Trends in the Incidence of Cardiovascular Diseases and their Risk Factors in a Rural Japanese Population

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To relate the morbidity trends with changes in risk factors for stroke and coronary heart disease between the 1960's and the 1980's, the data of disease surveillance and population surveys of risk characteristics in a northeast rural community of Japan (1965 census population 7,030) are combined. Between 1964 and 1987, the incidence of all stroke declined about 70% for both men and women aged 40–69. A decline in the stroke incidence was also observed for men and women aged 70 and over in the 1980's. There was about a 50% decline in the prevalence of stroke patients and the number of "bed-ridden" patients with severe disability among men and women aged 40 and over between the 1970's and the 1980's. The incidence of coronary heart disease did not change significantly and was lower than that for stroke. There was an over 10 mmHg systolic and 4 mmHg diastolic blood pressure decline for men and women aged 40–69, primarily in the second decade. The blood pressure decline may have been in part due to increased use of antihypertensive medication which was observed from the first decade. However, part of the blood pressure decline may be attributed to changes in related behaviors and environmental factors such as decreased salt intake and the improvement of working conditions, since the substantial decline occurred in the second decade. Between the 1960's and the 1980's, daily average salt intake decreased from 20 g to 14 g for men aged 40–59. Animal fat intake doubled from 4.5% to 9.6%. The most of the increase of fat intake was seen in the first decade due to an increased intake of meat, eggs and dairy products. Mean serum cholesterol increased 22 mg/dl to the 1980's mean level of 179 mg/dl in men aged 40–69, and 29 mg/dl to 192 mg/dl in women age 40–69. The increase of serum cholesterol level paralleled the increased intake of animal fat. A cohort of men and women aged 40–69 were followed from 1963–1966 to 1973 (2,257 persons) to examine risk factors of stroke. According to multivariate regression analyses, blood pressure levels and end organ effects in the electrocardiogram and fundus photographs were significantly associated with the incidence of cerebral hemorrhage and infarction. Serum total cholesterol was inversely
associated with cerebral hemorrhage. Reliable estimates of risk factors for coronary heart disease in this population was not obtained because of the small number of cases. Surveillance and risk factor surveys are continuing in order to clarify trends in cardiovascular diseases in the rural Japanese population in the future.

Population study, Cardiovascular disease trends, Serum cholesterol trends, Blood pressure trends, Japanese diet

INTRODUCTION

During the past couple of decades, Japan has experienced rapid change in living and eating patterns due to socioeconomic growth. This provides an unique opportunity to observe a natural experiment in which population risk of cardiovascular disease may change. To relate morbidity trends to changes in risk factors for stroke and coronary heart disease (CHD), we combined morbidity surveillance and population surveys of risk characteristics in a rural population of northeast Japan since 1963.


METHODS

The survey population was residents of Ikawa Town, a farming community in Akita Prefecture with a total census of 7,030 in 1965 and 6,386 in 1980. Surveillance of stroke and CHD was conducted since 1964 in men and women ages 40 and over. Three cross-sectional surveys of cardiovascular disease risk characteristics were conducted for men and women aged 40–69 in 1963–1966, 1972–1975, and 1980–1983. The participation rates for each survey are between 75% and 89%. For comparison, the data of clerical and manual workers in Osaka, the second largest city in Japan, were presented.

The morbidity surveillance collected disease data on men and women ages 40 and over in Ikawa town and investigated all hospitalized cases plus six other ascertainment sources: (1) national insurance claims, (2) reports by local physicians, (3) ambulance records, (4) death certificates, (5) reports by public health nurses and health volunteers, and (6) annual risk factor surveys. The completeness of the combined case-finding sources was established at the beginning of surveillance when a single detailed household survey revealed no cases undetected by the system. For workers in Osaka, ascertainment sources included (1) work records for days off due to sickness, (2) reports by company physicians and nurses, (3) death certificates and (4) annual risk factor surveys.

To validate the diagnosis, all living cases were visited to obtain a history from their families, and systematic neurological examinations were conducted by study physicians. Medical records in the local clinics and hospitals were reviewed. For deaths,
histories were obtained from families and/or attending physicians and medical records were reviewed.

The criteria for stroke and type of stroke are the same as Millikan's(2), except they exclude headache in the diagnosis of cerebral hemorrhage. Stroke is categorized as cerebral hemorrhage, cerebral infarction, subarachnoid hemorrhage, and stroke of undetermined type, and does not include transient ischemic attacks. The criteria for CHD were modified from those of the early WHO Expert Committee(3). The details of the criteria were reported elsewhere(4). Myocardial infarction and effort angina pectoris were regarded as CHD.

