International Journal of Colorectal Disease (2025) 40:74
https://doi.org/10.1007/s00384-025-04853-6

RESEARCH

Survival analysis and prediction of early-onset colorectal cancer patients post-chemotherapy: an analysis based on the SEER database

Zhiguo Tang[1] · Guojia Zhou[1] · Yu Xu[1] · Yinxu Zhang[1]

Accepted: 5 March 2025

Abstract

Background The incidence of Early-Onset Colorectal Cancer (EOCRC) has risen markedly in recent years, garnering widespread attention due to its distinctive clinical and biological features. However, systematic research on prognostic risk factors and long-term survival prediction for EOCRC patients undergoing postoperative chemotherapy remains scarce. This study seeks to pinpoint critical prognostic factors for EOCRC patients receiving postoperative chemotherapy and to devise a survival prediction tool employing a Nomogram model.

Methods Patients diagnosed with EOCRC between 2010 and 2015, who underwent postoperative chemotherapy, were extracted from the SEER (Surveillance, Epidemiology, and End Results) database. Only those meeting the inclusion criteria were included. Univariate and multivariate Cox regression analyses were performed to determine independent risk factors influencing overall survival (OS). A Nomogram model was then developed using significant variables. The model's predictive accuracy and clinical utility were assessed through the concordance index (C-index), calibration curves, receiver operating characteristic (ROC) curves, and decision curve analysis (DCA).

Results A cohort of 9,205 patients was analyzed, with 6,445 randomly allocated to the training group and 2,760 to the validation group from the SEER database. Independent prognostic factors, including gender, race, marital status, primary tumor location, histological type, TNM stage, CEA levels, bone metastasis, liver metastasis, and lung metastasis, were identified through univariate and multivariate Cox regression analyses. A Nomogram model constructed from these factors yielded a C-index of 0.76 (0.75, 0.77) in the training group and 0.76 (0.75, 0.78) in the validation group, reflecting robust discriminative ability and consistency. The area under the curve (AUC) for predicting 1-year OS was calculated as 0.84 (0.81, 0.86) in the training group and 0.82 (0.78, 0.85) in the validation group. For 3-year OS, AUCs were recorded at 0.83 (0.82, 0.84) and 0.82 (0.80, 0.84), respectively, while for 5-year OS, AUCs reached 0.81 (0.80, 0.82) and 0.82 (0.80, 0.84). Calibration curves demonstrated close alignment between predicted and observed survival rates. Additionally, DCA affirmed the model's clinical decision-making value.

Conclusion Prognostic risk factors for EOCRC patients receiving postoperative chemotherapy were systematically evaluated in this study, leading to the development of a Nomogram-based survival prediction model. This tool offers a robust scientific foundation for tailoring individualized treatment and guiding follow-up strategies.

Keywords Early-onset colorectal cancer · Postoperative chemotherapy · Survival analysis · Nomogram · SEER database

✉ Yinxu Zhang
zhangyinxu@163.com

Zhiguo Tang
tzg203184@163.com

Guojia Zhou
zhouguojia1020@163.com

Yu Xu
xuyu0407@163.com

[1] Department of General Surgery, The First Affiliated Hospital of Jinzhou Medical University, Jinzhou 121000, China

Introduction

Colorectal cancer (CRC) is one of the most prevalent malignant tumors worldwide, ranking as the third most common cancer and the second leading cause of cancer-related mortality in the United States [1]. With advancements in screening and early diagnostic technologies, the early detection rate of colorectal cancer has gradually increased. In developed countries, both incidence and mortality rates have stabilized or declined [2]. However, in recent years, the incidence of

Published online: 22 March 2025

EOCRC, defined as colorectal cancer occurring in patients under the age of 50, has exhibited a significant increasing trend. This trend is particularly evident in some developed countries and certain developing nations [3]. The diagnosis of EOCRC is often delayed, and patients face a higher risk of recurrence following treatment. The biological characteristics and clinical manifestations of the disease differ from those observed in older patients [4].

