Cancer Management and Research

Open Access Full Text Article

ORIGINAL RESEARCH

# Development and Validation of a Traditional Chinese Medicine Constitution-Based Risk Score for Advanced Colorectal Neoplasia in Asymptomatic Chinese Adults

Chenxi Huang[1,2], Yue Hou[3], Qing-hua Liu[3], Qian Kang[3,*], Ya-jing Fan[3,*], Ling-qin Zhu[3,*], Li Sun[4,*], Rui-cheng Men[4,*], Xiao-yan Li[4,*], Yun-long Gu[4,*], Qingtao Ni[5,*], Hui Wang[6], Yuqi He[3]

[1]Department of Physical Examination Center, Taizhou Fourth People's Hospital, Taizhou, Jiangsu, People's Republic of China; [2]Department of Physical Examination Center, Jinzhou Medical University, Panjin Liaohe Oilfield Gem Flower Hospital, Panjin, Liaoning, People's Republic of China; [3]Department of Gastroenterology, Beijing Chest Hospital, Capital Medical University, Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing, People's Republic of China; [4]Department of Gastroenterology, Wuhai Hospital of Traditional Chinese and Mongolian Medicine, Wuhai City, Inner Mongolia, People's Republic of China; [5]Department of Oncology, The Affiliated Taizhou People's Hospital of Nanjing Medical University, Taizhou School of Clinical Medicine, Nanjing Medical University, Taizhou, Jiangsu, People's Republic of China; [6]Department of Urology, The Affiliated Taizhou People's Hospital of Nanjing Medical University, Taizhou School of Clinical Medicine, Nanjing Medical University, Taizhou, Jiangsu, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yuqi He, Department of Gastroenterology, Beijing Chest Hospital, Capital Medical University, Beijing Tuberculosis and Thoracic Tumor Research Institute, No. 9, Beijing, 101149, People's Republic of China, Email endohe@163.com; Hui Wang, Department of Urology, The Affiliated Taizhou People's Hospital, Nanjing Medical University, Taizhou School of Clinical Medicine, Taizhou, 225300, People's Republic of China, Email wh0131@vip.qq.com

**Objective:** The objective of this study was to develop and validate an innovative risk-stratification tool that integrates Traditional Chinese Medicine (TCM) constitution with clinical factors to enhance colorectal cancer (CRC) screening among asymptomatic Chinese adults.

**Methods:** Conducted as a multicenter investigation, the study involved the randomization of 1430 asymptomatic participants into a derivation cohort (n=953) for model development and a validation cohort (n=477). Data on demographics, TCM constitution, and colonoscopy results were gathered using the TCM-Asia-Pacific Colorectal Screening (TCM-APCS) Questionnaire. A risk score was constructed through multivariable logistic regression analysis and its performance was assessed using receiver operating characteristic (ROC) analysis.

**Results:** The TCM-APCS model proficiently stratified participants into low-, medium-, and high-risk categories. Among individuals classified within the high-risk group, there was a significantly elevated prevalence of both low-grade adenoma (44.1% compared to 7.3%, p<0.001) and advanced colorectal neoplasia (17.2% compared to 3.6%, p<0.001) when contrasted with the low-risk group. The model demonstrated strong discriminatory capability for advanced neoplasia, exhibiting enhanced predictive performance relative to the original Asia-Pacific CRC Screening score. Additionally, at the optimal threshold, the model accurately identified 71.1% of advanced neoplasia cases within the validation cohort.

**Conclusion:** The TCM-APCS score is an effective, validated tool for risk-stratified CRC screening in China, enabling targeted resource allocation and enhanced screening efficiency in resource-constrained settings. Further external validation in diverse populations is warranted.

**Keywords:** traditional Chinese medicine constitution, risk stratification model, colorectal cancer screening, asymptomatic subjects

## Introduction

Colorectal cancer (CRC) represents a significant global health burden, with increasing incidence and mortality observed worldwide. In many Asian countries, rapid urbanization and accompanying lifestyle changes have contributed to a notable rise in CRC rates.[1] In China, improved living standards and dietary shifts towards a more Westernized pattern have been associated with steadily increasing CRC incidence and mortality.[2] In 2024, approximately 517,100 new CRC cases and 240,000 related deaths were reported in China, ranking it second and fifth, respectively, among all malignant tumors.[3] The incidence of CRC

https://doi.org/10.2147/CMAR.S568884
Received: 27 October 2025
Accepted: 26 March 2026
Published: 31 March 2026

begins to increase rapidly after the age of 50 in the Chinese population.[4] Moreover, the rising incidence of CRC among younger individuals presents additional challenges worldwide.[5]

There is growing evidence that CRC screening reduces both morbidity and mortality associated with this disease.[6] China's guidelines recommend screening via fecal occult blood tests, including the guaiac-based fecal occult blood test (gFOBT) and the fecal immunochemical test (FIT), as well as endoscopy for individuals over 45 or 50 years old.[7] In resource-limited settings, the implementation of CRC screening programs faces numerous obstacles. One of the key advantages of CRC screening is its established cost-effectiveness.[8] In China, the screening process predominantly relies on questionnaire-based surveys.[9] Integrating a scoring system as an initial screening tool could improve cost-effectiveness. While risk-stratified screening has the potential to reduce CRC incidence and mortality, such models are not yet widely used in China. The Asia-Pacific Colorectal Screening (APCS) score is utilized for assessing the risk of CRC and advanced adenomas (Table S1),[10] and FIT is recommended as an effective method. However, low compliance with fecal testing due to its undesirable nature remains a concern. Thus, patient adherence and the effectiveness of screening strategies are critical for successful CRC screening. An easily accepted strategy could simplify the screening process. CRC risk varies across populations and is influenced by factors such as age, gender, family history, obesity, excessive alcohol consumption, and smoking.[11]

