ORIGINAL ARTICLE

Retrospective Cohort Study

Characteristics of and risk factors for colorectal neoplasms in young adults in a screening population

Seung Eun Lee, Hee Bum Jo, Won Gun Kwack, Yun Jin Jeong, Yeo-Jin Yoon, Hyoun Woo Kang

Seung Eun Lee, Hee Bum Jo, Won Gun Kwack, Yun Jin Jeong, Yeo-Jin Yoon, Hyoun Woo Kang, Department of Internal Medicine, Dongguk University Ilsan Hospital, College of Medicine, Dongguk, Goyang, Gyeonggi-do 410-773, South Korea

Correspondence to: Hyoun Woo Kang, MD, PhD, Department of Internal Medicine, Dongguk University Ilsan Hospital, College of Medicine, Dongguk, Goyang, Gyeonggi-do 410-773, South Korea. gangmali@naver.com
Telephone: +82-31-9617128
Fax: +82-31-9617131

Abstract

AIM: To investigate prevalence and risk factors for colorectal neoplasms in adults aged < 50 years, for whom screening is not recommended.

METHODS: This cross-sectional study compared prevalence and characteristics of colorectal and advanced adenomas in patients aged < 50 years who underwent colonoscopy screening with subjects aged ≥ 50 years. To evaluate risk factors for colorectal and advanced adenoma in young adults, we used multivariable logistic regression models. Colorectal neoplasm characteristics were evaluated and compared with those in older patients.

RESULTS: Among 2819 patients included, prevalences of colorectal adenoma and advanced adenoma were 19.7% and 1.5%, respectively. As patient age increased, so did the prevalence of colorectal neoplasm. However, prevalence of advanced adenoma did not differ between age-groups 45-49 years and ≥ 50 years (OR = 0.43, 95%CI: 0.17-1.07, *P* = 0.070). In younger age-group (< 50 years), colorectal adenoma was significantly associated with older age, waist circumference (OR = 1.72, 95%CI: 1.15-2.55, *P* = 0.008), and current smoking (OR = 1.60, 95%CI: 1.07-2.41, *P* = 0.023). Alcohol consumption was

an independent risk factor for colorectal advanced adenoma (OR = 3.69, 95%CI: 1.08-12.54, *P* = 0.037). Multiple neoplasms and large neoplasms (⩾ 1 cm) were more prevalent in subjects ⩾ 50 years.

CONCLUSION: Current screening strategies for colorectal cancer may need to be amended to account for patient age, especially in young subjects with abdominal obesity, current smoking and alcohol consumption.

Key words: Colorectal adenoma; Advanced adenoma; Colorectal cancer; Cancer screening; Young patients

Core tip: We investigated prevalence and risk factors for colorectal neoplasms in adults aged < 50 years. The study demonstrated that, in terms of advanced adenoma, the groups aged < 40 years and 40-44 years showed significantly lower risk compared with the group aged ⩾ 50 years. However, no significant difference was found between the age-groups 45-49 years and ⩾ 50 years. In the young age-group, age, waist circumference, and current smoking were associated with a higher risk of colorectal adenoma, and alcohol consumption was associated with a higher risk of advanced adenoma.

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer-related mortality in North America[1,2]. In addition, the incidence of colorectal neoplasm is increasing in Asia, including South Korea[3,4]. Fortunately, CRC screening has demonstrated ability to reduce the incidence of CRC and CRC-related mortality[5-8]. Thus, many countries have adopted screening strategies that accord with their particular medical and socioeconomic environment.

Influential guidelines, including those in the United States and Europe, recommend screening for CRC beginning at age 50 years for average-risk patients[9-12]. These recommendations are based on the fact that CRC occurs infrequently before age 50[13,14]. However, in the past decades, the incidence of CRC in young adults has been increasing, in contrast to cases in older adults, which have been decreasing[15-17]. Furthermore,

the prevalence of advanced colorectal adenoma is still significant: 3.5% in patients aged < 50 years[15]. These epidemiological data imply that it may be necessary to modify strategies for CRC screening programs. It has been well documented that most CRCs arise from colorectal adenoma by a process referred to as the "adenoma-carcinoma sequence"[18,19]. Identifying the characteristics and risk factors for colorectal adenoma and advanced neoplasms in the population aged < 50 years may help in the development of new preventive and early detection strategies.

The aim of this study was to investigate the characteristics of colorectal neoplasm, including prevalence and risk factors, in subjects < 50 years old (young age group), and to compare them with subjects ⩾ 50 years old (old age group) within a screening population.

MATERIALS AND METHODS

Study population and design

This was a cross-sectional, retrospective study that reviewed the medical records of subjects who underwent colonoscopy as a part of routine health checkups from January 2012 to June 2014 at Dongguk University Ilsan Hospital Medical Screening Center (Goyang, South Korea). We reviewed all the subjects who received a colonoscopy, filled out the question-naire, were physically examined, and had various blood tests during the screening period. We excluded subjects who met the following exclusion criteria: significant missing information, incomplete examination due to poor bowel preparation or cecal intubation failure, colonic examination in the previous 10 years, and history of colonic diseases (*e.g.*, CRC, inflammatory bowel disease, bowel resection). Most subjects paid for the health examination themselves; employers covered the remaining costs. We divided the enrolled subjects into 4 groups according to age: < 40 years, 40-44 years, 45-49 years, and ⩾ 50 years. The study design was approved by the Institutional Review Board of Dongguk University Ilsan Hospital.

Clinical and laboratory evaluations

All participants were required to fill out self-administered questionnaires, which included questions about smoking status (current, former, never), alcohol consumption, physical activity, family history of CRC in first-degree relatives, medical history of diabetes, hypertension, and use of aspirin. The patients' height and weight were obtained by a trained nurse. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). As recommended, waist circumference (WC) was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest[20]. Venous samples were drawn after an overnight 12-h fast to determine serum complete cell counts, total cholesterol, triglycerides, high-density lipoprotein (HDL)

cholesterol, low-density lipoprotein (LDL) cholesterol, high-sensitivity C-reactive protein (hsCRP), and fasting glucose. All other biochemical tests were carried out using an automatic analyzer (cobas® 6500 model, Roche, Basel, Switzerland) within the Department of Laboratory Medicine at Dongguk University Ilsan Hospital, which is accredited by the Korean Society for Laboratory Medicine and the Korean Association of Quality Assurance.

