Risk Factors for Colorectal Cancer in Korea: A Population-Based Retrospective Cohort Study

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Purpose: The incidence of colorectal cancer in Korea has recently increased, making it the second most common cancer in men and the third most common cancer in women. Risk factors for colorectal cancer have been studied worldwide, but risk factors specific for the Korean population have not been established. In this study, we investigated incidence trends and risk factors of colorectal cancer in Korea.

Methods: A total of 8,846,749 subjects were included. Colorectal cancer incidence was investigated using Korea National Health Insurance Service claim data from 2004 to 2014. Colorectal cancer diagnoses were obtained by evaluating colorectal cancer diagnostic codes and the cancer registry for cost sharing. Risk factor identification for colorectal cancer was obtained from National Health Examination data from 2004 to 2005. Cox proportional hazard model statistical analysis was used to determine risk factors of colorectal cancer.

Results: The incidence of colorectal cancer gradually increased from 2006 to 2014 (from 45.4/100,000 to 54.5/100,000). There was a predominance among men (1.47:1), but incidence trends were similar in both sexes. Old age, high body mass index, and no history of colonoscopy were identified as risk factors in both sexes. High fasting blood glucose, familial history of cancer, frequent alcohol intake, and current smoker were identified as risk factors, especially in men.

Conclusion: The incidence of colorectal cancer has been increasing in Korea. Colonoscopy screening was a protective factor for colorectal cancer, and active use of colonoscopy may reduce incidence. Early diagnosis and care are important, particularly for the high-risk group.

Keywords: Colorectal neoplasms; Incidence; Risk factors; Population Characteristics

INTRODUCTION

Colorectal cancer is the third most common malignancy worldwide and, after skin cancer, the second most common malignancy in most western countries [1, 2]. In the United States, there are 141,220 new cases and 49,380 deaths annually due to colorectal cancer [3]. The incidence has recently increased in some Asian countries, including Korea. Colorectal cancer has become the second leading cancer in men and the third most frequent cancer in women in Korea [4].

Because of the high and increasing incidence, research has been conducted on colorectal cancer risk factors. Colorectal cancer is associated with dietary factors. Red meat and processed meat diets are known to increase the incidence of colorectal cancer, and dietary fiber intake reduces the risk of colorectal cancer [5]. Smoking is also associated with risk of colorectal cancer [6]. Medical conditions including obesity and diabetes are known risk factors of colorectal cancer [7]. Most studies on colorectal cancer risk factors have been performed in the United States and Europe, and risk factors for colorectal cancer may not be the same in Korea because of differences in race, region, and economic level. Azeem et al. [8] reported that spicy foods and tapioca increase colorectal

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cancer in the Asian population. In India, studies have shown that spicy foods, low-calorie meals, and alcohol consumption may increase the incidence and severity of colorectal cancer [9].

The fecal occult blood test (FOBT) is widely used to screen for colorectal cancer. FOBT use is associated with reduced colorectal cancer mortality [10]. However, the FOBT has relatively low specificity and sensitivity for colorectal neoplasms and cancer [11]. In addition, the positive predictive value of FOBT is relatively low (3%–10%) [12]. Colonoscopy screening during health examination reduces both the incidence and mortality of colorectal cancer [13]. Distal colon flexible sigmoidoscopy also reduces the mortality of colorectal cancer [14]. Colonoscopy can be performed in conjunction with polypectomy, which is also associated with reduced mortality [15]. However, due to economic reasons and bowel preparation difficulties, routine colonoscopy is difficult to execute as a mass screening tool [16].

The general risk factors of colorectal cancer have been studied worldwide, but specific risk factors for the Korean population have not been researched. In this study, we investigate incidence trends and risk factors of colorectal cancer in Korea.

METHODS

Database

The universal health insurance system for all citizens in Korea began in 1977, and the universal health care system was introduced in 1989. Everyone born in Korea is given a unique social security number, and almost all medical records are also registered in the National Health Insurance Service (NHIS) system. Data registered in the NHIS system include patient sociodemographic information, detailed billing details, prescription drug type and dosage, hospital information, and information obtained from periodic inspections during health examination. The inspections consist mainly of questions about lifestyle and results of basic diagnostic tests. All diseases are coded according to the Korean Classification of Disease (KCD), which is similar to the International Classification of Disease, 10th Revision. Many studies have been conducted using the KCD. This study was reviewed and approved by the Institutional Review Board (IRB) of National Health Insurance Service Ilsan Hospital (IRB No. 2017-01-021-001), and a waiver of informed consent was granted for data collection from existing medical records of patients.

