



Risk factors for colorectal cancer

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Colorectal cancer is one of the most common cancers in human population. It causes significant morbidity and mortality in our country. The incidence of colorectal cancer increases in the fifth decade of life. The aim of this study was to evaluate the association between colorectal cancer and potential risk factors. A case-control study of colorectal cancer was carried out between 1998 and 1999 in Clinical Center of Serbia, Center for Digestive Surgery. A total of 100 cases of newly diagnosed patients with colorectal cancer confirmed by histopathology and an equal number of controls, individually matched by gender and age (+/-5 years), were chosen from patients from the same hospital with no history of cancer at all. McNemar test and conditional logistic regression were used in the analysis. According to logistic regression analysis the following risk factors were independently related with the occurrence of colorectal cancer: cigarette smoking, alcohol consumption, and diet rich in red meat and fat promote the carcinogenic process; food rich in vegetables, fruits, grains, vitamin C, physical activity, and oral contraceptive use inhibit the same process. A family history of cancer and long standing inflammatory bowel diseases also have significant role. There is convincing evidence that nutrition affects colorectal carcinogenesis in a complex fashion.

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INTRODUCTION

Colorectal cancer is one of the most common tumors and represents about 30 percent of all cancers in our population (1). In Serbia, it is the third malignant tumor in men, after the cancer of lungs and prostate. Among women it is in second place, after breast cancer, and is one of the most frequent cause of mortality from malignant tumors (2,3). The incidence is similar, mostly after the age of 50 years.

In our country the data about the incidence and mortality are different, depending of regions. Standardize rate of the incidence in Serbia for the period from 1980 to 1995 was 37.5 per 100 000 inhabitants. The mortality rate for the same interval was 12.6 per 100 000 inhabitants. For central Serbia the incidence rate for given period was 44 to 44.8 per 100 000 inhabitants, for Belgrade it was 61.1, for Vojvodina 61.5, and for Kosovo 7.1. The mortality

rate in the region of central Serbia was 6.5 for cancer of colon, and 7.9 for cancer of rectum. In Vojvodina it was 9.5 for cancer of colon and 12.0 for cancer of rectum, and finally, in Kosovo and Metohija it was 0.65 for cancer of colon and 1.2 for cancer of rectum (4). The incidence rate for cancer of colon in the city of Nis in 1987 was 16.6 per 100 000 in men and 20.6 per 100.000 in women, while for cancer of rectum it was 19.2 per 100 000 for men and 11.2 per 100 000 for women (5).

Colorectal cancer is the second leading cause of death from cancer in the United States, also. It is a third leading cause of cancer death in men after lung and prostate cancer, respectively, and after lung and breast cancer deaths among women. More than 130,000 cases are diagnosed in the United States every year with over 56,000 of those patients dying.

The incidence of colorectal cancer increases during the fifth decade of life with its maximum at the age 75 years, but every year there are numerous cases in younger people. Six percent of the United States population will develop colorectal cancer in their lifetime.

Risk factors that have been identified include a personal history of colorectal cancer or adenomas, a family history of colon cancer or adenomas, inherited colorectal cancer syndromes, and long standing inflammatory bowel disease. There is convincing evi-

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dence that nutrition affects colorectal carcinogenesis in a complex fashion. A diet high in fat and red meat, low in fruits and vegetables, high caloric intake, low levels of physical activity, and obesity, smoking and excessive alcohol intake, may play a role in colon cancer development. Dietary components either promote or inhibit the carcinogenic process.

The aim of the present investigation was to evaluate the association between colorectal cancer and potential risk factors, with special reference to nutritional and life-style aspects.

MATERIAL AND METHODS

This hospital-based case-control study of colorectal cancer (CRC) was carried out between 1998 and 1999 in Clinical Center of Serbia. A total of 100 patients with colorectal cancer histopathologically confirmed were recruited from the Institute of Digestive Diseases, Clinical Center of Serbia, in Belgrade. An equal number of controls, individually matched by sex and age (± 2 years) were chosen among patients from the same hospital with no history of cancer at all. They have suffered from hernia. Only a few patients were chosen among patients from the Institute for Cardiovascular Diseases with rupture abdominal aorta.

A standardized questionnaire with 193 variables was used to obtain information on demographic characteristics of CRC patients and their controls: age, marital status, formal education, occupation, personal and family history, residence, body mass index, life style, physical activity, and some habits: diet, cigarette smoking, alcohol consumption and coffee drinking were compared and statistically analyzed. An interviewer-administered food frequency questionnaire covering 148 food items, including the quantity consumed, was used to assess the typical dietary pattern. In participants who reported previous malignant tumors, medical records were checked in order to verify diagnosis. The same person always interviewed all participants of the project.

McNemar test (10) was the first test applied in the analysis. The confidence intervals (95% CI) of the odds ratio (OR) were determined with the help of Miettinen's (11) simple test-based procedure. In order to account simultaneously for the potential confounding effect of various risk factors, the conditional logistic regression analysis was used (12). According to McNemar test, out of 193 variables only 21 were significantly related to colorectal cancer (Table 2). Its significance is seen by its consistent association as an independent predictor of colon cancer as well as by its impact on the odds ratios associated with other factors. All of these variables entered the model of conditional regression analysis. According to multiple logistic regressions analysis 17 variables were independently related to colorectal cancer (Table 3).

