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Relationship of Diet to the Incidence of Esophageal and Stomach Cancer in Japan

Masaki Nagai, Tsutomu Hashimoto, Hiroshi Yanagawa,
Hideaki Yokoyama, and Masumi Minowa

Abstract

The food intake of households in 1,040 census tracts sampled in 1974, 1975, and 1976 for the nationwide nutrition survey of the Japanese Ministry of Health and Welfare, and the standardized mortality ratios (SMRs) of stomach and esophageal cancers from 1969 to 1974 for the cities, towns, and villages of the nutrition survey areas, were linked and their relationship was observed statistically by correlation analysis and multiple regression analysis. The results obtained are summarized as follows:

- 1. The food items positively related to the SMR for stomach cancer were wheat, pickled vegetables, and beef, while tofu (soybean curd) was negatively related.*
- 2. Foods positively related to esophageal cancer were wheat, pork, and dried or salted fish.*
- 3. Pickled vegetables and dried or salted fish contain a high percentage of salt (NaCl), and thus the positive relationship of these foods to both stomach and esophageal cancers suggests a relationship between salt and these diseases.*

Introduction

Both the esophagus and the stomach are under the direct influence of diet, and it is believed that diet may play a major role in the onset of cancer in these organs. This study aims to clarify similarities and differences in the geographical distributions of stomach and esophageal cancer, and to clarify regional differences in diet that may have a bearing on cancer incidence.

The age-adjusted mortality rate for stomach cancer in Japan reached its peak around 1960, steadily declining thereafter for both males and females. However, the mortality rate of stomach cancer in Japan is still higher than that of any other cancer. Among males, the stomach cancer mortality rate is approximately twice that for lung cancer, which ranks second in male mortality, whereas among females it is more than 3 times the mortality rate for uterine cancer,

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which ranks second among females for mortality. The mortality rate for esophageal cancer is substantially lower than that for stomach cancer, and has been declining since the latter half of the 1960's for females and since approximately 1970 for males.

The geographical distribution of stomach and esophageal cancer in Japan shows that the former is found more frequently in the northeast region of the nation and less frequently in the southwest region, with the exception of the Kii Peninsula. The geographical distribution of the mortality rate for esophageal cancer basically corresponds to that of stomach cancer, except that in the southern part of Japan the mortality rate for esophageal cancer is relatively high while that for stomach cancer is relatively low.

In this paper, the relationship between the mortality rates for cancer and the foods consumed in various regions of Japan will be observed statistically.

Materials and Methods

Each year, the Japanese Ministry of Health and Welfare conducts a nationwide nutrition survey. About 300 areas within Japan are selected at random, each consisting of approximately 70 persons in about 20 households. Using this sample, the foods consumed over a period of 3 days are studied in detail.

In the present study, the results of the nationwide nutrition surveys conducted in 1974, 1975, and 1976, covering 1,040 areas, were compiled and compared with the standardized mortality ratios (SMRs) for cancer of the stomach and esophagus in the municipality in which each sample area is located. The SMR was the ratio of the number of deaths in the 6-year period ending in 1974 in each study area broken down by sex to the expected number of deaths in each study area computed on the basis of the mortality rate of the entire nation during the same period.

Since the pattern of food consumption in each area is closely related to socioeconomic background, the 1975 census-based population ratio of "first industries" (i.e., agriculture, fishery, and forestry) and "third industries" (i.e., wholesale finance, real estate, transport, services, etc.) and the individual income index of 1978 for each area were also included in the analysis.

Table 1 shows the mean value and standard deviation of the items of consumption chosen for the study as well as the 3 items indicating socioeconomic background. All of the items were selected with consideration of their possible relationship to deaths from stomach and esophageal cancer, their relevance in terms of total volume of food consumed, and their mutual exclusivity.

The correlation coefficients between the SMRs and the amount of each category of food consumed as well as the socioeconomic indices were calculated. A multiple regression analysis was also conducted, using the SMRs as the criterion variables and the amount of food in each category as the predictor variables. The predictor variables were selected by means of backward-elimination, in which the variable of the minimal partial regression coefficient whose level of significance is not less than 5% is eliminated.

