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Retrospective Study

Development and validation of a prediction model for early screening of people at high risk for colorectal cancer

Ling-Li Xu, Yi Lin, Li-Yuan Han, Yue Wang, Jian-Jiong Li, Xiao-Yu Dai

Specialty type: Gastroenterology and hepatology**Provenance and peer review:** Unsolicited article; Externally peer reviewed.**Peer-review model:** Single blind**Peer-review report's scientific quality classification**Grade A (Excellent): 0
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Colorectal cancer (CRC) is a serious threat worldwide. Although early screening is suggested to be the most effective method to prevent and control CRC, the current situation of early screening for CRC is still not optimistic. In China, the incidence of CRC in the Yangtze River Delta region is increasing dramatically, but few studies have been conducted. Therefore, it is necessary to develop a simple and efficient early screening model for CRC.

AIM

To develop and validate an early-screening nomogram model to identify individuals at high risk of CRC.

METHODS

Data of 64448 participants obtained from Ningbo Hospital, China between 2014 and 2017 were retrospectively analyzed. The cohort comprised 64448 individuals, of which, 530 were excluded due to missing or incorrect data. Of 63918, 7607 (11.9%) individuals were considered to be high risk for CRC, and 56311 (88.1%) were not. The participants were randomly allocated to a training set (44743) or validation set (19175). The discriminatory ability, predictive accuracy, and clinical utility of the model were evaluated by constructing and analyzing receiver operating characteristic (ROC) curves and calibration curves and by decision

curve analysis. Finally, the model was validated internally using a bootstrap resampling technique.

RESULTS

Seven variables, including demographic, lifestyle, and family history information, were examined. Multifactorial logistic regression analysis revealed that age [odds ratio (OR): 1.03, 95% confidence interval (CI): 1.02-1.03, $P < 0.001$], body mass index (BMI) (OR: 1.07, 95% CI: 1.06-1.08, $P < 0.001$), waist circumference (WC) (OR: 1.03, 95% CI: 1.02-1.03 $P < 0.001$), lifestyle (OR: 0.45, 95% CI: 0.42-0.48, $P < 0.001$), and family history (OR: 4.28, 95% CI: 4.04-4.54, $P < 0.001$) were the most significant predictors of high-risk CRC. Healthy lifestyle was a protective factor, whereas family history was the most significant risk factor. The area under the curve was 0.734 (95% CI: 0.723-0.745) for the final validation set ROC curve and 0.735 (95% CI: 0.728-0.742) for the training set ROC curve. The calibration curve demonstrated a high correlation between the CRC high-risk population predicted by the nomogram model and the actual CRC high-risk population.

CONCLUSION

The early-screening nomogram model for CRC prediction in high-risk populations developed in this study based on age, BMI, WC, lifestyle, and family history exhibited high accuracy.

Key Words: Colorectal cancer; Early screening model; High-risk population; Nomogram model; Questionnaire survey; Dietary habit; Living habit

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Core Tip: This was the first large-scale study to investigate early screening for detection of colorectal cancer (CRC) in Ningbo, China, which was part of the national early screening CRC program. The study focused on collecting information on the general population who attended annual health checks. Our findings showed that the area under the curve was 0.734 for the final validation set receiver operating characteristic (ROC) curve and 0.735 for the training set ROC curve. Therefore, we developed an early screening model with high accuracy for CRC.

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INTRODUCTION

Colorectal cancer (CRC) has become the third most common cancer worldwide[1]. The incidence of CRC in China increased from 42.74/100000 in 1990 to 8.95/100000 in 2019 and has been increasing annually in the Yangtze River Delta region[2]. A cross-sectional study on CRC knowledge and awareness in the Caribbean in 2020 revealed that only 54.7% of people were aware of the risk factors for CRC[3]. In addition, a questionnaire survey of diagnostic delays and their predictive factors in 303 CRC patients in southern China in 2020 found that the incidence of prolonged diagnostic delays was 57.8%[4]. The study found that the diagnostic delays were attributed to a variety of factors, such as a lack of knowledge of the risk factors for CRC and a reluctance to undergo CRC screening. This suggests that awareness of high-risk factors for CRC in China is insufficient, and colonoscopic screening has yet to become popular. Therefore, it is critical to identify individuals with high-risk CRC at an early stage.

In 2022, a study conducted at Memorial Sloan-Kettering Cancer Center found that altered bowel habits accounted for 24.7% of the common symptoms of CRC[5]. Some people recognize such symptoms and visit a hospital for treatment; however, a unified approach has yet to be developed in China for early screening of people at high risk of CRC. Previously, CRC screening was based on colonoscopy, fecal occult blood test, and abdominal computed tomography[6], which have some limitations, such as high cost and poor compliance. Therefore, it is important to utilize risk factors that are easily obtained in screening settings to develop simple and convenient early screening models capable of identifying those at high risk of CRC.

Some CRC risk-prediction models have been constructed. For instance, a risk-prediction model for advanced CRC in asymptomatic adults in the United States established by Imperiale *et al*[7], a risk-prediction model for CRC in Caucasian patients in Poland established by Kaminski *et al*[8], and a risk-prediction model for advanced CRC in Germany established by Tao *et al*[9]. Most of these models based their predictions on demographic information. In contrast, most of the CRC risk-prediction models developed in China were based on genomics, lifestyle habits, and dietary habits, such as those developed by Wong *et al*[10] and Sung *et al*[11]. Cai *et al*[12] constructed a CRC risk-prediction model in a retrospective cohort study of a population with poor dietary habits. This model was based on logistic regression and afforded an area under the curve (AUC) of 0.74 [95% confidence interval (CI): 0.70-0.78], indicating that it has moderate predictive ability. In summary, most of the CRC risk-prediction models are beneficial for screening high-risk CRC individuals in the

general population but are of little use for early screening of populations with high-risk CRC. Moreover, while some models are based on a single method or not well validated, others are complex and thus not feasible or practical for clinical application. Most importantly, compared with the factors affecting CRC incidence in western countries, those affecting CRC incidence in China are more complex. Thus, there is a need for CRC risk-prediction models based on data from the Chinese population, as these will allow the risk of CRC development to be effectively assessed in Chinese people and improve the accuracy of early-screening programs.

CRC has many causes; therefore, assessing and screening high-risk groups for CRC can be complicated. It requires examination of dietary habits[13], lifestyle habits[14], genetic factors[15], environmental factors[16], and emotional and psychological factors[17]. High-calorie, high-fat, and high-protein diets; consumption of pickled foods; and unhealthy lifestyle habits, such as staying up late, smoking, and drinking alcohol, can cause CRC[18]. China is a huge country with 56 ethnic groups, and the large variations in lifestyles, dietary habits, and environmental factors in the country mean that constructing a prediction model for early screening of CRC in high-risk groups may be complex.

