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Research Article

Exploratory correlations of dietary nutrients with prostate cancer mortality using over two decades of observations in Korea

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Prostate cancer is now the eighth leading cause of cancer mortality among Korean males. We investigated the relationship between various nutrients in the diet and prostate cancer deaths. Nutrient intake data were obtained from the Korean Nutrition Survey between 1963 and 1995 and the Korean National Health and Nutrition Examination Survey since 1998. Prostate cancer mortality rates for these time periods were obtained from the National Statistics Office. The correlations between different nutrients in the diet and mortality were calculated using Spearman's rank correlation analysis with a lag period. Carbohydrates and grains showed significant negative correlations while protein, fat, iron, and riboflavin, and the food groups including fruits, seafood, seasonings and drinks, meat, eggs, fish, and milk showed significant positive correlations. In addition, the correlation results for age-specific rates virtually coincided with the crude rate correlations. However, we urge caution in interpreting these results because they could merely be a consequence of the changing patterns of food consumption and the recording of deaths in Korea.

Keywords: Lag period / Mortality / Nutrients / Prostate cancer / Spearman's rank correlation coefficient

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1 Introduction

Prostate cancer is the third most common cancer in men globally and is more frequent in Western countries [1]. Mortality due to prostate cancer appears to be relatively low in some Oriental countries. In Korea, for example, prostate cancer deaths were very rare until 1980. The mortality rate was only 0.13 *per* 100 000 in 1983 but this rate gradually increased to 4.11 *per* 100 000 by 2006, so that prostate cancer is now the eighth most common cancer among Korean males (National Statistics Office, Vital Statistics for Causes of Deaths Analysis, 1983–2006). Between 1999 and 2002, 1589 patients on average were diagnosed annually with an incidence rate of 6.6 *per* 100 000 (National Cancer Information Center, National Cancer Center: http://www.cancer.go.kr/cms/statics/incidence/index.html#2).

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Abbreviations: FSU, final sampling units; **KNHANES,** Korean National Health and Nutrition Examination Survey; **KNS,** Korean Nutrition Survey

Some recent studies investigating the causes of prostate cancer have emphasized the importance of diet. Several studies showed that the consumption of dairy products could contribute to prostate cancer while calcium and low-fat milk in the diet were associated with a reduced risk of developing prostate cancer [2–4]. Despite the increasing mortality rate in Korea, few studies have attempted to quantitatively correlate the relationship between prostate cancer and diet. Yoon *et al.* described positive associations between prostate cancer and the consumption of milk, dairy products, and protein and fat from animals, and negative associations for the consumption of carbohydrates and grains [5].

The diets of Koreans have changed dramatically in association with the country's development and prosperity of the past few decades. Using the year 1969 as a reference standard, we compared the subsequent yearly changes in the consumption of the major food groups by Koreans and demonstrated some interesting points. The overall consumption of fat, milk, and meat have generally increased while that of vitamin A, niacin, grains, fruits, seasonings, drinks, and eggs have generally decreased during this time (Moon, H. K., Changing the method for measuring diet in the Korean National Nutrition Survey: from household to individual, unpublished).

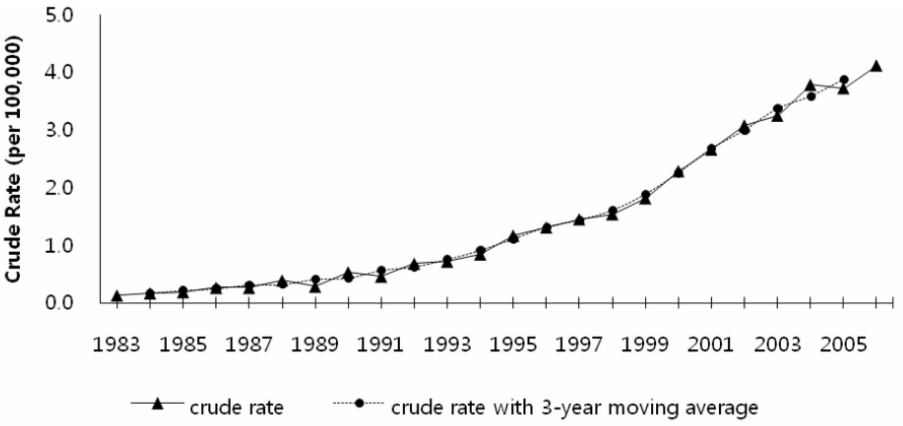


Figure 1. Yearly changes from 1983 to 2006 of calculated prostate cancer mortality rates in Korean males.