Beyond these conventional risk factors, emerging evidence suggests that TCM is a holistic system that classifies individuals into distinct constitutional types, believed to reflect inherent physiological predispositions and disease susceptibilities. Modern research has begun to link specific TCM constitutions with biological states relevant to carcinogenesis, such as chronic low-grade inflammation and metabolic dysregulation, which are established risk factors for CRC.[12] Integrating TCM constitutional assessment into established risk scoring systems like the APCS could thus provide a more comprehensive risk stratification by capturing these intrinsic biological predispositions. As Traditional Chinese Medicine (TCM) theory has evolved,[13] it has been increasingly linked to conditions such as colonic adenoma. This study aims to develop and validate a novel TCM-based risk stratification model for ACN, which may improve screening efficiency in resource-limited settings.

# Methods

## Study Design and Participants

This prospective study followed the STROBE reporting guidelines for observational studies (see Checklist). Between January 2022 and December 2023, 1500 subjects undergoing opportunistic screening were recruited from three centers: The Fourth People's Hospital of Taizhou City, Beijing Chest Hospital (Capital Medical University), and Wuhai Mongolian and Chinese Medicine Hospital. Subjects were consecutively enrolled and then randomly assigned (using computer-generated random numbers) in a 2:1 ratio to either a derivation cohort (n=953) or an independent validation cohort (n=477). All participants were aged over 40 years, asymptomatic for CRC (no rectal bleeding, change in bowel habits, or abdominal pain attributable to CRC), and provided written informed consent. Exclusion criteria included: a personal history of CRC, colorectal polyps, or inflammatory bowel disease (IBD); a history of colorectal surgery; and contraindications to colonoscopy. The study flowchart detailing enrollment is presented in Figure 1.

## Questionnaire and Data Collection

Participants in both cohorts completed three components: 1) A basic demographic and clinical questionnaire covering age, sex, height, weight, family history of CRC (defined as having at least one first-degree relative with CRC), and detailed smoking history (never, past, current). 2) The validated Traditional Chinese Medicine Constitution Identification Questionnaire (TCM-CCQ).[13] This 60-item tool assesses nine constitutional types: Balanced Constitution (BC), Yang Deficiency Constitution (YADC), Yin Deficiency Constitution (YIDC), Qi Deficiency Constitution (QDC), Qi Stagnation Constitution (QSC), Phlegm-Dampness Constitution (PDC), Damp-Heat Constitution (DHC), Blood Stasis Constitution (BSC), and Inherited Special Constitution (ISC). Participants were classified into their predominant constitution type based on established scoring and conversion algorithms (Table S2). To ensure reliability, all TCM questionnaires were administered and scored by two trained TCM physicians who were blinded to the colonoscopy results. Inter-rater reliability was assessed using Cohen's kappa ($\kappa = 0.85$, indicating excellent agreement). 3) The Asia-Pacific Colorectal Screening (APCS) questionnaire.[10] All questionnaires were completed with the assistance of trained research staff prior to colonoscopy.


