Caspian Journal of Internal Medicine 2025 (Summer); 16(3): 451-457
DOI: 10.22088/cjim.16.3.451

Original Article

Colon lesions in elderly individuals with positive and negative fecal immunochemical test results among PERSIAN Guilan cohort study (PGCS) population

Heydar Ali Balou (MD) [1]
Farahnaz Joukar (PhD) [1]
Mahdi Orang Goorabzarmakhi(MD) [1]
Milad Shahdkar (MD) [1]
Soheil Hassanipour (PhD) [1]
Saman Maroufizadeh (PhD) [2]
Mehrnaz Asgharnezhad (PhD) [1]
Paridokht Karimian (MD) [1]
Fariborz Mansour-Ghanaei (MD) [1*]

1. Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran
2. Department of Biostatistics, School of Health, Guilan University of Medical Sciences, Rasht, Iran

*** Correspondence:**
Fariborz Mansour-Ghanaei (M.D., AGAF), Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran Razi Hospital, Sardar-Jangle Ave., P.O. Box: 41448-95655, Rasht, Iran

E-mail:
fmansourghanaei@gmail.com
Tel: +98 1315535116

Received: 24 Dec 2023
Revised: 1 Feb 2024
Accepted: 2 March 2024
Published: 23 June 2025

Abstract

Background: Early colorectal cancer (CRC) detection helps reduce the mortality rate. This study aimed to investigate colon lesions in individuals with positive and negative fecal immunochemical test (FIT) results among the (PERSIAN) Guilan cohort study (PGCS) population.

Methods: This cross-sectional study was conducted on 1158 participants over 50 who were volunteers for the FIT stool test at the Endoscopy Department of Razi Hospital, Rasht, Iran, from 2021 to 2022. The FIT test was screened for all participants, and for 172 individuals (86 individuals from each group with positive and negative FIT results), a colonoscopy was performed to investigate the colon lesions. Demographic/clinical characteristics, FIT results, colonoscopy findings, and the Bristol Stool Chart were completed. All data were analyzed using SPSS Version 16, considering a significant level<0.05.

Results: Out of 1,158 participants, 86 had positive FIT results, and 172 (52.3%) were females. The colonoscopy results showed that 34.3% of the patients had colon lesions. Individuals with positive FIT exhibited a significantly higher prevalence of colon lesions ($p<0.001$). No statistically significant differences were observed between positive and negative FIT results, demographic and clinical characteristics, and the location of lesions in individuals with colon lesions ($p>0.05$). Moreover, there was a significant difference in pathological findings and the presence of adenomatous polyps regarding the FIT results ($p<0.001$).

Conclusion: The effectiveness of FIT in the initial stages of screening for early lesion detection is considerable, especially for individuals with upper age.

Keywords: Colonic neoplasms, Colonoscopy, Colorectal neoplasms.

Citation:
Balou HA, Joukar F, Orang Goorabzarmakhi M, et al. Colon lesions in elderly individuals with positive and negative fecal immunochemical test results among PERSIAN Guilan cohort study (PGCS) population. Caspian J Intern Med 2025; 16(3): 451-457.

Colorectal cancer (CRC) is the third most common malignancy worldwide and the second leading cause of cancer-related death in the United States (1, 2). CRC is one of the most common cancers of the gastrointestinal tract in Iran, and it has been ranked third and fourth in Iranian males and females, respectively (3). CRC screening emerges as a cost-effective strategy, with early diagnosis for reducing mortality. The adenoma-carcinoma sequence is a well-established pathway for CRC development, with an estimated two-thirds of CRCs originating from adenomatous polyps (4, 5). Various approaches exist for CRC screening, and colonoscopy is an effective means of diagnosing colon diseases. While colonoscopy has a high sensitivity and specificity in screening, many patients decline to undergo the procedure due to its invasive and painful nature (4, 6).