Especially with regard to the concomitant increased rate of prostate cancer in Korea, it is very interesting and important to quantitatively investigate the significance of any possible correlation between prostate cancer and diet. Therefore, the purpose of this study was to conduct an exploratory analysis to search for any association between the prostate cancer mortality rate and the general patterns of dietary change in Korea.

2 Materials and methods

2.1 Data

The Korean government has been conducting the Korean Nutrition Survey (KNS) on an annual basis since 1963. Because the survey's smallest final sampling unit (FSU) was originally the household, some of our analysis of food intake for individuals with prostate cancer was also based on individual households. Typically, a trained interviewer determined the weight of all the different foods consumed by the members of a household for two consecutive days and nutrient values were calculated using the food-composition table developed by the Rural Development Administration in Korea (Moon, H. K., Changing the method for measuring diet in the Korean National Nutrition Survey: from household to individual, unpublished). Consequently, the actual data values that we used were the average food intakes per adult household member.

After 1995, the nutrition survey was merged with the existing health interview survey and enforced to become the Korean National Health and Nutrition Examination Survey (KNHANES), which have been conducted every 3 years since 1998. Additionally, since 1998, the survey's smallest FSU was changed to the individual with a 24 h recall method, so that more precise individual correlations with prostate cancer became possible. Consequently, we used the total household intake data until 1995, after 1998; however, we were able to consider the implications of age and sex with regard to food intake and prostate cancer [6].

The National Statistics Office (NSO) collects all of the vital events with deaths due to prostate cancer and publishes them annually (National Statistics Office, Vital Statistics for Causes of Deaths Analysis, 1983–2006). Using these statistics, the denominator for the total population was obtained by interpolation between the population censuses or directly from civil registration data, and the mortality rates were calculated *per* 100 000 persons (Fig. 1). Based on the incidence data, which are available only for recent years, it appears that prostate cancer has a relatively high survival rate, but generally, the statistics suffer from some inaccuracy and incompleteness. However, the 5-year survival rate for prostate cancer was 59.1 between 1993 and 1997 and improved to 70.6 between 1998 and 2002 (National Cancer Information Center, National Cancer Center: http://www.cancer.go.kr/cms/statics/incidence/index.html#2).

2.2 Statistical analysis

After obtaining the mortality and food intake data, we searched for correlations between the intake of each nutrient and prostate cancer mortality. Initially, an analysis was performed to search for associations between food intake and crude mortality rates. Subsequently, analysis was refined to examine associations between food intake and prostate cancer deaths for specific age categories.

Since our period of observation covered more than 20 years, we made use of two different measures prior to analyzing the associations. The first measure was to use a 3-year moving average that was retained throughout the analysis, to detrend the cancer death rates and the food intake data over years. The second was to adopt a lag period. We used lag periods of 5, 10, and 15 years. The lag period of 0 year was omitted because we are interested in whether accumulated food consumption may a cause of prostate cancer. For each meaningful lag period, we examined correlations between the crude death rates and the intake of each nutrient. Finally, we applied the corresponding age-specific death rates and food intake for each lag