Using these standardized criteria, final diagnoses of stroke and CHD were made by a panel of four study physician-epidemiologists. Five-year incidence was calculated as the number of new cases per 1,000 census population in 1964–1968, 1969–1973, 1974–1978, 1979–1983, and 1984–1987.

In risk factor surveys, the blood was drawn from the participant quietly seated with minimal use of tourniquets. The serum was separated and stored at -20 to -70°C for a month until analyzed by the laboratory at the Center for Adult Diseases in Osaka. Serum total cholesterol was measured by the Zak-Henly method(5) in 1963–1966, and by the Liebermann-Burchard method(6) using a Technicon Autoanalyzer II in 1972–1975 and 1980–1983. The values of the two methods were found to be comparable(4). Quality control of the laboratory was maintained by Lipid Standardization Program of the Centers for Disease Control in Atlanta, Georgia(7,8).

Nutrition studies were conducted for samples of men ages 40 to 59 from those who participated in the surveys. A weighing method(9) was used in 1969 and 24-hour dietary recalls(10) in the latter two surveys. The data from 1969 are not strictly comparable as they are derived from twelve male volunteers and are used here as a general reference. Subjects of the latter two surveys were randomly selected from all participants in the population surveys and nutritional intake was calculated using the third revision of standard Japan Food Tables(11).

First and fifth-phase diastolic blood pressures were measured by physician epidemiologists with a standard mercury sphygmomanometer in the right arm of participants, who had sat quietly for at least five minutes. The physicians had been trained in epidemiological methods of blood pressure measurement and recording by experienced observers(12). The training was repeated until systematic observer error was minimized. This procedure was repeated among observers for each survey period to reduce observer differences. Methods of examination for other risk variables were reported elsewhere(4).

To examine risk factors for stroke, a prospective cohort study was conducted. A cohort of 2,257 men and women ages 40–69 was constructed at baseline (the participation rate of the baseline survey = 82%) in 1963–1966 and followed until 1973. During the follow-up, 79 participants died from all causes, and only 20 participants (0.9%) migrated and were lost to follow-up.

A logistic regression model was applied to determined risk factors associated with cerebral hemorrhage and infarction. Persons with a history of stroke were excluded from the analyses. Regression coefficients of independent variables and an intercept were estimated by a discriminant function method(13).

RESULTS

Figure 1 illustrates trends of incidence for all stroke, cerebral hemorrhage, and infarction respectively for men and women in Akita. There was a consistent decline in incidence of all
stroke for men and women aged 40–69. Between 1964–1968 and 1984–1987, the incidence of all strokes declined 74% for men (p < 0.001) and 71% for women (p < 0.001). The incidence of hemorrhage decreased 67% in men (p < 0.01) and 91% in women (p < 0.01). The respective percent decline for cerebral infarction was 79% in men (p < 0.01) and 61% in women (p < 0.01).

For men and women aged 70 and over, trends for all stroke were less clear until the end of 1970's. However, between 1979–1973 and 1984–1987, the incidence declined. A similar trend was observed for the incidence of cerebral infarction whereas a consistent decline was seen for the incidence of cerebral hemorrhage.

Figure 1 Incidence trends for all stroke, cerebral hemorrhage, and infarction by age and sex in a Akita rural community.
Figure 2 shows the number and prevalence rate of stroke patients among men and women aged 40 and over in Akita in 1976 and 1986. There was a 40% decline in the number of stroke patients between 1976 and 1986, although the population had increased 15%. The prevalence rate of stroke patients also declined 50% (p < 0.01). The number of patients with severe disability (so called bed-ridden patients) also decreased in both men and women between 1976 and 1989 (Figure 3).

Figure 4 shows trends of incidence for CHD in Akita, and urban manual and clerical workers for men aged 40 to 59. The incidence of CHD was low in Akita and there was no clear trend. On the other hand, there was an increase in the incidence of CHD in urban manual and clerical workers. Women and older men also showed the low incidence of CHD and no significant trends for CHD incidence.