On the other hand, considering colonoscopy as the gold standard for diagnosing colorectal diseases, the fecal immunochemical test (FIT) is noticed as the leading non-invasive method for screening asymptomatic individuals. This method relies on the breakdown of globulin induced by digestive bleeding through digestive enzymes (7). It is conducted qualitatively using immunochromatography and quantitatively through immunoturbidimetry (8). It is one of the highly recommended methods for colorectal cancer screening. This method is characterized by its non-invasiveness, cost-effectiveness, and high sensitivity and specificity in CRC detection. It has been reported that while FITs effectively detect most CRCs at stages II-IV, their sensitivity is significantly lower for CRC stage I and especially for T1 CRC. This highlights the necessity and potential for further enhancing the performance of FITs in the early detection of CRC. Also, further diagnostic evaluation through colonoscopy is recommended in case of a positive FIT test (9, 10). According to the Centers for Disease Control and Prevention (CDC) protocol, regular screening from 50 years old can prevent CRC. Stool examinations have become the predominant method in screening programs to recognize the prevalent reluctance among patients to undergo colonoscopy due to its invasive and painful nature and high cost. Hence, our study aimed to compare colon lesions in individuals with positive and negative FIT results among the elderly population of the Prospective Epidemiological Research Studies (PERSIAN) Guilan cohort study (PGCS) in Guilan, Iran.

Methods

Study design and participants: This cross-sectional study is a part of PGCS (11, 12), which has been conducted on 1158 participants (out of 6000 eligible individuals) aged over 50 who were volunteers for the FIT stool exam at the Endoscopy Department of Razi Educational and Medical Center Rasht, Iran, from Jan 2021 to Jan 2022. The study was confirmed by the Ethics Committee of the Guilan University of Medical Sciences, Rasht, Iran (IR.GUMS.REC.1399.459), and all individuals gave their consent to participate in the study. Demographic and clinical information was gathered via questionnaires, examinations, and face-to-face interviews. Data collected included age, gender, environment, marital status, education level, occupation, BMI (categorized as low weight under 18.5 kg/m², normal weight 18.5-24.99 kg/m², overweight 25-29.9 kg/m², and obesity 30 kg/m²), smoking history, alcohol and opium use, types of oil consumed, hypertension, diabetes, gastrointestinal cancer history, and constipation. This comprehensive approach aimed to obtain a detailed profile of each participant's health and lifestyle factors relevant to the study. The screening FIT test was performed on stool samples of volunteers, and according to the results, participants were divided into positive and negative FIT groups (figure 1). Also, a colonoscopy was applied to evaluate the colon lesions. Individuals over 50 and with the Sowmeh' E Sara residency were included. Exclusion criteria involved less than two years of residency in Sowmeh' E Sara, dementia, severe mental illness at the time of registration, residence in elderly care centers/nursing homes, and acute physical problems/disabilities. The FIT was performed through a qualitative immunologic method (Vitrotec, Iran). After collecting stool samples, they were stored at -20 °C until the test. The FIT test involved using a strip in the stool, and a positive result indicated abnormal bleeding in the lower gastrointestinal tract. Bristol chart related to excretory habits (13) was also completed for each individual as types 1 and 2: constipation, 3 and 4: normal stool, and 5-7: diarrhea.

Statistical analysis: The variables have been reported by numbers (percentage) and mean ± standard deviation (SD). The normality of data was evaluated using Kolmogorov-Smirnov and Levin tests. The Independent T-test, Mann-Whitney, and Chi-Square were used to compare the variables between individuals. Univariate and multivariate logistic regression were performed to determine the association between variables by considering a confidence interval (CI) of 95%. All statistical analysis was performed using SPSS Version 16.0 based on a significant level less than 0.05.