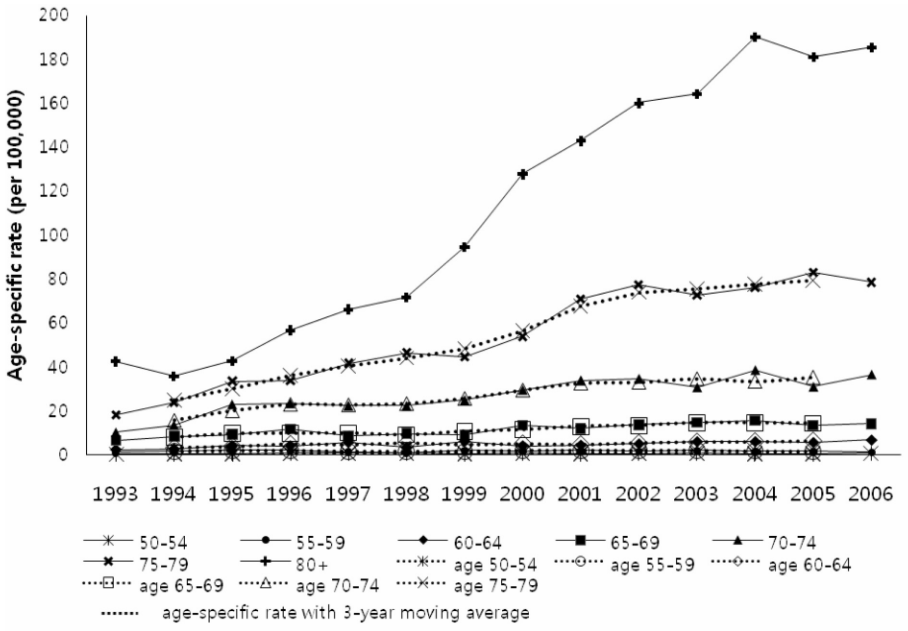


Figure 2. Trends in the incidence of prostate cancer for different age groups from 1993 to 2006.

period. Since the mortality rates and food intake data were appropriate for a nonparametric approach, Spearman's rank correlation coefficients were calculated.

3 Results

3.1 Incidence of prostate cancer in Korea

The prostate cancer death rate was 0.132 *per* 100 000 in 1983, and has increased rapidly since that time with remarkably similar crude and 3-year moving average death rates as represented in Fig. 1 by the solid and dotted lines, respectively. The rate tripled between 1983 and 1988, tripled again by 1996, and more than tripled yet again between 1996 and 2006 to 4.11 *per* 100 000. However, mortality from prostate cancer is low relative to lung cancer, which is regarded as one of the most common cancers of Korean males and for which the rate is more than ten-fold higher at 41.6 *per* 100 000 (National Statistics Office, Vital Statistics for Causes of Deaths Analysis, 1983–2006).

The temporal changes of the crude (solid line) and 3-year moving average (dotted line) prostate cancer death rates as a function of age indicate generally low rates below 60 years of age and dramatically increased rates over 70 years of age, a trend particularly evident since the year 2000 (Fig. 2).

3.2 Correlation of crude prostate cancer death rates

Table 1 shows the correlation coefficients calculated using the 3-year moving average mortality rates and lag periods of 5, 10, or 15 years, with each of the various consumed nutrients that were analyzed. Energy, carbohydrates, and grains exhibited significantly strong negative correlations for each lag period. In contrast, strong positive correlations were observed for protein, fat, iron, and riboflavin. Additionally, the food groups including fruits, seafood, seasonings, and drinks, meat, eggs, fish, and milk exhibited significant positive correlations for all lag periods. However, vitamin A, niacin, and beans showed significant negative correlations for the 5-year lag but significant positive correlations for the 15-year lag, whereas the nutrients calcium and vitamin C showed significant positive correlations for the 5-year lag but significant negative correlations for the 15-year lag. Finally, the vegetable and animal fat nutrients exhibited strong positive correlations with the prostate cancer mortality rate only for the 5- and 10-year lag periods.

