

Review

Japanese Dietary Lifestyle and Cardiovascular Disease

Norio Tada¹, Chizuko Maruyama², Shinji Koba³, Hiroaki Tanaka⁴, Sadatoshi Birou⁵,
Tamio Teramoto⁶ and Jun Sasaki⁷

¹Division of Metabolism and Nutrition, Department of Internal Medicine, The Jikei University Graduate School of Medicine, Tokyo, Japan

²Department of Food and Nutrition, Japan Women's University, Tokyo, Japan

³Department of Medicine, Division of Cardiology, Showa University, Tokyo, Japan

⁴Laboratory of Exercise Physiology, Faculty of Sports and Health Science, Fukuoka University, Fukuoka, Japan

⁵Department of Internal Medicine, Tsukasa Health Care Hospital, Kagoshima, Japan

⁶Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan

⁷Graduate School of Pharmaceutical Medicine, International University of Health and Welfare, Fukuoka, Japan

To demonstrate the reasons for low morbidity and mortality from coronary artery disease (CAD) and reconfirm the effectiveness of the Japanese dietary lifestyle for preventing CAD, we herein review the CAD risk transition, and post-war changes in Japanese food and nutrient intake.

Large-scale cohort studies in Japan were selectively reviewed. Low serum total cholesterol contributed to preventing CAD, and decreased blood pressure was the major factor favoring stroke reduction. Japanese consumed more plant and marine origin foods, but fewer animal foods with saturated fatty acids (SFA) during the 1960-70s than in recent decades. Adequate control of total energy with restriction of saturated fatty acids from animal foods, increased intake of n-3 polyunsaturated fatty acids, including fish, soybean products, fruits and vegetables together with low salt intake are responsible for promoting CAD and stroke prevention.

A diet with adequate total calories and increased intake of fish and plant foods, but decreased intake of refined carbohydrates and animal fat, a so-called Japan diet, appears to be quite effective for prevention of CAD risk factors and is recommended as dietary therapy for preventing CAD.

J Atheroscler Thromb, 2011; 18:723-734.

Key words; Nutrients, Food intake, Atherosclerosis, Coronary artery disease, Stroke

Introduction

The average life span of Japanese increased from 1947 to 2009, from 50.1 to 79.6 years in men and from 54.0 to 86.4 years in women. Currently, Japanese women have the longest and men have the second longest life span in the world with consistently low morbidity and mortality from coronary artery disease (CAD) and declines in those associated with stroke;

however, there is the so-called Japanese paradox, i.e. Japanese people have lower CAD incidence and mortality from CAD than other industrialized countries despite high smoking rates¹. Ueshima concluded that the low CAD mortality rate is attributable to a lower serum total cholesterol level in middle-aged and elderly people, as compared with Western countries, as well as the tendency for declines in blood pressure and smoking rates². On the other hand, Japanese foods are widely regarded as healthy, i.e. CAD preventive, based on research conducted in many geographic areas, such as the Seven Countries Study³⁻⁸ and the Ni-Hon-San Study⁹⁻¹¹.

Herein, we discuss CAD and stroke risk transitions in Japan and changes in Japanese food and nutrient intake, in order to reconfirm the efficacy of the Japan diet in preventing CAD and other cardiovascu-

Address for correspondence: Norio Tada, Division of Metabolism and Nutrition, Department of Internal Medicine, Kashiwa Hospital, The Jikei University Graduate School of Medicine, Kashiwashita 163-1, Kashiwa, 277-8567, Chiba Japan

E-mail: n-tada27@jikei.ac.jp

Received: December 20, 2010

Accepted for publication: March 11, 2011

lar diseases. We also describe how foods that may be useful for preventing CAD are traditionally prepared and served in Japan.

Changes in CAD, stroke and associated risk factors in Japan

In Japan, the age-adjusted all stroke mortality rate increased after World War II until 1965 and then showed a significant decline until 1990, whereas age-adjusted CAD mortality increased until 1970, but was still the lowest in industrialized countries, and then continuously decreased thereafter²⁾. Comparing the incidences of stroke and acute myocardial infarction (AMI) in several Japanese populations with those of the MONICA Project confirmed stroke risk to not be markedly higher and that of AMI to be much lower than in Western countries^{2, 12)}.

The Seven Countries Study, which carried out a baseline study between 1958 to 1964, involving an agricultural district and a fishing village in southern parts of Japan, indicated that the average total cholesterol level in Japanese was low at approximately 160 mg/dL, and the CAD mortality rate was the lowest among participating countries despite a high smoking rate in Japan^{4, 6)}. Furthermore, the Ni-Hon-San Study on Japanese men living in Japanese cities, Hiroshima and Nagasaki, and Japanese immigrants living in Honolulu, Hawaii, and the San Francisco Bay Area, revealed the total cholesterol level and incidence of CAD to be higher in the subjects living in San Francisco and Hawaii than those living in Hiroshima and Nagasaki^{10, 11)}. This study showed that Japanese are not naturally more resistant to atherosclerotic disorders. According to epidemiologic cohort studies in Japan, such as the National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged, 1980 (NIPPON DATA 80)¹³⁾, the Hiroshima/Nagasaki study¹⁴⁾ and the Hisayama study¹⁵⁾, there are no differences in relative CAD risk factors, i.e. hypertension, hypercholesterolemia, smoking and diabetes mellitus, between Japan and other industrialized countries¹²⁾. The lower total cholesterol level in Japanese in comparison with their Western counterparts might be a one of the major factors associated with CAD prevention. Furthermore, hereditary predisposition did not protect Japanese against the onset of CAD while lifestyle-related factors that contributed to maintaining low total cholesterol levels were found to be important for prevention, as shown in the Ni-Hon-San Study^{10, 11)}. As regards stroke, these studies identified hypertension and smoking as major factors¹⁶⁻²⁰⁾. Meanwhile, blood pres-

sure and smoking prevalence in elderly people have clearly decreased²⁾. This was credited with decreasing stroke mortality²⁾ in the last two decades of the 20th century.

With respect to changes in risk factors for cardiovascular diseases, the Hisayama Study, which investigated cohorts from 1961, 1974 and 1988, revealed another recent risk profile in the Japanese population. Despite gradual significant decreases in the prevalence of hypertension and smoking, rates of obesity, hypercholesterolemia, and impaired glucose tolerance apparently rose in both genders^{15, 21-23)}. Based on the results of a meta-analysis of 16 Japanese cohorts followed from 1985 to 2005, excess weight was also associated with increased risks of cerebral infarction and myocardial infarction (MI)²⁴⁾. The National Health and Nutrition Survey in Japan (NHNSJ), initiated in 1946, indicated ongoing increases in obesity and diabetes mellitus. Obesity in men and subjects at considerable risk for diabetes mellitus increased from 24.3 % to 31.2% and from 13.7 to 22.1 million people, respectively, from 1997 to 2007²⁵⁾. As regards serum cholesterol in particular, NIPPON DATA80 indicated a positive correlation between the risk of CAD and the total cholesterol concentration²⁰⁾. Total cholesterol in Japanese showed a gradual increase, reaching a level similar to that of the American population (**Fig. 1**)²⁶⁻²⁸⁾. Conversely, in the United States, the total cholesterol level has gradually decreased in both genders with the establishment of national strategies for prevention of CAD²⁹⁻³¹⁾; however, the incidence of CAD in Japanese remained lower, i.e. approximately 1/5 to 1/3 of that in Americans in each plasma total cholesterol level³²⁻³⁴⁾. Considering the unique status of atherosclerotic disease in Japanese, not only physical and biochemical parameters, but also lifestyle factors, including diet, can be merits to emphasize.