Here, we collected the demographic information, living habits, dietary habits, and family history of a large CRC early screening cohort in the China Urban Cancer Early Diagnosis and Treatment Program, Ningbo, from 2014 to 2017. These data were examined *via* a backward Wald logistic regression analysis to identify the risk factors for CRC. These risk factors were used to establish a prediction model for screening groups at high risk for CRC at an early stage. We believe that this model will provide a basis for the accurate identification of high-risk groups in future CRC screening efforts.

MATERIALS AND METHODS

Study design and participants

This retrospective study was conducted in Ningbo Hospital, China, from 2014 to 2017. Of the 64448 participants, 530 were excluded due to missing or incorrect data. Of the remaining participants, 7607 (11.9%) were considered high risk for CRC, and 56311 (88.1%) were not. The inclusion criteria were as follows: (1) Permanent household registration in the city (living in the local area for > 3 years); (2) age 40-74 years; and (3) ability to sign the informed consent form unaided. The exclusion criteria were as follows: (1) An abnormal identifier number; and (2) a previous CRC diagnosis. All the participants provided written informed consent. The study protocol complied with the Declaration of Helsinki and was approved by the Ethical Review Board of Ningbo No. 2 Hospital (approval number: YJ-NBEY-KY-2023-060-01).

Selection of variables

Demographic information, dietary habits, living habits, and family history of the participants in the validation and training sets were obtained *via* questionnaires. The questionnaires collected details of dietary habits, including usual food intake, food preference, and dietary behavior, using the food frequency questionnaire. The questionnaires were administered by uniformly trained and qualified investigators through face-to-face questioning. We selected variables based on prior knowledge of the underlying biology and epidemiology of CRC and relevant predictors. This yielded seven variables that covered basic information, lifestyle, and family history.

Basic information comprised age, sex, ethnicity, body mass index (BMI), and waist circumference (WC). Age was categorized according to the United Nations New Standard for the Classification of Human Ages: young adults ≤ 65 years and middle-aged and older adults > 65 years[19]. Minors < 18 years of age were not included in the study. Sex was categorized as male or female. Ethnicity was divided into Han nationality and other ethnic groups, according to the results of the questionnaire. BMI was based on the BMI classification standard for Chinese adults[20]: Underweight < 18.50 kg/m², normal weight 18.50-23.99 kg/m², overweight 24.0-27.99 kg/m², and obese ≥ 28.0 kg/m². The median WC was 80 cm (SD: 50-184 cm).

Lifestyle included dietary habits and living habits. With reference to the standards of Dietary Guidelines for Chinese Residents (2007 edition) and the Dietary Reference Intake of Nutrients for Chinese Residents (2013 edition) and based on the discussion involving a group of relevant experts and scholars, we used the following definitions to determine the intake of substances and their frequencies (dietary habits) and the specific behaviors (living habits) in the questionnaire survey.

Dietary habits included taste, oil consumption, frequency of pickled and sun-cured food intake, and weekly consumption of fresh vegetables, fresh fruits, meat, and coarse grains. Taste was classified into three levels based on salt consumption: double-salt taste (> 5 g/d), moderate-salt taste (5 g/d), and low-salt taste (< 5 g/d). Oil consumption was classified into three levels based on the amount of cooking oil ingested per day: High oil consumption (> 30 g/d), moderate oil consumption (25-30 g/d), and low oil consumption (< 25 g/d). The frequency of pickled and sun-cured food intake was classified into the following three levels: never, < 3 times/wk (*i.e.*, sometimes), and ≥ 3 times/wk (*i.e.*, often). Weekly consumption of fresh vegetables, fresh fruits, meat, and coarse grains was classified as follows: fresh vegetables (0 kg/wk, < 2.5 kg/wk, or ≥ 2.5 kg/wk); fresh fruits (0 kg/wk, < 1.25 kg/wk, or ≥ 1.25 kg/wk); meat (0 kg/wk, < 0.35 kg/wk, or ≥ 0.35 kg/wk), and coarse grains (0 kg/wk, < 0.5 kg/wk, or ≥ 0.5 kg/wk).

Living habits included smoking, alcohol consumption, and physical activity. Smoking was defined as having smoked > 1 cigarette/d for > 6 consecutive or cumulative months, and smoking cessation was defined as not having smoked for ≥ 2 years. Thus, smoking was classified into three levels: never smoker (no), current smoker (yes), and ever smoker but currently not a smoker (quit smoking). Drinking alcohol was defined as having consumed an average of at least 1 drink/wk for > 6 mo, and abstinence was defined as not having had a drink for ≥ 1 year. Thus, alcohol consumption was classified into three levels: never drinker (no), current drinker (yes), and ever drinker but currently abstaining (quit drinking). Physical activity was defined as effective physical activity of > 30 min/session, with an average of ≥ 3

sessions/wk, and was categorized into two levels: ≤ 3 times/wk (no) and > 3 times/wk (yes). Family history was categorized as no family history of CRC (no) and a family history of CRC (yes).

Diagnosis of participants with a high risk of CRC

The diagnosis of participants with a high risk of CRC was made by at least two experienced anorectal surgeons who were experts in the field, based on the following conditions: (1) A positive test for fecal occult blood[21]; (2) a first-degree relative with a history of CRC[22]; (3) a history of intestinal polyps or adenomas[23]; (4) a history of cancer or other malignancies[24]; (5) a change in bowel habits[25]; and (6) any two of the following conditions: chronic diarrhea, chronic constipation, mucus bloody stools, a history of chronic appendicitis or appendectomy, a history of chronic cholecystitis or cholecystectomy, and chronic mental depression[24]. Participants were diagnosed as having a high risk of CRC if they had any one of the conditions from 1 to 5 and any two of the conditions listed in 6. After a series of evaluations, those without any of the above conditions were not considered high risk for CRC.

