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Original Article

Study on the relationship between diet and environmental exposure-related factors and the incidence of colorectal cancer

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Abstract: Objective: The purpose of this study was to analyze the relationship between dietary and environmental exposure-related factors and the incidence of colorectal cancer (CRC). Methods: Eighty cases of CRC patients diagnosed by colonoscopy and pathological biopsy were selected as the case group. Eighty non-CRC patients without digestive tract symptoms served as the control group. The composition ratio of age, pathological type and diseased parts of CRC patients were calculated, and a questionnaire was designed for the research methods and purposes. The baseline data was compared between the two groups, including demographic characteristics, dietary factors, environmental factors, and psychological factors. Results: Eighty CRC patients were approximately aged 46-60 years with a high morbidity of rectal cancer, and their main pathological type was tubular adenocarcinoma. The unconditional multivariate logistic regression analysis confirmed that consumption of fried and smoked foods (2 times/week), animal liver (2 times/week), preserved food (4-7 times/week), the presence of sewage plant around the residence, smoking and drinking habits, psychological stimulation lasting for more than 10 years, and CPSS scores of 26-56 points may be risk factors for CRC (OR>1, P<0.05); while consumption of fresh vegetables (4-7 times/week) may be a protective factor for CRC (OR<1, P<0.05). Conclusion: The incidence of CRC was closely related with dietary habits, environmental exposure and psychological factors. Unhealthy dietary habits, poor living environments, smoking and drinking history and excessive psychological pressure will increase the risk of CRC. Therefore, it is necessary to pay attention to the above risk factors to prevent the occurrence of CRC by strengthening health education, arranging regular physical examination, cultivating healthy eating habits and maintaining a positive mentality.

Keywords: Colorectal cancer, diet, environmental exposure, related factors

Introduction

Colorectal cancer (CRC) refers to gastrointestinal malignant tumors with malignant lesions in the intestinal mucosal epithelium. It includes both colon cancer and rectal cancer, according to the areas of the lesion. Since early clinical symptoms may not be present, most patients can only be diagnosed when intestinal obstruction, hematochezia and intestinal irritation have already occurred, thus missing the best opportunity for treatment [1-3]. The prognosis of CRC patients is closely related to early diagnosis and timely treatment. Data show that the 5-year survival rates of patients with early and advanced CRC are 90% and 10%, respectively, after surgery [4, 5]. Therefore, early screening, early detection, early diagnosis and treatment are crucial steps to prevent CRC and improve the survival rate.

Molecular biology studies have found that CRC develops in multiple stages mediated by varying genes, involving inactivation of tumor suppressor genes, oncogene activation of genetic mutations, gene overexpression, and mutations in mismatch repair genes [6-8]. At present, there are many studies on the risk factors of CRC worldwide, but there are no definite criteria for the determination of the high-risk population for CRC. Therefore, this study conducted a retrospective investigation of the factors relat-

ed to diet and environmental exposure in CRC patients, so as to provide a theoretical basis for better prevention and treatment of CRC.

Materials and methods

General materials

Eighty patients with CRC admitted to our hospital from March 2017 to July 2019 were selected as the case group. Inclusion criteria: those who were diagnosed by colonoscopy and pathological biopsy; those with complete medical data; those who had lived in the same region for more than 10 years. Exclusion criteria: those with a history of psychological and mental diseases; those with cognitive impairment who could not complete the questionnaire independently; those with other malignancies.

There were 49 males and 31 females aged 30-90 years old, with an average age of (58.93 ± 6.12) years. According to the pair matching principle, a total of eighty non-CRC patients without digestive tract symptoms who were treated in our hospital during the same period were served as the control group, including 49 males and 31 females ranging from 30-90 years old, with an average age of (57.14 ± 5.98) years. Matching criteria: those with same gender showed negative results of colonoscopy; age difference of matched patients was <5 years. The gender and age ratio of the case group and control group were well balanced, which was comparable (P>0.05). This study was approved by the Ethics Committee of our hospital. The research subjects and their families were informed and signed a fully-informed consent form.