Definitions

Current smoking was defined as smoking regularly or some days during the previous 1 year; former smoking was defined as no smoking at all during the previous 1 year[21]. Alcohol consumption was defined as drinking > 140 g alcohol per week. Hypertension was defined as blood pressure $\geq$ 140/90 mmHg; diabetes mellitus was defined as a fasting plasma glucose concentration of $\geq$ 126 mg/dL. Subjects taking anti-hypertensive or anti-diabetic drugs were considered to have hypertension or diabetes mellitus. Regular medication was defined as drug use for $\geq$ 3 mo during the preceding 12 mo. Individuals were diagnosed as having metabolic syndrome by the presence of $\geq$ 3 of the following criteria[22]: (1) WC $\geq$ 90 cm in men and $\geq$ 80 cm in women; (2) blood pressure $\geq$ 130/85 mmHg; (3) fasting plasma glucose $\geq$ 110 mg/dL; (4) triglyceride levels $\geq$ 150 mg/dL; and (5) HDL cholesterol < 40 mg/dL for men and < 50 mg/dL for women.

Colonoscopy and detection of colorectal adenoma

Colonoscopy was performed using a model H260 flexible endoscope (Olympus Optical, Tokyo, Japan) by 6 experienced gastroenterologists who had gastroenterology and endoscopy specialty board certifications. Bowel preparation was conducted using 2 L of polyethylene glycol with ascorbate (Coolprep®; TaeJoon Pharmaceuticals, Seoul, South Korea). Most subjects were consciously sedated with midazolam and pethidine. The location, size, number, and type of all adenomatous polyps were recorded. The locations of colorectal adenomas were categorized as either within the proximal colon (*i.e.*, the cecum, ascending colon, or transverse colon) or within the distal colon (*i.e.*, the splenic flexure, descending colon, sigmoid colon, or rectum). Polyp sizes were estimated using 7-mm diameter open-biopsy forceps. Histopathologically, colorectal adenomas were categorized either by grade or by amount of villous component (tubular, tubulovillous, or villous; serrated polyps/adenoma). An advanced adenoma was defined as advanced if it had a diameter $\geq$ 10 mm, high-grade dysplasia, or $\geq$ 25% villous features. Hyperplastic polyps were excluded.

Statistical analysis

To evaluate the relationship between age and colorectal neoplasms, subjects were categorized into 4 age-groups: < 40 years, 40-44 years, 45-49

years, and $\geq$ 50 years. In addition to age-group, other independent variables evaluated included sex, smoking status, hypertension, diabetes mellitus, BMI, WC, cholesterol parameters, and hsCRP. In order to compare the patients' baseline characteristics, one-way analysis of variance was used for continuous variables, and the linear-by-linear association test was used for categorical variables.

Risk factors for adenoma and advanced colorectal neoplasm in young subjects were determined by performing univariate analysis for each variable separately; then, multivariate analysis was done using multivariate conditional logistic regression. In conducting our univariate analysis, we used Student's *t* test for continuous variables and the χ^2 test for categorical variables. About colorectal adenoma and advanced adenoma, variables with a *P* value < 0.05 in the univariate analysis were added to the multivariate conditional logistic regression model. ORs and 95%CIs were calculated to evaluate each risk factor. A *P* value of < 0.05 was considered statistically significant. We also conducted hierarchical cluster analysis to find the surge point of age for prevalences of colorectal adenoma and advanced adenoma. All analyses were conducted using SPSS software version 20.0 for Windows (SPSS, Chicago, IL, United States).

RESULTS

Baseline characteristics of the study subjects

A total of 4668 patients underwent colonoscopy. All participants were requested to fill out the questionnaire and undergo physical examination and various blood tests during the review period. Among the 4668 patients, 1849 met the exclusion criteria. After exclusion, the final sample size was 2819 participants (Figure 1), among whom the prevalence of colorectal adenoma and advanced adenoma was 19.7% and 1.5%, respectively. The baseline characteristics of subjects categorized as < 40 years, 40-44 years, 45-49 years, and $\geq$ 50 years are summarized in Table 1. No statistically significant difference was found between the groups in terms of sex. The prevalence of hypertension, diabetes mellitus, and metabolic syndrome increased with age, and the presence of alcohol consumption and smoking decreased with age. Subjects in the age-group $\geq$ 50 years had higher mean BMI, WC, triglyceride levels, hsCRP, total cholesterol, and LDL cholesterol levels, but lower HDL cholesterol levels. In hierarchial cluster analysis, the age groups were divided in two groups for colorectal adenoma (age < 46 or age $\geq$ 46) (Figure 2A) and for advanced adenoma (age < 49 or age $\geq$ 49), respectively (Figure 2B).

Risk factors for colorectal adenoma and advanced adenoma

We examined the risk factors for colorectal adenoma and advanced adenoma. After performing a univariate
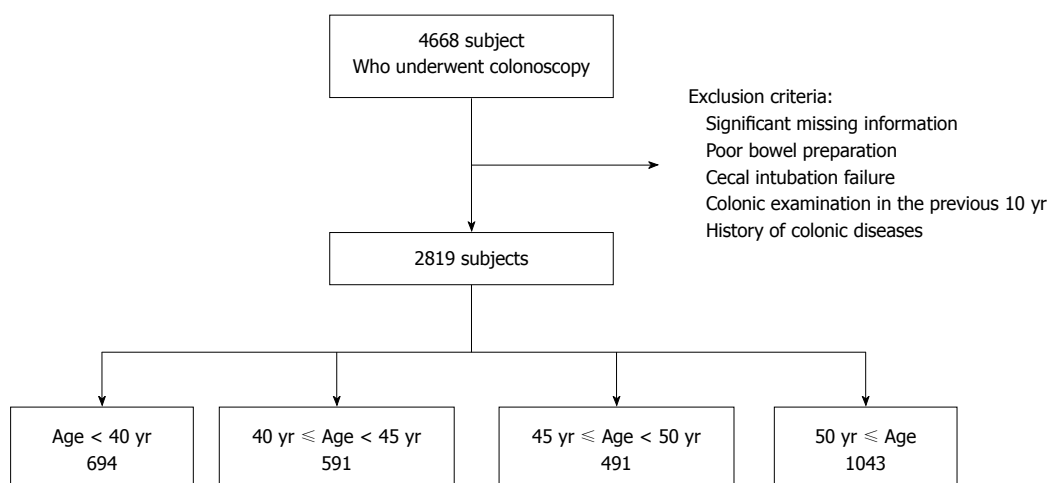
Figure 1 Study population. In total, 4668 subjects who underwent screening colonoscopy were reviewed during study period. 1849 subjects were excluded for the reasons stated in the Methods section. The remaining 2819 subjects were enrolled and divided to 4 groups according to age (< 40 years, 40-44 years, 45-49 years, and ⩾ 50 years).