3.3 Correlation of age-specific prostate cancer death rates

Because of the two general trends that food intake decreased and prostate cancer mortality increased with increase in age, we controlled for age-related negative correlations of nutrient intakes with cancer death rates by considering the same age groups over the years. Spearman's correlation coefficients for the various nutrients and death rates were displayed only for the group above 60 years of age because the cancer death rates were very low in the group below 60 years of age and the correlation patterns were rather irregular for the younger group (Table 2). In addition, lags up to 15 years were analyzed. Variability made it very difficult to draw any meaningful conclusions despite the presence of some consistent results. Generally, the results for the 5-year lag were less informative. Virtually

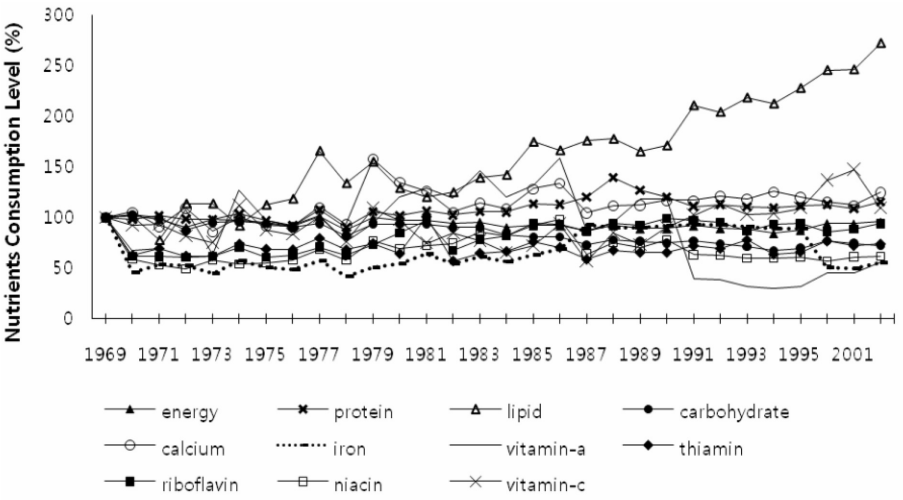
Table 1. Correlation of prostate cancer with food intake by nutrient categories and lag years

Lag years	Energy	Protein	Fat	Carbohydrate	Calcium	Iron	Vit_a	Thiamin	Riboflavin
5	**–0.95**	**0.64**	**0.94**	**–0.97**	–0.25	**0.91**	**–0.70**	–0.20	**0.83**
10	**–0.88**	**0.83**	**0.92**	**–0.95**	0.34	**0.92**	–0.29	–0.29	**0.92**
15	**–0.79**	**0.85**	**0.91**	**–0.93**	**0.56**	**0.73**	**0.61**	–0.19	**0.92**

Lag years	Niacin	Vit_c	Grains	Beans	Potatoes	Vegetables	Fruits	Seafood	
5	**–0.54**	0.42	**–0.99**	**–0.57**	–0.05	0.11	**0.95**	**0.99**	–
10	0.19	0.12	**–0.98**	0.08	–0.34	0.25	**0.90**	**0.83**	–
15	**0.72**	**–0.65**	**–0.98**	**0.54**	–0.29	–0.13	**0.78**	**0.75**	–

	Lag years	Seasonings and drinks	Vegetable fat	Meat	Egg	Fish	Milk	Animal fat	
5	**0.72**	**0.78**	**0.97**	**0.90**	**0.69**	**0.99**	**0.75**	–	–
10	**0.72**	**0.88**	**0.97**	**0.94**	**0.86**	**1.00**	0.10	–	–
15	**0.44**	0.38	**0.97**	**0.72**	**0.95**	**0.95**	–0.43	–	–

Note: Bold font indicates significant correlation coefficients ($p < 0.05$).



Source : Korean National Health and Nutrition Examination Survey[7)]

Figure 3. Nutrient intake levels from 1969 to 2002 (all data are displayed relative to 100% for 1969).

consistent negative correlations were observed between the prostate cancer death rate and energy, niacin, grains, and beans. In contrast, positive correlations were observed for protein, riboflavin, iron, and potatoes and also for the food groups including fruits, seafood, seasonings, and drinks, meat, eggs, fish, milk, and both vegetable and animal fat.

