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Urinary salt excretion and stomach cancer mortality among four Japanese populations

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A relationship between salt intake and the occurrence of stomach cancer has been suggested by both epidemiologic and experimental data. To test this hypothesis, urinary excretion of salt in 24 hours and dietary intake of salt were measured in four male populations with different levels of stomach cancer mortality. Age-adjusted mortality rate of stomach cancer showed a high correlation ($r^2 = 0.995$) with the average amount of salt excretion in 24-hour urine. This strong correlation, however, was not shown ($r^2 = 0.265$) with dietary salt intake calculated from the standard food-composition table. The results confirmed the important role of salt in the development of stomach cancer in Japan, and raised the problem of evaluating the level of salt intake by using the uniform composition table.

Key words: Cross-sectional study, Japan, nutrition, sodium chloride, stomach cancer, urine.

Introduction

The geographic difference in mortality from stomach cancer is noteworthy even within the homogenous population of Japan. The highest age-adjusted mortality rate in males of Niigata Prefecture is 53.8 per 100,000 (adjusted to the standard World population), which is almost three times higher than that of the lowest value of 19.8 in Okinawa Prefecture in 1985.[1] Decreased mortality from stomach cancer has been observed among Japanese immigrants in the United States, but mortality is still high among Japanese immigrants in São Paulo, Brazil (48.5 in 1979-81).[2] These descriptive data suggest that any risk factor for stomach cancer should exist in the lifestyle in each area.

Generally, prefectures with higher mortality of stomach cancer are located in the northern part of Japan, while those with lower mortality are in the southern part.[1] This distribution is similar to that of the cerebrovascular disease mortality[1] together with the level of dietary salt intake.[3] The recent decreasing trend of stomach cancer incidence and mortality in Japan[4] is considered to be parallel to the decreasing salt intake and the promoting action of salt, as evidenced in animal experiments.[5]

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The purpose of this study is to verify the positive correlation between stomach cancer mortality and dietary salt intake in populations in the representative areas by a cross-sectional approach.

Materials and methods

This study is a part of our cross-sectional study to find the factors which could generate the geographic differences of various sites of cancer in Japan using multiple biologic markers.[6] Each study area has a population of approximately 100,000 covered by the prefectural health center, which supervises the health administration of several cities, towns, and villages. Four areas were selected for this study according to the degree of age-adjusted mortality rates of stomach cancer: Yokote in Akita Prefecture has one of the highest rates; Saku in Nagano Prefecture has one of the higher; Ninohe in Iwate Prefecture has one of the lower; and Ishikawa in Okinawa Prefecture has one of the lowest rates. Geographic location and age-adjusted male mortality rates of stomach cancer (adjusted to the standard World population) for 1985 to 1987 in these areas are shown in Figure 1.

Volunteer subjects for this study were recruited from participants of the main study, which selected 170 to 175 men aged 40 to 49 years old from the list of resident registration. The participant rates of the main study were 77 percent (134/175) in Ninohe, 78 percent (133/170) in Yokote, 71 percent (120/170) in Saku, and 76 percent (129/170) in Ishikawa.

Twenty-four-hour urine samples were collected on weekdays (except holidays) from February to March 1989 in Ninohe and Ishikawa areas, and in 1990 in Yokote and Saku areas. A simple portable device (Urine Mate P, Sumitomo Bakelite, Tokyo) was used for collecting urine.[7] After measuring the total urinary volume, samples were frozen ($-80°C$) until analysis. Sodium and creatinine concentrations were analyzed by the flame photometry method and by the method using alkaline picric acid, respectively.

A three-day record of the amount and type of each food eaten also was obtained to detect the level of dietary salt intake. The salt content of each food was calculated by using the food composition table (the fourth revised edition of Standard Food Composition Tables in Japan[8]). The survey was conducted in three consecutive days (except Saturdays, Sundays, and holidays) between March and April of 1989 and 1990. The participants of this nutrition survey were given explanations of the recording method by trained nutritionists before the survey, and were advised at least one