Study design and participants

Claims data from the NHIS database from January 1, 2004, to December 31, 2014 were used. For a diagnosis of colorectal cancer, 2 criteria had to be fulfilled. First, the person had to have a KCD diagnostic code of C18, C19, or C20; second, the person had to meet the exception rule for cost sharing (V193). The cost sharing code is a disease classification code with high accuracy because it requires registration by the national cancer management project. To determine colorectal cancer risk factors, a cohort

dataset was constructed. A total of 21,313,265 people had national health screening examinations from January 1, 2004 to December 31, 2005. Of these, 10,783,876 persons were selected as subjects by removing duplicates based on 2004 examiners. Patients with newly diagnosed cancer (codes C00-C97 by KCD) from January 1, 2004 to December 31, 2005 were excluded. Since people with Korean Medical Care (medical insurance system for low income persons) have no or low income and are susceptible to many diseases, they were excluded from this study. To eliminate measurement and observation errors, subjects with health examination data outliers were excluded. These outliers are described in the supplement, and the detailed flow chart for analysis is shown in Fig. 1.

Statistical analysis

Data are expressed in the form of frequency (%), and chi-square tests were performed to determine statistical significance. Most variables were changed to categorical data by setting continuous data intervals. The criteria for separating categories were not specific, but the criteria did not violate data uniformity. Based on previous studies, most results were reported according to sex. Cox proportional hazard model analysis was used to determine the risk factors of colorectal cancer. Results were expressed as hazard ratio (HR) and 95% confidence interval (CI). The basic assumption of the Cox model was confirmed by log(-log) curves. First, significant variables were identified by univariate analysis. Multi-
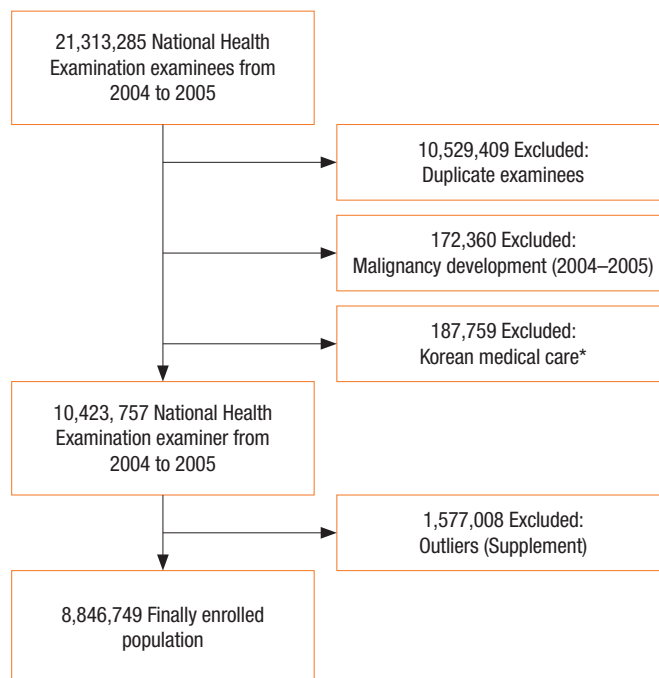
Fig. 1. Flow chart of subjects included in analysis of colorectal cancer risk factors. *Korean medical care: Special medical insurance system for the low-income population.

variate analysis was performed using the result of univariate analysis and correcting for necessary variables. Statistical analysis was performed using SAS ver. 9.4 (SAS Institute Inc., Cary, NC, USA). P-value <0.05 was considered statistically significant.

RESULTS

To estimate the incidence of colorectal cancer among Koreans, the number of newly diagnosed colon cancer cases was counted every year from 2006 to 2014, and the incidence and prevalence per 100,000 people was calculated. Because of differences in incidence, occurrence and incidence data were presented according to age and sex. Overall, there is a pattern of increasing incidence until 2012. The incidence per 100,000 people in 2006 was 45.4/100,000, and this incidence increased to 54.4/100,000 in 2014. A similar pattern was observed when incidence was analyzed by sex (Table 1).

Men had higher colorectal cancer incidence than women. The peak incidence occurred in 2012 in both sexes, with incidence of 67.9/100,000 in men and 45.3/100,000 in women (Table 1). In 2008, the male age group with highest incidence was the 70- to 79-year-old age group (372.7/100,000); after 2009 this changed to the over 80-year-old age group (401.7/100,000). In those under 40-year-old age, incidence was 2.9/100,000 in 2006 and 3.2/100,000 in 2014. In those aged 40–49, incidence was 31.7/100,000 in 2006 and 29.1/100,000 in 2014, reflecting a fairly high incidence of colorectal cancer in people below 50-year-old age. In 2014, the incidence was 212.0/100,000 for men in their 60s, 347.4/1000,000 for men in their 70s, and 412.2/100,000 for men in the over 80-year-old age group. These data indicate a high incidence of colorectal cancer in men over 60-year-old age. In women, the highest incidence was observed in women in their 70s in 2007 (183.2/100,000) and in those over 80-year-old age beginning in 2008 (189.0/100,000). In the group under 40-year-old age, incidence was 2.7/100,000 in 2006 and 2.9/100,000 in 2014.