Results

Distribution of Each Index

Figure 1 shows the distribution of the SMRs for stomach and esophageal cancer in the 1,040 areas of the nationwide nutrition survey. The distribution of the SMR for stomach cancer is basically symmetrical for both sexes, while the distribution for esophageal cancer shows substantially more instances of zero values due to the relatively lower mortality rate of this cancer, with the right half of the figure showing a more tapered decline. For stomach cancer, the mean values and standard deviations were 99.6 and 20.5 for males and 98.3 and 20.7 for females. For esophageal cancer, the values were 102.8 and 46.9 for males and 98.8 and 62.9 for females.

The mean values and standard deviations of the foods consumed and the socioeconomic indices used as predictor variables are shown in Table 1. In most cases these variables did not show great differences from normal distribution.

Table 1. Average Value and Standard Deviation of the Variables Studied

Variables	Mean value	Standard deviation
Food consumption		
Calorie ratio (observed/required)	115.0%	12.6%
Protein ratio (observed/required)	117.6%	11.7%
Rice	247.4g	51.1g
Wheat	92.4g	23.6g
Potatoes	60.8g	16.8g
Sugar	14.8g	5.2g
Confectionery	28.0g	10.3g
Fat	16.4g	4.9g
Miso	20.6g	7.1g
Tofu (soybean curd)	31.3g	11.4g
Fruits	181.7g	47.2g
Green vegetables	52.0g	13.5g
White vegetables	193.9g	35.6g
Pickled vegetables	38.4g	18.2g
Soy sauce	23.5g	7.5g
Sake	20.2g	13.6g
Fresh fish	41.9g	16.7g
Dried or salted fish	13.7g	7.8g
Beef	12.8g	9.9g
Pork	26.7g	10.2g
Egg	41.0g	8.1g
Milk	93.8g	28.1g
Social conditions		
Population ratio of first industry	12.7%	15.1%
Population ratio of third industry	53.3%	13.5%
Income ratio (all Japan = 100)	101.8%	30.5%

Correlation Analysis

The simple correlation coefficients between the SMRs for both types of cancer and the amounts of food consumed indicate that wheat, pickled vegetables, and beef have a positive correlation with stomach cancer, while sugar and tofu have a negative correlation with stomach cancer. Wheat, oil and fat, white vegetables, dried or salted fish or shellfish, pork, and milk have a positive correlation with esophageal cancer, while rice, potatoes, sugar, and fresh fish have a negative correlation, as shown in Table 2. The two types of cancer were also correlated with social conditions. The population ratio of the first industries had a negative correlation with both cancers, while that of the third industries had a positive correlation with esophageal cancer. The income index had a positive correlation with both cancers (Table 2).

The food consumption values for all of the items studied show mutual correlation as well as a close relationship with the specific characteristics of the area. For example, rice, potatoes, sugar, miso (salted and fermented soybean), tofu, white vegetables, pickled vegetables, soy sauce, sake, fresh fish, and dried or salted fish, which have a significant positive correlation with the population ratio of the first industries, have mutually positive correlations in most cases, as shown in Table 3. The majority of foods mentioned above are traditional Japanese foods.

