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Original Article

Predictive Factors and Prediction Model for Advanced Colorectal Neoplasia in Pattani, Thailand

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ABSTRACT

Background: Understanding the predictive factors of advanced colorectal neoplasia (ACN) is crucial for constructing a prediction model for its detection.

Objective: We aimed to determine the predictive factors associated with advanced colorectal neoplasia in the Pattani population appointed for colonoscopies.

Method: A prognostic factor research with a retrospective, cross-sectional design including 637 patients from Pattani Hospital was conducted between July 2020 to April 2024. All participants had a complete colonoscopy to determine the presence of advanced neoplasia. Variables were examined based on the Asia Pacific Colorectal Screening (APCS) score, and additional variables, such as the history of alcohol use, diabetes mellitus, and body mass index (BMI), were included. We use multivariable logistic regression to identify the predictive factors and develop a prediction model for predicting ACN.

Results: 87 people were recognized to have ACN, while 530 participants were not. Multivariable analyses revealed significant increased risks for men (OR, 2.69; 95% CI, 1.51, 4.79), aged 50-69 years (OR, 3.36; 95% CI, 1.39, 5.44), age > 70 years (OR, 4.57; 95% CI, 2.12, 9.87), and individuals who currently or formerly smoked (OR, 1.93; 95% CI, 1.04, 3.57). No significant association was observed between a family history of colon cancer in first-degree relatives, alcohol consumption, diabetes mellitus, and a body mass index greater than 23. The prediction model was developed using six predictive factors: gender, age, smoking, family history of colon cancer in first-degree relatives, alcohol consumption, and body mass index (BMI). The model demonstrated a greater area under the receiver operating characteristic curve (AuROC) of 0.71 (95% CI, 0.65, 0.76) compared to the APC score of 0.61 (95% CI, 0.56, 0.67), with a significant difference ($p < 0.001$).

Conclusions: The predictive factors for advanced colorectal neoplasia (ACN) detected in this study may be helpful in clinical applications for predicting ACN risk in Pattani.

Keywords: Advanced colorectal neoplasia, Colorectal cancer screening, Risk stratification

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Introduction

Colorectal cancer (CRC) accounts for around 10.0% of all diagnosed cancers and is the second most significant cause of cancer-related mortality globally.[1,2] Most colorectal cancers develop slowly from precursor lesions. The duration for an early adenoma to establish colorectal cancer is uncertain. However, existing information indicates it is at least ten years. Advanced adenomatous polyps may require less time, especially serrated adenomas with dysplasia.[3] This gradual development provides an opportunity to detect precursor lesions and early cancer.

Colonoscopy nowadays is an essential technique for colorectal cancer diagnosis. Mucosal staining and magnification endoscopy facilitate the visual identification of precancerous lesions. Upon diagnosis, endoscopic polypectomy can efficiently eliminate malignant polyps.[4] It is widely accepted as an effective screening procedure for colorectal cancer and an effective strategy for decreasing its mortality by up to 68%[5]. Nonetheless, adherence is usually inadequate and less accessible in countries with limited resources. The restricted capacity of colonoscopy impedes the conduct of colorectal cancer screening in many countries. Thus, it is beneficial to understand predictive factors for detecting advanced colorectal neoplasia and develop risk stratification to enhance the cost-effectiveness of screening. It offers a systematic approach to optimizing CRC screening and identifying precancerous lesions, improving resource allocation.

Using risk factors and patient information for stratification has been helpful, leading to different colorectal cancer screening risk-stratification methods. The Asia Pacific Colorectal Screening (APCS) consists of four factors: age, sex, family history of colorectal cancer, and smoking status. The APCS score has been validated to predict advanced colorectal neoplasia (ACN)[6]. The modified APCS scoring system incorporates body mass index (BMI) as a further determinant of the APCS score. A recent Japanese study updated the APCS score from a 6-point to an 8-point system for the Japanese population, thereby improving the score's discriminative potential[7]. The new scoring system for evaluating risk stratification is complicated, necessitating precise information regarding a patient's smoking history duration. The adjusted Asia-Pacific colorectal screening score (A-APCS) system for predicting advanced colorectal neoplasia in asymptomatic Chinese individuals employed a threshold of 23.5 kg/m^2 for BMI and a history of one or more first-degree relatives with colorectal cancer (CRC)[8].