In women in their 40s, incidence was 26.0/100,000 in 2006 and 23.0/100,000 in 2014, also reflecting a high incidence of colorectal cancer in women below 50-year-old age. In 2014, the incidence was 101.9/100,000 for women in their 60s, 181.3/1000,000 for women in their 70s, and 220.9/100,000 for women in the over 80-year-old age group, indicating high incidence in these age groups similar to men. In both sexes, incidence in the 70- to 79-year-old age groups showed a decreasing trend, while incidence in over 80-year-old age groups showed substantial increases.

Risk factors for colorectal cancer were analyzed by sex. First, the results in men are as follows. Risk of colorectal cancer increased with age, and HR was highest in the over 80-year-old age group (HR, 19.190; P < 0.001). Increased age was a risk factor for colorectal cancer in men (Table 2). Risk of colorectal cancer increased with increasing BMI, and BMI over 23 kg/m^2 was revealed to be a risk factor of colorectal cancer (23–25 kg/m^2: HR, 1.111; P = 0.0272; ≥25 kg/m^2: HR, 1.254; P < 0.001). The risk of colorectal cancer was higher when fasting blood glucose was higher than 126 mg/dL (HR, 1.217; P < 0.001). The risk of total cholesterol level was analyzed among 3 groups of less than 200 mg/dL, 200–240 mg/dL, and more than 240 mg/dL. There were no significant relationships among the 3 groups and risk of colorectal cancer. Family history of diabetes mellitus (DM) and malignancy was also analyzed. Family history of DM showed no significant association with risk of colorectal cancer, but family history of malignancy showed increased risk of colorectal cancer (HR, 1.163; P < 0.001). Alcohol consumption was analyzed based on 5 groups: none, 2–3 times a month, 1–2 times a week, 3–4 times a week, and almost every day. The results showed that risk increased with more frequent alcohol consumption. Smoking status was analyzed by non-smoker, ex-smoker, and current smoker. Current smokers showed significantly higher risk of colorectal cancer than non-smokers and ex-smokers (HR, 1.093; P = 0.021). Colonoscopy during health examinations reduced the risk of

Table 1. Prevalence and incidence of colorectal cancer

Year	Overall	Men	Women
2005	39,000 (79.3)/-	22,752 (92.1)/-	16,248 (66.5)/-
2006	67,336 (136.8)/22,332 (45.4)	39,114 (158.1)/13,038 (52.7)	28,222 (115.2)/9,294 (37.9)
2007	85,816 (172.8)/22,225 (44.7)	49,979 (200.4)/13,086 (52.5)	35,837 (144.9)/9,139 (37.0)
2008	103,112 (206.2)/22,980 (46.0)	60,308 (240.2)/13,674 (54.5)	42,804 (171.9)/9,306 (37.4)
2009	121,765 (242.1)/25,200 (50.1)	71,537 (283.4)/15,132 (59.9)	50,228 (200.5)/10,068 (40.2)
2010	140,895 (278.6)/26,421 (52.2)	83,138 (327.6)/15,836 (62.4)	57,757 (229.2)/10,585 (42.0)
2011	160,642 (315.5)/28,326 (55.6)	95,250 (373.0)/17,165 (67.2)	65,392 (257.7)/11,161 (44.0)
2012	180,708 (353.2)/28,973 (56.6)	107,349 (418.6)/17,413 (67.9)	73,359 (287.4)/11,560 (45.3)
2013	199,693 (388.1)/28,628 (55.6)	118,769 (460.7)/17,226 (66.8)	80,924 (315.3)/11,402 (44.4)
2014	217,955 (421.1)/28,161 (54.4)	129,636 (499.9)/16,804 (64.8)	88,319 (342.0)/11,357 (44.0)

Values are presented as prevalence (per 100,000)/incidence (per 100,000).

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Table 2. Incidence and risk factors of colorectal cancer in men (n=5,105,889)

