Review

Lifestyle and Cardiovascular Disease in Japan

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The aim was to give an overview of the profile of cardiovascular disease, vascular pathology and the relationships between lifestyle and cardiovascular disease in Japanese. Compared with the United States and Europe, the higher mortality from stroke and lower mortality from coronary heart disease constitute a unique cardiovascular profile for Japan.

A selective review of population-based pathology, trend and prospective cohort studies was performed to clarify the characteristics of cardiovascular disease and vascular pathology, trends in the incidence and mortality of cardiovascular disease, and the relationships between lifestyle and cardiovascular disease among Japanese adults. Since the 1970s, mortality from coronary heart disease as well as stroke has declined substantially in Japan, probably due to a major decline in blood pressure levels and for men a more recent decline in smoking, in spite of an increase in body mass index and total cholesterol levels. However, the decline in mortality was smaller and plateaued in middle-aged men aged 30-49 in the metropolitan cities of Tokyo and Osaka. The incidence of coronary heart disease has increased among middle-aged men residing in the suburbs of Osaka. As for the associations between lifestyle and cardiovascular disease, higher sodium, lower calcium and lower animal protein content in the diet and for men higher alcohol consumption may account for the higher prevalence of hypertension and higher risk of stroke for Japanese than for western populations. On the other hand, lower saturated fat (meat) and higher n3 polyunsaturated fat (fish) in the Japanese diet may contribute to the lower prevalence of hypercholesterolemia and lower risk of coronary heart disease among Japanese.

Japan is unique among developed countries in that coronary heart disease mortality has been low and has continued to decline, while stroke mortality has declined substantially. However, a recent trend for coronary heart disease incidence to increase among urban men is a cause for concern as a potential source of future problems for public health and clinical practice in Japan.


Key words: Epidemiology, Lifestyle, Coronary heart disease, Stroke, Japan

Characteristics of Stroke in Japanese

After ranking first as the cause of death between 1951 and 1980, stroke is now the third-ranked cause of death in Japan, with cancer and heart disease first and second. The mortality rate for stroke (per 100,000) in 2007 was 99.2 for men and 102.3 for women.

Hypertension is a universally reported strong risk factor for stroke, while low HDL-cholesterol and diabetes mellitus are risk factors for ischemic stroke, however, the associations of total or LDL-cholesterol and triglycerides with the risk of total or ischemic stroke are weak or non-existent. The proportion of intraparenchymal hemorrhage is higher for Japanese than for western populations: 20-30% versus 5-10%. Along with a major decline in mean systolic blood pressure for the population as a whole, stroke mortality declined one-third to one-fourth for Japanese between 1970 and 2005, whereas the mortality decline was not so manifest in the United States and England.

To examine changes in the contribution of hypertension to stroke risk, we explored three cohort...
data of residents aged 40-69 years in Japanese communities obtained from 1963-1971, 1975-1984 and 1985-1994 baseline surveys, with a mean follow-up period for each cohort of ten years. From the first to third cohorts, the blood pressure category with a majority of stroke incidence shifted from severe or moderate to mild hypertension. The population attributable risk fractions of the severe hypertension category for the first, second and third cohorts were 20%, 14% and 9%, respectively, those of the moderate hypertension category were 19%, 24% and 11%, and those of the mild hypertension category were 17%, 26% and 23%. The shift of stroke burden from severe to moderate to mild hypertension provides strong support for the value of early management of hypertension and primary prevention of high blood pressures for the prevention of stroke.

Characteristics of Coronary Heart Disease in Japanese

Heart disease is the second most common cause of death in Japan, and coronary heart disease (CHD) accounts for approximately half of heart disease-related deaths. The mortality rate for CHD (per 100,000) in 2007 was 66.7 for men and 52.8 for women. High total and LDL-cholesterol, low HDL-cholesterol and high triglycerides as well as hypertension and glucose abnormality have been established as risk factors for CHD in western countries. The low prevalence of hypercholesterolemia and glucose abnormality in Japanese as compared with that in western populations may contribute to the low CHD mortality in Japan, i.e. 1/3 to 1/5 of that in the United States. There is growing concern about a possible increase in atherosclerosis among Japanese subpopulations.

