Yield of repeat colonoscopy in asymptomatic individuals with a positive fecal immunochemical test and recent colonoscopy

Nam Hee Kim, MD,[1] Yoon Suk Jung, MD, PhD,[2] Jae Wan Lim, MD,[2] Jung Ho Park, MD, PhD,[2] Dong Il Park, MD, PhD,[2] Chong Il Sohn, MD, PhD[2]

Seoul, Korea

Background and Aims: A fecal immunochemical test (FIT) is often repeated annually, even after a recent colonoscopy. However, there are no published data on the proper approach to FIT-positive patients after a recent colonoscopy. We compared colorectal cancer (CRC) and advanced colorectal neoplasia (ACRN) prevalence based on the interval since the last colonoscopy.

Methods: We reviewed asymptomatic screenees aged ≥50 years who underwent FIT and colonoscopy.

Results: Of 2228 FIT-positive participants, 514 had a colonoscopy less than 3 years before (group 1), 427 had a colonoscopy had a colonoscopy 3 to 10 years before (group 2), and 1287 had a colonoscopy >10 years before or no colonoscopy (group 3). The prevalence of CRC in groups 1, 2, and 3 was 2.1%, 1.6%, and 7.2%, respectively, and that for ACRN was 10.9%, 12.6%, and 26.0%, respectively. Even after adjusting for confounders, CRC and ACRN detection rates in group 1 were lower than those in group 3 but not lower than those in group 2. Among 6135 FIT-negative participants, the prevalence of CRC in the 3 groups was .7%, .4%, and 3.4%, respectively, and that for ACRN was 6.0%, 6.1%, and 14.7%, respectively. CRC and ACRN detection rates were significantly higher in FIT-positive participants than in FIT-negative participants in all 3 groups.

Conclusions: In FIT-positive patients who underwent colonoscopy within the prior 3 years, CRC and ACRN prevalence was not low. Our findings support the U.S. Multi-Society Task Force on the CRC screening recommendation that repeat colonoscopy be offered to patients with positive FIT results and recent colonoscopy. (Gastrointest Endosc 2019;89:1037-43.)

Colorectal cancer (CRC) is the third most common cancer and the fourth most common cause of cancer-related death worldwide.[1] CRC screening aids in early detection of CRC and reduces mortality rates by up to 53%.[2] The U.S. Multi-Society Task Force on Colorectal Cancer Screening recommends colonoscopy every 10 years or an annual fecal immunochemical test (FIT) as first-tier options for CRC screening.[3] It is generally accepted that a follow-up colonoscopy is not needed for 10 years after a negative colonoscopy in individuals at an average risk for CRC. The Centers for Disease Control and Prevention and several guidelines also recommend suspending guaiac-based fecal occult blood testing (gFOBT) for at least 5 to 10 years after a negative colonoscopy.[4-6] However, this recommendation is based on expert opinion, and data supporting this are lacking. There are limited data to support the optimal approach for individuals with a positive gFOBT who had a recent colonoscopy.

gFOBT has been criticized because of poor sensitivity for diagnosis of CRC and advanced colorectal neoplasia

Abbreviations: ACRN, advanced colorectal neoplasia; CI, confidence interval; CRC, colorectal cancer; CRN, colorectal neoplasia; FIT, fecal immunochemical test; gFOBT, guaiac-based fecal occult blood testing; NCSP, National Cancer Screening Program; OR, odds ratio.

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Current affiliations: Preventive Healthcare Center (1), Division of Gastroenterology, Department of Internal Medicine (2), Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea.

Reprint requests: Yoon Suk Jung, MD, PhD, Division of Gastroenterology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29, Saemunan-ro, Jongno-gu, Seoul 03181, Korea.

