Available online at www.sciencedirect.com
ScienceDirect
Preventive Medicine 44 (2007) 349–355
Preventive Medicine
www.elsevier.com/locate/ypmed

The joint impact of cardiovascular risk factors upon medical costs

Kaori Ohmori-Matsuda [a,*], Shinichi Kuriyama [a], Atsushi Hozawa [a,b], Naoki Nakaya [a], Taichi Shimazu [a], Ichiro Tsuji [a]

[a] *Division of Epidemiology, Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, 2-1 Seiryo-machi, Aoba-ku, Sendai, 980-8575, Japan*
[b] *Department of Health Science, Shiga University of Medical Science, Japan*

Available online 7 February 2007

Abstract

Objective. The joint impact of obesity, hypertension, and hyperglycemia upon medical costs is not well known. Our objective was to evaluate the joint impact of these cardiovascular risk factors upon medical costs in the rural Japanese population.

Methods. The data were derived from a 6-year prospective observation of National Health Insurance beneficiaries in rural Japan. Data on blood chemistry tests, blood pressure, weight, and height were obtained from an annual health check-up provided by the local municipalities in 1995. We prospectively collected data on medical costs over a 6-year period for 12,340 subjects (5306 men and 7034 women) without prior histories of cardiovascular disease or cancer.

Results. Mean medical costs for individuals being overweight/obese, hypertensive, and hyperglycemic were 91.0% higher than those for individuals without any of these three cardiovascular risk factors. In this cohort, 17.2% of total medical costs were attributable to these three risk factors.

Conclusion. Overweight/obesity, hypertension, and hyperglycemia could have a large impact on health care resources in rural Japan.

Keywords: Hypertension; Obesity; Hyperglycemia; Health care costs

Introduction

Medical costs are increasing much faster than Gross Domestic Product in most industrialized countries (Organisation for Economic Co-operation and Development, 2005), and this imbalance is now becoming a serious threat to the sustainability of national health insurance systems. Reducing the need and demand for medical services through health promotion and disease prevention is expected to stabilize medical costs and alleviate this imbalance (Fries et al., 1993). Several studies have estimated the economic impact of modifiable cardiovascular risk factors including hypertension, hyperglycemia, dyslipidemia, or obesity. Most of them were focused on the economic impact of a single risk factor (Nakamura et al., 2005; Brown et al., 1999; Nichols and Brown, 2005; Chenoweth, 2004; Selby et al., 1997; Thompson and Wolf, 2001; Quesenberry et al., 1998; Raebel et al., 2004; Kuriyama et al., 2002) or were based on hypothetical, cross-sectional, or retrospective study designs (Ray et al., 2000; Oliva et al., 2004; Hodgson and Cohen, 1999; Hogan et al., 2003). These cardiovascular risk factors often occurred together in the same individual (Ford et al., 2002; Greenland et al., 2003; Haffner and Taegtmeyer, 2003), and their combination synergistically increased the risk of morbidity and mortality (Stamler et al., 1993, 1999; Wilson et al., 1998; Greenland et al., 2003), consequently raising medical costs. However, the joint impact of these cardiovascular risk factors upon medical costs is still unclear.

A few previous cohort studies have tried to estimate the relationship between medical costs and combination of cardiovascular risk factors (Daviglus et al., 1998; Goetzel et al., 1998; Anderson et al., 2000; Jee et al., 2001; Lynch et al., 2005). Most of them were limited to working individuals, who were healthy enough to work at entry into the cohort and would later drop out when they ceased to work because of age or illness. Therefore, these studies would have underestimated the impact of cardiovascular risks upon medical costs. To fully examine the impact of cardiovascular risk factors upon medical

* Corresponding author. Fax: +81 22 717 8125.
E-mail address: ohmori-k@umin.ac.jp (K. Ohmori-Matsuda).

0091-7435/$ - see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.ypmed.2006.11.020

costs, it is necessary to follow-up a large-scale population-based cohort that retains all individuals, regardless of age or health status.

Our objective was to evaluate the joint impact of cardiovascular risk factors upon medical costs in the rural Japanese population. The present data were derived from a 6-year follow-up observation of National Health Insurance (NHI) beneficiaries in rural Japan, known as the Ohsaki NHI Cohort Study (Tsuji et al., 1998, 2003; Izumi et al., 2001; Kuriyama et al., 2004; Anzai et al., 2005).

Methods

Study setting and design

The setting and design of the Ohsaki NHI Cohort Study have already been reported in detail (Tsuji et al., 1998). In brief, this prospective cohort study started in 1994, when we delivered a self-administered questionnaire on various health-related lifestyles to all NHI beneficiaries aged 40–79 years living in the catchments area of Ohsaki Public Health Center, Miyagi Prefecture, Japan. NHI in Japan is used by farmers, the self-employed, pensioners, and their dependents. Ohsaki Public Health Center, a local government agency, provides preventive health services for the residents of 14 municipalities. The questionnaires were delivered to and collected from the subjects' residences by public health officials in each municipality. This procedure yielded a high response rate of 94.6% (N=52,029). We excluded 774 subjects because they had withdrawn from the NHI before January 1, 1995, when we started the prospective collection of NHI claim files. Thus, 51,255 subjects formed the study cohort. This study was approved by the Ethics Committee of the Tohoku University Graduate School of Medicine. We considered the return of self-administered questionnaires signed by the subjects to imply their consent to participate in the study.

Exposure data

Data on cardiovascular risk factors were obtained from an annual health check-up conducted by physicians and provided by the local municipalities in 1995. This annual health check-up is provided free, or at low charge, to all people aged 40 years and over in Japan. The examinations include an interview, measurement of weight, height and blood pressure (BP), physical examination, and blood chemistry tests for serum total cholesterol, serum high-density lipoprotein (HDL), plasma glucose, and other parameters, without instructions to fast beforehand.

In this study, we defined hypertension as either a self-report of taking antihypertensive medication or systolic BP $\geq$140 mm Hg or diastolic BP $\geq$90 mm Hg (Chobanian et al., 2003), and dyslipidemia as either a self-report of taking lipid-lowering medication or a serum total cholesterol level $\geq$220 mg/dl or serum HDL level <40 mg/dl (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001). Hyperglycemia was defined as either a self-reported history of diabetes or a plasma glucose level $\geq$150 mg/dl (Schauffler et al., 1993). Body Mass Index (BMI) was calculated as the weight (kg)/height (m)^2. We defined overweight/obesity as a BMI $\geq$25 (World Health Organization, 2000).

Follow-up

Among the participants of the Ohsaki NHI Cohort Study, 17,065 (33.3%) received the annual health check-up between June and November in 1995, and gave their consent for us to analyze their results for this study. We prospectively collected NHI claims files from the local NHI Association for all individuals in the cohort for the period from January 1, 1996, to the date of withdrawal from the NHI because of death or emigration, or until December 31, 2001. When a beneficiary withdraws from the NHI, the date and reason are entered in the NHI withdrawal files. Both NHI claims and withdrawal files were linked to our baseline survey data and annual health check-up data files, using each beneficiary's identification number as the key code.

Out of 17,065 examines, we excluded 439 because they had withdrawn from the NHI before January 1, 1996. We also excluded 1522 subjects who reported having had cancer, stroke, or myocardial infarction and 2764 subjects who had missing data for BP, body measurements, and blood tests. Consequently, 12,340 subjects (5306 men and 7034 women) were included in this analysis.

Assessment of medical costs

NHI covers almost all medical care, including diagnostic tests, medication, and surgery. When medical providers treat a patient, they receive co-payment from the patient and then file a claim to the local NHI Association for reimbursement. Payment to medical providers is made on a fee-for-service basis, where the price of each service is determined by a uniform national fee schedule. The local NHI Association has provided us with subjects' NHI claim files every month.

Monthly medical costs for each subject were calculated by dividing the total medical costs throughout the observation period by the number of months observed. We used monthly values rather than cumulative values to avoid underestimating medical costs for subjects who died or emigrated during the follow-up (Kuriyama et al., 2004; Anzai et al., 2005).

Statistical analysis

Like previous studies (Daviglus et al., 1998; Kuriyama et al., 2004; Anzai et al., 2005), we chose an ordinary least-squares model based on non-log-transformed data in a general linear model because the results in the original dollar units are more easily interpretable and because total medical costs for groups can be estimated from adjusted mean-per-individual costs.

We estimated the relative contribution of each of four cardiovascular risk factors (hypertension, dyslipidemia, hyperglycemia, and overweight/obesity) to medical costs. We estimated medical costs within three categories-inpatient, outpatient, and total cost-for subjects with and without these index risk factors using analysis of covariance (ANCOVA) adjusted by age at the baseline (continuous variable), sex, smoking (current smoker, past smoker, or never smoker), alcohol drinking (current drinker, past drinker, or never drinker), and comorbidity of the other three cardiovascular risk factors.

To assess the joint impact of cardiovascular risk factors upon medical costs, we classified the subjects into categories according to the combination of risk factors that were significantly associated with medical costs, and calculated the adjusted mean monthly medical costs of each category by ANCOVA.

We estimated the proportion of risk-attributable medical costs (RAC%) related to the cardiovascular risk factors. First, we calculated the adjusted excess costs per individual for each risk category by subtracting the mean medical costs among those without any of overweight/obesity, hypertension, and hyperglycemia from the mean medical costs for each risk category. Second, to estimate risk-attributable medical costs for each risk category, the adjusted excess costs per individual for each risk category were multiplied by the person-months for each risk category observed. Risk-attributable medical costs were divided by total medical costs for the entire cohort. The results provided the estimates of RAC%.

All analyses were conducted with SAS software version 9.1 (SAS Institute Inc., 2004). We estimated the P-value using the F-value of the general linear model and estimated the 95% confidence interval (CI) from the least squares standard error. For multiple comparisons, we used the Tukey test. All of the statistical tests reported here were two-sided, and differences at P <0.05 were accepted as statistically significant. In this paper, monetary values are converted to U.S. dollars ($) using an exchange rate of $1.00=115 Japanese yen.

Results

Among 51,255 participants in the Ohsaki NHI Cohort Study, 24.1% (N=12,340) were available for the present study. They were more likely to be female, current nonsmoker, normotensive, and normoglycemic as compared with non-participants (N=38,915) (Table 1).

Table 1
Baseline characteristics of the Ohsaki Study subjects in 1995, Japan

	Non-participants	Study participants	P-value [a]	Overweight/Obesity [b]		Hypertension [c]		Hyperglycemia [d]		Dyslipidemia [e]	
				(−)	(+)	(−)	(+)	(−)	(+)	(−)	(+)
N	38,915	12,340		8152	4188	7158	5182	11,292	1048	6790	5550
Age (year) (SD)	61.0 (10.6)	61.1 (9.4)	0.25	61.2 (9.6)	61.0 (8.9)	59.1 (9.7)	63.9 (8.2)	60.8 (8.3)	64.0 (8.3)	60.5 (9.8)	61.8 (8.9)
Male (%)	49.4	43.0	<0.0001	45.5	38.2	41.7	44.8	41.6	58.2	47.1	38.0
Current smoker (%)	30.0	22.3	<0.0001	24.7	17.7	23.0	21.3	21.6	30.3	23.9	20.4
Current drinker (%)	42.1	42.6	<0.0001	43.6	40.8	41.3	44.4	42.0	49.6	47.9	36.2
Overweight/obesity (%)	28.7 [f]	28.8 [f]	0.75	0.0 [b]	100.0 [b]	27.8 [b]	42.5 [b]	33.7 [b]	36.1 [b]	27.9 [b]	41.4 [b]
Hypertension (%)	27.5 [g]	23.8 [g]	<0.0001	36.6 [c]	52.5 [c]	0.0 [c]	100.0 [c]	41.0 [c]	52.5 [c]	39.5 [c]	45.1 [c]
Hyperglycemia (%)	7.2 [h]	4.7 [h]	<0.0001	8.2 [d]	9.0 [d]	7.0 [d]	10.6 [d]	0.0 [d]	100.0 [d]	7.9 [d]	9.2 [d]
Dyslipidemia (%)	–	–		39.9 [e]	54.9 [e]	42.6 [e]	48.3 [e]	44.6 [e]	48.9 [e]	0.0 [e]	100.0 [e]

SD denotes standard deviation.
[a] Variables were compared between study participants and non-participants by the t-test or the χ^2 test, as appropriate.
[b] Measured Body Mass Index ≥25.0.
[c] Blood pressure ≥140/90 mm Hg or self-report of taking antihypertensive medication.
[d] Casual blood glucose ≥150 mg/dl or self-reported history of diabetes.
[e] Casual serum cholesterol ≥220 mg/dl, or HDL <40 mg/dl, or self-report of taking lipid-lowering medication.
[f] Body Mass Index calculated by self-reported weight/(height*height) ≥25.0.
[g] Self-reported history of hypertension.
[h] Self-reported history of diabetes.

