

Colon Cancer Risk Factors in Jiashan County of Zhejiang Province, the Highest Incidence Area in China

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OBJECTIVE To investigate the risk factors of colon cancer in Jiashan county, the highest incidence area in China and to provide a scientific basis for monitoring and prevention.

METHODS With a population-based case-control study, 109 colon cancer patients with 1:7 matched controls were interviewed with uniform questionnaires. Conditional logistic regression was used for univariate and multivariate analysis of colon cancer.

RESULTS High monthly pork consumption (OR=1.608), and high monthly animal fat consumption (OR=1.391) over a ten-year period, psychological depression (OR=9.887), negative emotion (OR=1.723), lower digestive-tract diseases (OR=4.163), and history of colorectal cancer in first-degree relatives (OR=3.421) were the main risk factors of colon cancer. During that time, high monthly vegetable consumption was a protective factor for colon cancer (OR=0.422).

CONCLUSIONS Colon cancer in Jiashan county was related to dietary factors. The research results support the colon cancer etiological hypothesis of "fat-bile acid" and "deficiency of dietary fibre". Psychological depression, inheritance and lower digestive tract diseases were also correlated with colon cancer.

KEYWORDS: colorectal neoplasms/epidemiology, colonic neoplasms/epidemiology, risk factors, case-control study.

The colon cancer incidence rate in North America, Australia and West Europe is high, but it is low in Asia and Africa. China belongs to a low-incidence area of colon cancer, but colon cancer incidence rates in cities are greater than that in rural areas. During 1988–1992, the world standardized incidence rates of colorectal cancer in men and women in Jiashan county were 26.3/10⁵ and 18.6/10⁵ respectively. The rate of there is highest in China and even greater than that in Shanghai city and Beijing city^[1]. To investigate the risk factors of colon cancer in the highest incidence area, Jiashan county, and provide scientific basis for monitoring and prevention, we conducted a case-control study of colon cancer based on the whole population in Jiashan county in 1990–2000.

MATERIALS AND METHODS

Subjects

Colon cancer patients were identified in the Jiashan County Registry.

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Eligibility criteria for entry in the study were as follows: patients with a diagnosis of adenocarcinoma of the colon between January 1, 1997 to December 31, 1999; residing in Jiashan county for more than 20 years. Controls were matched to cases by sex, age (over 5-year intervals) and residential location, in a 7:1 ratio. Controls also lived in Jiashan county more than 20 years without histories of cancer. A total of 109 pairs of case-controls were interviewed.

Interviews

Uniform questionnaires were adopted. The questionnaire included characteristics of the population such as social-economic status, sex, age, marriage, education, occupation, monthly income, body height and weight, etc; living circumstances: the degree of industrial pollution; diet history: the diet history questionnaire included participant's average consumption frequency and amount of common foods (Food items were arranged into six food groups: meat, fish and eggs; dairy products; starches and sweets; vegetables; fruits and beverages); hobbies and habits: smoking, drinking wine and tea, physical exercise and psychological status; medical history and family cancer history; history of female menses and child-bearing.

Trained professional medical staff conducted personal interviews in the participants' homes.

Data analysis

A common protocol was used for questionnaire editing and coding. All variables were inputted into computers according to the form of the data base of Epiinfo software. Through logical examination some errors were rejected. There were more than 340 original variables included in the data base plus new born variables which were ranked and provided with a value.

Statistical methods: Odds ratio (OR) was used to measure the relationship between the studied variables and colon cancer, and to compare differences between the cases and controls. Confidence intervals (95%) of OR were calculated. The statistical differences were also calculated. Conditional logistic regression was used for single variable analyses among all variables and according to the level of $\alpha \leq 0.10$ preliminarily selected 24 variables interrelated with the risk for colon cancer. Multivariate conditional logistic regression was used for the above 24 variables, and according to the level of $\alpha \leq 0.05$ the main effect mode was established.

Regression analyses were performed with STATA 5.0 software.

RESULTS

Univariate analyses

Table 1 shows the results of univariate analyses of conditional logistic regression of colon cancer risk factors in Jiashan county. Based on the $\alpha \leq 0.10$ level, 24 variables were statistically interrelated with colon cancer. Among them, 14 variables were diet factors. Monthly mean consumption of pork, mutton and beef, domestic fowl and animal fat over a 10-year period; and during the reference year, monthly mean consumption of fried foods, smoked foods, pickled foods and roast foods were risk factors for colon cancer. Monthly mean consumption of vegetables for a period of 10 years and during the reference year were a protective factor for colon cancer occurrence. Besides diet factors, colorectal cancer history of first-degree relatives, lower digestive tract diseases, psychic trauma, psychic depression, residence in environmental pollution for 10 years, drinking the surface water and well water were all risk factors for colon cancer.