(ACRN).[7] A major disadvantage of gFOBT is that it is not specific for human blood and thus can be affected by foods containing peroxidase.[8] The most important recent advances in fecal screening have centered around FIT compared with traditional guaiac methods. FITs offer many advantages over gFOBTs, including specificity for human blood and hence removing any need for dietary restrictions.[9,10] Prior studies have demonstrated that FIT is superior to gFOBT with respect to sensitivity for detection of CRC and ACRN.[9-12] Additionally, a meta-analysis reported that FIT was superior to gFOBT both for the detection of CRC (relative risk, 1.96; 95% confidence interval [CI], 1.2-3.2) and ACRN (relative risk, 2.28; 95% CI, 1.68-3.10).[13]

Recently, the U.S. Multi-Society Task Force suggested that given the superior test performance of FIT compared with that of gFOBT, those with a positive FIT result and a recent colonoscopy generally should be offered a repeat colonoscopy.[7] However, this is a weak recommendation with low-quality evidence. Currently, no consensus supports or disproves the concomitant use of annual FIT with colonoscopy. However, in clinical practice interval FIT is often performed despite a recent colonoscopy. This may occur more frequently, especially in countries such as Korea, where annual FIT has been adopted as the test conducted in a population-based screening program.

In this situation, it is clinically important to identify the proportion of CRC and ACRN in individuals with a positive FIT result who had a recent colonoscopy. It may be helpful to provide data to inform clinicians on the appropriate approach to such individuals. Therefore, we conducted this study to assess the prevalence of CRC and ACRN in relation to the duration since the last colonoscopy in asymptomatic individuals with a positive FIT result. In addition, we compared the prevalence of CRC and ACRN between FIT-positive and FIT-negative individuals to identify whether interval FIT selects out patients at elevated risk for CRC and ACRN.

METHODS

Patients

The National Cancer Screening Program (NCSP) of Korea provides a single annual FIT for adults aged ≥50 years as initial CRC screening and a confirmatory colonoscopy as a secondary test for those with a positive FIT result.[14] The NCSP provides a free FIT to all Koreans aged ≥50 years without considering history of previous colonoscopy. In other words, an annual FIT is provided uniformly to all Koreans aged ≥50 years, even if they have recently received a colonoscopy. Therefore, the FIT is often performed despite a recent colonoscopy because of the medical environment in Korea where an annual FIT is adopted as a population-based CRC screening program. We retrospectively reviewed participants who underwent an FIT for CRC screening through the NCSP at Kangbuk Samsung Hospital in Korea between January 2013 and July 2017. We then identified participants who underwent colonoscopy. Because patients with positive FIT results can undergo colonoscopy in any NCSP-designated hospital, some FIT-positive participants did not undergo colonoscopy at our hospital, and some FIT-negative participants underwent colonoscopy based on personal preference despite their negative FIT results.

Before the colonoscopies, interviews by general practitioners were conducted to ensure that all participants were asymptomatic (ie, no abdominal pain or hematochezia). Persons with symptoms were urged to seek medical care.

The exclusion criteria were as follows: a history of CRC or colorectal surgery, a history of inflammatory bowel disease, and poor bowel preparation. The quality of bowel preparation was assessed using the Boston Bowel Preparation Scale, and poor bowel preparation was defined as a score of 0 or 1 in any colon segment.[15]

This study was approved by the Institutional Review Board of Kangbuk Samsung Hospital. The requirement for informed consent was waived because only deidentified data were retrospectively assessed.

Clinical measurements and FIT

The data source for this study was the CRC screening database of the NCSP. Examinees who receive cancer screening through the NCSP must fill out a questionnaire developed by the NCSP. The questionnaire contains information on medical history and health-related behaviors. The examinees must submit the self-administered questionnaire on the day of colonoscopy, and the contents of the questionnaire are entered by the staff into an electronic medical database. Data on smoking habits, family history of CRC, and comorbidities were retrieved using the electronic medical database based on the self-administered questionnaires. Data on the time of previous colonoscopy were collected through interviews by nurses. The nurses asked the examinees about previous colonoscopy history including the date and entered this information directly into the electronic medical database. Height and weight were measured by trained staff before colonoscopy on the day of the procedure, and these physical measurements were also entered into the electronic medical database by the staff. A family history of CRC was defined as CRC in ≥1 first-degree relatives at any age. Obesity was defined as body mass index ≥25 kg/m^2, which is the proposed cut-off value for a diagnosis of obesity in Asians.[16]