Statistical analysis

We used χ^2 tests to assess the characteristic differences in baseline data, 2014-2017 separately, between the high-risk and non-high-risk groups. Cluster analysis was used to categorize the participants based on their dietary and living habits as either having a healthy or an unhealthy lifestyle. A healthy lifestyle was considered an intake of fresh vegetables, fresh fruits, and coarse grains and participation in physical activity. An unhealthy lifestyle was considered an intake of meat, pickled and sun-cured food, oily food, and double-salted food; smoking; and alcohol consumption. A random sampling method was used to allocate the participants to a training set or a validation set in the ratio of 7:3. Each participant was considered as a randomized unit with the same probability of being selected. We performed a multifactorial logistic regression analysis by introducing variables with $P < 0.05$ as independent predictor variables into the training set. The strength of the association between predictors and participants with a high risk of CRC was assessed by calculating the ORs and 95% CIs. Meaningful variables were selected based on a backward Wald logistic regression analysis and were used to construct a nomogram model. The discriminative ability, predictive accuracy, and clinical value of the model were evaluated by constructing and analyzing the ROC and calibration curves and by performing decision curve analysis (DCA). Five hundred bootstrap resamples were used to reduce overfitting bias. All of the statistical analyses were conducted using R (version 4.3.0) and SPSS (version 25.0), and $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Basic characteristics and risk factors of participants at high risk for CRC

Table 1 shows the basic information, dietary habits, living habits, and family histories of both groups in 2014-2017. Compared with the CRC non-high-risk group, the basic information revealed that the CRC high-risk group had more men and the participants were older, and had higher BMI and WC. The dietary habits data revealed that the CRC high-risk group had a lower weekly intake of fresh vegetables, fresh fruits, and coarse grains; had a higher weekly intake of meat; had more participants with double-salt taste and high oil consumption; and consumed pickled and sun-cured foods more frequently. Furthermore, participants in the CRC high-risk group were more likely to smoke, drink alcohol, and not perform physical activity. The family history data showed that the CRC high-risk group typically had a family history of the disease.

A cluster analysis of the dietary and living habits of all the participants was performed to categorize them as having a healthy or unhealthy lifestyle. A healthy lifestyle was considered an intake of fresh vegetables, fresh fruits, and coarse grains and participation in physical activities. An unhealthy lifestyle was considered an intake of meat and pickled and sun-cured foods, high oil consumption, a double-salt taste, smoking, and alcohol consumption. The analysis revealed that 39134 (61.2%) participants had a healthy lifestyle and 24783 (38.8%) had an unhealthy lifestyle. All of the participants were then randomly divided into a training set ($n = 44743$) and a validation set ($n = 19175$) in a 7:3 ratio.

Table 2 shows the results of univariate and multivariate analyses of the training set. The univariate analysis indicated that BMI and WC were significantly associated with a high risk of CRC, as was lifestyle and family history. The backward Wald logistic regression model, after excluding variables with $P > 0.05$, demonstrated that there were five predictors associated with a high risk of CRC: age, BMI, WC, lifestyle, and family history (Figure 1).

Development and validation of a nomogram model for early screening of individuals with a high risk of CRC

A nomogram for the early screening of individuals at high risk of CRC was constructed based on a logistic regression model (Figure 1). To estimate the probability of high-risk CRC individuals being detected during early screening, each predictor observation was assigned a certain number of points by drawing a vertical line toward the vertex table. The sum of the points for each variable corresponded to the probability of an individual being identified during early screening as having a high risk of CRC. Finally, we analyzed the 500 resamples using the bootstrap method and determined the AUC of the nomogram model as 0.734 for the validation set (Figure 2A) and 0.735 for the training set (Figure 2B). The calibration curves demonstrated good agreement between the actual observations in the model validation set (Figure 3A) and training set (Figure 3B). The DCA of the validation set (Figure 4A) and training set (Figure 4B) indicated that the model has potential clinical value.

Table 1 Basic information, dietary habits, living habits, and family history of colorectal cancer high-risk and non-high-risk groups in 2014-2017

Variable		2014			2015			2016			2017		
Basic information		Non-high risk group, n (%)	High risk group, n (%)	P value	Non-high risk group, n (%)	High risk group, n (%)	P value	Non-high risk group, n (%)	High risk group, n (%)	P value	Non-high risk group, n (%)	High risk group, n (%)	P value
Sex	Male	8514 (43.24)	888 (43.94)	0.545	14277 (53.80)	1486 (57.46)	0.0002	2359 (54.82)	711 (54.61)	0.892	3276 (56.68)	899 (50.70)	0.004
	Female	11177 (56.76)	1133 (56.06)		12260 (46.20)	1092 (42.36)		1944 (45.18)	591 (45.39)		2504 (43.32)	807 (47.30)	
Age (yr)	≤ 65	16311 (82.83)	1573 (77.83)	< 0.001	22960 (86.52)	2139 (82.97)	< 0.001	3186 (74.04)	979 (75.19)	0.405	4499 (77.84)	1287 (75.44)	0.038
	> 65	3380 (17.17)	448 (22.17)		3577 (13.48)	439 (17.03)		1117 (25.96)	323 (24.81)		1281 (22.16)	419 (24.56)	
Ethnicity	The Han nationality	19641 (99.75)	2015 (99.70)	0.717	26474 (99.76)	2572 (99.77)	0.963	4298 (99.88)	1302 (100)	0.219	5766 (99.76)	1701 (99.71)	0.714
	Other	50 (0.25)	6 (0.30)		63 (0.24)	6 (0.23)		5 (0.12)	0 (0.00)		14 (0.24)	5 (0.29)	
BMI (kg/m ²)	< 18.50	541 (2.75)	46 (2.28)	< 0.001	644 (2.43)	59 (2.29)	< 0.001	104 (2.42)	26 (2.00)	< 0.001	132 (2.28)	33 (1.93)	< 0.001
	18.50-23.99	10988 (55.80)	869 (43.00)		16050 (60.48)	1211 (46.97)		2497 (28.03)	694 (53.30)		3376 (58.41)	852 (49.94)	
	24-27.99	6899 (35.04)	773 (38.25)		8586 (32.35)	1011 (39.22)		1502 (34.91)	444 (34.10)		1971 (34.10)	650 (38.10)	
	≥ 28.00	1263 (6.41)	333 (16.48)		1257 (4.74)	297 (11.52)		200 (4.65)	138 (10.60)		301 (5.21)	171 (10.02)	
WC (cm)	≤ 80	10038 (50.98)	762 (37.70)	< 0.001	14239 (53.66)	1139 (44.18)	< 0.001	2225 (51.71)	650 (49.92)	0.259	2951 (51.06)	830 (48.65)	0.081
	> 80	9653 (49.02)	1259 (62.30)		12298 (46.34)	1439 (55.82)		2078 (48.29)	652 (50.08)		2829 (48.94)	876 (51.35)	
Dietary habit													
Fresh vegetables (kg/wk)	0	79 (0.40)	20 (0.99)	< 0.001	151 (0.57)	18 (0.70)	< 0.001	22 (0.51)	10 (0.77)	< 0.001	16 (0.28)	14 (0.82)	< 0.001
	< 2.5	8839 (44.89)	1265 (62.59)		14860 (56.00)	1727 (66.99)		2386 (55.45)	952 (73.12)		3329 (57.60)	1188 (69.64)	
	≥ 2.5	10773 (54.71)	736 (36.42)		11526 (43.43)	833 (32.31)		1895 (44.04)	340 (26.11)		2435 (42.13)	504 (29.54)	
Fresh fruits (kg/wk)	0	472 (2.40)	71 (3.51)	< 0.001	457 (1.72)	228 (8.84)	< 0.001	61 (1.42)	39 (3.00)	< 0.001	62 (1.07)	51 (2.99)	< 0.001
	< 1.25	12209 (62.00)	1496 (74.02)		17073 (64.34)	1793 (69.55)		2722 (63.26)	998 (76.65)		4080 (70.59)	1312 (76.91)	
	≥ 1.25	7010 (35.60)	454 (22.46)		9007 (33.94)	557 (21.61)		1520 (35.32)	265 (20.35)		1638 (28.34)	343 (20.11)	
Meat (kg/wk)	0	641 (3.26)	103 (5.10)	< 0.001	427 (1.61)	49 (1.90)	< 0.001	54 (1.25)	17 (1.31)	0.843	64 (1.11)	22 (1.29)	< 0.001
	< 0.35	12542 (63.69)	1047 (51.81)		17393 (65.54)	1179 (45.73)		2781 (64.63)	830 (63.75)		4123 (71.33)	1075 (63.01)	
	≥ 0.35	6508 (33.05)	871 (43.10)		8717 (32.85)	1350 (52.37)		1468 (34.12)	455 (34.95)		1593 (27.56)	609 (35.70)	