APCS is based on data from nine ethnic background populations. Consequently, a thorough regionalization study is essential in various countries, taking into account the unique demographic characteristics. Hence, the risk stratification capabilities of the Pattani people

remain unidentified. Consequently, comprehending the predictive features of advanced colorectal neoplasia is essential for developing a detection prediction model. We aim to investigate the predictive characteristics of advanced colorectal neoplasia by applying the APCS to predict ACN in the Pattani community.

Methods

We conducted a cross-sectional analysis of patients who underwent their first colonoscopy and collected consecutive data. A retrospective analysis was conducted in Pattani Hospital, Thailand, from July 2020 to September 2023.

Study population

The inclusion criteria for the study encompass all patients aged 15 and older who underwent colonoscopy, regardless of whether they presented with symptomatic or asymptomatic lower gastrointestinal symptoms. The exclusion criteria included incomplete colonoscopy, inadequate bowel preparation, inadequate colonoscopy report specifying the quantity and dimensions of colorectal neoplasms, incomplete pathology report regarding the histological analysis and dysplasia grading of colorectal neoplasms, prior history of colonoscopy, prior history of colorectal polyps, malignancy, or surgical intervention, and the presence of inflammatory bowel disease. The Pattani Hospital ethics committee approved this study, which conformed with the Helsinki Declaration's ethical guidelines. (ethical approval number: PTN-026-2567). Furthermore, all individually identifiable information has been previously anonymized to protect patient privacy.

Study definitions and data collection

Medical records contained relevant data about the patient, including BMI, demographic details, family history of colorectal cancer in first-degree relatives, colonoscopy findings, and pathological features. In this study, people were classified as current or former smokers and current or previous drinkers.

Advanced colonic neoplasia is characterized by an adenoma of 10 mm or larger, a villous or tubulovillous adenoma, or an adenoma demonstrating high-grade dysplasia or any combination thereof, as well as invasive malignancy, all of which are categorized as advanced colorectal neoplasia, for example, tubular adenomas of 10 mm or larger or containing high-grade dysplasia are advanced adenomas.[9]

Individuals who had carcinoma in situ or intramucosal carcinoma were classified into the high-grade dysplasia category. Invasive cancer generally penetrates the muscularis mucosae into the submucosa, indicating that carcinoma has at least invaded the submucosa of the colorectum.[10] Patients were categorized according to a highly histologically advanced lesion[11]. The dimensions

and characteristics of the largest polyp or the neoplasms exhibiting advanced disease were documented for those with multiple neoplasms. This study utilizes an ACN discovered during colonoscopy and evaluated pathologically as the primary outcome measure.

Four experienced endoscopists performed colonoscopies with standard colonoscopes (OLYMPUS CV-190, Tokyo, Japan). Cecal intubation denotes the insertion of the colonoscope's tip into the cecum.[12] Using the Boston bowel preparation scale, the bowel preparation grading scale was assessed; each segment received a score of ≥ 2, which is considered "adequate."In this case, some segments that had an inadequate and incomplete colonoscopy were excluded. The adenoma detection rate indicates the proportion of patients diagnosed with at least one conventional adenoma during their initial primary colonoscopy. Individuals classified as current or past smokers were those who smoked seven or more cigarettes weekly, while current or past drinkers were defined as those who consumed alcohol two or more times per week.[8]

Statistical analysis

Statistical analyses and sample size estimation were conducted utilizing STATA version 16 (StataCorp, Lakeway, Texas, USA). Continuous variables were described by the mean and standard deviation, and histograms showed how the data was distributed. Frequency and percentage were employed for categorical data. Fisher's exact probability test was employed to compare categorical variables among the various groups, and an independent *t*-test and Mann-Whitney test were utilized to compare continuous variables as considered appropriate. All parameters went through exploratory analysis by univariable logistic regression. The odds ratio (OR), p-value, and 95% confidence interval were examined individually for each variable. A multivariable logistic regression analysis was conducted to identify the ACN predictor. The removal of non-contributing predictors was determined by their correlation with ACN and statistical significance. Variables unrelated to ACN, including diabetes, were sequentially removed using backward elimination. The insignificant statistical parameters considered clinically relevant with ACN were retained in the model as appropriate. A predictive model was developed specifically for predicting ACN. The ROC curve was utilized to evaluate the model's discriminative and predictive efficacy. The ROC of the models was compared. *P*-values for statistical tests below 0.05 have been determined statistically significant.

