RESEARCH ACTIVITIES OF EPIDEMIOLOGY IN JAPAN
Cardiovascular Disease
Epidemiology of Cerebrovascular Disease: Stroke Epidemic in Japan

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Japan had the highest mortality from stroke among developed countries in 1960, but experienced rapid changes in diet and other lifestyles with economic growth between the 1960s and the 1980s, which provided an unique opportunity to observe a natural experiment of changes in risk factors and stroke. Blood pressure levels declined due to improvements of drug treatment for hypertension and to dietary improvements such as sodium reduction. An increase in mean values of ethanol intake and body mass index did not correspond with a decline of blood pressure levels. Serum total cholesterol increased with an increased intake of meat, egg, milk and dairy products. Age-adjusted mortality rate of stroke declined 70% between 1960 and 1990. The changes of diet, blood pressure levels and stroke were more evident in rural populations than in urban populations. Risk factors of stroke has been investigated prospectively, and hypertension was found to be the most important risk factor. A low blood cholesterol was associated with the increased risk of intracerebral hemorrhage, which has been confirmed in several Japanese populations, Japanese Americans and Caucasian Americans. Thus, a rise in serum cholesterol suggested to contribute in part to a decline in intracerebral hemorrhage. Risk factors for cerebral infarction include age, atrial fibrillation and hypertensive endorgan effects such as resting electrocardiogram and fundoscopic examination. A community-based hypertension control program for stroke prevention has been evaluated; a larger decline in stroke incidence in the intervention community (69%) than in the reference community (49%, the difference: p<0.001). Effective community programs stimulated the formation of the 1982 national act on health and medical care in which every municipal government is required to conduct health screenings and education for residents aged 40 and over to prevent cardiovascular diseases. J Epidemiol, 1996; 6: S43-S47.

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Japan has a higher mortality from stroke and a lower mortality from coronary heart disease than western countries, and stroke rate was the highest among developed countries in 1960.2 The high rate of stroke incidence and mortality was confirmed by a WHO stroke registry3 and autopsy studies4,5. The epidemic of stroke in Japan has contributed to the development of stroke epidemiology and preventive programs. A major methodology for stroke epidemiology is a prospective study for community residents under stroke prevention programs based on blood pressure control through detection, follow-up and treatment of hypertensives and health education6-10.

The combination of observational prospective studies and prevention program has been an practical way to maintain a long-term follow-up for community residents because the support of municipal government can be obtained.

Between 1960 and 1990, Japan showed a 70% decline in age-adjusted mortality rate of stroke, and in 1985 ranking 9 to 11 among developed countries; Japan has shown the lowest mortality of coronary heart disease, one-fifth of the rate compared to the United States11. The proportion of intracerebral hemorrhage ranged between 15% and 30% which was higher than reported proportions from Western countries (about 10%}

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There are several important questions in stroke epidemiology in Japan: 1) Why was a high rate of stroke in Japanese? 2) What has contributed to the substantial decline in stroke mortality in Japan? and 3) Is a community-based program of hypertension control effective to prevent stroke?

**Why was a High Rate of Stroke in Japanese?**

Because hypertension is an universal risk factor for stroke, we can easily assume that blood pressure levels are higher in Japan than in Western Countries such as the United Sates. Two international studies,[15,13] however, did not show that blood pressure difference explain the higher rate of stroke in Japan than in the United Sates. In Seven Countries Study,[20] blood pressure levels were lower in Japanese men than in US men. In Ni-Hon-San study[12], Japanese living in Japan showed a higher blood pressure level than Japanese in Hawaii, but a lower blood pressure level than Japanese in California. There was a large geographical difference in blood pressure levels in Japan; blood pressure levels were higher in northern part of Japan than in western part of Japan.[15,16] It should be notified that the surveyed Japanese populations in both Seven Countries and the Ni-Hon-San studies were located in western part of Japan which might represent populations with lower blood pressure levels compared to the national level.