Although the pathogenesis of EOCRC remains incompletely understood, the interaction between genetic factors, environmental factors, and lifestyle choices is considered to be a key etiological foundation. Firstly, hereditary colorectal cancer-related conditions such as familial adenomatous polyposis (FAP) and Lynch syndrome are closely associated with the onset of EOCRC [5]. Furthermore, studies have demonstrated that EOCRC patients often exhibit molecular features distinct from those of elderly colorectal cancer patients. For example, microsatellite instability (MSI) is detected in a higher proportion of EOCRC patients, with approximately 15–20% exhibiting MSI positivity. This condition is typically triggered by mismatch repair (MMR) system defects, resulting in elevated gene mutations in microsatellite regions. Consequently, MSI-positive EOCRC patients often present a higher tumor mutational burden and a more pronounced immune response. These characteristics may promote tumor development and influence its biological behavior [6, 7]. In addition to genetic factors, lifestyle factors such as diet, obesity, smoking, and physical inactivity may also play a significant role in its development. Notably, major risk factors, such as a high-fat, low-fiber diet and chronic inflammation, are also implicated in EOCRC etiology [8, 9].

Postoperative chemotherapy regimens, including 5-fluorouracil (5-FU) with leucovorin, FOLFOX (5-FU + oxaliplatin), FOLFIRI (5-FU + irinotecan), and XELOX (capecitabine + oxaliplatin), are typically administered based on tumor staging, histological type, and patient health status [10]. In high-risk cases, targeted therapies like anti-EGFR (cetuximab) or anti-VEGF (bevacizumab) antibodies are frequently employed [11]. Standardized protocols for EOCRC align with those for late-onset colorectal cancer (LOCRC) [12], effectively reducing recurrence and metastasis rates. However, overall survival benefits remain limited for stage II and III diseases [13]. Given their younger age, EOCRC patients generally tolerate chemotherapy well, though long-term toxicity and quality-of-life impacts warrant close monitoring [14]. Emerging research continues to explore EOCRC's unique molecular characteristics and their influence on chemotherapy response, paving the way for personalized approaches. Neoadjuvant chemotherapy is increasingly considered for locally advanced EOCRC, offering benefits such as reduced tumor volume, enhanced surgical resectability, and improved survival outcomes. Furthermore, immune checkpoint inhibitors exhibit notable efficacy in MSI-high (MSI-H) colorectal cancer [15], providing optimism for this subgroup. Lifestyle interventions, including a balanced diet and regular exercise, are recognized as vital in reducing postoperative recurrence risk [16]. Future investigations will prioritize precision medicine, molecularly guided chemotherapy, and holistic management to enhance treatment efficacy and survival quality for EOCRC patients.

This study focuses on the unique population of EOCRC and aims to selectively identify patients who may benefit from chemotherapy. Utilizing large-scale data from the Surveillance, Epidemiology, and End Results (SEER) database, a systematic analysis of the independent prognostic risk factors for postoperative chemotherapy is conducted, and an individualized survival prediction nomogram model specifically for EOCRC is developed. The goal is to provide valuable information for clinical decision-making and reduce unnecessary medical expenses.

Materials and methods

Patient selection

The data for this study were obtained from the SEER database (www.SEER.cancer.gov), which includes 17 registries, as of November 2022 (covering data from 2000 to 2022). Patient data were downloaded using SEER*Stat version 8.4.4. As SEER does not include personally identifiable information, approval from an institutional review board or informed consent was not required for this study. A total of 24,001 patients aged under 50 years were downloaded from the database. Patients with invalid or missing information were excluded from the study. The final analysis included a total of 9,205 patients, who were randomly assigned to training and validation groups at a 7:3 ratio. The data selection process is outlined in Fig. 1.

Statistical analysis

All statistical analyses in this study were performed using R software (version 3.6.1), with a two-sided p-value of < 0.05 considered statistically significant. The patients were randomly divided into a training group and a validation group using R software. Chi-square tests or Fisher's exact tests were used to compare the distribution of variables between the two groups.