The study's sample size was determined based on a pilot study of individuals who received colonoscopy at Pattani Hospital, achieving 80% power and assuming that significant differences in the variables of gender, age, and smoking history

between the two groups could be identified at a *p*-value of 0.05. Based on this premise, the investigation necessitated a minimum population of 413 patients.

Results

Study population

Between July 2020 and September 2023, a total of 637 patients underwent colonoscopy at Pattani Hospital. Twenty patients were excluded from the analysis due to incomplete or inappropriate reports. Figure 1 illustrates a flowchart depicting the study population. Among the 617 patients who underwent their initial colonoscopy, 315 were male (51.03%), whereas 302 were female (49.95%). The average age was 56.67 ± 15.76 years. A total of 133 patients (21.55%) received a diagnosis of colorectal neoplasm. Of these patients, 28 (21.05%) presented with advanced colorectal polyp, whereas 59 (44.36%) exhibited invasive carcinoma. Advanced colorectal neoplasia was present in 14.10% (87/617) of cases. The clinical characteristics of the individuals and baseline features of patients are shown in Table 1. The ACN group exhibited a considerably higher male gender and was older than the non-ACN group, and the ACN group had a significantly greater smoking rate. The findings from the colonoscopy indicate that a colorectal tumor was identified in 9.56% (59/617) of cases, and a polyp was present in 11.99% (74/617) (Table 2). Table 3 delineates the clinicopathological features of Colorectal neoplasia(CRN) discovered

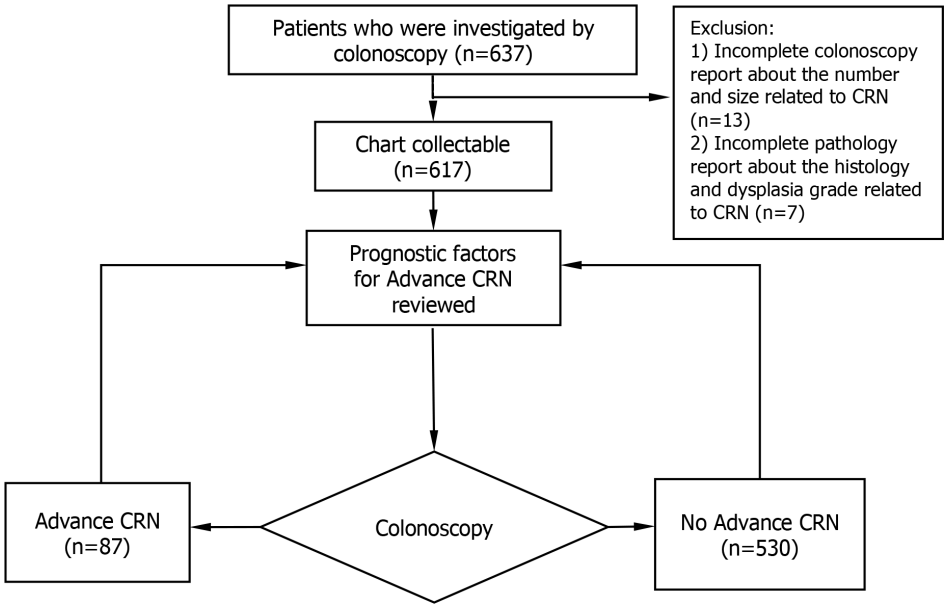

Figure 1 A flow diagram of the study population
CRN; Colorectal neoplasia

in the study. The predominant component of the ACN group is adenocarcinoma. Other components that encompass advanced colorectal polyps like villous adenoma, serrated adenoma, tubular adenoma with high-grade dysplasia, and intramucosal adenocarcinoma.

