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Alimentary Tract

A combination of clinical risk stratification and fecal immunochemical test is useful for identifying persons with high priority of early colonoscopy

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ABSTRACT

Background: We aimed to develop a combination screening strategy for advanced colorectal neoplasia based on the Asia-Pacific Colorectal Screening score and fecal immunochemical test results.
Methods: We reviewed the records of participants who had undergone a colonoscopy and fecal immunochemical test as part of a comprehensive health screening program. The prevalence of advanced colorectal neoplasia in participants 40–49 years old was analyzed according to Asia-Pacific Colorectal Screening scores and fecal immunochemical test results.
Results: We analyzed the data of 9205 participants 40–49 years old and 3215 participants ≥50 years old. The prevalence of advanced colorectal neoplasia in participants 40–49 years old was 1.0%, 2.1%, 7.1%, and 13.4% in the "fecal immunochemical test (−) & Asia-Pacific Colorectal Screening < 2," "fecal immunochemical test (−) & Asia-Pacific Colorectal Screening ≥ 2," "fecal immunochemical test (+) & Asia-Pacific Colorectal Screening < 2," and "fecal immunochemical test (+) & Asia-Pacific Colorectal Screening ≥ 2" subgroups, respectively. The prevalence of advanced colorectal neoplasia in "fecal immunochemical test (+) & Asia-Pacific Colorectal Screening ≥ 2" subgroup was higher than in participants ≥50 years old with Asia-Pacific Colorectal Screening ≥ 4 (13.4% vs. 5.8%, $P < 0.001$).
Conclusions: Fecal immunochemical test-positive individuals 40–49 years old with an Asia-Pacific Colorectal Screening ≥ 2 have a higher risk of advanced colorectal neoplasia than individuals ≥50 years old with an Asia-Pacific Colorectal Screening ≥ 4.

1. Introduction

In order to prevent colorectal cancer (CRC), current guidelines recommend that persons with an average risk of CRC begin undergoing screening colonoscopies at the age of 50 years old [1–3]. Consequently, the incidence and mortality of CRC have decreased in adults ≥50 years old over the past few decades [4,5]. On the other hand, the incidence of CRC is increasing among adults <50 years old [4,6]. Moreover, younger patients with CRC tend to have more aggressive disease and worse outcomes than older patients [7,8]. Accordingly, some researchers suggest that the age for commencing CRC screening may be lowered in higher-risk individuals [9,10].

However, the most important concern with screening colonoscopies performed before the age of 50 is its low cost-effectiveness, because the risk of CRC or advanced colorectal neoplasia (ACRN) is relatively low in this population [4,11]. To improve cost-effectiveness of CRC screening in individuals <50 years old, clinical risk stratification models such as the Asia-Pacific Colorectal Screening (APCS) scoring system may be an alternative strategy to primary screening with colonoscopy [12,13]. Its advantage is that individuals who require colonoscopy can be identified easily in a clinical situation. However, risk of CRC in individuals <50 years old is usually underestimated with the clinical risk stratification models, because individuals <50 years old are assigned 0 points for age in these models [12,13]. Therefore, judging the risk of CRC based only on the clinical risk stratification model is limited in this population.

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Table 1
The Asia-Pacific Colorectal Screening score.

Criteria	Points
Age, year	
<50	0
50–69	2
≥70	3
Sex	
Female	0
Male	1
Family history of CRC in a first degree relative	
Absent	0
Present	2
Smoking habits	
Never smoker	0
Former or current smoker	1
CRC, colorectal cancer	

The fecal immunochemical test (FIT) may be another reasonable alternative to primary screening with colonoscopy in a young population because it is non-invasive, inexpensive, and easy to perform. A recent study suggested that screening with FIT could be extended to individuals 40–49 years old [9]. However, FIT screening for all individuals 40–49 years old may not be cost-effective.

In this situation, the APCS scoring system and FIT would complement each other in selecting and prioritizing asymptomatic individuals 40–49 years old for early colonoscopy. We designed a strategy where younger adults with a high clinical risk of ACRN would undergo a FIT, and then those with positive FIT results would undergo a confirmative colonoscopy. In this study, we aimed to determine the cut-off value of the APCS score for identifying individuals requiring FIT and then assess the predictive performance of a combination strategy based on the APCS score and FIT results.