Participants were instructed to collect a 1-time stool sample in a sampling tube (Eiken Chemical Company, Tokyo, Japan) containing 2.0 mL of buffer designed to minimize hemoglobin degradation. The collected fecal material was sealed in a plastic bag and sent to the

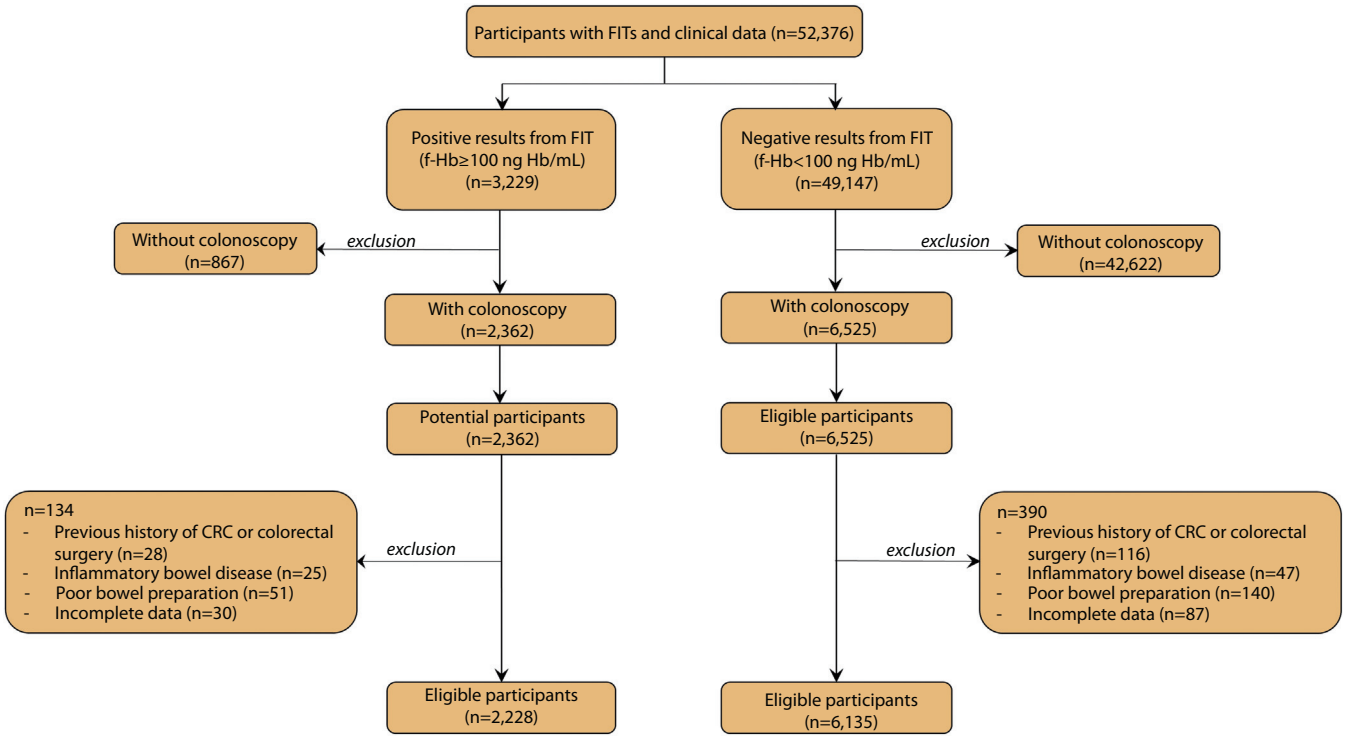

Figure 1. Study flow diagram. *FIT*, Fecal immunochemical test; *f-Hb*, fecal hemoglobin; *CRC*, colorectal cancer.

