RESEARCH COMMUNICATION

Correlation between Food Consumption and Colorectal Cancer: An Ecological Analysis in Japan

Chun-Xia Yang[1,2], Tetsuo Kuroishi[1], Xin-En Huang[1], Manami Inoue[1], Kazuo Tajima[1]

Abstract

Objectives: **Incidence rates for colorectal cancer are universally high in western countries while values in the orient are very variable. Japan is one of the oriental countries with a high incidence but any association with food components remains to be clarified. To explore specific nutrient effects on risk of colorectal cancer in Japan, we here conducted a correlation analysis between change in the diet and incidence rates.**

Methods: **Incidence data for 1976-1996 and national values for per capita daily food nutrient intake in 1956-1995 were used. We first analyzed chronological changes of food nutrients and colorectal cancer, and then calculated correlation coefficients with time lags of 5, 10, 15 or 20 years. To adjust for the confounding effects of total energy, we also performed a partial correlation analysis.**

Results: **Incidences of colorectal cancer gradually increased during 1976-1996 with the highest incidence rates for colon and rectal cancers, 25.31 and 13.75 per 100,000, respectively, in 1996. Food nutrient intake also demonstrated major variation during 1956-1995, total fats and oils increasing most, followed by animal protein and animal fats. Incidences of colorectal cancer were positively associated with fat and oil intake, of both plant and animal types; a positive link was noted with animal protein but the association with plant protein consumption was inverse, as was also the case for carbohydrate and cereals; no simple association was evident with total energy intake.**

Conclusions: **Food nutrients play roles in risk of colon and rectal cancers. Lower animal protein and fat intake, and higher carbohydrate and cereal consumption might reduce the risk of colon and rectal cancers.**

Key Words: food nutrients - colorectal cancer - correlation

Asian Pacific J Cancer Prev, **3**, 77-83

Introduction

Colorectal cancer is the fourth most common cancer in the world (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997), and its incidence rate appears to be increasing in almost all countries. With regard to geographical variation, developed countries generally show greater incidences than developing countries and urban populations have higher values than their counterparts in rural areas (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997; Parkin et al., 1997; Tajima et al., 1985). Immigrant and chronological studies suggest that such variation is due mainly to change in environmental exposure (Danna et al., 2000; Whittemore et al., 1985; Doll and Peto, 1981). For example, foods and nutrients are important environmental factors that can modify risk of colorectal cancer (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997; Tajima et al., 1985; Doll and Peto, 1981). However, actual effects of specific foods on risk of colorectal cancer are still not very clear. Most previous studies have dealt with specific food items, each of which contains a variety of nutrients. The approach adopted for the present study was to focus on nutrients themselves.

Incidence rates for colorectal cancer are universally high in western countries but vary greatly in the orient (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997). Japan is one of the oriental countries with a high prevalence, mortality rates

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obviously fluctuating with time (Tominaga et al., 1999). Change in dietary habits has also been obvious (Ministry of Health and Welfare, 1956-1995). Therefore a correlation analysis between food nutrients and colorectal cancer risk in Japan during this period might be expected to provide some clues to effects of specific food types.

For this purpose the time lag between exposure and tumor development must naturally be taken into account. In one previous analysis, the statistically estimated time lag was approximately 10 years with a range of 4-16 years (Tominaga and Kato, 1990). Therefore, we here used data for 1976-1996 colorectal cancer incidences and 1956-1995 food intake (values for animal fats, plant oils, percentage of energy supplied by cereals and percentage of animal proteins were absent for 1956-1965; data for iron were also lacking in 1964-1970) to describe chronological changes and analyze correlation coefficients with time lags of 5 years, 10 years, 15 years or twenty years.

Materials and Methods

1) National Nutritional Survey

The Ministry of Health and Welfare of Japan has conducted a National Nutritional Survey every year since 1946 to estimate the nutritional status of the Japanese. In this survey, about 15,000-20,000 members from 5000-6000 households sampled from 300 regional health centers have been interviewed in mid-November every year since 1972. Information on food consumption was collected on three consecutive days (avoiding weekends and festivals) by interviewing sample households, with names of food materials and weights, cooking information and leftover diet filling into special questionnaires (Ministry of Health and Welfare, 1956-1995). All the data are summarized at the Statistics and Information Department, Ministers Secretariat, Ministry of Health and Welfare.