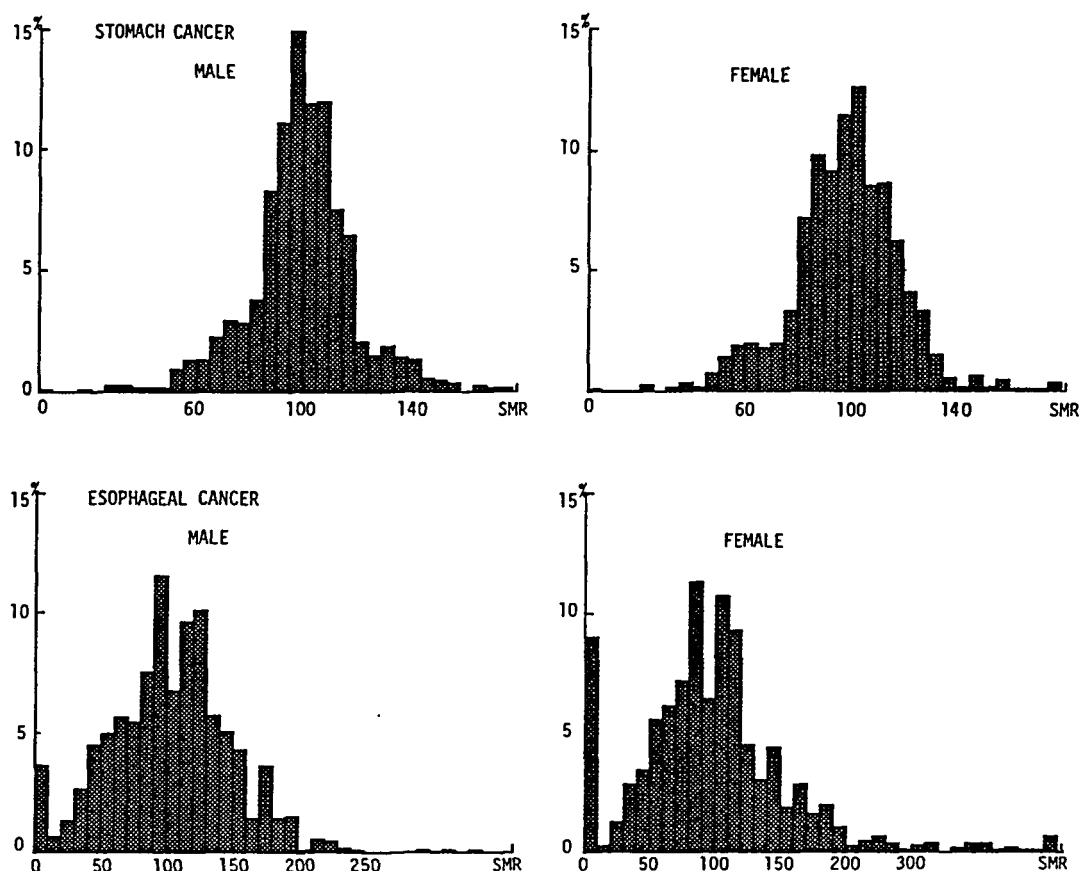


Figure 1. Distribution of the standardized mortality ratios of stomach cancer and esophageal cancer in 1,040 observation areas in Japan from 1969 to 1974.

Wheat, oil and fat, beef, pork, eggs, and milk, on the other hand, have a significantly positive correlation with the population ratio of the third industries (Table 4). These are rather western types of food. All of the correlation coefficients between the foods in this group are positive, with the exception of the correlation between beef and pork.

Multiple Regression Analysis

Multiple regression analysis was performed using each of the 22 categories of food consumption as the predictor variables and the SMRs of stomach and esophageal cancer as the criterion variables.

As shown in Table 5, wheat has a positive correlation with stomach and esophageal cancer, while sugar has a negative correlation for both cancers. Beef has a positive correlation for stomach cancer, while the correlation of tofu is negative. Potatoes, confectionery, and fresh fish have positive correlations only with stomach cancer, while oil, soy sauce, salted or dried fish, and pork have positive correlations only with esophageal cancer. The positive coefficient between pickled vegetables and male stomach cancer and the negative coefficient between rice and male esophageal cancer are relatively large.

Table 2. Statistical Significance of Correlation Coefficients Between the Standardized Mortality Ratio of Stomach and Esophageal Cancer and Data on Food Consumption and Social Conditions

