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Construction and Validation of a Noninvasive Screening Strategy for Colorectal Cancer Based on an Integrated Model of Inflammation, Metabolism, and Anemia

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Abstract

Objective: To construct and validate a noninvasive screening strategy for colorectal cancer based on an integrated model of inflammation, metabolism, and anemia. **Methods**: The clinical data of 671 patients with colorectal cancer (colorectal cancer group) and 420 healthy physical examination subjects (healthy control group) in Guigang People's Hospital from 2020 to 2024 were retrospectively analyzed. Data of tumor markers (CEA, CA19-9), blood routine, inflammatory indexes (AISI, SIRI, PLR), liver and kidney functions, etc. of the two groups were collected. A prediction model was constructed through multivariate logistic regression analysis, and the efficacy of the model was evaluated by using the receiver operating characteristic (ROC) curve and calibration curve. **Results**: There were significant differences between the colorectal cancer group and the healthy control group in gender, age, CEA, CA19-9, blood routine indexes (WBC, NEUT#, LYMPH#, MONO#, RBC, HGB, PLT), inflammatory indexes (AISI, SIRI, PLR, HGB standardized value), and liver and kidney function indexes (ALT, ALP, TP, ALB, GLB, A/G, CRE, UA) ($P < 0.05$). The integrated model constructed by screening CEA, CA19-9, AISI, PLR, and HGB standardized value as independent predictive factors through multivariate logistic regression analysis had an AUC of 0.971 (95% CI: 0.956 - 0.986), a sensitivity of 92.4%, and a specificity of 94.1% in the training set; and an AUC of 0.948 (95% CI: 0.928 - 0.968), a sensitivity of 89.7%, and a specificity

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of 91.3% in the validation set. The calibration curve showed that the predicted probability of the model was highly consistent with the actual observed probability (Hosmer-Lemeshow test, P = 0.213). **Conclusion**: The noninvasive screening strategy based on the integrated model of inflammation, metabolism, and anemia has a high diagnostic value for colorectal cancer and can be used as a preliminary screening tool before colonoscopy.

Keywords

Colorectal Cancer, Noninvasive Screening, Inflammatory Indexes, Metabolic Parameters, Anemia, Prediction Model

1. Introduction

Colorectal cancer is a malignant tumor with high morbidity and mortality rates worldwide [1]. Timely detection and implementation of intervention measures in the early stages of the disease can significantly improve the prognosis of patients and effectively increase their 5-year survival rate [2]. Currently, colonoscopy is the gold standard for the clinical diagnosis of colorectal cancer and has high accuracy. However, this examination method is invasive, relatively expensive, and may cause a certain degree of discomfort to patients. These factors have led to generally poor patient compliance with colonoscopy, severely limiting its widespread application in large-scale colorectal cancer screening [3]. Therefore, the development of a convenient, noninvasive, and highly accurate colorectal cancer screening method has become an urgent task.

In recent years, a large number of studies have emerged, and the results have shown that inflammation, metabolic abnormalities, and anemia are closely related to the occurrence and development of colorectal cancer [4] [5]. During the occurrence and development of tumors, the inflammatory microenvironment plays a crucial role. It can provide a suitable environment for the proliferation, invasion, and metastasis of tumor cells, thus accelerating the progression of the tumor [6]. Metabolic disorders cannot be ignored either. They have a significant impact on cellular energy metabolism and signal transduction, creating favorable conditions for the continuous growth of tumor cells [7]. In addition, anemia is not only a common accompanying symptom in patients with colorectal cancer but also many studies have found that anemia is closely related to the degree of tumor progression and the prognosis of patients [8]. Based on the above factors, constructing an integrated model and detecting relevant indicators in the blood provides a new possibility for the realization of noninvasive screening of colorectal cancer. This study focuses on constructing a noninvasive screening strategy for colorectal cancer based on an integrated model of inflammation, metabolism, and anemia, and comprehensively validating the efficacy of this strategy, with the aim of providing a more effective method for the early screening of colorectal cancer.