Variable	Total	Colorectal cancer		HR (95% CI)	P-value
		Yes	No		
Age (yr)					
<40	1,718,961 (33.7)	4,024 (6.2)	1,714,937 (34.0)	1.000	
40–49	1,550,303 (30.4)	12,122 (18.5)	1,538,181 (30.5)	2.685 (2.331–3.093)	<0.001
50–59	979,572 (19.2)	19,435 (29.7)	960,137 (19.0)	6.529 (5.689–7.492)	<0.001
60–69	608,683 (11.9)	20,637 (31.6)	588,046 (11.7)	13.376 (11.636–15.377)	<0.001
70–79	216,795 (4.2)	8,314 (12.7)	208,481 (4.1)	19.177 (16.334–22.513)	<0.001
≥80	31,575 (0.6)	817 (1.3)	30,758 (0.6)	19.190 (13.288–27.712)	<0.001
Body mass index (kg/m^2)					
<18.5	107,303 (2.1)	1,385 (2.1)	105,918 (2.1)	1.000	
18.5–23	1,628,404 (31.9)	19,892 (30.4)	1,608,512 (31.9)	1.071 (0.981–1.170)	0.125
23–25	1,428,447 (28)	18,725 (28.7)	1,409,722 (28)	1.111 (1.012–1.220)	0.027
>25	1,941,735 (38)	25,347 (38.8)	1,916,388 (38)	1.254 (1.141–1.377)	<0.001
Fasting blood glucose (mg/dL)					
<126	4,759,751 (93.2)	58,073 (88.9)	4,701,678 (93.3)	1.000	
≥126	346,138 (6.8)	7,276 (11.1)	338,862 (6.7)	1.217 (1.092–1.356)	<0.001
Total cholesterol (mg/dL)					
<200	3,038,715 (59.5)	37,931 (58.0)	3,000,784 (59.5)	1.000	
200–240	1,527,822 (29.9)	20,101 (30.8)	1,507,721 (29.9)	0.956 (0.891–1.025)	0.201
>240	539,352 (10.6)	7,317 (11.2)	532,035 (10.6)	1.018 (0.920–1.126)	0.734
Family history of DM					
No	4,371,505 (92.8)	56,628 (94.4)	4,314,877 (92.8)	1.000	
Yes	338,772 (7.2)	3,378 (5.6)	335,394 (7.2)	0.910 (0.794–1.042)	0.173
Family history of malignancy					
No	4,155,911 (87.9)	53,136 (88.2)	4,102,775 (87.9)	1.000	
Yes	569,367 (12.1)	7,099 (11.8)	562,268 (12.1)	1.163 (1.066–1.269)	<0.001
Alcohol consumption					
Never	1,694,201 (33.2)	23,087 (35.8)	1,671,114 (33.6)	1.000	
2–3 times/mo	1,099,887 (21.5)	10,481 (16.3)	1,089,406 (21.9)	1.105 (1.007–1.212)	0.035
1–2 times/wk	159,186 (3.1)	16,022 (24.8)	1,431,649 (28.8)	1.217 (1.118–1.325)	<0.001
3–4 times/wk	538,531 (10.5)	8,412 (13.0)	530,119 (10.7)	1.360 (1.223–1.511)	<0.001
Everyday	258,287 (5.1)	6,474 (10.0)	251,813 (5.1)	1.490 (1.320–1.682)	<0.001
Smoking					
None	2,072,613 (40.6)	29,168 (45.4)	2,043,445 (41.2)	1.000	
Ex-smoker	823,774 (16.1)	11,488 (17.9)	812,286 (16.4)	1.079 (0.994–1.173)	0.070
Current smoker	2,129,870 (41.7)	23,637 (36.8)	2,106,233 (42.4)	1.093 (1.013–1.180)	0.022
History of colonoscopy					
No	194,655 (39.2)	2,169 (47.9)	192,486 (39.1)	1.000	
Yes	301,849 (60.8)	2,362 (52.1)	299,487 (60.9)	0.501 (0.470–0.533)	<0.001

Values are presented as number (%) unless otherwise indicated.
HR, hazard ratio; CI, confidence interval; DM, diabetes mellitus.

Table 3. Incidence and risk factors of colorectal cancer in women (n=3,654,706)