Table 1 The clinical characteristics of the enrolled participants

Patient characteristics	Advance CRN n=87		Non-Advance CRN n=530		*p*-value
	n	%	n	%	
Demographics					
Male (n,%)	63	72.41	252	47.55	< 0.001
Age (year), mean (± SD)	63.48	± 12.89	55.55	± 15.91	< 0.001
BMI, mean (± SD)	22.28	± 4.36	22.59	± 4.01	0.502
Co-morbidities (n, %)					
DM	4	4.60	19	3.58	0.551
Family history of colorectal cancer in first-degree relatives (FDR)	2	2.30	26	4.94	0.407
Smoking					
No	55	63.22	428	80.75	0.001
Stop use	21	24.14	57	10.75	
Continuous use	11	12.64	45	8.49	
Alcohol					
No	71	81.61	465	87.74	0.217
Stop use	12	13.79	44	8.30	
Continuous use	4	4.60	21	3.96	
Asymptomatic	19	21.35	127	24.05	0.686
Symptom					
Abdominal pain	25	28.74	149	28.11	0.898
Chronic Constipation	11	12.64	86	16.23	0.524
Chronic diarrhea	7	8.05	21	3.96	0.097
Constipation and diarrhea	13	14.94	51	9.62	0.132
Hematochezia	2	2.30	17	3.23	1.000
Melena	2	2.30	7	1.32	0.370
Mucus bloody stool	26	29.89	128	24.15	0.285
Unexplained weight loss	6	6.90	17	3.22	0.119

CRN; Colorectal neoplasia, BMI; Body mass index, DM; Diabetes mellitus, FIT; Fecal Immunochemical Test, PEG; Polyethylene glycol, RC; Right side colon, TC; Transverse colon, LC; Left side colon

Table 1 The clinical characteristics of the enrolled participants (continue)

Patient characteristics	Advance CRN n = 87		Non-Advance CRN n = 530		*p*-value
	n	%	n	%	
FIT test					
No	80	91.95	454	85.66	0.325
Negative	1	1.15	12	2.26	
Positive	6	6.90	64	12.08	
Bowel preparation					
Swiff 45 mil 2 doses	30	34.48	258	48.68	0.243
PEG 2 litre	52	59.77	233	43.96	
PEG 4 litre	5	5.75	39	7.36	
Bowel preparation(Boston scale), mean (± SD)					
RC	1.76	± 1.10	2.41	± 0.70	< 0.001
TC	2.06	± 1.05	2.63	± 0.65	< 0.001
LC	2.70	± 0.54	2.33	± 0.86	< 0.001
Total	**6.19**	**± 2.66**	**7.74**	**± 1.69**	**< 0.001**
Time to cecum (min), mean (± SD)	**11.73**	**± 7.51**	**11.91**	**± 8.40**	**0.894**
Time withdraws (min), mean (± SD)	**8.44**	**± 5.32**	**7.77**	**± 4.18**	**0.223**

CRN; Colorectal neoplasia, BMI; Body mass index, DM; Diabetes mellitus, FIT; Fecal Immunochemical Test, PEG; Polyethylene glycol, RC; Right side colon, TC; Transverse colon, LC; Left side colon

Table 2 Colonoscope findings of all participants

Colonoscope finding	N = 617	%
Normal Study	380	61.58
Diverticulum	58	9.57
Colitis	14	2.31
Polyp	74	11.99
Tumor	59	9.56
Other benign	41	6.77

Table 3 Histopathology finding

Histopathology finding	Advance CRN n = 87		No-Advance CRN n = 530	
	n	%	n	%
Normal Study	0	0	380	72.54
Non-significant finding	0	0	104	19.62
Tubular adenoma	8*	9.19	46	8.71
Villous adenoma	2	2.25	0	0
Tubular adenoma, High-grade dysplasia	5	5.62	0	0
Tubulovillous adenoma, low-grade dysplasia	3	3.37	0	0
Tubulovillous adenoma, High-grade dysplasia	3	3.37	0	0
High-grade dysplasia	1	1.12	0	0
Serrated adenoma low-grade dysplasia	2	2.25	0	0
Intramucosal adenocarcinoma	4	4.49	0	0
Adenocacinoma	59	66.29	0	0

CRN; Colorectal neoplasia

* Tubular adenoma, if smaller than 10 mm. was categorized in non-ACN groups, and ≥10 mm were categorized in ACN groups