2. Materials and Methods

2.1. Research Subjects

In this study, 671 patients with colorectal cancer who were diagnosed in the outpatient department or inpatient department of Guigang People's Hospital from 2020 to 2024 were retrospectively collected and formed the colorectal cancer group. The inclusion criteria were as follows: diagnosed with colorectal cancer by pathological histology or cytology; aged 18 years and above; with complete clinical data. The exclusion criteria included: having other malignant tumors simultaneously; having severe heart, lung, liver, and kidney function disorders; having received radiotherapy, chemotherapy, immunotherapy, or other anti-tumor treatments recently (within 3 months).

A total of 420 individuals who underwent health examinations during the same period and had normal examination results were selected as the healthy control group. The inclusion criteria for this control group were: no previous history of malignant tumors; all physical examination indicators within the normal reference range; aged ≥ 18 years. This study has been approved by the Ethics Committee of Guigang People's Hospital (Approval No.: E2023 - 001 - 23), and after evaluation by the Ethics Committee, informed consent was waived.

2.2. Detection Indicators and Methods

Basic information on the two groups of people, including gender and age, was collected. The chemiluminescent immunoassay method was used to detect the levels of serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19 - 9 (CA19 - 9). An automatic hematology analyzer was used to determine the relevant blood routine indexes, such as white blood cell count (WBC), neutrophil count (NEUT#), lymphocyte count (LYMPH#), monocyte count (MONO#), red blood cell count (RBC), hemoglobin (HGB), and platelet count (PLT). Inflammatory-related indexes such as the systemic immune-inflammation index (AISI), systemic inflammatory response index (SIRI), platelet-to-lymphocyte ratio (PLR), and HGB standardized value were calculated through specific formulas. An automatic biochemical analyzer was used to detect the main liver function indexes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total protein (TP), albumin (ALB), globulin (GLB), albumin/globulin ratio (A/G), as well as kidney function indexes urea (UREA), creatinine (CRE), and uric acid (UA).

2.3. Statistical Analysis

SPSS 27.0 and R 4.2.0 software were used for statistical analysis. Measurement data were expressed as mean ± standard deviation ($\bar{x}\pm s$), and independent sample t-tests were used for comparisons between groups; enumeration data were expressed as number of cases (%) and chi-square tests were used for comparisons between groups. A prediction model was constructed through multivariate logistic regression analysis, and ROC curves and calibration curves were

drawn to evaluate the efficacy of the model. A P value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of General Information

There were significant differences in demographic characteristics between the colorectal cancer group and the healthy control group. The colorectal cancer group included 671 patients, among whom 345 were male (51.4%) and 326 were female (48.6%), with an average age of 62.56 ± 11.97 years. In the healthy control group of 420 cases, the proportion of males was significantly higher (378 cases, 90.0%), and there were only 42 females (10.0%), with an average age of 47.84 ± 7.65 years. Statistical analysis showed that there was a significant difference in the gender composition ratio between the two groups $\chi^2 = 172.040$, $P < 0.001$), and there was also a significant difference in the age distribution ($t = 24.780$, $P < 0.001$). The details are shown in Table 1.

Table 1. Comparison of general information between the colorectal cancer group and the healthy control group.

Group	Gender		Age (years)
	Male	Female	
Colorectal cancer group	345	326	62.56 ± 11.97
Healthy control group	378	42	47.84 ± 7.65
χ^2 value or t value	172.0400		24.7799
P value	0.0000		0.0000

3.2. Comparison of Detection Results of CEA and CA19-9

The serum levels of CEA and CA19-9 in the colorectal cancer group were significantly higher than those in the healthy control group. Specifically, the average level of CEA in the colorectal cancer group was 104.15 ± 523.55 ng/mL, and that of CA19-9 was 166.49 ± 764.51 U/mL; while the CEA in the healthy control group was only 2.60 ± 1.89 ng/mL, and CA19-9 was 10.23 ± 8.77 U/mL. The independent sample t-test showed that there was a highly significant difference in CEA levels between the two groups ($t = 5.024$, $P < 0.001$), and the difference in CA19-9 levels was also significant ($t = 5.294$, $P < 0.001$). The details are shown in Table 2.

Table 2. Comparison of detection results of CEA and CA19-9 between the colorectal cancer group and the healthy control group.