Dietary changes in Japan

After World War II, the Japanese lifestyle, especially dietary features, changed markedly with westernization and diversification, as reflected by changes in the amounts and types of foods consumed per capita annually, as recorded in "Food Balance Sheets" issued by the Ministry of Agriculture, Forestry and Fisheries (**Fig. 2**)³⁵⁾. From 1960 to 2005, the amounts of animal products and total fats and oils increased markedly by approximately 4- and 3-fold, respectively, while rice consumption decreased by half.

The food group-based intake per capita obtained by NHNSJ showed a marked increase in the intake of meat and poultry, milk and other dairy products, but

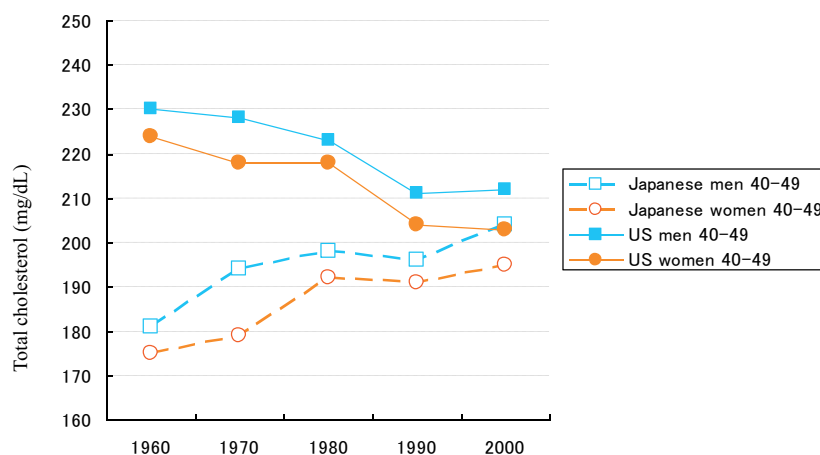


Fig. 1. Comparison of changes in serum total cholesterol level between Japanese and American adults in their 40s

The cholesterol level in Japanese showed a gradual increase and reached a similar level to that of the United States (Ref. 26-28).

kg per capita/year

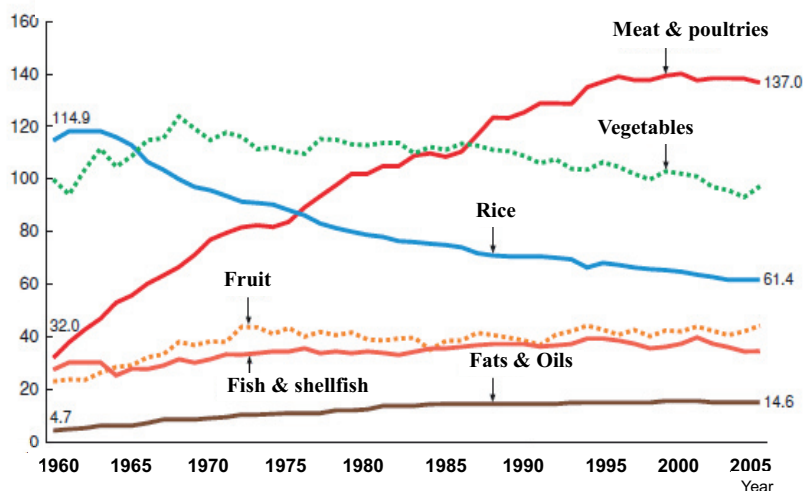


Fig. 2. Changes in food supply per capita in Japan

The annual food consumption per capita was regarded as the annual food supply per year. The supply of animal foods, excluding whale meat, has markedly increased since 1960. The total fat and oil intake has also risen approximately 3-fold. On the other hand, rice supply has markedly decreased, and vegetable intake has serially reduced. Data were obtained from the “Food balance sheet” reported by the Ministry of Agriculture, Forestry and Fisheries (Ref. 35).

decrease in the intake of rice, as mentioned earlier. The mean intake of fish and beans slightly increased and mean vegetable intake seemed to be constant³⁶; however, a clear difference with higher intake of vegetables, fruit, seafood and bean products in the elderly versus lower intake in the younger generation has become apparent in recent years³⁷.

Based on the results of the NHNSJ, the percentage of energy derived from fat has gradually but clearly increased from 7.0% in 1946 to 26.6% in 2000, despite almost the same average total energy intake during this 54-year period (**Fig. 3**). This suggests that qualitative changes involved in an increase in the percentage of energy derived from fat are attributable to

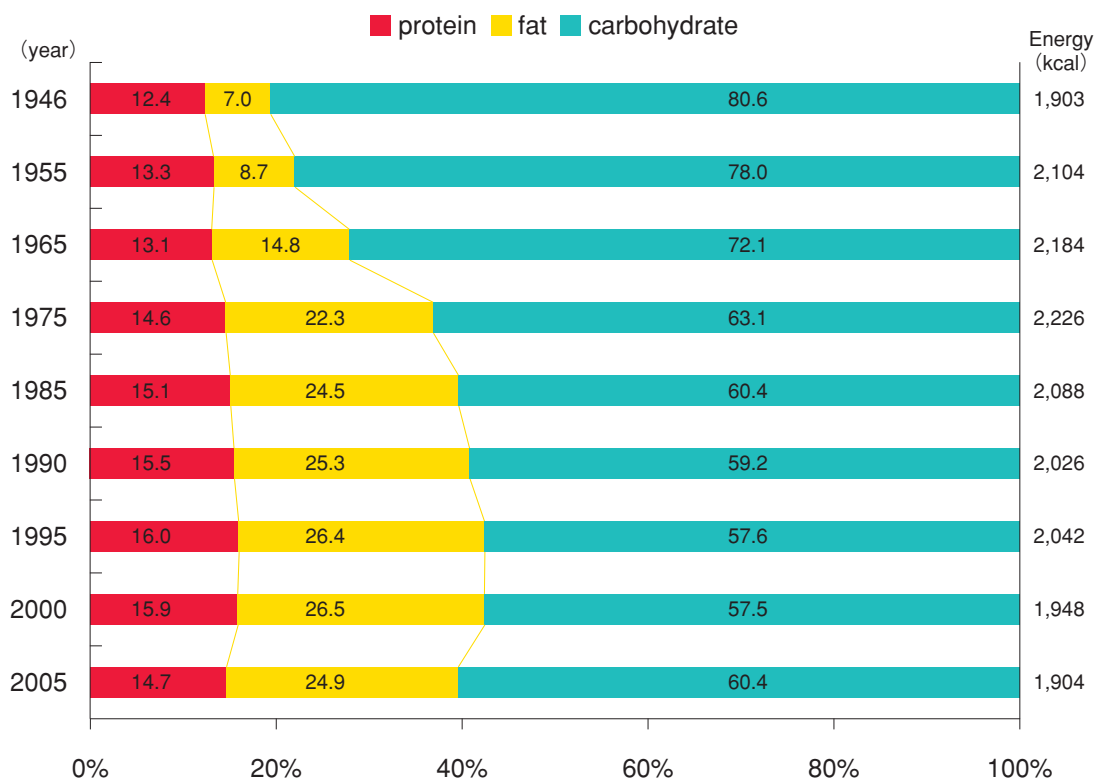


Fig. 3. Changes in energy intake in Japan

The energy percentage derived from fat has gradually increased since 1946, although there have been no marked changes in the average total energy intake among Japanese. The data were obtained from the results of the National Nutrition and Health Survey by The Ministry of Health, Labour and Welfare (Ref. 38).

increased intake of fat contained in animal products and artificially produced from plant oil by hydrogenation. The mean salt intake in Japanese in 1976 was 13.7 g/day, gradually decreasing to 11.7 g/day by 1987. It then increased with a rise in the frequency of restaurant dining and the widespread consumption of fast foods, but had apparently decreased to 10.6 g/day in 2006³⁸).