Studies of cardiovascular risk factors for the national representative samples existed both in Japan[15] and in the United Sates,[16] and the data of blood pressure in the two studies were found comparable because of similarity of the study methods[17]. For men, age-adjusted systolic blood pressure level was higher in Japanese than in US white and black. Japanese showed a similar diastolic blood pressure to US white and a lower diastolic blood pressure than US black. For women, Japanese showed a higher systolic blood pressure level than in US white, but similar level to US black. Diastolic blood pressure was similar between Japanese and US white and higher in US black. The result indicated that systolic blood pressure was higher in Japanese men than in American men.[17] The INTERSALT study suggested that a higher systolic blood pressure level in Japanese than in US white may be attributable to a higher sodium intake for men and women, and to a higher alcohol intake for men.[10] Other environmental factors related with a low economic status in the 1960s such as high labor work and poor house heating, although they have been improved since the 1970s, may contributed to a high systolic blood pressure level in Japanese.[2,10] The racial difference in systolic blood pressure level was not explained by the difference in body mass index because mean body mass index was much lower in Japanese than in US white.[10] Higher systolic blood pressure level in Japanese men may contributed to a higher mortality rate of stroke in Japanese men than in American men.

What other factors may contribute to a high stroke mortality and incidence in Japan? A low population level of serum total cholesterol due to a low intake of animal foods such as meat, egg, milk and dairy products is another candidate.[10] Our epidemiologic observation in rural Japanese, first found an inverse association of serum total cholesterol and the incidence of cerebral hemorrhage[14,19]. The inverse association was reported from several other Japanese cohorts[8,20], and from a prospective study of Japanese Americans living in Hawaii[22] and from a 6-year follow-up study of over 350,000 American men screened for the Multiple Risk Factor Intervention Trial (MRFIT)[23]. In the MRFIT follow-up study, serum total cholesterol was inversely associated with the death rate from cerebral hemorrhage, and positively associated with the death rate from cerebral infarction. The inverse association was primarily observed in a high blood pressure subgroup. The recent report has shown that a similar finding persisted in the 10.5-year follow-up[24]. A low serum cholesterol related with cerebral hemorrhage was also reported from an autopsy study[25]. On the other hand, a high serum cholesterol has not been appeared as a risk fator for cerebral infarction[8,10]. Risk factors for cerebral infarction include age, atrial fibrillation and hypertensive endorgan effects such as resting electrocardiogram and fundscopic examination. Recent epidemiologic studies using CT scan are showing that risk factors vary between lacunar infarction and larger thromboembolic infarction[26].

An international study[20] and our population-based study[14,27] demonstrated that Japanese showed a lower mean and distribution of serum total cholesterol than in US white. A lower cholesterol level in Japanese was due to a lower dietary intake of fat[10,12,16]. Among Japanese populations, serum cholesterol was low in rural men, intermediate in urban men, progressively higher in urban blue collar workers, white collar workers and physicians.[14] Serum cholesterol levels were correlated well with fat intake among populations[27].

A high alcohol intake in Japanese men may be a factor of a high stroke rate because heavy drinking raises the risk of intracerebral hemorrhage[28]. The INTERSALT study suggested that Japanese men has a higher alcohol intake than the US white[8]. The Ni-Hon-San study[12] indicated that alcohol intake was high in Japanese living in Japan and intermediate in Japanese in Hawaii and low in Japanese in California. Finding of lower plasma fibrinogen levels[29] and higher serum n-3 fatty acids[30] in Japanese than in US white are considered to be factors contributing to the higher risk of hemorrhagic stroke in Japanese because of their effects of lower coagulability and reduced platelet aggregation. Prospective studies and experiments will be required to confirm this hypotheses.

