Regional Differences in Stroke Mortality and Alcohol Consumption in Japan

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SUMMARY  The relationship between alcohol consumption and stroke mortality in 1975 in 46 prefectures of Japan was investigated. This was done by adjusting salt intake and several socio-economic factors, i.e., the annual per capita income, the number of persons who received public aid, the number of tatamis (a Japanese traditional floor unit) per household, the unemployment rate, and the unmarried or divorce rate, using a stepwise multiple regression analysis. As dependent variables, the sex-specific and age-adjusted mortality for the middle-aged (35-59 years) and for all ages due to stroke were used. For men, alcohol consumption was significantly related to age-adjusted stroke mortalities for the middle-aged and for all ages independent of salt intake and several socio-economic factors. Alcohol consumption was more strongly related to age-adjusted stroke mortality for the middle-aged than for all ages. For women alcohol was weakly correlated with the stroke mortality of the middle-aged. Salt intake was significantly correlated with stroke mortality for women but not for men. Furthermore, the male:female ratios of the age-adjusted stroke mortality for the middle aged and for all ages were analyzed as well, because alcohol is mostly consumed by men in Japan, and it was expected that the sex ratios would be well correlated to alcohol consumption. The results were as expected. Therefore, it was suggested that the regional difference in stroke mortality in Japan may be explained in part by that of alcohol consumption.

STROKE has been one of the leading causes of death in Japan. Hypertension is a major risk factor for stroke. Mortality, the incidence of stroke, and the prevalence of hypertension have been higher in the northeastern part than in the southwestern part of Japan. These areas with high stroke mortality and high prevalence of hypertension correspond to high salt intake. However, alcohol intake is higher in the northeastern part of the main island (Honshu) of Japan, especially in Akita Prefecture, than in any other area. It is well documented not only by cross-sectional epidemiological studies but also by follow-up studies that moderate or heavy level of alcohol drinking is related to hypertension. Furthermore, several animal and epidemiological studies suggest that alcohol is a risk factor for stroke independent of hypertension. Therefore, whether or not the regional difference in stroke mortality across 46 prefectures is related to alcohol consumption, and independent of salt and several socio-economic factors in Japan, was analyzed by a stepwise multiple regression analysis.

Materials and Methods

Statistics for 46 prefectures, excluding Okinawa, in 1975 were used to analyze the relationship between stroke mortality and alcohol consumption. Age-specific stroke mortality data by prefecture and sex were available in the Special Report of Vital Statistics in Japan, 1975. The age-adjusted stroke mortalities for all ages by sex were calculated using the national population census and five-year age-specific mortality rate in 1975. In this study, the age-adjusted stroke mortality for the middle-aged (35-59 years) as well as for all ages were calculated. This is because it was observed that the decreasing rate of middle-aged men's mortality due to all causes of death slowed down in comparison with other age and sex groups, and because most of the alcohol was consumed by middle-aged men. Furthermore, male:female ratios of age-adjusted stroke mortality were also calculated for the middle-aged and for all ages to analyze the relationship between the sex ratio and alcohol consumption. Alcohol consumption per person per year by prefecture was calculated from the Annual Report of the Tax Administration Agency, total alcohol consumption by prefecture was divided by the population aged 20 years and over. No data on sex-specific alcohol consumption was available. To estimate salt intake by prefecture, data on salt excretion per creatinine (g/g) in the spot urine of three-year-old children by prefecture was used. Since it was found that the data of the salt excretion was correlated with the salt intake recorded in the National Nutrition Survey, this data seems to reflect the variation of salt consumption by prefecture. Several socio-economic factors for each prefecture were used in a stepwise multiple regression analysis. These factors were, the annual income per capita, the number of men per 100,000 who are receiving public aid, the number of tatamis (a Japanese traditional floor unit) per household, the unemployment rate per 100,000 men, the unmarried rate per 100 men aged 35-49, and the annual incidence rate of divorce per 1000 persons. Data on these factors was obtained from the Statistics on Social Life and the Annual Report of Social Welfare, 1975, the Population Census of Japan, 1975 and Vital Statistics, 1975.