Identifying risk predictors

Univariable and multivariable predictors of ACN

Table 4 demonstrates the associations between patient variables and ACN using analysis of univariable and multivariable regression methods. In the univariable analysis, older age, male gender, and current or previous smoking exhibited a significant association with ACN. The independent predictors identified included older age (50-69 years: OR, 3.36; 95% CI, 1.39-5.44, *p*-value=0.001; ≥ 70 years: OR, 4.57; 95% CI, 2.12-9.87, *p*-value < 0.001), male gender (OR, 2.69; 95% CI, 1.51-4.79, *p*-value=0.001), and present or previous smoking (OR, 1.93; 95% CI, 1.04-3.57, *p*-value=0.037).

Table 4 Univariable and Multivariable logistic regression analysis, Predictive factors associated with advanced colorectal neoplasm (ACN)

Predictors	Crude OR		Adjusted OR[§]	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Gender				
Male	3.01 (1.83,4.96)	< 0.001	2.69 (1.51,4.79)	0.001
Female	reference		reference	
Age				
≥ 70	2.75 (1.39,5.44)	0.004	4.57 (2.12,9.87)	< 0.001
50-69	3.91 (1.86,8.20)		3.36 (1.39,5.44)	0.001
< 50	reference		reference	
Smoking				
Yes	2.34 (1.14,3.80)	0.001	1.93 (1.04,3.57)	0.037
No				
Family History of Colon Cancer in first degree relative				
Yes	0.44 (0.10,1.88)	0.270	0.56 (0.13,2.47)	0.654
No				
Alcohol				
Yes	1.28 (0.83,1.96)	0.256	0.70 (0.41,1.19)	0.197
No				
DM				
Yes	1.26 (0.42,3.79)	0.680	0.96 (0.29,3.12)	0.950
No				
BMI				
≥ 23	0.98 (0.92,1.03)	0.428	0.99 (0.93,1.05)	0.850
< 23				

[§] Multivariable logistic regression

OR, Odds ratio; CI, confidence interval, BMI; Body mass index, DM; Diabetes mellitus

Development of the prediction model

Three factors, age, gender, and smoking that had a significant association with ACN were part of the prediction model and also included consumption of alcohol and BMI ≥ 23 kg/m^2 according to the modified colorectal screening score[7], and a first-degree relative's history of colorectal cancer (FDR) based on APCS. However, the latter three factors were not statistically significant but clinically relevant. The model's predictive capability was assessed using a receiver operating characteristic (ROC) curve, which obtained an area under the curve (AUC) of 0.71 (95% CI, 0.65-0.76). When comparing our model to the APCS score, our model was considerably superior (P = 0.0002) (Figure 2A).