2) Cancer Statistics

Data for age-adjusted incidence rates of colorectal cancer by sex in 1976-1996 were collected from the research group for population based cancer registration (The Research Group for Population-based Cancer Registration in Japan, 2001); data of Japanese male and female numbers in 1976-1996 was collected from Journal of health and welfare statistics (Health and Welfare Statistics Association, 1977-1997). Total age-adjusted incidence rates of colon and rectal cancers in 1976-1996 were calculated by using male proportion time male age-adjusted incidence rate plus female proportion time female age-adjusted incidence rate annually.

3) Statistical Analysis

All data were analyzed with the SPSS PC software package, version 10 (SPSS Inc.). Following a descriptive analysis, 4 sets of correlation coefficients were separately calculated between food nutrients and colon and rectal cancers with a 5, 10, 15 or 20 years time lag. To adjust for the confounding effects of total energy, we also performed a partial correlation analysis.

Results

1.Chronological Change in Food Nutrient Intake and Colorectal Cancer Incidence:

Incidences gradually increased during 1976-1996 with the highest rates for colon and rectal cancers, of 25.31 and 13.75, respectively, in 1996 (Table 1, Figure 1). Food nutrient intake also demonstrated large variation during 1956-1995 (Table 1). Among food nutrients, total fats and oils increased most, followed by animal protein and animal fats (Figure 2, Figure 3). Total fats and oils, animal protein, calcium and animal fats obviously increased during 1956-1976, thereafter demonstrating little change (Figure 2, Figure 3). Plant protein consumption decreased gradually during 1956-1995. Up

Table 1. Variation in Colorectal Cancer Incidence Rate (1976-1996) and Food Nutrient Intake (1956-1995)

	Minimum	Maximum	Mean	SD
Incidence Rates for Colorectal Cancers:				
Colon Cancer Incidence (1/100,000 person-years)	7.84	25.31	15.95	5.94
Rectal Cancer Incidence (1/100,000 person-years)	7.33	13.75	10.94	2.01
Food Nutrient Intake:				
Total Energy (Kcal)	2023	2287	2135	74.7
Total Protein (g)	69.1	84.1	77.1	4.3
Animal Protein (g)	22.6	44.4	35.7	6.8
Plant Protein (g)	37.1	46.5	41.5	3.1
Total Fats and Oils (g)	21.8	59.9	47.3	13.0
Animal Fats and Oils (g)	17.8	29.8	26.4	3.3
Plant Oils (g)	21.9	30.6	28.0	2.7
Carbohydrate (g)	280	406	304.2	44.9
Calcium (mg)	379	585	510.3	64.3
Iron (mg)	10.4	16.0	12.0	1.5
Energy supplies from cereals (%)	40.7	61.8	49.1	4.7
Protein supplies from animal (%)	39.2	54.5	49.1	3.9

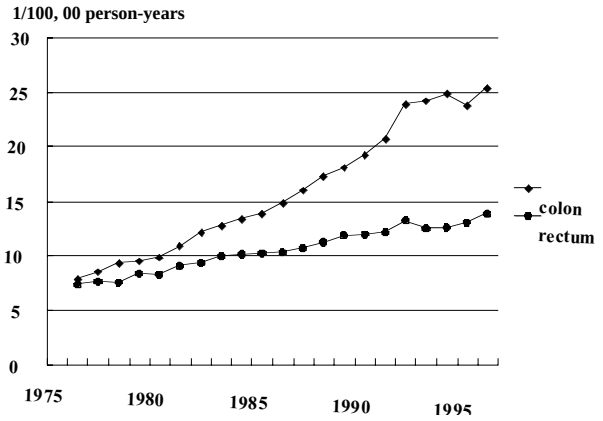

Figure 1. Estimated Incidence Rates of Colon and Rectal Cancers (1976-1996) in Japan