Coarse grains (kg/wk)	0	1090 (5.54)	203 (10.04)	< 0.001	1309 (4.93)	437 (16.95)	< 0.001	296 (6.88)	227 (17.43)	< 0.001	164 (2.84)	133 (7.80)	< 0.001
	< 0.5	13140 (66.73)	1535 (75.95)		18394 (69.31)	1714 (66.49)		2937 (68.25)	947 (72.73)		4277 (74.00)	1314 (77.02)	
	≥ 0.5	5461 (27.73)	283 (14.00)		6834 (25.75)	427 (16.56)		1070 (24.87)	128 (9.83)		1339 (23.17)	259 (15.18)	
Taste	Double salt	2492 (12.66)	522 (25.83)	< 0.001	3073 (11.58)	985 (38.21)	< 0.001	965 (22.43)	754 (57.91)	< 0.001	803 (13.89)	620 (36.34)	< 0.001
	Moderate	13520 (68.66)	1183 (58.54)		19823 (74.70)	1239 (48.06)		2905 (67.51)	482 (37.02)		4351 (75.28)	882 (51.70)	
	Light	3679 (18.68)	316 (15.64)		3641 (13.72)	354 (13.73)		433 (10.06)	66 (5.07)		626 (10.83)	204 (11.96)	
Oil consumption	High oil consumption	1597 (8.11)	536 (26.52)	< 0.001	2311 (8.71)	981 (38.05)	< 0.001	604 (14.04)	585 (44.93)	< 0.001	620 (10.73)	639 (37.46)	< 0.001
	Moderate oil consumption	15323 (77.82)	1271 (62.89)		21196 (79.87)	1364 (52.91)		3318 (77.11)	657 (50.46)		4699(81.30)	921 (53.99)	
	Low oil consumption	2771 (14.07)	214 (10.59)		3030 (11.42)	233 (9.04)		381 (8.85)	60 (4.61)		461 (7.98)	146 (8.56)	
Pickled and sun-cured food	Never	1805 (9.17)	161 (7.97)	< 0.001	1964 (7.40)	138 (5.35)	< 0.001	290 (6.74)	48 (3.69)	< 0.001	550 (9.52)	63 (3.69)	< 0.001
	Sometimes	15686 (79.66)	1385 (68.53)		20894 (78.74)	1430 (55.47)		3114 (72.37)	561 (43.09)		4480 (77.51)	1098 (64.36)	
	Often	2200 (11.17)	475 (23.50)		3679 (13.86)	1010 (39.18)		899 (20.89)	693 (53.23)		750 (12.98)	545 (31.95)	
Living habit													
Smoking	No	14265 (72.44)	1358 (67.19)	< 0.001	21116 (79.57)	1682 (65.24)	< 0.001	3180 (73.90)	810 (62.21)	< 0.001	4338 (75.05)	1047 (61.37)	<0.001
	Yes	4401 (22.35)	521 (25.78)		4445 (16.75)	724 (28.08)		839 (19.50)	364 (27.96)		1127 (19.50)	482 (28.25)	
	Quit smoking	1025 (5.21)	142 (7.03)		976 (3.68)	172 (6.67)		284 (6.60)	128 (9.83)		315 (5.45)	177 (10.38)	
Alcohol drinking	No	14190 (72.06)	1287 (63.68)	< 0.001	20691 (77.97)	1523 (59.08)	< 0.001	3148 (73.16)	789 (60.60)	< 0.001	4352 (75.29)	986 (57.80)	< 0.001
	Yes	4885 (24.81)	647 (32.01)		5177 (19.51)	903 (35.03)		997 (23.17)	445 (34.18)		1247 (21.57)	619 (36.28)	
	Quit drinking	616 (3.13)	87 (4.30)		668 (2.52)	152 (5.90)		158 (3.67)	68 (5.22)		181 (3.13)	101 (5.92)	
Physical activities	No	9188 (46.66)	1094 (54.13)	< 0.001	11132 (41.95)	1477 (57.29)	< 0.001	1917 (44.55)	845 (64.90)	< 0.001	2865 (49.57)	917 (53.75)	0.002
	Yes	10503 (53.34)	927 (45.87)		15405 (58.05)	1101 (42.71)		2386 (55.45)	457 (35.10)		2915 (50.43)	789 (46.25)	
Family history	No	14438 (73.32)	1032 (51.06)	< 0.001	21524 (81.11)	1174 (45.54)	< 0.001	2960 (68.79)	527 (40.48)	< 0.001	3660 (63.32)	486 (28.49)	< 0.001
	Yes	5253 (26.68)	9989 (48.94)		5013 (18.89)	1404 (54.46)		1343 (31.21)	775 (59.52)		2120 (36.68)	1220 (71.51)	

BMI: Body mass index; WC: Waist circumference.

Table 2 Univariate and multivariate analyses of the training set

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	P value	OR	95%CI	P value
Age (≤ 65 yr <i>vs</i> >65 yr)	1.03	1.02-1.03	< 0.001	1.03	1.02-1.03	< 0.001
Sex (male <i>vs</i> female)	0.98	0.93-1.04	0.540			
Ethnicity (Han nationality <i>vs</i> other)	0.90	0.48-1.67	0.731			
BMI (< 18.50 kg/m ² , 18.50-23.99 kg/m ² , 24-27.99 kg/m ² <i>vs</i> ≥ 28.00 kg/m ²)	1.07	1.06-1.08	< 0.001	1.05	1.04-1.06	< 0.001
WC (≤ 80 cm <i>vs</i> > 80 cm)	1.03	1.02-1.03	< 0.001	1.02	1.01-1.02	< 0.001
Family history (no <i>vs</i> yes)	4.28	4.04-4.54	< 0.001	4.30	4.04-4.56	< 0.001
Lifestyle (unhealthy lifestyle <i>vs</i> healthy lifestyle)	0.45	0.42-0.48	< 0.001	0.44	0.41-0.47	< 0.001

BMI: Body mass index; WC: Waist circumference.