Mean systolic and diastolic blood pressure levels declined for every age-sex group in Akita, with a 15-mmHg age-adjusted decline in systolic, 4-mmHg decrease in diastolic blood pressure for men aged 40–69, and a 11-mmHg systolic and 4-mmHg diastolic decrease for women. Figure 5 illustrated distributions of systolic blood pressure for men aged 40–49 in Akita, and urban and clerical male workers during the three survey periods. Trends of the distributions are similar for the other age groups. Between 1963–1966 and 1972–1975, the prevalence of systolic blood pressures in excess of 180 mmHg declined in Akita. The distribution shifted downwards in Akita between 1972–1975 and 1980–1983. Urban manual and clerical workers showed a lower distribution of blood pressure and no shift in the distribution. Distributions of diastolic blood pressure showed a similar trend.
Figure 3  The number of “bed-ridden” patients in men and women aged 40 and over in Akita between 1976 and 1989.

Figure 4  Incidence trends for coronary heart disease for men aged 40–59 in Akita, and urban clerical and manual workers.
The frequency percent of all hypertensives taking antihypertensive medication (hypertensive defined as those with systolic blood pressure greater than 160 mmHg, or diastolic blood pressure greater than 95 mmHg, and/or taking antihypertensive medication), was between 14% and 22% for every age-sex group of Akita in 1963–1966. Over time, the percent significantly increased in a stepwise fashion: 30–70% in 1972–1975 and 55–84% in 1980–1983.

Figure 6 indicates the trend in the proportion of normotensives (ie. persons with systolic blood pressure less than 140 mmHg and diastolic blood pressure less than 90 mmHg) without history of antihypertensive medication use among men aged 40–69 in Akita. There was no trend in the proportion between 1963–1966 and 1972–1975, but a large increase in the proportion between 1972–1975 and 1980–1983. A similar trend was observed in women aged 40–69.

**Figure 5** Distributions of systolic blood pressure for men aged 40–49 in Akita, and urban clerical and manual workers.
Age-adjusted mean serum cholesterol levels increased 22 mg/dl to the 1980–1983 mean of 179 mg/dl for men aged 40–69 and 29 mg/dl to the 1980–1983 mean of 192 mg/dl for women in Akita. Figure 7 illustrates distributions of serum total cholesterol for men aged 40–49 in Akita, and urban manual and clerical workers during the three survey periods. Trends of the distributions are similar for the other age groups. The distribution shifted upwards in Akita between 1963–1966 and 1980–1983. The shift was larger in the first decade than in the second. An upward shift was also observed in manual workers, although the magnitude was smaller. Clerical workers showed a higher mean cholesterol level (200 mg/dl) than Akita and manual workers, with no significant trend.

Figure 8 shows the trend in dietary intake of salt and fat for men aged 40–59 in Akita. Salt intake declined from 20 g in 1969 to 14 g in 1980–1983. There was a 38% increase in percent calories from total fat with animal fat doubling between 1969 and 1980–1983. The increase in animal fat intake occurred in the first decade primarily due to an increase in meat and dairy products.

Table 1 shows regression coefficients of risk variables for the risk of cerebral hemorrhage and infarction. Systolic blood pressure, ST-T changes in the electrocardiogram (ECG), and hypertensive changes in the fundus were positively associated with hemorrhage incidence. Total serum cholesterol was inversely associated with hemorrhage. For cerebral infarction, sex, age, high R wave amplitude in the ECG, and hypertensive changes in the fundus were significantly associated.
Figure 7  Distributions of serum total cholesterol for men aged 40–49 in Akita, and urban clerical and manual workers.

Table 1  Regression coefficients of risk variables for the risk of cerebral hemorrhage and infarction for men and women aged 40–69 in Akita.

<table>
<thead>
<tr>
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<th>Hemorrhage (n=20)</th>
<th>Infarction (n=45)</th>
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<tbody>
<tr>
<td>Sex (men=1, women=2)</td>
<td>-0.34</td>
<td>-0.54*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>-0.01</td>
<td>0.07**</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>0.02*</td>
<td>0.01</td>
</tr>
<tr>
<td>Serum Chol (mg/dl)</td>
<td>-0.02**</td>
<td>0.01</td>
</tr>
<tr>
<td>ST-T Changes (ECG)</td>
<td>1.19*</td>
<td>0.07</td>
</tr>
<tr>
<td>High R Waves (ECG)</td>
<td>-0.29</td>
<td>0.80*</td>
</tr>
<tr>
<td>Hypertensive (Fundus)</td>
<td>0.99**</td>
<td>0.64**</td>
</tr>
<tr>
<td>Arteriosclerotic (Fundus)</td>
<td>0.30</td>
<td>-0.17</td>
</tr>
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* p < 0.05,  ** p < 0.01
DISCUSSION