Of the 12,340 study participants, 12,054 (97.7%), 4215 (34.2%), and 12,047 (97.6%) used total, inpatient, and outpatient medical care and had more than zero costs for the 6-year period. During the follow-up, 584 subjects (4.7%) died and 921 (7.5%) were lost to follow-up. Table 1 shows the baseline characteristics of the subjects in terms of presence/absence of overweight/obesity, hypertension, hyperglycemia, and dyslipidemia. Cardiovascular risk factors were often present together in the same individual. Among the study participants, 39.1% had no risk factor, 39.3% had a single risk factor, and 21.6% had two or more risk factors. In comparison with those without overweight/obesity, those with overweight/obesity had a higher prevalence of the other three cardiovascular risk factors and were less likely to be current smokers or current drinkers. Also, hypertension, hyperglycemia, and dyslipidemia were associated with a higher prevalence of the other three cardiovascular risk factors.

Table 2 shows the adjusted monthly medical costs of the subjects in terms of presence/absence of these cardiovascular risk factors. The adjusted mean total and outpatient medical costs among overweight/obese subjects were significantly higher than those among subjects who were not overweight/obese (P=0.013, 0.030, respectively). The mean inpatient cost among overweight/obese subjects was higher than that among subjects who were not overweight/obese, but the difference was not significant (P=0.068). The adjusted mean total, inpatient, and outpatient medical costs among subjects with hypertension were significantly higher than among subjects without hypertension (P <0.0001, 0.0008, <0.0001). The adjusted mean total, inpatient, and outpatient medical costs among subjects with hyperglycemia were significantly higher than among subjects without hyperglycemia (P <0.0001, 0.0004, <0.0001). There was no difference in total, inpatient, and outpatient medical costs between subjects with and without dyslipidemia (P=0.74, 0.50, 0.55).

Table 2
Adjusted monthly medical costs by the presence/absence of the cardiovascular risk factors in the Ohsaki Study, Japan, 1996–2001

		N	Adjusted inpatient cost [a], $		Adjusted outpatient cost [a], $		Adjusted total cost [a], $		Increasing rate (%)
			(95%CI)	P-value	(95%CI)	P-value	(95%CI)	P-value	
Overweight/obesity [b]	(−)	8152	87.1 (78.8–95.5)	(Referent)	139.5 (135.4–143.6)	(Referent)	226.6 (216.9–236.3)	(Referent)	(Referent)
	(+)	4188	100.6 (88.9–112.3)	0.068	147.4 (141.6–153.2)	0.030	248.0 (234.4–261.6)	0.013	9.4
Hypertension [c]	(−)	7158	81.5 (72.5–90.5)	(Referent)	122.0 (117.6–126.4)	(Referent)	203.5 (193.0–213.9)	(Referent)	(Referent)
	(+)	5182	105.8 (95.1–116.4)	0.0008	170.1 (164.8–175.3)	<0.0001	275.9 (263.5–288.2)	<0.0001	35.6
Hyperglycemia [d]	(−)	11,292	88.0 (80.9–95.0)	(Referent)	137.8 (134.3–141.3)	(Referent)	225.8 (217.6–234.0)	(Referent)	(Referent)
	(+)	1048	131.8 (108.4–155.1)	0.0004	189.4 (177.9–200.9)	<0.0001	321.1 (294.0–348.2)	<0.0001	42.2
Dyslipidemia [e]	(−)	6790	93.8 (84.7–103.0)	(Referent)	141.3 (136.7–145.8)	(Referent)	235.1 (224.5–245.7)	(Referent)	(Referent)
	(+)	5550	89.1 (79.0–99.2)	0.50	143.3 (138.3–148.3)	0.55	232.4 (220.6–244.2)	0.74	−1.1

CI denotes confidence interval. The plus (+) denotes the presence of each of the index risk factors. The minus (−) denotes the absence of each of the index risk factors.
[a] Tested by analysis of covariance (ANCOVA) using non-log-transformed data on charges adjusted by age at baseline (continuous variable), sex, smoking (current smoker, past smoker, or never smoker), alcohol drinking (current drinker, past drinker, or never drinker), and comorbid condition of other three cardiovascular risk factors.
[b] Body Mass Index ≥25.0.
[c] Blood pressure ≥140/90 mm Hg or self-report of taking antihypertensive medication.
[d] Casual blood glucose ≥150 mg/dl or self-reported history of diabetes.
[e] Casual serum cholesterol ≥220 mg/dl, or HDL <40 mg/dl, or self-report of taking lipid-lowering medication.

Table 3
The joint impact of cardiovascular risk factors upon medical costs in the Ohsaki Study, Japan, 1996–2001

No. of risks	N	Person-months	Inpatient costs				Risk-attributable costs[b], $	RAC%[c] (%)	Outpatient costs	
			Adjusted cost[a], $	(95%CI)	P-value	Increasing rate (%)			Adjusted cost[a], $	(95%CI)
0	4821	323,036	76.2	(65.3–87.1)	(Referent)	(Referent)			117.2	(111.9–122.6)
1										
Overweight/obesity[d]	1839	123,039	82.8	(65.2–100.4)	0.99	8.7	812,054	1.1	120.4	(111.8–129.0)
Hypretension[e]	2661	177,066	95.3	(80.6–110.0)	0.47	25.1	3,381,967	4.5	161.9	(154.7–169.1)
Hyperglycemia[f]	349	23,080	126.7	(86.6–166.8)	0.25	66.3	1,165,524	1.5	160.2	(140.5–179.9)
2										
Overweight/obesity[d] + Hypretension[e]	1971	131,829	111.1	(94.2–128.1)	0.017	45.8	4,600,825	6.1	170.1	(161.8–178.4)
Overweight/obesity[d] + Hyperglycemia[f]	149	10,117	105.4	(44.2–166.7)	0.98	38.3	295,418	0.4	173.4	(143.4–203.5)
Hypretension[e] + Hyperglycemia[f]	321	20,718	134.7	(92.7–176.7)	0.13	75.8	1,211,976	1.6	223.5	(202.9–244.1)
3										
Overweight/obesity[d] + Hypretension[e] + Hyperglycemia[f]	229	15,173	158.2	(108.7–207.7)	0.034	107.6	1,244,169	1.6	211.2	(186.9–235.5)
Total	12,340	824,056					12,711,934	16.8		

CI denotes confidence interval. RAC% denotes percentage of risk-attributable medical costs.
[a] Tested by analysis of covariance (ANCOVA) adjusted by age at baseline (continuous variable), sex, smoking (current smoker, past smoker, or never smoker), and alcohol drinking (current drinker, past drinker, or never drinker).
[b] The increment in medical costs attribute to cardiovascular risk factors were calculated by multiplying the adjusted excess costs by the number of person-months observed.
[c] The proportion of medical costs in the entire cohort that would not occur if no one had cardiovascular risk factors, which were calculated by dividing the risk-attributable medical costs by the total medical costs for entire cohort during the 6-years of observation period.
[d] Body Mass Index ≥25.
[e] Blood pressure ≥140/90 mm Hg or self-report of taking antihypertensive medication.
[f] Casual blood glucose ≥150 mg/dl or self-reported history of diabetes.

Table 3 lists the monthly mean medical costs according to the combination of cardiovascular risk factors. Medical costs increased significantly as the number of risk factors increased. Subjects without any of overweight/obesity, hypertension, and hyperglycemia (the 'no-risk-factor' group) had an adjusted mean total medical cost of $193.4 per month. Relative to this group, among subjects who had one risk factor, the presence of overweight/obesity alone was associated with a 5.1% increase in total medical costs, but this was not statistically significant; the presence of hypertension alone was associated with a 33.0% significant increase in total medical costs, and the presence of hyperglycemia alone was associated with a 48.3% significant increase. The combinations of overweight/obesity+hypertension, overweight/obesity+hyperglycemia, and hypertension+hyperglycemia were associated with 45.4%, 44.2%, and 85.2% increases in total medical costs, respectively. Subjects who had all three risk factors had total medical costs that were 91.0% higher than those of the no-risk-factor group.

During the 6-year observation period, the whole study population consumed medical costs totaling $192.6 million (824,056 person-months). Risk-attributable medical costs for each risk category were estimated by multiplying the excess cost and the person-months for each risk category observed. For example, the risk-attributable total medical cost for overweight/obesity alone was estimated by multiplying the adjusted total excess cost per individual who had the single risk factor of overweight/obesity ($9.8) by the associated person-months (123,039 person-months). By multiplying these values, it was estimated that a medical cost of $1.2 million (0.6%) was attributable to this risk factor. Although the degree of increase in medical cost per individual was greater among subjects with hyperglycemia alone than among subjects with hypertension alone, the RAC% for hyperglycemia alone was smaller than that for hypertension because of its lower prevalence. Total RAC% was 17.2%. RAC% for inpatient medical care was 16.8%, and that for outpatient care was 17.5%. There was no notable interaction between risk categories and age or sex in adjusted mean total cost.

For sensitivity analysis, we redefined overweight/obesity, hypertension, hyperglycemia, and dyslipidemia and re-estimated the economic impact of these factors (Table 4). Among subjects who had BP ≥140/90 mm Hg, 42.2% reported taking antihypertensive medication. Among subjects who had a casual blood glucose level of ≥150 mg/dl, 32.0% reported a history of diabetes. Among subjects who had a casual serum cholesterol level of ≥220 mg/dl or HDL <40 mg/dl, 4.0% reported taking lipid-lowering medication. Self-reporting of antihypertensive medication and a self-reported history of diabetes, and a BMI of ≥30 were associated with significantly increased total medical cost (P <0.0001, <0.0001, 0.0030, respectively). Subjects who self-reported taking lipid-lowering

				Total costs					
		Risk-attributable costs[b], $	RAC%[c] (%)	Adjusted cost[a], $				Risk-attributable total costs[b], $	RAC%[c] (%)
P-value	Increasing rate (%)				(95%CI)	P-value	Increasing rate (%)		
(Referent)	(Referent)			193.4	(180.8–206.0)	(Referent)	(Referent)		
0.99	2.7	393,723	1.3	203.2	(182.8–223.6)	0.99	5.1	1,204,956	0.6
0.0010	38.1	7,914,864	6.8	257.2	(240.1–274.3)	<0.0001	33.0	11,298,260	5.9
<0.0001	36.7	992,427	0.8	286.9	(240.3–333.5)	0.038	48.3	2,157,869	1.1
0.0074	45.1	6,973,743	6.0	281.2	(261.5–300.9)	<0.0001	45.4	11,575,527	6.0
0.0003	48.0	568,579	0.5	278.9	(207.7–350.0)	0.28	44.2	864,735	0.4
<0.0001	90.7	2,202,274	1.9	358.3	(309.5–407.0)	<0.0001	85.2	3,415,376	1.8
<0.0001	80.2	1,426,243	1.2	369.4	(311.9–426.9)	<0.0001	91.0	2,670,227	1.4
		20,471,853	17.5					33,186,950	17.2

medication had a higher mean cost than those with a serum cholesterol level of <220 mg/dl and HDL ≥40 mg/dl and who did not self-report taking lipid-lowering medication, but the difference was not significant ($P=0.76$). Among subjects who did not self-report a history of diabetes, those who had a blood glucose level of ≥150 mg/dl and <200 mg/dl had a significantly higher mean total cost than those who had a blood glucose level of <150 mg/dl ($P=0.017$).