In the training group, univariate Cox regression analysis was conducted to identify risk factors linked to postoperative chemotherapy in EOCRC patients. Variables with p-values < 0.05 were subsequently incorporated into multivariate Cox regression analysis to confirm independent risk

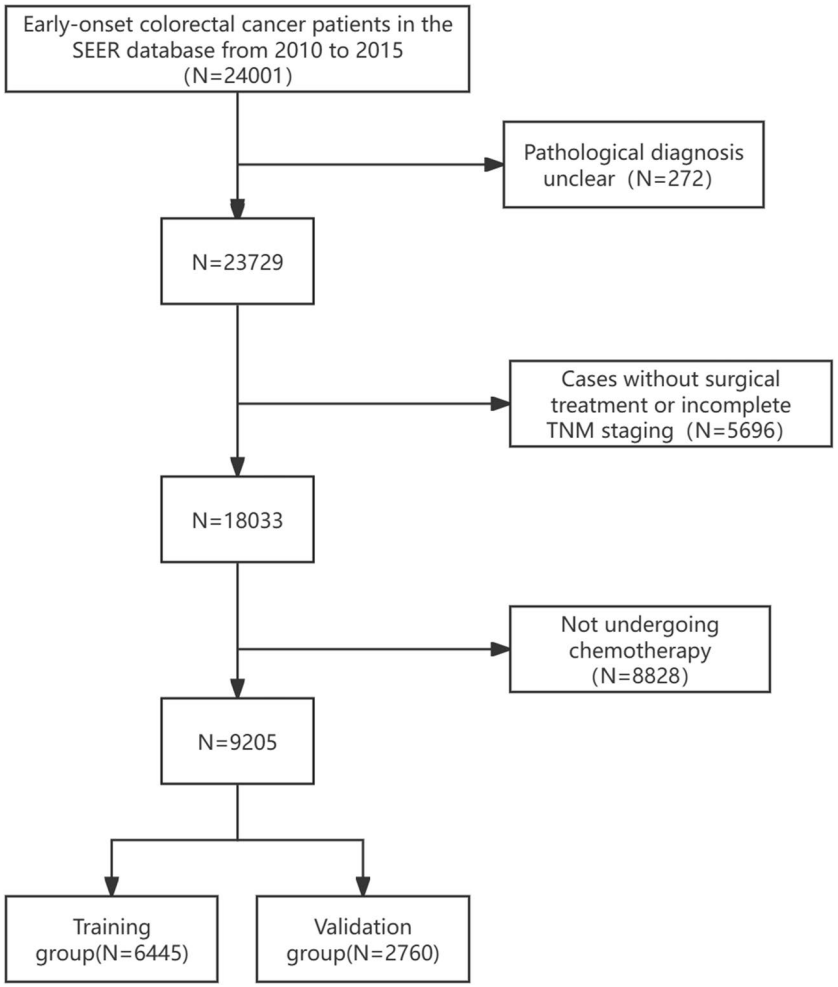

Fig. 1 Flowchart of the selection of patients for inclusion in EOROC in this study

factors. A diagnostic Nomogram was then established using the "rms" package based on these factors.

The model's performance was validated using the validation group. The C-index was employed to gauge discriminative power, ROC curves were utilized to evaluate classification accuracy, calibration curves were applied to assess predictive consistency, and DCA was performed to verify clinical utility across various risk thresholds, ensuring practical applicability.

This study was conducted in accordance with the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines (www.equator-network.org).

Result

Characteristics of included cases

A total of 9,205 cases were included in this study based on the inclusion criteria. 6,445 cases were randomly assigned to the training group, and 2,760 cases were assigned to the validation group. Among all patients, 453 (4.9%) were aged under 30 years, while 95.1% were aged between 31 and 49 years. The patient cohort consisted of 4,842 (52.6%) males and 47.4% females. The marital status distribution was as follows: 29.5% unmarried, 59.1% married, and 11.4% widowed or divorced. Rectal cancer accounted for 28.9% of cases, while colon cancer accounted for 71.1%, with left-sided colon cancer being the most prevalent at 41.9%. Bone metastasis was observed in 0.5% of patients, liver metastasis in 16.7%, and lung metastasis in 3.3%. Patients with stage III and IV disease accounted for 53.0% and 25.1%, respectively, while those with stage I and II disease collectively accounted for 21.9%. A history of radiotherapy was reported in 2,108 patients (32.8%), and 2,125 patients (33.0%) tested positive for CEA. No significant differences were observed between the training and validation groups for any of the included variables (Table 1).