Variable	Total	Colorectal cancer		HR (95% CI)	P-value
		Yes	No		
Age (yr)					
<40	565,986 (15.5)	1,743 (4.7)	564,243 (15.6)	1.000	
40–49	1,192,095 (32.6)	7,619 (20.4)	1,184,476 (32.7)	2.011 (1.624–2.490)	<0.001
50–59	925,748 (25.3)	10,032 (26.8)	915,716 (25.3)	2.987 (2.407–3.707)	<0.001
60–69	657,412 (18.0)	11,496 (30.7)	645,916 (17.9)	5.207 (4.184–6.479)	<0.001
70–79	273,253 (7.5)	5,831 (15.6)	267,422 (7.4)	8.186 (6.452–10.386)	<0.001
≥80	40,212 (1.1)	669 (1.8)	39,543 (1.1)	9.72 (5.929–15.934)	<0.001
Body mass index (kg/m²)					
<18.5	127,463 (3.5)	842 (2.3)	126,621 (3.5)	1.000	
18.5–23	1,519,420 (41.6)	12,711 (34.0)	1,506,709 (41.7)	1.110 (0.975–1.265)	0.116
23–25	892,897 (24.4)	9,479 (25.4)	883,418 (24.4)	1.221 (1.073–1.388)	0.002
>25	1,114,926 (30.5)	14,358 (38.4)	1,100,568 (30.4)	1.250 (1.103–1.417)	0.001
Fasting blood glucose (mg/dL)					
<126	347,2851 (95.0)	34,541 (92.4)	3,438,310 (95.1)	1.000	
≥126	181,855 (5.0)	2,849 (7.6)	179,006 (4.9)	1.183 (0.997–1.404)	0.054
Total cholesterol (mg/dL)					
<200	2,093,347 (57.3)	18,267 (48.9)	2,075,080 (57.4)	1.000	
200–240	1,091,988 (29.9)	12,699 (34.0)	1,079,289 (29.8)	1.067 (0.974–1.170)	0.165
>240	469,371 (12.8)	6,424 (17.2)	462,947 (12.8)	1.059 (0.939–1.195)	0.346
Family history of DM					
No	3,113,793 (92.2)	32,115 (93.1)	3,081,678 (92.2)	1.000	
Yes	262,790 (7.8)	2,390 (6.9)	260,400 (7.8)	1.115 (0.961–1.294)	0.152
Family history of malignancy					
No	2,921,230 (86.2)	29,605 (85.4)	2,891,625 (86.2)	1.000	
Yes	469,388 (13.8)	5,069 (14.6)	464,319 (13.8)	1.103 (0.990–1.230)	0.076
Alcohol consumption					
Never	2,839,365 (77.7)	30,648 (83.8)	2,808,717 (79.2)	1.000	
2–3 times/mo	457,398 (12.5)	3,513 (9.6)	453,885 (12.8)	0.973 (0.844–1.122)	0.705
1–2 times/wk	222,337 (6.1)	1,752 (4.8)	220,585 (6.2)	0.925 (0.758–1.129)	0.443
3–4 times/wk	39,489 (1.1)	387 (1.1)	39,102 (1.1)	1.111 (0.740–1.668)	0.612
Everyday	22,483 (0.6)	269 (0.7)	22,214 (0.6)	1.494 (0.959–2.327)	0.076
Smoking					
None	3,419,049 (93.6)	34,777 (95.9)	3,384,272 (96.4)	1.000	
Ex-smoker	39,908 (1.1)	434 (1.2)	39,474 (1.1)	1.293 (0.919–1.821)	0.140
Current smoker	88,959 (2.4)	1,057 (2.9)	87,902 (2.5)	0.988 (0.743–1.313)	0.934
History of colonoscopy					
No	117,231 (34.4)	1,097 (41.4)	116,134 (34.3)	1.000	
Yes	223,914 (65.6)	1,555 (58.6)	222,359 (65.7)	0.609 (0.560–0.663)	<0.001

Values are presented as number (%) unless otherwise indicated.
HR, hazard ratio; CI, confidence interval; DM, diabetes mellitus.

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colorectal cancer (HR, 0.501; P < 0.001) (Table 2).

In women, risk increased with age, and the risk was highest in patients over 80 years (HR, 9.720; P < 0.001) (Table 3). Risk increased with increasing BMI, and BMI over 23 kg/m^2 was revealed as a risk factor of colorectal cancer (23–25 kg/m^2: HR, 1.221; P = 0.0024; ≥25 kg/m^2: HR, 1.250; P = 0.0005). The level of fasting blood glucose and total cholesterol were not significant risk factors for colorectal cancer. DM and malignancy showed no significant relationship with increased colorectal cancer risk in women. Frequency of alcohol consumption and smoking were not found to be risk factors in women. Colonoscopy also reduced the risk of colorectal cancer in women (HR, 0.609; P < 0.001) (Table 3).

Risk factors were also analyzed according to location of colorectal cancer. In men, right colon cancer had the greatest increase in risk with increasing age, and rectal cancer had the lowest increase (Table 4). Frequent alcohol consumption was a risk factor, but was not a risk factor in left colon cancer (Table 4). In women, total cholesterol level was not a risk factor of colorectal cancer overall, but was a risk factor in left colon cancer (Table 5).