Results

Among 1158 volunteers for the FIT stool exam, 86 (7.42%) were indicated as FIT positive. Therefore, the study compared two groups of 86, with positive and negative FIT results. There was a significant difference comparing the presence of lesions in FIT positive (52.32%) and negative (6.27%) groups ($p<0.001$) (figure 1). Of these participants, 49.41% were under 60 and 52.32% were females. About 55.23%, 35.46%, and 10.46% of individuals had a history of hypertension, diabetes, and a family history of gastrointestinal cancer, respectively, table 1. No statistically significant difference between the demographic and clinical characteristics of patients with lesions and the results of FIT were observed ($p>0.05$), table 2. The results showed a statistically significant association between pathology findings and FIT results ($p<0.001$). In this study, 52.32% of

FIT-positive and 16.27% of FIT-negative individuals had pathological findings. Also, a significant association was illustrated between the presence of adenomatous polyp and FIT ($p<0.001$). Furthermore, in positive FIT, adenomatous polyp was more prevalent than in negative FIT (table 3). The most common location of colon lesions was the sigmoid in FIT-positive patients and the rectum in FIT-negative patients. However, there was no statistically significant relationship between the location of the lesion and FIT results ($p>0.05$) (table 4).

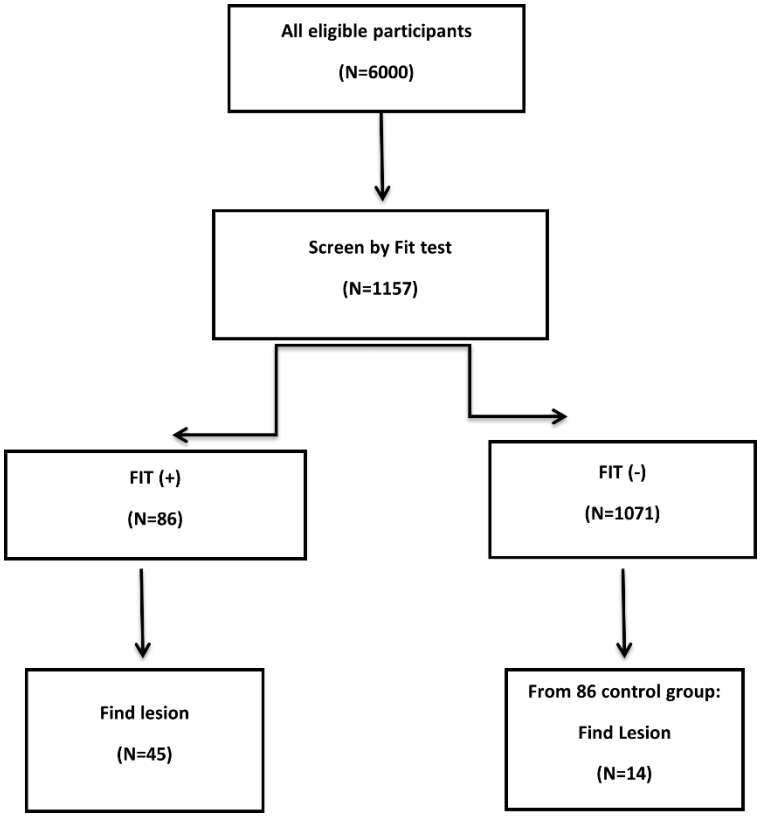

Figure 1. Flowchart

Table 1. Demographic and clinical characteristics of included subjects in the study (N=172)

Variable	Category	FIT + (n=86)	FIT – (n=86)	*P*-value
Age	< 60 years	42 (48.8)	43 (50)	0.999
	> 60 years	44 (51.2)	43 (50)	
Gender	Male	40 (46.5)	42 (48.8)	0.760
	Female	46 (53.4)	44 (51.2)	
Residence	Urban	25 (29)	28 (32.5)	0.621
	Rural	61 (71)	58 (67.5)	
Education level	Illiterate	7 (8.1)	8 (9.3)	0.181
	1-5 years	30 (37)	27 (31.4)	
	6-12 years	46 (39.5)	43 (50)	
	> 12 years	3 (3.4)	8 (9.3)	
BMI	18.5 – 24.9	20 (23.2)	16 (18.6)	0.925
	25-29.9	32 (37.2)	34 (39.5)	
	> 30	34 (39.5)	36 (41.8)	