Variables	Stomach cancer			Esophageal cancer		
	Total	Male	Female	Total	Male	Female
Food consumption						
Calorie ratio (observed/required)	NS	NS	NS	NS	NS	NS
Protein ratio (observed/required)	NS	NS	NS	NS	NS	NS
Rice	NS	NS	NS	--	--	NS
Wheat	++	++	++	++	++	++
Potatoes	NS	NS	NS	--	--	NS
Sugar	--	-	--	--	--	NS
Confectionery	NS	NS	NS	NS	NS	NS
Fat	NS	NS	NS	++	++	++
Miso	NS	NS	--	NS	++	NS
Tofu (soybean curd)	--	-	--	NS	NS	NS
Fruits	NS	NS	NS	NS	NS	NS
Green vegetables	NS	NS	NS	NS	NS	+
White vegetables	NS	+	NS	++	++	NS
Pickled vegetables	+	++	NS	++	++	NS
Soy sauce	NS	NS	-	NS	NS	++
Sake	NS	NS	NS	NS	NS	++
Fresh fish	NS	NS	NS	--	NS	--
Dried or salted fish	NS	NS	NS	++	++	++
Beef	+	NS	++	NS	-	NS
Pork	NS	NS	NS	++	++	++
Egg	NS	NS	NS	NS	-	NS
Milk	NS	NS	NS	+	+	NS
Social conditions						
Population ratio of first industry	--	--	--	--	--	NS
Population ratio of third industry	NS	NS	NS	++	++	NS
Income ratio (all Japan = 100)	++	+	++	++	++	NS
NS: not significant. --, ++: $p \leq 0.01$. -: negative correlation, $0.01 < p \leq 0.05$. +: positive correlation, $0.01 < p \leq 0.05$.						

Table 3. Correlation Coefficients Between the 11 Food Items Positively Correlated to the First Industries

Food items	First industry	Rice	Potatoes	Sugar	Miso	Tofu	White vegetables	Pickled vegetables	Soy sauce	Sake	Fresh fish
Rice	0.464										
Potatoes	0.330	0.256									
Sugar	0.071	0.060	0.162								
Miso	0.488	0.410	0.347	0.010							
Tofu (soybean curd)	0.167	0.090	0.139	0.046	0.155						
White vegetables	0.377	0.297	0.351	0.096	0.525	0.150					
Pickled vegetables	0.430	0.371	0.275	0.128	0.545	0.071	0.655				
Soy sauce	0.403	0.312	0.273	0.257	0.348	0.180	0.325	0.360			
Sake	0.145	0.182	0.108	0.131	0.078	0.052	0.178	0.176	0.216		
Fresh fish	0.321	0.244	0.074	0.021	0.295	0.148	0.207	0.257	0.211	0.097	
Dried or salted fish	0.134	0.067	0.098	0.038	0.212	-0.012	0.291	0.301	0.112	0.081	-0.022

Table 4. Correlation Coefficients Between the 6 Food Items Positively Correlated to the Third Industries

Food items	Third industry	Wheat	Fat	Beef	Pork	Egg
Wheat	0.451					
Fat	0.208	0.301				
Beef	0.345	0.230	0.051			
Pork	0.197	0.290	0.443	-0.284		
Egg	0.140	0.156	0.207	0.294	0.022	
Milk	0.187	0.409	0.242	0.104	0.231	0.237

Table 5. Standardized Partial Regression Coefficients of 22 Food Consumption Variables on Stomach and Esophageal Cancer SMR

Variables	Stomach cancer		Esophageal cancer	
	Male	Female	Male	Female
Calorie ratio (observed/required)	-0.004	0.029	0.041	-0.028
Protein ratio (observed/required)	0.008	0.001	0.025	0.039
Rice	0.003	0.004	-0.127 ^a	0.036
Wheat	0.185 ^a	0.102 ^b	0.177 ^a	0.103 ^b
Potatoes	0.096 ^a	0.063	-0.049	-0.032
Sugar	-0.089 ^b	-0.099 ^b	-0.140 ^a	-0.013
Confectionery	0.035	0.082 ^b	-0.044	-0.018
Fat	0.028	0.009	0.101 ^b	0.080
Miso	-0.026	-0.082	0.160 ^a	-0.110 ^b
Tofu (soybean curd)	-0.094 ^a	-0.091 ^a	-0.030	0.020
Fruits	-0.027	-0.060	-0.003	-0.025
Green vegetables	-0.013	-0.032	-0.049	0.021
White vegetables	-0.003	0.066	0.078	0.046
Pickled vegetables	0.152 ^a	0.073	0.035	-0.028
Soy sauce	0.048	-0.039	0.013	0.141 ^a
Sake	0.048	0.018	-0.007	0.088 ^a
Fresh fish	0.092 ^b	0.058	-0.018	-0.076 ^b
Dried or salted fish	0.052	-0.026	0.091 ^a	0.069 ^b
Beef	0.135 ^a	0.144 ^a	0.044	-0.042
Pork	0.007	0.016	0.104 ^a	0.061
Egg	0.022	-0.024	-0.071 ^b	-0.015
Milk	0.003	0.004	-0.031	-0.012
R ² (%)	7.3	5.9	17.1	7.2
^a p ≤ 0.01				
^b 0.01 < p ≤ 0.05				

