

Performance of APCS Risk Score and Fecal Immunochemical Test in Predicting Colorectal Cancer: A Retrospective Diagnostic Accuracy Study.

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Abstract

Objective: To evaluate the diagnostic performance of APCS and FIT for predicting colorectal cancer (CRC), and to develop an enhanced predictive model incorporating clinical and laboratory parameters.

Methods: A retrospective study of 662 patients undergoing colonoscopy at Rattanaaburi Hospital, Thailand (January 2022–April 2025). Clinical data, quantitative FIT, APCS scores, and histopathology were analyzed.

Results: Mean age was 61.3 years; 42.45% were male. Adenomas comprised 93.96% of lesions, and adenocarcinomas (CA) 2.87%. The subgroup with APCS ≥ 4 and positive FIT had the highest CA detection rate (6.29%). For predicting CA, FIT alone had an AUROC of 0.56 (sensitivity 68.4%, specificity 45.3%), while APCS ≥ 4 alone had an AUROC of 0.59 (sensitivity 68.4%, specificity 50.7%). Combining FIT and APCS ≥ 4 increased specificity to 79.0% (sensitivity 47.4%, AUROC 0.64). Multivariable regression identified FIT positivity (OR=7.66), APCS ≥ 4 (OR=4.54), diabetes mellitus (OR=8.84), and hematocrit (OR=0.70) as independent CA predictors ($p < 0.01$ for all except APCS $p = 0.01$). An enhanced model combining these variables significantly improved performance (AUROC 0.86).

Conclusion: Standalone APCS or FIT scores offer limited predictive accuracy (AUROC < 0.65). However, incorporating diabetes and hematocrit into an enhanced model significantly improves diagnostic performance (AUROC 0.86), showing high potential for risk-based screening.

Keywords: APCS Risk Score, Fecal Immunochemical Test (FIT), Colorectal

INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies found worldwide and remains a leading cause of cancer-related mortality. According to GLOBOCAN 2020, there were approximately 1.93 million new CRC cases and 935,000 deaths, accounting for about 10% of all cancer deaths.¹ The severity of CRC largely stems from the fact that many patients present with advanced stages when treatment outcomes are suboptimal. Nevertheless, CRC is a preventable disease through effective screening, since most cases develop from adenomatous polyps that undergo malignant transformation over several years. Early detection and removal of such polyps can significantly reduce both incidence and mortality.² Several CRC screening modalities are currently available, including the fecal immunochemical test (FIT), colonos-

copy, flexible sigmoidoscopy, and CT colonography.³ Among these, colonoscopy offers the highest sensitivity and specificity. However, its widespread implementation is constrained by resource availability, trained personnel, and cost, making its population-wide use impractical. Therefore, the tools that help to identify high-risk individuals for colonoscopy referral are of particular importance.

In Asia, the Asia-Pacific Colorectal Screening (APCS) score was developed using regional population data to estimate the risk of advanced colorectal neoplasia. This scoring system incorporates fundamental risk factors, such as age, sex, smoking status, and family history of CRC.⁴ The APCS categorizes individuals into three risk groups: low risk (0–1 points), moderate risk (2–3 points), and high risk (≥ 4 points). In parallel, FIT is widely used as a simple, non-invasive, and low-cost screening tool

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that detects occult blood in stool, potentially arising from tumors or CRC, and is well-suited for large-scale population screening.⁵ However, the diagnostic performance of FIT may vary across different populations and clinical contexts, and may be limited in non-bleeding lesions or small polyps, resulting in reduced sensitivity in certain real-world settings.

Previous studies have demonstrated that combining APCS with FIT improves screening accuracy compared with using either tool alone. Individuals with a high APCS score and positive FIT have been shown to have a substantially higher probability of advanced colorectal neoplasia than those with low-risk scores and negative FIT results.⁶ For instance, a Thai study reported that APCS combined with FIT yielded markedly higher detection rates of advanced adenoma.⁶ However, most prior studies primarily focused on advanced neoplasia rather than histologically confirmed colorectal cancer, and many were conducted under controlled research conditions. Therefore, their findings may not fully reflect the true performance of these tools in routine clinical service, particularly in opportunistic colonoscopy cohorts.