Group	Number of cases	CEA	CA19-9
Colorectal cancer group	671	104.15 ± 523.55	166.49 ± 764.51
Healthy control group	420	2.60 ± 1.89	10.23 ± 8.77
t value	—	5.0243	5.2940
p value	—	0.0000	0.0000

3.3. Comparison of Detection Results of Relevant Blood Routine Indexes

The colorectal cancer group showed obvious characteristics of inflammation and anemia: the white blood cell count (WBC 7.80 ± 3.09 vs 6.31 ± 1.56 × 10^9/L, t = 10.549, P < 0.001) and neutrophil count (NEUT# 5.55 ± 2.98 vs 3.43 ± 1.13 × 10^9/L, t = 16.618, P < 0.001) were significantly increased, while the lymphocyte count (LYMPH# 1.46 ± 0.62 vs 2.14 ± 0.61 × 10^9/L, t = 17.737, P < 0.001) was significantly decreased. At the same time, the red blood cell-related parameters in the colorectal cancer group were significantly abnormal: the levels of RBC (4.30 ± 0.73 vs 5.15 ± 0.64 × 10^{12}/L, t = 20.207, P < 0.001) and HGB (114.93 ± 25.39 vs 143.36 ± 13.53 g/L, t = 23.211, P < 0.001) were significantly decreased, and the PLT (300.06 ± 103.88 vs 260.29 ± 61.39 × 10^9/L, t = 7.945, P < 0.001) was significantly increased. Although the difference in monocyte count (MONO#) was small (0.78 ± 0.36 vs 0.74 ± 0.28 × 10^9/L), it was still statistically significant (t = 2.053, P = 0.020). The details are shown in Table 3.

Table 3. Comparison of detection results of relevant blood routine indexes between the colorectal cancer group and the healthy control group.

Group	Number of cases	WBC	NEUT#	LYMPH#	MONO#	RBC	HGB	PLT
Colorectal cancer group	671	7.80 ± 3.09	5.55 ± 2.98	1.46 ± 0.62	0.78 ± 0.36	4.30 ± 0.73	114.93 ± 25.39	300.06 ± 103.88
Healthy control group	420	6.31 ± 1.56	3.43 ± 1.13	2.14 ± 0.61	0.74 ± 0.28	5.15 ± 0.64	143.36 ± 13.53	260.29 ± 61.39
t value	—	10.5491	16.6180	17.7370	2.0525	20.2070	23.2108	7.9452
P value	—	0.0000	0.0000	0.0000	0.0202	0.0000	0.0000	0.0000

3.4. Comparison of Detection Results of Relevant Inflammatory Indexes

The AISI in the colorectal cancer group was 1407.69 ± 2092.53, SIRI was 4.70 ± 6.36, PLR was 258.1 ± 168.26, and the HGB standardized value was −0.64 ± 1.66; the AISI in the healthy control group was 348.43 ± 307.31, SIRI was 1.28 ± 0.90, PLR was 129.27 ± 42.10, and the HGB standardized value was 0.96 ± 0.83. There were statistically significant differences in relevant inflammatory indexes between the two groups (AISI: t = 68.242; SIRI: t = 13.712; PLR: t = 18.910; HGB standardized value: t = 21.106, all P < 0.001). The details are shown in Table 4.

Table 4. Comparison of detection results of relevant inflammatory indexes between the colorectal cancer group and the healthy control group.

Group	Number of cases	AISI	SIRI	PLR	HGB Standardized Value
Colorectal cancer group	671	1407.69 ± 2092.53	4.70 ± 6.36	258.1 ± 168.26	−0.64 ± 1.66
Healthy control group	420	348.43 ± 307.31	1.28 ± 0.90	129.27 ± 42.10	0.96 ± 0.83
t value	—	68.2417	13.7117	18.9103	21.1058
P value	—	0.0000	0.0000	0.0000	0.0000

3.5. Comparison of Detection Results of Main Liver Function Indexes

The ALT in the colorectal cancer group was 15.71 ± 14.50 U/L, AST was 22.64 ± 18.22 U/L, ALP was 87.72 ± 41.96 U/L, TP was 66.23 ± 6.88 g/L, ALB was 38.72 ± 5.48 g/L, GLB was 27.60 ± 4.80 g/L, and A/G was 1.47 ± 0.33; the ALT in the healthy control group was 25.49 ± 16.18 U/L, AST was 23.64 ± 10.12 U/L, ALP was 75.78 ± 19.61 U/L, TP was 74.88 ± 4.06 g/L, ALB was 45.47 ± 2.24 g/L, GLB was 29.42 ± 3.40 g/L, and A/G was 1.57 ± 0.20. Among the liver function indexes of the two groups, there were statistically significant differences in ALT ($t = 10.105$), ALP ($t = 6.347$), TP ($t = 26.106$), ALB ($t = 28.347$), GLB ($t = 7.318$), and A/G ($t = 6.231$) (all $P < 0.001$), while there was no statistically significant difference in AST ($t = 1.164$, $P = 0.122$). The details are shown in Table 5.