Discussion

Mean medical cost among subjects who were overweight/obese, hypertensive, and hyperglycemic was 91.0% higher than that among subjects without any of these three risk factors, after adjustment for a variety of potential confounders. In this cohort, 17.2% of the total medical cost was attributable to these three cardiovascular risk factors.

One cohort study in Korea (Jee et al., 2001) and one cohort study in the U.S. (Anderson et al., 2000) have estimated RAC % for combination of cardiovascular risk factors in terms of total medical costs. Anderson et al., based on a prospective observation of a large employee cohort in the U.S., reported the RAC% for obesity, hyperglycemia, and hypertension of 6.3% (Anderson et al., 2000). In their study, dyslipidemia was not associated with any increase in medical cost. Jee et al. (2001) found that the RAC% for obesity, hyperglycemia, and hypertension was 10.4% for men and 5.5% for women, using a large employee cohort in Korea. In the present study, the RAC% for overweight/obesity, hyperglycemia, and hypertension was 17.2%, and was thus higher than in the previous studies. This may have been partly due to the fact that the previous studies were based on observations of healthy young workers; the impact of cardiovascular risk factors upon medical costs would become larger with age. In addition, as these previous studies excluded subjects who became too ill to work during the follow-up, they would have underestimated the impact of cardiovascular risks upon medical costs.

The result of sensitivity analysis (Table 4) showed that being on treatment at the baseline rather than having a raised level of risk factors without treatment was associated with higher cost. Especially in hyperglycemia, most of the costs associated with hyperglycemia were attributable to diabetes rather than prediabetic hyperglycemia.

Study limitations and strengths

The present study had a number of strengths. First, we followed up a large population-based cohort retaining the elderly and those who became ill during follow-up. In our cohort, only 921 subjects (7.5%) withdrew from the NHI and were thus lost to follow-up because of emigration. Second,

Table 4
Adjusted monthly medical costs by the cardiovascular risk status in the Ohsaki Study, Japan, 1996–2001

		N	Adjusted cost[a], $ (95%CI)	P-value	Increasing rate (%)
Overweight/Obesity	Body Mass Index <25	8152	226.6 (216.8–236.3)	(Referent)	(Referent)
	Body Mass Index ≥25 and <30	3747	242.3 (228.0–256.7)	0.17	7.0
	Body Mass Index ≥30	421	299.9 (257.2–342.5)	0.0030	32.4
Hypertension	Without self-report of taking antihypertensive medication				
	Systolic BP <140 mm Hg and diastolic BP <90 mm Hg	7158	202.9 (192.5–213.3)	(Referent)	(Referent)
	Systolic BP ≥140 mm Hg or diastolic BP ≥91 mm Hg	2247	223.0 (204.6–241.4)	0.15	9.9
	Self-report of taking antihypertensive medication	2935	317.7 (301.3–334.1)	<0.0001	56.6
Hyperglycemia	Without self-reported history of diabetes				
	Casual blood glucose <150 mg/dl	11,292	225.8 (217.6–234.0)	(Referent)	(Referent)
	Casual blood glucose ≥150 mg/dl and <200 mg/dl	354	296.6 (250.2–343.0)	0.017	31.4
	Casual blood glucose ≥200 mg/dl	111	255.9 (173.2–338.6)	0.89	13.3
	Self-reported history of diabetes	583	348.5 (312.2–384.8)	<0.0001	54.4
Dyslipidemia	Without self-report of taking lipid-lowering medication				
	Casual serum cholesterol <220 mg/dl and HDL ≥40 mg/dl	6790	235.1 (224.5–245.7)	(Referent)	(Referent)
	Casual serum cholesterol ≥220 mg/dl or HDL <40 mg/dl	5328	231.4 (219.4–243.4)	0.9	−1.6
	Self-report of taking lipid-lowering medication	222	256.5 (198.0–315.1)	0.76	9.1

CI denotes confidence interval. BP denotes blood pressure. HDL denotes high-density lipoprotein.
[a] Tested by analysis of covariance (ANCOVA) using non-log-transformed data on charges adjusted by age at baseline (continuous variable), sex, smoking (current smoker, past smoker, or never smoker), alcohol drinking (current drinker, past drinker, or never drinker), and comorbid condition of other three cardiovascular risk factors.

because NHI claim files were obtained directly from the local NHI Association and included almost all available medical treatment, our charge calculation was accurate. Third, in this study, the joint impact of cardiovascular risk factors was analyzed after adjustment for a variety of potential confounders.

Our study also had some limitations. Among all this study population, participation rate in the annual health check-up was as low as 33.3%. However, the participation rate in the annual health check-up was similar to that for Japan as a whole. According to the Ministry of Health, Labour and Welfare, the participation rate in the annual health check-up in Japan was 36.5% in 1995. Second, only 24.1% of the study population participated in the annual health check-up and had no prior history of cancer, stroke, or myocardial infarction and were available for the present study. The present study subjects were less likely to be hypertensive and hyperglycemic and might have been healthier than the rest of the study population. Therefore, we might have underestimated the RAC% because of the lower prevalence of cardiovascular risk factors in these individuals. Third, the present study does not prove whether prevention of these cardiovascular risk factors can reduce medical costs. Further interventional strategies could reduce these cardiovascular risk factors and potentially lower medical costs. Fourth, we did not identify individual reasons for medical treatment, and thereby we were unable to distinguish treatment costs from comorbid costs. However, each of the cardiovascular risk factors was associated with an increase not only in outpatient medical costs but also inpatient medical cost. In Japan, because hypertension and obesity rarely become main reasons for hospitalization, inpatient costs mainly reflect the costs of comorbidity. Moreover, the fact that RAC% for inpatient care was comparable to RAC% for outpatient care (16.8% vs. 17.5%) implies that overweight/obesity, hypertension, and hyperglycemia are related to not only high prescription costs for treatment of the primary disease but also severe medical events requiring inpatient treatment.

Conclusion

We have demonstrated that 17.2% of medical costs are attributable to overweight/obesity, hypertension, and hyperglycemia. These cardiovascular risk factors could have a large impact on health care resources in rural Japan.

Acknowledgments

This study was supported by a Health and Labour Sciences Research Grants for Research on Policy Planning and Evaluation (H16-Seisaku-023) from the Ministry of Health, Labour and Welfare, Japan. The authors are grateful to Dr. S. Hisamichi for his valuable comments and to Y. Nakata, M. Wagatsuma, and N. Sato for their helpful secretarial assistance.

References

Anderson, D.R., Whitmer, R.W., Goetzel, R.Z., Ozminkowski, R.J., Dunn, R.L., Wasserman, J., Serxner, S., Health Enhancement Research Organization (HERO) Research Committee, 2000. The relationship between modifiable health risks and group-level health care expenditures. Health Enhancement Research Organization (HERO) Research Committee. Am. J. Health Promot. 15, 45–52.

Anzai, Y., Kuriyama, S., Nishino, Y., Takahashi, K., Ohkubo, T., Ohmori, K., Tsubono, Y., Tsuji, I., 2005. Impact of alcohol consumption upon medical care utilization and costs in men: 4-year observation of National Health Insurance beneficiaries in Japan. Addiction 100, 19–27.

Brown, J.B., Nichols, G.A., Glauber, H.S., Bakst, A.W., 1999. Type 2 diabetes: incremental medical care costs during the first 8 years after diagnosis. Diabetes Care 22, 1116–1124.

Chenoweth, D., 2004. The medical cost of high serum cholesterol in Harris County, Texas. Tex. Med. 100, 50–53.

Chobanian, A.V., Bakris, G.L., Black, H.R., Cushman, W.C., Green, L.A., Izzo Jr., J.L., Jones, D.W., Materson, B.J., Oparil, S., Wright Jr., J.T., Roccella, E.J., National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, National High Blood Pressure Education Program Coordinating Committee, 2003. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. JAMA 289, 2560–2572.

Daviglus, M.L., Liu, K., Greenland, P., Dyer, A.R., Garside, D.B., Manheim, L., Lowe, L.P., Rodin, M., Lubitz, J., Stamler, J., 1998. Benefit of a favorable cardiovascular risk-factor profile in middle age with respect to Medicare costs. N. Engl. J. Med. 339, 1122–1129.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 285, 2486–2497.

Ford, E.S., Giles, W.H., Dietz, W.H., 2002. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 287, 356–359.

Fries, J.F., Koop, C.E., Beadle, C.E., Cooper, P.P., England, M.J., Greaves, R.F., Sokolov, J.J., Wright, D., The Health Project Consortium, 1993. Reducing health care costs by reducing the need and demand for medical services. N. Engl. J. Med. 329, 321–325.

Goetzel, R.Z., Anderson, D.R., Whitmer, R.W., Ozminkowski, R.J., Dunn, R.L., Wasserman, J., 1998. The relationship between modifiable health risks and health care expenditures. An analysis of the multi-employer HERO health risk and cost database. The Health Enhancement Research Organization (HERO) Research Committee. J. Occup. Environ. Med. 40, 843–854.

Greenland, P., Knoll, M.D., Stamler, J., Neaton, J.D., Dyer, A.R., Garside, D.B., Wilson, P.W., 2003. Major risk factors as antecedents of fatal and nonfatal coronary heart disease events. JAMA 290, 891–897.

Haffner, S., Taegtmeyer, H., 2003. Epidemic obesity and the metabolic syndrome. Circulation 108, 1541–1545.

Hodgson, T.A., Cohen, A.J., 1999. Medical care expenditures for diabetes, its chronic complications, and its comorbidities. Prev. Med. 29, 173–186.

Hogan, P., Dall, T., Nikolov, P., American Diabetes Association, 2003. Economic costs of diabetes in the US in 2002. Diabetes Care 26, 917–932.

Izumi, Y., Tsuji, I., Ohkubo, T., Kuwahara, A., Nishino, Y., Hisamichi, S., 2001. Impact of smoking habit on medical care use and its costs: a prospective observation of National Health Insurance beneficiaries in Japan. Int. J. Epidemiol. 30, 616–621.

Jee, S.H., O'Donnell, M.P., Suh, I., Kim, I.S., Korea Medical Insurance Corporation, 2001. The relationship between modifiable health risks and future medical care expenditures: the Korea Medical Insurance Corporation (KMIC) Study. Am. J. Health Promot. 15, 244–255.

Kuriyama, S., Tsuji, I., Ohkubo, T., Anzai, Y., Takahashi, K., Watanabe, Y., Nishino, Y., Hisamichi, S., 2002. Medical care expenditure associated with body mass index in Japan: the Ohsaki Study. Int. J. Obes. Relat. Metab. Disord. 26, 1069–1074.