In this context, the present study aimed to evaluate the diagnostic performance of APCS and FIT for identifying individuals at risk of histologically confirmed colorectal cancer in a real-world opportunistic colonoscopy cohort. Rather than assuming superior performance, this study sought to objectively determine whether these tools provide adequate and clinically useful discrimination in routine practice. The ultimate goal is to inform the potential roles of APCS and FIT in supporting risk-based prioritization of colonoscopy in resource-limited healthcare settings.

RESEARCH OBJECTIVE

The objective of this study was to evaluate the diagnostic performance of the Asia-Pacific Colorectal Screening (APCS) score and the Fecal Immunochemical Test (FIT) in relation to histopathological findings of colorectal lesions, and to assess their ability to predict cancer.

MATERIALS AND METHODS

This was a retrospective diagnostic accuracy study. The study population represented a real-world opportunistic colonoscopy cohort at Rattanaaburi Hospital. It consisted predominantly of asymptomatic individuals undergoing colorectal cancer screening, together with a smaller proportion of participants with mild, non-alarming

gastrointestinal symptoms who were referred for early evaluation. This pattern reflects the routine CRC screening service model in district and provincial hospitals, rather than a strictly asymptomatic screening cohort.

All eligible individuals who underwent colonoscopy between January 2022 and April 2025 and had complete APCS, FIT, and histopathological results were included in the study. Clinical, colonoscopy, and pathology data were retrospectively retrieved from medical records.

Fecal immunochemical test (FIT) All participants underwent a quantitative fecal immunochemical test (FIT) before colonoscopy. FIT was performed using a quantitative immunoturbidimetric assay (Hangzhou AllTest Biotech Co., Ltd, Manufacturer, China). Results were reported in $\mu\text{g Hb/g}$ of feces (cutoff 100 ng/ml). In accordance with the manufacturer's recommendation and institutional practice, $\text{FIT} \geq 10 \mu\text{g Hb/g}$ was defined as positive, and values below this threshold were considered negative. This predefined cut-off was consistently applied in all diagnostic and regression analyses.

APCS Risk Stratification The Asia-Pacific Colorectal Screening (APCS) score was calculated based on age, sex, smoking history, and family history of colorectal cancer. Participants were categorized into three risk groups: low risk (0–1 points), moderate risk (2–3 points), and high risk (≥ 4 points). For diagnostic and regression analyses, APCS was further dichotomized into high-risk ($\text{APCS} \geq 4$) and non-high-risk ($\text{APCS} < 4$), consistent with previous APCS validation studies.

Endoscopic and histopathological classification In this retrospective analysis, we included only participants who had at least one biopsy or polypectomy specimen submitted for histopathological examination. As a result, individuals with completely normal colonoscopy findings and no biopsy were not captured in the analytic dataset. For each participant, endoscopic and histopathological findings were summarized per patient according to the most advanced lesion identified (adenocarcinoma > adenoma > colitis or other non-neoplastic lesions). Thus, the high proportion of adenomas observed in this cohort reflects an enriched subset of colonoscopy-and-biopsy cases rather than the adenoma detection rate in the entire screening-eligible population.

Outcomes

The primary outcome of interest was colorectal cancer (CRC), defined as histologically confirmed colorectal adenocarcinoma on biopsy or polypectomy specimens. For

descriptive purposes, histological findings were categorized into three groups: (1) colitis or other non-neoplastic inflammatory lesions; (2) adenoma (including tubular, tubulovillous, or villous adenomas without invasive carcinoma); and (3) adenocarcinoma (CRC).

Inclusion criteria

Participants were eligible if they had met the following criteria:

1. Age ≥ 18 years.
2. Underwent colonoscopy at Rattanaaburi Hospital between January 2022 and April 2025 as part of colorectal cancer (CRC) screening or early evaluation of mild, non-alarming gastrointestinal symptoms (e.g., functional constipation or vague abdominal discomfort) in an outpatient setting.
3. Had an Asia-Pacific Colorectal Screening (APCS) score assessed before colonoscopy.
4. Underwent a quantitative fecal immunochemical test (FIT) prior to colonoscopy.
5. Had at least one biopsy or polypectomy specimen with available histopathological results.

Exclusion criteria

Participants were excluded if they met any of the following conditions:

1. Having a history or diagnosis of chronic inflammatory bowel disease (IBD), such as Crohn's disease or ulcerative colitis
2. Having received a previous diagnosis of colorectal cancer prior to the current screening
3. Having had incomplete or inadequate colonoscopies (e.g., poor bowel preparation, incomplete examination)
4. Presenting with alarm gastrointestinal features suggestive of a diagnostic rather than screening indication (e.g., overt gastrointestinal bleeding, suspected bowel obstruction, or severe unexplained anemia).