In order to make the relationships easier to visualize, predictor variables were selected by the backward-elimination method. The partial regression coefficients and the simple correlation coefficients of the variables remaining after the elimination for stomach cancer in males are illustrated in Figure 2. Pickled vegetables, wheat, beef, potatoes, and fresh fish have positive partial regression coefficients, while tofu has a negative partial regression coefficient. As shown in Figure 3 for females, potatoes and fresh fish were excluded from those foods with positive partial regression coefficients, but confectionery was included with a positive value and sugar was included with a negative value. The results for esophageal cancer of males and females are shown in Figures 4 and 5, respectively. Wheat, pork, and dried or salted fish and shellfish are the foods with positive partial regression coefficients for both sexes. Miso has a positive partial regression coefficient for males, but a negative coefficient for females.

One of the 3 indices of analysis, i.e., population ratio of the first industries, that of the third industries, and the income indices, was added to the food categories, and variables were selected by backward elimination. The addition of socioeconomic indices did not have a marked influence on the partial regression coefficients of food categories (see, for example, the results obtained when the population ratio of the first industries was entered as the 23rd predictor variable, shown in Table 6).

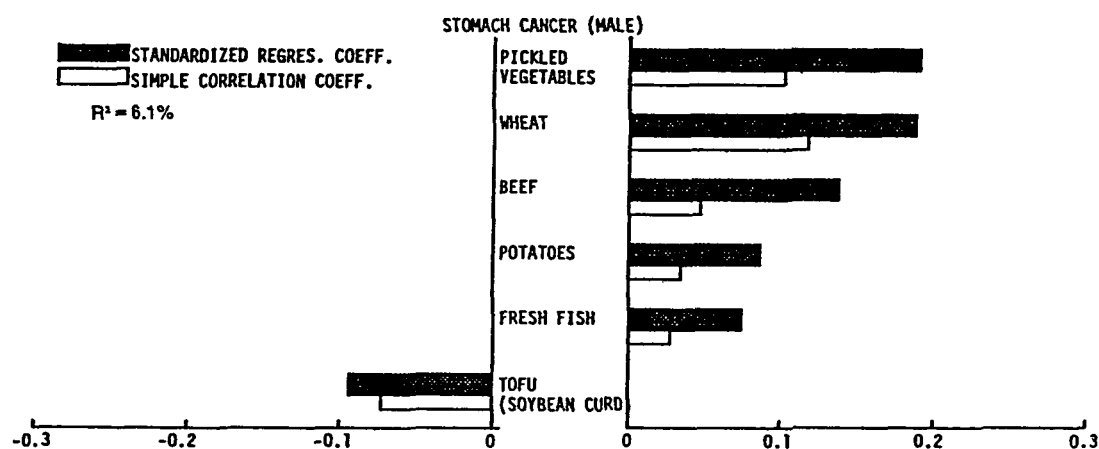


Figure 2. For stomach cancer in males, the standardized regression coefficients of the predictor variables on the SMR selected by the backward-elimination method, as compared with simple correlation coefficients.