Kuriyama, S., Hozawa, A., Ohmori, K., Suzuki, Y., Nishino, Y., Fujita, K., Tsubono, Y., Tsuji, I., 2004. Joint impact of health risks on health care charges: 7-year follow-up of National Health Insurance beneficiaries in Japan (the Ohsaki Study). Prev. Med. 39, 1194–1199.

Lynch, W.D., Chikamoto, Y., Imai, K., Lin, T.F., Kenkel, D.S., Ozminkowski, R.J., Goetzel, R.Z., 2005. The association between health risks and medical expenditures in a Japanese corporation. Am. J. Health Promot. 19, 238–248.

Nakamura, K., Okamura, T., Kanda, H., Hayakawa, T., Kadowaki, T., Okayama, A., Ueshima, H., Health Promotion Research Committee of the Siga National Insurance Organizations, 2005. Impact of hypertension on medical economics: a 10-year follow-up study of national health insurance in Shiga, Japan. Hypertens. Res. 28, 859–864.

Nichols, G.A., Brown, J.B., 2005. Higher medical care costs accompany impaired fasting glucose. Diabetes Care 28, 2223–2229.

Oliva, J., Lobo, F., Molina, B., Monereo, S., 2004. Direct health care costs of diabetic patients in Spain. Diabetes Care 27, 2616–2621.

Organisation for Economic Co-operation and Development, 2005. OECD Health Data 2005: Statistics and Indicators for 30 Countries 2005 Edition. OECD Publishing (CD-ROM).

Quesenberry Jr., C.P., Caan, B., Jacobson, A., 1998. Obesity, health services use, and health care costs among members of a health maintenance organization. Arch. Intern. Med. 158, 466–472.

Raebel, M.A., Malone, D.C., Conner, D.A., Xu, S., Porter, J.A., Lanty, F.A., 2004. Health services use and health care costs of obese and nonobese individuals. Arch. Intern. Med. 164, 2135–2140.

Ray, G.T., Collin, F., Lieu, T., Fireman, B., Colby, C.J., Quesenberry, C.P., Van den Eeden, S.K., Selby, J.V., 2000. The cost of health conditions in a health maintenance organization. Med. Care Res. Rev. 57, 92–109.

SAS Institute Inc., 2004. SAS/STAT 9.1 User's Guide. SAS Institute Inc, Cary, NC.

Schauffler, H.H., D'Agostino, R.B., Kannel, W.B., 1993. Risk for cardiovascular disease in the elderly and associated Medicare costs: the Framingham. Study. Am. J. Prev. Med. 9, 146–154.

Selby, J.V., Ray, G.T., Zhang, D., Colby, C.J., 1997. Excess costs of medical care for patients with diabetes in a managed care population. Diabetes Care 20, 1396–1402.

Stamler, J., Dyer, A.R., Shekelle, R.B., Neaton, J., Stamler, R., 1993. Relationship of baseline major risk factors to coronary and all-cause mortality, and to longevity: findings from long-term follow-up of Chicago cohorts. Cardiology 82, 191–222.

Stamler, J., Stamler, R., Neaton, J.D., Wentworth, D., Daviglus, M.L., Garside, D., Dyer, A.R., Liu, K., Greenland, P., 1999. Low risk-factor profile and long-term cardiovascular and noncardiovascular mortality and life expectancy: findings for 5 large cohorts of young adult and middle-aged men and women. JAMA 282, 2012–2018.

Thompson, D., Wolf, A.M., 2001. The medical-care cost burden of obesity. Obes. Rev. 2, 189–197.

Tsuji, I., Nishino, Y., Ohkubo, T., Kuwahara, A., Ogawa, K., Watanabe, Y., Tsubono, Y., Bando, T., Kanemura, S., Izumi, Y., Sasaki, A., Fukao, A., Nishikori, M., Hisamichi, S., 1998. A prospective cohort study on National Health Insurance Beneficiaries in Ohsaki, Miyagi Prefecture, Japan: study design, profiles of the subjects and medical cost during the first year. J. Epidemiol. 8, 258–263.

Tsuji, I., Takahashi, K., Nishino, Y., Ohkubo, T., Kuriyama, S., Watanabe, Y., Anzai, Y., Tsubono, Y., Hisamichi, S., 2003. Impact of walking upon medical care expenditure in Japan: the Ohsaki Cohort Study. Int. J. Epidemiol. 32, 809–814.

Wilson, P.W., D'Agostino, R.B., Levy, D., Belanger, A.M., Silbershatz, H., Kannel, W.B., 1998. Prediction of coronary heart disease using risk factor categories. Circulation 97, 1837–1847.

World Health Organization, 2000. Obesity. Preventing and Managing the Global Endemic. WHO Technical Report Series no 894. WHO, Geneva.

2．日本食パターンと死亡リスクに関する前向きコホート研究：大崎コホート研究

【目的】先行研究では因子分析により同定された日本食パターンが報告されている。しかし、日本食パターンが全死因・疾患別死因に与える影響は、ほとんど調べられていない。因子分析により得られた日本食パターンと全死因・疾患別死因の関連を、前向きコホート研究デザインにて検討する。

【方法】1994年、宮城県大崎保健所管内に在住する40歳から79歳の国民健康保険加入者に自記式調査票を配布し52,029名(95.0%)より有効回答を得た。40項目の食事摂取頻度調査票に25項目以上無回答、総エネルギー摂取が上位0.5%または下位0.5%、がん・脳血管疾患・心疾患・糖尿病いずれかの既往者、追跡開始以前に国民健康保険から異動した者を除外した40,547名を解析対象とした。

40項目の食事摂取頻度調査票から各食品項目の一日あたりの摂取量を算出し、これらについて因子分析（主成分）をおこなった結果、日本食パターン、動物性食品パターン、洋風健康食パターンを同定した。各パターンとの関連性をあらわす因子得点を個人ごとに算出した。エンドポイントは、全死因・循環器疾患・がん死亡とした。死因は人口動態調査調査票により確認した。各パターンの因子得点の最小四分位を基準としたハザード比（95%信頼区間）をCoxモデルにて算出した。共変量は年齢・性・喫煙状況・歩行時間・総エネルギー摂取・教育歴とした。

【結果および考察】7年間の追跡により、全死因死亡2,922人、循環器疾患死亡875人、がん死亡1,169人を確認した。日本食パターンは、野菜・果物・魚・大豆製品の摂取、動物性食品パターンは、肉類・脂肪性食品・アルコール摂取と相関が高かった。洋風健康食パターンは、野菜・乳製品との相関が高かったが、ご飯、味噌汁の摂取とは負の相関がみられた。日本食パターンは、循環器疾患・全死因死亡と負の関連を認めたが、がん死亡とは関連を認めなかった。動物食品パターンは循環器疾患・全死因死亡と正の関連を認めた。洋風健康食パターンについては、いずれのエンドポイントとも関連を認めなかった。本研究結果より、日本食パターンが循環器疾患および全死因死亡リスクの低下に関与している可能性が示唆された。

Published by Oxford University Press on behalf of the International Epidemiological Association

Advance Access publication 22 February 2007

International Journal of Epidemiology 2007;**36**:600–609
doi:10.1093/ije/dym005

CARDIOVASCULAR DISEASE

Dietary patterns and cardiovascular disease mortality in Japan: a prospective cohort study

Taichi Shimazu,[1]* Shinichi Kuriyama,[1] Atsushi Hozawa,[1,2] Kaori Ohmori,[1] Yuki Sato,[1,3] Naoki Nakaya,[1] Yoshikazu Nishino,[4] Yoshitaka Tsubono[5] and Ichiro Tsuji[1]

Accepted 4 January 2007

Background Although ecological observations suggest that the Japanese diet may reduce the risk of cardiovascular disease (CVD), the impact of a Japanese dietary pattern upon mortality due to CVD is unclear.

Methods We prospectively assessed the association between dietary patterns among the Japanese and CVD mortality. Dietary information was collected from 40 547 Japanese men and women aged 40–79 years without a history of diabetes, stroke, myocardial infarction or cancer at the baseline in 1994.

Results During 7 years of follow-up, 801 participants died of CVD. Factor analysis (principal component) based on a validated food frequency questionnaire identified three dietary patterns: (i) a Japanese dietary pattern highly correlated with soybean products, fish, seaweeds, vegetables, fruits and green tea, (ii) an 'animal food' dietary pattern and (iii) a high-dairy, high-fruit-and-vegetable, low-alcohol (DFA) dietary pattern. The Japanese dietary pattern was related to high sodium intake and high prevalence of hypertension. After adjustment for potential confounders, the Japanese dietary pattern score was associated with a lower risk of CVD mortality (hazard ratio of the highest quartile vs the lowest, 0.73; 95% confidence interval: 0.59–0.90; P for trend = 0.003). The 'animal food' dietary pattern was associated with an increased risk of CVD, but the DFA dietary pattern was not.

Conclusion The Japanese dietary pattern was associated with a decreased risk of CVD mortality, despite its relation to sodium intake and hypertension.

Keywords Diet, factor analysis, statistical, cardiovascular diseases, mortality, prospective studies, Japan

The traditional Japanese diet has drawn considerable attention since the 1960s because of its association with an extremely low rate of coronary heart disease (CHD).[1,2] On the other hand, this diet used to be characterized by high consumption of salt[2] and low consumption of animal fat and protein,[3] which would increase the risk of stroke, especially intracerebral haemorrhage (ICH).[4]

Over the past 40 years, however, the Japanese diet has changed. Average consumption of fruits, dairy products, eggs and meat has increased, while the high consumption of vegetables, soy products and fish has been maintained.[5] In parallel with the change from a traditional Japanese diet, the stroke mortality rate has fallen dramatically,[6] and the CHD mortality rate is still lower than in Western countries.[7] The age-adjusted rate of mortality due to cardiovascular disease (CVD) is lower than in the UK (~40%) and the US (~30%).[7] Thus, the contemporary Japanese diet may have beneficial effects in terms of lower CVD mortality.

While several single food items in the Japanese diet such as fish[8–10] and soybean[10,11] have been studied for CVD association, the results have not always been consistent. As food variables

[1] Division of Epidemiology, Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan.

[2] Department of Health Science, Shiga University of Medical Science, Shiga, Japan.

[3] Department of Health Policy, National Research Institute for Child Health and Development, Tokyo, Japan.

[4] Division of Epidemiology, Miyagi Cancer Center Research Institute, Natori, Japan.

[5] Division of Health Policy, Tohoku University School of Public Policy, Sendai, Japan.

* Corresponding author. Division of Epidemiology Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, 2-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi 980-8575, Japan. E-mail: tshimazu-thk@umin.ac.jp

are highly intercorrelated and possibly have biochemical interactions, it is difficult to examine their separate effects.[12] To address the difficulties of the single food approach, many studies have investigated the association between dietary patterns and CVD among Western populations.[13–19]

Among the Japanese, previous studies on the association with specific cancers[20–22] or all-cause mortality[23] have identified a dietary pattern correlated with distinctive Japanese foods by using factor analysis.[24] However, no study has investigated the contribution of 'Japanese' dietary patterns to lower CVD mortality.

Our study objectives were to identify contemporary dietary patterns among the Japanese by factor analysis and to investigate their impact upon CVD mortality in a large-scale population-based prospective cohort study.

Methods

Study population

The details of the Ohsaki National Health Insurance (NHI) Cohort study have been described previously.[25,26] Briefly, we delivered a self-administered questionnaire including items on dietary intake [40-item food frequency questionnaire (FFQ)], medical history, smoking status and physical health status, between October and December 1994 to all NHI beneficiaries aged 40–79 years living in the catchment area of Ohsaki Public Health Center, Miyagi Prefecture, northeast Japan. Ohsaki Public Health Center, a local government agency, provides preventive health services for residents of 14 municipalities in Miyagi Prefecture. Of 54 996 eligible individuals, 52 029 (95.0%) responded.