Table 1 Baseline demographic and clinical characteristics of EOCRC patients

Variables	Training ($N=6445$)	Validation ($N=2760$)	Overall ($N=9205$)	P-value
Age				0.94
≤30	316 (4.9%)	137 (5.0%)	453 (4.9%)	
31–49	6129 (95.1%)	2623 (95.0%)	8752 (95.1%)	
Sex				0.63
Female	3066 (47.6%)	1297 (47.0%)	4363 (47.4%)	
Male	3379 (52.4%)	1463 (53.0%)	4842 (52.6%)	
Race				0.98
White	4847 (75.2%)	2073 (75.1%)	6920 (75.2%)	
Black	835 (13.0%)	357 (12.9%)	1192 (12.9%)	
Other	763 (11.8%)	330 (12.0%)	1093 (11.9%)	
Marital.status				0.1
Married	3852 (59.8%)	1588 (57.5%)	5440 (59.1%)	
UnaMarried/Single	1861 (28.9%)	856 (31.0%)	2717 (29.5%)	
Divorced/Separated/Widowed	732 (11.4%)	316 (11.4%)	1048 (11.4%)	
Histologic				0.98
Adenocarcinoma	5715 (88.7%)	2449 (88.7%)	8164 (88.7%)	
Mucinous adenocarcinoma	592 (9.2%)	251 (9.1%)	843 (9.2%)	
Signet ring cell carcinoma	138 (2.1%)	60 (2.2%)	198 (2.2%)	
Site				0.2
Left-side	2701 (41.9%)	1200 (43.5%)	3901 (42.4%)	
Right-side	1464 (22.7%)	599 (21.7%)	2063 (22.4%)	
Rectum	1864 (28.9%)	808 (29.3%)	2672 (29.0%)	
Other	416 (6.5%)	153 (5.5%)	569 (6.2%)	
Tumor.size				0.22
>5 cm	2625 (40.7%)	1163 (42.1%)	3788 (41.2%)	
≤5 cm	3820 (59.3%)	1597 (57.9%)	5417 (58.8%)	
Stage				0.41
I	200 (3.1%)	69 (2.5%)	269 (2.9%)	
II	1246 (19.3%)	540 (19.6%)	1786 (19.4%)	
III	3396 (52.7%)	1477 (53.5%)	4873 (52.9%)	
IV	1603 (24.9%)	674 (24.4%)	2277 (24.7%)	
T				0.57
T1	201 (3.1%)	95 (3.4%)	296 (3.2%)	
T2	489 (7.6%)	200 (7.2%)	689 (7.5%)	
T3	4105 (63.7%)	1730 (62.7%)	5835 (63.4%)	
T4	1650 (25.6%)	735 (26.6%)	2385 (25.9%)	
N				0.45
N0	1733 (26.9%)	718 (26.0%)	2451 (26.6%)	
N1	2738 (42.5%)	1211 (43.9%)	3949 (42.9%)	
N2	1974 (30.6%)	831 (30.1%)	2805 (30.5%)	
M				0.67
M0	4842 (75.1%)	2086 (75.6%)	6928 (75.3%)	
M1	1603 (24.9%)	674 (24.4%)	2277 (24.7%)	
Radiotherapy				0.8
None/Unknown	4337 (67.3%)	1849 (67.0%)	6186 (67.2%)	
Yes	2108 (32.7%)	911 (33.0%)	3019 (32.8%)	
CEA				0.89
Negative	2432 (37.7%)	1047 (37.9%)	3479 (37.8%)	
Positive	2125 (33.0%)	918 (33.3%)	3043 (33.1%)	
Unknown	1888 (29.3%)	795 (28.8%)	2683 (29.1%)	

Table 1 (continued)

Variables	Training ($N=6445$)	Validation ($N=2760$)	Overall ($N=9205$)	P-value
Bone.metastasis				0.46
No	6410 (99.5%)	2749 (99.6%)	9159 (99.5%)	
Yes	35 (0.5%)	11 (0.4%)	46 (0.5%)	
Liver.metastasis				0.81
No	5376 (83.4%)	2296 (83.2%)	7672 (83.3%)	
Yes	1069 (16.6%)	464 (16.8%)	1533 (16.7%)	
Lung.metastasis				0.8
No	6229 (96.6%)	2671 (96.8%)	8900 (96.7%)	
Yes	216 (3.4%)	89 (3.2%)	305 (3.3%)	

Nomogram establishment

To identify the independent risk factors affecting the survival of EOCRC patients after surgery, univariate Cox regression analysis was performed. The analysis revealed that variables such as age, gender, race, marital status, pathological classification, primary tumor location, tumor size, tumor grade, T stage, N stage, M stage, radiotherapy, CEA levels, bone metastasis, liver metastasis, and lung metastasis were significantly associated with postoperative survival (Table 2).