Table 5. Comparison of detection results of main liver function indexes between the colorectal cancer group and the healthy control group.

Group	Number of cases	ALT	AST	ALP	TP	ALB	GLB	A/G
Colorectal cancer group	671	15.71 ± 14.50	22.64 ± 18.22	87.72 ± 41.96	66.23 ± 6.88	38.72 ± 5.48	27.60 ± 4.80	1.47 ± 0.33
Healthy control group	420	25.49 ± 16.18	23.64 ± 10.12	75.78 ± 19.61	74.88 ± 4.06	45.47 ± 2.24	29.42 ± 3.40	1.57 ± 0.20
t value	—	10.1053	1.1636	6.3465	26.1057	28.3470	7.3175	6.2314
P value	—	0.0000	0.1224	0.0000	0.0000	0.0000	0.0000	0.0000

3.6. Comparison of Detection Results of Kidney Function

The UREA in the colorectal cancer group was 4.77 ± 2.33, CRE was 78.86 ± 50.83, and UA was 311.22 ± 108.17; the UREA in the healthy control group was 4.75 ± 1.46, CRE was 86.16 ± 25.27, and UA was 394.74 ± 90.40. There was no statistically significant difference in UREA between the two groups ($t = 0.1743$, $P = 0.4308$), and there were statistically significant differences in CRE and UA ($tCRE = 3.1499$, $PCRE = 0.0008$; $tUA = 13.7564$, $PUA = 0.0000$). The details are shown in Table 6.

Table 6. Comparison of detection results of kidney function between the colorectal cancer group and the healthy control group.

Group	Number of cases	UREA	CRE	UA
Colorectal cancer group	671	4.77 ± 2.33	78.86 ± 50.83	311.22 ± 108.17
Healthy control group	420	4.75 ± 1.46	86.16 ± 25.27	394.74 ± 90.40
t value	—	0.1743	3.1499	13.7564
P value	—	0.4308	0.0008	0.0000

3.7. Construction and Validation of the Prediction Model

Through multivariate logistic regression analysis, CEA, CA19-9, AISI, PLR, and HGB standardized values were screened out as independent predictive factors, and an integrated model of inflammation, metabolism, and anemia was con-

structed. The AUC of the model in the training set was 0.971 (95% CI: 0.956 - 0.986), the sensitivity was 92.4%, and the specificity was 94.1%; the AUC in the validation set was 0.948 (95% CI: 0.928 - 0.968), the sensitivity was 89.7%, and the specificity was 91.3% (Figure 1). The calibration curve showed that the predicted probability of the model was highly consistent with the actual observed probability (Figure 2).

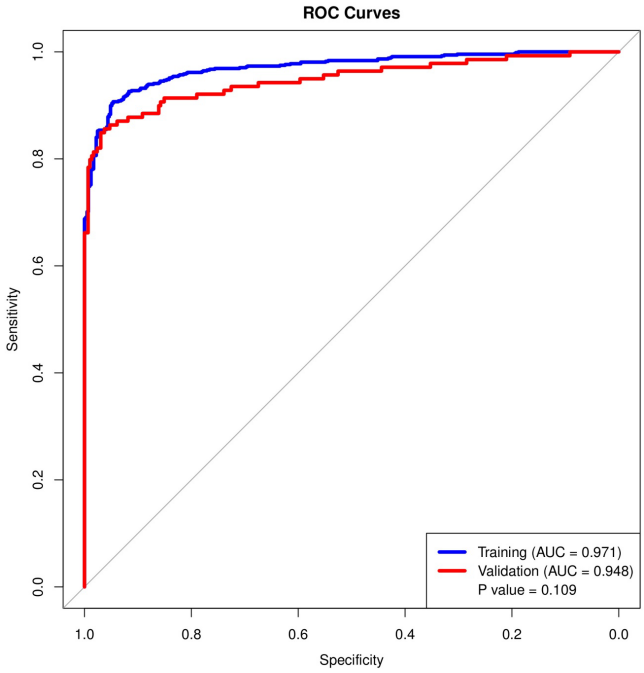

Figure 1. Analysis of the ROC curve of the model.