Variable	Category	FIT + (n=86)	FIT – (n=86)	*P*-value
Smoking	Yes	21 (24.4)	19 (22)	0.935
	No	65 (75.6)	67 (78)	
Alcohol	Yes	8 (9.3)	9 (10.4)	0.874
	No	78 (90.7)	77 (89.6)	
Opium	Yes	5 (5.8)	4 (4.6)	0.999
	No	81 (94.2)	82 (95.4)	
Family history of GI cancer	Yes	10 (11.6)	8 (9.3)	0.944
	No	76 (88.4)	78 (90.7)	
Constipation	Yes	28 (32.5)	29 (33.7)	0.999
	No	58 (67.5)	57 (66.3)	
Hypertension	Yes	47 (54.6)	48 (55.8)	0.999
	No	39 (45.4)	38 (44.2)	
Diabetes	Yes	32 (37.2)	29 (33.7)	0.572
	No	54 (62.8)	57 (66.3)	

Table 2. Demographic and clinical characteristics of included subjects in the study with the lesion (N=59)

Variable	Category	FIT + (N=45)	FIT – (N=14)	OR (95% CI)	*P*-value
Age	< 60 years	24 (53.3)	8 (57.1)	Ref	0.803
	> 60 years	21 (46.6)	6 (42.9)	1.16 (0.34-3.91)	
Gender	Male	23 (51.1)	5 (35.7)	1.88 (0.54-6.50)	0.310
	Female	22 (48.9)	9 (64.3)	Ref	
Residence	Urban	10 (22.2)	3 (21.4)	1.04 (0.24-4.49)	0.950
	Rural	35 (77.8)	11 (78.6)	Ref	
Education level	Illiterate	5 (11.1)	1 (7.1)	1.62 (0.17-15.20)	0.670
	1-5 years	16 (35.5)	7 (50)	0.55 (0.16-1.85)	0.336
	6-12 years	21 (46.7)	5 (35.8)	1.57 (0.45-5.44	0.473
	> 12 years	3 (6.7)	1 (7.1)	Ref	-
Body mass index (BMI)	18.5 – 24.9	8 (17.7)	3 (21.5)	Ref	-
	25-29.9	19 (42.2)	3 (21.5)	2.67 (0.65-10.94)	0.170
	> 30	17 (37.8)	8 (57)	0.45 (0.13-1.53)	0.206
Smoking	Yes	14 (31.1)	2 (7)	2.71 (0.52-13.75)	0.229
	No	31 (68.9)	12 (93)	Ref	
Alcohol	Yes	5 (11.1)	3 (21.4)	0.45 (0.09-2.22)	0.333
	No	40 (88.9)	11 (78.6)	Ref	
Opium	Yes	4 (8.9)	1 (7)	1.26 (0.13-12.38)	0.838
	No	41 (91.1)	13 (93)	Ref	
Family history of GI cancer	Yes	7 (15.5)	1 (7)	2.39 (0.26-21.35)	0.434
	No	38 (84.5)	13 (93)	Ref	

Variable	Category	FIT + (N=45)	FIT – (N=14)	OR (95% CI)	*P*-value
Constipation	Yes	13 (28.9)	5 (35.8)	0.73 (0.20-2.60)	0.629
	No	32 (71.2)	9 (64.2)	Ref	
Hypertension	Yes	25 (55.5)	4 (28.6)	3.12 (0.85-11.46)	0.086
	No	20 (44.5)	10 (71.4)	Ref	
Diabetes	Yes	18 (40)	4 (28.6)	1.66 (0.45-6.13)	0.443
	No	27 (60)	10 (71.4)	Ref	

