

Original Article



Association between Nutrient Intake and Metabolic Syndrome in Patients with Colorectal Cancer

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Conflict of Interest

The authors declare that they have no competing interests.

ABSTRACT

The purpose of this study was to investigate the difference of nutritional status according to metabolic syndrome in colorectal cancer patients. The subjects were divided into 2 groups (metabolic syndrome group and normal group) according to the presence or absence of metabolic syndrome in 143 patients diagnosed with colorectal cancer, and their lifestyle and nutritional status were analyzed. Recall method was used for the dietary survey, and metabolic syndrome was defined as the presence of 3 or more of waist circumference, fasting blood glucose, triglyceride, high-density lipoprotein (HDL)-cholesterol, and blood pressure. This study showed that the metabolic syndrome group had a low age, a high body mass index (BMI), and a high drinking rate. The intake of energy, protein, fat, calcium, and phosphorus was significantly higher in the metabolic syndrome group than in the normal group, and the intake of β -carotene, vitamin C, and folic acid was significantly low. The intake of cholesterol, fatty acid, saturated fatty acid, and polyunsaturated fatty acid was also higher in the metabolic syndrome group. Higher BMI, alcohol consumption, intake of fat, total fatty acid, or saturated fatty acid increased the risk of metabolic syndrome, but fiber, vitamin C, or folic acid intake lowered the risk. Weight management and balanced nutritional intake should be emphasized to prevent metabolic syndrome and to improve the condition in patients with colorectal cancer.

Keywords: Colorectal cancer; Metabolic syndrome; Nutrient intake; Diet; Lifestyle

INTRODUCTION

Colorectal cancer is the third most common cancer in Korea following thyroid cancer and stomach cancer. Although it occurs mainly in patients older than 50 years, the number of patients with colon cancer in their 40s or younger is increasing [1]. Colon cancer is caused by environmental factors such as dietary habits, smoking, and frequent alcohol consumption as well as genetic factors. Therefore, smoking cessation, alcohol abstinence, restriction of red meat intake, and adequate vegetable intake are recommended to reduce the risk of colorectal cancer [2-4]. Many studies have shown that food is an important carcinogen, and the risk of colon cancer is known to be closely related to dietary factors. Consumption of antioxidant

vitamins, green vegetables, and animal fat are associated with the development of colorectal polyps [5-7]. Although there are many studies of dietary factors such as excessive animal fat, sugar, alcohol consumption, and fiber intake, the results are not consistent due to the variability of study subjects and methods among studies [8,9].

Colonoscopically observed adenoma is a pathologic precursor lesion of colon cancer. Alcohol consumption, smoking, and obesity increase the risk of colon polyps. Hyperglycemia and hypertriglyceridemia are closely related to the presence of colon polyps [10,11]. Obesity, high blood sugar, and elevated blood pressure are major diagnostic factors for metabolic syndrome. According to Wang et al. [12], metabolic syndrome is also associated with the development of colonic polyps, and the greater the number of metabolic syndrome diagnostic criteria, the greater the incidence of colonic polyps. Insulin resistance is also known to play an important role in the development of metabolic syndrome directly or indirectly. Metabolic syndrome factors include insulin, estrogen, cytokines, and growth factors [13-15]. One study indicates that these factors affect the association between the metabolic syndrome and colorectal cancer and engage in the component of colorectal cancer screening system used in other countries [16,17].

The risk of metabolic syndrome is higher in cancer patients than in healthy people even after surgery, radiotherapy, hormone therapy, the recovery period, and the management period after a cancer diagnosis. In addition, in the case of colorectal cancer, it is very important to maintain a healthy lifestyle through weight management and balanced diet during treatment.

There have been many studies which investigated the aspect of metabolic syndrome in the development of various chronic diseases. However, there are very few studies on metabolic syndrome and dietary factors in colorectal cancer patients. The aim of this study was to investigate the incidence of metabolic syndrome in patients with colorectal cancer and to compare whether nutrient intake differed according to the presence or absence of metabolic syndrome.

MATERIALS AND METHODS

Patients

The subjects of the study were the patients who were diagnosed colorectal cancer at general hospitals and were preparing for surgery. The purpose of this study and the contents of the study were explained and the research consent was obtained. Patients were asked to agree on their participation in the study and direct interviews were conducted to ensure the validity of all data. The total number of patients under investigation was 168, but the number of final research subjects was 143, except for patients who withdrew and information was omitted. And chronic diseases such as diabetes, hyperlipidemia and hypertension were excluded.