Age-adjusted stroke mortalities for all ages and for the middle-aged by sex, and the male:female ratio of age-adjusted stroke mortality for the middle-aged and all ages were used as dependent variables, while alcohol consumption, salt intake and socio-economic factors were used as independent variables in a stepwise multiple regression analysis. The same independent variables were used for the stepwise multiple regres-
TABLE 1  Mean and Standard Deviation of Stroke Mortality, Alcohol Consumption, Salt Excretion, and Other Socio-economic Variables in 46 Prefectures of Japan, 1975

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-adjusted stroke mortality for the middle-aged (35–59 years old)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men (number of death per 100,000 population per year)</td>
<td>81.84</td>
<td>18.21</td>
</tr>
<tr>
<td>Women (number of death per 100,000 population per year)</td>
<td>43.46</td>
<td>6.71</td>
</tr>
<tr>
<td>Male:female ratio</td>
<td>1.89</td>
<td>0.32</td>
</tr>
<tr>
<td>Age-adjusted stroke mortality for all ages</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men (number of death per 100,000 population per year)</td>
<td>124.36</td>
<td>19.73</td>
</tr>
<tr>
<td>Women (number of death per 100,000 population per year)</td>
<td>111.13</td>
<td>15.33</td>
</tr>
<tr>
<td>Male:female ratio</td>
<td>1.12</td>
<td>0.08</td>
</tr>
<tr>
<td>Annual alcohol consumption per person aged 20 years and over (equivalent volume to 100 ml of sake)</td>
<td>508.30</td>
<td>88.25</td>
</tr>
<tr>
<td>Number of tatamis per household</td>
<td>27.89</td>
<td>5.11</td>
</tr>
<tr>
<td>Unemployment rate (number of unemployment per 100,000 men)</td>
<td>100.32</td>
<td>40.54</td>
</tr>
<tr>
<td>Annual income per capita (1,000 Yen)</td>
<td>972.06</td>
<td>163.43</td>
</tr>
<tr>
<td>Unmarried rate (number of person per 100 men aged 35–49 years)</td>
<td>3.51</td>
<td>1.05</td>
</tr>
<tr>
<td>Annual incidence of divorce (number of divorce per 1,000 persons)</td>
<td>0.99</td>
<td>0.21</td>
</tr>
<tr>
<td>NaCl/creatinine in spot urine of three-year-old children (g/g)</td>
<td>18.72</td>
<td>3.56</td>
</tr>
<tr>
<td>Rate of receipt of public aid (number of person per 100,000 population)</td>
<td>102.45</td>
<td>56.35</td>
</tr>
</tbody>
</table>

*SD is standard deviation

sion analysis of both men and women. Either the unmarried rate or the divorce rate was used as an independent variable.

Results

Characteristics of the Variables

Table 1 shows the mean and standard deviations of the variables used in this study. Stroke mortality for middle-aged (35–59 years old) men was higher than that for women, and the male:female ratio of it was 1.9. However, there was no large difference between male and female stroke mortality for all ages.

Annual alcohol consumption per capita was 50,800 ml of sake — about 18g of ethanol per day. Average excretion of salt per creatinine was 18.7 (g/g) in the spot urine of three years old children.

Simple Correlation Analysis

The matrix of the simple correlation coefficient is shown in table 2. Alcohol consumption correlated highly and significantly with the stroke mortality for middle-aged men (fig. 1) and the male:female ratio of the stroke mortality for the middle-aged (fig. 2) and all ages. The correlation coefficient between the age-adjusted stroke mortality for middle-aged women and annual alcohol consumption per capita was far lower than that for men \(r = 0.322, p < 0.05\).

On the other hand, salt intake correlated significantly but moderately with women's stroke mortality for the middle-aged and for all ages and weakly with men's stroke mortality for all ages. Salt intake correlated neither with the male:female ratio of the stroke mortality for the middle-aged nor for all ages. There was no correlation between alcohol consumption and salt intake across 46 prefectures. Annual income correlated significantly and negatively with 5 of 6 cases of stroke mortality.