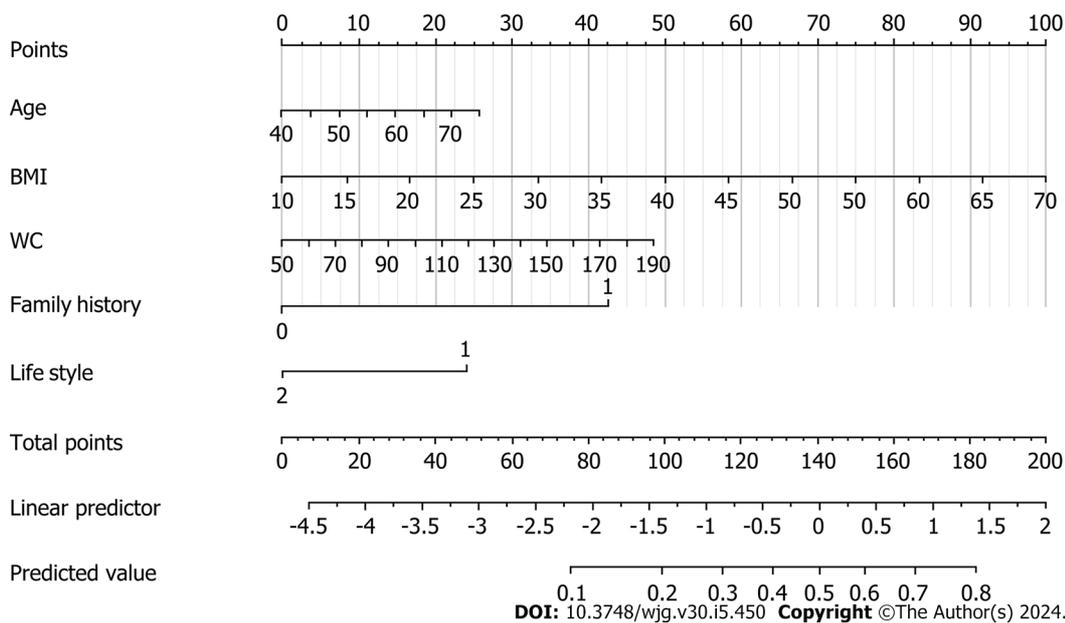


Figure 1 Nomogram for predicting early screening of individuals at high risk of colorectal cancer. The value of each variable was scored on a point scale from 0 to 100, after which the scores for each variable were added together. The total sum was located on the total points axis, which enabled us to predict the probability of early screening of individuals at high risk of colorectal cancer. Age, body mass index, and waist circumference were used as continuous variables. The family history group 0 = no and 1 = yes, and lifestyle group 1 = unhealthy lifestyle and 2 = healthy lifestyle. BMI: Body mass index; WC: Waist circumference.

DISCUSSION

Our findings indicated that age, BMI, WC, family history, and lifestyle significantly contributed to the prediction of individuals at high risk for CRC. Therefore, these variables were used to validate an early screening model for individuals at high risk for CRC, and the model demonstrated potential clinical utility.

Compared with the current study, a multicenter study combining genetic and environmental risk scores for risk stratification of early-onset CRC [16] placed more emphasis on scores for polygene variants, environmental factors, and lifestyle. The results showed that an increase in the lifestyle score was associated with an increase in the relative risk of early-onset CRC, in line with our findings, which demonstrated a significant association between lifestyle and high risk for CRC. However, unlike this multicenter study, our study incorporated dietary habits in addition to living habits and family history to assess lifestyle. We found five factors to be significantly associated with high risk for CRC, two of which were non-modifiable variables (age and family history), in line with previous findings [22,26]. A healthy lifestyle had an OR of 0.44 (95% CI: 0.41-0.47) in individuals at high risk of CRC, indicating that a healthy lifestyle is a protective factor.

A similar study found that in addition to a high intake of red and processed meat, sex, ethnicity, sedentary lifestyle, and inflammatory bowel disease were associated with a low, intermediate, and high risk of early-onset CRC [27]. The study was a meta-analysis of the literature retrieved from PubMed and Web of Science. Eighteen articles were screened for inclusion, and 10 were ultimately reviewed to afford baseline data on the case group ($n = 32843$) and control group (n

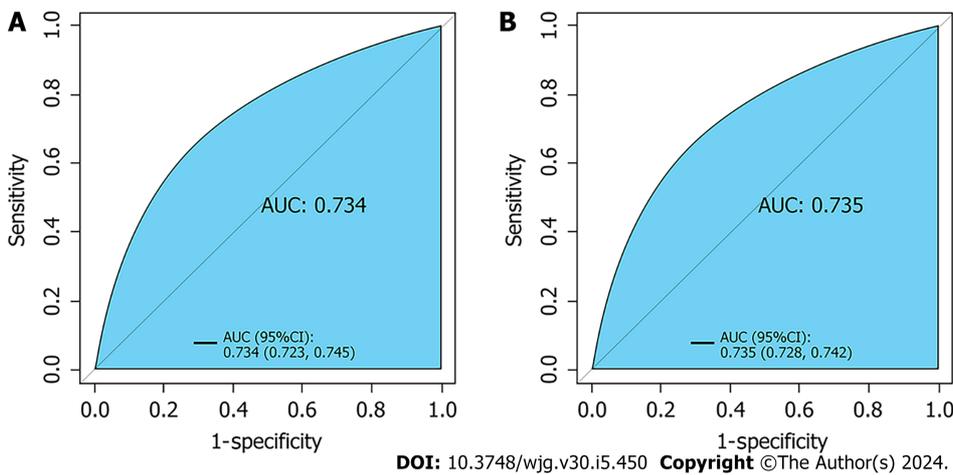


Figure 2 Receiver operating characteristic curves curve for predicting early screening of individuals at high risk of colorectal cancer. A: Validation set: Receiver operating characteristic curves (ROC) curve for the nomogram generated using bootstrap resampling (500 times); B: Training set: ROC curve for the nomogram generated using bootstrap resampling (500 times). AUC: Area under the curve.