Definition of metabolic syndrome

In addition, to define the metabolic syndrome, subjects with 3 or more risk factors for metabolic syndrome were diagnosed as the metabolic syndrome group based on National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) and Asia-Pacific criteria. Among the 5 factors of metabolic syndrome, waist circumference, and blood pressure were directly measured. Blood was collected from the upper arm vein after 12 hours of fasting for blood tests. Serum centrifuged at 2,000–4,000 rpm for 10 minutes

was analyzed using a biochemical automatic analyzer (Hitachi 7170; Hitachi Ltd., Tokyo, Japan). Blood pressure were measured using an automatic sphygmomanometer (HEM-770A; OMRON, Kyoto, Japan) after the blood pressure was stabilized, and the mean blood pressure of the right upper arm was measured twice. The waist circumference was measured at the umbilicus in a comfortable posture using a tape measure, and the widest part between the upper and lower ends of the iliac bone was measured around the hip. A blood glucose, triglycerides, and high-density lipoprotein (HDL)-cholesterol were recorded as a result of blood tests. The subjects were divided into the metabolic syndrome group (n = 49) and the normal group (n = 94) according to the risk factors of metabolic syndrome.

Anthropometric and lifestyle survey

Age, sex, height, and body weight were examined retrospectively. Body mass index (BMI) was calculated from obtained height and weight. The waist circumference was measured by spreading the legs 25 to 30 cm, spreading the weight evenly, measuring tape measure to 0.1 cm so that the skin was not pressed by the tape measure at the lowest position of the ribs and the highest position of the pelvis. Drinking and smoking are categorized as drinking or smokers if they are present or have been performed within the last 1 month. Regular exercise was divided into subjects who exercised 3 or more times a week for at least 40 minutes.

Nutrient intake survey

In order to evaluate nutrient intake, 3-day food record method were conducted and analyzed using the computer-aided nutritional analysis program (CAN-Pro 4.0; Korean Nutrition Society, Seoul, Korea). Energy 3 types of nutrients, fiber, vitamins and minerals, cholesterol and fatty acids were analyzed. The ratio of Polyunsaturated fatty acid:Monounsaturated fatty acid:Saturated fatty acid (P:M:S) by the way that the sum of total fatty acids was divided by the amount of polyunsaturated, monounsaturated or saturated fatty acids.

Statistical analysis

To identify the difference in numeric values of factors between the groups, lifestyle, and nutrient factors were compared using independent t-tests and the equal-variance, χ^2 , or Fisher's exact test for categorical variables. Then, factors differing significantly between the 2 groups were subjected to univariate logistic regression analysis. These factors were included in initial multiple logistic regression and were eliminated in a step-by-step manner using backward selection. The Akaike information criterion (AIC) and Nagelkerke's R² statistic were used to assess the fit of the multiple logistic regression model. All statistical analyses were conducted using SPSS software (version 14.0; SPSS Inc., Chicago, IL, USA) and R (version 3.1.3; The R Foundation for Statistical Computing, Vienna, Austria). The level of statistical significance was set at 5%.

RESULTS

Comparison of anthropometric and lifestyle data

The proportion of patients accompanied with metabolic syndrome was 34.3% (n=49) among 143 subjects. The mean age was 52.5 years in the metabolic syndrome group and 58.0 in the normal group. In the metabolic syndrome group, 57.1% were men versus 62.8% in the normal group. The mean BMI was 27.7 kg/m² in the metabolic syndrome group. Smoking rates were 42.9% in the metabolic syndrome group and 36.2% in the normal group, and the alcohol consumption rate was significantly higher in the metabolic syndrome group (61.2%) than in the

normal group (42.6%). There was no significant difference in lower exercise rates between the groups, 26.5% and 26.6% for the metabolic and normal group, respectively. (Table 1)

Comparison of metabolic syndrome profile

There were significant differences between the 2 groups in terms of the metabolic syndrome diagnoses. Waist circumference, triglycerides, HDL-cholesterol, and systolic blood pressure were significantly different between the 2 groups. The average waist circumference was significantly higher in the metabolic syndrome group (93.3 cm) than in the normal group (76.3 cm), and the mean triglycerides were 189.1 mg/dL and 130.5 mg/dL, respectively. The metabolic syndrome group had higher HDL-cholesterol, 50.2 mg/dL vs. 38.5 mg/dL in the normal group. For systolic blood pressure, the metabolic syndrome group was 133.3 mmHg and the normal group was 116.4 mmHg. There was a difference in the level of triglycerides and HDL-cholesterol between groups, but the level of triglycerides were in normal range in both groups and HDL-cholesterol was in the normal range in the metabolic syndrome group (Table 2).

