.42-1.80)	0.57(0.36-0.90)*	0.048	0.103
Global health status											
Poor current health	0.95(0.72-1.25)	1.04(0.79-1.36)	0.85(0.51-1.42)	0.92(0.66-1.28)	1.05(0.70-1.57)	0.353	0.99(0.63-1.58)	1.44(0.87-2.38)	1.01(0.73-1.38)	0.924	0.442
Sleep problems											
Sleeping time (<6 hours/day)	0.71(0.57-0.88)**	0.62(0.50-0.78)***	0.65(0.44-0.96)*	0.71(0.55-0.92)*	0.70(0.48-0.94)*	0.699	0.48(0.32-0.72)***	0.85(0.55-1.31)	0.61(0.47-0.79)***	0.211	0.837
Snoring	1.34(1.08-1.67)**	1.53(1.23-1.90)***	1.26(0.86-1.84)	1.17(0.90-1.51)	1.84(1.28-2.65)**	0.059	1.22(0.86-1.75)	1.96(1.23-3.14)**	1.58(1.24-2.02)***	0.147	0.056
Sleep apnea	1.44(1.09-1.91)*	1.48(1.12-1.95)**	1.09(0.66-1.81)	1.41(1.02-1.95)*	1.78(1.20-2.65)**	0.079	1.46(0.94-2.27)	2.12(1.29-3.49)**	1.42(1.04-1.94)*	0.801	0.893

*p<0.05, **p<0.01, ***p<0.001.

Multivariable-adjusted relative odds ratios (95% confidence interval) are shown.

Physical activity was adjusted for age, socioeconomic status, eating habits score, and alcohol consumption.

Eating habits were adjusted for age, socioeconomic status, regular physical activity, and alcohol consumption.

Alcohol consumption was adjusted for age, socioeconomic status, regular physical activity, and eating habits score.

Other variables were adjusted for age, socioeconomic status, regular physical activity, eating habits score, and alcohol consumption.

Global health status and sleeping time: Number of current smokers, ex-smokers and non-smokers were 874, 914 and 914, respectively.

Snoring: Number of current smokers, ex-smokers and non-smokers were 763, 815 and 737, respectively. Sleep apnea: Number of current smokers, ex-smokers and non-smokers were 664, 675 and 626, respectively.

[a]The test for trend was calculated across increasing categories of daily cigarette consumption for current smokers only.

[b]The test for trend was calculated across increasing categories of years after cessation for ex-smokers only.

[c]The test for trend was calculated across increasing categories of years after cessation for ex-smokers and current smokers (duration was assumed to be 0).

Table 3 Adjusted odds ratios of current smokers and ex-smokers versus nonsmokers in females