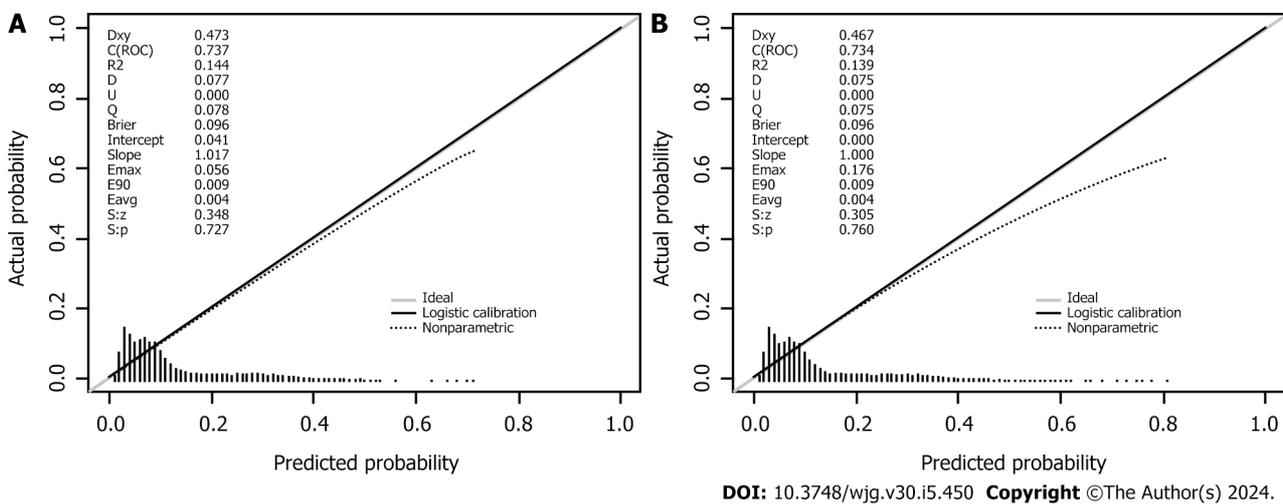


Figure 3 Calibration plot for predicting early screening of individuals at high risk of colorectal cancer. A: Validation set nomogram calibration plot; B: Training set nomogram calibration plot. When the solid line (performance nomogram) is closer to the dotted line (ideal model), the prediction accuracy of the nomogram is better.

= 25806408), which were used to construct a risk assessment model. Risk factors associated with early-onset CRC in the baseline data were screened by meta-analysis, and those with $P < 0.05$ were included in the final model. The model differed from ours in that it categorized the population into low-, intermediate-, and high-risk groups based on risk trend scores. Moreover, their participants were < 50 years of age, thus predominantly comprising young adults. In contrast, the current study consisted of a wider range of age groups, although primarily focusing on those aged 40-74 years. It aimed to develop a prediction model that would enable accurate primary screening of groups at high risk for CRC.

One of the major strengths of our study was that it integrated multiple factors including age, sex, ethnicity, BMI, WC, healthy and unhealthy lifestyle, and family history. Second, our sample size, which was obtained from the population in Ningbo, Zhejiang, China, was large. Third, compared with other models, our model enabled better and earlier screening of CRC in high-risk populations in Ningbo. In addition, previous studies have demonstrated that CRC development can be prevented by altering the modifiable risk factors[28]. In our model, all of the risk factors, except age and family history, could be modified by improving lifestyle habits, changing dietary habits, and increasing physical activities. Age and family history are non-modifiable variables and must be carefully examined in early screening of CRC, especially because they are inextricably linked to CRC development[22,26]. Therefore, the combination of modifiable and non-modifiable risk factors in our model can help facilitate early screening of individuals at high risk for CRC. Furthermore, our model makes it easier to screen patients for CRC risk than colonoscopy, which can be painful and complex. The Colorectal Cancer Early Screening Model can also be convenient for clinicians and may help them improve the rate of clinical diagnosis and reduce the rate of underdiagnosis of CRC in high-risk populations.

However, this study had some limitations. First, given that the study population was from a single region in China (Ningbo, Zhejiang), the model lacked generalizability. China is a large country with differences in living environments, lifestyles and habits, diets, and cultures. Second, although we examined four risk factors, there are many other factors

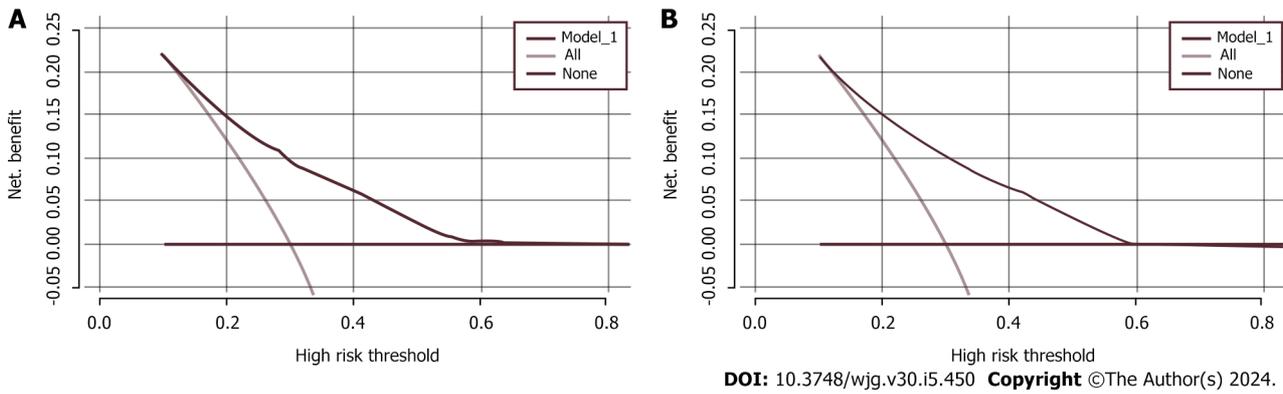


Figure 4 Decision curve analysis for predicting early screening of individuals at high risk of colorectal cancer. A: Decision curve analysis (DCA) of the validation set prediction model; B: DCA of the training set prediction model. Red solid lines indicate the prediction models, gray solid lines indicate all populations at high risk for colorectal cancer (CRC), and solid horizontal lines indicate non-high-risk populations for CRC. The graph depicts the expected net gain for each individual relative to the high-risk CRC Nuo plot forecast. Net gain increases with the model curve.

associated with dietary habits, living habits, and family history, and our study design could not incorporate them all. Therefore, future studies should include more variables to further validate our model. Third, our model did not include emotional and psychological factors. It is worth noting that a relationship between mental trauma and CRC has been reported in previous studies[29]. Although the exact mechanism underlying this relationship remains unclear, it may be because great mental trauma leads to neurological dysfunction, resulting in bowel disorders and stress ulcers, ultimately leading to the development of malignant intestinal lesions. Alternatively, excessive mental stress weakens the immune system, thereby increasing the susceptibility to disorders of the intestinal flora and the risk of developing CRC[30]. Therefore, future studies must examine the effect of emotional and psychological factors on CRC risk.