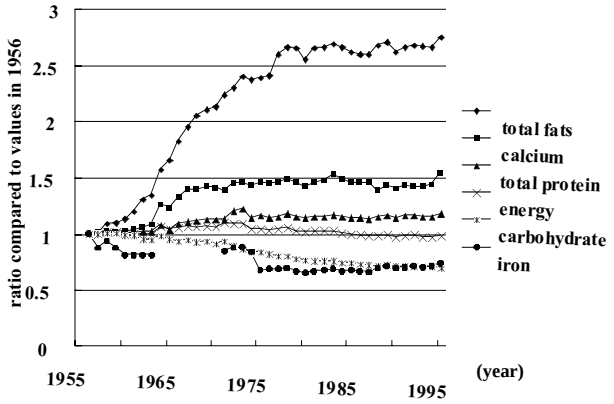

Figure 2. Chronological change in intake of food nutrients (1956-1995) in Japan

until 1970, energy intake increased, and then decreased gradually. Total protein consumption only increased slightly (Figure 2).

2. Univariate Correlation Coefficients:

Total energy was inversely associated with colon and rectal cancers with a 5 or 10 year time lag, but exhibited positive association with a 20 year time lag; animal protein, total fats and oils, animal fats and oils and percentage of protein supplies from animal were always positively associated with incidences of colon and rectal cancers; plant protein, carbohydrate and percentage of energy supplies from cereals demonstrated inverse associations. Findings for calcium, iron, plant oils and total protein are listed in Tables 2 and 3.

3. Partial Correlation Coefficients:

Partial correlation coefficients after adjusting for total energy are given in Tables 4 and 5. Incidences of colon and rectal cancers exhibited good correlations with food nutrients with a 15 year time lag; total protein, animal protein, total fats and oils, animal fats and oils, plant oils, calcium and percentage of proteins from animal sources demonstrated positive associations; plant protein, carbohydrate and percentage of energy supplies from cereals were inversely associated with incidences; iron demonstrated no obvious correlation.

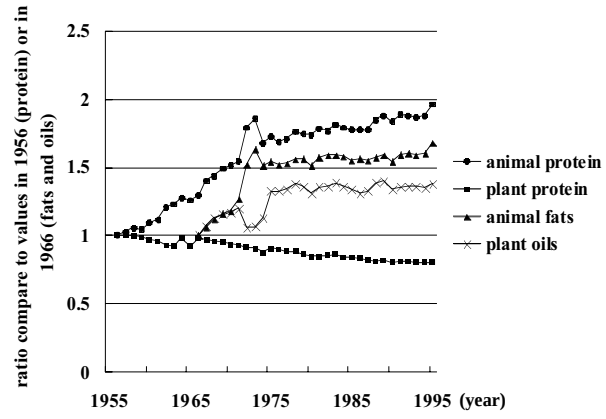

Figure 3. Chronological change in protein (1956-1995) and fat (1966-1995) supplied by animals and plants in Japan

Discussion

Most previous studies on food and colorectal cancer have dealt with individual food items but it can be argued that attention should be concentrated on specific nutrients directly. In the present study the results suggested that previous food nutrient intake had a particularly strong association with incidence rates of colorectal cancer after a 15 year time lag (Table 2-5). Our data thus indicate that a high carbohydrate intake and high proportion of energy supplies from cereals are inversely associated with colorectal cancer, even after adjustment for total energy. One cohort study in a male population in the USA similarly found a high carbohydrate intake to confer a lower risk of colorectal adenomas (Giovannucci et al., 1992), and 3 case-control studies gave concordant results (Hoff et al.,1986; Neugut et al., 1993; Sandler et al., 1993). However, two more recent case-control studies (Slattery et al., 1997; Ghadirian et al., 1997) and one prospective study (Kato et al., 1997) of 14,727 women found no relation. While protective effects of carbohydrate intake on cancer risk are therefore inconsistent, high amounts of non-digestible carbohydrates have been concluded to have preventive potential (Scheppach et al., 2001). The possible mechanisms are: (a) degradation in the colon by anaerobic bacteria increases fecal nitrogen excretion in a process called fermentation, giving rise to short chain fatty acids evaluated as new therapeutics for acute colitis (Scheppach et al., 2001); (b) low-digestible carbohydrates are trophic to the colonic epithelium, and hinder bacterial translocation (Scheppach et al., 2001); (c) non-fermented carbohydrates increase fecal bulk and may prevent chronic functional constipation and the irritable bowel syndrome (Scheppach et al., 2001).