Sample size

The sample size for this study was determined using a single-proportion formula to estimate the predictive performance of each tool. Based on the study by Chiu et al. (2016).⁸ which evaluated the effectiveness of an APCS combined with a FIT in a prospective international multi-center setting, the combination of APCS and FIT demonstrated the accurate identification of individuals requiring colonoscopy at an early stage, detecting up to

70.6% of those with advanced neoplasia (AN). Using the single-population proportion formula, the following parameters were applied:

$$n = \frac{Z^2_{\alpha/2} P(1-P)}{d^2}$$

Alpha (α)	=	0.05
Standard normal value (Z)	=	1.96
Prevalence (P)	=	0.70
Absolute precision (d)	=	0.035
95% confidence interval		

The calculated sample size was 662 participants.

Ethical approval

The study was approved by the Ethics Committee for Human Research, Surin Provincial Public Health Office, Ministry of Public Health, Thailand (Ethics approval number: 85/2568). The review process was conducted under the expedited review category. The study adhered to the principles of the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines, and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Data analysis and statistical methods

All data were processed and analyzed using STATA software.

1. Descriptive statistics: For the normally distributed data, the results were presented as means $\pm$ standard deviation (SD). For the non-normally distributed data, the results were reported as medians with interquartile ranges (IQRs), along with minimum and maximum values.

2. Comparisons of histopathological distribution between groups in Tables 3–5 were analyzed using the Chi-square test (or Fisher's exact test when expected cell counts were <5). A p -value <0.05 was considered statistically significant.

3. Diagnostic performance: Sensitivity, specificity, and accuracy of the individual and combined models were calculated.

4. Multivariable logistic regression was performed to identify factors associated with colorectal cancer (CRC). The dependent variable was defined as the presence of CRC, based on histologically confirmed colorectal adenocarcinoma (CRC = 1) versus all other histological

findings (CRC = 0). A total of 19 participants in the cohort had CRC, and this limited number of outcome events was explicitly considered when specifying the number of predictors included in the models to reduce the risk of overfitting. Results were presented as adjusted odds ratios (aORs) with 95% confidence intervals (CIs) and *p*-values. Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test and visually inspected using a calibration plot. Multicollinearity was evaluated using variance inflation factors (VIFs), with values >10 indicating substantial multicollinearity.

5. Model performance: Discriminative ability was assessed using the area under the receiver operating characteristic curve (AUROC) to evaluate the capacity for each model to distinguish between cancer and non-cancer cases.

RESULTS

Among 662 participants, 19 (2.87%) were diagnosed with histologically confirmed colorectal cancer (CRC), while 643 (97.13%) had non-CRC lesions. Univariable logistic regression analysis showed that age, diabetes mellitus, hematocrit, hemoglobin, neutrophil percentage, and lymphocyte percentage were significantly associated with CRC (*p* < 0.05). Sex, body mass index, smoking history, alcohol consumption, hypertension, dyslipidemia, family history of colorectal cancer, and platelet count were not significantly associated with CRC. (Table 1).

Colonoscopy findings revealed that 72.66% of participants were asymptomatic. Among those with symptoms, constipation was the most common (19.49%), followed by abdominal pain (6.80%). The most frequent diagnosis after colonoscopy was colonic polyps (93.81%), followed by colitis (3.02%) and colorectal cancer (2.42%). Histopathological examination confirmed that most lesions were adenomas (93.96%), which are precursor lesions of colorectal cancer, while adenocarcinoma accounted for 2.87% and colitis for 3.17% (Table 2).