These data collectively indicate that the Japanese younger generation decreased the intake of plant and marine origin foods, while increasing that of animal (other than seafood) products. Such changes have resulted in decreased n-3 polyunsaturated fatty acids, dietary fiber and salt intake, but increased saturated fatty acid intake.

Reports on nutrient and diet in relation to CAD and stroke risk and mortality reduction in Japan

The findings of Japanese cohort studies, having

the advantage of being able to evaluate long-term effects of exposure, on nutrient and food intake show significant multivariate hazard ratios for the incidence and mortality of CAD and stroke, summarized in **Table 1**. Among these major studies, the Japan Public Health Center-based (JPHC) and Japan Collaborative Cohort (JACC), NIPPON DATA80 studies were conducted to obtain nationwide population-based samples.

CAD and diet

As for CAD incidence and mortality, negative associations were confirmed with the intake of fish and n-3 polyunsaturated fatty acids, soybean and soybean products and isoflavones, fruit, potassium, folate, vitamin B6 and alcohol. This food and nutrient intake has contributed to the lower mortality from CAD in the Japanese population.

Fish and n-3 PUFA

In the JPHC study, the incidence of total CAD

Table 1. Effects of food and nutrient intake on coronary artery disease and stroke in Japan

Author (reference)	Population	Multivariate hazard ratios (95% CI)
Iso H <i>et al.</i> (39)	27,063 men and 27,435 women aged 40-59 followed from 1990 to 2001 (JPHC)	RR=0.43 (0.23-0.81) for nonfatal coronary events and 0.63 (0.38-1.04) for incidence of total CAD, and 0.44 (0.24-0.81) for definite MI in the highest (8 times/week or median intake 180 g/day) vs lowest (once/week or median intake=23 g/day) fish intake groups. RR=0.35 (0.18-0.66) for incidence of definite MI and 0.33 (0.17-0.63) for nonfatal coronary events in those with the highest (median 2.1 g/day) vs the lowest (median 0.3 g/day) n3 PUFA intake .
Yamagishi K <i>et al.</i> (40)	22,881 men and 35,091 women aged 40-79 followed from 1988-90 to 2003 (JACC)	RR=0.77(0.53-1.10) for mortality from MI in those with the highest (median (male) 86 g/day, median (female) 85 g/day) vs the lowest (median (male) 20 g/day, median (female) 21 g/day) fish intake . RR=0.75 (0.47-1.19) for mortality from MI in those in the highest vs lowest quintiles (volume are not shown) of n-3 PUFA intake .
Nakamura Y <i>et al.</i> (41)	3,945 men and 4,935 women followed from 1980 to 1998	RR=0.91 (0.35-2.35) for CAD mortality, 1.26 (0.70-1.27) for stroke mortality in those who ate fish more than twice daily vs 1 to 2 times weekly
Kokubo Y <i>et al.</i> (47)	40,462 men and women aged 40-59 followed from 1990-92 to 2002 (JPHC)	RR=0.55 (0.26-1.09) for incidence of MI and 0.64 (0.43-0.95) for cerebral infarction in women with the highest (>5 times /week) vs the lowest (0-2 times /week) soy consumption . RR=0.35 (0.21-0.59) for incidence of cerebral infarction and 0.37 (0.14-0.98) for MI in women with the highest (mean 45.2 mg/day) vs the lowest (mean 10.6 mg/day) isoflavone intake
Sasazuki S <i>et al.</i> (48)	632 nonfatal AMI aged 40-79 versus (vs) 1,214 age, sex, and residence matched controls from 1996-1998	RR=0.5 (0.3-0.9) for incidence of nonfatal AMI in women with high (>4 times/week) vs low (<2 times / week) tofu consumption .
Nagura J <i>et al.</i> (49)	25,206 men and 34,279 women aged 40-79 followed from 1988-90 to 2003 (JACC)	RR=0.79 (0.58-1.08, <i>p</i> for trend 0.061) from CAD, 0.65 (0.53-0.80) for mortality from total stroke and 0.59 (0.42-0.82) from hemorrhagic stroke in those with the highest (5.9 servings/week) vs the lowest (0.9 servings/week) fruit intake .
Umesawa M <i>et al.</i> (50)	23,119 men and 35,611 women aged 40-79 from 1988-90 to 2003 (JACC)	RR=0.65 (0.39-1.06) for mortality from CAD in those with the highest (median 68 mmol/day) vs the lowest (median 35 mmol/day) potassium intake . RR=1.55 (1.21-2.00) for mortality from total stroke and 2.04 (1.41-2.94) for ischemic stroke in those with the highest (median 135 mmol/day) vs the lowest (median 50 mmol/day) sodium intake .
Ishihara J <i>et al.</i> (51)	19,343 men and 21,460 women (37,477 non-multivitamin supplement users) aged 40-59 followed from 1990 to 2001 (JPHC)	RR=0.63 (0.38-1.04) for incidence of definite MI in non-multivitamin supplement users who had the highest (mean 436 µg/day) vs the lowest (mean 290 µg/day) folate intake. RR=0.52 (0.29-0.91) for incidence of definite MI in non-multivitamin supplement users who had the highest (mean 1.60 mg/day) vs lowest (mean 1.30 mg/day) vitamin B6 intake . RR=0.53 (0.29-0.95) for incidence of definite MI in non-multivitamin supplement users who had the highest (mean 11.1 µg/day) vs lowest (mean 6.5 µg/day) vitamin B12 intake .
Cui R <i>et al.</i> (52)	23,119 men and 35,611 women aged 40-79 followed from 1988-1990 to 2003 (JACC)	RR=0.57 (0.34-0.96) for mortality from CAD in those who had the highest (mean 619 µg/day) vs lowest (mean 225 µg/day) folate intake , and RR=0.47 (0.21-1.04) for mortality from CAD in those who had the highest (mean 1.5 mg/day) vs lowest (mean 0.7 mg/day) vitamin B6 intake in women.