Table 1 Baseline characteristics of the subjects according to age *n* (%)

Variable	Age group				*P* value
	< 40 (*n* = 694)	40-44 (*n* = 591)	45-49 (*n* = 491)	⩾ 50 (*n* = 1043)	
Males	465 (67.0)	443 (75.0)	363 (73.9)	717 (68.7)	0.790
Body mass index (kg/m^2)	23.1 ± 3.3	23.8 ± 3.3	24.0 ± 3.0	24.0 ± 3.0	< 0.001
Waist circumference (cm)	81.5 ± 10.3	82.9 ± 9.5	83.7 ± 8.8	84.1 ± 8.7	< 0.001
Diabetes mellitus	17 (2.4)	21 (3.6)	33 (6.7)	130 (12.5)	< 0.001
Hypertension	89 (12.8)	146 (24.7)	155 (31.6)	462 (44.3)	< 0.001
Metabolic syndrome	48 (6.9)	67 (11.3)	77 (15.7)	226 (21.7)	< 0.001
High hsCRP	54 (7.8)	55 (9.3)	41 (8.4)	131 (12.6)	0.001
Triglyceride (mg/dL)	116.0 ± 91.2	125.4 ± 85.3	130.2 ± 90.2	123.8 ± 83.6	0.039
HDL cholesterol (mg/dL)	58.7 ± 15.1	57.5 ± 14.7	56.3 ± 14.6	56.7 ± 15.1	0.018
LDL cholesterol (mg/dL)	132.0 ± 50.3	136.6 ± 34.1	139.5 ± 36.8	137.4 ± 35.1	0.006
Total cholesterol (mg/dL)	202.1 ± 37.5	208.0 ± 36.0	210.8 ± 41.6	208.2 ± 39.4	0.001
Alcohol consumption	272 (39.2)	263 (44.5)	235 (47.9)	348 (33.4)	0.005
Smoking status					
Never	312 (45.0)	212 (35.9)	181 (36.9)	449 (43.0)	< 0.001
Former	134 (19.3)	136 (23.0)	131 (26.7)	366 (35.1)	
Current	248 (35.7)	243 (41.1)	179 (36.5)	228 (21.9)	
Colorectal adenoma	61 (8.8)	87 (14.7)	105 (21.4)	302 (29.0)	< 0.001
Advanced neoplasm	6 (0.9)	4 (0.7)	6 (1.2)	26 (2.5)	0.004
⩾ 1 cm	5 (0.7)	3 (0.5)	5 (1.0)	24 (2.3)	0.001
Villous	1 (0.1)	1 (0.2)	1 (0.2)	7 (0.7)	0.055
High grade	0 (0.0)	1 (0.2)	1 (0.2)	4 (0.4)	0.091
Multiplicity	8 (1.2)	18 (3.0)	33 (6.7)	121 (11.6)	< 0.001

hsCRP: High-sensitivity C-reactive protein; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

analysis, older age, male sex, alcohol consumption, smoking, BMI, WC, diabetes mellitus, hypertension and metabolic syndrome, hsCRP, triglyceride level, and total cholesterol were significantly associated with an increased risk of colorectal adenoma. To determine whether age independently increased the risk of colorectal adenoma, multivariate analysis was performed, following which age remained a statistically significant risk factor (Table 2). In addition to age, male sex (OR = 1.88, 95%CI: 1.35-2.61, *P* < 0.001), WC (OR = 1.50, 95%CI: 1.14-4.97, *P* = 0.004), and current smoking (OR = 1.56, 95%CI: 1.16-2.10, *P* = 0.003) were significant risk factors for colorectal

adenoma (Table 2).

For advanced colorectal adenoma, univariate analysis and subsequent multivariate analysis were done in the same manner. Patients aged < 40 years (OR = 0.34, 95%CI: 0.13-0.85, *P* = 0.022) and 40-44 years (OR = 0.24, 95%CI: 0.08-0.71, *P* = 0.010) showed significantly lower risk for advanced adenoma compared with those aged ⩾ 50 years. However, the group aged 45-49 years had no significant difference with the group aged ⩾ 50 years (OR = 0.43, 95%CI: 0.17-1.07, *P* = 0.070). According to multivariate analysis, alcohol consumption was a significant risk factor for advanced adenoma (OR = 2.39, 95%CI:

Table 2 Risk factors of colorectal adenoma in this study population *n* (%)