Table 2 Colonoscopy findings, post-operative diagnoses, and histopathology results (n = 662)

Variables	Mean ± SD or n (%)
Clinical signs	
Bowel habit change	7 (1.06)
Constipation	129 (19.49)
Abdominal pain	45 (6.80)
No clinical signs	481 (72.66)
Post-operative diagnoses (Post-op Dx)	
Rectal polyp	2 (0.30)
Rectal cancer	3 (0.45)
Colitis	20 (3.02)
Colon cancer	16 (2.42)
Colonic polyp	621 (93.81)
Histopathology (Patho)	
Colitis	21 (3.17)
Adenocarcinoma	19 (2.87)
Adenoma	622 (93.96)

Table 1 The baseline characteristics of the participants (n = 662)

Variables	non-CRC (n=643)	CRC (n=19)	Total	OR (95%CI)	<i>p</i> -value
Age (years)	61.05±7.03	69.21±5.55	61.30 ± 7.12	1.17 (1.09-1.25)	<0.01
Male (%)	274(42.61)	7 (36.84)	281 (42.45)	1.27 (0.49-3.27)	0.61
Body mass index	24.45±7.55	22.60±4.46	24.40 ± 7.49	0.90 (0.80-1.01)	0.09
Smoking history	184(28.62)	8 (42.11)	192 (29.0)	1.81 (0.71-4.58)	0.20
Alcohol consumption	151(23.58)	6 (31.58)	157 (23.72)	1.50 (0.56-4.02)	0.41
Comorbidities					
HT	186(28.93)	9(47.37)	195 (29.46)	2.21(0.88-5.52)	0.09
DM	54 (8.40)	8 (42.11)	62 (9.37)	7.93 (3.06-20.56)	<0.01
DLP	37 (5.75)	3 (15.79)	40 (6.04)	3.07 (0.85-11.01)	0.08
Family history of colorectal cancer	190 (29.55)	9 (47.37)	199 (30.06)	2.15 (0.85-5.36)	0.10
Laboratory findings					
HCT (%)	38.24±4.44	33.94±3.43	38.12 ± 4.47	0.84 (0.77-0.91)	<0.01
HB (g/dL)	12.34±1.62	11.04±1.30	12.30 ± 1.63	0.65 (0.51-0.83)	<0.01
PLT (T/μL)	258388.8 ± 69904	268473.7 ± 106931	258,678.2 ± 71,136.09	1.00 (0.99-1.00)	0.54
Neutrophils%	58.29 ± 10.22	67.57 ± 8.27	58.56 ± 10.28	1.07 (1.03-1.12)	<0.01
Lymphocytes%	31.22 ± 9.11	23.0 ± 6.93	30.98 ± 9.15	0.91 (0.86-0.95)	<0.01

When comparing the fecal immunochemical test (FIT) results with the histopathology, 297 participants had tested FIT–, of whom 92.26% had adenomas. Among 365 FIT+ participants, 95.34% had had adenomas. Adenocarcinoma was more common in the FIT+ group (3.56%) compared to the FIT– group (2.02%). Conversely, colitis had been more frequently detected in the FIT– group (5.72%) than in the FIT+ group (1.10%) (**Table 3**).

Table 3 A comparison between the FIT results and the histopathology findings

Histopathology	FIT– (n = 297)	FIT+ (n = 365)	p-value
Colitis	17 (5.72)	4 (1.10)	< 0.01
Adenocarcinoma	6 (2.02)	13 (3.56)	
Adenoma	274 (92.26)	348 (95.34)	

A comparison of histopathology by APCS score showed that participants with APCS ≥ 4 (the high-risk group) had a higher proportion of adenocarcinoma than those with APCS < 4 (3.94% vs. 1.81%). Adenomas were common in both groups but more frequent in the APCS < 4 group (95.18% vs. 92.73%). The prevalence of colitis was similar between the two groups (3.01% vs. 3.33%) (**Table 4**).

Table 4 A comparison between the APCS scores and the histopathology findings

Histopathology	APCS < 4 (n = 332)	APCS ≥ 4 (n = 330)	p-value
Colitis	10 (3.01)	11 (3.33)	0.24
Adenocarcinoma	6 (1.81)	13 (3.94)	
Adenoma	316 (95.18)	306 (92.73)	

When combining the APCS and FIT results, the highest proportion of adenocarcinoma was observed in the high-risk (APCS ≥ 4) + FIT+ group (6.29%), which was followed by APCS ≥ 4 + FIT– (2.14%). In contrast, groups with APCS < 4 , regardless of their FIT statuses, had exhibited lower proportions (approximately 1.80–1.82%). Adenomas were highly prevalent across all groups, particularly in APCS < 4 + FIT+ (97.30%). Colitis, a non-cancerous lesion, was found to be more common in the FIT-groups (APCS < 4 + FIT–: 7.27%; APCS ≥ 4 + FIT–: 4.81%) compared with the FIT+ groups. These differences were determined to be statistically significant ($p < 0.01$) (**Table 5**).