laboratory. Fecal hemoglobin quantitation was performed using OC-Sensor Diana (Eiken Chemical Company). FIT results were expressed in nanograms of hemoglobin per milliliter of buffer (ng Hb/mL), and the FIT-positive cut-off value was set at 100 ng Hb/mL (equivalent to 20 mg Hb/g feces).[17]

Colonoscopy and histologic examination

All colonoscopies were performed by experienced board-certified endoscopists, using the Evis Lucera CV-260 colonoscope (Olympus Medical Systems, Tokyo, Japan). Suspicious neoplastic lesions were examined or removed by biopsy sampling, polypectomy, or EMR. All specimens were histopathologically assessed by experienced GI pathologists. CRN was defined as a cancer or any adenoma, and ACRN was defined as a cancer or advanced adenoma. Advanced adenoma was defined as the presence of one of the following features: ≥10 mm diameter, tubulovillous or villous structure, and high-grade dysplasia.[18]

Statistical analysis

FIT-positive and FIT-negative participants were classified into 3 groups according to previous colonoscopy intervals: <3 years, 3-10 years, and >10 years or no colonoscopy. Baseline characteristics between groups were compared using the χ^2 test and 1-way analysis of variance for categorical and continuous variables, respectively. The prevalence of CRN was compared among groups using the χ^2 test.

To evaluate the association between the duration since the last colonoscopy and CRN risk, logistic regression models were used. In these models well-known risk factors for CRN, including age, sex, smoking status, family history of CRC, obesity, hypertension, and diabetes, were adjusted as confounding variables. All reported P values were 2-tailed, and $P < .05$ was considered statistically significant. SPSS version 18 (SPSS Inc, Chicago, Ill) was used for statistical analyses.

RESULTS

Baseline characteristics of the study population

We reviewed 52,376 participants who underwent FIT for CRC screening through the NCSP (Fig. 1), and 3229 of them (6.2%) had positive FIT results. Of the participants with positive FIT results, 2362 (73.1%) underwent colonoscopy. Of these participants, 134 were excluded because of a history of CRC or colorectal surgery (n = 28), history of inflammatory bowel disease (n = 25), poor bowel preparation (n = 51), or incomplete data of previous colonoscopy (n = 30). Finally, 2228 participants with positive FIT results were examined. Meanwhile, of the 49,147 participants who had negative FIT results, 6525 underwent colonoscopy. Of these participants, 390 were excluded because of a history of CRC or colorectal surgery

TABLE 1. Baseline characteristics and prevalence of colorectal neoplasia according to previous colonoscopy intervals