Atherosclerosis typically observed in the aorta, coronary arteries, carotid arteries and basal cerebral arteries, while arteriolosclerosis usually occurs in small penetrating arterioles in basal ganglions of the brain. Atherosclerosis, a large vascular pathology, is characterized by lipid accumulation with proliferative changes leading to plaque formation (left side of Fig. 1). Arteriolosclerosis, on the other hand, a small vascular pathology, is characterized by the necrosis or apoptosis of smooth muscle cells within the media, leading to the formation of microaneurysms (intraparenchymal hemorrhage) and fibrous proliferative changes (lacunar stroke) (right side of Fig. 1).

Characteristics of Vascular Pathology in Japanese and Western Populations

As shown in the figure, atherosclerosis, a large vascular pathology, is characterized by lipid accumulation with proliferative changes leading to plaque formation (left side of Fig. 1). Arteriolosclerosis, on the other hand, a small vascular pathology, is characterized by the necrosis or apoptosis of smooth muscle cells within the media, leading to the formation of microaneurysms (intraparenchymal hemorrhage) and fibrous proliferative changes (lacunar stroke) (right side of Fig. 1).

Atherosclerosis is typically observed in the aorta, coronary arteries, carotid arteries and basal cerebral arteries, while arteriolosclerosis usually occurs in small penetrating arterioles in basal ganglions of the brain. Major risk factors for atherosclerosis are dyslipidemia, glucose abnormality and metabolic syndrome as well as hypertension and smoking while those for arteriolosclerosis are primarily hypertension, and secondarily glucose abnormality, metabolic syndrome and smoking. Atherosclerosis is very common in western populations and is reflected in high CHD mortality, while the same holds true for arteriolosclerosis in Japanese and is reflected in high stroke mortality. For example, the ratios of stroke subtypes for Japanese were approximately 20% for large artery occlusive infarction, 20-30% for intraparenchymal hemorrhage and 40% for lacunar infarction, while those for western populations were 40%, 5-10%, and 20%; however, the recent rise in CHD incidence among urban middle-aged men may indicate a potential increase in atherosclerosis among Japanese subpopulations.

Nevertheless, the major ethnic differences in the
prevalence of vascular pathology and cardiovascular disease may be in part due to differences in lifestyle, in particular in terms of the diet. Higher sodium, lower calcium and lower animal protein intake and, for men, higher alcohol consumption may contribute to the higher prevalence of hypertension and higher risk of stroke in Japanese. On the other hand, lower saturated fat (meat) and higher n3 polyunsaturated fat (fish) intake may contribute to the lower prevalence of hypercholesterolemia and lower risk of CHD in Japanese.

Relationships between Lifestyle and Cardiovascular Disease

Sodium and Potassium Intake

According to a 13-year population-based cohort study of 58,730 Japanese aged 40-79 years (JACC study), sodium intake was positively associated with mortality from total stroke, ischemic stroke, and total cardiovascular disease. Multivariable hazard ratios for the highest versus lowest quintiles of sodium intake were 1.55 (95% CI, 1.21-2.00; \( p \) for trend=0.001) for total stroke, 2.04 (1.41-2.94; \( p \) for trend=0.001) for ischemic stroke, and 1.42 (1.20-1.69; \( p \) for trend=0.001) for total cardiovascular disease. Potassium intake was inversely associated with mortality from CHD and total cardiovascular disease. The multivariable hazard ratios for the highest versus the lowest quintiles of potassium intake were 0.65 (95% CI, 0.39-1.06; \( p \) for trend=0.083) for CHD and 0.73 (0.59-0.92; \( p \) for trend=0.018) for total cardiovascular disease. A recent report of the JPHC Study has shown that the amount rather than concentrations of sodium in the diet has an adverse effect on stroke risk.

Calcium Intake

Another report of the JACC study showed that dietary intake of total calcium tended to be inversely associated with mortality from total stroke but not from CHD or total cardiovascular disease for both men and women. The associations with cardiovascular disease were more evident for dairy than for non-dairy calcium intake. The multivariable hazard ratios for men with highest versus lowest quintiles of dairy calcium intake were 0.53 (95% CI, 0.34 to 0.81) for total stroke, 0.46 (0.23 to 0.91) for hemorrhagic stroke, and 0.53 (0.29 to 0.99) for ischemic stroke; the corresponding hazard ratios for women were 0.57 (0.38 to 0.86), 0.51 (0.28 to 0.94), and 0.50 (0.27 to 0.95). We also investigated the association between dairy calcium intake and the incidence of cardiovascular disease during the 13-year follow-up for a JPHC study of 41,526 Japanese men and women age 40-59.
years\(^{19}\). Dairy calcium intake was found to be inversely associated with risks of total and ischemic stroke with respective multivariable hazard ratios (95% CIs) of 0.69 (0.56 to 0.85; \(p\) for trend=0.007) and 0.69 (0.52 to 0.93; \(p\) for trend=0.05). Dietary calcium intake was not associated with the risk of CHD.