Table 5 The distribution of histopathology findings according to APCS and quantitative Fecal Immunochemical Test (FIT) results

Histopathology	APCS ≥ 4 + FIT+	APCS ≥ 4 + FIT–	APCS < 4 + FIT+	APCS < 4 + FIT–	p-value
Colitis	2 (1.40)	9 (4.81)	2 (0.90)	8 (7.27)	< 0.01
Adenocarcinoma	9 (6.29)	4 (2.14)	4 (1.80)	2 (1.82)	
Adenoma	132 (92.31)	174 (93.05)	216 (97.30)	100 (90.91)	

In evaluating the diagnostic performance of screening tools for predicting cancer, FIT alone had yielded a sensitivity of 68.4% but a low specificity (45.3%), with an AUROC of 0.56, indicating poor discriminative performance. Using APCS ≥ 4 alone, the same sensitivity (68.4%) was achieved, with a slightly higher specificity (50.7%) and an AUROC of 0.59. Combining FIT with APCS ≥ 4 increased specificity to 79.0% but reduced sensitivity to 47.4%. Nevertheless, the AUROC had improved to 0.64 (**Table 6**).

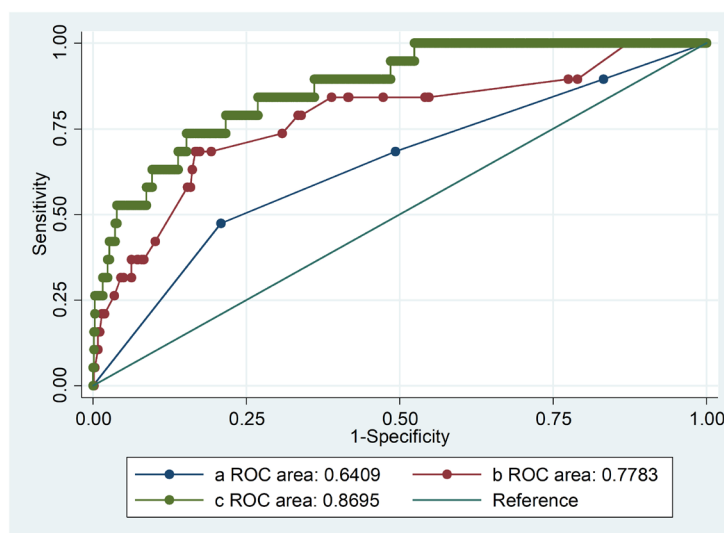
Table 6 The diagnostic performance for predicting colorectal cancer

	Sensitivity	Specificity	ROC areas
FIT positive	68.4 (43.4–87.4)	45.3 (41.4–49.2)	0.56 (0.45–0.67)
APCS ≥ 4	68.4 (43.4–87.4)	50.7 (46.8–54.6)	0.59 (0.48–0.70)
FIT positive and APCS ≥ 4	47.4 (24.4–71.1)	79.0 (75.8–82.2)	0.64 (0.51–0.74)

Multivariate analysis of the factors associated with colorectal cancer (CA) was performed using three models (**Table 7**). In Model 1, which included only FIT and APCS, FIT+ showed a non-significant trend toward increased risk (OR = 2.23, $p = 0.11$), while APCS ≥ 4 was determined to be borderline significant (OR = 2.66, $p = 0.05$). The AUROC was 0.64, indicating low accuracy. Model 2, which added risk behaviors (alcohol consumption) and comorbidities, identified diabetes mellitus as a strong independent predictor (OR = 7.62, $p < 0.01$). FIT+ also reached statistical significance (OR = 3.51, $p = 0.03$), with the AUROC increasing to 0.77. Model 3 achieved the highest AUROC of 0.86, demonstrating improved discriminative performance when FIT, APCS, diabetes mellitus, and HCT had been combined.