	FIT-positive participants (n = 2228)				FIT-negative participants (n = 6135)			
	<3 years (n = 514)	3-10 years (n = 427)	>10 years or no colonoscopy (n = 1287)	*P* value	<3 years (n = 1365)	3-10 years (n = 1774)	>10 years or no colonoscopy (n = 2996)	*P* value
Age, y	64.1 ± 8.0	64.0 ± 8.2	64.6 ± 8.6	.343	63.4 ± 7.7	62.7 ± 7.6	63.0 ± 8.3	.042
Male sex	304 (59.1)	228 (53.4)	664 (51.6)	.015	792 (58.0)	989 (55.7)	1425 (47.6)	<.001
Current or ex-smoker	185/409 (45.2)	142/354 (40.1)	390/993 (39.3)	.114	485/1092 (44.4)	616/1449 (42.5)	838/2331 (36.0)	<.001
Family history of CRC	52 (10.1)	33 (7.7)	55 (4.3)	<.001	123 (9.0)	131 (7.4)	149 (5.0)	<.001
Obesity (BMI ≥25 kg/m^2)	147/367 (40.1)	97/311 (31.2)	318/905 (35.1)	.052	347/999 (34.7)	410/1311 (31.3)	731/2116 (34.5)	.100
Hypertension	206 (40.1)	168 (39.3)	539 (41.9)	.584	551 (40.4)	696 (39.2)	1197 (40.0)	.800
Diabetes mellitus	74 (14.4)	66 (15.5)	209 (16.2)	.618	190 (13.9)	218 (12.3)	426 (14.2)	.158
Colorectal neoplasia								
Any CRN	283 (55.1)	240 (56.2)	843 (65.5)	.001	654 (47.9)	866 (48.8)	1656 (55.3)	<.001
ACRN	56 (10.9)	54 (12.6)	335 (26.0)	<.001	82 (6.0)	108 (6.1)	441 (14.7)	<.001
CRC	11 (2.1)	7 (1.6)	93 (7.2)	<.001	10 (.7)	7 (.4)	101 (3.4)	<.001
Intramucosal cancer	2 (18.2)	1 (14.3)	24 (25.8)	.576	1 (10.0)	1 (14.3)	27 (26.7)	.550
I- II	4 (36.4)	2 (28.6)	38 (40.9)		5 (50.0)	2 (28.6)	43 (42.6)	
III-IV	3 (27.3)	4 (57.1)	25 (26.9)		3 (30.0)	4 (57.1)	25 (24.8)	
Unknown	2 (18.2)	0 (.0)	6 (6.5)		1 (10.0)	0 (.0)	6 (5.9)	

Values are mean ± standard deviation or n and n/N (%).
FIT, Fecal immunochemical test; *BMI*, body mass index; *CRN*, colorectal neoplasia; *ACRN*, advanced colorectal neoplasia; *CRC*, colorectal cancer.

(n = 116), history of inflammatory bowel disease (n = 47), poor bowel preparation (n = 140), or incomplete data of previous colonoscopy (n = 87). Finally, 6135 participants with negative FIT results were examined. The mean age of the total study population was 63.4 ± 8.1 years, and the proportion of men was 52.6%.

Table 1 shows the baseline characteristics and the prevalence of CRN according to the previous colonoscopy intervals. Among 2228 participants with positive FIT results, the number of those who had a colonoscopy <3 year prior, 3 to 10 years prior, and >10 years prior or no colonoscopy was 514 (23.1%), 427 (19.2%), and 1287 (57.8%), respectively. The proportion of men and family history of CRC was highest in those who had a colonoscopy <3 year prior and lowest in those who had a colonoscopy >10 years prior or no colonoscopy. The prevalence of any CRN, ACRN, and CRC was significantly highest in those who had a colonoscopy >10 years prior or no colonoscopy. The prevalence of ACRN in those who had a colonoscopy <3 year prior, 3 to 10 years prior, and >10 years prior or no colonoscopy was 10.9%, 12.6%, and 26.0%, respectively ($P < .001$) and that for CRC was 2.1%, 1.6%, and 7.2%, respectively ($P < .001$).

Among 6135 participants with negative FIT results, the number of those who had a colonoscopy <3 year prior, 3 to 10 years prior, and >10 years prior or no colonoscopy was 1365 (22.2%), 1774 (28.9%), and 2996 (48.8%), respectively (Table 1). The proportion of men, smokers, and those with a family history of CRC was highest in those who had a colonoscopy <3 year prior. The prevalence of any CRN, ACRN, and CRC was significantly highest in those who had a colonoscopy >10 years prior or no colonoscopy. The prevalence of ACRN in those who had a colonoscopy <3 year prior, 3 to 10 years prior, and >10 years prior or no colonoscopy was 6.0%, 6.1%, and 14.7%, respectively ($P < .001$) and that for CRC was .7%, .4%, and 3.4%, respectively ($P < .001$).