Methods

CRC patients were given regimens such as surgery or chemotherapy with XELOX. Among them, patients with colon cancer stage I, II and III were treated with radical resection + regional lymph node dissection, and the surgical scope and method were determined according to the location of the tumor. For stage IV patients with intestinal obstruction and severe intestinal bleeding, palliative resection was feasible. Patients with rectal cancer stage II and III were treated with preoperative chemoradiotherapy, and then received radical surgery. The surgical methods for rectal cancer mainly included total mesorectal excision, transanal resection, low anterior resection, transabdominal sphincter abdominal perineum combined resection, *etc*. The composition ratio of age, pathological type and lesion site of CRC patients were calculated, and a questionnaire was designed, and the items included demographic data (occupation, marital status, education, annual income, BMI), dietary factors (fried and smoked food, animal liver, preserved food, fresh vegetables, meat, eggs, milk, *etc*.), environmental factors (sewage plants, smoking, drinking, physical exercise), psychological factors (whether suffering from mental stimulation and psychological pressure within the past 10 years). BMI = weight (kg)/height (m^2). BMI ≥ 24 kg/m^2 was considered overweight, and BMI between 18-24 kg/m^2 was normal. The patient's psychological pressure was assessed by the Perceived Psychological Stress Scale (CPSS) from 14 items, comprising six negative (items 1, 2, 3, 8, 11 and 14) and four positive items (items 6, 7, 9 and 10). A score of 0-25 indicated no pressure and 25-56 indicated pressure. The psychological pressure was positively correlated with the scores.

Statistical analysis

SPSS 22.0 was used for data processing. The measurement data was expressed as (χ±S) and examined by t test. The count data was expressed as percentage, and compared by χ^2. The possible influencing factors were evaluated through unconditional multiple logistic regression analysis. P<0.05 indicated a significant difference.

Results

Analysis of the composition of age, pathological type and lesion sites of CRC

In CRC patients, the proportion of age was 8.75% between 30-45 years old, 45% between 40-60 years old, 30% between 61-75 years old, and 16.25% between 76-90 years old, with the highest proportion of patients aged between 40-60 years. In the pathological type, mucinous adenocarcinoma accounted for 3.75%, tubular adenocarcinoma accounted for 77.50%, papillary adenocarcinoma accounted for 17.50%, signet ring cell carcinoma (SRCC) accounted for 1.25%, among which tubular adenocarcinoma accounted for the highest pro-

Table 1. Analysis of the composition ratio of the age, pathological type and lesion parts in 80 patients with CRC

Item		Case (n)	Percentage (%)
Age (year)	30-45	7	8.75
	46-60	36	45.00
	61-75	24	30.00
	76-90	13	16.25
Pathological type	Mucinous adenocarcinoma	3	3.75
	Tubular adenocarcinoma	62	77.50
	Papillary adenocarcinoma	14	17.50
	Signet ring cell carcinoma	1	1.25
Lesion part	Rectal cancer	57	71.25
	Colon cancer	23	28.75

portion. The incidence of rectal cancer was 71.25%, and that of colon cancer was 28.75%. This suggested that CRC patients in this group were mainly aged 46-60 years, the main pathological type was tubular adenocarcinoma, and rectal cancer had the highest incidence (**Table 1**).

Mono-factor analysis

General demographic characteristics: There was no significant difference in occupation, marital status, education level, annual economic income and BMI between the case group and the control group. These indicators may have no significant effect on the incidence of CRC (**Table 2**).

Dietary factors: The consumption frequency of fried and smoked food, animal liver, preserved food and fresh vegetables in the case group was significantly different from that in the control group ($P<0.05$), indicating that the above dietary habits may increase the risk of CRC (**Table 3**).

Environmental factors: The ratio of the presence of sewage factories around the residence, smoking and drinking in the case group were higher than those in the control group ($P<0.05$), indicating that the above environmental factors may increase the risk of CRC (**Table 4**).

Psychological factors: The proportion of patients suffering from mental stimulation for the past 10 years and the number of patients with CPSS scores of 26-56 points in the case group were higher than those in the control group ($P<0.05$), indicating that excessive psychological pressure may increase the risk of CRC (**Table 5**).