https://doi.org/10.2147/CMAR.S568884

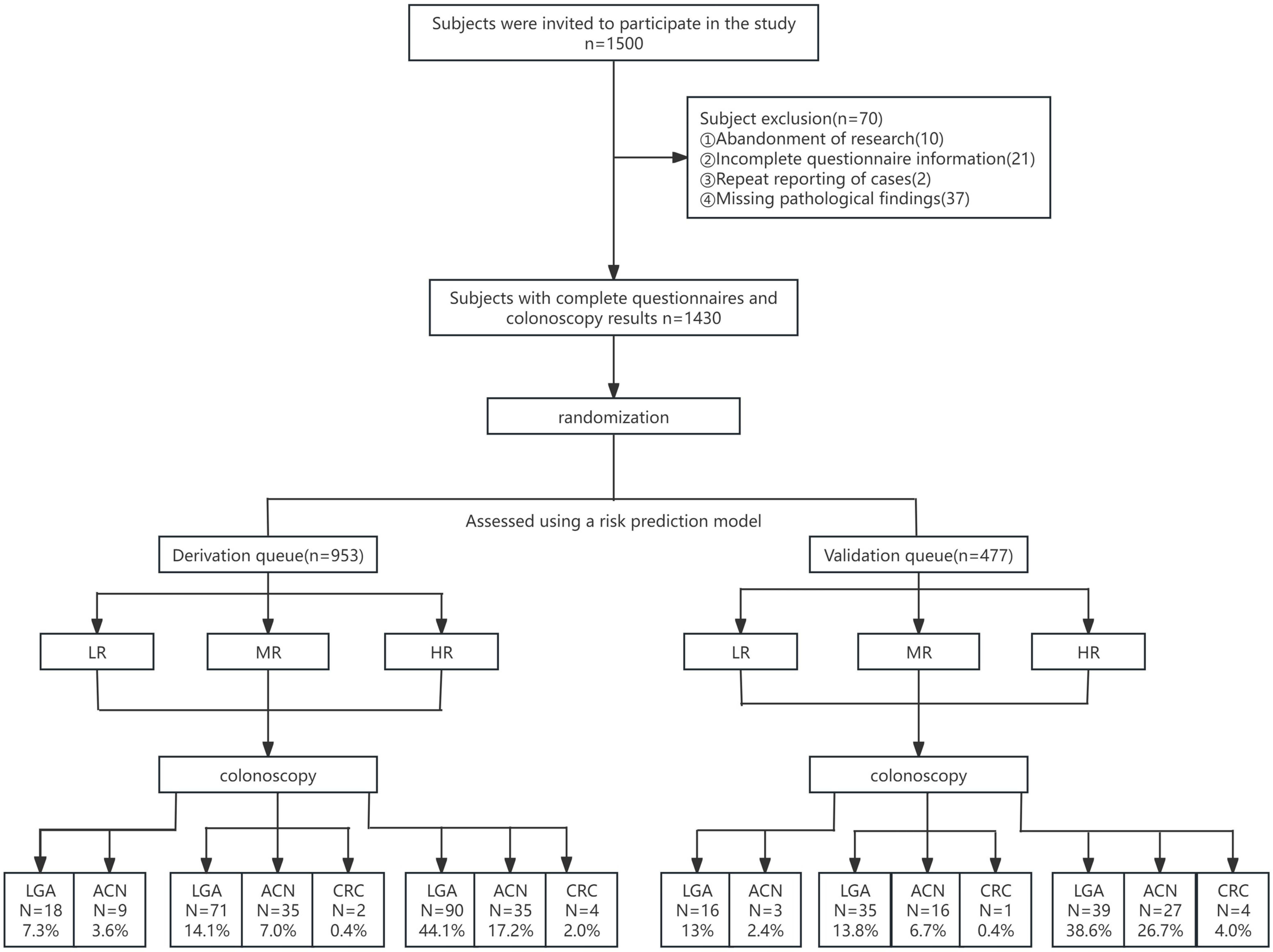


**Figure 1** Flow chart of participant enrollment, allocation, and colonoscopy.

## Colonoscopy and Histopathological Assessment

Colonoscopies were performed by experienced endoscopists (each with >5 years of experience and >1000 procedures) at each center. To ensure quality, the withdrawal time was mandated to be at least 6 minutes. All detected polyps were resected or biopsied for histopathological examination by expert gastrointestinal pathologists blinded to the questionnaire results. Lesions were classified according to the World Health Organization criteria. Advanced Colorectal Neoplasia (ACN): Defined as colorectal cancer (CRC) or advanced adenoma. Advanced adenoma was defined as an adenoma with one or more of the following features: size ≥10 mm, villous or tubulovillous histology (≥25%), or high-grade dysplasia. Low-Grade Adenoma (LGA): Adenomas not meeting the criteria for advanced adenoma. Non-Advanced Colorectal Neoplasia (NACN): Included hyperplastic polyps and LGA. The primary study endpoint was the detection of ACN.

## Statistical Analysis

Statistical analyses were performed using SPSS 26.0 (IBM Corp.) and R software (version 4.2.1). A two-sided P-value <0.05 was considered statistically significant. Continuous variables were compared using Student's *t*-test or Mann–Whitney *U*-test, and categorical variables using the Chi-square test or Fisher's exact test, as appropriate. Specifically, SPSS 26.0 was primarily used for data management, descriptive statistics, univariate and multivariate logistic regression analyses, and model goodness-of-fit tests (eg, Hosmer–Lemeshow test). R software (version 4.2.1) was mainly employed for generating ROC curves, calculating the AUC, and performing DeLong's test for comparing ROC curves.

## Model Development and Internal Validation

In the derivation cohort, univariate logistic regression analyses were performed to identify factors associated with LGA and ACN. Variables with $P<0.10$ in univariate analysis were entered into multivariate logistic regression models using backward stepwise selection (entry $P<0.05$, removal $P>0.10$). Multicollinearity was assessed using the variance inflation factor (VIF <5 for all retained variables). Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. The final model was used to develop the TCM-APCS risk score.

## Risk Score Derivation

Risk factors were assigned point values based on established criteria, with distinct values designated for various age groups and types of TCM. Subsequently, these points were adjusted in the multivariate logistic regression analysis by weighting them according to the corresponding adjusted ORs. For the purpose of facilitating scoring, the adjusted ORs were halved and rounded to the nearest whole number. The scoring system for smoking history was allocated a value of 1 point, reflecting its significant association with the development of colorectal tumors, although its influence on advanced tumors did not reach statistical significance (refer to Table S4). Using the Youden index derived from the ROC curve, a score of 3.5 was identified as the optimal cut-off for detecting any colorectal neoplasia (LGA/ACN/CRC), and a score of 5.5 for detecting CRC specifically. For clinical practicality, these continuous cut-offs were translated into three risk strata: Low Risk (0–3 points), Medium Risk (4–5 points), and High Risk (6–8 points).

## Model Performance and Risk Stratification

The discriminatory ability of the TCM-APCS score for predicting ACN was evaluated using the area under the receiver operating characteristic curve (AUC-ROC). The Youden index was used to determine optimal cut-off points for risk stratification. Calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test. The model's performance was then validated in the independent validation cohort.

## Comparison with APCS Score

To evaluate the incremental value of adding TCM constitution, we compared the performance (AUC, sensitivity, specificity) of the new TCM-APCS score against the original APCS score alone in both cohorts using DeLong's test for paired ROC curves.