Table 7 A comparison of the multivariable logistic regression models for the predictors of colorectal cancer

Variables	Model 1		Model 2		Model 3	
	Adj.OR	p-value	Adj.OR	p-value	Adj.OR	p-value
FIT positive	2.23 (0.81-6.08)	0.11	3.51 (1.12-11.04)	0.03	7.66 (1.96-30.0)	< 0.01
APCS ≥ 4	2.66 (0.97-7.24)	0.05	2.70 (0.92-7.88)	0.06	4.54 (1.29-16.02)	0.01
Alcohol			1.80 (0.60-5.36)	0.28	0.83 (0.20-3.35)	0.80
Underlying						
HT			1.81 (0.67-4.86)	0.24	2.28 (0.74-7.04)	0.14
DM			7.62 (2.60-22.32)	< 0.01	8.84 (2.70-28.96)	< 0.01
DLP			2.19 (0.45-10.56)	0.32	3.66 (0.69-19.26)	0.12
LAB						
HCT (%)					0.70 (0.54-0.89)	< 0.01
HB (g/dL)					1.59 (0.85-2.99)	0.14
PL (T/ μ L)					1.00 (0.99-1.00)	0.33
Neutrophils (%)					1.01 (0.90-1.14)	0.74
Lymphocytes (%)					0.93 (0.81-1.08)	0.38
ROC CURVE	0.64 (0.49-0.78)		0.77 (0.65-0.90)		0.86 (0.83-0.96)	

**Figure 1** A comparison of the diagnostic performance for predicting colorectal cancer

DISCUSSION

This study aimed to evaluate the diagnostic performance of the Asia-Pacific Colorectal Screening (APCS) score and the Fecal Immunochemical Test (FIT), both individually and in combination, to predict colorectal cancer (CRC) using data from 662 participants who had undergone colonoscopy. Quantitative Fecal Immunochemical Test (FIT) results, APCS scores, and histopathological findings were analyzed retrospectively. Our analysis revealed that adenoma had been the most commonly detected lesion (93.96%), whereas adenocarcinoma was found in only 2.87% of cases. This finding indicated that the screening program had been more effective at detecting precursor lesions than advanced cancer, which is valuable

for population-level prevention strategies. This aligned with Lieberman et al.⁹ who followed 1,915 participants over 10 years and reported adenoma detection rates of 25–30% and advanced neoplasia (AN) rates of approximately 6%, which was comparable to the APCS ≥ 4 + FIT+ group in the present study.

Another important explanation for the modest diagnostic performance of FIT observed in this study is the very high proportion of adenomas in our cohort. Histopathological analysis revealed that 93.96% of lesions were adenomas, while only 2.87% were adenocarcinomas. Since FIT primarily detects occult gastrointestinal bleeding, its sensitivity is inherently lower in populations dominated by non-bleeding precursor lesions such as small

or non-advanced adenomas. Many adenomas do not bleed consistently and, therefore, may not produce detectable fecal hemoglobin, resulting in reduced FIT sensitivity and AUROC in this real-world screening cohort.

When considering FIT alone to predict CRC, sensitivity was 68.4%, specificity was 45.3%, and the AUROC was 0.56. The low specificity indicated a high false-positive rate. This contrasted with the meta-analysis by Anastasia Katsoula et al.,¹⁰ which included 12 studies ($n = 6,204$) using colonoscopy as the reference standard and which reported a FIT sensitivity of 93% and a specificity of 91%. The discrepancy may be explained by our study population being asymptomatic, with a high prevalence of adenoma (93.96%) and a low prevalence of adenocarcinoma (2.87%). FIT is known to have limitations in detecting non-bleeding or small adenomas, which can lead to false negatives and reduce overall accuracy, unlike the high-risk or symptomatic populations analyzed by Katsoula et al.

For APCS ≥ 4 alone, the sensitivity was 68.4%, specificity was 50.7%, and the AUROC was 0.59, which was slightly lower than the meta-analysis by Mai Ngoc Luu et al.,¹¹ who reviewed 69,762 colonoscopy participants and reported an APCS sensitivity of 42% (95% CI: 40–44%) and a specificity of 86% (95% CI: 85–86%) for predicting advanced colorectal neoplasia (ACN), with a weighted AUROC of 0.642 (95% CI: 0.610–0.657). The difference may reflect the APCS score's limitations when applied to new, asymptomatic populations with low AN prevalence.