These variables were identified as potential risk factors for EOCRC patients receiving postoperative chemotherapy. Subsequently, a multivariate Cox regression analysis was conducted, which identified gender, race, marital status, pathological classification, primary tumor location, T stage, N stage, M stage, CEA levels, bone metastasis, liver metastasis, and lung metastasis as independent risk factors for EOCRC patients undergoing postoperative chemotherapy. Based on these independent risk factors, OS nomogram models were developed for predicting 1-year, 3-year, and 5-year survival (Fig. 2).

Nomogram validation

The C-index results demonstrated good discrimination ability and consistency of the nomogram, with values of 0.76 (0.75, 0.77) in the training group and 0.76 (0.75, 0.78) in the validation group (Fig. 3). The area under the receiver operating characteristic curves (AUCs) for predicting 1-year OS were 0.84 (0.81, 0.86) and 0.82 (0.78, 0.85) in the training and validation groups, respectively. For 3-year OS prediction, the AUCs were 0.83 (0.82, 0.84) and 0.82 (0.80, 0.84) in the training and validation groups, while for 5-year OS prediction, the AUCs were 0.81 (0.80, 0.82) and 0.82 (0.80, 0.84), respectively (Fig. 4). The accuracy of the model was further validated by the calibration curves in both the training and validation groups, with the close alignment of the red line to the 45° calibration line indicating strong agreement between the predicted and actual outcomes (Fig. 5). Moreover, the DCA confirmed the clinical utility of the nomogram in decision-making processes (Fig. 6).

Discussion

In this study, Cox regression analysis was performed to identify 12 independent prognostic factors out of 16 candidate factors, which were then utilized to construct a prognostic Nomogram model for EOCRC patients. This finding suggests that, compared to late-onset colorectal cancer, the prognosis of postoperative chemotherapy patients with EOCRC is likely associated with a greater number of variables. The 1-, 3-, and 5-year AUC values and calibration curves of the developed model indicate that it possesses good discriminatory power and can be employed to provide personalized treatment for EOCRC patients by considering multiple risk factors, thereby identifying those who are most likely to benefit from chemotherapy. However, no statistically significant survival difference was found between the age groups ≤ 30 years and 31–49 years; consequently, age was not included as a variable in the model. This result implies that, despite the wide age range among EOCRC patients, age may not be an independent prognostic factor for survival outcomes in those receiving postoperative chemotherapy. A cohort study from the Anderson Cancer Center proposed that the molecular characteristics of younger patients may differ from those of late-onset patients, and survival rates are primarily influenced by biological behavior rather than age itself [7, 17]. Interestingly, being female was identified as a protective factor in the Nomogram; moreover, marriage was also considered a protective factor. This finding emphasizes the significance of social support in cancer management [18] and provides new directions for optimizing postoperative follow-up and comprehensive treatment. The integration of psychological and social support resources holds promise for further improving the survival prognosis of EOCRC patients. Histological subtypes significantly influence postoperative survival in EOCRC. Characterized

Table 2 Univariate and multivariate analysis of overall survival in the training group