From January 1, 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 774 participants because they had withdrawn from the NHI before collection of the NHI withdrawal history files. Thus, 51 255 participants formed the study cohort. The study protocol was reviewed and approved by the Ethics Committee of Tohoku University School of Medicine. We considered the return of self-administered questionnaires signed by the study participants to imply their consent to participate.

For current analysis, we excluded participants who died before collection of NHI withdrawal history files ($n = 37$), who left blank more than 24 of the 40 food items on the FFQ ($n = 3941$) and who reported daily energy intakes at the extreme 0.5% upper or lower ends of the range (sex-specific cut-off points were used: 1759 kJ, 14 884 kJ for men and 1256 kJ, 9609 kJ for women, respectively) ($n = 478$). We followed the exclusion criteria for the number of blanks on the FFQ reported in previous studies[17,18] of dietary patterns. We also excluded participants who reported a history of cancer ($n = 1533$), myocardial infarction ($n = 1325$), stroke ($n = 1040$) or diabetes mellitus at the baseline ($n = 3092$), because these diseases could have changed their diet and lifestyle. Consequently, our analysis included 40 547 participants.

Dietary assessment

The 40-item FFQ asked about the average frequency of consumption of each food. Regarding the foods that showed different patterns of consumption between seasons, the FFQ asked about the frequency in the season when these foods were consumed most frequently within a year. However, the FFQ did not refer a specific time frame. Five frequency categories were used for the majority of food items (almost never, 1–2 days/month, 1–2 days/week, 3–4 days/week and almost every day). For rice and miso (fermented soybean paste) soup, the number of bowls consumed daily was asked. For current drinkers, the frequency of alcohol consumption was asked using four frequency categories (once or less/week, 1–2 days/week, 3–4 days/week, almost every day) and the usual amount was asked using six categories. For consumption of four non-alcohol beverages (green tea, black tea coffee and Chinese tea), five categories were used (almost never, sometimes, 1–2 cups/day, 3–4 cups/day, 5 or more cups/day).

We had previously conducted a validation study of the FFQ.[27] In brief, 113 participants (55 men and 58 women), who were a subsample of the cohort, provided four 3-day diet records (DRs) within a 1-year period and subsequently responded to the FFQ. We computed the Spearman correlation coefficients between the amounts consumed according to the DRs and the amounts consumed according to the FFQ. For 40 food items, medians (range) of the age and total energy-adjusted correlation coefficients were 0.35 (−0.30–0.72) in men and 0.34 (−0.06–0.75) in women. Medians (range) of the age and total energy-adjusted correlation coefficients of the two FFQs administered 1 year apart were 0.43 (0.14–0.76) in men and 0.45 (0.06–0.74) in women for the 40 food items.

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 the DRs. To calculate nutrients, we developed a food composition table that corresponded to the food items listed in the FFQ. Using the Standard Tables of Food Composition published by the Science and Technology Agency of Japan,[28] we calculated nutrients from the DRs and grouped the food codes to form food categories that best corresponded to the listing of the FFQ. We assigned relative weights to the food codes grouped into a single category based on the DR data.

Dietary pattern derivation

To derive dietary patterns, factor analysis (principal component analysis) was conducted by using the daily consumption (weight in grams) of 40 food items from the FFQ. If the reported frequency was blank, we assumed that the item was never consumed. We used the PROC FACTOR procedure in SAS version 9.1[29] to perform the analyses. To determine the number of factors to retain, we considered eigenvalue, Scree test and factor interpretability.[24] Because 10 factors satisfied the criteria for eigenvalues greater than one, and the Scree plot indicated five factors that were retained, we selected solutions ranging from 2 to 5 for rotation. To achieve a simpler structure with greater interpretability, the factors were rotated by an orthogonal transformation (varimax rotation function in SAS).

With regard to factor interpretability, a three-factor solution appeared to describe most meaningfully the distinctive dietary patterns of the study population. We named them (i) a Japanese pattern, (ii) an 'animal food' pattern and (iii) a high-dairy, high-fruit-and-vegetable, and low-alcohol (DFA) pattern, according to the food items showing high factor loading (absolute value) with respect to each dietary pattern. These dietary patterns were consistent with those reported previously in Japanese men.[20] For each pattern and each participant, we calculated a factor score by summing the consumption from each food item weighted by its factor loading.[24]

We conducted additional sensitivity analysis of dietary pattern derivation. When we also performed factor analyses for six subgroups stratified by sex and three age groups (aged 40–59, 60–69 and 70–79 years), the derived patterns appeared similar. Thus, in our analyses, we used a factor solution including both men and women, and all age groups. Among the participants who left no blanks for food items ($n = 17\,010$), the derived dietary patterns closely resembled those derived from the total participants. As an additional analysis with stricter cut-off points of total energy intake for inclusion, we excluded participants who reported of daily energy intakes at the extreme 2.5% upper or lower ends of the range. The derived dietary patterns were similar to those of the main analysis.

Additional analyses using the maximum likelihood method instead of the principal component method as the initial factor-extracting method, and oblique rotation (promax rotation function in SAS) as a factor rotation method made the factor loadings for the three dietary patterns similar. The same criteria as the main analysis indicated three factors that were retained, and each factor was correlated to with (i) vegetables, fruits, seaweeds, soy products, and fish, (ii) meat and fat and (iii) rice (negatively), miso soup (negatively) and dairy products, respectively.

Follow-up

The primary endpoint was CVD mortality. Secondarily, we conducted analyses of CHD and stroke mortality. We investigated cause of death by reviewing the death certificates filed at Ohsaki Public Health Center. Cause of death was coded by trained physicians according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10).[30] We identified deaths from CVD (codes I00-I99), CHD (codes I20-I25), total stroke (codes I60-I69), cerebral infarction (code I63) and ICH (code I61).

Statistical analyses

From January 1, 1995 to December 31, 2001, 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 follow-up, whichever occurred first.

Cox proportional hazards regression analysis was used to calculate the hazard ratio (HR) and 95% confidence interval (CI) of CVD mortality according to quartiles of the dietary pattern score and to adjust for potentially confounding variables, using SAS.[29] For all models, the proportional hazards assumptions were tested and met using time-dependent covariates.[31] Dummy variables were created for the quartiles of each dietary pattern score. The lowest quartile of a dietary pattern score was used as a reference category. The *P*-values for analysis of linear trends were calculated by scoring the quartiles of a dietary pattern score, from one for the lowest quartile to four for the highest, entering the number as a continuous term in the regression model. Interaction between sex and quartiles of each dietary pattern score was tested by addition of cross-product terms to the multivariate model. The association between each dietary pattern and CVD mortality did not vary by sex (P for interaction $n = 0.55$). All reported *P*-values are two-tailed.

Multivariate models were adjusted for the following variables: age (in years), sex, smoking status (never, former, currently smoking <20 cigarettes per day and currently smoking ⩾20 cigarettes per day), walking duration (<1 hour per day and ⩾1 hour per day), total energy intake (as a continuous variable), body mass index ($<18.5\,kg/m^2$, 18.5–$24.9\,kg/m^2$ and $\geqslant 25.0\,kg/m^2$) and history of hypertension (yes or no). Two multivariate models not including and including body mass index and history of hypertension were used, since these two factors could be regarded as intermediate in the causal pathway between dietary pattern and CVD mortality. Walking duration was used as a parameter of physical activity because it is the most common type of physical activity among middle-aged and older individuals in rural Japan. The validity and reproducibility of the question on walking time has been reported elsewhere.[32]

All analyses were repeated after exclusion of participants who had died in the first 3 years of follow-up. To minimize any possible bias caused by physically inactive participants, we performed additional analysis that was restricted to participants who were able to perform vigorous activity [Medical Outcome Study (MOS) Short Form General Health Survey[33] score of 5–6] and with a well self-perceived health status. As an additional analysis, dietary pattern scores were adjusted for total energy by using the residual method.[34]

Results

Table 1 shows factor loadings, which are equivalent to simple correlations between the food items and dietary patterns. A positive loading indicates that a food item is positively associated with the dietary pattern, and a negative loading indicates an inverse association with the dietary pattern. That is, food items highly loaded within a dietary pattern are highly correlated with each other.

The Japanese dietary pattern was loaded heavily on soybean products, fish, seaweeds, vegetables, fruits and green tea, whereas the 'animal food' pattern was loaded heavily on various animal-derived foods (beef, pork, ham, sausage, chicken, liver and butter), coffee and alcoholic beverages. The DFA dietary pattern was heavily loaded on dairy products (milk and yoghurt), margarine, fruits and vegetables (carrot, pumpkin and tomato), and negatively loaded on rice, miso soup and alcoholic beverages. These three dietary patterns explained 26.2% of the variance.

Table 2 compares the characteristics of participants according to the quartiles of each dietary pattern score. Participants

Table 1 Factor-loading matrix for the major dietary pattern identified by factor analysis

	Japanese pattern	'Animal food' pattern	DFA[a] pattern
Rice			−0.59
Miso soup	0.25		−0.39
Beef		0.48	
Pork (excluding ham, sausage)		0.55	
Ham, sausage		0.56	
Chicken		0.49	
Liver		0.43	
Egg	0.34	0.32	
Milk	0.26		0.28
Yoghurt			0.50
Cheeses		0.44	
Butter		0.50	
Margarine		0.37	0.40
Deep fried-dishes, tempura	0.28	0.39	
Fried vegatable	0.43		
Raw fish, fish boiled with soy, roast fish	0.51		
Boiled fish paste	0.39	0.32	
Dried fish	0.37		
Green vegetables	0.64		
Carrot, pumpkin	0.59		0.36
Tomato	0.45		0.32
Cabbage, lettuce	0.59		
Chinese cabbage	0.62		
Wild plant	0.27		
Mushrooms (shiitake, enokitake)	0.42		
Potato	0.61		
Seaweeds	0.59		0.26
Pickles (radish, chinese cabbage)	0.41		
Food boiled with soy			
Boiled beans			
Soybean (tofu, fermented soybeans)	0.57		
Orange	0.50		0.42
Other fruits	0.49		0.47
Fresh juice			
Confectioneries	0.27		
Green tea	0.29		
Black tea			
Coffee		0.29	
Chinese tea			
Alcoholic beverages		0.27	−0.50
Variance explained (%)	15.1	6.4	4.8

[a] DFA means high-dairy, high-fruit-and-vegetable, low-alcohol.
Absolute values <0.25 were not listed for simplicity.

with a higher Japanese dietary pattern score tended to be older, were more likely to walk and have a history of hypertension, and less likely to be current drinkers and smokers. Participants with a higher 'animal food' dietary pattern score tended to be younger and male, were more likely to be current smokers and drinkers, and less likely to have a history of hypertension. Participants with a higher DFA dietary pattern score tended to be female, and were similar to those with a higher Japanese dietary pattern score except for walking duration, education and history of hypertension.

Table 3 shows total energy-adjusted daily nutrient and food intakes according to dietary pattern score quartiles. Although the fat and protein intakes in any given quintile of dietary patterns were almost equivalent, their sources varied among dietary patterns. Participants with a higher Japanese dietary pattern score consumed more fish and soybean, a higher 'animal food' dietary pattern score was associated with higher meat and fat intake, and a higher DFA dietary pattern was associated with a higher intake of dairy products. Although the Japanese and DFA dietary patterns were similar in terms of high vegetable and fruit intake, the Japanese dietary pattern differed from the DFA pattern in terms of high intakes of sodium, fish, soybean, seaweeds and green tea.