DISCUSSION

This study showed a trend of increasing colorectal cancer in Korea. The incidence has increased from 45.4/100,000 in 2012 to 54.4/100,000 in 2014. Analysis of old Korean data shows that incidence in men was 1999 in 27.0/100,000, which increased to 50.2 in 2009. In women, the incidence in 1999 was 17.2/100,000, which increased to 26.9/100,000 in 2009 [17]. In our data, the incidence in 2014 was 64.8/100,000 in men and 44.0/100,000 in women. This demonstrates that the incidence of colorectal cancer in Korea has been dramatically increasing. Compared to other countries, the incidence of colorectal cancer in Korea is high. In 2012, the incidence in men was highest in Korea (50.0/100,000), followed by New Zealand (49.1/100,000). Korea had the third highest total incidence including men and women the world (Koreans, 37.3/100,000) after New Zealand (43.5/100,000) and the Netherlands (38.9/100,000) [17]. The United States used to have the highest incidence in the world, but it has been decreasing since the 1990s [18]. Compared to Singapore, the incidence is very high in Korea. The age-standardized rate in 2008–2012 was 20.5/100,000 in Singapore [19]. Meat consumption per person in Korea was 41.0 kg in 2006 and 51.9 kg in 2014 [20]. The increase of meat consumption may be related to the increased incidence of colorectal cancer. The incidence of colorectal cancer in Korea has been increasing dramatically, with a plateau in incidence since 2012. The cause of the plateau is unknown, but may be due to the increased interest in health care, healthy lifestyle, and eating habits. Since 2009, colonoscopy has been performed for those who are FOBT positive through National Health Examinations. An increase in health examinations and colonoscopies may have slowed down the increasing trend. Additional research is needed to find the exact cause.

Unlike other malignancies, the genetic and molecular biological pathogenesis of colorectal cancer has been extensively studied. Transition from adenoma to carcinoma describes the natural history of colon cancer development. In addition, the development of colorectal cancer due to microorganisms and intestinal factors also has been well-studied [21]. The functions of the large intestine are to deliver food from the small intestine to the rectum and to absorb water and electrolytes. Intestinal microorganisms metabolize the remaining food and digestive fluids. Cells in the colon crypts are active and proliferative, requiring nutrients. The proliferative process is affected by dietary changes [22]. Genetic changes that develop during dietary changes accumulate and lead to genomic instability. These changes result in colorectal cancer development [23]. By-products of protein digestion are fermented by colonic bacteria to produce ammonia, phenol, and hydrogen sulfide. Nitrate and nitrite are introduced into the colonic mucosa when processed meat is ingested. These substances cause inflammation and damage to the colon mucosa [24].

To ascertain the risk factors of colorectal cancer, variables included in the National Health Examination data and reported as risk factors in other studies were analyzed. In our study, increased age and BMI were revealed as risk factors in both men and women. Colonoscopy performance as part of health examinations was a protective factor for colorectal cancer. Especially in men, high fasting blood glucose and family history of malignancy were risk factors. Frequent alcohol consumption and current smoking were also risk factors for colorectal cancer in men. The relationship between increased age and colorectal cancer has been well-studied [25]. Our data also demonstrated that increased age is a risk factor for both sexes. Obesity is also a risk factor for colorectal cancer [26, 27]. Shin et al. [28] reported that high BMI is a risk factor for colorectal cancer in men, and low BMI is a protective factor in women.

The relationship of colorectal cancer with family history has been well-studied. Familial history of colorectal cancer increases the risk of colorectal cancer [29]. Familial history of other malignancies, such as gastric cancer and prostate cancer, also increases the risk of colorectal cancer [30, 31]. In this study, family history of DM and any malignancy was investigated, and familial history of DM-related malignancy was a risk factor in men. Disease presence is a risk factor for colorectal cancer. A personal history of DM is well known to increase the risk of colorectal cancer [7]. In our study, serum cholesterol level was not a significant risk factor for colorectal cancer, and high serum glucose level was a risk factor only in men.

Dietary habits are known to be important risk factors. Ingestion of red meat and processed meat such as bacon, ham, or sausage are well known risk factors [32]. Eating fried meat increases the risk of colorectal cancer [33]. Every 30-g increase of daily red meat and processed meat consumption increases colorectal cancer risk by 10% [34]. Increased total meat intake increases the risk