Variable	Number of persons		Univariate analysis		Multivariate analysis[1]	
	Non-adenoma	Adenoma	OR (95%CI)	*P* value	OR (95%CI)	*P* value
	(*n* = 2264)	(*n* = 555)				
Males	1530 (67.6)	458 (82.5)	2.27 (1.79-2.87)	< 0.001	1.88 (1.35-2.61)	< 0.001
Age (yr)						
≥ 50	741 (32.7)	302 (54.4)	1	< 0.001	1	
45-49	386 (17.0)	105 (18.9)	0.67 (0.52-0.86)		0.64 (0.49-0.84)	0.001
40-44	504 (22.3)	87 (15.7)	0.42 (0.33-0.55)		0.40 (0.30-0.53)	< 0.001
< 40	633 (28.0)	61 (11.0)	0.24 (0.18-0.32)		0.25 (0.18-0.34)	< 0.001
Body mass index (kg/m^2)						
mean ± SD	23.6 ± 3.2	24.4 ± 3.0				
< 25	1468 (64.8)	321 (57.8)	1	< 0.001	1	
25.0-29.9	624 (27.6)	203 (36.6)	1.52 (1.25-1.86)		0.94 (0.72-1.23)	0.644
≥ 30	76 (3.4)	18 (3.2)	1.11 (0.65-1.88)		0.68 (0.37-1.24)	0.204
Waist circumference (cm)						
mean ± SD	82.6 ± 9.4	85.5 ± 8.7				
Male < 90, female < 80	1658 (73.2)	353 (63.6)	1	< 0.001	1	
Male ≥ 90, female ≥ 80	606 (6.8)	202 (36.4)	1.57 (1.28-1.91)		1.50 (1.14-1.97)	0.004
Diabetes mellitus	144 (6.4)	57 (10.3)	1.69 (1.22-2.33)	0.001	1.12 (0.79-1.57)	0.533
Hypertension	623 (27.5)	229 (41.3)	1.85 (1.53-2.24)	< 0.001	1.27 (0.96-1.67)	0.095
Metabolic syndrome	308 (13.6)	110 (19.8)	1.57 (1.23-2.00)	< 0.001	0.86 (0.59-1.26)	0.445
hsCRP						
< 0.10			1	0.020	1	
≥ 0.10			1.25 (1.04-1.51)		1.05 (0.82-1.34)	0.725
Triglyceride (mg/dL)						
mean ± SD	119.7 ± 85.8	138.1 ± 91.0				
< 150	1742 (76.9)	376 (67.7)	1	< 0.001	1	
≥ 150	522 (23.1)	179 (32.3)	1.59 (1.30-1.95)		1.15 (0.92-1.45)	0.227
HDL cholesterol (mg/dL)						
mean ± SD	57.9 ± 15.0	54.9 ± 14.6				
Male < 40, female < 50	277 (12.2)	77 (13.9)	1	0.296		
Male ≥ 40, female ≥ 50	1987 (87.8)	478 (86.1)	0.87 (0.66-1.14)			
LDL cholesterol (mg/dL)						
mean ± SD	135.7 ± 40.3	138.5 ± 36.1				
≤ 100	354 (15.6)	76 (13.7)	1	0.070		
101-129	699 (30.9)	152 (27.4)	1.01 (0.75-1.37)			
≥ 130	1211 (53.5)	327 (58.9)	1.26 (0.95-1.66)			
Total cholesterol (mg/dL)						
mean ± SD	206.7 ± 38.5	209.0 ± 40.0				
< 200	1033 (45.6)	226 (40.7)	1	0.037	1	
≥ 200	1231 (54.4)	329 (59.3)	1.22 (1.01-1.48)		1.09 (0.89-1.34)	0.390
Current alcohol	871 (38.5)	247 (44.5)	1.28 (1.06-1.55)	0.009	0.93 (0.75-1.16)	0.513
Smoking status						
Never	994 (43.9)	160 (28.8)	1	< 0.001	1	
Former	584 (25.8)	18 (33.0)	1.90 (1.54-2.46)		1.21 (0.90-1.63)	0.215
Current	68 (30.3)	21(38.2)	1.90 (1.53-2.41)		1.56 (1.16-2.10)	0.003

[1]Adjusted for sex, age, body mass index, waist circumference, diabetes mellitus, hypertension, metabolic syndrome, hsCRP, triglyceride, alcohol, and smoking. hsCRP: High-sensitivity C-reactive protein; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

1.14-4.99, *P* = 0.021) (Table 3).

Risk factors for colorectal adenoma and advanced adenoma in young subjects

We also examined risk factors for colorectal adenoma and advanced adenoma in young subjects. In univariate analysis, older age, male sex, alcohol consumption, smoking, BMI, WC, diabetes mellitus, hypertension, metabolic syndrome, triglyceride levels, and total cholesterol were significant risk factors for colorectal adenoma in young subjects. After performing multivariate analysis, increasing age, WC (OR = 1.72, 95%CI: 1.15-2.55, *P* = 0.008), and

current smoking (OR = 1.60, 95%CI: 1.07-2.41, *P* = 0.023) were independent, significant risk factors (Table 4). Risk factors for colorectal advanced adenoma in young subjects were analyzed using the same method. Alcohol consumption was found to be the only significant risk factor in the younger age-groups (OR = 3.69, 95%CI: 1.08-12.54, *P* = 0.037) (Table 5).

Comparison of adenoma characteristics by patient age

We further compared the characteristics of colorectal adenoma in the young and the old age-groups. Villous adenomas, high-grade adenoma, and large (> 1 cm) adenomas were more prevalent in subjects aged ≥ 50

Table 3 Risk factors of colorectal advanced adenoma in this study population *n* (%)