CONCLUSION

This study showed that older age, a high BMI, a large WC, an unhealthy lifestyle, and a family history of CRC are significantly associated with a high risk of CRC. A CRC risk-prediction model was also developed for accurate primary screening of groups with a high risk of CRC. This model could enable clinicians to develop early CRC screening strategies and may support public health campaigns for reducing CRC deaths and disease burden.

ARTICLE HIGHLIGHTS

Research background

The establishment of early screening model for high risk of colorectal cancer (CRC) may become a potential new method for early screening. It is different from traditional invasive screening and is a noninvasive, simple and rapid screening methods. Although there are many studies on early screening model for high risk of CRC, there is still a lack of large sample size studies and clinical validation. Our study focused on collecting information in the general population who attended annual health checks. At the same time, this is also the first study with a large sample size for early screening for CRC in Ningbo, China, which was part of national early screening for CRC.

Research motivation

Constructing an early screening model for CRC high-risk groups by means of basic information such as lifestyle has gradually become a major topic in CRC early screening research, which is mainly aimed at solving the problem of the more complicated means of early screening for colorectal cancer high-risk groups.

Research objectives

This study aimed to establish an efficient early screening model to identify individuals at high risk of CRC, and reduce CRC prevalence and mortality.

Research methods

This retrospective study included data from the health screening population in Ningbo Hospital, China from 2014 to 2017 to analyze the basic information, living habits and dietary habits, so that the early screening model of CRC was constructed and conducted for internal verification.

Research results

Retrospective analysis of 63918 individuals eligible for health screening, comprising studies with seven variables. The area under the curve was 0.734 [95% confidence interval (CI): 0.723-0.745] for the final validation set receiver operating characteristic curve (ROC) and 0.735 (95%CI: 0.728-0.742) for the training set ROC curve. The calibration curve demonstrated a high correlation between the CRC high-risk population predicted by the nomogram model and the actual CRC high-risk population.

Research conclusions

This study has an early screening model for high risk of CRC based on basic population information, lifestyle and family history.

Research perspectives

This study has the potential to revolutionize primary detection by accurately identifying groups at high risk of developing CRC.

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FOOTNOTES

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Co-corresponding authors: Jian-Jiong Li and Xiao-Yu Dai.

Author contributions: Xu LL, Lin Y, Li JJ and Dai XY participated in the study design; Xu LL and Lin Y statistically analyzed, interpreted, and drafted the manuscript; Xu LL and Lin Y revised the manuscript; Han LY and Wang Y contributed to data collection and organization; all authors contributed to the revision of the final manuscript and approved the final version of the manuscript; Li JJ and Dai XY provided financial support and study supervision.

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REFERENCES

- 1 Baidoun F, Elshiwly K, Elkeraiye Y, Merjaneh Z, Khoudari G, Sarmini MT, Gad M, Al-Husseini M, Saad A. Colorectal Cancer Epidemiology: Recent Trends and Impact on Outcomes. *Curr Drug Targets* 2021; **22**: 998-1009 [PMID: 33208072 DOI: 10.2174/1389450121999201117115717]