### Animal Protein Intake

A population-based, cross-sectional study of 7,585 men and women aged 40-69 years in five communities showed that dietary animal protein intake, estimated on the basis of a single 24-h dietary recall, was associated with blood pressure levels after adjustment for age, sex, community, body mass index, antihypertensive medication use, ethanol intake, smoking, and dietary intakes of sodium, potassium, and calcium\(^{20}\). A 19.9-g/d increment in animal protein intake was associated with a decrease in systolic blood pressure of 1.09 mm Hg (\(p<0.001\)) and in diastolic blood pressure of 0.41 mm Hg (\(p=0.003\)). Further adjustment for nutritional factors weakened the associations, but the inverse associations of animal protein intake with systolic blood pressure remained statistically significant. The findings of a 14-year prospective study of 4,775 men and women aged 40-69 years indicated that animal protein intake tends to be inversely associated with the risk of intraparenchymal hemorrhage, since the hazard ratio with a one-standard deviation increase in animal protein intake (17.6 g/day) was 0.79 (95% CI, 0.61-1.02; \(p=0.07\))\(^{21}\).

### Intake of Fish and \(\omega-3\)-polyunsaturated Fatty Acids

According to an 11-year follow-up of the JPHC Study of 41,578 men and women aged 40 to 59 years\(^{22}\), dietary intake of fish and \(\omega-3\)-polyunsaturated fatty acids (PUFA) was inversely associated with the risk of CHD. Multivariate hazard ratios for the highest (8 times per week, or median intake 180 g/d) versus the lowest (once a week, or median intake 23 g/d) quintiles of fish intake were 0.63 (95%CI, 0.38-1.04) for total CHD, 0.44 (0.24-0.81) for definite myocardial infarction, and 1.14 (0.36-3.63) for sudden cardiac death. Stronger inverse associations existed between the dietary intake of \(\omega-3\) polyunsaturated fatty acids (PUFA) and risk of definite myocardial infarction with an HR of 0.35 (0.18 to 0.66) and nonfatal coronary events with an HR of 0.33 (0.17 to 0.63).

In a 13-year follow-up of the JACC Study of 57,972 men and women aged 40-79 years\(^{23}\), we found that fish and \(\omega-3\) PUFA intakes was inversely associated with mortality from total cardiovascular disease and manifestly so for mortality from heart failure. Multivariate hazard ratios (95%CI) for highest versus lowest quintiles were 0.76 (0.53-1.09) for fish and 0.58 (0.36-0.93) for \(\omega-3\) PUFA.

### Physical Activity

The JACC Study of 7,3265 men and women aged 40-79 years\(^{24}\) indicated that men and women who reported the highest category of physical activity in (i.e., walking ≥1 hour/day or doing sports ≥5 hours/week) had lower mortality from cardiovascular disease than did those in the second lowest physical activity category (i.e., walking 0.5 hour/day, or sports participation for 1-2 hours/week). Multivariate hazard ratios for the highest versus the second lowest categories of walking or sports participation were 0.71 (95%CI, 0.54-0.94) and 0.80 (0.48-1.31), respectively, for ischemic stroke, 0.84 (0.64-1.09) and 0.51 (0.32-0.82) for CHD, and 0.84 (0.75-0.95) and 0.73 (0.60-0.90) for total cardiovascular disease.