Variable	Number of persons		Univariate analysis		Multivariate analysis[1]	
	Non-advanced adenoma	Advanced adenoma	OR (95%CI)	*P* value	OR (95%CI)	*P* value
	(*n* = 2778)	(*n* = 41)				
Males	1955 (70.4)	33 (80.5)	1.74 (0.80-3.78)	0.159	0.80 (0.27-2.43)	0.697
Age (yr)						
≥ 50	1018 (36.6)	25 (61.0)	1	0.003	1	
45-49	485 (17.5)	6 (14.6)	0.50 (0.21-1.24)		0.43 (0.17-1.07)	0.070
40-44	587 (21.1)	4 (9.8)	0.28 (0.10-0.80)		0.24 (0.08-0.71)	0.010
< 40	688 (24.8)	6 (14.6)	0.36 (0.15-0.87)		0.34 (0.13-0.85)	0.022
Body mass index (kg/m^2)						
mean ± SD	23.7 ± 3.1	24.5 ± 3.0				
< 25	1764 (63.5)	25 (61.0)	1	0.518		
25.0-29.9	814 (29.3)	13 (31.7)	1.15 (0.59-2.25)			
≥ 30	92 (3.3)	2 (4.9)	1.57 (0.37-6.70)			
Waist circumference (cm)						
mean ± SD	83.1 ± 9.4	85.9 ± 7.1				
Male < 90, female < 80	1985 (71.5)	26 (63.4)	1	0.258		
Male ≥ 90, female ≥ 80	793 (28.5)	15 (36.6)	1.44 (0.76-2.74)			
Diabetes mellitus	196 (7.1)	5 (12.2)	1.83 (0.71-4.72)	0.204		
Hypertension	835 (30.1)	17 (41.5)	1.65 (0.88-3.08)	0.114	1.03 (0.45-2.38)	0.947
Metabolic syndrome	409 (14.7)	9 (22.0)	1.63 (0.77-3.44)	0.196	1.06 (0.40-2.80)	0.907
hsCRP (mg/dL)						
< 0.10	1747 (62.9)	24 (58.5)	1	0.567		
≥ 0.10	1031 (37.1)	17 (41.5)	1.20 (0.64-2.25)			
Triglyceride (mg/dL)						
mean ± SD	123.1 ± 87.3	136.8 ± 75.3				
< 150	2091 (75.3)	27 (65.9)	1	0.166	1	
≥ 150	687 (24.7)	14 (34.1)	1.58 (0.82-3.03)		1.23 (0.62-2.45)	0.555
HDL cholesterol (mg/dL)						
mean ± SD	57.3 ± 15.0	56.2 ± 15.7				
Male < 40, female < 50	348 (12.5)	6 (14.6)	1	0.686		
Male ≥ 40, female ≥ 50	2430 (87.5)	35 (85.4)	0.84 (0.35-2.00)			
LDL cholesterol (mg/dL)						
mean ± SD	136.3 ± 39.4	137.2 ± 46.3				
≤ 100	423 (15.2)	7 (17.1)	1	0.876		
101-129	840 (30.2)	11 (26.8)	0.79 (0.31-2.06)			
≥ 130	1515 (54.5)	23 (56.1)	0.92 (0.39-2.15)			
Total cholesterol (mg/dL)						
mean ± SD	207.1 ± 38.5	208.7 ± 52.1				
< 200	1240 (44.6)	19 (46.3)	1	0.827		
≥ 200	1538 (55.4)	22 (53.7)	0.93 (0.50-1.73)			
Current alcohol	1093 (39.3)	25 (61.0)	2.41 (1.28-4.53)	0.005	2.39 (1.14-4.99)	0.021
Smoking status						
Never	1143 (41.1)	11 (26.8)	1	0.106	1	
Former	753 (27.1)	14 (34.1)	1.93 (0.87-4.28)		1.40 (0.50-3.92)	0.516
Current	882 (31.7)	16 (39.0)	1.89 (0.87-4.08)		1.61 (0.58-4.45)	0.363

[1]Adjusted for sex, age, hypertension, metabolic syndrome, triglyceride, alcohol, and smoking. hsCRP: High-sensitivity C-reactive protein; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

years, but no statistically significant differences were found between the 2 groups. For continuous variables, the number of adenomas was higher in the old age-group (1.82 ± 1.39 *vs* 1.31 ± 0.66, *P* < 0.001); for categorical variables, multiplicity was significantly predominant in subjects aged ≥ 50 years (40.1% *vs* 23.3%, *P* < 0.001). The prevalence of right-sided adenomas was higher in the old age-group, but there was no significant difference compared with the young age-group (51.7% *vs* 44.3%, *P* = 0.083) (Table 6).

Comparison of sessile serrated adenoma/polyp characteristics by patient age
We also evaluated relationship between age and the prevalence of sessile serrated adenoma/polyp (SSA/P) was more prevalent in subjects aged ≥ 50 years (2.1% *vs* 5.5%, *P* < 0.001). In subjects who had SSA/SSP, we further analyzed whether the number and location was associated with age or not. There were no differences between 2 groups in terms of the number and location (Table 7).

DISCUSSION

This population-based study showed no significant difference in the prevalence of advanced colorectal adenoma between the age-groups 45-49 years and ≥ 50 years. The incidence of colorectal neoplasm in

Table 4 Risk factors for colorectal adenoma in young subjects *n* (%)