Multi-factors analysis

The unconditional multiple logistic regression analysis confirmed that consumption of fried and smoked food (≥2 times/week), animal liver (≥2 times/week), preserved food (4-7 times/week), presence of sewage factories around the residence, smoking, drinking, suffering from psychological stimulation within the past 10 years, and CPSS score of 26-56 points may be risk factors for the onset of CRC (OR>1, $P<0.05$), while consumption of fresh vegetables (4-7 times/week) may be a protective factor of CRC (OR<1, $P<0.05$) (**Table 6**).

Discussion

CRC is a common clinical malignant tumor of the digestive tract with high morbidity and mortality. The incidence of the disease has been increasing in recent years and is now more common in the young population [9]. Colorectal cancer may not present with any symptoms in the early stages. Most of the patients are in the middle and advanced stages at the time of diagnosis, which poses a serious threat to the patients [10]. Therefore, it is of great significance to analyze the risk factors of CRC actively and carry out prevention and treatment as early as possible.

Diet is associated with the incidence of CRC. Although clinical studies on the relationship between diet and CRC have been conducted for nearly 30 years, its oncogenesis has not been fully revealed yet. In this study, the unconditional multiple logistic regression analysis is confirmed that consumption of fried and smoked food (≥2 times/week), animal liver (≥2 times/week), and preserved food (4-7 times/week) may be risk factors for CRC. In the study of An et al [11], the COX regression model was used for mono-factor and multi-factors analysis, and the results found that more consumption of animal liver, preserved food, fried and grilled food over a period of 10 years were all CRC-related dietary risk factors and eating more fresh vegetables for 10 years was a protective factor, which was similar to the results of

Table 2. Comparison of general demographic characteristics in both groups (n)

Events		Case group (n=80)	Control group (n=80)	χ^2	*P*
Occupation	Worker	20	22		
	Farmer	37	32		
	Others	23	26		
Marital status	Married	64	68	0.693	0.405
	Others	16	12		
Education level	Primary school or below	36	39		
	Middle school	24	22		
	Senior high school or above	20	19		
Annual economic income (Ten thousand yuan)	<3	21	25	0.488	0.485
	≥3	59	55		
BMI (kg/m^2)	18-24	48	42	0.914	0.339
	>24	32	38		

Table 3. Comparison of diet in both groups (n)

Events	Times/week	Case group (n=80)	Control group (n=80)	χ^2	*P*
Fired and smoked food	<2	61	71	4.329	0.037
	≥2	19	9		
Animal liver	<2	72	79	5.769	0.016
	≥2	8	1		
Preserved food	<2	9	16	11.042	0.004
	2-3	21	35		
	4-7	50	29		
Fresh vegetables	<2	14	2	34.542	0.000
	2-3	51	28		
	4-7	15	50		
Meat egg milk	<2	10	7	0.888	0.641
	2-3	29	27		
	4-7	41	46		

Table 4. Comparison of environmental factors in both groups (n)

Events		Case group (n=80)	Control group (n=80)	χ^2	*P*
Presence of sewage plants around the residence	Yes	54	25	21.028	0.000
	No	26	55		
Smoking	Yes	47	29	8.120	0.004
	No	33	51		
Drinking	Yes	43	30	4.258	0.039
	No	37	50		
Physical exercise	Yes	29	35	0.938	0.333
	No	51	45		

this study. The reasons may be that (1) fried, spicy food and animal offal are unhealthy components of diets that may cause CRC. Animal offal and fried foods can stimulate the secretion of bile acids, which are decomposed into secondary bile acids by intestinal flora, and damage the DNA. It leads to proliferation and inflammation of intestinal mucosal cells and

Table 5. Comparison of psychological factors in both groups (n)

Events		Case group (n=80)	Control group (n=80)	χ^2	*P*
Suffering psychological stimulation in the past 10 years	Yes	28	11	9.799	0.002
	No	52	69		
CPSS scores	0-25	18	33	6.476	0.011
	26-56	62	47		