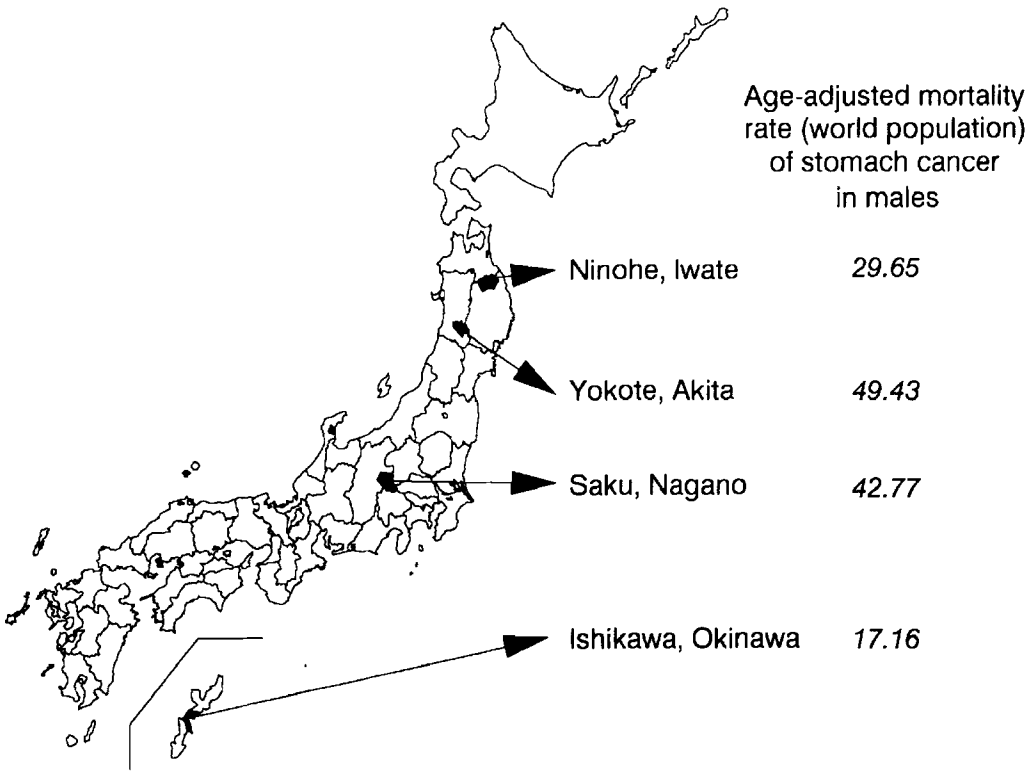

Figure 1. Location of survey areas and age-adjusted mortality rates (adjusted to standard World population).

time during the three-day recording period. Furthermore, final assessments were made on the occasion of submitting the result of recording. The method was almost the same as the one applied in the National Nutrition Survey.[3]

Subjects of the two studies, *i.e.*, urine collection and nutrition survey, did not always match.

Results

A total of 159 men (33 in Ninohe, 43 in Yokote, 48 in Saku, and 32 in Ishikawa) participated in the 24-hour urine collection, while a total of 144 men (26 in Ninohe, 50 in Yokote, 41 in Saku, and 27 in Ishikawa) were involved in the nutritional survey. Of the total, 77 men (10 in Ninohe, 20 in Yokote, 31 in Saku, 16 in Ishikawa) participated in both studies. The final response rates were 23 percent (19 percent in Ninohe, 25 percent in Yokote, 28 percent in Saku, and 19 percent in Ishikawa) for urine collection and 21 percent (15 percent in Ninohe, 29 percent in Yokote, 24 percent in Saku, and 16 percent in Ishikawa) for the nutrition survey.

Mean values and standard deviations of the urinary volume, creatinine, and salt in 24-hour urine samples are shown in Table 1. For creatinine excretion of 0.5 g per day or more, the same values are also given due to the possibility of incomplete urine collection. The highest value of 13.41 g for salt was obtained in Yokote, while the lowest value of 7.99 g was obtained in Ishikawa.

The estimated salt intake calculated from the nutrition survey is also shown in Table 1. The values estimated by the nutrition survey resulted in higher amounts than the actual urinary salt excretion, the differences being 1 g for Yokote and Saku, 4 g for Ishikawa, and 6 g for Ninohe. Larger differences were noted for the areas where urinary excretion was actually lower.

A strong correlation between the urinary salt excretion and stomach cancer mortality is shown in Figure 2. The r^2 value is 0.995; whereas, the r^2 value between the estimated dietary salt intake and stomach cancer mortality is only 0.265.

Discussion

An almost complete correlation between the urinary salt excretion in 24-hour urine samples and the age-adjusted stomach cancer mortality was shown by the cross-sectional survey in four areas with different mortality levels.