Prevalence of CRN according to FIT results

The prevalence of CRN based on previous colonoscopy intervals was compared in FIT-positive and FIT-negative participants (Table 2). The prevalence of any CRN (61.3% vs 51.8%, $P < .001$), ACRN (20.0% vs 10.3%, $P < .001$), and CRC (5.0% vs 1.9%, $P < .001$) was significantly higher in FIT-positive participants than in FIT-negative participants. Additionally, the prevalence of any CRN, ACRN, and CRC was significantly higher in FIT-positive participants than in FIT-negative participants in all 3 groups based on previous colonoscopy intervals.

Risk of CRN according to previous colonoscopy intervals among FIT-positive participants

Logistic regression models for risk of ACRN and CRC according to previous colonoscopy intervals among FIT-positive participants are presented in Table 3. In multivariate analysis adjusted for confounding factors,

TABLE 2. Comparison of prevalence of colorectal neoplasia based on previous colonoscopy intervals between FIT-positive and FIT-negative participants

	All			<3 years			3-10 years			>10 years or no colonoscopy		
	FIT positive (n = 2228)	FIT negative (n = 6135)	*P* value	FIT positive (n = 514)	FIT negative (n = 1365)	*P* value	FIT positive (n = 427)	FIT negative (n = 1774)	*P* value	FIT positive (n = 1287)	FIT negative (n = 2996)	*P* value
Any CRN	1366 (61.3)	3176 (51.8)	<.001	283 (55.1)	654 (47.9)	.006	240 (56.2)	866 (48.8)	.006	843 (65.5)	1656 (55.3)	<.001
ACRN	445 (20.0)	631 (10.3)	<.001	56 (10.9)	82 (6.0)	<.001	54 (12.6)	108 (6.1)	<.001	335 (26.0)	441 (14.7)	<.001
CRC	111 (5.0)	118 (1.9)	<.001	11 (2.1)	10 (.7)	.010	7 (1.6)	7 (.4)	.004	93 (7.2)	101 (3.4)	<.001

Values are n (%).
FIT, Fecal immunochemical test; *CRN*, colorectal neoplasia; *ACRN*, advanced colorectal neoplasia; *CRC*, colorectal cancer.

TABLE 3. Association between previous colonoscopy intervals and colorectal neoplasia risk among FIT-positive participants

	ACRN				CRC			
	Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Previous colonoscopy intervals								
<3 y	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
3-10 y	1.18 (.80-1.76)	.406	1.17 (.71-1.93)	.542	.76 (.29-1.98)	.578	.58 (.17-1.93)	.370
>10 y or no colonoscopy	2.88 (2.12-3.90)	<.001	3.63 (2.48-5.31)	<.001	3.56 (1.89-6.71)	<.001	3.66 (1.74-7.73)	.001
Age, y	1.03 (1.02-1.04)	<.001	1.03 (1.02-1.05)	.001	1.03 (1.002-1.05)	.030	1.02 (.99-7.73)	.219
Male sex	2.24 (1.79-2.79)	<.001	1.77 (1.23-2.55)	.002	1.33 (.90-1.97)	.149	1.19 (.63-2.24)	.600
Current or ex-smoker	2.01 (1.59-2.55)	<.001	1.56 (1.10-2.21)	.013	1.29 (.84-1.97)	.249	1.27 (.68-2.37)	.448
Family history of CRC	1.05 (.69-1.60)	.821	1.36 (.80-2.31)	.262	.85 (.37-1.96)	.696	.96 (.34-2.73)	.941
Obesity (BMI $\geq$25 kg/m^2)	1.19 (.92-1.53)	.181	1.13 (.86-1.49)	.373	.70 (.43-1.14)	.149	.72 (.43-1.20)	.201
Hypertension	1.31 (1.06-1.62)	.011	1.28 (.97-1.69)	.087	1.06 (.72-1.56)	.764	.88 (.54-1.41)	.587
Diabetes mellitus	1.23 (.94-1.62)	.134	.99 (.72-1.35)	.932	1.35 (.84-2.19)	.218	1.15 (.66-1.99)	.623

FIT, Fecal immunochemical test; *ACRN*, advanced colorectal neoplasia; *CRC*, colorectal cancer; *OR*, odds ratio; *CI*, confidence interval; *BMI*, body mass index.

those who had a colonoscopy >10 years prior or who had never had a prior colonoscopy had a significantly higher risk of ACRN than those who had a colonoscopy <3 years prior (adjusted odds ratio [OR], 3.63; 95% CI, 2.48-5.31). However, the risk of ACRN was not significantly different between those who had a colonoscopy <3 years prior and 3 to 10 years prior (adjusted OR, 1.17; 95% CI, .71-1.93).