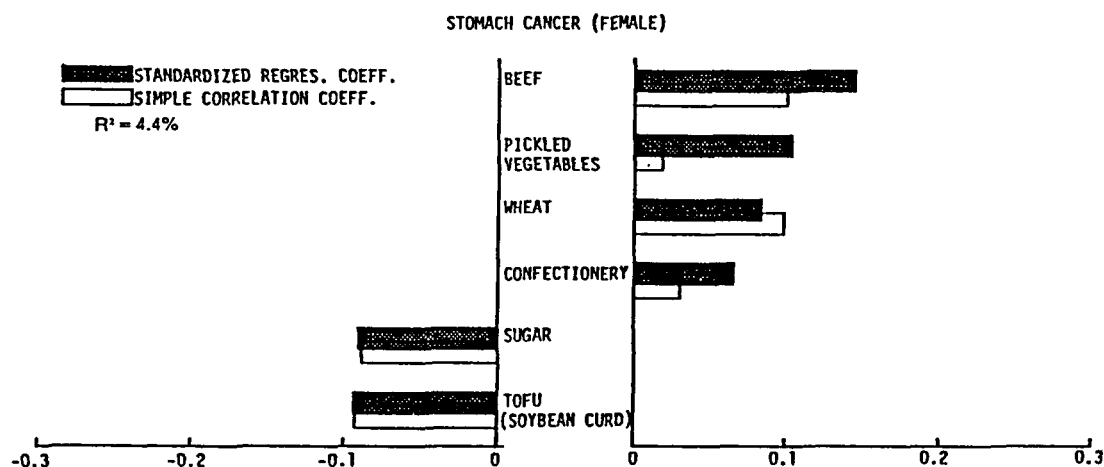


Figure 3. For stomach cancer in females, the standardized regression coefficients of the predictor variables on the SMR selected by the backward-elimination method, as compared with simple correlation coefficients.

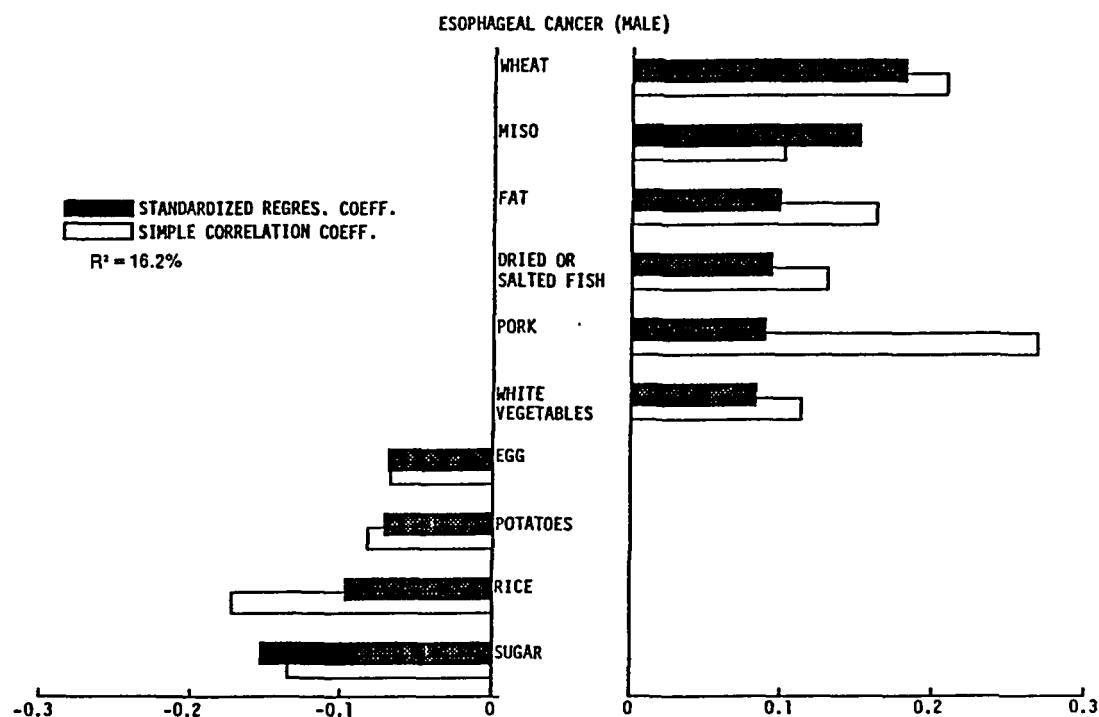


Figure 4. For esophageal cancer in males, the standardized regression coefficients of the predictor variables on the SMR selected by the backward-elimination method, as compared with simple correlation coefficients.