The national study indicated that smoking rate was surprisingly high 80% for men and low 15% for women in 1960[31], although smoking rate declined to 61% in 1990 for men and did not change for women[32]. A high smoking rate in Japanese men, however, does explain a little for a high rate of stroke because the contribution of smoking is small, if exists to stroke occurrence except for subarachnoid hemorrhage[30].
What has Contributed to the Substantial Decline in Stroke Mortality in Japan?

Japan has experienced a substantial decline in blood pressure level for men and women, a decline in smoking rate in men, and an increase in serum total cholesterol level for men and women between 1960 and 1990. A substantial reduction of labor work and an improvement of house heating since the 1970s might contribute to the blood pressure decline. A decline of blood pressure was largely attributed to a decline of sodium intake. An improvement of detection and treatment of hypertension contributed to the decline of blood pressure levels, too. An increase of serum total cholesterol corresponded with an increase of fat intake. According to the National Nutrition Survey, mean systolic blood pressure level declined between 1960 and 1990. The national data on serum cholesterol were available in 1980 and 1990. During the last ten years, serum total cholesterol level increased 13-16 mg/dl for both men and women. Fat intake per capita doubled from 11% of total calorie in 1960 to 25% in 1990. The increase of fat intake was primarily due to an increase of meat, and to a lesser extent due to an increase of milk, egg, dairy products, and oils. Salt intake declined from 13.7 g/day in 1976 to 12.5 g/day in 1990. Smoking rate declined from 80% in 1960 to 61% in 1990 for men, and for women smoking rate remained low during the last 30 years. Smoking rate was reported from a population of urban male employees. Our population-based study in a northeast rural Japanese population demonstrated the stronger trends in blood pressure, serum total cholesterol and sodium intake between 1963 and 1991.

Is a Community-Based Hypertension Control Program Effective to Prevent Stroke?

A community-based program of hypertension control was launched in several communities in Japan in the 1960s to ameliorate the epidemic of stroke. The basic strategies for hypertension control included 1) systematic blood pressure screening for detection of hypertensives, 2) referral of high risk individuals to local physicians when antihypertensive medication was required, 3) health education for hypertensives at blood pressure screening sites, at adult classes, and via nurse home visits, 4) training of “healthy diet” volunteers to give health education for dietary improvement, and 5) community-wide media-disseminated education to encourage persons to participate in blood pressure screening and to reduce salt intake. Stroke incidence declined significantly more (p<0.001) in the intervention community (population aged 30 and over in 1965: n=3,219, a 69 % decline between 1964-69 and 1982-87) than in the reference community (n=1,468, a 48% decline). The result indicated that the intensive hypertension control in a community was effective to reduce stroke incidence.

In 1969-70, the national government supported a three-year pilot study of the feasibility and effects of community-based hypertension control programs in twelve prefectures with a high mortality from stroke. Our community study received this support. Early successful results of the community-based hypertension control program stimulated the national government to enlarge the financial support for blood pressure screening to every prefecture after 1973, and for electrocardiography and fundus examinations after 1978. These movements led to the 1982 national act on health and medical care in which every municipal government was required to conduct health screenings and education for residents aged 40 and over to prevent cardiovascular diseases. More recently, the national government has supported for community-based stroke registry to enhance community care for stroke patients.

CONCLUSIONS

Stroke epidemic in Japan was caused by a high level of systolic blood pressure and possibly by a low level of serum total cholesterol. These two risk factors, however, have been attenuated by improvements of hypertension treatment and changes of diets such as reduction of sodium intake and an increase of fat and protein intake. The nation-wide activities of hypertension control and dietary education have accelerated these trends, which contributed to reduce stroke mortality in Japanese. There has been no evidence on an increase of age-adjusted mortality of coronary heart disease in Japan although increasing trend in the incidence of coronary heart disease was reported from a population of urban male employees. Surveillance on cardiovascular disease and its risk factors is underway in both rural and urban Japanese populations to clarify trends in the incidence of coronary heart disease as well as stroke.

REFERENCES