Table 6. Multi-factors analysis of CRC

Related factors	*B*	SE	*Wald*	*P*	*OR*	95% CI
Fried and smoked food (≥2 times/week)	0.899	0.441	4.161	0.041	2.457	1.036-5.829
Animal liver (≥2 times/week)	2.172	1.073	4.098	0.043	8.778	1.071-71.913
Preserved food (4-7 times/week)	0.681	0.230	8.767	0.003	1.975	1.259-3.099
Fresh vegetables (4-7 times/week)	-1.709	0.321	28.403	0.000	0.181	0.097-0.339
Presence of sewage plants around the residence	1.519	0.339	20.045	0.000	4.569	2.350-8.886
Smoking	0.918	0.325	7.978	0.005	2.505	1.325-4.736
Drinking	0.661	0.322	4.218	0.040	1.937	1.031-3.640
Suffering psychological stimulation in the past 10 years	1.217	0.400	9.239	0.002	3.378	1.541-7.404
CPSS scores (26-56 points)	0.883	0.351	6.327	0.012	2.418	1.215-4.813

changes the intestinal mucosal structure and function, resulting in the increases of the risk of CRC [12, 13]. Spicy and fried foods contain high calories and high fat, which can slow down the gastrointestinal tract peristalsis and cause constipation, thus making it difficult to expel the intestinal toxins.

Chinese people eat more preserved foods and smoked foods since it was not easy to store foods in the past [14]. Nowadays, people marinate or smoke various ingredients, such as sauerkraut, salted fish, pickles, cured meat, bacon, *etc*. to increase the flavor of ingredients. A large amount of salt needs to be added during this production process; however, excessive salt can cause a heavy burden on many organs such as the heart, kidney and gastrointestinal tract [15]. The higher content of dimethyl nitrite in preserved food will be converted into the carcinogens dimethyl ammonium nitrite in the human body. In addition, the results of this study found that fresh vegetables may be a protective factor for the onset of CRC. Fresh vegetables contain a large amount of dietary fiber that cannot be easily decomposed and absorbed in the intestine, but can generate short-chain fatty acids such as propionic acid and acetic acid. They can reduce the acidity of the intestinal tract, thereby inhibiting the production of toxic metabolites, protecting the intestinal mucosa and improving the body's immunity [16].

The results of this study indicated that the presence of sewage plants around the residence, smoking and drinking may also be risk factors for CRC. This may be attribute to the fact that cigarette smoke contains a variety of carcinogens such as heterocyclic aromatic amines, polycyclic aromatic hydrocarbons and so on, which can induce malignant tumors such as CRC through the blood circulation. At the same time, the smoking history and smoking volume are positively correlated with the risk of CRC. That is, the longer the smoking history and the greater the number of cigarettes smoked, the higher the risk of CRC [17]. Tobacco contains a variety of carcinogens that will reach the intestine tissue through blood circulation, which has an impact on the cellular metabolism process. It can induce gene mutations and eventually cause tumors through methylation of cellular DNA. Therefore, smoking is closely related to the incidence of CRC, and patients should be actively encouraged to quit smoking.

Drinking a small amount of alcohol has a protective effect on the cardiovascular system. However, long-term excessive drinking can increase the risk of CRC. In the study of the rela-

tionship between alcohol consumption and the risk of colorectal cancer by Wang et al [18], it was found that heavy drinking can increase the risk of colorectal cancer, which was consistent with the results of this study. The main reasons were that ethanol reached the intestine and then was converted into acetaldehyde, which directly affected the cells of the intestine and caused damage, thereby increasing the risk of CRC [19, 20]. Ethanol can stimulate the secretion and synthesis of highly reactive oxygen species, causing damage to DNA and changing its methylation. It can also increase the incidence of intestinal malignant tumors. In addition, ethanol can promote tumor growth through angiogenesis and immunosuppression, reducing the therapeutic effect of chemotherapy drugs [21]. It has been clinically confirmed that alcohol consumption is an important culprit in the pathogenesis of many diseases, and the amount of alcohol consumption is positively correlated with the risk of CRC [22]. Therefore, patients with a history of alcohol consumption can be initially assessed for CRC risk, and healthy people should be reminded not to drink too much.