Comparison of nutrient intake status

Table 3 showing differences in nutrient intake between the 2 groups. The intake of energy, total fat, animal fat, total calcium, animal calcium, and phosphorus was significantly higher in the metabolic syndrome group, and the consumption of fiber, β -carotene, vitamin C, and

Table 1. Anthropometric and life habit status

Variables	Colorectal cancer (n = 143)		
	MS (n = 49)	Normal (n = 94)	p value
Age, yr	52.5 \pm 13.0	58.0 \pm 9.3	0.041
Gender (male/female)	28/21	59/35	0.056
Height, cm	166.8 \pm 15.3	163.2 \pm 8.4	0.362
Weight, kg	62.6 \pm 14.2	54.0 \pm 11.1	0.006
BMI, kg/m ²	27.7 \pm 3.0	23.4 \pm 4.6	0.002
Smoking			0.048
Smoker	21 (42.9)	34 (36.2)	
Nonsmoker	28 (57.1)	60 (63.8)	
Alcohol consumption			< 0.001
Drinker	30 (61.2)	40 (42.6)	
Nondrinker	19 (38.8)	54 (57.4)	
Regular exercise			0.714
Yes	13 (26.5)	25 (26.6)	
No	36 (81.2)	69 (78.1)	

The data is presented as mean \pm standard deviation for continuous variables by the independent t-test and frequency (%) for categorical variables by the χ^2 test. MS, metabolic syndrome group; BMI, body mass index.

Table 2. Metabolic syndrome profile

Variables	Colorectal cancer (n = 143)		
	MS (n = 49)	Normal (n = 94)	p value
Waist circumference, cm (n = 82)*	93.3 \pm 3.8	76.3 \pm 6.2	0.001
Fasting plasma glucose, mg/dL (n = 51)	108.4 \pm 10.7	96.8 \pm 8.4	0.125
Triglyceride, mg/dL (n = 63)	189.1 \pm 55.3	130.5 \pm 38.6	0.003
HDL-cholesterol, mg/dL (n = 70)	38.5 \pm 4.5	50.2 \pm 3.5	< 0.001
Blood pressure, mmHg (n = 55)			
Systolic	133.3 \pm 10.5	116.4 \pm 13.4	< 0.001
Diastolic	78.7 \pm 5.6	71.2 \pm 8.3	0.339

The data is presented as mean \pm standard deviation for continuous variables by the independent t-test and frequency (%) for categorical variables by the χ^2 test. MS, metabolic syndrome group; HDL, high-density lipoprotein.

*The number in parentheses means the number of subjects corresponding to each definition element of metabolic syndrome.

Table 3. Nutrient intake status

Variables	Colorectal cancer (n = 143)		
	MS (n = 49)	Normal (n = 94)	p value
Energy, kcal	2,048.1 ± 505.0	1,699.5 ± 492.2	0.005
Protein, g	88.9 ± 12.9	67.2 ± 14.4	0.014
Animal	56.6 ± 28.0	43.9 ± 10.5	0.022
Plant	36.3 ± 12.0	34.3 ± 13.7	0.358
Fat, g	71.2 ± 14.1	58.5 ± 13.5	0.001
Animal	42.0 ± 12.6	34.0 ± 10.2	0.031
Plant	29.9 ± 10.3	23.6 ± 9.0	0.341
Carbohydrate, g	257.6 ± 75.7	229.4 ± 80.8	0.228
Fiber, g	124.8 ± 3.4	193.8 ± 5.7	0.007
Calcium, mg	536.5 ± 190.5	416.5 ± 204.6	0.004
Animal	337.8 ± 142.2	255.9 ± 181.9	0.010
Plant	258.6 ± 123.4	230.6 ± 117.6	0.310
Phosphorous, mg	1,281.2 ± 200.2	946.3 ± 326.1	0.006
Iron, mg	14.1 ± 4.8	13.8 ± 3.0	0.459
Animal	4.6 ± 1.1	4.7 ± 1.3	0.701
Plant	10.7 ± 2.7	10.9 ± 3.2	0.848
Sodium, mg	4,343.8 ± 1,679.6	3,994.48 ± 1,152.7	0.206
Potassium, mg	2,071.0 ± 451.5	2,251.6 ± 336.2	0.152
Zinc, mg	8.1 ± 2.4	8.5 ± 3.0	0.623
Vitamin A, µgRE	653.8 ± 227.6	709.6 ± 334.1	0.570
Retinol, µg	140.4 ± 79.2	151.8 ± 61.3	0.236
β-carotene, µg	2,966.9 ± 1,953.4	3,832.3 ± 1,730.7	0.026
Vitamin B ₁ , mg	1.5 ± 0.3	1.6 ± 0.3	0.497
Vitamin B ₂ , mg	1.0 ± 0.3	1.2 ± 0.3	0.123
Vitamin B ₆ , mg	2.0 ± 0.7	2.4 ± 0.6	0.086
Niacin, mgNE	17.0 ± 4.0	18.8 ± 3.9	0.110
Vitamin C, mg	63.1 ± 34.0	92.7 ± 21.3	< 0.001
Folic acid, mg	206.6 ± 94.4	262.2 ± 87.6	< 0.042
Vitamin E, mg	12.7 ± 4.8	12.6 ± 5.4	0.287