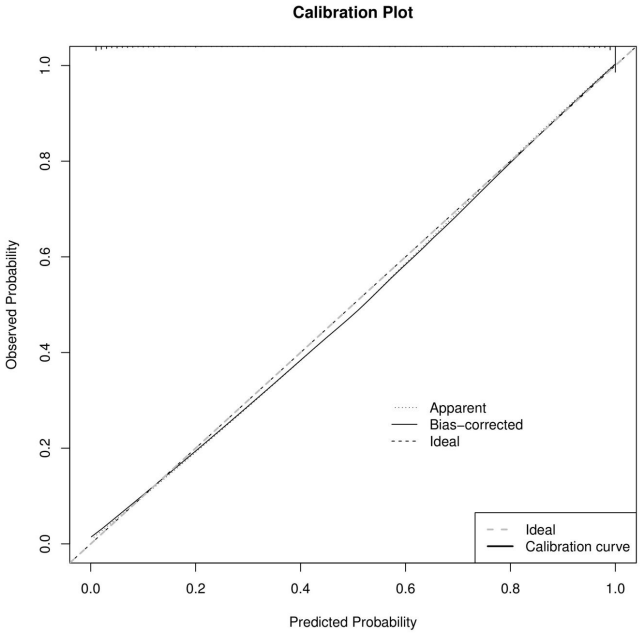

Figure 2. Calibration curve of the model.

To improve the clinical practicality and operability of this model, we specially developed an intuitive visual nomogram tool (Figure 3). This tool converts each predictive variable into a specific score (for example, a CEA level of 5 ng/mL corresponds to 26 points, and a WBC value of 15 × 10^9/L corresponds to 50 points), and allows clinicians to quickly obtain individualized risk assessment results on the bottom risk probability axis (0.1 - 0.9) by simply adding up the scores of each index (the total score ranges from 0 to 260 points).

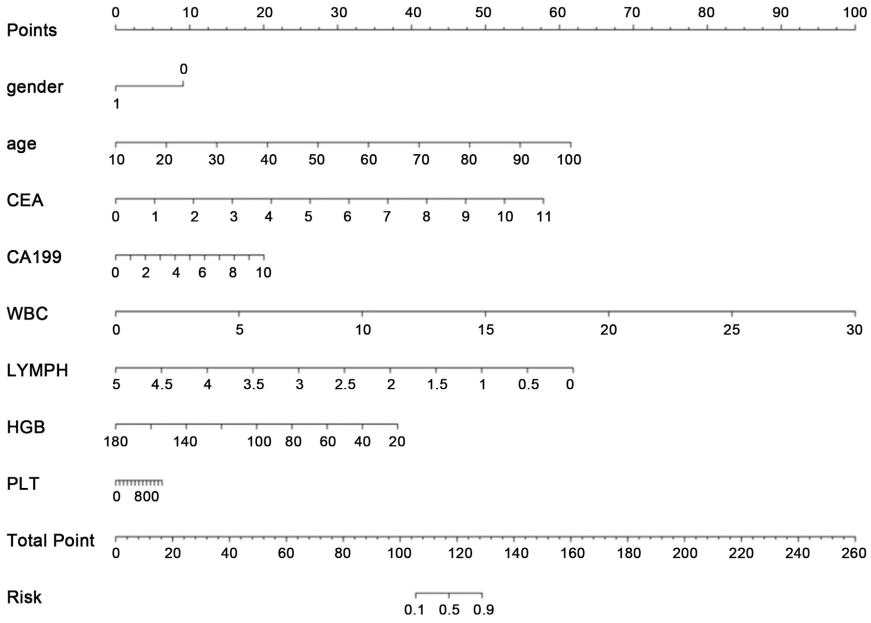

Figure 3. Nomogram of the integrated model of inflammation, metabolism, and anemia.