In this study, people suffering from psychological stimulation for 10 years and CPSS scores of 26-56 points may be risk factors for CRC. High psychological pressure can increase the risk of CRC. The main reasons are that psychological pressure can activate the thalamus-pituitary-adrenal cortex, promote the synthesis and secretion of glucocorticoids such as catecholamines, corticosteroids, thus inhibiting the activity of natural killer cells. It can also reduce immune function and increase the risk of tumor development [23, 24]. At the same time, excessive psychological pressure may cause diseases such as obesity and insulin resistance, and increase the onset of CRC. It may also affect intestinal peristalsis and prolong the residence time of carcinogens in the intestinal tract, thus affecting the pathogenesis of CRC. Besides, those with high psychological pressure are more likely to smoke and drink, which will also increase the risk of CRC [25]. Therefore, it is necessary to maintain good emotions, eliminate negative emotions, relieve psychological pressure and maintain a good mentality.

In summary, the occurrence of CRC is the result of the combined effects of diet, environmental exposure and psychological factors. Unhealthy diet patterns, poor living environment, smoking and drinking, and excessive psychological pressure will increase the risk of CRC. Therefore, it is necessary to pay attention to the above risk factors to prevent CRC by strengthening health education, arranging regular physical examination, cultivating healthy eating habits and maintaining a good mentality. However, the study has certain limitations. This study only discussed the dietary and environmental exposure factors of colorectal cancer from a macro perspective. Further clinical studies should be conducted from the perspective of molecular biology.

Disclosure of conflict of interest

None.

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References

[1] Lee CH, Cheng SC, Tung HY, Chang SC, Ching CY and Wu SF. The risk factors affecting survival in colorectal cancer in Taiwan. Iran J Public Health 2018; 47: 519-530.

[2] Rybakov EG, Shelygin YA, Khomyakov EA and Zarodniuk IV. Risk factors for postoperative ileus after colorectal cancer surgery. Colorectal Dis 2017; [Epub ahead of print].

[3] Demb J, Earles A, Martínez ME, Bustamante R, Bryant AK, Murphy JD, Liu L and Gupta S. Risk factors for colorectal cancer significantly vary by anatomic site. BMJ Open Gastroenterol 2019; 6: e000313.

[4] Jones P, Cade J, Evans C, Burley V, Hancock N and Greenwood D. P74 Adherence to the WCRF/AICR cancer prevention guidelines and risk of colorectal cancer in the UK Women's Cohort Study. Br J Nutr 2016.

[5] Morris JS, Bradbury KE, Cross AJ, Gunter MJ and Murphy N. Physical activity, sedentary behaviour and colorectal cancer risk in the UK Biobank. Br J Cancer 2018; 118: 920-929.

[6] Chubak J, Boudreau DM, Rulyak SJ and Mandelson MT. Colorectal cancer risk in relation to antidepressant medication use. Int J Cancer 2011; 128: 227-232.

[7] Munakata S, Sugimoto K, Honjo K, Kawai M, Kawano S, Kamiyama H, Ouchi M, Takahashi M, Tomiki Y and Sakamoto K. Neutrophil-lymphocyte ratio as a prognostic factor in in-