Several experimental[5] and epidemiologic[9-11] findings support the etiologic role of salt in the development of stomach cancer. Indicators of the degree of salt intake, however, varied among epidemiologic studies. Most case-control and cohort studies use the intake-frequency of highly salted foods, such as Japanese pickles and salted fish, and the taste for salt as indicators of salt intake.[9] Contrarily, a cross-sectional study using *per capita* salt consumption or urinary excretion failed to show the relationship with stomach cancer mortality in Japan.[12-13] Salt-intake levels calculated by the standard food-composition table failed to show any relationships in the present study. This standard table gives the same sodium value even though the sodium concentration in the food item is different, resulting in a poor estimated value.

The differences between the estimated level of salt intake calculated from the nutrition survey and from

Table 1. Mean and standard deviation of volume, creatinine, and salt in 24-hour urine samples from male inhabitants aged 40 to 49 years old in four areas of Japan

	Area, Prefecture			
	Ninohe, Iwate	Yokote, Akita	Saku, Nagano	Ishikawa, Okinawa
All samples				
Number	33	43	48	32
Volume (ml)	1335±599	1360±792	1367±712	1153±486
Creatinine (g)	0.88±0.36	1.00±0.42	0.89±0.50	1.04±0.42
Salt (g)	8.97±4.04	12.27±6.84	10.19±5.81	7.50±3.41
Samples with creatinine ≥0.5				
Number	28	37	38	29
Volume (ml)	1433±591	1497±761	1562±651	1211±469
Creatinine (g)	0.97±0.29	1.12±0.34	1.05±0.43	1.11±0.37
Salt (g)	9.92±3.56	13.41±6.58	11.92±5.26	7.99±3.21
Estimated dietary salt intake[a]				
Number	26	50	41	27
Salt (g)	15.5±4.4	15.0±3.2	13.2±2.8	12.0±3.3

[a]Calculated by dietary food intake using standard food-composition table.

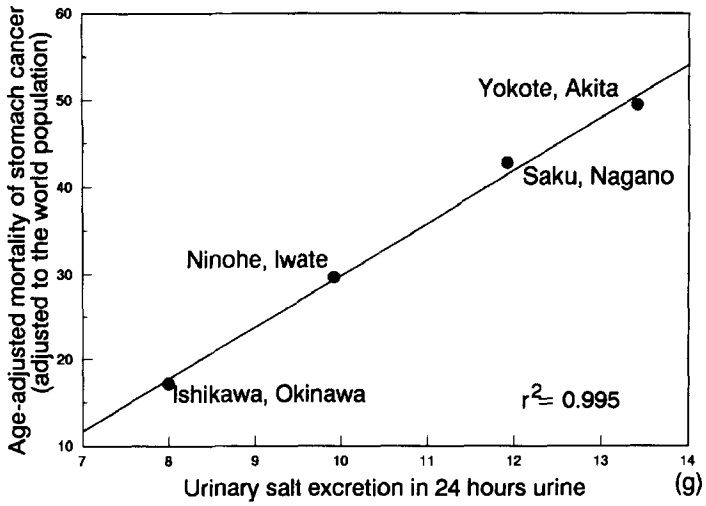

Figure 2. Correlation between age-adjusted male stomach cancer mortality and urinary salt excretion.

the 24-hour urine samples are worth noting for the Ninohe and Ishikawa areas where urinary excretion was actually low. The sodium concentration in the food is expected to be low in these areas, indicating that food with high sodium concentrations common in Yokote and Saku can be risk factors for stomach cancer.

The final response rate of 23 percent (range 19 to 28 percent) was not sufficient to provide representative values of urinary salt excretion in 24-hour urine samples in each of the study areas, even though the response rates were high (from 71 to 78 percent) in the main study. The participants in the 24-hour urine collection may be biased in that they are more health conscious or that they work at home. The comparability, however, is expected to be good among these four areas since the same method was used for recruiting the participants of the urine survey. The same applies to the nutrition survey.

The present study confirmed the importance of salt restriction to reduce the stomach cancer incidence and suggested that a 40 percent reduction (from 13.41 to 7.99) of salt intake could produce a 65 percent decline (from 49.43 to 17.16) of stomach cancer mortality in Yokote, or a corresponding 26 percent reduction (to 9.92) of salt intake could produce a 40 percent decline (to 29.65).

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