The results for CRC were similar. The risk of CRC was higher in those who had a colonoscopy >10 years prior or who had never had a prior colonoscopy than in those who had a colonoscopy <3 years prior (adjusted OR, 3.66; 95% CI, 1.74-7.73). However, it was not significantly different between those who had a colonoscopy <3 years prior and 3 to 10 years prior (adjusted OR, .58; 95% CI, .17-1.93).

DISCUSSION

In this study we found that CRC and ACRN were detected in a non-negligible proportion of patients who were FIT positive, even though they had a colonoscopy within the prior 3 years. CRC and ACRN were detected in 2.1% and 10.9% of those who had a colonoscopy <3 years prior, respectively. Although the CRC and ACRN detection rates in patients who had a colonoscopy <3 years prior were lower than those in patients who had colonoscopy >10 years prior or who had never had a prior colonoscopy, the rates were similar to those in patients who had a colonoscopy 3 to 10 years before.

Some previous studies have suggested that in a high-risk population, the use of FIT in the intervals between surveillance colonoscopies aids the detection of cancer and advanced adenoma that might be otherwise missed or that might develop rapidly.[19,20] Lane et al[19] reported that in patients who had at least 2 prior colonoscopy examinations and a family or personal history of CRN, interval FIT detected 12 of 14 CRCs (86% sensitivity) and 60 of 96 advanced adenomas (63% sensitivity) during follow-up evaluation. Bampton et al[20] showed that a 1-off interval FIT detected clinically significant neoplasia (ACRN or >3 adenomas) in 1.8% of subjects who were enrolled in a colonoscopy-based surveillance program because of a personal history of CRN or a significant family history. Our study showed that among asymptomatic

patients who were FIT positive and had a recent colonoscopy, the prevalence of ACRN was not low. FIT detected ACRN in 10.9% of patients (56/514) who had a colonoscopy <3 years before. However, in contrast to the research by Lane et al and Bampton et al, the proportion of patients with a family history of CRC in our study was only 6.3% (140/2228), and patients with a history of CRC were strictly excluded. Although some patients in our study may have had a history of colorectal adenoma, our results suggest that interval FIT may also be helpful in detecting ACRN, even in an average-risk population.

A study reported inconsistent results compared with those in our study.[21] Liu et al[21] demonstrated that in asymptomatic average-risk persons with a negative colonoscopy within the prior 5 years, the prevalence of ACRN was very low (1.1%, 2/183), despite a positive gFOBT result. These findings support the Centers for Disease Control and Prevention recommendation to suspend annual gFOBT for up to 5 years after a negative colonoscopy. However, FIT has superior diagnostic performance compared with traditional gFOBT because it has an increased sensitivity for the detection of fecal hemoglobin compared with gFOBT.[7,9-13] If Liu et al had used FIT instead of gFOBT, the study might have shown different results. Given the superior performance characteristics of FIT compared with that of gFOBT, the U.S. Multi-Society Task Force recommends that those with positive FIT results and recent colonoscopy should be offered a repeat colonoscopy. Our study provides data to support this recommendation.