RESULTS

Table 1 gives the distribution of patients with colorectal cancer and their controls according to age, marital status, education, occupation and place of residence.

Table 1. Demographic characteristics of colorectal cancer patients and their controls

Demographic characteristics	Number of patients	Number of controls
<i>Age</i>		
20-29	5	4
30-39	16	15
40-49	24	27
50-59	36	36
60-69	17	16
70+	2	2
Total	100	100
<i>Marital status</i>		
Never married	10	10
Married	77	76
Divorced	1	
Widowed	12	13
Illegitimate partnership		1
Total	100	100
<i>Formal education</i>		
Illiterate		
Incomplete primary	8	6
Primary	18	23
Secondary	33	32
Higher	40	39
Total	100	100
<i>Occupation</i>		
Agriculture worker	8	10
Blue-collar worker	20	15
White-collar worker	15	17
Expert-Artist	29	30
Unemployment-Housewife	14	17
Shopkeeper	14	11
Total	100	100
<i>Residence</i>		
Rural area	31	31
Urban area	69	69
Total	100	100

The youngest patient was 24 and the oldest 79 years old, the median age being 52 years. Most of patients were married and urban dwellers, and had primary or secondary school education. They were of various occupations. No significant difference in the aforementioned socio-demographics between patients and controls emerged.

The most predominant type was adenocarcinoma (89/100). The second type in our study was mucinous carcinoma (9/100). The most frequent localization was rectum (73), followed by colon sigmoid (10).

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Table 2. Risk factors for colorectal cancer - McNemars test

Risk factors	Discordant pairs		P
	Patient + Control -	Patient - Control +	
Cigarette smoking	41	13	0.001
Brandy	24	6	0.001
Cognac	19	5	0.05
Vine	1	9	0.001
Fat	36	4	0.001
Chilly pepper	31	16	0.05
Vitamin C	7	31	0.001
Bowel disease	23	5	0.001
Hemorrhoids	23	5	0.001
Hypertension	13	31	0.05
Sport	8	19	0.05
Recreation	6	36	0.001
Butter	8	37	0.001
Eggs	27	57	0.05
Peach	28	59	0.001
Apricot	30	48	0.001
Cherry	25	46	0.05
Strawberry	33	41	0.05
Blackberry	5	12	0.001
Grilled meat	59	83	0.05
Boiled beef meat	59	84	0.05

Table 3. Risk factors for colorectal cancer - conditional logistic regression analysis

Risk factor	Coefficient	Standard error	P value	Odds ratio	95% confidence interval
Cigarette smoking	2.547	0.561	0.000	12.766	4.248-38.366
Alcohol intake (brandy)	1.612	0.567	0.004	5.012	1.649-15.230
Cognac	2.192	0.685	0.001	8.950	2.339-34.238
Pork meat	2.572	0.678	0.000	13.087	3.466-49.422
Poultry	1.821	0.819	0.026	6.177	1.240-30.772
Fish	-1.776	0.616	0.004	0.169	0.051-0.567
Salad	0.276	0.137	0.044	0.758	0.580-0.992
Lentil	-0.586	0.191	0.002	0.557	0.383-0.810
French beans	-0.547	0.199	0.006	0.570	0.392-0.584
Carrot	-1.595	0.368	0.000	4.930	2.398-10.135
Potato	1.119	0.498	0.025	3.061	1.155-8.118
Maize (corn)	-1.144	0.0447	0.011	0.319	0.133-0.765
Apple	-0.956	-0.211	0.000	0.385	0.254-0.581
Hazelnut	-0.590	0.201	0.003	0.554	0.374-0.822
Vitamin. C	-1.297	0.448	0.004	0.273	0.148-0.801
Sport	-1.066	0.431	0.013	0.344	0.148-0.801
Oral contraceptive use	-1.799	0.805	0.026	0.166	0.034-0.803

The number of cigarette smoking among patients was statistically significantly higher than in the control group with OR=12.766. Concerning regular alcohol consumption for 28 years on the average, in a quantity of 4.6 dl for patients and 2.1 dl for controls, there was significant difference between types and kinds of alcohol drinks. Plum brandy and cognac with brand name Vinjak show statistically significant difference between patients and control group, for plum brandy with OR=5.012 and for Vinjak with OR=8.950. We did not find statistically significant difference between patients and control group concerning wine and beer consumption.

As concerning fat in diet there was also statistically significant difference between patients and control group. The number of patients was nine times higher then in control group: 36 vs. 4. In McNemar test P was 0.001.

Out of 100 patients 24 had history of previous colon diseases, especially hemorrhoids. In the control group, according to

McNemar test, there was statistically significant difference, and previous colon diseases were reported only in 6 patients. Malignant tumors in the first-degree relatives were also significantly more frequent in patients than in their controls. Among the relatives of both patients and controls, mother was most frequently affected by malignant tumor and the most frequent tumor was cancer of uterus.