The data is presented as mean ± standard deviation for continuous variables by the independent t-test.

MS, metabolic syndrome group.

folic acid was significantly higher in the normal group. There was no significant difference in other nutrients (**Table 3**).

Comparison of fat intake status

We analyzed whether there was any difference in fat intake between the 2 groups. The intake of cholesterol, total fatty acid, saturated fatty acid, and monounsaturated fatty acid was significantly higher in the metabolic syndrome group than in the normal group. However, the ratio of polyunsaturated fatty acid to total fatty acid was not significantly different between the 2 groups (**Table 4**).

Table 4. Fat intake status

Variables	Colorectal cancer (n = 143)		
	MS (n = 49)	Normal (n = 94)	p value
Cholesterol, mg	391.7 ± 143.8	289.9 ± 159.5	0.002
TFA, mg	38.6 ± 7.5	29.4 ± 6.0	0.023
SFA, mg	15.5 ± 5.5	11.2 ± 3.6	0.001
MUFA, mg	16.2 ± 6.4	13.7 ± 5.2	0.044
PUFA, mg	7.4 ± 2.6	8.3 ± 3.0	0.095
P:M:S ratio	0.54:1.05:1.00	0.67:1.13:1.00	0.231

The data is presented as mean ± standard deviation for continuous variables by the independent t-test.

MS, metabolic syndrome group; TFA, total fatty acid; SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; P:M:S ratio, Polyunsaturated:Monounsaturated:Saturated fatty acids ratio.

Table 5. Risk of the individual components of metabolic syndrome in patients with colorectal cancer (n = 143)

Variables	Metabolic syndrome	
	Model 1, OR (95% CI)	Model 2, OR (95% CI)
BMI	1.15 (0.90–1.48)	1.50 (1.15–1.96)*
Smoker	0.99 (0.95–1.03)	1.04 (0.97–1.11)
Alcohol consumption	1.19 (1.11–1.27) [†]	1.73 (1.64–1.83) [†]
Energy	1.16 (0.94–1.28) [‡]	1.04 (0.84–1.22)
Protein	1.01 (1.00–1.14)	1.11 (1.00–1.12)
Fat	1.01 (0.79–1.29)	1.51 (1.39–2.06)*
Fiber	0.96 (0.92–1.01)	0.93 (0.89–0.98)*
Calcium	0.95 (0.90–1.35)	0.99 (0.96–1.10)
Phosphorous	1.04 (0.82–1.32)	1.02 (0.82–1.80)
β-carotene	0.99 (0.95–1.03)	1.10 (0.93–1.27)
Vitamine C	0.95 (0.91–0.99) [‡]	0.89 (0.84–0.94) [‡]
Folic acid	0.93 (0.89–0.97)*	0.87 (0.81–0.93)*
Cholesterol	1.01 (0.94–1.09)	0.95 (0.88–1.35)
TFA	1.08 (1.00–1.17)	1.05 (0.99–1.12)
SFA	1.22 (1.16–1.28) [†]	1.29 (1.20–1.39) [†]
MUFA	1.05 (0.99–1.12)	0.96 (0.91–1.00)

Model 1: crude model; Model 2: adjusted for variable.

OR, odds ratio; CI, confidence interval; BMI, body mass index; TFA, total fatty acid; SFA, saturated fatty acid; MUFA, Monounsaturated fatty acid.

 *p < 0.01, [†]p < 0.001, [‡]p < 0.05.

Risk factors of metabolic syndrome in patients with colorectal cancer

Factors which have shown significantly different values between groups in above results were further analysed for assessing the degree of relationship with metabolic syndrome. Significant results in single regression analysis were found for alcohol consumption, energy, vitamin C, folic acid, and total fatty acids intake. However, multiple regression analysis showed that BMI, alcohol consumption, intake of fat, fiber, vitamin C, folic acid, and total fatty acids had a significant effect on the incidence of metabolic syndrome in patients with colorectal cancer (**Table 5**).