Table 2. Correlation Coefficients between Colon Cancer (1976-1996) and Intake of Food Nutrient with Five, Ten, Fifteen and Twenty Years' Time-lag (1956-1991)

	5 years	10 years	15 years	20 years
Total Energy	-0.92**	-0.83**	0.01	0.72**
Total Protein	-0.29	0.34	0.75**	0.94**
Animal Protein	0.67**	0.75**	0.89**	0.99**
Plant Protein	-0.95**	-0.94**	-0.86**	-0.83**
Total Fats and Oils	0.75**	0.89**	0.93**	0.97**
Animal Fats and Oils	0.44*	0.76**	0.83**	##
Plant Oils	0.61**	0.81**	0.87**	##
Carbohydrate	-0.91**	-0.96**	-0.98**	-0.95**
Calcium	-0.12	0.75**	0.77**	0.92**
Iron	0.52*	-0.71**	##	##
Energy supplies from cereals %	-0.88**	-0.87**	-0.94**	##
Protein supplies from animal %	0.89**	0.85**	0.86**	##

#: Pearson correlation coefficients, 2-tailed test.
*: P<0.05; **: P<0.01; ##: data absent

The present study suggested that incidences of colon and rectal cancers were positively associated with total protein, especially with animal protein, and inversely associated with plant protein. Recently, some animal experiments suggested that soybean, one plant protein, might reduce risk for colorectal cancer (Azuma et al., 2000; Wang and Higuchi, 2000). Up to now, at least eight case-control studies found high total protein intake to be associated with increased risk of colorectal cancer (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997; Benito et al., 1991), notably animal protein (Benito et al., 1991). Because animal protein is the main component of meat, especially of red meat, our results support the hypothesis that increased consumption of red meat causes an increased incidence of colon and rectal cancer, consistent with much previous research (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997; Norat and Riboli, 2001; Ogimmoto et al., 2000; Zhuo and Watanabe, 1999; Levi et al., 1999; Hsing et al., 1998; Koo et al., 1997; Tominaga and Kuroishi, 1997). In the book of Food, Nutrition and the Prevention of Cancer: a global perspective (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997), the panel reached the conclusion that consumption of diets high in red meat probably increases the risk of colorectal cancer. In a recent review of the epidemiological evidence on colorectal cancer risk and meat consumption from 32 case-control and 13 cohort studies published in English from 1970 to 1999 and retrieved from the Medline database, the results also supported the hypothesis that meat consumption is associated with a modest increase in colorectal cancer risk (Norat and Riboli, 2001).

Table 3. Correlation Coefficients between Rectal Cancer(1976-1996) and Intake of Food Nutrient with Five, Ten, Fifteen and Twenty Years' Time-lag (1956-1991)

	5 years	10 years	15 years	20 years
Total Energy	-0.95**	-0.79**	0.13	0.74**
Total Protein	-0.36	0.42	0.81**	0.92**
Animal Protein	0.62**	0.82**	0.92**	0.96**
Plant Protein	-0.96**	-0.97**	-0.80**	-0.82**
Total Fats and Oils	0.81**	0.93**	0.97**	0.97**
Animal Fats and Oils	0.45**	0.84**	0.85**	##
Plant Oils	0.69**	0.81**	0.84**	##
Carbohydrate	-0.95**	-0.97**	-0.95**	-0.92**
Calcium	0.005	0.75**	0.85**	0.94**
Iron	0.31	-0.32	##	##
Energy supplies from cereals %	-0.86**	-0.95**	-0.94**	##
Protein supplies from animal %	0.87**	0.91**	0.88**	##

#: Pearson correlation coefficients, 2-tailed test.
*:P<0.05; **: P<0.01; ##: data absent

Table 4. Partial Correlation Coefficients between Colon Cancer Incidences (1976-1996) and Corresponding Food Nutrient Intake with Five, Ten, Fifteen and Twenty Years' Time-lag (1956-1991)

	5 years	10 years	15 years	20 years
Total Protein	0.52*	0.79**	0.92**	0.90**
Animal Protein	0.54*	0.82**	0.94**	0.97**
Plant Protein	-0.60**	-0.85**	-0.90**	-0.88**
Total Fats and Oils	0.22	0.86**	0.99**	0.96**
Animal Fats and Oils	0.08	0.77**	0.88**	##
Plant Oils	-0.14	0.57**	0.78**	##
Carbohydrate	-0.19	-0.86**	-0.99**	-0.98**
Calcium	-0.05	0.81**	0.93**	0.86**
Iron	0.47*	0.07	##	##
Energy supplies from cereals (%)	-0.24	-0.81**	-0.95**	##
Protein supplies from animal (%)	0.60**	0.84**	0.90**	##