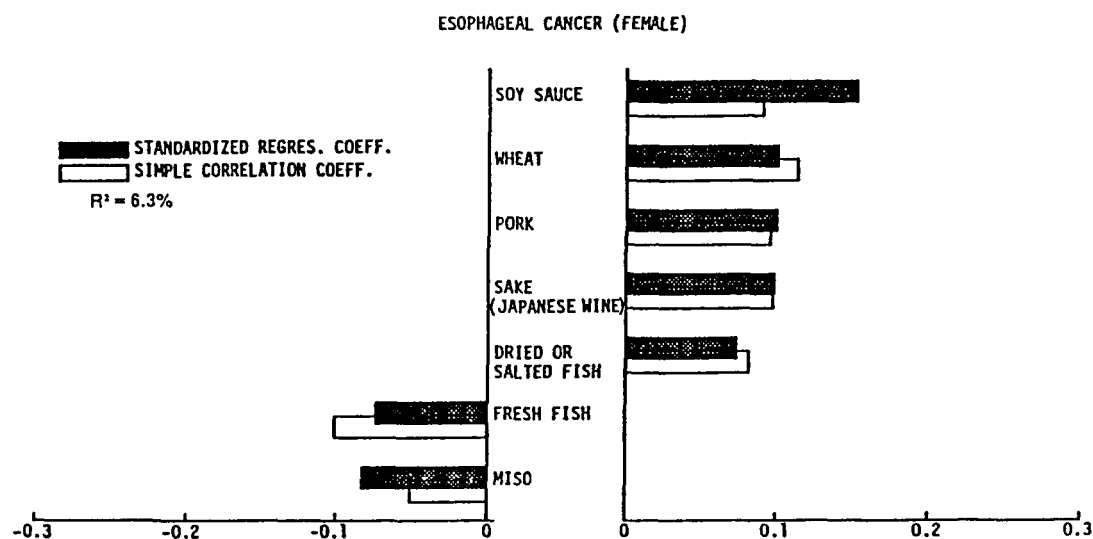


Figure 5. For esophageal cancer in females, the standardized regression coefficients of the predictor variables on the SMR selected by the backward-elimination method, as compared with simple correlation coefficients.

Table 6. Standardized Regression Coefficients of the Predictor Variables on the SMR Selected by Backward Elimination Method

Predictor variables	Stomach cancer Male		Esophageal cancer Male	
	(1)	(2)	(1)	(2)
Calorie ratio	—	—	—	—
Protein ratio	—	—	—	—
Rice	—	—	-0.097	-0.083
Wheat	0.188	0.126	0.181	0.162
Potatoes	0.087	0.108	-0.072	—
Sugar	—	—	-0.153	-0.147
Confectionery	—	—	—	—
Fat	—	—	0.098	0.101
Miso	—	—	0.151	0.173
Tofu (soybean curd)	-0.094	-0.076	—	—
Fruits	—	—	—	—
Green vegetables	—	—	—	-0.066
White vegetables	—	—	0.083	0.106
Pickled vegetables	0.191	0.226	—	—
Soy sauce	—	—	—	—
Sake	—	—	—	—
Fresh fish	0.075	0.097	—	—
Dried or salted fish	—	—	0.093	0.099
Beef	0.138	0.104	—	—
Pork	—	—	0.089	0.071
Egg	—	—	-0.069	-0.080
Milk	—	—	—	—
Population ratio of first industry	#	-0.193	#	-0.143
R ² (%)	6.1	8.3	16.2	17.3
(1): 22 food consumption variables were used as predictor variables.				
(2): Population ratio of first industry was used as 23rd predictor variable with the food variables.				
—: Variable eliminated by backward elimination method.				
#: Variable not included in the predictor variables.				

Discussion

There were about 300,000 stomach cancer deaths and 30,000 esophageal cancer deaths in Japan from 1969 to 1974, the period on which the SMR calculation of this study was based. The age-standardized mortality ratios for about 3,000 wards, cities, towns, and villages were compiled from this data.

As the total number of deaths in each municipality, especially esophageal cancer deaths, was rather small, the statistics for 6 years were accumulated. This reduced the variances of the estimated SMRs usually observed in small areas. The authors believe that the 6-year death values represent the localities of the mortality with enough confidence to make statistical observations.

The purpose of the government-conducted nationwide nutrition survey was not to evaluate the nutrition intake in small regions such as cities or towns, but rather in the whole nation. The

data for food consumption in each area, which are the result of 3 day's surveying of about 30 households, also show some variation.