Multivariate analyses

Table 2 shows the results of multivariate analyses of conditional logistic regression of colon cancer risk factors in Jiashan county. Monthly mean consumption of pork and animal fat over a 10-year period, psychological depression, psychic repression, lower digestive tract diseases, colorectal cancer history of the first-degree relatives and residence in industrial pollution for 10 years were risk factors for colon cancer. Meanwhile monthly mean consumption of vegetables for a 10-year period was a protective factor for colon cancer occurrence.

DISCUSSION

Diet factors

Epidemiological studies conducted in the USA and France showed that a high intake of meat and fat was a risk factor for colon cancer^[2,3]. In univariate analyses of conditional logistic regression of the present study, monthly mean consumption of pork, domestic fowl, animal fat, mutton and beef for 10 years and in the reference year were related to colon cancer risk. The OR values indicated middle to strong positive associations between colon cancer risk and these variables. In multivariate analyses of conditional logistic regression of the study, monthly mean consumption of pork and animal fat for 10 years both were main effects that entered into the model. OR values of colon cancer risk were 1.608 and 1.391 respectively.

The univariate analyses of the study also showed

Table 1. Results of univariate analyses of conditional logistic regression of colon cancer risk factors in Jiashan county

Variable	β_i	OR	95%CI
Monthly mean consumption of pork during the reference year*	0.598	1.818*	1.448-2.284
Monthly mean consumption of pork for 10 years	0.743	2.102*	1.652-2.673
Monthly mean consumption of mutton and beef during the reference year	1.509	4.524*	2.664-7.682
Monthly mean consumption of mutton and beef for 10 years	1.328	3.773*	2.043-6.968
Monthly mean consumption of domestic fowl during the reference year	0.554	1.740*	1.241-2.442
Monthly mean consumption of domestic fowl for 10 years	0.296	1.345	0.944-1.918
Monthly mean consumption of vegetables during the reference year	-1.532	0.216*	0.138-0.338
Monthly mean consumption of vegetables for 10 years	-1.162	0.313*	0.223-0.440
Monthly mean consumption of animal fat during the reference year	0.592	1.808*	1.450-2.253
Monthly mean consumption of animal fat for 10 years	0.501	1.651*	1.327-2.054
Monthly mean consumption of fried foods	0.835	2.305*	1.759-3.022
Monthly mean consumption of smoked foods	2.559	12.921*	4.425-37.729
Monthly mean consumption of pickled foods	0.625	1.869*	1.534-2.277
Monthly mean consumption of roast foods	0.429	1.536	0.955-2.468
Negative emotion	0.719	2.053*	1.340-3.144
Abnormal relations with people	0.438	1.549	0.972-2.468
Psychic trauma	1.569	4.801*	2.307-9.988
Psychic depression	2.046	7.735*	3.881-15.417
Colorectal cancer history of first-degree relatives	1.580	4.855*	1.848-12.757
Chronic colitis	1.588	4.893*	1.805-13.267
Lower digestive tract diseases	1.267	3.550*	1.994-6.321
Drinking surface water and well water for 10 years	1.363	3.909*	2.287-6.679
Residence industrial pollution during the reference year	1.563	4.773*	2.287-10.000
Residence in industrial pollution 10 years	0.894	2.444*	1.042-5.734

Notes: ★ In year before diagnosis (cases) or interview (controls). β_i , regression coefficient. * $P < 0.01$ compared to control.

Table 2. Results of multivariate analyses of conditional logistic regression of colon cancer risk factors in Jiashan county

Variable	β_i	OR	95%CI
Monthly mean consumption of pork 10 years	0.475	1.608**	1.224-2.113
Monthly mean consumption of vegetables 10 years	-0.863	0.422**	0.308-0.579
Monthly mean consumption of animal fat 10 years	0.330	1.391**	1.109-1.744
Monthly mean consumption of smoked foods	0.030	1.030**	1.014-1.046
Psychic depression	2.291	9.887**	3.973-24.603
Negative emotion	0.544	1.723*	1.045-2.842
Lower digestive tract diseases	1.426	4.163**	1.964-8.823
Colorectal cancer history of the first degree relatives	1.230	3.421*	1.040-11.253
Residence industrial pollution 10 years	1.359	3.893*	1.329-11.407