Figure 3 shows the geographic variations of age-adjusted stroke mortality for middle-aged men (35–59 years old) and annual alcohol consumption per capita by quintiles and prefecture. The stroke mortality and alcohol consumption in the north-eastern part of the main island (Honshu) and southern island (Kyushu) were higher than in other prefectures. Most of the prefectures belong to the top or second class of the quintiles for stroke mortality and alcohol consumption.

Since most alcohol is consumed by men in Japan, the male:female ratio of the stroke mortality was expected to correlate with alcohol consumption. The results were as expected (fig. 2, table 2).

Stepwise Multiple Regression Analysis

The results of a stepwise multiple regression analysis showed that alcohol consumption was significantly related to the age-adjusted stroke mortality for middle-aged men and women independent of salt intake (table 3). The F value of alcohol was far lower in women than in men. Therefore, the multiple correlation coefficient (multiple R) was far higher in men than in women. Salt intake was significant for the analysis of women but not for men. For men, the number of tatamis was significant as well.

Table 4 shows the result of the analysis on the age-adjusted stroke mortality for all ages. For men, alcohol consumption and annual income were significant. For women, salt intake was significantly related to the age-adjusted stroke mortality for all ages. Thus, alcohol was significantly correlated to the male stroke mortality for all ages independent of salt intake and other socio-economic variables.
STROKE AND ALCOHOL CONSUMPTION

In this study, we first demonstrated that the geographic variation of stroke mortality in 1975 among 46 prefectures in Japan was significantly related to alcohol consumption which was independent of salt intake and several socio-economic factors. Recently, several epidemiological studies have revealed that alcohol drinking is related to high blood pressure, although there is controversy about the threshold effect. A Japanese epidemiological study revealed that there was a graded relationship between alcohol consumption and the blood pressure level; it was independent of obesity, smoking habits, hemoglobin concentration, serum uric acid and serum lipid levels. Two follow-up studies in Chicago, U.S.A. show that alcohol drinking induces hypertension. It is also reported that the patients who stopped drinking show decreasing blood pressure levels, while those who started to drink again show an increase in blood pressure levels not found in those who did not start to drink again. The mechanism explaining why drinking more alcohol increases the blood pressure level or induced hypertension has not yet been clearly delineated, although there are some findings that the adreno-cortico and medullar hormone system, renin-angiotensin system and vaso-pressin system are related to alcohol ingestion.

Several follow-up studies on stroke risk factors reveal that alcohol drinking is a risk factor in stroke. It is reported that alcohol concentration which parallels that needed for its graded effects of euphoria, mental haziness, muscular incoordination, stupor and coma in humans induces graded contractile responses in rat cerebral arterioles and venules in vivo and in isolated canine basilar and middle cerebral arteries. Thus, alcohol ingestion may play a role in causing stroke by increasing blood pressure and contracting cerebral arteries.

The people who are living in the northeastern part of the main island of Japan where the consumption of sake is high also have a high consumption of salt and engage in manual farm labor. Such factors as high...
TABLE 2  Matrix Showing the Simple Correlation of Alcohol Consumption, Salt Intake and Selected Socio-economic Variables in 46 Prefectures of Japan, 1975

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stroke mortality for the middle-aged</th>
<th>Stroke mortality for all ages</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>Stroke mortality for the middle-aged men</td>
<td>0.609‡</td>
<td>0.719‡</td>
</tr>
<tr>
<td>Stroke mortality for all ages men</td>
<td>0.688‡</td>
<td>0.669‡</td>
</tr>
<tr>
<td>Stroke mortality for all ages women</td>
<td>0.670‡</td>
<td>0.670‡</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0.618‡</td>
<td>0.493‡</td>
</tr>
<tr>
<td>Salt</td>
<td>-0.427†</td>
<td>-0.266</td>
</tr>
<tr>
<td>Income</td>
<td>0.219</td>
<td>0.008</td>
</tr>
<tr>
<td>Tatamis</td>
<td>0.06 - 0.101</td>
<td>0.123</td>
</tr>
<tr>
<td>Unemployment</td>
<td>0.163</td>
<td>0.004</td>
</tr>
<tr>
<td>Unmarried rate</td>
<td>-0.050</td>
<td>-0.044</td>
</tr>
<tr>
<td>Divorce rate</td>
<td>0.011</td>
<td>-0.049</td>
</tr>
</tbody>
</table>

*Selection criteria is F = 2.0.