Sauvaget C <i>et al.</i> in Hiroshima/Nagasaki study (60)	14,966 men and 23,471 women aged 34-97 followed from 1980-81 to 1998	RR=0.77 (0.62-0.95) and 0.81 (0.68-0.96) for mortality from total stroke and 0.68 (0.50-0.94) and 0.70 (0.55-0.90) for cerebral infarction in those with the highest (daily) vs lowest (0-1/week) green-yellow vegetable intake in men and women. RR=0.65 (0.53-0.80) and 0.75 (0.64-0.88) for mortality from total stroke and 0.63 (0.41-0.97) and 0.68 (0.49-0.94) for hemorrhage, RR=0.63 (0.47-0.83) and 0.77 (0.61-0.96) for cerebral infarction in those with the highest (daily) vs the lowest (0-1/week) fruit intake in men and women.
Umesawa M <i>et al.</i> (64)	46,465 men and 64,327 women aged 40-79 followed from 1988-90 to 2003 (JACC)	RR=0.53 (0.34-0.81) for mortality from total stroke, 0.46 (0.23-0.91) for hemorrhagic stroke and 0.53 (0.29-0.99) for ischemic stroke in men with the highest (median 150 mg/day) vs the lowest (median 0 mg/day) dairy calcium intake ; corresponding relative risks for women were 0.57 (0.38-0.86), 0.51 (0.28-0.94) and 0.50 (0.27-0.95) in those with the highest (median 173 mg/d) vs the lowest (median 0 mg/d) dairy calcium intake .
Umesawa M <i>et al.</i> (63)	19,947 men and 21,579 women aged 40-59 followed from 1990-95 to 2003 (JPHC)	RR=0.69 (0.56-0.85) for incidence of total stroke and RR=0.69 (0.52-0.93) for incidence of ischemic stroke in those with the highest (median 116 mg/d) vs the lowest (median 0 mg/day) dairy calcium intake .
Iso H <i>et al.</i> (65)	2,269 men and 2,506 women aged 40-69 followed from 1973 to 1997	RR=0.30 (0.12-0.71) for incidence of intra-parenchymal hemorrhage in the highest (17 g/day) vs lowest (5 g/day) of SFA intake quartiles.
Iso H <i>et al.</i> (68)	19,544 men aged 40-59 followed from 1990 to 2001 (JPHC)	RR=1.43 (1.05-1.96) for incidence of total stroke, 1.37 (0.98-1.92) for definite total stroke, 2.15 (1.22-3.79) for hemorrhagic stroke, and 2.07 (1.12-3.83) for intra-parenchymal hemorrhage in those with the highest (>450 g/week) vs occasional ethanol intake . RR=0.98 (0.71-1.36) for incidence of total stroke, 1.73 (0.98-3.07) for hemorrhagic stroke, 0.59 (0.37-0.93) for ischemic stroke, and 0.43 (0.22-0.87) for lacunar infarction in those consuming 1-149 g/week ethanol vs occasional drinkers
Nakamura Y <i>et al.</i> (57)	23,062 men aged 40-69 followed from 1993 to 2001 (JPHC)	RR=0.46, 0.53, 0.28 and 0.70 (<i>P</i> for trend=0.005) for incidence of AMI in those with 1-149, 150-299, 300-449 and >450 g/week of ethanol vs non- drinkers in non-flusher. Same trend (<i>P</i> =0001) was observed in flusher.

CI: confidence interval, JPHC: Japan Public Health Center-based study, JACC: Japan Collaborative Cohort study, NIPPON DATA: National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged, CAD: coronary artery disease, MI: myocardial infarction, AMI: acute MI, SFA: saturated fatty acid, PUFA: polyunsaturated fatty acid Dietary surveys were performed employing food frequency questionnaires except in the study reported by Iso (reference 33) which employed the 24-hour recall method.

was 37% lower in persons who consumed an average of 180 g/day (or 8 times/week) of fish (2.4 g/day of n-3 polyunsaturated fatty acids) than in those ingesting 23 g/day or once/week (0.3 g/day). This significantly reduced risk, confined to nonfatal coronary events, not fatal coronary events, was attributed to Japanese consuming higher amounts of fish than the populations of Western countries³⁹). In the JACC study including elderly people, the median 85 g/day intake of fish was equivalent to 2.2 g/day of n-3 polyunsaturated fatty acids intake and was associated with an 18% to 19% lower risk of MI mortality as compared to 20 g/day intake of fish; however, these findings were not statistically significant⁴⁰). The NIPPON DATA 80 also did not observed significant differences in CAD between subjects who ate fish twice daily ver-

sus who ate it 1-2 times weekly, as the Japanese consumed fish more than the threshold level presumably shown to be beneficial⁴¹). However, the Japan EPA Lipid Intervention Study (JELIS) involving 18,645 Japanese patients with a total cholesterol of 6.5 mmol/L or greater followed for a mean 4.6 years indicated that the combination of a statin and 1.8 g of highly purified eicosapentaenoic acid (EPA) preparations significantly prevented the onset of major coronary events, as compared to a statin alone⁴²).

Saturated fatty acids

The NIPPON DATA80/90 Research Group compared fatty acids intake obtained from NHNSJ and serum lipid profiles from the National Survey on Circulatory Disorders (NSCD) in Japan conducted in

1990. They found that saturated fatty acid and total fat intake (%kcal) was positively associated with age- and body mass index (BMI)- adjusted serum total cholesterol, HDL-C, and LDL-C in women but not in men⁴³). The majority of studies have documented an increased risk of CAD with the intake of saturated fatty acid since the Seven Countries Study showed the association^{3, 4}). Saturated fatty acid intake was correlated with blood cholesterol concentrations also among Japanese females, as shown above, and high blood cholesterol was a strong risk factor for CAD⁴⁴). Multivariate linear regression analyses using the data from the Seven Countries Study including Japan also showed that the population intake of saturated fatty acid was positively associated with all-cause mortality rates⁸). However, a recent meta-analysis of prospective studies failed to show significant evidence to conclude that dietary SFA is associated with an increased risk of CAD⁴⁵). The JACC Study Group have recently reported that no multivariable-adjusted association was observed between saturated fatty acid intake and mortality from heart disease [$n = 836$; 0.89 (0.68, 1.15); P for trend = 0.59] after 14.1-year follow-up of 58,453 Japanese middle-aged men and women⁴⁶), although the distribution of saturated fatty acid intake among Japanese is far lower than that among Americans.

Soybean and soybean products and isoflavones

Soybean and soybean products are rich in protein, n-6 polyunsaturated fatty acids, lecithin, folate, calcium, fiber and isoflavones. Significant inverse associations of soy and isoflavone intake with the risk of MI and cardiovascular disease mortality were observed in women but not in men. Similar but weaker inverse associations were observed between the intake of miso soup and beans and risk of cardiovascular disease mortality in women but not in men⁴⁷). Tofu (soybean curd) consumption was associated with both low risk and mortality from AMI in women⁴⁸). Consuming soybeans and soybean products on an almost daily basis might be effective for CAD prevention.

Fruit and potassium

Higher fruit intake, with the exception of 100% juice, tended to be associated with both low risk and low total mortality from CAD^{49, 50}), the findings of which were more apparent in women⁵⁰). As potassium, which can reduce the risk of hypertension, is obtained from fruits, vegetables, seaweed and potatoes, lower mortality from CAD might reflect the combined effect of consuming these foods.

Folate, vitamin B6 and vitamin B12

High dietary folate, vitamin B6 and B12 intakes were associated with both a low incidence of CAD and a low mortality rate from CAD, primarily MI^{51, 52}). Japanese formerly consumed more dietary folate than their western counterparts⁵³⁻⁵⁵). Among middle-aged Japanese without any prior diagnosis of CAD and cancer, intake of folate, vitamin B6 and B12 was inversely associated with the incidence of CAD and definite MI and the combination of below median intake of these 3 vitamins or only B6 conferred a 70 to 80 % higher risk of CAD⁵¹).