When combining FIT and APCS and specifically selecting the high-risk group (APCS ≥ 4 + FIT+), specificity increased significantly to 79.0%, while sensitivity decreased to 47.4%, with the AUROC rising to 0.64. This demonstrated improved discrimination between participants with and without CRC when using both tools together. This finding was consistent with Chiu et al. (8), who reported that combining APCS and FIT in a prospective multicenter study accurately identified participants who should undergo early colonoscopy, detecting 70.6% of those with advanced neoplasia. Although an AUROC value of 0.64 indicates fair discrimination (0.6–0.7), the combined use of APCS and FIT can improve the ability to distinguish participants with CRC, increase specificity, and reduce unnecessary colonoscopies in low-risk groups while still detecting a substantial proportion of advanced lesions.

Although combining a positive FIT result with a high APCS score (≥ 4) improved diagnostic performance compared with either tool alone, the AUROC of the combined strategy remained below 0.7. This modest discrimination is biologically and methodologically plausible. First, the

APCS score was originally developed to predict advanced colorectal neoplasia rather than histologically confirmed colorectal cancer alone; therefore, its predictive ability is expected to decrease when CRC is used as the sole outcome. Second, the performance of FIT depends on

occult gastrointestinal bleeding, and many adenomas and some early cancers are non-bleeding lesions, which lowers sensitivity. Third, the relatively low CRC prevalence in this cohort (2.87%) may attenuate predictive performance due to spectrum and base-rate effects. In addition, our dataset was a colonoscopy-and-biopsy cohort enriched for neoplastic lesions rather than a true population screening cohort, and the number of CRC events was limited, which may contribute to modest AUROC estimates. These factors together likely explain why the combined approach, although superior to either tool alone, still demonstrated only poor discrimination.

Multivariable logistic regression analysis revealed that, in addition to FIT positivity (adjusted OR = 7.66) and APCS ≥ 4 (adjusted OR = 4.54), diabetes mellitus (DM) (adjusted OR = 8.84; 95% CI: 2.70–7.04) had been significantly associated with CRC risk, demonstrating a stronger predictive effect than FIT or APCS alone. Larsson et al.¹² analyzed 15 studies (6 case-control and 9 cohort, total $n = 2,593,935$) and found that DM had increased the risk of colorectal cancer compared with non-diabetic individuals (RR = 1.30, 95% CI: 1.20–1.40) and had been associated with higher CRC mortality (RR = 1.26, 95% CI: 1.05–1.50). Mechanistically, chronic hyperinsulinemia and insulin resistance may elevate IGF-1 levels, thereby stimulating abnormal cell proliferation, while chronic inflammation and oxidative stress in DM participants may promote DNA damage and tumorigenesis.

Laboratory parameters were also significant predictors. Hematocrit (HCT) showed an inverse association with CRC risk (adjusted OR = 0.70; 95% CI: 0.54–0.89), which is consistent with the clinical observation that anemia, especially in older adults, may be an early sign of CRC. HCT may be used in conjunction with other screening tools, such as FIT or APCS, to enhance the accuracy of risk assessment.

Limitations

1. This was a retrospective, single-center study, potentially introducing selection and recording bias and thereby limiting generalizability.

2. Most participants were asymptomatic, and the CRC prevalence was only 2.87%. These factors may have caused spectrum bias and reduced sensitivity/AUROC esti-

mates compared to studies with higher disease prevalence.

3. The AUROC for APCS + FIT may underestimate the true potential in settings with higher AN/CRC prevalence, optimized FIT cut-offs, population-specific APCS adjustments, and controlled colonoscopy quality and confounding factors.

4. Colonoscopy quality indicators such as CIR and ADR could not be fully assessed due to incomplete documentation, which may limit the interpretation of screening performance.

5. Formal internal and external validation of the predictive model was not performed in this study. The development of a validated prediction equation or nomogram will be addressed in future studies using independent datasets.

CONCLUSION

The combination of APCS ≥ 4 and a positive FIT result improves the identification of participants at risk for colorectal cancer (CRC) compared with either tool used alone. This combined approach substantially improved specificity (79.0%), suggesting its clinical utility in prioritizing colonoscopy among high-risk individuals. and had raised the AUROC to 0.64, representing fair discrimination. Whereas, FIT or APCS alone had yielded lower AUROC values of 0.56 and 0.59, respectively. Furthermore, a predictive model incorporating FIT, APCS ≥ 4 , diabetes mellitus (DM), and hematocrit (HCT) demonstrated high performance (AUROC = 0.86), suggesting that adding comorbidity and laboratory indicators to the APCS + FIT screening strategy could enhance practical screening accuracy in both district-level and provincial-level hospitals.

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