During 7 years of follow-up (252 647 person-years), we documented 801 deaths from CVD. These deaths included 181 CHDs, 432 total strokes (163 cerebral infarctions, 129 ICHs). Table 4 shows the association between the three dietary pattern score quartiles and CVD mortality. The Japanese dietary pattern was associated with a reduced risk of CVD mortality. On the other hand, the 'animal food' dietary pattern was associated with an increased risk of CVD mortality, and the DFA dietary pattern was not associated with CVD mortality.

After adjustment for age, sex, smoking status, walking duration, education and total energy intake, the multivariate HRs (95% CI) of CVD mortality across increasing quartiles of the Japanese dietary pattern score were 1.00, 0.76 (0.63–0.93), 0.71 (0.58–0.87) and 0.73 (0.59–0.90) (P for trend = 0.003), whereas for the 'animal food' dietary pattern, the corresponding multivariate HRs (95% CI) of CVD mortality were 1.00, 0.93 (0.76–1.13), 1.13 (0.92–1.38) and 1.22 (0.99–1.51) (P for trend = 0.03). With additional adjustment for body mass index and history of hypertension, the results were essentially unchanged. Furthermore, the results of analysis using body mass index as a continuous variable and history of hypertension remained similar.

As the Japanese and 'animal food' dietary patterns were associated with CVD mortality, their associations with CHD and stroke were further investigated (Table 5). After adjusting for potential confounders, the point estimate of the HR for CHD mortality of participants with the highest quartile of the Japanese dietary pattern score was 20% lower than the lowest, whereas those with the highest quartile of the 'animal food' dietary pattern score was 49% higher.

The multivariate HRs (95% CI) of CHD mortality across increasing quartiles of the Japanese dietary pattern score were 1.00, 0.84 (0.56–1.26), 0.70 (0.45–1.08) and 0.80 (0.51–1.25) (P for trend = 0.24), and the corresponding multivariate HRs (95% CI) of the 'animal food' dietary pattern score were 1.00,

Table 2 Baseline characteristics of the participants according to dietary pattern score quartiles

	Dietary pattern score quartiles			
Characteristic	1 (lowest)	2	3	4 (highest)
Age (years), mean (SD)				
Japanese pattern	57.7 (11.1)	59.3 (10.5)	60.6 (9.9)	61.9 (9.3)
'Animal food' pattern	63.8 (8.9)	60.6 (10.1)	58.2 (10.4)	57.0 (10.6)
DFA[a] pattern	58.5 (10.1)	60.5 (10.4)	60.5 (10.4)	60.1 (10.4)
Male (%)				
Japanese pattern	55.3	48.3	43.4	41.3
'Animal food' pattern	23.5	42.2	53.4	69.1
DFA[a] pattern	89.8	53.0	28.8	16.7
Body mass index (kg/m^2), mean (SD)				
Japanese pattern	23.4 (3.3)	23.5 (3.2)	23.5 (3.1)	23.6 (3.1)
'Animal food' pattern	23.8 (3.4)	23.6 (3.2)	23.5 (3.1)	23.3 (3.0)
DFA[a] pattern	23.5 (3.0)	23.5 (3.3)	23.7 (3.3)	23.5 (3.2)
Current smoker (%)				
Japanese pattern	44.8	35.1	28.6	24.4
'Animal food' pattern	18.1	30.0	36.1	46.9
DFA[a] pattern	58.0	35.7	21.3	14.8
Walking duration ⩾1 hour/day (%)				
Japanese pattern	41.2	45.0	47.7	52.1
'Animal food' pattern	43.9	44.8	47.7	49.5
DFA[a] pattern	54.8	47.3	44.0	40.0
Current drinker (%)				
Japanese pattern	55.6	51.1	46.9	43.5
'Animal food' pattern	29.6	45.9	54.6	64.8
DFA[a] pattern	80.0	49.6	34.4	29.8
Education until age ⩾19 years (%)				
Japanese pattern	8.3	7.7	7.6	7.8
'Animal food' pattern	5.8	7.3	8.9	9.4
DFA[a] pattern	4.4	5.8	7.8	13.4
History of hypertension (%)				
Japanese pattern	22.2	23.4	25.7	27.0
'Animal food' pattern	31.6	26.2	21.7	18.9
DFA[a] pattern	22.3	25.0	25.7	25.4

[a] DFA means high-dairy, high-fruit-and-vegetable, low-alcohol.
SD, standard deviation.

1.12 (0.73–1.72), 1.38 (0.89–2.15) and 1.49 (0.94–2.34) (*P* for trend = 0.06).

The Japanese dietary pattern was associated with a decreased risk of total stroke, cerebral infarction and ICH mortality. The multivariate HRs (95% CI) of total stroke mortality across increasing quartiles of the Japanese dietary pattern score were 1.00, 0.70 (0.54–0.92), 0.66 (0.50–0.87) and 0.64 (0.47–0.85) (*P* for trend = 0.003). The 'animal food' dietary pattern was not positively associated with the risk of total stroke.

We analysed the association between the Japanese dietary pattern derived from participants who left no blanks for food items ($n = 17010$) and CVD mortality, and the results were similar. The multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.74 (0.51–1.07) (*P* for trend = 0.04). After exclusion of participants who reported daily energy intakes at the extreme 2.5% instead of the extreme 0.5% of the upper or lower ends of the range, we analysed the association between the Japanese dietary pattern derived and CVD mortality ($n = 38937$), and the results were similar. The multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.75 (0.60–0.93) (*P* for trend = 0.005).

After excluding the 287 participants who died from CVD in the first 3 years of follow-up, the multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.70 (0.54–0.92)

Table 3 Daily nutrient and food intakes of the participants according to dietary pattern score quartiles

	Dietary pattern score quartiles			
Variable	1 (lowest)	2	3	4 (highest)
Daily nutrient and food intakes[a] (median)				
Energy (kJ)				
Japanese pattern	5046	5793	6227	6861
'Animal food' pattern	5128	5826	6430	7458
DFA[b] pattern	8346	5956	5537	5466
Fat (g)				
Japanese pattern	31	35	38	41
'Animal food' pattern	34	35	37	41
DFA[b] pattern	32	35	37	41
Protein (g)				
Japanese pattern	61	66	70	74
'Animal food' pattern	65	66	68	72
DFA[b] pattern	68	67	67	69
Sodium (mg)				
Japanese pattern	2418	2762	2925	3152
'Animal food' pattern	2909	2824	2768	2822
DFA[b] pattern	2684	2865	2897	2878
Rice (g)				
Japanese pattern	814	684	620	567
'Animal food' pattern	617	647	734	744
DFA[b] pattern	885	739	601	524
Total meats (g)				
Japanese pattern	20	21	22	22
'Animal food' pattern	14	19	24	34
DFA[b] pattern	21	21	21	22
Dairy products (g)				
Japanese pattern	127	191	217	223
'Animal food' pattern	192	198	201	206
DFA[b] pattern	86	142	226	268
Total Fish (g)				
Japanese pattern	50	64	73	96
'Animal food' pattern	68	67	66	69
DFA[b] pattern	69	67	66	68
Total vegetables (g)				
Japanese pattern	59	79	99	138
'Animal food' pattern	101	89	86	87
DFA[b] pattern	66	82	96	118
Soybean (g)				
Japanese pattern	64	82	98	101
'Animal food' pattern	95	88	85	87
DFA[b] pattern	87	86	89	92
Seaweeds (g)				
Japanese pattern	3	5	6	9
'Animal food' pattern	6	5	5	5
DFA[b] pattern	4	5	6	7
Total fruits (g)				
Japanese pattern	111	145	173	204
'Animal food' pattern	178	155	147	147
DFA[b] pattern	79	132	183	238
Green tea consumption ≥5 cups/day (%)				
Japanese pattern	16	26	33	44
'Animal food' pattern	39	31	26	25
DFA[b] pattern	29	30	30	32

[a] Nutrient and food intakes presented in this table are adjusted for total energy intake.
[b] DFA means high-dairy, high-fruit-and-vegetable, low-alcohol.

(P for trend = 0.009). We performed additional analysis restricted to participants who performed vigorous activity and with a well self-perceived health status (n = 27 239, 312 deaths from CVD), and a similar result was obtained. The multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.71 (0.50–1.01) (P for trend = 0.07). When we used the model adjusted for total energy intake by the residual method, the multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.78 (0.64–0.96) (P for trend = 0.03).

The results of further analysis stratified by smoking status on the association between the Japanese dietary pattern and CVD mortality are shown in Table 6. Although the point estimates of the HR for CVD mortality were consistently below unity compared with the reference category, the inverse association was less pronounced among current smokers than among never or past smokers (P = 0.07 for interaction with smoking). No interaction between the other covariates and quartiles of the Japanese dietary pattern score was observed (data not shown).

Discussion

We identified three dietary patterns among the Japanese population: the Japanese, 'animal food' and DFA dietary patterns. The Japanese dietary pattern was associated with a decreased risk of CVD mortality. In contrast, the 'animal food' dietary pattern was associated with an increased risk of CVD mortality, and the DFA dietary pattern was not.

Three dietary patterns we identified were consistent with previously reported patterns observed among different Japanese populations.[20–23] Corresponding to the (i) Japanese, (ii) 'animal food' and (iii) DFA dietary patterns, the previous studies reported dietary patterns that were correlated with (i) vegetables, fruits, seaweeds, soy products and fish,[20–23] (ii) meat and fat[20–23] and (iii) rice (negatively), miso soup (negatively) or bread and dairy products.[20,22,23] Although our FFQ is short, it includes these key foods, especially Japanese foods.

Table 4 Age, sex-adjusted and multivariate-adjusted hazard ratio for cardiovascular disease mortality according to dietary pattern score quartiles

	Dietary pattern score quartiles				
Dietary pattern	1 (low)	2	3	4 (high)	***P* for Trend**
Japanese pattern					
No. of deaths	243	189	179	190	
Person-years	62 529	63 035	63 316	63 767	
Age, sex-adjusted HR (95% CI)	1	0.73 (0.60–0.88)	0.64 (0.53–0.78)	0.63 (0.52–0.77)	<0.001
Multivariate-adjusted HR1[a] (95% CI)	1	0.76 (0.63–0.93)	0.71 (0.58–0.87)	0.73 (0.59–0.90)	0.003
Multivariate-adjusted HR2[b] (95% CI)	1	0.77 (0.63–0.94)	0.71 (0.58–0.88)	0.74 (0.59–0.91)	0.004
'Animal food' pattern					
No. of deaths	244	188	184	185	
Person-years	63 113	63 396	63 143	62 996	
Age, sex-adjusted HR (95% CI)	1	0.90 (0.74–1.09)	1.04 (0.85–1.27)	1.07 (0.88–1.32)	0.31
Multivariate-adjusted HR1[a] (95% CI)	1	0.93 (0.76–1.13)	1.13 (0.92–1.38)	1.22 (0.99–1.51)	0.03
Multivariate-adjusted HR2[b] (95% CI)	1	0.93 (0.76–1.13)	1.14 (0.93–1.39)	1.24 (1.00–1.54)	0.02
DFA[c] pattern					
No. of deaths	180	251	211	159	
Person-years	63 303	62 878	62 848	63 618	
Age, sex-adjusted HR (95% CI)	1	1.27 (1.04–1.55)	1.17 (0.94–1.45)	0.94 (0.74–1.19)	0.38
Multivariate-adjusted HR1[a] (95% CI)	1	1.18 (0.96–1.45)	1.07 (0.85–1.35)	0.88 (0.68–1.13)	0.14
Multivariate-adjusted HR2[b] (95% CI)	1	1.18 (0.96–1.45)	1.10 (0.87–1.38)	0.89 (0.69–1.14)	0.19

[a] Multivariate-adjusted HR1 was adjusted for age (in years), sex, smoking status (never, former, currently smoking <20 cigarettes/day and currently smoking 20 cigarettes/day), walking duration (<1 hour/day and 1 hour/day), education (until age up to 15 years, until age 16–18 years, and until age 19 years) and total energy intake (continuous).