# Results

## Baseline Characteristics

A total of 1430 participants completed the study (953 in derivation, 477 in validation). The baseline characteristics were well-balanced between the two cohorts (Table 1). In the derivation cohort, the majority of participants were aged 45 years or older, 56.8% were male, and the prevalence of ACN was 8.9% (n=85). Among the pathological TCM constitutions, the most common TCM constitutions were Phlegm-Dampness (PDC, 4.4%) and Damp-Heat Constitution (DHC, 5.6%). Only a small proportion of participants reported a family history of CRC.

## Factors Associated with Colorectal Neoplasia

Univariate and multivariate analyses for LGA and ACN within the derivation cohort are detailed in Table S3. In the final multivariate model for ACN (Table 2), independent predictors were identified as follows: age ≥60 years (OR=3.46, 95% CI 1.30–9.21), current smoking, which demonstrated a trend toward significance (OR=1.95, 95% CI 0.92–4.11), and a family history of CRC in first-degree relatives (OR=4.43, 95% CI 1.43–17.32, P=0.033). Notably, specific TCM constitutions were significantly associated with an increased risk of ACN, particularly the Damp-Heat Constitution (DHC, OR=42.45, 95% CI 15.55–115.86) and the Phlegm-Dampness Constitution (PDC, OR=41.25, 95% CI 11.94–142.51). These estimates, while striking, should be interpreted with caution due to the modest number of ACN cases in these subgroups (eg, 12 ACN cases among 145 DHC individuals).


https://doi.org/10.2147/CMAR.S568884

**Table 1** Comparison of Subjects' Clinical Characteristics and Colonoscopy Findings

| Characteristics | All Subjects Prevalence, n (%) | Derivation Cohort | Validation Cohort |
|---|---|---|---|
| Age (y) | | | |
| < 45 | 213 (14.9) | 142 (14.9) | 71 (14.9) |
| 45–59 | 816 (57.1) | 548 (57.5) | 268 (56.2) |
| ≥ 60 | 401 (28.0) | 263 (27.6) | 138 (28.9) |
| BMI upon admission (kg/m$^2$) | | | |
| Normal and low (BMI <24.0) | 845 (59.1) | 557 (58.4) | 288 (60.4) |
| Overweight (BMI 24.0–27.9) | 494 (34.5) | 331 (34.7) | 163 (34.2) |
| Obese (BMI ≥28.0) | 91 (6.4) | 65 (6.8) | 26 (5.4) |
| Family history of CRC among first-degree relatives | | | |
| No | 1403 (98.1) | 936 (98.2) | 467 (97.9) |
| Yes | 27 (1.9) | 17 (1.8) | 10 (2.1) |
| Gender | | | |
| Male | 818 (57.2) | 541 (56.8) | 277 (58.1) |
| Female | 612 (42.8) | 412 (43.2) | 200 (41.9) |
| Hospital | | | |
| The Beijing Chest Hospital affiliated to the Capital Medical University | 93 (6.5) | 66 (6.9) | 27 (5.7) |
| The Wuhai Meng Medicine Hospital | 238 (16.6) | 155 (16.3) | 83 (17.4) |
| The Fourth People's Hospital of Taizhou City | 1099 (76.9) | 732 (76.8) | 367 (76.9) |
| Cigarette smoking | | | |
| Nonsmoker | 974 (68.1) | 647 (67.9) | 327 (68.6) |
| Past smoker | 152 (10.6) | 100 (10.5) | 52 (10.9) |
| Current smoker | 304 (21.3) | 206 (21.6) | 98 (20.5) |
| TCM constitution | | | |
| BC | 1040 (72.7) | 698 (73.2) | 342 (71.7) |
| YADC | 68 (4.8) | 44 (4.6) | 24 (5.0) |
| DHC | 78 (5.5) | 53 (5.6) | 25 (5.2) |
| QDC | 57 (4.0) | 42 (4.4) | 15 (3.1) |
| QSC | 26 (1.8) | 19 (2.0) | 7 (1.5) |
| PDC | 71 (5.0) | 42 (4.4) | 29 (6.1) |
| BSC | 27 (1.9) | 16 (1.7) | 11 (2.3) |
| YIDC | 47 (3.3) | 31 (3.3) | 16 (3.4) |
| ISC | 16 (1.1) | 8 (0.8) | 8 (1.7) |
| APCS | | | |
| Low risk | 370 (25.9) | 247 (25.9) | 123 (25.8) |
| Moderate risk | 755 (52.8) | 502 (52.7) | 253 (53.0) |
| High risk | 305 (21.3) | 204 (21.4) | 101 (21.2) |
| Outcome | | | |
| NCN | 1024 (71.6) | 689 (72.3) | 335 (70.2) |
| LGA | 269 (18.8) | 179 (18.8) | 90 (18.9) |
| ACN, CRC | 137 (9.6) | 85 (8.9) | 52 (10.9) |

**Abbreviations**: n, quantity; BMI, Body Mass Index; FDR, first-degree relative; BC, Balanced Constitution; YADC, Yang Deficiency Constitution; YIDC, Yin Deficiency Constitution; QDC, Qi Deficiency Constitution; QSC, Qi Stagnation Constitution; PDC, Phlegm-Dampness Constitution; DHC, Damp-Heat Constitution; BSC, Blood Stasis Constitution; ISC, Inherited Special Constitution; APCS, Asia-Pacific Colorectal Cancer Screening Scoring System; NCN, non-colorectal neoplastic lesions; LGA, low-grade adenoma; ACN, advanced colorectal tumors; CRC, colorectal cancer.