- 2 **GBD 2019 Colorectal Cancer Collaborators.** Global, regional, and national burden of colorectal cancer and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Gastroenterol Hepatol* 2022; **7**: 627-647 [PMID: 35397795 DOI: 10.1016/S2468-1253(22)00044-9]
- 3 **Rocke KD.** Colorectal Cancer Knowledge and Awareness Among University Students in a Caribbean Territory: a Cross-sectional Study. *J Cancer Educ* 2020; **35**: 571-578 [PMID: 30798462 DOI: 10.1007/s13187-019-01499-1]
- 4 **Jin Y, Zheng MC, Yang X, Chen TL, Zhang JE.** Patient delay to diagnosis and its predictors among colorectal cancer patients: A cross-sectional study based on the Theory of Planned Behavior. *Eur J Oncol Nurs* 2022; **60**: 102174 [PMID: 35952459 DOI: 10.1016/j.ejon.2022.102174]
- 5 **Park L, O'Connell K, Herzog K, Chatila W, Walch H, Palmairia RLD, Cercek A, Shia J, Shike M, Markowitz AJ, Garcia-Aguilar J, Schattner MA, Kantor ED, Du M, Mendelsohn RB.** Clinical features of young onset colorectal cancer patients from a large cohort at a single cancer center. *Int J Colorectal Dis* 2022; **37**: 2511-2516 [PMID: 36441197 DOI: 10.1007/s00384-022-04286-5]
- 6 **Wu W, Huang J, Tan S, Wong MCS, Xu W.** Screening methods for colorectal cancer in Chinese populations. *Hong Kong Med J* 2022; **28**: 183-185 [PMID: 35470808 DOI: 10.12809/hkmj219917]
- 7 **Imperiale TF, Monahan PO, Stump TE, Glowinski EA, Ransohoff DF.** Derivation and Validation of a Scoring System to Stratify Risk for Advanced Colorectal Neoplasia in Asymptomatic Adults: A Cross-sectional Study. *Ann Intern Med* 2015; **163**: 339-346 [PMID: 26259154 DOI: 10.7326/M14-1720]
- 8 **Kaminski MF, Polkowski M, Kraszewska E, Rupinski M, Butruk E, Regula J.** A score to estimate the likelihood of detecting advanced colorectal neoplasia at colonoscopy. *Gut* 2014; **63**: 1112-1119 [PMID: 24385598 DOI: 10.1136/gutjnl-2013-304965]
- 9 **Tao S, Hoffmeister M, Brenner H.** Development and validation of a scoring system to identify individuals at high risk for advanced colorectal neoplasms who should undergo colonoscopy screening. *Clin Gastroenterol Hepatol* 2014; **12**: 478-485 [PMID: 24022090 DOI: 10.1016/j.cgh.2013.08.042]
- 10 **Wong MC, Lam TY, Tsoi KK, Hirai HW, Chan VC, Ching JY, Chan FK, Sung JJ.** A validated tool to predict colorectal neoplasia and inform screening choice for asymptomatic subjects. *Gut* 2014; **63**: 1130-1136 [PMID: 24045331 DOI: 10.1136/gutjnl-2013-305639]
- 11 **Sung JJY, Wong MCS, Lam TYT, Tsoi KKF, Chan VCW, Cheung W, Ching JYL.** A modified colorectal screening score for prediction of advanced neoplasia: A prospective study of 5744 subjects. *J Gastroenterol Hepatol* 2018; **33**: 187-194 [PMID: 28561279 DOI: 10.1111/jgh.13835]
- 12 **Cai QC, Yu ED, Xiao Y, Bai WY, Chen X, He LP, Yang YX, Zhou PH, Jiang XL, Xu HM, Fan H, Ge ZZ, Lv NH, Huang ZG, Li YM, Ma SR, Chen J, Li YQ, Xu JM, Xiang P, Yang L, Lin FL, Li ZS.** Derivation and validation of a prediction rule for estimating advanced colorectal neoplasm risk in average-risk Chinese. *Am J Epidemiol* 2012; **175**: 584-593 [PMID: 22328705 DOI: 10.1093/aje/kwr337]
- 13 **Song M, Garrett WS, Chan AT.** Nutrients, foods, and colorectal cancer prevention. *Gastroenterology* 2015; **148**: 1244-60.e16 [PMID: 25575572 DOI: 10.1053/j.gastro.2014.12.035]
- 14 **Wang C, Miller SM, Egleston BL, Hay JL, Weinberg DS.** Beliefs about the causes of breast and colorectal cancer among women in the general population. *Cancer Causes Control* 2010; **21**: 99-107 [PMID: 19787437 DOI: 10.1007/s10552-009-9439-3]
- 15 **Ahmad R, Singh JK, Wunna A, Al-Obeed O, Abdulla M, Srivastava SK.** Emerging trends in colorectal cancer: Dysregulated signaling pathways (Review). *Int J Mol Med* 2021; **47** [PMID: 33655327 DOI: 10.3892/ijmm.2021.4847]
- 16 **Archambault AN, Jeon J, Lin Y, Thomas M, Harrison TA, Bishop DT, Brenner H, Casey G, Chan AT, Chang-Claude J, Figueiredo JC, Gallinger S, Gruber SB, Gunter MJ, Guo F, Hoffmeister M, Jenkins MA, Keku TO, Le Marchand L, Li L, Moreno V, Newcomb PA, Pai R, Parfrey PS, Rennert G, Sakoda LC, Lee JK, Slattery ML, Song M, Win AK, Woods MO, Murphy N, Campbell PT, Su YR, Lansdorf-Vogelaar I, Peterse EFP, Cao Y, Zeleniuch-Jacquotte A, Liang PS, Du M, Corley DA, Hsu L, Peters U, Hayes RB.** Risk Stratification for Early-Onset Colorectal Cancer Using a Combination of Genetic and Environmental Risk Scores: An International Multi-Center Study. *J Natl Cancer Inst* 2022; **114**: 528-539 [PMID: 35026030 DOI: 10.1093/jnci/djac003]
- 17 **Peng YN, Huang ML, Kao CH.** Prevalence of Depression and Anxiety in Colorectal Cancer Patients: A Literature Review. *Int J Environ Res Public Health* 2019; **16** [PMID: 30709020 DOI: 10.3390/ijerph16030411]
- 18 **Boi-Dsane NAA, Amari V, Tsatsu SE, Bachelie SV, Bediako-Bowan AAA, Koney NK, Dzudzor B.** Cross-Sectional Study for Investigation of the Association Between Modifiable Risk Factors and Gastrointestinal Cancers at a Tertiary Hospital in Ghana. *Cancer Control* 2023; **30**: 10732748231155702 [PMID: 37129188 DOI: 10.1177/10732748231155702]
- 19 **Yao A, Liang L, Rao H, Shen Y, Wang C, Xie S.** The Clinical Characteristics and Treatments for Large Cell Carcinoma Patients Older than 65 Years Old: A Population-Based Study. *Cancers (Basel)* 2022; **14** [PMID: 36358648 DOI: 10.3390/cancers14215231]
- 20 **Kokkinos P, Faselis C, Myers J, Pittaras A, Sui X, Zhang J, McAuley P, Kokkinos JP.** Cardiorespiratory fitness and the paradoxical BMI-mortality risk association in male veterans. *Mayo Clin Proc* 2014; **89**: 754-762 [PMID: 24943694 DOI: 10.1016/j.mayocp.2014.01.029]
- 21 **Jayasinghe M, Prathiraja O, Caldera D, Jena R, Coffie-Pierre JA, Silva MS, Siddiqui OS.** Colon Cancer Screening Methods: 2023 Update. *Cureus* 2023; **15**: e37509 [PMID: 37193451 DOI: 10.7759/cureus.37509]
- 22 **Kastrinos F, Samadder NJ, Burt RW.** Use of Family History and Genetic Testing to Determine Risk of Colorectal Cancer. *Gastroenterology* 2020; **158**: 389-403 [PMID: 31759928 DOI: 10.1053/j.gastro.2019.11.029]
- 23 **Sano W, Hirata D, Teramoto A, Iwatate M, Hattori S, Fujita M, Sano Y.** Serrated polyps of the colon and rectum: Remove or not? *World J Gastroenterol* 2020; **26**: 2276-2285 [PMID: 32476792 DOI: 10.3748/wjg.v26.i19.2276]
- 24 **Zhu N, Huang YQ, Song YM, Zhang SZ, Zheng S, Yuan Y.** [Efficacy comparison among high risk factors questionnaire and Asia-Pacific colorectal screening score and their combinations with fecal immunochemical test in screening advanced colorectal tumor]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2022; **25**: 612-620 [PMID: 35844124 DOI: 10.3760/cma.j.cn441530-20211127-00478]
- 25 **Siegel RL, Jakubowski CD, Fedewa SA, Davis A, Azad NS.** Colorectal Cancer in the Young: Epidemiology, Prevention, Management. *Am Soc Clin Oncol Educ Book* 2020; **40**: 1-14 [PMID: 32315236 DOI: 10.1200/EDBK_279901]
- 26 **Sninsky JA, Shore BM, Lupu GV, Crockett SD.** Risk Factors for Colorectal Polyps and Cancer. *Gastrointest Endosc Clin N Am* 2022; **32**: 195-213 [PMID: 35361331 DOI: 10.1016/j.giec.2021.12.008]
- 27 **Gu J, Li Y, Yu J, Hu M, Ji Y, Li L, Hu C, Wei G, Huo J.** A risk scoring system to predict the individual incidence of early-onset colorectal cancer. *BMC Cancer* 2022; **22**: 122 [PMID: 35093005 DOI: 10.1186/s12885-022-09238-4]
- 28 **Keum N, Giovannucci E.** Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. *Nat Rev Gastroenterol Hepatol* 2019; **16**: 713-732 [PMID: 31455888 DOI: 10.1038/s41575-019-0189-8]
- 29 **Simonton OC, Matthews-Simonton S.** Cancer and stress: counselling the cancer patient. *Med J Aust* 1981; **1**: 679, 682-683 [PMID: 7278751]

DOI: [10.5694/j.1326-5377.1981.tb135959.x](https://doi.org/10.5694/j.1326-5377.1981.tb135959.x)]

- 30 **Geremia A**, Arancibia-Cárcamo CV. Innate Lymphoid Cells in Intestinal Inflammation. *Front Immunol* 2017; **8**: 1296 [PMID: [29081776](https://pubmed.ncbi.nlm.nih.gov/29081776/) DOI: [10.3389/fimmu.2017.01296](https://doi.org/10.3389/fimmu.2017.01296)]



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