Variables are listed in order when they are included in the equation.

In Japan, in contrast to Europe and North America, few women drink alcoholic beverages, although recently the number who drink beer or whiskey has been increasing. A national survey shows that only 3 percent of females drink alcoholic beverages every day, compared with 47 percent of males. If those who drink sometimes are included in addition to those who drink every day, the rate for women is still only 21 percent, while that for men is 74 percent. Therefore, men contribute the most to the consumption of alcoholic beverages, and this has resulted in higher simple and multiple correlation coefficients between alcohol consumption and stroke mortality in men than in women. It has also resulted in high simple and multiple correlation coefficients between alcohol consumption and male:female ratios of stroke mortality. Alcohol consumption was weakly but significantly correlated to stroke mortality in middle-aged women, however this might be induced by possible confounding factors. Since data was not available on women’s alcohol consumption by prefecture, we could not conclusively state whether or not alcohol consumption explains, even in part, the regional differences in stroke mortality of women as well.

For the analysis of age-adjusted stroke mortality for the middle-aged, the coefficients of alcohol were far higher than for those of all ages. One of the possible reasons is that there is a difference in the alcohol drinking pattern between the middle-age group and all age groups, i.e., few people under age 20 in Japan drink publicly, and the rate of drinkers over 70 years old is

salt intake and hard manual labor may be confounding factors. Salt was significantly related to stroke mortality for women in a multiple regression analysis. Since it seems that men and women have the same tendency of salt intake when salt intake in 46 prefectures is compared, salt may relate to stroke mortality for men as well. As a matter of fact, the simple correlation coefficient between salt and male stroke mortality for all ages was significant.

TABLE 3  Stepwise Multiple Regression Analysis* of Age-adjusted Stroke Mortality for the Middle-aged (35-59 years) in 46 Prefectures, Using the Independent Variables of Alcohol Consumption, Salt Intake, Annual per Capita Income, Unemployment Rate, Rate of Receipt of Public Aid, Number of Tatamis (Japanese traditional floor unit) and Rate of Unmarried Men

<table>
<thead>
<tr>
<th>Variable</th>
<th>Standardized coefficient</th>
<th>F value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>Alcohol</td>
<td>0.672</td>
<td>38.495</td>
</tr>
<tr>
<td></td>
<td>Tatamis</td>
<td>0.290</td>
<td>6.474</td>
</tr>
<tr>
<td></td>
<td>Salt</td>
<td>0.178</td>
<td>2.511</td>
</tr>
<tr>
<td></td>
<td>Multiple R = 0.726</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>Alcohol</td>
<td>0.320</td>
<td>5.419</td>
</tr>
<tr>
<td></td>
<td>Salt</td>
<td>0.293</td>
<td>4.545</td>
</tr>
<tr>
<td></td>
<td>Multiple R = 0.435</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05, †p < 0.01, ‡p < 0.001.

Variables are listed in order when they are included in the equation.
lower than that of drinkers in the 30–69 years age group. The number of tatamis was significantly related to stroke mortality in 2 of 6 analyses. Since relatively large houses in Japan tend to be farm houses located in the country-side, as compared with the small houses found in cities, this does not mean that rich people or prefectures with relatively large houses is a risk factor in stroke. The result shows rather that people who are living in poor prefectures with large farm houses have a high stroke mortality rate. The annual income was weakly and negatively related to the stroke mortality for men of all ages and the male:female ratio of stroke mortality for all ages. Prefectures with low annual income seem to have many factors that increase stroke mortality.

This study does not show how alcohol was related to stroke risk on an individual base. That the relationship between stroke and the alcohol drinking habit should be investigated further by case-control and/or prospective follow-up studies, addressing both the acute and chronic effects of alcohol drinking. The impact of alcohol drinking on stroke may be strong if the relationship between them is real because the alcohol drinking habit is prevalent in industrialized societies.

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