DISCUSSION

Colorectal cancer is associated with male, smoking, and alcohol consumption, and the risk of colon adenomas is higher in individuals with high BMI [4]. In a study of the relationship between lipoproteins, blood sugar and colorectal cancer, it was shown that an increase in triglycerides increased bile acids, and bile acid in the stool affected the intestinal mucosa [17,18]. In Korea, total cholesterol and triglycerides are correlated with colonic adenoma. Elevated blood sugar has been found to have a stronger association with colorectal cancer than with colorectal adenoma. There is also evidence that insulin resistance plays an important role in the differentiation of colon polyps into cancer and that the homeostasis model assessment-insulin resistance (HOMA-IR) value is significantly increased in colorectal cancer patients [14].

Because factors known to be involved in the etiology of colorectal cancer are the main items used in the diagnosis of metabolic syndrome, we predicted that there would be differences in lifestyle and dietary habits according to the presence of metabolic syndrome in colorectal cancer patients. BMI was significantly higher in colon cancer patients with metabolic syndrome, and smokers and drinkers were more likely to be in the metabolic syndrome group than in the normal group [4]. Metabolic syndrome has been associated with alcohol consumption and smoking, and it has been suggested that increased triglycerides and cholesterol resulting from alcohol consumption lead to obesity, an increased risk of cardiovascular disease, and increased mortality [19].

In middle-aged men, weight and waist-to-hip ratios are reported to be positively correlated with colorectal cancer, but the waist circumference findings are still controversial and further studies are needed [20]. In the present study, abdominal obesity, systolic blood pressure, and triglycerides were significantly higher in the metabolic syndrome group and lower in the HDL-cholesterol level, but the triglyceride level was within the normal range.

In a study of patients with rectal cancer, dietary patterns were associated with the development of rectal cancer, and high frequency of the pork, processed meat, and potatoes dietary pattern had an increased risk of developing colon and rectal cancer. It has been reported that consumption of fruits, vegetables, and dairy products reduces the risk of developing rectal cancer [21]. Metabolic syndrome and dietary factors have been reported in a variety of ways. High caloric intake and high fat intake increase the risk of metabolic syndrome by increasing oxidative stress [22]. It has been recommended that saturated fat be replaced with monounsaturated or polyunsaturated fatty acids, as well as reducing the total amount of fat [23]. In Korea, the westernization of dietary habits has increased overall food consumption and fast food, intake which consequently lead to an increased intake of fat and salt, and accelerate the incidence of cardiovascular disease. There are studies that have higher carbohydrate intake in metabolic syndrome group [24] but there was no difference between the 2 groups in this study. However, in the metabolic syndrome group, the intake of cholesterol was high and the intake of fiber and folic acid was lower [23]. Therefore, to prevent metabolic syndrome, the younger age group needs to reduce fat intake and carbohydrate intake as their age increases.

In this study, the metabolic syndrome group consumed significantly higher energy, protein, and fat than the normal group and consumed fewer factors that lower blood cholesterol such as fiber, β -carotene, vitamin C, and folate, or consumed fewer antioxidant nutrients. Fatty acid intake rate was not significantly different but both groups showed unbalanced state. Since patients with colon cancer need to change their dietary habit to healthier pattern for recovery and cure after surgery, the diet should be managed to improve the health condition of metabolic syndrome if the patient has metabolic syndrome.

This study is a cross-sectional study and it is difficult to observe temporal causality in the occurrence of colorectal cancer and metabolic syndrome. In addition, we could not analyze the clinical condition of accompanying diseases more closely. The results of this study can not be generalized to patients with colorectal cancer. The absence of a control group in this study is considered to be a lack of research design. However, the results of this study suggest that the proportion of metabolic syndrome accompanying the metabolic syndrome is 34.3%, and the intake of alcohol, saturated fatty acids, fiber, vitamin C, and folic acid correlate the risk of metabolic syndrome occurrence, respectively.

In conclusion, we confirmed that weight management, decreases in fat and saturated fatty acid intake, and increases of fiber and vitamin intake should be implemented to prevent metabolic syndrome in colorectal cancer patients. In the management of patients with colorectal cancer, confirmation of the presence of metabolic syndrome and implementation of a balanced and proper diet are considered very important. Based on the present study, the effects of metabolic syndrome on disease treatment and health status along with the interaction of nutrient intake or dietary habit with risk factors need to be investigated in future prospective studies.

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