As a surrogate marker of physical activity, we examined body mass index and its effect on cardiovascular disease. A 10-year follow-up of the JACC Study for 104,928 men and women aged 40-79 years\(^{25}\) indicated that compared with persons with a body mass index (BMI) 23.0 to 24.9, those with BMI ≥27.0 kg/m\(^2\) had a higher risk of CHD, with the respective multivariate relative risks (95% CI) for men and women being 2.05 (1.35 to 3.13) and 1.58 (0.95 to 2.62). Persons with BMI <18.5 kg/m\(^2\) had a higher risk of total stroke and intraparenchymal hemorrhage, with the respective multivariate relative risk for men and women being 1.29 (1.01 to 1.49) and 1.92 (1.49 to 2.47) for total stroke and 1.96 (1.16 to 3.31) and 2.32 (1.36 to 3.97) for intraparenchymal hemorrhage, respectively. An 11-year follow-up of the JPHC Study of 43,235 men and 47,444 women aged 40-69 years added to the evidence that weight gain is associated with an increased risk of CHD. When weight change was examined according to BMI at the age of 20 years, men with an initial BMI <21.7 kg/m\(^2\) who gained more than 10 kg compared with men with no weight change had a twofold higher risk of CHD.

### Alcohol Consumption

An 11-year follow-up of the JPHC Study of 19,544 men aged 40 to 59 years\(^{26}\) showed that alcohol consumption was associated with an elevated risk of total stroke for drinkers with an alcohol intake of 450 g ethanol per week compared with occasional drinkers. This excess risk was confined primarily to hemorrhagic stroke with a multivariable HR of 2.15 (95% CI: 1.22-3.79). There was a lower risk of ischemic stroke, more specifically lacunar infarction, a
higher risk of hemorrhagic stroke, and no excess risk of total stroke for drinkers with an intake of 1 to 149 g ethanol per week compared with occasional drinkers. The multivariate hazard ratios were 0.59 (0.37 to 0.93) for ischemic stroke, 0.43 (0.22 to 0.87) for lacunar infarction, 1.73 (0.98 to 3.07) for hemorrhagic stroke, and 0.98 (0.71 to 1.36) for total stroke.

We further examined whether the protective effect of light-to-moderate alcohol consumption on the risk of ischemic stroke was affected by social support. The multivariate hazard ratios of ischemic stroke associated with light-to-moderate alcohol consumption (1 to 299 g/wk) were 1.53 (0.95 to 2.46) for the low social support group and 0.82 (0.60 to 1.13) for the high social support group (p for interaction = 0.002). There was no association between alcohol consumption and social support in relation to the risk of CHD. Alcohol consumption is strongly and inversely associated with the risk of CHD.

**Smoking and Smoking Cessation**

Smoking was found to be associated with an elevated risk of stroke, more specifically, subarachnoid hemorrhage and ischemic stroke. An 11-year follow-up of the JPHC Study of 41,282 men and women aged 40 to 59 years showed that the multivariate hazard ratios (95% CIs) for current smokers compared with never-smokers were 1.27 (1.05 to 1.54) for total stroke, 3.60 (1.62 to 8.01) for subarachnoid hemorrhage, and 1.66 (1.25 to 2.20) for ischemic stroke. The corresponding hazard ratios for women were 1.98 (1.42 to 2.77), 2.70 (1.45 to 5.02) and 1.57 (0.86 to 2.87). There was a dose-response relationship for men between the number of cigarettes smoked and risks of ischemic stroke, lacunar infarction and large-artery occlusive infarction but not embolic infarction. Another report of the JPHC study showed that smoking was strongly and positively associated with the risk of CHD, as has been reported universally.

According to a 10-year follow-up of the JACC Study of 94,683 men and women aged 40-79 years, the decline in the risk for CHD and total cardiovascular disease started to take effect within 2 years and for total stroke 2-4 years after smoking cessation. For every endpoint and for both age subgroups (40-64 and 65-79 years), most of the benefit of cessation occurred 10-14 years after cessation, indicating the importance of smoking cessation at any age to prevent cardiovascular disease.

A recent pooled analysis of 300,000 men and women aged 40-79 years confirmed that the HRs for ex-smokers compared with current smokers in relation to the time elapsed since smoking cessation started to decrease approximately 5 years after smoking cessation, and had reached the same level as the HR for lifelong non-smokers approximately 10 years after smoking cessation for both men and women.

In conclusion, we have presented an overview of the distinctive trends for mortality, incidence of stroke and CHD in Japan. Although it is hard to predict future CHD trends in Japan, middle-aged men, especially in urban areas, may be vulnerable to an CHD epidemic, which would present major issues for both public health and clinical practice.

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**References**