Notes: β_i , regression coefficient. Compared to control: ** $P < 0.01$, * $P < 0.05$.

that monthly mean consumption of fried foods, smoked foods, pickled foods and roasted foods were greater for colon cancer cases than that for controls, odds ratios for the each variable were 2.305, 12.921, 1.536 and 1.896 respectively. Fried, smoked and roast foods contain many kinds of heterocyclic amines. Pickled foods contain more nitrosamines. They are

cancerogenic substances for colon cancer^[4]. Although only smoked foods eventually entered the multivariate conditional logistic regression model and showed a weak positive relationship, yet the variable still should be regarded as a risk factor and should be monitored.

High intake of pork and animal fat can promote secretion of bile. Under the effects of bacterioflora in

the bowel, bile acids became secondary bile acids such as deoxycholic acid and lithocholic acid. Secondary bile acids had cytotoxic effects on epithelial cells of colon crypts, and seriously damaged DNA that could not be repaired. Besides the effects of the secondary bile acids, heterocyclic amines in scorched meat and nitrosamines in pickled foods all cause damage to DNA of colon-crypt epithelial cells. Under normal conditions an organism can eliminate seriously damaged cells with unrepaired DNA by a mechanism of cell apoptosis. Over a period of several decades, due to the effects of secondary bile acids in high concentration and carcinogenic substances in the diet, some mutated cells or gradually changed cells resisting apoptosis overcome DNA damage, selectively survive, proliferate and gradually replace nearby dead epithelia of the colon. These over-proliferated epithelial cells resist apoptosis and gradually evolve from mutation or anaplasia to adenoma and adenocarcinoma^[5]. In South Africa the incidence of colon cancer in white people is 15 times that of colon cancer in black people. The main food of the white people is meat, while main food of the black people is corn. Biopsies showed that colon mucosa of the white people proliferated markedly compared to the colon mucosa of the black people^[6]. Whether in univariate analyses or in multivariate analyses of the study, monthly mean consumption of vegetables for 10 years was a protective factor for colon cancer occurrence, the odds ratios being 0.313 and 0.422 respectively. Vegetables mainly provide more fiber that play a protective role against colon cancer occurrence^[4].

Other factors

Social and psychological factors: in the course of cancer occurrence, social and psychological factors should not be ignored. Negative life events such as losing family members, discord among family members, being disappointed in work, abnormal relationships with people and so on could easily give rise to psychological depression. So called C type action mode, such as long-time psychological depression, not being suited to local conditions, negative emotions because of an inability to adjust oneself, anxiety, strong stress and so on was regarded as a susceptible action mode to cancer^[7]. In the study long-time psychological depression and negative emotions because of an inability to adjust oneself were similar to C type action. The odds ratio of psychological depression was 9.887. It is the strongest risk factor of all risk factors for colon cancer in the study. The odds ratio of negative emotion was 1.732. It is an intermediate risk factor for colon cancer.

Lower digestive tract diseases: lower digestive tract diseases include chronic colitis, intestinal polyps and so on. Ulcerative colitis and intestinal polyps were closely related to colon cancer. Extensive ulcerative colitis and more than a 10-year course of the disease along with colorectal polyps increased risk of colon cancer^[8,9]. Results of the present study showed that whether in univariate analyses or in multivariate analyses, lower digestive tract diseases were risk factors for colon cancer. The odds ratios were 3.550 and 4.163 respectively.

Heredity and environment factors: heredity factors played an important role in at least 20% of colorectal cancer. A cohort study in Sweden showed that if the mothers suffered from colorectal cancer, the cumulative risk of their offspring before 50 years of age was 3 times the cumulative risk of the general Swedish population^[10]. An epidemiological study in the State of Utah in the United States showed that the risk of colon cancer among the people whose first-degree relatives suffered from colorectal cancer was 1.77 times the risk in the general population. Results in our study in Jiashan county showed that the risk of colon cancer in the people whose first-degree relatives had colorectal cancer history was 3.421 times the risk in the common people.

The present study showed that residency in an industrial polluted area for 10 years was a risk factor for colon cancer whether in univariate analyses or in multivariate analyses, achieving a middle to strong positive relation. More studies are needed in order to further clarify the relationship between residency in an industrial polluted area and colon cancer occurrence.

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