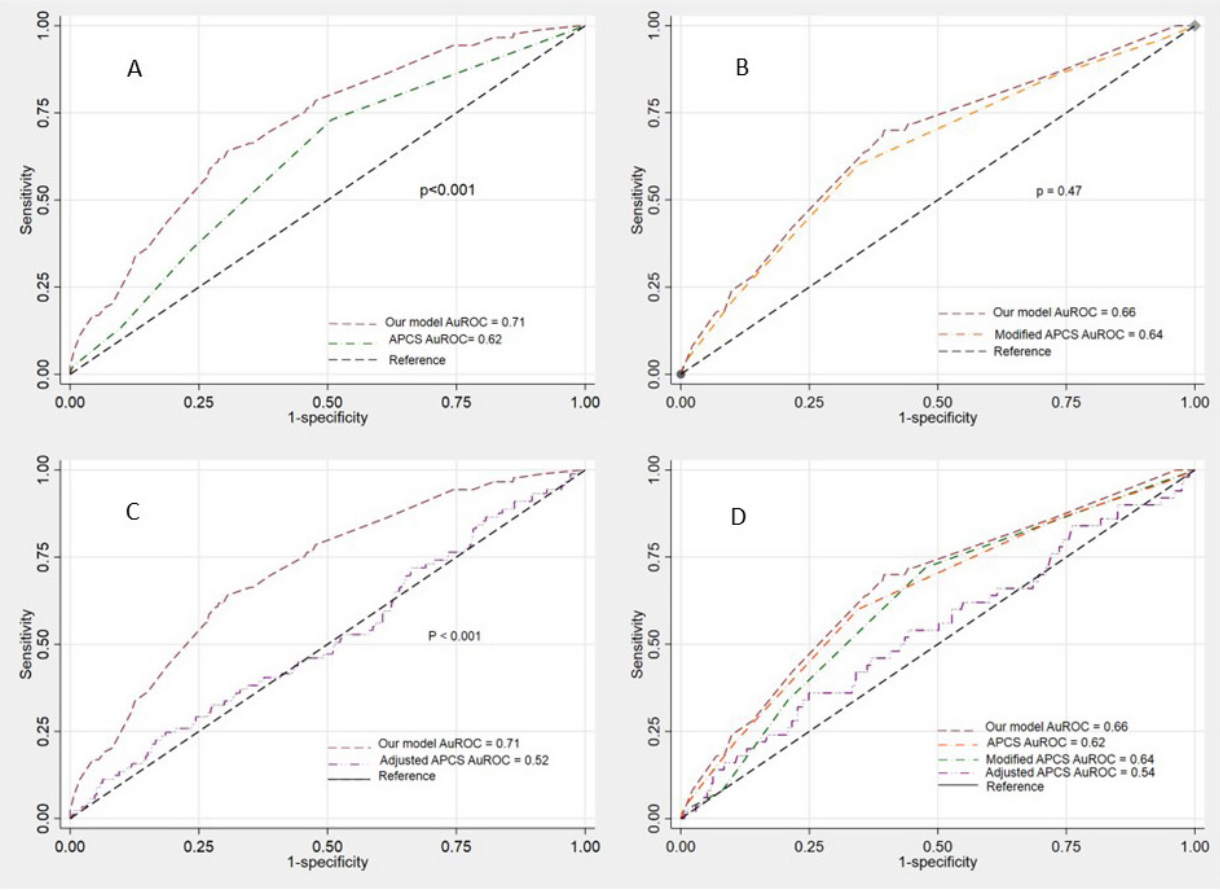

Figure 2 The model's predictive capability compared the receiver operating characteristic (ROC) curve. 2A compares our model to the APCS score, 2B compares our model to the modified colorectal screening score, 2C compares our model to the adjusted colorectal screening score, and 2D compares all models.

In evaluating the AUC for our model compared to the modified colorectal screening score, we found that our model achieved 0.66 (95% CI, 0.58-0.74), which was not significantly higher than the modified colorectal screening score of 0.64 (95% CI, 0.56-0.72) (*p*-value = 0.47) (Figure 2B). Our model exhibited a considerably higher AUC of 0.71 (95% CI, 0.65–0.76) compared to the adjusted Asia-Pacific colorectal screening score of 0.52 (95% CI, 0.45–0.58) ($P < 0.001$) (Figure 2C). When comparing the AUC of all models, our model had the highest AUC but non-statistic significantly (Figure 2D).

Discussion

Thailand has instituted a countrywide colorectal cancer screening program utilizing fecal immunochemical testing (FIT) for individuals aged 50 to 70. A stool-based test, such as FIT, may be limited to just serving as a screening tool for early identification of colorectal cancer. Single-application FITs exhibit moderate to high sensitivity and specificity for colorectal cancer, depending upon the positive threshold. The sensitivity of single-instance testing for advanced adenomas is low, irrespective of the threshold.[13]

Recognition of the predictive factors associated with advanced adenomas offers a logical approach to enhancing colorectal cancer screening and prevention, optimizing resource utilization. The availability of a reliable risk assessment tool is an important prerequisite for the risk stratification procedure. Cancer prevention testing is preferable to cancer diagnosis because it allows for the removal of advanced CRN and the prevention of CRC. CRC screening should prioritize prevention through polypectomy rather than detection[14]. Our result from investigating the predictive characteristics of advanced colorectal neoplasia by applying the APCS to predict ACN in the Pattani community by deriving a prediction model and stratifying the risk of the patient and prioritizing high-risk patients to colonoscopic schedule because resource limitation and prediction model using in patient 90% of target population that not included in colorectal cancer screening program policy of Thailand (only 10% of target population).