Table 3. Comparison of pathology result in FIT (+) and FIT (-)

Result of pathology	Fit (+)	Fit (-)	Total	P-value
Adenomatous	24	6	30	< 0.001
Sessile serrated	8	4	12	0.227
inflammatory	1	1	2	0.999
Adenocarcinoma	1	0	1	0.314
Non-polyp	11	3	14	0.024
Total	45	14	59	< 0.001

Table 4. Comparison of FIT (+) and FIT (-) in location of lesion

Location	Fit (+)	Fit (-)	Total	P-value
Cecum	2	0	2	0.785
Rectum	10	5	15	0.134
Ileum	4	0	4	0.121
Transverse colon	2	1	3	0.796
Ascending colon	7	2	9	0.756
Descending colon	5	2	7	0.691
Sigmoid	13	1	14	0.067
Splenic flexure	2	2	4	0.999
Hepatic flexure	0	1	1	0.788

Discussion

Colorectal cancer (CRC) is a prevalent and life-threatening disease, emphasizing the importance of early detection and removal of precancerous lesions through screening tests (1, 14). Our results showed that about 7.5% of participants over 50 represented positive results for FIT. Similarly, Doubeni et al. demonstrated that the frequency of FIT-positive results among patients aged 50-75 was 4.4% (2.6-8%) (15). Comparing the demographic and clinical characteristics of FIT-positive and negative individuals, our results indicated no significant differences between the two groups. More pathological damage was reported in individuals with a positive FIT. Some studies suggested a significant association between positive FIT results and demographical factors such as increasing age, male gender, and low socioeconomic status (16, 17). These findings may vary due to the diversity of populations across studies. Our findings revealed that more than half of the individuals exhibited pathological lesions with a higher frequency of adenomatous polyps. Wilen et al. reported that the positive results of FIT might make patients susceptible to adenomatous polyps with stalk shape and high-risk dysplasia (18). In contrast, Chang et al. demonstrated that positive FIT results did not show a significant difference between individuals with adenomatous polyps and those without, compared to colonoscopy findings. Overall, it has

been suggested that the FIT test illustrated low sensitivity in identifying serrated adenomatous polyps compared to normal polyps (19). FIT might help identify adenomas with a pedunculated shape and high-risk dysplasia, and patients with flat or extensive adenomas may be missed in screening. Moreover, evidence suggests that pedunculated lesions are more likely to be identified by FIT than flat lesions (20). Although the positive result of FIT is more frequent in patients with polyps, it has low sensitivity in identifying the type of polyp. Stool tests can identify the initial phases of CRC and precancerous polyps. These polyps can be eliminated through a colonoscopy that should be conducted for all patients who were positive for stool tests. Evidence revealed that patients with positive FIT results were more prone to having polyps detected during colonoscopy than those without prior stool tests (21, 22). Consequently, incorporating these tests for screening purposes can enhance the number of individuals referred for colonoscopy and require the removal of significant lesions. Our findings showed that the location of the lesion was not associated with the result of FIT.

On the contrary, it has been reported that the positive result of FIT is associated with the location of neoplasia, in which distal neoplasia resulted in a stool hemoglobin concentration of >20 mg (23). However, other studies have reported that FIT was less sensitive for detecting right-sided neoplasia (20, 24). Levy et al. demonstrated that the sensitivity of FIT for advanced distal lesions was higher than for advanced proximal lesions (25). Other studies have also identified a higher sensitivity of FIT for distal versus proximal adenomas, particularly those equal to or greater than 10 mm in diameter (26, 27). Further research is necessary to improve understanding of FIT's effectiveness and limitations in detecting various types and locations of polyps during colorectal cancer screening.