Variable	Number of persons		Univariate analysis		Multivariate analysis[1]	
	Non-adenoma	Adenoma	OR (95%CI)	*P* value	OR (95%CI)	*P* value
	(*n* = 1523)	(*n* = 253)				
Males	1060 (69.6)	211 (83.4)	2.19 (1.55-3.11)	< 0.001	1.43 (0.89-2.28)	0.136
Age (yr)						
45-49	386 (25.3)	105 (41.5)	1	< 0.001	1	
40-44	504 (33.1)	87 (34.4)	0.64 (0.46-0.87)		0.64 (0.46-0.88)	0.006
< 40	633 (41.6)	61 (24.1)	0.35 (0.25-0.50)		0.39 (0.28-0.56)	< 0.001
Body mass index (kg/m²)						
mean ± SD	23.5 ± 3.2	24.4 ± 3.1				
18.5-24.9	993 (65.2)	144 (56.9)	1	0.002	1	
25.0-29.9	402 (26.4)	94 (37.2)	1.66 (1.25-2.20)		0.90 (0.61-1.33)	0.599
≥ 30	55 (3.6)	9 (3.6)	1.16 (0.56-2.40)		0.55 (0.24-1.27)	0.161
Waist circumference (cm)						
mean ± SD	82.1 ± 9.7	85.2 ± 9.3				
Male < 90, female < 80	1161 (76.2)	164 (64.8)		< 0.001	1	
Male ≥ 90, female ≥ 80	362 (23.8)	89 (35.2)	1.74 (1.31-2.31)		1.72 (1.15-2.55)	0.008
Diabetes mellitus	55 (3.6)	16 (6.3)	1.80 (1.02-3.20)	0.041	1.29 (0.71-2.35)	0.403
Hypertension	309 (20.3)	81 (32.0)	1.85 (1.38-2.48)	< 0.001	1.36 (0.92-2.02)	0.127
Metabolic syndrome	154 (10.1)	38 (15.0)	1.57 (1.07-2.30)	0.020	0.88 (0.53-1.46)	0.612
hsCRP (mg/dL)	128 (8.4)	22 (8.7)				
< 0.10	1004 (65.9)	156 (61.7)	1	0.187		
≥ 0.10	519 (34.1)	97 (38.3)	1.20 (0.91-1.58)			
Triglyceride (mg/dL)						
mean ± SD	119.2 ± 86.4	146.2 ± 101.3				
< 150	1168 (76.7)	165 (65.2)	1	< 0.001	1	
≥ 150	355 (23.3)	88 (34.8)	1.76 (1.32-2.33)		1.18 (0.85-1.63)	0.330
HDL cholesterol (mg/dL)						
mean ± SD	58.0 ± 14.8	55.4 ± 15.4				
Male < 40, female < 50	162 (10.6)	30 (11.9)	1	0.563		
Male ≥ 40, female ≥ 50	1361 (89.4)	223 (88.1)	0.89 (0.59-1.34)			
LDL cholesterol (mg/dL)						
mean ± SD	135.1 ± 43.0	138.7 ± 36.8				
≤ 100	244 (16.0)	38 (15.0)	1	0.106		
101-129	493 (32.4)	67 (26.5)	0.87 (0.57-1.34)			
≥ 130	786 (51.6)	148 (58.5)	1.21 (0.82-1.78)			
Total cholesterol (mg/dL)						
mean ± SD	205.8 ± 38.1	210.9 ± 39.6				
< 200	715 (46.9)	100 (39.5)	1	0.028	1	
≥ 200	808 (53.1)	153 (60.5)	1.35 (1.03-1.78)		1.08 (0.81-1.44)	0.595
Current alcohol	637 (41.8)	133 (52.6)	1.54 (1.18-2.01)	0.001	1.04 (0.77-1.40)	0.806
Smoking status						
Never	639 (42.0)	66 (26.1)	1	< 0001	1	
Former	339 (22.3)	62 (24.5)	1.77 (1.22-2.57)		1.23 (0.79 -1.93)	0.359
Current	545 (35.8)	125 (49.4)	2.22 (1.61-3.06)		1.60 (1.07-2.41)	0.023

[1]Adjusted for sex, age, body mass index, waist circumference, diabetes mellitus, hypertension, metabolic syndrome, triglyceride, total cholesterol, alcohol, and smoking. hsCRP: High-sensitivity C-reactive protein; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

young adults is increasing[15-17], but beginning CRC screening at age 50 was established as a guideline in the remote past. CRC in younger adults has been reported to differ from that found in older adults in several respects. For example, CRC in younger adults often takes a more aggressive, advanced form than in older adults[16]. Another implication of the patient's age is that if CRC has the same stage and clinical features, younger adults may be reluctant to select chemotherapy and radiation because of their negative effects on fertility[16]. Therefore, the ability to detect premalignant lesions, such as adenoma and advanced adenoma, is important even in patients aged < 50 years. However, in order to do so, risk factors for colorectal neoplasms in young adults must be ascertained. Our study showed that age, WC, and current smoker status were independent risk factors for colorectal adenoma in young adults, and alcohol consumption was a risk factor for advanced colorectal adenoma in young adults. A previous study has argued that often, CRC diagnosis is delayed in younger adults because physicians, as well as patients, do not attribute the symptoms to cancer in this age-group[16]. If risk factors could be confidently established by future studies, then physicians could decide whether to proceed with further workup or observation and follow-up of young adults who present to the clinic with discomfort.

Table 5 Risk factors of colorectal advanced adenoma in young subjects *n* (%)

Variable	Number of persons		Univariate analysis		Multivariate analysis[1]	
	Non-advanced adenoma (*n* = 1760)	Advanced adenoma (*n* = 16)	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Males	1258 (71.5)	13 (81.3)	1.73 (0.49-6.09)	0.388		
Age (yr)						
45-49	485 (27.6)	6 (37.5)	1	0.570		
40-44	587 (33.4)	4 (25.0)	0.55 (0.16-1.96)			
< 40	688 (39.1)	6 (37.5)	0.71 (0.23-2.20)			
Body mass index (kg/m^2)						
mean ± SD	23.6 ± 3.2	24.8 ± 2.8				
< 25	79 (4.5)	0 (0.0)	1	0.862		
25.0-29.9	492 (28.0)	4 (25.0)	1.66 (1.25-2.20)			
≥ 30	63 (3.6)	1 (6.3)	1.16 (0.56-2.40)			
Waist circumference (cm)						
mean ± SD	82.5 ± 9.7	86.1 ± 6.6				
Male < 90, female < 80	1313 (74.6)	12 (75.0)	1	0.971		
Male ≥ 90, female ≥ 80	447 (25.4)	4 (25.0)	0.98 (0.31-3.05)			
Diabetes mellitus	70 (4.0)	1 (6.3)	1.61 (0.21-12.36)	0.644		
Hypertension	388 (22.0)	2 (12.5)	0.51 (0.11-2.23)	0.359		
Metabolic syndrome	191 (10.9)	1 (6.3)	0.55 (0.07-4.17)	0.555		
High hsCRP						
mean ± SD	148 (8.4)	2 (12.5)				
< 0.10	1149 (65.3)	11 (68.8)	1	0.772		
≥ 0.10	611 (34.7)	5 (31.3)	0.86 (0.30-2.47)			
Triglyceride (mg/dL)						
mean ± SD	123.0 ± 89.3	121.1 ± 72.3				
< 150	1321 (75.1)	12 (75.0)	1	0.996		
≥ 150	439 (24.9)	4 (25.0)	1.00 (0.32-3.13)			
HDL cholesterol (mg/dL)						
mean ± SD	57.6 ± 14.8	60.1 ± 19.3				
Male < 40, female < 50	191 (10.9)	1 (6.3)	1	0.555		
Male ≥ 40, female ≥ 50	1569 (89.1)	15 (93.8)	1.83 (0.24-13.90)			
LDL cholesterol (mg/dL)						
mean ± SD	135.5 ± 41.9	139.1 ± 43.9				
≤ 100	278 (15.8)	4 (25.0)	1	0.703		
101-129	559 (31.8)	1 (6.3)	0.12 (0.01-1.12)			
≥ 130	923 (52.4)	11 (68.8)	0.83 (0.26-2.62)			
Total cholesterol (mg/dL)						
mean ± SD	206.4 ± 38.3	214.1 ± 41.3				
< 200	810 (46.0)	5 (31.3)	1	0.238		
≥ 200	950 (54.0)	11 (68.8)	1.88 (0.65-5.42)			
Current alcohol	758 (43.1)	12 (75.0)	3.97 (1.27-12.34)	0.010	3.69 (1.08-12.54)	0.037
Smoking status						
Never	701 (39.8)	4 (25.0)	1	0.129	1	
Former	398 (22.6)	3 (18.8)	1.32 (0.29-5.93)		0.81 (0.17-3.86)	0.789
Current	661 (37.6)	9 (56.3)	2.39 (0.73-7.79)		1.38 (0.39-4.93)	0.620