	Current smoker/ Nonsmoker (N=177/1,312)	Ex-smoker/ Nonsmoker (N=131/1,312)	Current smoker/Nonsmoker				Ex-smoker/Nonsmoker				
			1–10 cigarettes/day (N=108/1,312)	11–20 cigarettes/day (N=62/1,312)	≥21 cigarettes/day (N=7/1,312)	P-value for trend[a]	<3 years since cessation of smoking (N=39/1,312)	3–4 years since cessation of smoking (N=12/1,312)	≥5 years since cessation of smoking (N=80/1,312)	P-value for trend[b]	P-value for trend[c]
Physical activity											
Little regular exercise	1.29(0.83–2.01)	1.24(0.76–2.03)	1.60(0.89–2.86)	1.04(0.53–2.05)	0.59(0.11–3.11)	0.246	1.52(0.59–3.94)	2.53(0.32–1.98)	1.03(0.57–1.85)	0.552	0.667
Little regular physical activity	1.13(0.54–2.33)	1.29(0.54–3.08)	1.21(0.47–3.10)	1.16(0.35–3.87)	0.41(0.05–3.53)	0.517	2.16(0.29–16.15)	0.60(0.08–4.83)	1.27(0.45–3.63)	0.881	0.942
Eating habits											
Overeating											
Go to bed within 1–2 hours after dinner	0.92(0.62–1.38)	1.37(0.90–2.08)	0.76(0.45–1.29)	1.27(0.69–2.31)	0.67(0.08–5.59)	0.306	1.34(0.64–2.80)	0.74(0.16–3.44)	1.52(0.91–2.55)	0.436	0.112
Frequently eat until full	0.93(0.67–1.29)	1.38(0.93–2.05)	0.79(0.53–1.19)	1.25(0.72–2.17)	0.86(0.19–3.89)	0.170	4.92(1.73–13.97)**	2.53(0.55–11.68)	0.83(0.52–1.33)	0.002	0.926
Eat snack (almost every day)	0.63(0.45–0.89)**	1.16(0.80–1.67)	0.67(0.44–1.03)	0.65(0.37–1.12)	0.26(0.03–2.18)	0.685	1.05(0.55–2.01)	1.40(0.44–4.38)	1.15(0.72–1.82)	0.621	0.012
Drink sugar-sweetened beverage (almost every day)	1.93(1.39–2.68)***	1.46(0.99–2.15)	1.63(1.08–2.47)*	2.35(1.40–3.96)**	3.37(0.85–17.56)	0.093	1.69(0.87–3.27)	0.54(0.18–2.50)	1.55(0.96–2.51)	0.855	0.297
Frequently eat quickly	1.15(0.84–1.58)	1.34(0.93–1.93)	1.03(0.70–1.54)	1.35(0.81–2.27)	1.39(0.31–6.31)	0.347	1.51(0.79–2.88)	1.23(0.39–3.87)	1.24(0.78–1.96)	0.714	0.597
Fat consumption											
Eat fried food (almost every day)	1.05(0.72–1.54)	1.33(0.88–2.02)	0.80(0.48–1.34)	1.66(0.94–2.93)	0.72(0.09–6.11)	0.441	1.01(0.47–2.16)	3.17(0.99–10.02)	1.25(0.73–2.13)	0.942	0.313
Eat eggs (almost every day)	0.65(0.45–0.93)*	0.77(0.52–1.15)	0.64(0.41–0.99)*	0.68(0.38–1.21)	0.72(0.13–3.92)	0.874	0.88(0.44–1.74)	0.94(0.29–3.03)	0.70(0.42–1.18)	0.468	0.851
Eat fatty meat (≥3 days/week)	0.81(0.58–1.13)	1.03(0.71–1.50)	0.81(0.53–1.24)	0.76(0.43–1.32)	1.38(0.30–6.33)	0.759	0.97(0.50–1.88)	2.79(0.83–9.36)	0.88(0.54–1.42)	0.770	0.479
Eat seafood (<3 days/week)	1.16(0.84–1.60)	1.23(0.84–1.79)	1.09(0.73–1.63)	1.16(0.69–1.96)	2.17(0.41–11.34)	0.419	1.19(0.61–2.30)	0.96(0.30–3.06)	1.28(0.80–2.06)	0.427	0.579
Salt consumption											
Frequently prefer strong flavors	1.64(1.17–2.28)**	0.71(0.46–1.11)	1.62(1.07–2.45)*	1.74(1.02–2.95)*	1.13(0.22–5.88)	0.974	0.74(0.33–1.63)	1.04(0.28–3.87)	0.66(0.38–1.17)	0.673	0.004
Eat miso or other soup (≥2 times/day)	0.97(0.53–1.79)	1.01(0.51–2.01)	1.11(0.54–2.27)	0.88(0.31–2.48)	2.23(0.26–19.17)	0.726	1.32(0.46–3.82)	0.96(0.12–7.58)	1.04(0.43–2.47)	0.589	0.950
Drink almost all noodle soup	1.05(0.67–1.65)	0.77(0.44–1.37)	0.85(0.47–1.57)	1.15(0.57–2.32)	3.95(0.86–18.03)	0.077	0.73(0.26–2.10)	0.65(0.08–5.09)	0.92(0.47–1.78)	0.759	0.658
Eat salty foods (≥3 days/week)	0.59(0.30–1.16)	0.72(0.35–1.47)	0.60(0.26–1.41)	0.66(0.23–1.87)	1.41(0.17–12.02)	0.544	0.89(0.27–2.96)	1.17(0.15–9.29)	0.64(0.25–1.62)	0.505	0.990
Add soy sauce to cooked meal	1.92(1.20–3.06)**	1.65(0.95–2.88)	1.82(1.01–3.28)*	2.14(1.05–4.36)*	1.84(0.22–15.62)	0.647	1.30(0.45–3.76)	1.10(0.14–8.63)	2.06(1.09–3.90)*	0.457	0.911
Eat pickles (≥2 times/day)	1.71(0.99–2.97)	0.84(0.37–1.87)	1.41(0.68–2.93)	2.18(0.99–4.81)	2.15(0.25–18.48)	0.495	1.85(0.63–5.41)	1.73(0.22–13.78)	0.55(0.17–1.79)	0.114	0.080