The present study demonstrated a significant decline in the incidence of stroke, the prevalence rate of stroke and the number of bed-ridden patients in a Akita rural community between the 1960's and the 1980's. The incidence of CHD was low and showed no significant trend. The decline in stroke incidence was attributable primarily to a decline in systolic and diastolic blood pressure levels. Our prospective analyses indicated that blood pressure or hypertensive end organ effects in ECG or fundus were significantly associated with both cerebral hemorrhage and infarction. The blood pressure decline in Akita may have been in part due to increased use of antihypertensive medication. However, it is hard to attribute over 10 mmHg systolic and 4 mmHg diastolic decline for both sexes solely to the improvement of hypertension control by medication. Furthermore, a large blood pressure decline occurred in the second decade, whereas the antihypertensive medication use increased significantly in the first decade. We infer that a considerable part of the blood pressure decline may be attributed to changes in related behaviors and environmental factors: for example, dietary change such as decreased salt intake. Our nutrition study indicated that average salt intake declined from 20 g/day in 1989 to 14 g/day in 1980–1983.
Socio-economic developments since the mid-1960s with an increase in cash income and improvements of food transport and refrigeration were associated with increased consumption of meat and dairy foods, while the intake of traditional salt-preserved food decreased. At the same time, community-based nutrition education campaigns were conducted in attempts to reduce salt and increase animal food intake in the general population. The percent of total fat calories increased from the 1960s to the 1970s, with animal fat intake doubling. The increase in animal fat intake, mostly due to an increase in meat intake, may contribute to the significant increase in mean serum cholesterol levels between the 1960s and the 1970s.

The incidence of CHD remained continually low for men and women ages 40 to 69 in Akita during the past two decades. We speculate that the significant rise in serum cholesterol levels is not yet sufficient to raise the overall incidence of CHD. It is noteworthy that the latest serum cholesterol levels in Akita were 179 mg/dl for men and 192 mg/dl for women ages 40–69. Mean values in Akita are 8 mg/dl lower for men and 5 mg/dl lower for women compared to national population-based samples in 1980. Mean values in Akita men was about 15–20 ml/dl lower than urban manual and clerical workers who showed a slight increase in CHD incidence. These cholesterol levels in Japanese were much lower than those in the U.S. for the same period. The substantial decline in blood pressure levels is assumed to contribute to CHD trends, countering any potential effect of the population serum cholesterol increase.

In the analysis of risk factors for stroke, a most noteworthy finding is the inverse association between baseline serum cholesterol level and subsequent risk of cerebral hemorrhage. This inverse association was reported from other prospective studies of Japanese and Japanese Americans and from the six-year follow-up study of 350,977 U.S. men screened for the Multiple Risk Factor Intervention Trial. There is no widely-accepted plausible explanation for an association between low serum cholesterol levels and cerebral hemorrhage. However, it is well known that the pathogenesis of hemorrhage differs from that of CHD. Arterionecrosis (fibrinoid necrosis) characterizes intracerebral arteries in cerebral hemorrhage, and atherosclerosis in coronary arteries in CHD.

We hypothesize that the fragility of intracerebral vascular walls is augmented by low serum cholesterol levels particularly in the presence of hypertension. A significant increase in glycerol permeability and osmotic fragility was observed in cholesterol-depleted/reduced cell membranes and erythrocytes. Our case-control study showed that both serum cholesterol and the cholesterol content of red cell membranes were significantly lower among cerebral hemorrhage than for non-cases, and osmotic fragility of erythrocytes was significantly greater. Experimental studies indicated that a rise in serum total cholesterol associated with diet in animals attenuates the development of angionecrosis in intracerebral arteries and stroke. Thus, we infer that the significant decline in the incidence of cerebral hemorrhage in Akita could be due to the combination of the serum cholesterol rise and blood pressure fall. However, we can not exclude potential confounding factors like relative protein deficiency and alcohol consumption.

In conclusion, trends of blood pressure and serum total cholesterol were associated with changes in behaviors and environmental factors in the Akita rural community during the past two decades. The substantial decline in stroke incidence was attributed mostly to decreased blood pressure levels and possibly to increased serum cholesterol levels. There was no significant change in CHD incidence in spite of the increased serum cholesterol levels in Akita, whereas an increasing trend was observed for urban clerical and manual workers. Surveillance is underway in both rural and urban populations to clarify trends in stroke and CHD incidence and changes in risk factors and behaviors in the future.
REFERENCES