## TCM-APCS Risk Score and Stratification

Based on the multivariate model, the TCM-APCS risk score was developed (Table 3, and detailed derivation in Table S4). Scores ranged from 0 to 14. For practical clinical application, we defined three risk strata based on ROC analysis: Low Risk (LR: 0–3 points), Medium Risk (MR: 4–5 points), and High Risk (HR: 6–8 points) (see Table S5).

**Table 2** Multivariate Logistic Regression Analysis of Risk Factors

| Risk Factors | *P* value | NCN vs LGA | | ACN/CRC | |
|---|---|---|---|---|---|
| | | OR (95% CI) | *P* value | OR (95% CI) | *P* value |
| Age (y) | 0.006 | | | | |
| < 45 | | Reference | | Reference | |
| 45–59 | | 1.824 (0.832–4.002) | 0.134 | 1.443 (0.55–3.784) | 0.456 |
| ≥ 60 | | 2.791 (1.220–6.388) | 0.015 | 3.457 (1.297–9.213) | 0.013 |
| Cigarette smoking | < 0.001 | | | | |
| Never | | Reference | | Reference | |
| Past smoker | | 8.135 (3.772–17.542) | < 0.001 | 4.069 (1.709–9.688) | 0.002 |
| Current smoker | | 4.379 (2.323–8.257) | < 0.001 | 1.95 (0.924–4.113) | 0.083 |
| TCM constitution | < 0.001 | | | | |
| BC | | Reference | | Reference | |
| YADC | | 34.866 (14.271–85.180) | < 0.001 | 19.576 (6.921–55.368) | < 0.001 |
| DHC | | 51.034 (20.224–128.780) | < 0.001 | 42.452 (15.554–115.863) | < 0.001 |
| QDC | | 20.669 (8.820–48.437) | < 0.001 | 16.376 (6.138–43.691) | < 0.001 |
| QSC | | 13.381 (4.621–38.745) | < 0.001 | 4.86 (0.953–24.784) | 0.057 |
| PDC | | 62.510 (20.216–193.288) | < 0.001 | 41.245 (11.938–142.506) | < 0.001 |
| BSC | | 35.493 (8.666–145.374) | < 0.001 | 10.873 (1.632–72.463) | 0.014 |
| YIDC | | 8.651 (3.648–20.513) | < 0.001 | 3.582 (0.963–13.32) | 0.057 |
| ISC | | 12.562 (2.439–64.688) | 0.002 | 5.214 (0.537–50.636) | 0.155 |
| BMI upon admission (kg/m$^2$) | 0.066 | | | | |
| Normal and low (BMI <24.0) | | Reference | | Reference | |
| Overweight (BMI 24.0–27.9) | | 1.767 (1.086–2.873) | 0.022 | 1.605 (0.903–2.852) | 0.107 |
| Obese (BMI ≥28.0) | | 2.631 (1.163–5.952) | 0.02 | 1.857 (0.666–5.177) | 0.237 |
| Gender | 0.035 | | | | |
| Male | | Reference | | Reference | |
| Female | | 2.147 (1.184–3.894) | 0.012 | 1.541 (0.792–2.996) | 0.203 |
| Family history of CRC among first-degree relatives | 0.053 | | | | |
| No | | Reference | | Reference | |
| Yes | | 1.159 (0.246–5.461) | 0.852 | 4.427 (1.427–17.318) | 0.033 |

**Abbreviations**: BC, Balanced Constitution; YADC, Yang Deficiency Constitution; YIDC, Yin Deficiency Constitution; QDC, Qi Deficiency Constitution; QSC, Qi Stagnation Constitution; PDC, Phlegm-Dampness Constitution; DHC, Damp-Heat Constitution; BSC, Blood Stasis Constitution; ISC, Inherited Special Constitution; BMI, Body Mass Index; FDR, first-degree relative; APCS, Asia-Pacific Colorectal Cancer Screening Scoring System; NCN, non-colorectal neoplastic lesions; LGA, low-grade adenoma; ACN, advanced colorectal tumors; CRC, colorectal cancer; OR, odds ratio; CI, confidence interval.

In the derivation cohort, the prevalence of ACN exhibited a significant increase across different risk strata: 3.6% in the LR group, 7.0% in the MR group, and 17.2% in the HR group (P for trend <0.001). According to the TCM-APCS risk assessment model, individuals categorized as MR and HR demonstrated a higher prevalence of LGA compared to those in the LR category (14.1% vs. 7.3%, p=0.006; 44.1% vs. 7.3%, p<0.001) (refer to Table S6). Compared to the original APCS score, the TCM-APCS score exhibited superior predictive performance, as evidenced by a larger area under the ROC curve. The Hosmer-Lemeshow test indicated a good model fit, with non-significant results observed in both the derivation and validation cohorts (P > 0.05).

## Comparison with APCS Score

Compared with the original APCS score, the TCM-APCS score demonstrated superior discriminative ability for ACN in both the derivation and validation cohorts, as evidenced by the larger area under the ROC curve (Figure 2A and B). Moreover, at the predefined high-risk threshold, the TCM-APCS score achieved a more favorable balance between sensitivity and specificity for detecting ACN relative to the APCS high-risk category.