[b] Multivariate-adjusted HR2 was adjusted for the same as HR1, body mass index (<18.5 kg/m^2, 18.5–24.9 kg/m^2 and 25 kg/m^2), and history of hypertension (yes or no).

[c] DFA means high-dairy, high-fruit-and-vegetable, low-alcohol.

HR, hazard ratio; CI, confidence interval.

The Japanese dietary pattern has partly similar characteristics to 'healthy' dietary patterns reported previously among Western populations that were inversely associated with CVD mortality. High consumption of vegetables and fruits is a common component of 'healthy' dietary patterns in Western populations.[13–19] These components might partly explain the possible protective effect of the Japanese dietary pattern against CVD mortality including CHD and stroke, although we might have failed to detect associations with CHD mortality due to insufficient statistical power. However, compared with 'healthy' dietary patterns among Western populations, the Japanese dietary pattern also has unique characteristics.

The Japanese diet has so far been considered to increase the risk of CVD because it includes a large amount of salt.[35] In the present study, the Japanese dietary pattern was related to higher sodium consumption (Table 3) and higher prevalence of hypertension (Table 2). In spite of these risk factors, the Japanese dietary pattern was associated with lower CVD mortality. Although some components of the Japanese diet (i.e. salt) increase the risk of hypertension, other components may compensate for this, and decrease the risk of CVD. Components unique to the Japanese diet would include items such as soybeans, seaweeds and green tea. The effect of those foods upon CVD risk has yet to be clarified.

Factor analysis has both strengths and limitations. On the one hand, it can overcome multicollinearity of various dietary variables, because it is a statistical dimension-reduction technique that exploits the correlation of each variable. However, factor analysis requires several decisions about the methods used for extracting initial factors and rotation.[36] Even after multiple sensitivity analyses using these methods and various groupings by age and sex, the dietary patterns were essentially unchanged.

Our study also had other limitations. First, healthy behaviour in adhering to a Japanese dietary pattern could have confounded the association between dietary patterns and mortality. Although we adjusted our data using measured potential confounders including non-dietary variables, we could not completely exclude the effects of unmeasured confounders. Second, 12% of the participants were lost to follow-up. This proportion did not vary across the quartiles of each dietary pattern score (13%, 13%, 12% and 11% of participants from the lowest to highest Japanese dietary pattern score quartiles, respectively). Therefore, we consider it unlikely that the association between each dietary pattern and CVD mortality was substantially distorted by the effect of loss to follow-up.

Third, our FFQ did not ask about individual portion size, and preparation of foods including added oil. Some misclassification of food consumption could have arisen in deriving dietary pattern scores and estimating the effect of the patterns on

Table 5 Multivariate-adjusted hazard ratio for coronary heart disease and stroke mortality according to dietary pattern score quartiles

Variable	Dietary pattern score quartiles				*P* for Trend
	1 (low)	2	3	4 (high)	
Coronary heart disease					
Japanese pattern					
No. of deaths	54	45	38	44	
Multivariate-adjusted HR1[a] (95% CI)	1	0.84 (0.56–1.26)	0.70 (0.45–1.08)	0.80 (0.51–1.25)	0.24
Multivariate-adjusted HR2[b] (95% CI)	1	0.86 (0.57–1.29)	0.71 (0.46–1.11)	0.82 (0.52–1.29)	0.29
'Animal food' pattern					
No. of deaths	42	44	46	49	
Multivariate-adjusted HR1[a] (95% CI)	1	1.12 (0.73–1.72)	1.38 (0.89–2.15)	1.49 (0.94–2.34)	0.06
Multivariate-adjusted HR2[b] (95% CI)	1	1.10 (0.72–1.70)	1.39 (0.89–2.16)	1.50 (0.95–2.37)	0.05
Total stroke					
Japanese pattern					
No. of deaths	138	100	97	97	
Multivariate-adjusted HR1[a] (95% CI)	1	0.70 (0.54–0.92)	0.66 (0.50–0.87)	0.64 (0.47–0.85)	0.003
Multivariate-adjusted HR2[b] (95% CI)	1	0.71 (0.54–0.92)	0.67 (0.51–0.88)	0.64 (0.48–0.86)	0.004
'Animal food' pattern					
No. of deaths	142	103	103	84	
Multivariate-adjusted HR1[a] (95% CI)	1	0.89 (0.68–1.15)	1.11 (0.84–1.43)	0.97 (0.72–1.31)	0.79
Multivariate-adjusted HR2[b] (95% CI)	1	0.89 (0.69–1.15)	1.11 (0.85–1.45)	1.00 (0.74–1.35)	0.66
Cerebral infarction					
Japanese pattern					
No. of deaths	48	44	38	33	
Multivariate-adjusted HR1[a] (95% CI)	1	0.89 (0.59–1.36)	0.73 (0.47–1.15)	0.60 (0.37–0.99)	0.03
Multivariate-adjusted HR2[b] (95% CI)	1	0.89 (0.59–1.36)	0.73 (0.47–1.15)	0.60 (0.37–0.99)	0.03
'Animal food' pattern					
No. of deaths	51	43	35	34	
Multivariate-adjusted HR1[a] (95% CI)	1	1.04 (0.68–1.57)	1.08 (0.69–1.70)	1.11 (0.69–1.78)	0.66
Multivariate-adjusted HR2[b] (95% CI)	1	1.03 (0.68–1.56)	1.09 (0.69–1.71)	1.14 (0.71–1.85)	0.57
Intracerebral hemorrhage					
Japanese pattern					
No. of deaths	45	29	25	30	0.04
Multivariate-adjusted HR1[a] (95% CI)	1	0.62 (0.38–1.00)	0.52 (0.31–0.87)	0.60 (0.35–1.01)	0.04
Multivariate-adjusted HR2[b] (95% CI)	1	0.63 (0.39–1.02)	0.52 (0.31–0.88)	0.60 (0.36–1.03)	
'Animal food' pattern					
No. of deaths	44	28	30	27	
Multivariate-adjusted HR1[a] (95% CI)	1	0.71 (0.44–1.15)	0.87 (0.53–1.43)	0.82 (0.48–1.41)	0.59
Multivariate-adjusted HR2[b] (95% CI)	1	0.71 (0.44–1.16)	0.89 (0.54–1.46)	0.86 (0.50–1.47)	0.71

[a] Multivariate-adjusted HR1 was adjusted for age (in years), sex, smoking status (never, former, currently smoking <20 cigarettes/day and currently smoking 20 cigarettes/day), walking duration (<1 hour/day and 1 hour/day), education (until age up to 15 years, until age 16–18 years, and until age 19 years), and total energy intake (continuous).

[b] Multivariate-adjusted HR2 was adjusted for the same as HR1, body mass index ($<18.5\,kg/m^2$, 18.5–$24.9\,kg/m^2$, and $25\,kg/m^2$) and history of hypertension (yes or no).

HR, hazard ratio; CI, confidence interval.

Table 6 Multivariate-adjusted hazard ratio for cardiovascular disease mortality according to the Japanese dietary pattern score quartiles stratified by smoking status

	Dietary pattern score quartiles				
Variable	1 (low)	2	3	4 (high)	***P* for Trend**
Never smoker					
No. of deaths	82	71	76	73	
Multivariate-adjusted HR1[a] (95% CI)	1	0.70 (0.50–0.97)	0.68 (0.48–0.95)	0.54 (0.38–0.78)	0.002
Multivariate-adjusted HR2[b] (95% CI)	1	0.70 (0.50–0.97)	0.68 (0.48–0.95)	0.54 (0.37–0.78)	0.002
Past smoker					
No. of deaths	53	28	30	27	
Multivariate-adjusted HR1[a] (95% CI)	1	0.53 (0.33–0.85)	0.53 (0.33–0.85)	0.53 (0.32–0.89)	0.01
Multivariate-adjusted HR2[b] (95% CI)	1	0.53 (0.33–0.85)	0.53 (0.33–0.86)	0.53 (0.32–0.89)	0.01
Current smoker					
No. of deaths	87	62	45	61	
Multivariate-adjusted HR1[a] (95% CI)	1	0.79 (0.57–1.10)	0.66 (0.46–0.97)	0.92 (0.64–1.33)	0.41
Multivariate-adjusted HR2[b] (95% CI)	1	0.79 (0.57–1.11)	0.66 (0.46–0.97)	0.93 (0.65–1.34)	0.44

HR, hazard ratio; CI, confidence interval.

[a] Multivariate-adjusted HR1 was adjusted for age (in years), sex, walking duration (<1 hour/day and ⩾ 1 hour/day), education (until age up to 15 years, until age 16-18 years, and until age ⩾ 19 years), and total energy intake (continuous).

[b] Multivariate-adjusted HR2 was adjusted for the same as HR1, body mass index (<18.5kg/m2, 18.5-24.9kg/m^2, and ⩾ 25kg/m2), and history of hypertension (yes or no).

CVD mortality. However, this misclassification may be non-differential and would tend to result in underestimation of the impact of the dietary patterns.

In conclusion, we have found that the Japanese dietary pattern is associated with lower CVD mortality, despite the fact that the Japanese dietary pattern appeared to be related to higher sodium intake and high prevalence of hypertension.

Acknowledgements

This study was supported by a Health Sciences Research Grant for Health Services (H18-Choju-Ippan-014, H16-Seisaku-Ippan-023, H18-Junkankitou (Seisyu)-Ippan-012), Ministry of Health, Labour and Welfare, Japan. The authors are grateful to all the participants of this study.

Conflict of interest: None declared.

KEY MESSAGES

- Although ecological observations suggest that the Japanese diet may reduce the risk of cardiovascular disease, the impact of a Japanese dietary pattern upon mortality due to CVD is unclear.
- The association between dietary patterns among 40 547 Japanese aged 40–79 years and CVD mortality was examined in a 7-year prospective cohort study.
- The Japanese dietary pattern was associated with a lower risk of CVD mortality, despite its relation to sodium intake.

References

[1] Keys AB. *Seven Countries: A Multivariate Analysis of Death and Coronary Heart Disease*. Cambridge, MA: Harvard University Press, 1980.

[2] Willett WC. Diet and health: what should we eat? *Science* 1994;**264**:532–7.

[3] Kromhout D, Keys A, Aravanis C *et al.* Food consumption patterns in the 1960s in seven countries. *Am J Clin Nutr* 1989;**49**:889–94.

[4] Takeya Y, Popper JS, Shimizu Y, Kato H, Rhoads GG, Kagan A. Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: incidence of stroke in Japan and Hawaii. *Stroke* 1984;**15**:15–23.

[5] Ministry of Health Labour and Welfare. *The National Nutrition Survey in Japan, 2002 (in Japanese)*. Tokyo: Daiichi-Shuppan, 2004.

[6] Ministry of Health Labour and Welfare. *Vital Statistics of Japan 2003 (in Japanese)*. Tokyo: Health Welfare Statistics Association, 2003.

[7] World Health Organization. *WHO Mortality Database*. Available from: http://www3.who.int/whosis/menu.cfm?path=whosis,mort&language=english (Accessed May 1, 2006).