In general, the correlation results for age-specific rates coincided with the crude rate correlations. In particular, vitamin A, niacin, and beans exhibited consistent positive correlations. All of the negative correlations were most significant using the 10-year lag period and the positive correlations were most significant using the 15-year lag period with the exception of riboflavin, seafood, and seasonings and drinks, which were most significant using the 10-year lag period.

4 Discussion

Several important considerations should be taken into account for this study. Until 1990, the accuracy of Korean vital statistics has been somewhat problematic because of incomplete death registrations and unknown causes of death, particularly among the most elderly. Recently, however, accuracy has improved dramatically, with the causes for the majority of elderly deaths properly recorded. Based

Table 2. Correlation of prostate cancer with food intake by age-groups and lag years

Age (years)	Lag years	Energy	Protein	Vit_a	Thiamin	Riboflavin	Niacin	Ascorbic acid	Calcium
60–64	5	–0.87	–0.50	**–1.00**	0.50	–0.50	**–1.00**	**1.00**	**1.00**
	10	–0.02	0.62	–0.60	0.17	0.67	–0.55	0.21	–0.12
	15	–0.60	0.36	0.10	–0.55	0.55	0.25	–0.50	–0.08
65–69	5	–0.87	–0.50	**–1.00**	0.50	–0.50	**–1.00**	**1.00**	**1.00**
	10	**–0.87**	0.07	–0.38	0.31	0.52	**–0.81**	**0.93**	0.33
	15	–0.53	**0.96**	0.04	0.09	**0.92**	0.28	**–0.75**	–0.05
70–74	5	–0.87	–0.50	**–1.00**	0.50	–0.50	**–1.00**	**1.00**	**1.00**
	10	–0.68	0.26	–0.64	0.17	**0.79**	**–0.95**	**0.81**	0.05
	15	**–0.70**	**0.90**	0.16	–0.19	**0.84**	0.37	**–0.81**	–0.12
75–79	5	–0.87	–0.50	**–1.00**	0.50	–0.50	**–1.00**	**1.00**	**1.00**
	10	**–0.83**	0.29	**–0.71**	0.12	**0.93**	**–0.98**	**0.88**	0.00
	15	**–0.71**	**0.94**	0.19	–0.20	**0.83**	0.39	**–0.82**	–0.14

Age (years)	Lag years	Iron	Grains	Beans	Potatoes	Vegetables	Fruits	Seafood	Seasonings and drinks
60–64	5	**1.00**	**1.00**	–0.50	–0.50	**1.00**	**1.00**	**1.00**	**1.00**
	10	0.57	–0.67	**–0.76**	0.07	–0.14	0.19	0.57	0.55
	15	0.44	–0.49	0.19	**0.73**	–0.10	**0.65**	**0.72**	0.07
65–69	5	**1.00**	**1.00**	–0.50	–0.50	**1.00**	**1.00**	**1.00**	**1.00**
	10	**0.86**	0.00	–0.40	–0.64	0.67	**0.74**	**0.86**	**0.81**
	15	**0.79**	**–0.83**	0.12	**0.83**	0.01	**0.77**	**0.96**	0.19
70–74	5	**1.00**	**1.00**	–0.50	–0.50	**1.00**	**1.00**	**1.00**	**1.00**
	10	**0.98**	–0.21	**–0.71**	–0.52	0.55	**0.76**	**0.98**	**0.95**
	15	**0.73**	**–0.82**	0.22	**0.94**	0.18	**0.84**	**0.96**	0.07
75–79	5	**1.00**	**1.00**	–0.50	–0.50	**1.00**	**1.00**	**1.00**	**1.00**
	10	**1.00**	–0.40	**–0.76**	–0.50	0.52	0.64	**1.00**	**0.98**
	15	**0.76**	**–0.85**	0.24	**0.92**	0.14	**0.87**	**0.99**	0.01