#: Adjusted by total energy; Pearson correlation coefficients, 2-tailed test.
*: P<0.05; **: P<0.01; ##: data absent

Another article covering 43 relevant papers including data from Japan searched by the MEDLINE for the period 1966 through 1997 also find that in general population, consumption of meat is probably a risk factor of colorectal cancer (Ogimmoto et al., 2000).

The present research also suggested that fats and oils both from animals and plants are positively associated with risk of colon and rectal cancers. A number of previous studies found that animal fats might be a risk factor of colorectal cancer (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997; Favro et al., 1999; Franceschi 1999; Franceschi and Favero, 1999; Willett et al., 1990). A prospective study among 88,751 women with 150 incident cases of colon cancer in 1980-1986 revealed animal fat to be positively associated with the risk (P for trend = 0.01); the relative risk for the highest as compared with the lowest quintile was 1.89 (95 percent confidence interval, 1.13 to 3.15) (Willett et al., 1990). On the other hand, combined analysis of data from 13 case-control studies of 5,287 cases and 10,470 controls previously conducted in populations with different colorectal cancer rates and dietary practices found no evidence of any energy-independent effect of either total fat or saturated fat on colorectal cancer (Howe et al., 1992). While the epidemiological data are equivocal, many experimental studies in animals and humans have indicated that fat influence the colonic concentrations of fecal diacylglycerols (DAGs), known to be activators of protein kinase C (PKC), which in turn can modulate colonic epithelial cell growth and therefore play a role in malignant transformation (Pickering et al., 1995). Guillem and Weinstein have proposed that interactions of fat, bile acids and bacteria produce excess intraluminal diacylglycerol, which may mimic and amplify cell-replication signals (Guillem and Weinstein,1990). Considering all the epidemiological and experimental evidence, a conclusion that fats may increase

Table 5. Partial Correlation Coefficients between Rectal Cancer Incidences (1976-1996) and Crresponding Food Nutrient Intake with Five, Ten, Fifteen and Twenty Years' Time-lag (1956-1991)

	Five years	Ten years	Fifteen years	Twenty years
Total Protein	0.42	0.86**	0.92**	0.81**
Animal Protein	0.42	0.90**	0.94**	0.92**
Plant Protein	-0.52*	-0.93**	-0.89**	-0.88**
Total Fats and Oils	0.47*	0.92**	0.99**	0.95**
Animal Fats and Oils	0.12	0.88**	0.91**	##
Plant Oils	0.11	0.60**	0.72**	##
Carbohydrate	-0.44	-0.93**	-0.98**	-0.95**
Calcium	0.32	0.77**	0.95**	0.89**
Iron	0.11	0.07	##	##
Energy supplies from cereals %	-0.38	-0.90**	-0.96**	##
Protein supplies from animal %	0.47*	0.92**	0.98**	##

#: Adjusted by total energy; 2-tailed test.
*: P<0.05; **: P<0.01; ##: data absent

risk of colorectal cancer appears warranted.

The present study provided some evidence that calcium intake is positively associated with colorectal cancer, in disagreement with earlier findings (World Cancer Research Fund in Association with the American Institute for Cancer Research, 1997). The link may thus be spurious because calcium intake was correlated with levels of other food nutrients so that confounding is conceivable. Our study found no association between iron and colorectal cancer.

As discussed above, colorectal cancer appears to be positively associated with high consumption of animal protein, fats and oils; and inversely associated with carbohydrate, plant protein and the proportion of energy supplied by cereals. Appropriate food intake should thus allow some percentage of colorectal cancers to be avoided. Further well-designed research is now necessary for verification and to develop effective intervention strategies.

Acknowledgments

This study was supported in part by a Grant-in Aid for Scientific Research on Cancer Epidemiology in a Special Priority Area (c) (Grant no. 12670383) from the Ministry of Education, Science, Sports, Culture and Technology of Japan. The first author is supported by the Japan-China Sasakawa Medical Fellowship.

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