In 2011, The Asia-Pacific Working Group on CRC developed the APCS score to assess ACN risk in asymptomatic individuals based on CRC risk factors. Gender, age, a family history of colorectal cancer, and tobacco use are the four components that create the APCS score.[6] Numerous studies adjusted the scoring method according to these four parameters, including a modified colorectal screening score; the model incorporated a BMI cutoff at > 23 kg/m^2 [7]. Compared to the APCS, the modified score's c-statistics showed better discriminatory ability (c-statistics = 0.65 vs. 0.60). An adjusted Asia-Pacific colorectal screening score system (A-APCS) the subsequent risk factors were evaluated to determine the point differential from

APCS: Age 40–49 0 points, 50–69 (1 point), ≥ 70 years (2 points); non-smoker (0 points), smokers either present or past (0.5 points); BMI <23.5 kg/m² (0 points), BMI ≥ 23.5 kg/m² (1 point); family history of colorectal cancer none (0 points), one (1 point), two or more (2 points). The A-APCS score demonstrated superior discriminative ability compared to using APCS predictors alone.[8]

A predictive model for advanced colorectal neoplasia reported by Hong et al. is a 5-item risk model that incorporates gender, age, smoking history, alcohol use, and aspirin usage, demonstrating good discrimination (AUC = 0.726). The model's discriminatory efficacy for high-risk patients with advanced colorectal neoplasia exceeds that of the APCS (AUC = 0.678, $P < 0.001$)[15].

Our analysis indicates that the independent predicted factors were age, male gender, and smoking status. According to a prior study, Our data indicate that age, male gender, and smoking status may be potential predictors for detecting ACN.[6-8] The age groups of 50-69 years and > 70 years exhibit an increase in the probability of detecting ACN when the older age group corresponds to the study of APCS, A-APCS, and a predictive model for advanced colorectal neoplasia, as reported by Hong et al.

The male gender increased the risk of identifying ACN in our investigation, consistent with the prior three models and the modified colorectal screening score.[7] Current or prior smoking increased the likelihood of identifying ACN in our study, similar to APCS, A-APCS, and modified colorectal screening scores. In contrast, a predictive model for advanced colorectal neoplasia developed by Hong et al. included continuous data on smoking duration (in years) as well as age. A family history of colon cancer in first-degree relatives increases the likelihood of identifying ACN in APCS, A-APCS, and modified colorectal screening scores. Conversely, our analysis did not indicate that A family history of colon cancer in first-degree relatives significantly elevated the risk for identifying ACN, as well as BMI, which may be due to the constrained sample size of our research. Our predictive model encompassed age, male gender, and current or past smoking, which were statistically significant, in conjunction with a family history of colorectal cancer in first-degree relatives (FDR) based on APCS, alcohol consumption following the predictive model for advanced colorectal neoplasia reported by Hong et al., and BMI ≥ 23 kg/m² according to the modified colorectal screening score, although each of the last three factors did not achieve statistical significance.

Our predictive model demonstrated superior discriminative power compared to the predictors of APCS alone and the adjusted Asia-Pacific colorectal screening score. This outcome may be attributed to the assessment in the model derived cohort. The model should undergo external

validation at other hospitals in the future. A prior study indicates that our outcome may be associated with three additional factors that, while not statistically significant, are clinically relevant. Nonetheless, our model exhibited inferior discriminative power compared to the modified colorectal screening score. The categorization of age groups, limited to those aged 50 years and older, resulted in a reduced sample size and diminished discriminatory power in our model.

Nonetheless, this study has some limitations. A single-center design initially recruited both asymptomatic and symptomatic individuals into the cohorts. This constrained the applicability of the results to screening contexts. The retrospective examination of the derivation cohort resulted in some data loss, leading to probable selection bias. However, due to the similarity of the included patients' demographic characteristics and predictive factors to prior studies, such data constraints are likely negligible. To avoid this bias in the future, a prospective validation study should be conducted. The predictive model should be parsimonious and validated before its application in clinical practice.

Conclusion

The predictive factors for advanced colorectal neoplasia (ACN) identified in this investigation may assist in practical applications for assessing ACN risk and formulating a prediction model to stratify ACN risk, hence improving the cost-effectiveness of screening. It provides an organized approach for enhancing CRC prevention and detecting precancerous lesions, hence improving resource allocation.

Conflicts of interest

none declared.

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none declared.

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