Age (years)	Lag years	Vegetable fat	Meat	Egg	Fish	Milk	Animal fat		
60–64	5	**1.00**	**–1.00**	**–1.00**	**–1.00**	**–1.00**	–0.50	–	–
	10	0.33	0.31	0.05	0.02	0.45	0.26	–	–
	15	0.52	**0.64**	0.49	**0.75**	**0.77**	**0.63**	–	–
65–69	5	**1.00**	**–1.00**	**–1.00**	**–1.00**	**–1.00**	–0.50	–	–
	10	**0.88**	–0.48	–0.57	–0.60	–0.33	–0.38	–	–
	15	**0.82**	**0.81**	**0.76**	**0.92**	**0.90**	**0.85**	–	–
70–74	5	**1.00**	**–1.00**	**–1.00**	**–1.00**	**–1.00**	–0.50	–	–
	10	**0.79**	–0.33	–0.60	–0.60	–0.19	–0.19	–	–
	15	**0.88**	**0.89**	**0.84**	**0.98**	**0.98**	**0.84**	–	–
75–79	5	**1.00**	**–1.00**	**–1.00**	**–1.00**	**–1.00**	–0.50	–	–
	10	0.52	–0.31	–0.62	–0.64	–0.17	–0.17	–	–
	15	**0.89**	**0.92**	**0.87**	**0.99**	**0.99**	**0.89**	–	–

Note: Bold font indicates significant correlation coefficients ($p < 0.05$).

on this pattern of events, the argument could be made that the variations made in recording the causes of death over the years could themselves be responsible for increased cancer death rates. However, while we point out and acknowledge the plausibility of this argument, we believe that a real increase in cancer deaths is occurring unrelated to any possible bias caused by inconsistent data recording.

The measurement of food intake in Korea has been recorded primarily during two distinct phases. Between 1969 and 1995, the KNS recorded food intake data; subsequently, the KHANES recorded food intake data every 3 years since 1998. The KNS initially sampled 1 000 and later 2 000 separate households using month-long recording periods between August and November and household-based food consumption diaries. Although the KNS had some limitations, the KNS data are the only national data available for statistical analysis. The most important consideration regarding this study is that due to the household-based method of the KNS, we could only determine the average food intake level for an individual between 1969 and 1995. The KHANES study, however, adopted a 24 h recall method and food frequency to determine food intake by single individuals. Despite the dramatic change in the smallest FSU from the household to the individual, the overall food intake of the general Korean population was not very different (Fig. 3). This is the primary reason that we decided to use the overall food measurement data to search for possible correlations with prostate cancer death rates.

The World Cancer Research Fund International (WCRF) and the American Institute for Cancer Research (AICR) summarized factors that modify the risk of prostate cancer [7]. Decreased risks were associated with the consumption of foods containing lycopene and selenium such as legumes, while foods containing alpha-tocopherol (vitamin E) were regarded as being limited/suggestive. Increased risk was associated with diets high in calcium while processed meats, milk, and dairy products were considered limited-suggestive. No conclusions were made, however, regarding many other important nutrients such as grains, potatoes, fruits, meats, fish, poultry, and eggs. We obtained some results that were consistent with those of previous studies. The negative correlation of beans in this study was consistent with Heald *et al.* [7] and Lee *et al.* [8], while the positive correlations of calcium, meat, milk, and dairy products were consistent with the findings of others [2–4, 9–11].

The negative correlation of the death rate with energy was interesting because decreased food consumption occurred simultaneously with increased cancer rate. This was true for every age group. When total food consumption decreased, certain key nutrients either decreased or increased significantly. Therefore, it was suggested that the correlations might be interpreted as a result of the food consumption pattern changing over time. For example, the negative correlation of carbohydrate and the positive correlations of protein and fat represented the most typical food consumption changes observed for Koreans during several decades.

The recent increased prostate cancer death rate could be related to the recent increased consumption of milk, meats, and fats. However, because the effect seems to be most prominent in the older age groups and the below60 age groups exhibited much lower deaths rates, we could determine more informative results by examining the incidence rate rather than the mortality rate for prostate cancer.

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The authors have declared no conflict of interest.

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