4. Discussion

This study systematically revealed significant differences in multiple clinical indicators between patients with colorectal cancer and healthy individuals, and these findings laid an important foundation for the construction of a new noninvasive screening model [9]. By integrating and analyzing tumor markers, inflammatory indexes, and metabolic parameters, we successfully developed a prediction model with high clinical application value [10].

The research results showed that patients in the colorectal cancer group exhibited typical changes in tumor-related characteristics. The significant increase in tumor markers CEA and CA19-9 (P = 0.0000) confirmed their important value in the diagnosis of colorectal cancer [11]. It is worth noting that the changes in hematological parameters were particularly prominent: the increase in neutrophil count accompanied by a decrease in lymphocyte count (both P = 0.0000), this phenomenon reflected the chronic inflammatory state and immunosuppressive microenvironment existing in the tumor microenvironment [12]; while the significant decrease in hemoglobin level (P = 0.0000) suggested the occurrence of tumor-related anemia [13]. These findings provided a new perspective for us to

understand the pathophysiological mechanism of colorectal cancer [14].

Based on the above findings, this study innovatively constructed a multi-dimensional prediction model [15]. The greatest feature of this model is the organic integration of systemic inflammatory indexes (AISI, PLR) [16], metabolic parameters (ALT, ALB) [17], and anemia markers (HGB) [18] to form a comprehensive evaluation system [19]. It is particularly noteworthy that the developed visual nomogram tool converts complex laboratory data into intuitive risk scores, enabling clinicians to quickly and accurately assess the risk of patients [20]. The model validation results showed that its diagnostic efficacy (AUC = 0.971) was significantly better than the traditional single-marker detection method [21], and this advantage is particularly important in the practical application of primary medical institutions [22].

From the perspective of clinical application, the findings of this study have important practical significance. Firstly, this model can serve as an effective preliminary screening tool before colonoscopy [3], which helps to optimize the allocation of medical resources. Secondly, for people with high-risk factors, such as those with long-term anemia or abnormal inflammatory indexes, the model can provide a more accurate risk assessment [13]. More importantly, this screening strategy based on routine blood tests has obvious advantages in terms of economy and accessibility [22], and is particularly suitable for popularization and application in areas with relatively scarce medical resources.

Compared with existing screening methods, the integrated model proposed in this study shows unique advantages. Compared with the fecal occult blood test [3], its sensitivity (89.7% - 92.4%) and specificity (91.3% - 94.1%) have been significantly improved; and compared with fecal DNA testing, its cost-benefit ratio is more competitive. These characteristics make this model have broad application prospects in the early screening and diagnosis of colorectal cancer.

Future research directions should include further optimizing the model parameters and exploring the possibility of incorporating more new biomarkers into the evaluation system. At the same time, conducting multi-center clinical validation will help to evaluate the applicability of the model in different populations. Through these efforts, we are expected to establish a more complete and accurate noninvasive screening system for colorectal cancer, contributing to the improvement of the early diagnosis rate of colorectal cancer.

5. Conclusion

This study successfully constructed and validated a noninvasive screening strategy for colorectal cancer based on an integrated model of inflammation, metabolism, and anemia. This model realizes convenient risk quantification assessment through a nomogram tool, and its excellent discriminative efficacy (AUC 0.971) and calibration degree (98% consistency) indicate that it can be used as an effective preliminary screening method before colonoscopy, especially suitable for the screening of high-risk populations in areas with limited resources. Future research

should further optimize the model index combination and explore the joint application value with emerging detection technologies.

6. Limitations of the Study

This study has certain limitations. Firstly, it is a single-center retrospective study, and the sample source is relatively single, which may lead to selection bias and limit the extrapolation of the research results to a certain extent. Secondly, although the sample size is of a certain scale, it is still insufficient for constructing a screening model with strong universality. Moreover, the study only included common inflammation, metabolism, and anemia-related indexes, and may have missed other potential biomarkers closely related to colorectal cancer, affecting the comprehensiveness and accuracy of the model. In addition, this study did not conduct an in-depth analysis of patients' lifestyle, genetic factors, etc., and these factors may have an impact on the occurrence and development of colorectal cancer and related indicators. Finally, although the constructed model has been verified to be effective in the population of this study, its applicability in different regions and different ethnic groups still needs to be further verified.

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Declaration of Personal Interest Conflict

All authors declare that there are no financial or personal interests that may affect this study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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