**Table 3** Predictive Performance of the TCM-APCS Score in Derivation and Validation Cohorts

| **Distinguish Between LGA, ACN, and CRC with a Score of 3.5** | | |
|---|---|---|
| **Variables** | **Derivation cohort (n=953)** | **Validation cohort (n=477)** |
| AUC (95% CI) | 0.870 (0.842, 0.898) | 0.875 (0.839, 0.910) |
| P value | < 0.001 | < 0.001 |
| Sensitivity, % (95% CI) | 72.7 (66.9, 78.0) | 71.1 (62.9, 78.4) |
| Specificity, % (95% CI) | 91.7 (89.4, 93.7) | 91.0 (87.5, 93.9) |
| Positive predictive value, % (95% CI) | 77.1 (71.4, 82.2) | 77.1 (68.9, 84.0) |
| Negative predictive value, % (95% CI) | 89.8 (87.3, 91.9) | 88.2 (84.3, 91.4) |
| Positive likelihood ratio, 95% CI | 8.8 (7.5, 10.3) | 7.9 (6.3, 9.9) |
| Negative likelihood ratio, 95% CI | 0.3 (0.3, 0.3) | 0.3 (0.3, 0.4) |
| **Distinguish between CRC with a score of 5.5** | | |
| **Variables** | **Derivation cohort (n=953)** | **Validation cohort (n=477)** |
| AUC (95% CI) | 0.796 (0.572, 1.000) | 0.800 (0.523, 1.000) |
| P value | 0.012 | 0.021 |
| Sensitivity, % (95% CI) | 83.3 (35.9, 99.6) | 80.0 (28.4, 99.5) |
| Specificity, % (95% CI) | 85.2 (82.8, 87.4) | 84.7 (81.2, 87.9) |
| Positive predictive value, % (95% CI) | 3.4 (1.1, 7.9) | 5.3 (1.5, 12.9) |
| Negative predictive value, % (95% CI) | 99.9 (99.3, 100.0) | 99.8 (98.6, 100.0) |
| Positive likelihood ratio, 95% CI | 5.6 (2.3, 13.6) | 5.2 (2.0, 14.0) |
| Negative likelihood ratio, 95% CI | 0.2 (0.1, 0.5) | 0.2 (0.1, 0.6) |

**Abbreviations**: n, quantity; AUC, area under the receiver operating characteristic curve; CI, confidence interval.

## Clinical Application and CRC Cases

Due to the limited number of pure CRC cases (n=6 in the derivation cohort), the study was not specifically designed to be sufficiently powered for an analysis focused solely on CRC. Nevertheless, an exploratory analysis of advanced ACN, which includes CRC, revealed that 35 out of 85 ACN cases (41.2%) in the derivation cohort were categorized within the high-risk stratum (score ≥6). The proposed high-risk threshold (≥6 points) demonstrated strong performance in detecting ACN, achieving a sensitivity of 71.1% at a cut-off score of 3.5 (refer to Table 3) and an 80.0% sensitivity for CRC at a cut-off score of 5.5 (refer to Table 3).

## Discussion

In this multicenter study, we developed and validated the TCM-APCS risk score, which integrates TCM constitutional assessment with established Western clinical risk factors. The score effectively stratifies asymptomatic Chinese individuals into low, medium, and high risk for ACN, with the high-risk group having a nearly five-fold higher prevalence of ACN compared to the low-risk group (17.2% vs. 3.6%). This tool could help prioritize colonoscopy resources in screening programs.

The incorporation of TCM constitution, DHC and PDC types, provided significant incremental predictive value beyond the APCS score. From a TCM perspective, these constitutions are characterized by internal “dampness” and “heat”, which are thought to create a microenvironment conducive to chronic inflammation and abnormal tissue growth.[12] Modern research links these patterns to systemic low-grade inflammation, insulin resistance, and gut microbiota dysbiosis—all established risk factors for colorectal carcinogenesis.[14,15] This provides a plausible mechanistic bridge between TCM theory and modern pathology. This integrative approach aligns with a growing body of research advocating for the combination of TCM diagnostics with conventional metrics to enhance the predictive power and clinical relevance of disease risk models,