Dietary fiber

A follow-up study of 58,730 Japanese middle-aged men and women over 14 years revealed that total, insoluble and soluble fiber intake was inversely associated with the risk of mortality from CAD and total cardiovascular disease for men and women⁵⁶).

Ethanol

The JPHC study of middle-aged Japanese men showed an inverse relationship between alcohol consumption and the risk of AMI during a mean follow-up of 8.7 years, and no increase in risk of AMI was seen among subjects with heavy alcohol consumption (>450 g/week) both in flushers or non-flushers⁵⁷).

Stroke and diet

As for stroke incidence and its mortality, a positive association was confirmed for sodium intake and excessive alcohol intake, while an inverse association for fruit, dairy calcium, soy and isoflavones, and saturated fatty acids intake.

Sodium

Mean sodium intake is reportedly higher in Japanese than in Caucasians^{58, 59}). A 100-mmol increment in uncalibrated daily sodium (=5.8 g of salt) intake was associated with an 83% higher total mortality rate from stroke⁵⁰). Japanese consume salt from seasonings such as salt itself, soy sauce, salted pickles, salty dried fish products and miso⁵⁹). Salt restriction to 10.6 g/day was achieved in 2006, as mentioned before, with reductions in the consumption of these foods and/or changes to reduced-salt foods in Japan³⁸).

Fruit and vegetables

Higher fruit intake (more than 5.9 servings/week), versus lower intake (0.9 servings/week), was associated with lower mortality from total stroke, including hemorrhage⁴⁹). Daily consumption of both green-yellow vegetables and fruit was associated with

lower mortality from cerebral hemorrhage and infarction in the Hiroshima/Nagasaki study⁶⁰. A meta-analysis of eight European cohort studies showed that vegetable and fruit intake was associated with a reduced risk of stroke, and consumption of more than 5 servings of vegetables and fruits per day was recommended⁶¹.

Dairy calcium

As in Western populations, an inverse association has been found between dairy calcium intake and mortality from stroke. Japanese consumption of milk and other dairy products is far lower than in Western countries⁶²; however, a median calcium intake of 116 mg/day from dairy products, suggested to be contained in half a glass of milk, was associated with an approximately 30% lower ischemic stroke incidence⁶³, and a cup of milk providing dairy calcium (150 mg/day in men, 173 mg/day in women) reduced the mortality from hemorrhagic, ischemic and total stroke⁶⁴.

Soy and isoflavones

Higher consumptions of soy and soy products containing isoflavones (more than 5 days/week) is associated with prevention of cerebral infarction in women and this association was observed primarily among postmenopausal women⁴⁷.

Saturated fatty acids

Very low saturated fatty acid intake (5 g/day) was confirmed to be associated with an increased risk of intra-parenchymal hemorrhage after adjustment for the serum total cholesterol level⁶⁵. Another survey conducted between 1988 and 1990 (JACC Study) also indicated an inverse association of saturated fatty acid intake with mortality from total stroke, intra-parenchymal hemorrhage, and ischemic stroke, except from sub-arachnoid hemorrhage⁴⁶. Similar trends were reported in American women 34-59 years of age, whose saturated fatty acid intake was approximately 3 times that of their Japanese counterparts⁶⁶.

Fish and n-3 polyunsaturated fatty acids

There have been no prospective studies on the preventive effects of fish and fish oil on recurrence of stroke. Subanalysis of the JELIS trial, mentioned before, showed that the administration of highly purified EPA appeared to reduce the risk for recurrent stroke in Japanese with hypercholesterolemia taking a statin, but not the risk for primary prevention of stroke⁶⁷.

Ethanol

The association of heavy ethanol consumption with the incidence of stroke is different from the incidence of CAD. Compared with occasional drinkers, heavy drinkers, i.e. those consuming >450 g/week had a 1.5- to 2-fold higher risk of total and hemorrhagic stroke. Light to moderate alcohol consumption, i.e., 1 to 149 g/week (<2 drinks/day), does not raise the total stroke risk⁶⁸.

The Japan Diet

Based on the substantial evidence above, adequate control of total energy and SFA intake, sufficient consumption of fish, soybeans and soybean products, fruits and vegetables, folate and vitamin B6, as well as modest alcohol intake, are useful for the prevention of CAD. In addition, specific foods, such as seaweed, mushrooms, konnyaku (boiled paste made from the arum root), and burdock, containing a large amount of dietary fiber but few calories, are frequently consumed in Japan. Japanese tea is high in antioxidants. These factors may all contribute collectively to the prevention of CAD and are presumably contained in the Japan diet.

Traditional Japanese cuisine

The so-called Japan diet characterized by consuming the foods described above, cooking by traditional Japanese methods, attributable to spiritual dietary culture partly derived from Zen, could promote a balanced intake of various nutrients while minimizing excess energy intake. Staple foods such as grains are commonly boiled without oil. Fish and shellfish, meat and poultry, eggs, soybeans and soybean products are used as main dishes. Main and side dishes are usually raw, steamed, boiled, grilled, roasted, or pan-fried with minimal addition of plant oil, but not animal fat. Vegetables and soybean products are prepared as side dishes and bonito soup, made from dried fish, konbu seaweed and dried shiitake mushrooms, which enhance the umami taste and flavor of glutamic and inosinic acids, are used for taste good. Japanese tea consumed without sugar contributes to low energy intake. The Japanese traditional method of combining foods and preparing dishes is notable for protecting against CAD.

Conclusions and message for the future

Recently, changes in societal structure have affected many aspects of the Japanese lifestyle, including

dietary habits. Food distribution systems and individual attitudes regarding eating have changed and people are consuming more meals outside of their homes, readily procuring salty prepared foods. The Japanese dietary style has become westernized, a diversification which has resulted in an increase in subjects with atherosclerotic risks, such as obesity, dyslipidemia, and hyperinsulinemia with impaired glucose tolerance. This tendency is particularly marked in younger persons. As a typical example of increasing metabolic syndrome in Japan, inhabitants of Okinawa prefecture were formerly the most long-lived population in Japan, as was apparent after World War II. Their traditional eating habits are recognized as preventive methods against cardiovascular disease⁶⁹; however, the mean life expectancy among males in Okinawa has not increased since 1980 and has remained below the national average since 2000^{70, 71}. People living in Okinawa are recognized as having changed early to a North American lifestyle, relative to the rest of Japan. In the near future, the risk of atherosclerotic disorders among Japanese is anticipated to increase if this lifestyle trend continues. In addition, it is important to prevent the global spread of metabolic syndrome, a lifestyle-related disease. It must be recognized that awareness of health and changes in dietary habits are the most useful strategies for both primary and secondary prevention of CAD, as described elsewhere⁷²⁻⁷⁴. The Japanese population has traditionally consumed foods and nutrients effective for preventing CAD, and this diet has been readily available in our daily lives; however, as mentioned previously, increased rates of obesity, hypercholesterolemia, and impaired glucose tolerance in both genders may become a health problem for the next generation in Japan. A recent epidemiological study revealed that elevated intake of white rice is associated with an increased risk of type 2 diabetes in Japanese women and is suggestive of a positive association in men who were not engaged in strenuous physical activity⁷⁵. Although rice consumption has decreased during the past several decades, nearly 30% of total energy intake for Japanese is still derived from rice⁷³. The Japan diet described herein, including less refined carbohydrate intake, may provide a useful tool for preventing, or at least ameliorating, metabolic syndrome and related disorders.