[8] Iso H, Kobayashi M, Ishihara J *et al.* Intake of fish and n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (JPHC) Study Cohort I. *Circulation* 2006;**113**:195–202.

[9] Nakamura Y, Ueshima H, Okamura T *et al.* Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980-99. *Am J Med* 2005;**118**:239–45.

[10] Nagata C, Takatsuka N, Shimizu H. Soy and fish oil intake and mortality in a Japanese community. *Am J Epidemiol* 2002;**156**:824–31.

[11] van der Schouw YT, Kreijkamp-Kaspers S, Peeters PH, Keinan-Boker L, Rimm EB, Grobbee DE. Prospective study on usual dietary phytoestrogen intake and cardiovascular disease risk in western women. *Circulation* 2005;**111**:465–71.

[12] Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic disease? *Am J Clin Nutr* 2001; **73**:1–2.

[13] Osler M, Heitmann BL, Gerdes LU, Jorgensen LM, Schroll M. Dietary patterns and mortality in Danish men and women: a prospective observational study. *Br J Nutr* 2001;**85**:219–25.

[14] Huijbregts P, Feskens E, Rasanen L, Fidanza F, Nissinen A, Menotti A, Kromhout D. Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and The Netherlands: longitudinal cohort study. *Br Med J* 1997;**315**:13–17.

[15] Kant AK, Schatzkin A, Graubard BI, Schairer C. A prospective study of diet quality and mortality in women. *JAMA* 2000;**283**: 2109–15.

[16] Michels KB, Wolk A. A prospective study of variety of healthy foods and mortality in women. *Int J Epidemiol* 2002;**31**:847–54.

[17] Hu FB, Rimm EB, Stampfer MJ, Ascherio A, Spiegelman D, Willett WC. Prospective study of major dietary patterns and risk of coronary heart disease in men. *Am J Clin Nutr* 2000;**72**: 912–21.

[18] Fung TT, Stampfer MJ, Manson JE, Rexrode KM, Willett WC, Hu FB. Prospective study of major dietary patterns and stroke risk in women. *Stroke* 2004;**35**:2014–19.

[19] Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* 2003;**348**:2599–608.

[20] Mizoue T, Yamaji T, Tabata S *et al.* Dietary patterns and colorectal adenomas in Japanese men: the self-defense forces health study. *Am J Epidemiol* 2005;**161**:338–45.

[21] Kim MK, Sasaki S, Sasazuki S, Tsugane S. Prospective study of three major dietary patterns and risk of gastric cancer in Japan. *Int J Cancer* 2004;**110**:435–42.

[22] Masaki M, Sugimori H, Nakamura K, Tadera M. Dietary patterns and stomach cancer among middle-aged male workers in Tokyo. *Asian Pac J Cancer Prev* 2003;4:61–6.

[23] Kumagai S, Shibata H, Watanabe S, Suzuki T, Haga H. Effect of food intake pattern on all-cause mortality in the community elderly: a 7-year longitudinal study. *J Nutr Health Aging* 1999;3:29–33.

[24] Kim J-O, Mueller CW. *Factor Analysis: Statistical Methods and Practical Issues*. Beverly Hills, CA: Sage Publications, 1978.

[25] Tsuji I, Nishino Y, Ohkubo T *et al.* A prospective cohort study on National Health Insurance beneficiaries in Ohsaki, Miyagi Prefecture, Japan: study design, profiles of the subjects and medical cost during the first year. *J Epidemiol* 1998;**8**:258–63.

[26] Tsuji I, Kuwahara A, Nishino Y, Ohkubo T, Sasaki A, Hisamichi S. Medical cost for disability: a longitudinal observation of national health insurance beneficiaries in Japan. *J Am Geriatr Soc* 1999;**47**:470–6.

[27] Ogawa K, Tsubono Y, Nishino Y *et al.* Validation of a food-frequency questionnaire for cohort studies in rural Japan. *Public Health Nutr* 2003;**6**:147–57.

[28] Science and Technology Agency. *Standard Tables of Food Composition in Japan (in Japanese)*. 5th edn. Tokyo: Printing Bureau, Ministry of Finance, 2000.

[29] SAS Institute. *SAS/STAT 9.1 User's Guide*. Cary, NC: SAS Institute, 2004.

[30] World Health Organization. *International Statistical Classification of Diseases and Related Health Problems. 10th Revision*. Geneva: World Health Organization, 1992.

[31] Cox DR, Oakes D. *Analysis of Survival Data*. London, New York: Chapman and Hall, 1984.

[32] Tsubono Y, Tsuji I, Fujita K *et al.* Validation of walking questionnaire for population-based prospective studies in Japan: comparison with pedometer. *J Epidemiol* 2002;**12**:305–9.

[33] Stewart AL, Hays RD, Ware JE Jr. The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care* 1988;**26**:724–35.

[34] Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. *Am J Epidemiol* 1986;**124**:17–27.

[35] Zhou BF, Stamler J, Dennis B *et al.* Nutrient intakes of middle-aged men and women in China, Japan, United Kingdom, and United States in the late 1990s: the INTERMAP study. *J Hum Hypertens* 2003;**17**:623–30.

[36] Martinez ME, Marshall JR, Sechrest L. Invited commentary: factor analysis and the search for objectivity. *Am J Epidemiol* 1998;**148**:17–9.

３．飲酒と自殺リスクに関する前向きコホート研究 ： 大崎コホート研究

【目的】飲酒と自殺リスクに関する先行研究では、アルコール依存症患者などで自殺リスクが上昇することが報告されてきた。

しかし、一般地域住民を対象とした疫学調査は少なく、少量飲酒者において自殺リスクが上昇するかは未だ一致した結果が得られていない。

本研究の目的は、一般地域住民を対象とした前向きコホート研究により少量飲酒者において自殺リスクが上昇するかどうかを明らかにすることである。

【方法】 1994 年に 40-79 歳の宮城県大崎保健所管内の国民健康保険加入者全員に自記式質問票を配布し、52,029 名 (94.6%) より有効回答を得た。本研究では、男性 24,895 名のみを調査対象とした。

解析対象者は追跡開始 (1995 年１月) 以前に死亡した者及び国民健康保険から異動した者、また飲酒に関する質問の未回答者を除いた 22,804 名 (86.1%) とした。

飲酒に関して、対象者は「飲む」「飲んだことがない」「飲んでいたがやめた」のうち１つを選択し、「飲む」「飲んでいたがやめた」

と回答した者は飲酒頻度と１日あたりの飲酒量を回答した。本研究では、飲酒カテゴリーを以下の４つに分類した；非現在飲酒者 (非飲酒者＋過去飲酒者)、現在飲酒者：アルコール摂取量 22.7g 以下/日、22.8 - 45.5g/日、45.6g 以上/日。

追跡調査は 2001 年 12 月末までの 7 年間行い、73 例の自殺死亡例を確認した。統計解析は、Cox 比例ハザードモデルを用い、非現在飲酒者に対する、他群の相対危険度を算出した (共変量は表に示す)。

【結果及び考察】 非現在飲酒者に対する多変量補正相対危険度 (95%信頼区間) は、22.7g 以下/日で 1.2 (0.5-2.7)、22.8 - 45.5g/日で 1.5 (0.7-3.4)、45.6g 以上/日で 2.3 (1.2-4.6) であり、有意な量－反応関係が示された。また、少量飲酒者における自殺リスクが上昇する傾向が示された。

さらに、ベースライン時から１年以内の死亡例を除外しても、少量飲酒者において自殺リスクが上昇する傾向は維持された (Multivariate HR2=1.7)。

以上の結果から、多量飲酒者のみならず少量飲酒者においても自殺リスクが上昇する傾向が示された。

ELSEVIER

ALCOHOL

Alcohol 41 (2007) 503–510

Alcohol consumption and suicide mortality among Japanese men: the Ohsaki Study

Naoki Nakaya[a,*], Nobutaka Kikuchi[a], Taichi Shimazu[a], Kaori Ohmori[a], Masako Kakizaki[a], Toshimasa Sone[a], Shuichi Awata[a,b], Shinichi Kuriyama[a], Ichiro Tsuji[a]

[a]*Division of Epidemiology, Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, 2-1 Seiryo, Sendai 980-8575, Japan*

[b]*Division of Neuropsychiatry and Center for Dementia, Sendai City Hospital, Sendai, Japan*

Received 17 May 2007; received in revised form 1 August 2007; accepted 1 August 2007

Abstract

The risk of suicide is well known to be increased among heavy alcohol drinkers. However, whether the risk is increased or decreased among light drinkers is still under debate. We investigated this association in a population-based sample of men in Japan. The Ohsaki Study was a population-based, prospective cohort study among Japanese adults aged from 40 to 79 years. Between October and December, 1994, 22,804 men in Miyagi Prefecture, Japan, completed a questionnaire on various health-related lifestyles, including alcohol drinking. During the subsequent 7 years follow-up, 73 participants committed suicide. We used the Cox proportional hazards regression model to estimate the hazard ratio (HR) for suicide mortality according to the quantity of alcohol consumed daily, with adjustment for potential confounders. There was a statistically significant positive and linear association between the amount of alcohol consumed and the risk of suicide: the multivariate HRs in reference to nondrinkers (95% confidence interval) were 1.2 (0.5–2.7), 1.5 (0.7–3.4), and 2.4 (1.2–4.6) in current drinkers who consumed ≤22.7 g, 22.8 g–45.5 g, and ≥45.6 g of alcohol per day, respectively (*P*-trend = .016). Even after the early death cases were excluded, a significant linear association was observed between alcohol consumption and the risk of suicide, with the risk of suicide also being nonsignificantly higher among the light drinkers than among nondrinkers (multivariate HR = 1.7). This prospective cohort study indicated a positive linear association between alcohol consumption and the risk of suicide, and the suicide risk among the light drinkers was not decreased as compared with that in nondrinkers.

Keywords: Alcohol consumption; Japanese; Men; Mortality; Prospective cohort study; Suicide

Introduction

Since 1998, over 30,000 people have committed suicide in Japan, and the number of people committing suicide continues to increase (30,553 suicide deaths in 2005) (Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare, 2005). In 2002, the World Health Organization reported that the suicide mortality rate in Japan was higher (23.8 per 100,000 population) (Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare, 2005) than in Western countries (France, 18.4/100,000 [data on 2000]; Germany, 13.5/100,000 [data on 2000]; Canada, 11.6/100,000; USA, 11.0/100,000; UK, 7.0/100,000 [data on 2004]; Italy, 7.1/100,000) (World Health Organization, Suicide Prevention, 2007). To develop effective strategies for suicide prevention, factors associated with an increased risk of suicide must be urgently investigated in Japan.

Various sociodemographic (male gender, 60 years of age or older, widowed or divorced, living alone, unemployed or having financial problems, and recent adverse event) and clinical variables (depression, schizophrenia, alcohol dependence, history of suicide attempts or ideation, feeling of hopelessness, panic attacks, severe anxiety, and severe anhedonia) have been identified as risk factors of suicide (Hirschfeld and Russell, 1997). Alcohol drinking is also one of the established risk factors for suicide (Akechi et al., 2006; Andreasson et al., 1991; Klatsky and Armstrong, 1993; Ross et al., 1990; Sorock et al., 2006).

Recently, a large population-based case-control study in the United States indicated that alcohol drinking was associated with an increased risk of suicide (Sorock et al., 2006), but the dose–response association between alcohol consumption and the risk of suicide was not able to be clarified in the study.

* Corresponding author. Tel.: +81-022-717-8123; fax: +81-022-717-8125.

E-mail address: nakaya-thk@umin.ac.jp (N. Nakaya).

0741-8329/07/$ – see front matter
doi: 10.1016/j.alcohol.2007.08.001