[1]Adjusted for alcohol and smoking. hsCRP: High-sensitivity C-reactive protein; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

In comparison with young age-group, age, male sex, WC, current smoker were independent risk factors for colorectal adenoma in overall age-group; age, alcohol consumption were for advanced colorectal adenoma. Prior studies reported that age, male sex, WC, and smoking were independent risk factors for colorectal neoplasm[23-27], findings that are consistent with our study. Even in young age-group, similar risk factors were elicited, though two differences were found between the young age-group and the overall age-group. First, male sex increased the risk of colorectal adenoma in the groups overall, but not in the young age-group. Recent studies have suggested that the tumor-promoting effect of testosterone could explain why men are at higher risk for developing colorectal adenomas[28]. Testosterone levels in men are at their highest in early adulthood and decline about 1 percent per year after age 30. Therefore we can anticipate the male sex may be an important risk factor in young age group. However, our data did not show this association. The duration of exposure to this hormone also may be important in tumorigenesis. Another recent study that evaluated risk factors for colorectal neoplasm stratified by age showed that male sex was an independent risk factor for colorectal adenoma in each age-group, but the OR for male sex was lower in the group aged 30-39 years than in the group aged 40-49 years[29]. These results are

Table 6 Comparison of neoplasm characteristics between young and old subjects *n* (%)

Characteristics of adenoma	Age group		*P* value
	Young age group, < 50 (*n* = 253)	Old age group, ≥ 50 (*n* = 302)	
Number	1.31 ± 0.66	1.82 ± 1.39	< 0.001
Multiple	59 (23.3)	121 (40.1)	< 0.001
Rt. side location	112 (44.3)	156 (51.7)	0.083
Advanced neoplasm	16 (6.3)	25 (8.3)	0.381
Villous or tubulovillous	3 (1.2)	7 (2.3)	0.318
High grade	2 (0.8)	4 (1.3)	0.545
Size > 1 cm	13 (5.1)	24 (7.9)	0.187

Table 7 Comparison of sessile serrated adenoma/polyp characteristics between young and old subjects *n* (%)

	Age group		*P* value
	Young age group, < 50 (*n* = 1776)	Old age group, ≥ 50 (*n* = 1043)	
SSA/P	37 (2.1)	57 (5.5)	< 0.001
Number of SSA/P	1.32 ± 0.58	1.32 ± 0.69	0.875
Right Side location	24 (64.9)	37 (64.9)	0.996

SSA/P: Sessile serrated adenoma/polyp.

also similar with ours. Second, age was a risk factor for advanced adenoma only in the overall age-group. In the young age-group, age was not significantly correlated with the occurrence of advanced adenoma. Thus, it can be surmised that age means duration of exposure to various risk factors. We assumed that there was surge point in the effect of age on advanced adenoma. To demonstrate this theory indirectly, we conducted hierarchical cluster analysis. For colorectal adenoma, the age groups were divided in two groups (age < 46 or age ≥ 46) (Figure 2A) and for age and advanced adenoma, (age < 49 or age ≥ 49) (Figure 2B). For this reason, age might not play a role in development of colorectal adenoma up to certain age.

Multiple studies have been done regarding the association between alcohol consumption and colorectal adenoma. A recent epidemiological study in South Korea[27] showed that chronic alcohol intake raises the risk for advanced adenoma and multiple adenomas, indicating that alcohol intake plays a role in colorectal carcinogenesis. In addition, some reports have linked colon cancer and alcohol consumption. Pedersen *et al*[30] addressed the positive correlation between alcohol intake and colon cancer in both men and women. Another study analyzed 8 cohort studies associating alcohol intake and CRC, suggesting that excessive alcohol intake may increase the risk of colon cancer[31].

Our study is significant because its results indicate a positive correlation between alcohol consumption and the occurrence of advanced adenoma in young adults who drink alcohol. The exact mechanisms by which alcohol intake leads to advanced adenoma, and
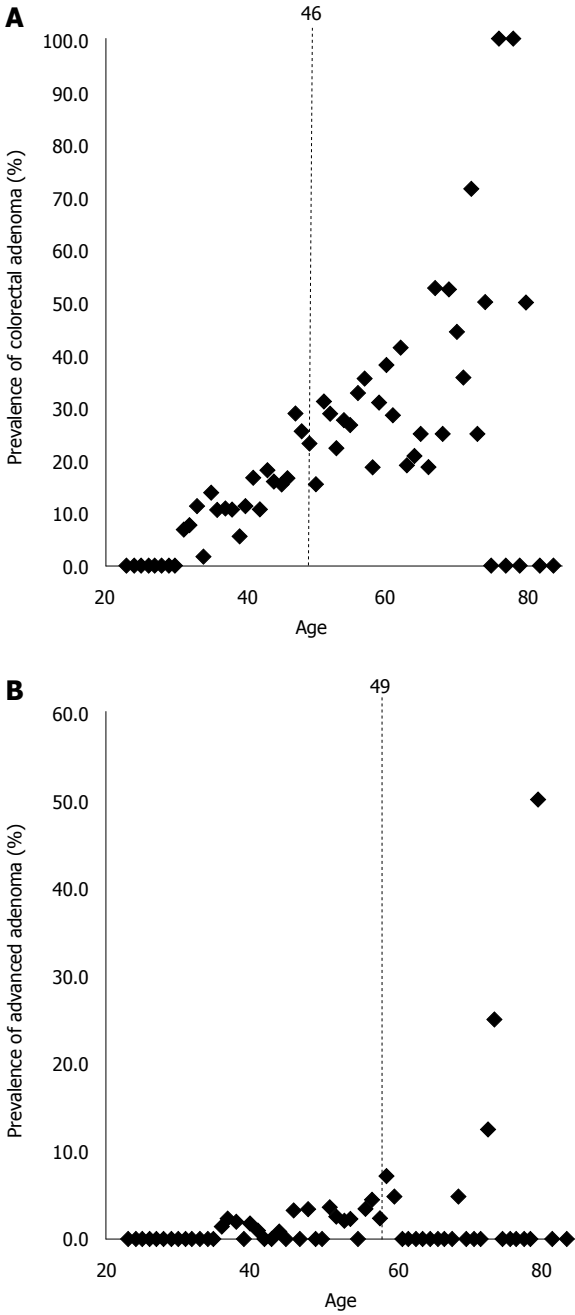