curable stage IV colorectal cancer. Open J Gastroenterol 2018; 8: 45-56.
[8] Symonds EL, Cock C, Meng R, Cole SR, Fraser RJL and Young GP. Uptake of a colorectal cancer screening blood test in people with elevated risk for cancer who cannot or will not complete a faecal occult blood test. Eur J Cancer Prev 2018; 27: 425-432.
[9] Hur SJ, Yoon Y, Jo C, Jeong JY and Lee KT. Effect of dietary red meat on colorectal cancer risk-a review. Compr Rev Food Sci Food Saf 2019; 18: 1812-1824.
[10] Hisabe T, Tsuda S, Hoashi T, Ishihara H, Yamasaki K, Yasaka T, Hirai F, Matsui T, Yao K, Tanabe H and Iwashita A. Validity of conventional endoscopy using "non-extension sign" for optical diagnosis of colorectal deep submucosal invasive cancer. Endosc Int Open 2018; 6: E156-E164.
[11] An Q, Li X, Gao X, Ma L and Cheng R. A case-control study on colorectal cancer and diet-related risk factors. China Public Health 2010; 26: 892-893.
[12] Zhang Q, Zheng X, Li X, Sun D, Xue P, Zhang G, Xiao M, Cai Y, Jin C, Yang J, Wu S and Lu X. The polymorphisms of miRNA-binding site in MLH3 and ERCC1 were linked to the risk of colorectal cancer in a case-control study. Cancer Med 2018; 7: 1264-1274.
[13] Ilgaz AE and Gözüm S. Determination of colorectal cancer risk levels, colorectal cancer screening rates, and factors affecting screening participation of individuals working in agriculture in Turkey. Cancer Nurs 2018; 41: E46-E54.
[14] Schwingshackl L, Schwedhelm C, Hoffmann G, Knüppel S, Laure Preterre A, Iqbal K, Bechthold A, De Henauw S, Michels N, Devleesschauwer B, Boeing H and Schlesinger S. Food groups and risk of colorectal cancer. Int J Cancer 2018; 142: 1748-1758.
[15] Jeon J, Du M, Schoen RE, Hoffmeister M, Newcomb PA, Berndt SI, Caan B, Campbell PT, Chan AT, Chang-Claude J, Giles GG, Gong J, Harrison TA, Huyghe JR, Jacobs EJ, Li L, Lin Y, Le Marchand L, Potter JD, Qu C, Bien SA, Zubair N, Macinnis RJ, Buchanan DD, Hopper JL, Cao Y, Nishihara R, Rennert G, Slattery ML, Thomas DC, Woods MO, Prentice RL, Gruber SB, Zheng Y, Brenner H, Hayes RB, White E, Peters U and Hsu L. Determining risk of colorectal cancer and starting age of screening based on lifestyle, environmental, and genetic factors. Gastroenterology 2018; 154: 2152-2164, e2119.
[16] Tabung FK. Inaccurate data in meta-analysis 'Dietary patterns and colorectal cancer risk: a meta-analysis'. Eur J Cancer Prev 2019; 28: 58-59.
[17] Wilson C, Flight I, Zajac IT, Turnbull D, Young GP and Olver I. Web-based communication strategies designed to improve intention to minimize risk for colorectal cancer: randomized controlled trial. JMIR Cancer 2018; 4: e2.
[18] Wang Y, Yang H, Shen CJ, Ge JN and Lin J. Association between alcohol consumption and colorectal cancer risk: a case-control study in the Han Chinese population. Eur J Cancer Prev 2018; 27: 433-437.
[19] Lin E and Katz S. Colorectal cancer risk and screening in geriatric patients. 2019.
[20] Park SY, Wilkens LR, Setiawan VW, Monroe KR, Haiman CA and Le Marchand L. Alcohol intake and colorectal cancer risk in the multiethnic cohort study. Am J Epidemiol 2019; 188: 67-76.
[21] Zheng Z, Yu H, Huang Q, Wu H, Fu Y, Shi J, Wang T and Fan X. Heterogeneous expression of Lgr5 as a risk factor for focal invasion and distant metastasis of colorectal carcinoma. Oncotarget 2018; 9: 30025-30033.
[22] Wang L, Ma J, Yang B, Jing F and Hu Y. XRCC2 polymorphisms and environmental factors predict high risk of colorectal cancer. Med Sci Monit 2018; 24: 2858-2863.
[23] Eto K, Kosuge M, Ohkuma M, Noaki R, Neki K, Ito D, Sugano H, Takeda Y and Yanaga K. Defunctioning Ileostomy is a key risk factor for small bowel obstruction after colorectal cancer resection. Anticancer Res 2018; 38: 1789-1795.
[24] Schullehner J, Hansen B, Thygesen M, Pedersen CB and Sigsgaard T. Nitrate in drinking water and colorectal cancer risk: a nationwide population-based cohort study. Int J Cancer 2018; 143: 73-79.
[25] Klusek J, Nasierowska-Guttmejer A, Kowalik A, Wawrzycka I, Lewitowicz P, Chrapek M and Głuszek S. GSTM1, GSTT1, and GSTP1 polymorphisms and colorectal cancer risk in Polish nonsmokers. Oncotarget 2018; 9: 21224-21230.