There was statistically significant difference between patients and their controls concerning to going in for sports with OR=0.344 according to multiple logistic regressions analysis (Table 3) and recreations with P =0.001 according to McNemar test (Table 2). Concerning the use of oral contraceptives, there was statistically significant difference, because women in control group used it almost four times more then women in patient group.

DISCUSSION

Colorectal cancer is one of the leading causes of mortality from malignant disease (1-5). Case-control and cohort studies provide strong support for a role of diet in the etiology of CRC. However, to establish causal relationships and to identify more precisely the dietary components involved, intervention studies in human subjects are required (27). Our study showed that the most predominant type was adenocarcinoma (89 out of 100). The second type in our study was mucinous carcinoma (9 out of 100). These results are in agreement with Morson and Dawson (35). The most frequent localization was rectum (73), followed by colon sigmoid (10). This similar distribution is also in agreement with Morson and Dawson (35).

Current data suggest that consuming a Western style diet, that is, one high in meat, refined grains, and sugar and low in vegetables and fiber, may contribute to risk of colon cancer. Risk factors that have been identified include a personal history of colorectal cancer or adenomas, a family history of colon cancer or adenomas, inherited colorectal cancer syndromes, and long standing inflammatory bowel disease (13-15, 26-33). Risk factors considered were obesity, physical inactivity, alcohol consumption, early adulthood cigarette smoking, red meat consumption, and low intake of folic acid from supplements. In the present study the risk of developing colorectal cancer was strongly related to other investigations. These include smoking, alcohol consumption, and diet (10,12,16-21,24,25,32-34). Dietary modifications along with secondary prevention measures may have a major impact on reducing the mortality from colorectal cancer (22). Our findings are in agreement with the results, recently reported by Scheppach et al. (17), and Slattery et al. (20).

The relation of cigarette smoking and alcohol drinking to colorectal cancer risk has been inconsistent in the epidemiological literature. Although cigarette smoking and alcohol drinking in general

were not risk factors for colorectal cancers in Shanghai, there were small excess risks for rectal cancer among heavy smokers and colon cancer among heavy drinkers (8,9,14). However, our data lend some additional support to the possibility that cigarette smoking and alcohol drinking may contribute to risk of colon cancer.

There is evidence of familial aggregation of colorectal cancer suggesting that genetic susceptibility may be important in the etiology of the disease (6). Only limited data are available comparing risk factors for colorectal cancer with and without a family history. There are arguments suggesting that individuals with a first-degree relative with colorectal cancer are at a greater risk from a diet high in energy than individuals without such a family history (14). Higher frequency of any cancer among family members in the present study is in agreement with the findings of some other authors (6, 14). Our findings are in agreement with the results Jedrychowski et al. (8) and Ji et al. (9) concerning exposure to alcohol.

Oral contraceptive drugs contain a hormone estrogen and progesterone in different proportion and relation, and these hormones may prevent or reverse the formation of polyps and colon cancer. Our results have shown that diets containing substantial amounts of red meat may increase the risk of colorectal cancer. The association with red meat intake may be due to a combination of factors, such as content of fat, protein, and iron, and/or meat preparation (e.g. cooking or preserving methods). Laboratory results have shown that meats cooked at high temperatures contain heterocyclic amines (HCAs) known to be mutagenic and carcinogenic in animals (17).

Our results show that fruit and vegetable have protective role, but there is currently no consensus as to recommendations on what type of fiber and the optimal amount that should be consumed. A high fiber intake (>25-30 g/day) based on a variety of food sources (fruit, vegetable, legumes, cereals) is the only way to avoid many of the disorders mentioned. The consumption of a particular type of fiber (soluble or insoluble) is limited to the treatment of certain processes, because its individual relationship with many disorders is still pending determination. High consumption of vegetables and fruits and the avoidance of highly refined sugar containing foods are likely to reduce risk of colon cancer (18, 23). We cannot explain almost opposite effect in our results concerning the role of carrots and potatoes in the diet. The only acceptable explanation is inaccurate answers in our interview.

Further studies covering larger groups of patients would probably make possible to draw at more reliable conclusion about precise calculation of risk factors and risk score. Larger study would also make possible the investigation of potential risk factors for individual histological types of colorectal cancer.

CONCLUSION

Cigarette smoking is positive risk factor and increases colorectal cancer risk. It is thought that it is an independent factor, which is very often in connection with alcohol intake and represents risk factor for many tumors of digestive system. Alcohol (plum brandy, cognac) also represents positive risk factor, and the risk increases in association with cigarette smoking. Meat (pork, poultry, and fish): red meat is positive-independent risk factor, while white meat (fish) is cancer protective.

On the basis of these data one can conclude that many factors may play a role in development of colorectal cancer. Some of them have protective significance, but also there are established predisposed risk factors. Balance between these two groups is cancer protective and maintains mucous membranes of the colon in normal status. The combined effect of these dietary factors, as well as modifiable non-dietary factors such as cigarette smoking, suggest that the majority of cases of colon cancer are preventable.

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