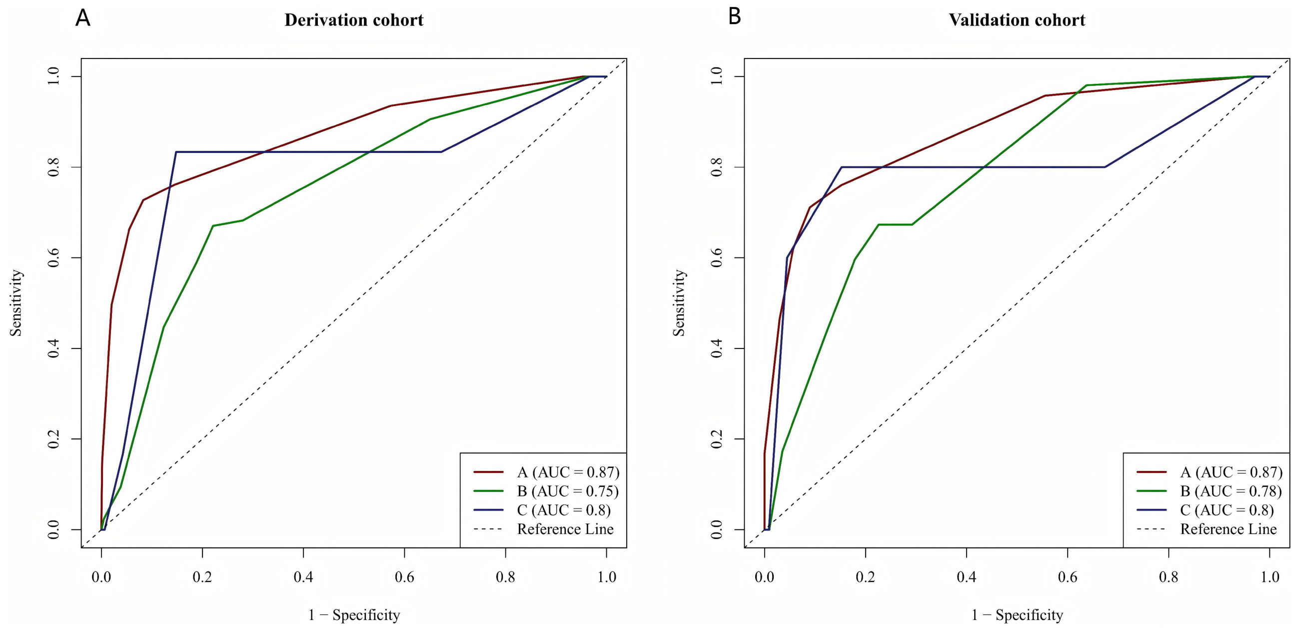


**Figure 2** ROC curves and AUC of multivariable regression models in the derivation and validation cohorts. (**A**) Derivation cohort. (**B**) Validation cohort.

particularly for complex, multifactorial conditions like cancer.[16] The scientific rationale lies in the potential of TCM constitution to capture latent, systemic biological tendencies, such as inflammatory or metabolic phenotypes, which may not be fully represented by discrete Western clinical variables alone.[17] However, the extraordinarily high ORs observed for DHC and PDC require cautious interpretation. They likely indicate a very strong relative risk within our study population but may be inflated due to the modest number of ACN events in these subgroups, a common issue in logistic regression with rare outcomes.[18] Future studies with larger samples are needed to obtain more precise estimates. Although family history of CRC in first-degree relatives was identified as an independent predictor in the multivariate model, its contribution should be interpreted with caution due to the low prevalence in our screening population, which resulted in wide confidence intervals and potential statistical instability.

The derivation process of our risk score was designed with an emphasis on transparency. The assignment of points was informed by the relative weight, or beta coefficient, of each predictor within the logistic regression model, adhering to a standard methodology for developing clinical prediction rules.[19] To facilitate practical application, we employed a straightforward linear transformation to convert these coefficients into integer points. The resulting three-tier stratification demonstrated strong calibration and discrimination in an independent validation cohort, indicating robustness against over-fitting. Nevertheless, it is important to acknowledge the limitations inherent in internal validation. The stability and general-izability of the model require further confirmation through studies involving broader and geographically diverse populations, as well as prospective implementation studies.

The primary strength of the TCM-APCS score lies in its potential clinical utility, particularly in resource-limited settings. By identifying a high-risk group that comprises approximately 16% of the asymptomatic population yet accounts for nearly half of the ACN cases, screening resources such as colonoscopy can be allocated more efficiently. This targeted approach is especially critical in light of the low coverage of organized CRC screening in China, which was estimated to be merely 3.0% among individuals aged 40–74 years in 2020.[20] Our analysis demonstrated that incorporating TCM constitution into the model enhanced its sensitivity for detecting ACN compared to the use of the APCS score alone, thereby potentially reducing the rate of missed diagnoses. The thresholds we propose are practical and align with a triage strategy: individuals classified as HR are strongly recommended to undergo colonoscopy, those at MR may be offered FIT or engaged in shared decision-making, and individuals at LR might be subjected to less intensive screening or longer screening intervals.

Importantly, the cost-effectiveness and practical implications of implementing this stratified strategy were not evaluated, underscoring the necessity for future research in this domain. Subsequent studies should include formal health economic evaluations, such as cost-effectiveness analyses or budget impact modeling. Recent evidence suggests that multivariable risk prediction algorithms, such as COLOFIT, which incorporate demographic and routine blood test data to prioritize patients for colonoscopy, have a high probability (98%) of being more cost-effective than single-test strategies by minimizing unnecessary procedures and reducing the burden on diagnostic services.[21] It is recommended that similar methodologies be employed to evaluate the TCM-APCS score within the framework of Chinese colorectal cancer screening programs.

## Conclusion

The TCM-APCS risk score, integrating TCM constitutional types with clinical risk factors, is a promising tool for risk-stratified CRC screening in the asymptomatic Chinese population. It identifies a high-risk group with a significantly greater yield of advanced neoplasia. The underlying biological mechanisms for this interaction warrant further investigation in future studies. By incorporating TCM constitutional assessment, the TCM-APCS score enhances the original APCS questionnaire through the addition of a novel, person-centered data dimension that reflects intrinsic biological predispositions, thereby providing a more holistic risk profile. While the model requires external validation in diverse populations and assessment of its cost-effectiveness, it represents a novel step towards personalized, integrative medicine approaches in cancer prevention. Future research should also focus on elucidating the biological underpinnings of high-risk TCM constitutions and testing the implementation of this tool in routine health check-ups.

## Data Sharing Statement

All of the data supporting this work will be made available from the corresponding author, Prof. Yuqi He, upon reasonable request.