2. Methods

We retrospectively analyzed data obtained from a prospectively established cohort that consisted of participants who had undergone colonoscopy and FIT as part of a comprehensive health screening program at the Total Healthcare Center of Kangbuk Samsung Hospital, Seoul and Suwon, Korea between 2010 and 2014. The setting of the study was a health examination center and not a clinic. Before colonoscopy, participants were interviewed by general practitioners to ensure that they were asymptomatic (i.e., they had no abdominal pain or hematochezia). If participants had any gastrointestinal symptoms, they were urged to seek medical care.

Participants were limited to persons 40 years old or older. The exclusion criteria were as follows: (1) previous colonic examination, colorectal surgery, or colorectal neoplasia (CRN); (2) a history of inflammatory bowel disease; (3) ischemic or infectious colitis diagnosed during colonoscopy; (4) poor bowel preparation, and (5) incomplete data for analysis.

This study was approved by the Institutional Review Board of Kangbuk Samsung Hospital.

2.1. Prioritizing participants 40–49 years old for early colonoscopy

The primary endpoint of our study was to identify a group at high risk for ACRN in participants 40–49 years old. The risk of ACRN or CRN in participants 40–49 years old was assessed according to their APCS scores, which consisted of age, sex, family history of CRC, and smoking habits (Table 1) [12]. APCS scores range from 0 to 7; however, participants 40–49 years old are graded from 0 to 4, because individuals less than 50 years old are assigned 0 points for age [12]. Participants 40–49 years old were further assessed for their ACRN or CRN risk based on FIT results.

In order to identify participants 40–49 years old for whom early colonoscopy was required, the prevalence of ACRN in each subgroup according to APCS scores and FIT results was compared to that in participants ≥50 years old with high APCS scores (≥4 points), who are usually recommended to undergo colonoscopy. In other words, participants ≥50 years old whose APCS scores were ≥4 points were considered a control group in this study.

Finally, based on the study outcomes, we suggested an algorithm to clinically determine whether early colonoscopy is warranted in persons 40–49 years old.

2.2. Colonoscopy and histopathologic examination

All colonoscopies were performed by experienced, board-certified endoscopists, using an Evis Lucera^{TM} CV-260 colonoscope (Olympus Medical Systems, Tokyo, Japan). The bowels were cleansed using 4 L of polyethylene glycol solution. Suspicious neoplastic lesions were examined via biopsy or removed with polypectomy or endoscopic mucosal resection (EMR).

All specimens obtained from biopsy, polypectomy, or EMR were evaluated via histopathological examination by experienced gastrointestinal pathologists. CRN was defined as a cancer or adenoma. ACRN was defined as a cancer or advanced adenoma. Advanced adenoma was defined as the presence of one of the following features: size ≥10 mm in diameter, tubulovillous or villous structure, and high-grade dysplasia [14].

2.3. Fecal immunochemical test

Participants collected a one-time stool sample in a sampling tube (Eiken Chemical Company, Tokyo, Japan) containing 2.0 mL of buffer designed to minimize hemoglobin degradation at home within 3 days before initiating bowel cleansing for colonoscopy.

The collected fecal material was sent to the laboratory sealed in a plastic bag. Fecal hemoglobin quantitation was performed using OC-SENSOR DIANA (Eiken Chemical Company, Tokyo, Japan). FIT results were expressed in nanograms of hemoglobin per mL buffer (ng Hb/mL), and the FIT positivity cut-off value was set at 100 ng Hb/mL (equivalent to 20 μg of Hb per gram of feces) [15].

2.4. Statistical analysis

Continuous variables such as age are presented as mean with standard deviation, and they were compared using the Student's *t*-test. Categorical variables are presented as numbers with percentages. The percentage of participants 40–49 years old with ACRN and CRN in each subgroup was compared with that in participants ≥50 years old with an APCS score ≥4 points using the chi-square test. A *P*-value of <0.05 was considered significant for group comparisons. All statistical analyses were conducted using the statistical software R (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Participants and baseline characteristics

We reviewed the medical records of 17,907 participants ≥40 years old who had undergone both colonoscopy and FIT. Of these, 1411 were excluded because of previous colonic examination, colorectal surgery, or CRN. In addition, 45 participants with inflammatory bowel disease were excluded. Thirteen participants who were diagnosed with ischemic or infectious colitis during the current colonoscopy were excluded because such conditions could influence FIT results. Of the remaining 16,438 participants, 1533 were excluded because of poor bowel preparation and 2485

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