These results suggest that the following strategies are useful for CAD and stroke prevention based on previous dietary changes in Japan: (1) a diet with adequate total calories, (2) increased intake of fish and plant foods, (3) decreased intake of refined carbohydrate and animal fat, (4) decreased intake of salt.

Acknowledgments

We thank Mitsuko Koseki and Makiko Suzuki, of the Academic Information Center, Jikei University School of Medicine, for providing nutrition-associated literature from Japan.

This report was presented at the Symposium of Message to the Future, Message from Committee on Lifestyle, "Changes in Lifestyle and Cardiovascular Disease in Japan" of the 41st Japan Atherosclerosis Society Annual Meeting on July 17, 2009 in Shimonoseki, Yamaguchi.

References

- 1) Wen C-P, Gershoff SN: Changes in serum cholesterol and coronary heart disease mortality associated with changes in the postwar Japanese diet. *Am J Clin Nutr*, 1973; 26: 616-619
- 2) Ueshima H: Explanation for the Japanese paradox: prevention of increase in coronary heart disease and reduction in stroke. *J Atheroscl Thromb*, 2007; 14: 278-286
- 3) Keys A: Coronary heart disease in seven countries. *Circulation*, 1970; 41(4 suppl): 101-112
- 4) Keys A, Menotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, Djordjevic BS, Dontas AS, Fidanza F, Keys MH, Kromhout D, Nedeljkovic S, Punsar S, Seccareccia F, Toshima H: The diet and 15-year death rate in the seven countries study. *Am J Epidemiol*, 1986; 24: 903-915
- 5) Kromhout D, Keys A, Aravanis C, Buzina R, Fidanza F, Giampaoli S, Jansen A, Menotti A, Nedeljkovic S, Pekkarinen M, Simic BS, Toshima H: Food consumption patterns in the 1960s in seven countries. *Am J Clin Nutr*, 1989; 49: 889-894
- 6) Kromhout D, Menotti A, Bloemberg B, Aravanis C, Blackburn H, Buzina R, Dontas AS, Fidanza F, Giampaoli S, Jansen A, Karvonen M, Katan M, Nissinen A, Nedeljkovic S, Pekkarinen J, Pekkarinen M, Punsar A, Räsänen L, Simic B, Toshima H: Dietary saturated and trans fatty acids and cholesterol and 25-year mortality from coronary heart disease: the Seven Countries Study. *Prev Med*, 1995; 24: 308-315
- 7) Menotti A, Kromhout D, Blackburn H, Fidanza F, Buzina R, Nissinen A: For the Seven Countries Study Research Group: Food intake patterns and 25-year mortality from coronary heart disease: cross-cultural correlations in the Seven Countries Study. *The Seven Countries Study Research Group. Eur J Epidemiol*, 1999; 15: 507-515
- 8) Kromhout D, Bloemberg B, Feskens E, Menotti A, Nissinen A : Saturated fat, vitamin C and smoking predict long-term population all-cause mortality rates in the Seven Countries Study. *Int J Epidemiol*, 2000; 29: 260-265
- 9) Tillotson JL, Kato H, Nichaman MZ, Miller DC, Gay ML, Johnson KG, Rhoads GG: Epidemiology of coronary heart disease and stroke in Japanese men living in Japan, Hawaii, and California: methodology for comparison of diet. *Am J Clin Nutr*, 1973; 26: 177-184

- 10) Marmot MG, Syme SL, Kagan A, Kato H, Cohen JB, Belsky J: Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: prevalence of coronary and hypertensive heart disease and associated risk factors. *Am J Epidemiol*, 1975; 102: 514-525
- 11) Benfante R: Studies of cardiovascular disease and cause-specific mortality trends in Japanese-American men living in Hawaii and risk factor comparisons with other Japanese populations in the Pacific region: a review. *Hum Biol*, 1992; 64: 791-805
- 12) Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A: Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation*, 1994; 90: 583-612
- 13) Tamaki J, Ueshima H, Hayakawa T, Choudhury SR, Kodama K, Kita Y, Okayama A: NIPPON DATA80 Research Group: Effect of conventional risk factors for excess cardiovascular death in men: NIPPON DATA80. *Circ J*, 2006; 70: 370-375
- 14) Kodama K, Sasaki H, Shimizu Y: Trend of coronary heart disease and its relationship to risk factors in a Japanese population: a 26-year follow-up, Hiroshima/Nagasaki study. *Jpn Circ J*, 1990; 54: 414-421
- 15) Nakashima Y, Kiyohara Y, Doi Y, Kubo M, Iida M, Sueishi K: Risk factors for coronary atherosclerosis in a general Japanese population: the Hisayama study. *Pathol Res Pract*, 2009; 205: 700-708
- 16) Lida M, Ueda K, Okayama A, Kodama K, Sawai K, Shibata S, Tanaka S, Keijnkai T, Horibe H, Minowa M, Yanagawa H, Hashimoto T: Nippon Data 80 Research Group. Impact of elevated blood pressure on mortality from all causes, cardiovascular diseases, heart disease and stroke among Japanese: 14 year follow-up of randomly selected population from Japanese - NIPPON DATA 80. *J Hum Hypertens*, 2003; 17: 851-857
- 17) Okayama A, Kadowaki T, Okamura T, Hayakawa T, Ueshima H; NIPPON DATA80 Research Group: Age-specific effects of systolic and diastolic blood pressures on mortality due to cardiovascular diseases among Japanese men (NIPPON DATA80). *J Hypertens*, 2006; 24: 459-462
- 18) Takagi S, Saitoh S, Nakano M, Hayashi Y, Obara F, Onishi H, Shimamoto K: Relationship between blood pressure level and mortality rate: an 18-year study conducted in two rural communities in Japan. *J Hypertens*, 2000; 18: 139-144
- 19) Ueshima H, Choudhury SR, Okayama A, Hayakawa T, Kita Y, Kadowaki T, Okamura T, Minowa M, Iimura O: Cigarette smoking as a risk factor for stroke death in Japan: NIPPON DATA 80. *Stroke*, 2004; 35: 1836-1841
- 20) NIPPON DATA80 Research Group: Risk assessment chart for death from cardiovascular disease based on a 19-year follow-up study of a Japanese representative population. *Circ J*, 2006; 70: 1249-1255
- 21) Ueda K, Omae T, Hirota Y, Takeshita M, Katsuki S, Tanaka K, Enjoji M: Decreasing trend in incidence and mortality from stroke in Hisayama residents, Japan. *Stroke*, 1981; 12: 154-160
- 22) Kubo M, Kiyohara Y, Kato I, Tanizaki Y, Arima H, Tanaka K, Nakamura H, Okubo K, Iida M: Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community: the Hisayama study. *Stroke*, 2003; 34: 2349-2354
- 23) Mannami T, Iso H, Baba S, Sasaki S, Okada K, Konishi M, Tsugane S; Japan Public Health Center-Based Prospective Study on Cancer and Cardiovascular Disease Group: Cigarette smoking and risk of stroke and its subtypes among middle-aged Japanese men and women: the JPHC Study Cohort I. *Stroke*, 2004; 35: 1248-1253
- 24) Yatsuya H, Toyoshima H, Yamagishi K, Tamakoshi K, Taguri M, Harada A, Ohashi Y, Kita Y, Naito Y, Yamada M, Tanabe N, Iso H, Ueshima H; for the Japan Arteriosclerosis Longitudinal Study (JALS) Group : Body mass index and risk of stroke and myocardial infarction in a relatively lean population: meta-analysis of 16 Japanese cohorts using individual data. *Circ Cardiovasc Qual Outcomes*, 2010; 3: 498-505
- 25) The Ministry of Health and Welfare: The report of Japanese National Health and Nutrition Survey in Japan, 2007. (in Japanese) http://www.mhlw.go.jp/toukei/kouhyo/indexkk_4_2.html
- 26) Research Committee on Serum Lipid Level Survey 1990 in Japan: Current state of and recent trends in serum lipid levels in the general Japanese population. *J Atheroscler Thromb*, 1996; 2: 122-132
- 27) Arai H, Yamamoto A, Matsuzawa Y, Saito Y, Yamada N, Oikawa S, Mabuchi H, Teramoto T, Sasaki J, Nakaya N, Itakura H, Ishikawa Y, Ouchi Y, Horibe H, Kita T: Serum lipid survey and its recent trend in the general Japanese population in 2000. *J Atheroscler Thromb*, 2005; 12: 98-106
- 28) Carroll MD, Lacher DA, Sorlie PD, Cleeman JI, Gordon DJ, Wolz M, Grundy SM, Johnson CL: Trends in serum lipids and lipoproteins of adults, 1960-2002. *JAMA*, 2005; 294: 1773-1781
- 29) Borhani NO: Coronary Heart Disease Prevention: The Multiple Risk Factor Intervention Trial (MRFIT). *West J Med*, 1974; 121: 418
- 30) The multiple risk factor intervention trial (MRFIT): A national study of primary prevention of coronary heart disease. *JAMA*, 1976; 235: 825-827
- 31) Stamler J, Wentworth D, Neaton JD: Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screens of the Multiple Risk Factor Intervention Trial (MRFIT). *JAMA*, 1986; 256: 2823-2828
- 32) Verschuren WM, Jacobs DR, Bloemberg BP, Kromhout D, Menotti A, Aravanis C, Blackburn H, Buzina R, and Dontas AS, Fidanza F: Serum total cholesterol and long-term coronary heart disease mortality in different cultures. Twenty-five-year follow-up of the seven countries study. *JAMA*, 1995; 274: 131-136
- 33) Menotti A, Blackburn H, Kromhout D, Nissinen A, Fidanza F, Giampaoli S, Buzina R, Mohacek I, Nedeljkovic S, Aravanis C, Toshima H: Changes in population cholesterol levels and coronary heart disease deaths in seven countries. *Eur Heart J*, 1997; 18: 566-571