## Acknowledgments

The authors sincerely thank all the participants, nurses, and endoscopy staff at the participating centers for their contributions to this study. We also acknowledge the statistical support provided by the Clinical Research Center of Beijing Chest Hospital.

## Funding

Supported by Capital's Funds for Health Improvement and Research (Grant No. 2022-1-5082), Grants from the National Natural Science Foundation of China (Grant No. 82273245), Inner Mongolia Autonomous Region Science and Technology Program (Grant No. 2022YFSH0041). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

## Disclosure

The authors report no conflicts of interest in this work.

## References

1. Siegel RL, Wagle NS, Cercek A, et al. Colorectal cancer statistics. *Ca A Cancer J Clin*. 2023;73(3):233–254. doi:10.3322/caac.21772
2. Akimoto N, Ugai T, Zhong R, et al. Rising incidence of early-onset colorectal cancer - a call to action. *Nat Rev Clin Oncol*. 2021;18(4):230–243. doi:10.1038/s41571-020-00445-1
3. Han B, Zheng R, Zeng H, et al. Cancer incidence and mortality in China. *J Nat Cancer Centre*. 2024;4(1):47–53.
4. Sena P, Mancini S, Pedroni M, et al. Expression of autophagic and inflammatory markers in normal mucosa of individuals with colorectal adenomas: a cross sectional study among italian outpatients undergoing colonoscopy. *Int J Mol Sci*. 2022;23(9):5211. doi:10.3390/ijms23095211
5. Ye S, Liu Y, Zhang T, et al. Analysis of the correlation between non-alcoholic fatty liver disease and the risk of colorectal neoplasms. *Front Pharmacol*. 2022;13:1068432. doi:10.3389/fphar.2022.1068432
6. de Klerk CM, van der Vlugt M, Smagge BA, et al. Urban density differences in colorectal cancer screening participation and screening yield in The Netherlands. *Preventive Med Rep*. 2022;27:101791. doi:10.1016/j.pmedr.2022.101791
7. 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(3):2123–2132.
8. Gong Y, Zheng Y, Wu R, et al. Detection rates of adenomas, advanced adenomas, and colorectal cancers among the opportunistic colonoscopy screening population: a single-center, retrospective study. *Chin Med J*. 2023;136(2):159–166. doi:10.1097/CM9.0000000000002435
9. Wang L, Chen H, Zhu Y, et al. One-sample quantitative and two-sample qualitative faecal immunochemical tests for colorectal cancer screening: a cross-sectional study in China. *BMJ Open*. 2022;12(5):e059754. doi:10.1136/bmjopen-2021-059754

10. Yeoh KG, Ho KY, Chiu HM, et al. The Asia-Pacific Colorectal Screening score: a validated tool that stratifies risk for colorectal advanced neoplasia in asymptomatic Asian subjects. *Gut*. 2011;60(9):1236–1241. doi:10.1136/gut.2010.221168
11. Wang J, Ding K, Wang Y, et al. Wumei Pill ameliorates AOM/DSS-induced colitis-associated colon cancer through inhibition of inflammation and oxidative stress by regulating s-adenosylhomocysteine hydrolase- (AHCY-) mediated hedgehog signaling in mice. *Oxid Med Cell Longev*. 2022;2022:4061713. doi:10.1155/2022/4061713
12. Wang J, Li YS, Yu T, et al. Metabolic characteristics of phlegm-dampness constitution: narrative review. *J Tradit Chin Med*. 2019;39(5):716–721.
13. Qi W. Classification of the 9 basic TCM body types and the basis of their diagnostic expressions. *J Beijing Univ Trad Chin Med*. 2005;28(4):1–8.
14. Tang Y, Wang Y, Wang J, et al. Association between damp-heat constitution and gastrointestinal symptoms: a cross-sectional study. *Chin Med*. 2021;16(1):45. doi:10.1186/s13020-021-00455-w
15. Song M, Chan AT. Environmental factors, gut microbiota, and colorectal cancer prevention. *Clin Gastroenterol Hepatol*. 2019;17(2):275–289. doi:10.1016/j.cgh.2018.07.012
16. Jiang M, Lu C, Zhang C. Integrating traditional Chinese medicine constitution with omics technologies: towards personalized medicine and disease prediction. *J Integr Med*. 2022;20(1):1–8. doi:10.1016/j.joim.2021.11.008
17. Wang Q, Liu J, Hu X. Bridging traditional Chinese medicine and modern science in preventive health: the role of body constitution. *Chin J Integr Med*. 2021;27(5):323–329. doi:10.1007/s11655-020-3189-1
18. Pavlou M, Ambler G, Seaman SR, et al. How to develop a more accurate risk prediction model when there are few events. *BMJ*. 2015;351:h3868. doi:10.1136/bmj.h3868
19. Sullivan LM, Massaro JM, Rb D Sr. Presentation of multivariate data for clinical use: the Framingham Study risk score functions. *Stat Med*. 2004;23(10):1631–1660. doi:10.1002/sim.1742
20. Li X, Dai M. Coverage of colorectal cancer screening in China: a systematic review and meta-analysis. *Int J Cancer*. 2024;154(3):460–471.
21. Liwen Huang J, Chen P, Yuan X, et al. An algorithm to predict advanced proximal colorectal neoplasia in Chinese asymptomatic population. *Sci Rep*. 2017;7:46493. doi:10.1038/srep46493