The limitations of this study include a small sample size due to the COVID-19 pandemic at the time of the conducting the investigation, the failure to calculate the sensitivity and specificity of the FIT test, an equal number of participants in the control and case groups, the lack of information regarding the location of the polyps, and the absence of investigation into the influence of heat and season on the FIT test. Additionally, no comparison was made between polyp size and the FIT test results. The study highlights the efficacy of non-invasive and cost-effective tests like FIT in the initial screening stages for early lesion detection. It should be measured in all individuals aged over 50 years. However, the necessity for colonoscopy persists to confirm the presence or absence of lesions in individuals with positive FIT results.

Acknowledgments

This study was driven from gastroenterology fellow-ship thesis of Heydar Ali Balou at the Guilan University of Medical Sciences (Registry Code: 1203).

Funding: None.

Ethics approval: This study was approved by the Ethics Committee of the Guilan University of Medical Sciences [IR.GUMS.REC.1399.459]. Informed consent was obtained from all individual participants.

Conflict of interests: The authors declare no conflict of interest.

Authors' contribution: Concept development (provided idea for the research): HA.B, F.J and F.MGH Design (planned the methods to generate the results): S.M, F.MGH, F.J, S.H Supervision (provided oversight, responsible for organization and implementation): F.J and F.MGH Data collection/processing (responsible for experiments, patient management, organization, or reporting data) and data analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): S.H, M.A, P.K, S.M Literature search (performed the literature search and writing of the manuscript): M.OG, P.K and M.SH Drafting the manuscript (responsible for writing a substantive part of the manuscript): All authors

Availability of data and materials: The study protocol and the datasets analyzed are available from the corresponding author upon request.

Consent for publication: Not applicable.

References

1. Batool R, Jamal K, Sheroze MW, et al. Clinical features of colorectal carcinoma at the Jinnah Postgraduate Medical Centre, Karachi, Pakistan: a cross-sectional study. J Med Res Heal Sci 2022; 5: 2203–9.
2. Saraiva MR, Rosa I, Claro I. Early-onset colorectal cancer: A review of current knowledge. World J Gastroenterol 2023; 29: 1289.
3. Tabesh E, Ghassami M, Rezayatmand R, Tahmasebi M, Adibi P. Adaptation of clinical practice guideline for colorectal cancer screening in people with average risk in Isfahan province. Int J Prev Med 2022; 13: 135.
4. Shaukat A, Levin TR. Current and future colorectal cancer screening strategies. Nat Rev Gastroenterol Hepatol 2022; 19: 521–31.
5. Lu C. Characterization of peripheral immune events in primary colorectal cancer patients. Doctoral dissertation, Klinikum der Ludwig-Maximilians-Universität München, Lmu; 2022.