Nutritional balance											
Frequently skip breakfast	5.42(3.79–7.73)***	2.80(1.82–4.32)***	4.87(3.14–7.54)***	6.81(3.94–11.77)***	6.85(1.44–32.63)*	0.345	2.65(1.27–5.53)*	2.89(0.84–9.95)	2.89(1.68–4.99)**	0.880	0.021
Eat vegetables (<3 times/day)	1.14(0.81–1.62)	1.36(0.90–2.05)	1.18(0.76–1.83)	0.94(0.54–1.61)	3.01(0.36–25.19)	0.824	1.20(0.59–2.44)	0.65(0.20–2.08)	1.62(0.94–2.78)	0.456	0.323
Eat fruit (<7 days/week)	2.62(1.76–3.88)***	1.34(0.90–1.98)	2.01(1.26–3.20)**	3.78(1.84–7.75)***	3.85(0.45–32.79)	0.096	1.99(0.93–4.26)	1.04(0.31–3.48)	1.17(0.72–1.89)	0.329	0.007
Eat soy products (<7 days/week)	1.45(1.03–2.05)*	1.33(0.90–1.96)	1.21(0.79–1.84)	1.75(0.97–3.13)	3.71(0.44–30.98)	0.135	1.05(0.54–2.05)	2.86(0.62–13.17)	1.34(0.82–2.18)	0.321	0.927
Eat milk products (<7 days/week)	1.46(1.06–2.01)*	1.33(0.92–1.92)	1.43(0.96–2.12)	1.50(0.89–2.50)	2.11(0.46–9.60)	0.832	1.43(0.75–2.72)	1.91(0.60–6.09)	1.22(0.77–1.93)	0.468	0.532
Alcohol consumption											
Daily alcohol consumption (≥23 grams/day)	3.24(2.23–4.71)***	2.22(1.41–3.49)**	2.58(1.61–4.15)***	4.42(2.52–7.77)***	6.19(1.32–28.97)*	0.113	2.14(0.98–4.66)	2.15(0.57–8.10)	2.35(1.32–4.20)**	0.937	0.183
Psychological health status											
Stressed	1.20(0.75–1.93)	0.79(0.42–1.47)	1.36(0.77–2.38)	0.67(0.26–1.71)	5.84(1.27–26.81)*	0.780	0.62(0.19–2.04)	1.50(0.32–7.00)	0.77(0.34–1.71)	0.986	0.291
Depressed	1.85(0.97–3.52)	1.15(0.48–2.76)	1.80(0.79–4.12)	1.99(0.75–5.29)	3.58(0.41–31.49)	0.509	1.91(0.56–6.54)	2.32(0.29–18.75)	0.58(0.14–2.48)	0.171	0.186
Global health status											
Poor current health	0.82(0.49–1.39)	1.41(0.83–2.39)	0.67(0.32–1.37)	0.77(0.34–1.77)	4.46(0.87–22.72)	0.145	2.28(1.02–5.10)*	1.71(0.35–8.40)	1.00(0.48–2.09)	0.157	0.592
Sleep problems											
Sleeping time (<6 hours/day)	0.94(0.62–1.41)	1.07(0.67–1.70)	1.11(0.69–1.79)	0.84(0.44–1.60)	0.56(0.07–4.73)	0.271	0.77(0.33–1.77)	2.85(0.88–9.21)	0.90(0.51–1.59)	0.460	0.740
Snoring	1.16(0.73–1.85)	1.64(0.95–2.83)	1.16(0.65–2.09)	1.08(0.51–2.26)	2.03(0.30–13.65)	0.708	1.52(0.60–3.87)	3.55(0.84–15.09)	1.44(0.70–2.95)	0.947	0.445
Sleep apnea	1.25(0.40–3.95)	2.15(0.60–7.79)	1.14(0.25–5.11)	1.39(0.29–6.73)	4.59(0.42–50.32)	0.491	3.13(0.38–25.63)	6.90(0.73–65.71)	2.28(0.49–10.69)	0.368	0.395

*p<0.05, **p<0.01, ***p<0.001.

Multivariable-adjusted relative odds ratios (95% confidence interval) are shown.

Physical activity was adjusted for age, socioeconomic status, eating habits score, and alcohol consumption.

Eating habits were adjusted for age, socioeconomic status, regular physical activity, and alcohol consumption.

Alcohol consumption was adjusted for age, socioeconomic status, regular physical activity, and eating habits score.

Other variables were adjusted for age, socioeconomic status, regular physical activity, eating habits score, and alcohol consumption.

Global health status and sleeping time: Number of current smokers, ex-smokers and non-smokers were 138, 97 and 1,067, respectively.

Snoring: Number of current smokers, ex-smokers and non-smokers were 102, 69 and 778, respectively. Sleep apnea: Number of current smokers, ex-smokers and non-smokers were 94, 60 and 746, respectively.

[a]The test for trend was calculated across increasing categories of daily cigarette consumption for current smokers only.

[b]The test for trend was calculated across increasing categories of years after cessation for ex-smokers only.

[c]The test for trend was calculated across increasing categories of years after cessation for ex-smokers and current smokers (duration was assumed to be 0).