Table 4. Risk factors of colorectal cancer by location in men

Variable	All	Colon	Rectum	Right colon	Left colon
Age (yr)					
<40	1.000	1.000	1.000	1.000	1.000
40–49	2.685 (2.331–3.093)*	3.187 (2.642–3.844)*	2.113 (1.699–2.629)*	3.673 (2.491–5.417)*	3.128 (1.896–5.163)*
50–59	6.529 (5.689–7.492)*	7.935 (6.611–9.524)*	4.935 (3.987–6.109)*	9.66 (6.623–14.089)*	7.164 (4.385–11.703)*
60–69	13.376 (11.636–15.377)*	17.217 (14.327–20.690)*	8.889 (7.131–11.081)*	20.668 (14.122–30.248)*	17.226 (10.548–28.132)*
70–79	19.177 (16.334–22.513)*	24.490 (19.917–30.113)*	13.119 (10.074–17.085)*	32.97 (21.622–50.274)*	31.258 (18.306–53.374)*
≥80	19.190 (13.288–27.712)*	24.431 (15.624–38.203)*	13.263 (6.889–25.534)*	30.096 (12.431–72.866)*	23.129 (6.759–79.152)*
Fasting blood glucose (mg/dL)					
<126	1.000	1.000	1.000	1.000	1.000
≥126	1.217 (1.092–1.356)*	1.231 (1.081–1.401)*	1.191 (0.977–1.452)	1.207 (0.927–1.572)	1.512 (1.1–2.078)*
Total cholesterol (mg/dL)					
<200	1.000	1.000	1.000	1.000	1.000
200–240	0.956 (0.891–1.025)	0.970 (0.893–1.055)	0.923 (0.814–1.046)	1.124 (0.952–1.327)	1.039 (0.833–1.296)
>240	1.018 (0.92–1.126)	0.973 (0.859–1.102)	1.117 (0.939–1.329)	1.041 (0.810–1.337)	1.114 (0.810–1.533)
Family history of DM					
No	1.000	1.000	1.000	1.000	1.000
Yes	0.910 (0.794–1.042)	0.821 (0.691–0.975)*	1.103 (0.884–1.376)	0.584 (0.388–0.881)*	0.953 (0.622–1.458)
Family history of malignancy					
No	1.000	1.000	1.000	1.000	1.000
Yes	1.163 (1.066–1.269)*	1.128 (1.014–1.254)*	1.243 (1.068–1.447)*	0.989 (0.787–1.243)	1.380 (1.058–1.801)*
Alcohol consumption					
Never	1.000	1.000	1.000	1.000	1.000
2–3 times/mo	1.105 (1.007–1.212)*	1.024 (0.914–1.146)	1.305 (1.109–1.536)*	1.220 (0.968–1.537)	0.975 (0.732–1.298)
1–2 times/wk	1.217 (1.118–1.325)*	1.153 (1.041–1.277)*	1.380 (1.186–1.607)*	1.475 (1.200–1.813)*	0.838 (0.633–1.110)
3–4 times/wk	1.360 (1.223–1.511)*	1.262 (1.110–1.435)*	1.607 (1.334–1.936)*	1.344 (1.025–1.763)*	0.947 (0.664–1.352)
Everyday	1.490 (1.320–1.682)*	1.523 (1.321–1.757)*	1.416 (1.123–1.785)*	2.011 (1.531–2.642)*	1.14 (0.765–1.698)
Smoking					
None	1.000	1.000	1.000	1.000	1.000
Ex-smoker	1.079 (0.994–1.173)	1.101 (0.997–1.216)	1.033 (0.890–1.200)	1.270 (1.045–1.544)*	1.198 (0.928–1.548)
Current smoker	1.093 (1.013–1.180)*	1.089 (0.992–1.195)	1.101 (0.963–1.259)	1.091 (0.903–1.318)	1.018 (0.789–1.312)
Experience of colonoscopy					
No	1.000	1.000	1.000	1.000	1.000
Yes	0.501 (0.470–0.533)*	0.539 (0.500–0.582)*	0.422 (0.377–0.472)*	0.289 (0.247–0.338)*	0.593 (0.484–0.726)*

Values are presented as hazard ratio (95% confidence interval).
HR, hazard ratio; CI, confidence interval; DM, diabetes mellitus.
*P < 0.05.

of colorectal cancer by 21%–28% [35]. An experimental study revealed that the fatty acids of animal fat act as a carcinogen in colorectal cancer [36]. Consumption of dietary fiber is a known protective factor for colorectal cancer [37]. As dietary fiber ferments in the large intestine, short chain fatty acids (SCFA), such as butyrate, acetate, and propionate, are produced. SCFA are used as a main energy source for colonic mucosa cells to maintain anti-inflammatory functions, preventing development of colorectal cancer [38]. Dietary risks are difficult to research because of difficulties in acquiring detailed data. In this study, acquisition of such data was impossible. The National Health Examination data questionnaire only differentiates among meat-eaters, eaters of both

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Table 5. Risk factors of colorectal cancer by location in women