6. Ajufo A, Adigun AO, Mohammad M, et al. Factors affecting the rate of colonoscopy among African Americans aged over 45 years. Cureus 2023; 15: e46525.
7. von Wagner C, Verstraete W, Hirst Y, et al. Public preferences for using quantitative faecal immunochemical test versus colonoscopy as diagnostic test for colorectal cancer: evidence from an online survey. BJGP Open 2020;4: bjgpopen20X101007.
8. Wang Q, Wang J, Xiao Z, et al. A fluorescent microsphere-based immunochromatographic strip is effective for quantitative fecal blood testing in colorectal cancer screening. Am J Transl Res 2022; 14: 2123.
9. Ferrari A, Neefs I, Hoeck S, Peeters M, Van Hal G. Towards novel non-invasive colorectal cancer screening methods: a comprehensive review. Cancers (Basel) 2021; 13: 1820.
10. Niedermaier T, Balavarca Y, Brenner H. Stage-specific sensitivity of fecal immunochemical tests for detecting colorectal cancer: Systematic review and meta-analysis. Am J Gastroenterol 2020; 115: 56-69.
11. Poustchi H, Eghtesad S, Kamangar F, et al. Prospective epidemiological research studies in Iran (the PERSIAN cohort study): Rationale, objectives, and design. Am J Epidemiol 2018 Apr 1; 187: 647–55. Available from: https://pubmed.ncbi.nlm.nih.gov/29145581. Accessed Apr 1, 2018.
12. Mansour-Ghanaei F, Joukar F, Naghipour MR, et al. The PERSIAN Guilan Cohort Study (PGCS). Arch Iran Med 2019; 22: 39–45.
13. Alijanpour S, Alimohamadi N, Khafri S, Rokni MA, Khorvash F. Caspian nursing process: Impactions on new-onset constipations in admission, discharge, and follow-up of acute stroke patients. Iran J Nurs Midwifery Res 2022; 27: 509.
14. Beniwal SS, Lamo P, Kaushik A, et al. Current status and emerging trends in colorectal cancer screening and diagnostics. Biosensors 2023; 13: 926.
15. Doubeni CA, Jensen CD, Fedewa SA, et al. Fecal immunochemical test (FIT) for colon cancer screening: Variable performance with ambient temperature. J Am Board Fam Med 2016; 29: 672–81.
16. Shin A, Choi KS, Jun JK, et al. Validity of fecal occult blood test in the national cancer screening program, Korea. PLoS One 2013; 8: e79292.
17. Mansouri D, McMillan DC, Grant Y, Crighton EM, Horgan PG. The impact of age, sex and socioeconomic deprivation on outcomes in a colorectal cancer screening programme. PLoS One 2013; 8: e66063.
18. Ribbing Wilén H, Blom J, Höijer J, Andersson G, Löwbeer C, Hultcrantz R. Fecal immunochemical test in cancer screening - colonoscopy outcome in FIT positives and negatives. Scand J Gastroenterol 2019; 54: 303–10.
19. Chang LC, Shun CT, Hsu WF, et al. Fecal immunochemical test detects sessile serrated adenomas and polyps with a low level of sensitivity. Clin Gastroenterol Hepatol 2017; 15: 872–9.
20. O'Reilly SM, MacNally S, O'Donoghue D, et al. Correlation of fecal immunochemical testing levels with pathology results in a national colorectal cancer screening program. Clin Transl Gastroenterol 2021; 12: bjgpopen20X101007.
21. Anderson JC, Hisey WM, Robinson CM, et al. Serrated polyp yield at colonoscopy in patients with positive FIT, positive mt-sDNA, and colonoscopy only: Data from the new hampshire colonoscopy registry. Cancer Epidemiol biomarkers Prev 2023; 32: 226–32.
22. Anderson JC, Robinson CM, Hisey WM, et al. Colorectal neoplasia detection in individuals with positive multitarget stool DNA tests: Data from the New Hampshire colonoscopy registry. J Clin Gastroenterol 2022; 56: 419–25.
23. Chen CH, Tsai MK, Wen C, Wen CP. A user-friendly objective prediction model in predicting colorectal cancer based on 234 044 Asian adults in a prospective cohort. ESMO Open 2021; 6: 100288.
24. Niedermaier T, Weigl K, Hoffmeister M, Brenner H. Diagnostic performance of flexible sigmoidoscopy combined with fecal immunochemical test in colorectal cancer screening: meta-analysis and modeling. Eur J Epidemiol 2017; 32: 481–93.
25. Levy BT, Bay C, Xu Y, et al. Test characteristics of faecal immunochemical tests (FIT) compared with optical colonoscopy. J Med Screen 2014; 21: 133–43.
26. Rutter CM, Nascimento de Lima P, Lee JK, Ozik J. Too good to be true? Evaluation of colonoscopy sensitivity assumptions used in policy models. Cancer Epidemiol Biomarkers Prev 2022; 31: 775-82.
27. Xu H, Tang RSY, Lam TYT, et al. Artificial intelligence-assisted colonoscopy for colorectal cancer screening: A multicenter randomized controlled trial. Clin Gastroenterol Hepatol 2023; 21: 337-46. e3.