Figure 2 Hierarchial cluster analysis. Scatter plot shows relationships among the age and incidence of adenoma. A and B indicates the age and incidence of colorectal adenoma and advanced adenoma, respectively. Red broken lines indicate demarcations from cluster analysis.

possibly colon cancer, have not yet been completely elucidated. However, it is possible that alcohol hinders folic acid absorption or inhibits enzymes responsible for folic acid synthesis, thereby causing folic acid deficiency in the colon and rectum and eventually leading to colon carcinogenesis[26].

In our study, a subgroup analysis showed that the number of adenomas and the rate of their multiplicity were higher in subjects aged ≥ 50 years, a finding that concurs with previous studies[32]. We also found that right-sided colorectal adenomas were predominant in subjects aged ≥ 50 years compared with younger

age-groups, but this was not statistically significant. Further studies about tumor localization according to age-group are needed. If their cost-effectiveness can be established, adscititious screening methods such as sigmoidoscopy may be helpful in younger age-groups.

The age is known to be an important risk factor for SSA/P[33]. In our study, SSA/P was more prevalent in subjects aged ≥ 50 years than in younger age group as predicted. The prevalence and location of SSA/P in this study were also consistent with those of previous studies[34,35]. A recent study showed that a significant proportion of Korean patients developed interval colorectal cancer, especially at the young age (subjects aged < 65 years) and in the proximal colon[36]. Therefore, a more complete and longer inspection of the proximal colon may be also important in subjects aged < 50 years, although the prevalence of SSA/P in this age group is low.

This study has several strengths. First, to the best of our knowledge, this was the first study to compare the incidence of colorectal neoplasm between the age-groups < 40 years, 40-44 years, 45-49 years, and ≥ 50 years. Many other studies have evaluated the risk factors for colorectal and advanced adenoma in the Korean population[25-27,37-41]. However, we grouped our study population by age and showed no significant differences in the incidence of advanced adenoma between age-groups 45-49 years and ≥ 50 years. These data indicate that more attention needs to be paid to the age-group < 50 years. Second, we collected high-quality data using a trained nurse with a standardized protocol. Third, we enrolled a relatively large number of patients, yielding high statistical power.

Even so, this study also had several limitations. First, our study conducted a survey of subjects in a health promotion center. The patients were self-motivated people seeking colonoscopy screening, and thus, selection bias might have occurred. In addition, regional study may affect generalizability. Second, we excluded several important variables which is associated with the risk of colorectal neoplasm (CRC family history, medication history, and physical activity) owing to low response rates. This might cause the different results. Third, we recruited subjects at a single center, and thus, our results might not be representative of the general population. Fourth, our study was performed using retrospective evaluation only of patients with colorectal adenoma and advanced adenoma and did not include early colon cancer or colon cancer patients. The prevalence of CRC in this population is too low to evaluate risk factors for CRC. Future large-scale studies about this issue are warranted.

In summary, among patients with colorectal adenoma, the prevalence increased significantly with older age (from < 40 years to 40-44 years to 45-49 years to ≥ 50 years). In terms of advanced adenoma, the groups aged < 40 years and 40-44 years showed significantly lower risk compared with the group aged ≥ 50 years. However, no significant difference was found between the age-groups 45-49 years and ≥ 50 years. In the young age-group, age, WC, and current smoking were associated with a higher risk of colorectal adenoma, and alcohol consumption was associated with a higher risk of advanced adenoma. In conclusion, current screening strategies for CRC may need to be amended to account for patient age, especially in young subjects with abdominal obesity, current smoking and alcohol consumption.

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COMMENTS

Background
Influential guidelines, including those in the United States and Europe, recommend screening for colorectal cancer (CRC) beginning at age 50 years for average-risk patients. However, in the past decades, the incidence of CRC in young adults has been increasing, in contrast to cases in older adults, which have been decreasing.

Research frontiers
The aim of this study was to evaluate the characteristics of colorectal neoplasm, including prevalence and risk factors, in subjects < 50 years old (young age group), and to compare them with subjects ≥ 50 years old (old age group) within a screening population. There are few studies focusing on this issue in subjects < 50 years old.

Innovations and breakthroughs
The study demonstrated that, in terms of advanced adenoma, the groups aged < 40 years and 40-44 years showed significantly lower risk compared with the group aged ≥ 50 years. However, no significant difference was found between the age-groups 45-49 years and ≥ 50 years. In the young age-group, age, waist circumference, and current smoking were associated with a higher risk of colorectal adenoma, and alcohol consumption was associated with a higher risk of advanced adenoma.

Applications
The identification of risk factors for CRC in young patients will offer a help in the revision of recent screening guidelines for young subjects.

Peer-review
In this study, the authors presented the characteristics of and risk factors for colorectal neoplasms in young adults in a screening population. The paper is well written and the themes of this study are unique and interesting.

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