- 34) Saito I, Folsom AR, Aono H, Ozawa H, Ikebe T, Yamashita T: Comparison of fatal coronary heart disease occurrence based on population surveys in Japan and the USA. *Int J Epidemiol*, 2000; 29: 837-844
- 35) Ministry of Agriculture, Ministry of Agriculture, Forestry and Fisheries: Abstract of statistics on agriculture forestry and fisheries in Japan. (in Japanese) <http://www.maff.go.jp/j/tokei/index.html>
- 36) Yoshiike N, Matsumura Y, Iwaya M, Sugiyama M, Yamaguchi M: The National Nutrition Survey in Japan. *J Epidemiol*, 1996; 6: S189-S200
- 37) Organization of the Ministry of Health, Labour and Welfare: The National Health and Nutrition Survey in 2000. pp42, Daiichi Shuppan, Tokyo, 2002 (in Japanese)
- 38) Organization of the Ministry of Health, Labour and Welfare. The National Health and Nutrition Survey in Japan. (in Japanese) http://www.nih.go.jp/eiken/chosa/kokumin_eiyou/index.html
- 39) Iso H, Kobayashi M, Ishihara J, Sasaki S, Okada K, Kita Y, Kokubo Y, Tsugane S; JPHC Study Group: 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
- 40) Yamagishi K, Iso H, Date C, Fukui M, Wakai K, Kikuchi S, Inaba Y, Tanabe N, Tamakoshi A: Japan Collaborative Cohort Study for Evaluation of Cancer Risk Study Group: Fish, omega-3 polyunsaturated fatty acids, and mortality from cardiovascular disease in a nationwide community-based cohort of Japanese men and women the JACC (Japan Collaborative Cohort Study for Evaluation of Cancer Risk) Study. *J Am Coll Cardiol*, 2008; 52: 988-996
- 41) Nakamura Y, Ueshima H, Okamura T, Kadowaki T, Hayakawa T, Kita Y, Tamaki S, Okayama A; NIPPON DATA80 Research Group: Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980-1999. *Am J Med*, 2005; 118: 239-245
- 42) Yokoyama M, Origasa H, Matsuzaki M, Matsuzawa Y, Saito Y, Ishikawa Y, Oikawa S, Sasaki J, Hishida H, Itakura H, Kita T, Kitabatake A, Nakaya N, Sakata T, Shimada K, Shirato K: Japan EPA lipid intervention study (JELIS) Investigators: A randomised open-label, blinded endpoint analysis. *Lancet*, 2007; 369: 1090-1098
- 43) Nakamura Y, Okuda N, Turin TC, Fujiyoshi A, Okamura T, Hayakawa T, Yoshita K, Miura K, Ueshima H; NIPPON DATA80/90 Research Group: Fatty acids intakes and serum lipid profiles: NIPPON DATA90 and the national nutrition monitoring. *J Epidemiol*, 2010; 20 Suppl 3: S544-S548
- 44) Prospective Studies Collaborations, Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J, Halsey J, Qizilbash N, Peto R, Collins R: Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. *Lancet*, 2007; 370: 1829-1839
- 45) Siri-Tarino PW, Sun Q, Hu FB, Krauss RM: Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *Am J Clin Nutr*, 2010; 91: 535-546
- 46) Yamagishi K, Iso H, Yatsuya H, Tanabe N, Date C, Kikuchi S, Yamamoto A, Inaba Y, Tamakoshi A; JACC Study Group: Dietary intake of saturated fatty acids and mortality from cardiovascular disease in Japanese: the Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC) Study. *Am J Clin Nutr*, 2010; 92: 759-765
- 47) Kokubo Y, Iso H, Ishihara J, Okada K, Inoue M, Tsugane S; JPHC Study Group: Association of dietary intake of soy, beans, and isoflavones with risk of cerebral and myocardial infarctions in Japanese populations: the Japan Public Health Center-based (JPHC) study cohort I. *Circulation*, 2007; 116: 2553-2562
- 48) Sasazuki S; Fukuoka Heart Study Group: Case-control study of nonfatal myocardial infarction in relation to selected foods in Japanese men and women. *Jpn Circ J*, 2001; 65: 200-206
- 49) Nagura J, Iso H, Watanabe Y, Maruyama K, Date C, Toyoshima H, Yamamoto A, Kikuchi S, Koizumi A, Kondo T, Wada Y, Inaba Y, Tamakoshi A; JACC Study Group: Fruit, vegetable and bean intake and mortality from cardiovascular disease among Japanese men and women: the JACC study. *Br J Nutr*, 2009; 102: 285-292
- 50) Umehara M, Iso H, Date C, Yamamoto A, Toyoshima H, Watanabe Y, Kikuchi S, Koizumi A, Kondo T, Inaba Y, Tanabe N, Tamakoshi A; JACC Study Group: Relations between dietary sodium and potassium intakes and mortality from cardiovascular disease: the Japan Collaborative Cohort Study for Evaluation of Cancer risks. *Am J Clin Nutr*, 2008; 88: 195-202
- 51) Ishihara J, Iso H, Inoue M, Iwasaki M, Okada K, Kita Y, Kokubo Y, Okayama A, Tsugane S; JPHC Study Group: Intake of folate, vitamin B6 and vitamin B12 and the risk of CHD: the Japan Public Health Center-Based Prospective Study Cohort I. *J Am Coll Nutr*, 2008; 27: 127-136
- 52) Cui R, Iso H, Date C, Kikuchi S, and Tamakoshi A; Japan Collaborative Cohort Study Group: Dietary folate and vitamin B6 and B12 intake in relation to mortality from cardiovascular diseases: Japan collaborative cohort study. *Stroke*, 2010; 41: 1285-1289
- 53) Selhub J, Jacques PF, Wilson PW, Rush D, Rosenberg IH: Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. *JAMA*, 1993; 270: 2693-2698
- 54) Melse-Boonstra A, de Bree A, Verhoef P, Bjoerke-Monsen AL, Verschuren WMM: Dietary monoglutamate and polyglutamate folate are associated with plasma folate concentrations in Dutch men and women aged 20-65 years. *J Nutr*, 2002; 132: 1307-1312
- 55) Ford ES, Ballew C: Dietary folate intake in US adults: findings from the third National Health and Nutrition Examination Survey. *Ethn Dis*, 1998; 8: 299-305
- 56) Eshak ES, Iso H, Date C, Kikuchi S, Watanabe Y, Wada Y, Wakai K, Tamakoshi A; JACC Study Group: Dietary fiber intake is associated with reduced risk of mortality from cardiovascular disease among Japanese men and women. *J Nutr*, 2010; 140: 1445-1453
- 57) Nakamura Y, Kita Y, Iso H, Ueshima H, Okada K, Konishi M, Inoue M, Tsugane S; JPHC Study Group: Alcohol consumption, alcohol-induced flushing and incidence of acute myocardial infarction among middle-aged men in