Variable	All	Colon	Rectum	Right colon	Left colon
Age (yr)					
<40	1.000	1.000	1.000	1.000	1.000
40–49	2.011 (1.624–2.490)*	1.824 (1.431–2.325)*	2.675 (1.701–4.207)*	2.388 (1.249–4.565)*	5.024 (1.553–16.254)*
50–59	2.987 (2.407–3.707)*	2.624 (2.052–3.354)*	4.341 (2.756–6.837)*	4.472 (2.341–8.544)*	7.939 (2.462–25.603)*
60–69	5.207 (4.184–6.479)*	4.565 (3.558–5.856)*	7.642 (4.826–12.101)*	7.252 (3.748–14.032)*	23.470 (7.327–75.178)*
70–79	8.186 (6.452–10.386)*	7.101 (5.402–9.335)*	12.329 (7.553–20.125)*	13.512 (6.723–27.157)*	41.612 (12.740–135.913)*
≥80	9.720 (5.929–15.934)*	6.561 (3.383–12.721)*	20.932 (9.533–45.963)*	20.429 (6.395–65.260)*	30.182 (4.986–182.694)*
Fasting blood glucose (mg/dL)					
<126	1.000	1.000	1.000	1.000	1.000
≥126	1.183 (0.997–1.404)	1.187 (0.970–1.452)	1.176 (0.853–1.623)	1.326 (0.843–2.088)	1.062 (0.654–1.724)
Total cholesterol (mg/dL)					
<200	1.000	1.000	1.000	1.000	1.000
200–240	1.067 (0.974–1.170)	1.051 (0.944–1.171)	1.112 (0.933–1.326)	0.979 (0.754–1.271)	1.320 (1.004–1.735)*
>240	1.059 (0.939–1.195)	1.043 (0.905–1.202)	1.105 (0.880–1.386)	0.852 (0.597–1.217)	1.614 (1.172–2.223)*
Family history of DM					
No	1.000	1.000	1.000	1.000	1.000
Yes	1.115 (0.961–1.294)	1.111 (0.934–1.321)	1.128 (0.844–1.507)	1.371 (0.922–2.037)	0.810 (0.479–1.370)
Family history of malignancy					
No	1.000	1.000	1.000	1.000	1.000
Yes	1.103 (0.990–1.230)	1.140 (1.006–1.292)*	1.001 (0.805–1.245)	0.870 (0.619–1.223)	1.000 (0.715–1.398)
Alcohol consumption					
Never	1.000	1.000	1.000	1.000	1.000
2–3 times/mo	0.973 (0.844–1.122)	1.036 (0.881–1.219)	0.803 (0.597–1.081)	0.958 (0.633–1.451)	0.726 (0.434–1.216)
1–2 times/wk	0.925 (0.758–1.129)	0.860 (0.675–1.096)	1.095 (0.771–1.554)	0.860 (0.477–1.552)	0.940 (0.494–1.785)
3–4 times/wk	1.111 (0.740–1.668)	1.181 (0.739–1.888)	0.945 (0.419–2.132)	1.860 (0.755–4.578)	1.360 (1.122–1.412)
Everyday	1.494 (0.959–2.327)	1.610 (0.965–2.685)	1.229 (0.506–2.983)	1.230 (0.917–1.650)	2.106 (0.672–6.603)
Smoking					
None	1.000	1.000	1.000	1.000	1.000
Ex-smoker	1.293 (0.919–1.821)	1.276 (0.856–1.902)	1.345 (0.692–2.613)	0.631 (0.156–2.551)	1.099 (0.350–3.456)
Current smoker	0.988 (0.743–1.313)	0.762 (0.522–1.112)	1.586 (1.026–2.450)*	1.115 (0.520–2.390)	0.172 (0.024–1.234)
Experience of colonoscopy					
No	1.000	1.000	1.000	1.000	1.000
Yes	0.609 (0.560–0.663)*	0.712 (0.645–0.787)*	0.406 (0.346–0.475)*	0.312 (0.246–0.397)*	0.673 (0.525–0.865)*

Values are presented as hazard ratio (95% confidence interval).
HR, hazard ratio; CI, confidence interval; DM, diabetes mellitus.
*P < 0.05.

meat and vegetables, and vegetarians. Increased consumption of alcohol is also a risk factor for colorectal cancer. One report concluded that that consumption of more than 45 g/day of ethanol increases risk of colorectal cancer by 41% [39]. Our data only assessed frequency of alcohol consumption; in the future, the kind and amount of alcohol consumption should be included for more detailed analyses.

Many tools have been developed for colorectal screening. These screening tools decrease colorectal cancer death through early identification and removal of polyps [40]. Colonoscopy is widely used to screen for colorectal cancer in many countries. Colonoscopy is the gold standard for colorectal cancer screening. Colo-

noscopy has high sensitivity and specificity, and simultaneous polypectomy is available during colonoscopy [41]. Even with normal findings, colonoscopy reduces the risk of colorectal cancer [42] and colorectal cancer-related death [43]. However, due to economic considerations and difficulties in bowel preparation, colonoscopy cannot always be used as a frequent screening tool. In many countries, colonoscopy for FOBT-positive individuals is widely used for colorectal cancer screening [44]. In our data, history of colonoscopy was a protective factor against colorectal cancer in both sexes. Routine use of colonoscopy reduces the incidence of colorectal cancer.

In this study, we identified a trend in colorectal cancer incidence in Korea over the past 10 years. The incidence substantially increased until 2012. We also analyzed risk factors of colorectal cancer in men and women. Because many factors are involved in the development of colorectal cancer, not all identified risk factors may be primary risk factors. However, this study analyzed risk factors for a large population in Korea. The National Health Examination data on lifestyle and eating habits are limited, and data that are more detailed may provide meaningful results about risk factors in the future.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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