One of the reasons for a higher rate of ACRN in our study compared with that reported by Liu et al[21] may be that their study included only persons with a negative colonoscopy, whereas our study did not investigate whether there was a history of adenoma; therefore, patients with such a history may have been included in our study. Current guidelines on postpolypectomy surveillance stratify adenomas into 2 risk groups based on the likelihood of developing ACRN during surveillance and recommend repeat screening colonoscopy at 5 to 10 years for patients with low-risk adenomas and at 3 years for those with high-risk adenomas.[18] Although some patients may have low- or high-risk adenomas on previous colonoscopy, the recommended surveillance colonoscopy intervals are 5 to 10 years and 3 years, respectively. Our study showed that the CRC and ACRN detection rates in patients who had a colonoscopy <3 years prior were similar to those in patients who had a colonoscopy 3 to 10 years prior. In other words, the diagnostic yield of CRC and ACRN by FIT before the time of surveillance colonoscopy was not inferior to that at the time of surveillance colonoscopy or later. These findings strongly indicate that even before the recommended time for surveillance colonoscopy, a colonoscopy should be performed again for patients who are FIT positive.

CRC and ACRN found in patients who underwent a colonoscopy <3 years prior are likely to be missed lesions rather than rapidly growing lesions. Based on our results, interval FIT may be a good solution to avoiding missed CRC or ACRN. However, the proportions of CRC in FIT-positive participants who had a colonoscopy <3 years before and 3 to 10 years before (positive predictive values of FIT) were only 2.1% and 1.6%, respectively, and those for ACRN were only 10.9% and 12.6%, respectively. In other words, the downside of performing interval FIT in a colonoscopy-based screening program is that it may lead to unnecessary colonoscopies that are not ultimately diagnostic of CRC or ACRN. Therefore, it may not be reasonable to offer interval FIT to all patients. We performed an analysis to identify the risk factors for CRC and ACRN among FIT-positive patients who had a colonoscopy <3 years prior but did not find any significant risk factors. Further research is needed to identify patients who might benefit from interval FIT.

In the present study, we compared the prevalence of CRC and ACRN based on previous colonoscopy intervals between FIT-positive and FIT-negative participants to identify if and to what extent FIT selects out patients at elevated risk for CRC and ACRN. As a result the prevalence of CRC and ACRN was significantly higher in FIT-positive participants than in FIT-negative participants in all 3 groups based on previous colonoscopy intervals. For example, among those who had a colonoscopy <3 years prior, the prevalence of CRC in FIT-positive and FIT-negative participants was 2.1% and .7%, respectively ($P = .010$), and that for ACRN was 10.9% and 6.0%, respectively ($P < .001$). These results suggest that interval FIT plays a significant role in detecting CRC and ACRN.

Our study will help to provide an appropriate approach for patients with positive FIT results who had a recent colonoscopy. Nevertheless, the current study has several limitations. First, the reliance on patient memory regarding previous colonoscopies performed at an outside hospital might result in possible recall bias. Second, the frequency of family history of CRC was higher in participants with shorter previous colonoscopy intervals. This suggests that interval FIT (early FIT) may have been performed more selectively in those with family history of CRC, and this might affect the proportion of ACRN or CRC in those who had received FIT early. Third, this study was hospital based rather than population based, and therefore there was likely some degree of selection bias. Finally, the quality of prior colonoscopy examination, such as bowel preparation quality and endoscopist adenoma detection rate, and the results of prior colonoscopy (eg, no adenoma, low-risk adenomas, or high-risk adenomas) were not considered. However, this represents a "real-world" scenario, where healthcare provision is often fragmented, screening programs are centrally driven, and primary care physicians are not involved with delivering or coordinating screening programs for their patients.

In conclusion, a non-negligible proportion of asymptomatic patients with FIT-positive results were detected

with CRC and ACRN, although they had a colonoscopy within the past 3 years. Furthermore, the CRC and ACRN detection rates in FIT-positive patients who had a colonoscopy <3 years prior were not lower than the rates in those who had a colonoscopy 3 to 10 years prior. Our results support the recommendations of the U.S. Multi-Society Task Force that those with positive FIT result and recent colonoscopy should be offered a repeat colonoscopy considering the superior performance characteristics of FIT compared with that of gFOBT.

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