- Japan-Japan Public Health Center-based prospective study. *Atherosclerosis*, 2007; 194: 512-516
- 58) Sodium intake among adults - United States, 2005-2006: Centers for disease control and prevention (CDC). *MMWR Morb Mortal Wkly Rep*, 2010; 59: 746-749
- 59) Ministry of Health, Labour and Welfare: The National Health and Nutrition Survey in Japan, 2004. pp Daiichi-Shuppan, 2006, Tokyo. (in Japanese)
- 60) Sauvaget C, Nagano J, Allen N, Kodama K: Vegetable and fruit intake and stroke mortality in the Hiroshima/Nagasaki Life Span Study. *Stroke*, 2003; 34: 2355-2360
- 61) He FJ, Nowson CA, MacGregor GA: Fruit and vegetable consumption and stroke: Independent significant difference from other plant foods was reported on fruit consumption and stroke mortality. *Meta-analysis of cohort studies. Lancet*, 2006; 367: 320-326
- 62) Higashiguchi M, Onoda T, Turin TC, Sakata K; NIPPON DATA80/90 Research Group: Calcium intake and associated factors in a general Japanese population: baseline data of NIPPON DATA80/90 and the National Nutrition Survey. *J Epidemiol*, 2010; 20 Suppl 3: S549-S556
- 63) Umesawa M, Iso H, Ishihara J, Saito I, Kokubo Y, Inoue M, Tsugane S; JPHC Study Group: Dietary calcium intake and risks of stroke, its subtypes, and coronary heart disease in Japanese: the JPHC Study Cohort I. *Stroke*, 2008; 39: 2449-2456
- 64) Umesawa M, Iso H, Date C, Yamamoto A, Toyoshima H, Watanabe Y, Kikuchi S, Koizumi A, Kondo T, Inaba Y, Tanabe N, Tamakoshi A: Dietary intake of calcium in relation to mortality from cardiovascular disease. *The JACC study. Stroke*, 2006; 37: 20-26
- 65) Iso H, Sato S, Kitamura A, Naito Y, Shimamoto T, Komachi Y: Fat and protein intakes and risk of intra-parenchymal hemorrhage among middle-aged Japanese. *Am J Epidemiol*, 2003; 157: 32-39
- 66) Iso H, Stampfer MJ, Manson JE, Rexrode K, Hu F, Hennekens CH, Colditz GA, Speizer FE, Willett WC: Prospective study of fat and protein intake and risk of intra-parenchymal hemorrhage in women. *Circulation*, 2001; 103: 856-863
- 67) Tanaka K, Ishikawa Y, Yokoyama M, Origasa H, Matsuzaki M, Saito Y, Matsuzawa Y, Sasaki J, Oikawa S, Hishida H, Itakura H, Kita T, Kitabatake A, Nakaya N, Sakata T, Shimada K, Shirato K; JELIS Investigators, Japan: Reduction in the recurrence of stroke by eicosapentaenoic acid for hypercholesterolemic patients: subanalysis of the JELIS trial. *Stroke*, 2008; 39: 2052-205
- 68) Iso H, Baba S, Mannami T, Sasaki S, Okada K, Konishi M, Tsugane S; JPHC Study Group: Alcohol consumption and risk of stroke among middle-aged men: the JPHC Study Cohort I. *Stroke*, 2004; 35: 1124-1112
- 69) Willcox DC, Willcox BJ, Todoriki H, Suzuki M: The Okinawan Diet: Health Implications of a low-calorie, nutrition-dense, antioxidant-rich dietary pattern low in glycemic load. *J Am College of Nutr*, 2009; 28: 500S-516S
- 70) Kagawa Y: Impact of Westernization on the nutrition of Japanese: changes in physique, cancer, longevity and centenarians. *Prev Med*, 1978; 7: 205-217
- 71) Tanaka H, Shimabukuro T, Oshiro T, Sasaki K: Relationship between metabolic syndrome and homeostasis model assessment (HOMA-R) on the complete physical check-up in Okinawa. *Prog in Med*, 2005; 25: 74-79 (in Japanese)
- 72) American Heart Association Nutrition Committee, Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, Franklin B, Kris-Etherton P, Harris WS, Howard B, Karanja N, Lefevre M, Rudel L, Sacks F, Van Horn L, Winston M, Wylie-Rosett J: Diet and lifestyle recommendations revision 2006. A scientific statement from the American Heart Association Nutrition Committee. *Circulation*, 2006; 114: 82-96
- 73) Hu FB, Willett W: Optimal diets for prevention of coronary heart disease. *JAMA*, 2002; 288: 2569-2578
- 74) Reddy KS, Katan MB: Diet, nutrition and the prevention of hypertension and cardiovascular diseases. *Pub Health Nutr*, 2004; 7: 167-186
- 75) Nanri A, Mizoue T, Noda M, Takahashi Y, Kato M, Inoue M, Tsugane S for the Japan Public Health Center-based Prospective Study Group: Rice intake and type 2 diabetes in Japanese men and women: the Japan Public Health Center-based Prospective Study. *Am J Clin Nutr*, 2010; 92: 1468-1477