Although several studies with descriptive analyses of the relationship between stomach cancer or esophageal cancer and diet in Japan have been conducted, their observations were made on prefecture levels. A nationwide observation on smaller geographical units such as towns or cities has not been conducted until now because of the difficulty of data compilation.

Food items in the nutrition survey were detailed, and those items thought to have importance in terms of cancer risk were used independently. Those thought to be less important or consumed in small amounts were categorized as larger-category items. In order to avoid large variances of data due to the small number of households observed or the brevity of the observation period, the combination of food categories with common features from the viewpoint of cancer risk was made with consideration of mutual exclusiveness with the other categories used in the analysis.

Deaths from stomach cancer correlate positively with consumption of wheat, pickled vegetables, and beef, but correlate negatively with tofu and sugar consumption. Strong correlation was observed among food items, which is one of the reasons that multiple regression analysis was performed. However, the results obtained by multiple regression analysis were almost the same as those obtained by simple correlation analysis.

The conclusive results of the above-mentioned analysis are the positive correlation of stomach cancer SMR with wheat, beef, and pickled vegetable consumption, and the negative correlation with tofu consumption. These relationships were observed for both males and females. The fact that stomach cancer is more prevalent in Japan than in European and North American countries, and that Japan has had a declining rate of stomach cancer mortality in recent years, may indicate an association between western foods and reduced cancer incidence. The positive relationship of stomach cancer SMR to beef or wheat consumption observed in this study seems to present opposite evidence. However, it is possible that western foods other than beef may relate to a reduction of stomach cancer. About half of wheat consumption is in the form of bread, while the remainder is in the form of noodles, which represent a traditional element of the Japanese diet. The relationship of stomach cancer incidence to pickled vegetable ingestion, which has already been observed by case-control studies [1-3], is concordant with this study. As pickled vegetables have a high concentration of salt (NaCl), it is interesting to consider the relationship of salt to stomach cancer. The negative relation between tofu and stomach cancer is also interesting, even though tofu is a typical Japanese food.

In summary, wheat, pork, and dried or salted fish showed positive relationships to esophageal cancer. These relationships were identical for both males and females. Other variables (i.e., miso, oil and white vegetables for males, and soy sauce and sake for females) also showed positive relationships. All these foods, except fat, showed statistically significant correlations with the SMR for 1 sex. Fat showed a positive correlation for both sexes in simple correlation analysis. Excessive drinking and smoking are considered risk factors for esophageal cancer [4], and tea-gruel and fernbrake are also suspected carcinogens [5,6]. The fact that dried fish contains a high percentage of salt may suggest a relationship of salt and esophageal cancer, as seen in the analysis of stomach cancer.

A relationship between pork consumption and esophageal cancer was also observed in the geographical study on the prefecture level. Okinawa prefecture, where diet is strongly influenced by Chinese culture, has a high esophageal cancer mortality rate for males and a high rate of pork consumption [7,8]. These facts are concordant with the results of this study. Wheat also shows a positive relationship to esophageal cancer. Further study may be needed to discover the effects on cancer incidence of westernization of the Japanese diet.

In this study, observations on the relationship between food consumption and cancer mortality were made in terms of correlation coefficients and multiple regression coefficients and the square of R (multiple correlation coefficient), which ranged from 4.4% to about 20%, too small to accurately predict the death rate based on food consumption data. Disadvantages of this

study are that the information on food consumption came from regional observation and not from the observation of individual cancer victims, and that the variances of SMR and food consumption data were rather large for the small size of the individual observation areas. It may be that the relationships of diet to cancer are actually stronger than they seemed to be under such unfavorable study conditions. This is especially true when the relationships between diet and cancer rates are consistent in both sexes.

The reason that squares of R were smaller and relationships of food to cancer were less significant in females than in males may be the lower female mortality rate and the resultant larger variances. However, esophageal cancer, which has a lower mortality rate than stomach cancer, showed significant correlation with a greater number of foods than did stomach cancer.

Two environmental factors other than diet (i.e., population ratio of the first industries and income index) showed significant relationships to cancer. However, in the multiple regression analysis the influence of these 2 factors on the relationships of foods to cancers was trivial. This observation may support the specific relationships of foods to cancer.

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