Variables	Univariate alysis		Multivariate alysis	
	HR(95%CI)	*P*-value	HR(95%CI)	*P*-value
Age				
≤ 30	Reference			
31–49	0.77(0.65,0.91)	0.002	0.99(0.84,1.18)	0.93
Sex				
Female	Reference			
Male	1.14(1.05,1.23)	0.001	1.17(1.08,1.26)	< 0.001
Race				
White	Reference			
Black	1.42 (1.28,1.58)	< 0.001	1.29(1.16,1.44)	< 0.001
Other	1.03 (0.91,1.16)	0.61	1.05(0.93,1.19)	0.42
Marital.status				
Married	Reference			
Unmarried/Single	1.38 (1.26,1.50)	< 0.001	1.33(1.21,1.45)	< 0.001
Divorced/Separated/Widowed	1.35 (1.2,1.52)	< 0.001	1.42(1.26,1.60)	< 0.001
Histologic				
Adenocarcinomas	Reference			
Mucinous adenocarcinoma	1.21 (1.06,1.37)	0.004	1.07(0.93,1.22)	0.34
Signet ring cell carcinoma	3.22 (2.64,3.93)	< 0.001	2.38(1.94,2.93)	< 0.001
Site				
Left-side	Reference			
Right-side	1.22 (1.11,1.34)	< 0.001	1.21(1.09,1.34)	< 0.001
Rectum	0.76 (0.69,0.84)	< 0.001	1.05(0.92,1.20)	0.46
Other	1.12 (0.96,1.31)	0.16	1.13(0.96,1.32)	0.14
Tumor.size				
≤ 5 cm	Reference			
> 5 cm	0.86 (0.79,0.93)	< 0.001	1.01(0.93,1.09)	0.89
Stage				
I	Reference			
II	0.89 (0.64,1.23)	0.481	-	-
III	1.6 (1.18,2.17)	0.002	-	-
IV	7.21 (5.32,9.78)	< 0.001	-	-
T				
T1	Reference			
T2	0.78 (0.57,1.08)	0.132	0.80(0.58,1.10)	0.16
T3	1.32 (1.02,1.72)	0.037	1.06(0.82,1.39)	0.64
T4	2.97 (2.28,3.87)	< 0.001	1.86(1.41,2.43)	< 0.001
N				
N0	Reference			
N1	1.51 (1.36,1.69)	< 0.001	1.61(1.44,1.80)	< 0.001
N2	2.96 (2.66,3.3)	< 0.001	2.38(2.13,2.66)	< 0.001
M				
M0	Reference			
M1	5.22 (4.83,5.64)	< 0.001	2.94(2.60,3.33)	< 0.001
Radiotherapy				
None/Unknown	Reference			
Yes	0.71 (0.65,0.77)	< 0.001	1.13(0.99,1.29)	0.06
CEA				
Negative	Reference			
Positive	2.26 (2.05,2.48)	< 0.001	1.44(1.31,1.59)	< 0.001

Table 2 (continued)

Variables	Univariate alysis		Multivariate alysis	
	HR(95%CI)	*P*-value	HR(95%CI)	*P*-value
Unknown	1.51 (1.36,1.67)	< 0.001	1.40(1.26,1.55)	< 0.001
Bone.metastasis				
No	Reference			
Yes	8.78 (6.12,12.6)	< 0.001	2.53(1.77,3.60)	< 0.001
Liver.metastasis				
No	Reference			
Yes	4.43 (4.08,4.81)	< 0.001	1.53(1.34,1.74)	< 0.001
Lung.metastasis				
No	Reference			
Yes	4.16 (3.58,4.84)	< 0.001	1.55(1.32,1.83)	< 0.001

by younger onset, EOCRC frequently exhibits signet-ring cells, poorly differentiated tumors, and heightened lymph node metastasis risk [19]. Mucinous adenocarcinoma and signet-ring cell carcinoma are associated with poorer prognoses compared to adenocarcinoma. Previous studies have demonstrated that mucinous adenocarcinoma may exhibit lower sensitivity to standard postoperative chemotherapy regimens (such as FOLFOX and CAPOX) [20], thus necessitating the exploration of new therapeutic strategies. The optimization of chemotherapy regimens or the utilization of molecular-based targeted therapies and immunotherapy could provide new therapeutic directions for these patients. Additionally, clinicians should incorporate histological subtype into the treatment decision-making process for EOCRC patients to provide better clinical benefits. Patients who test positive for CEA usually have a worse prognosis because it means they have a larger tumor burden [21], which is linked to advanced staging, a higher risk of metastasis, and aggressive molecular features like MSS and CIN. Furthermore, elevated CEA levels, indicative of reduced chemotherapy responsiveness and minimal residual disease (MRD), further elevate recurrence and mortality risks [22]. Prognosis is also tied to tumor location, influenced by anatomical, vascular, and molecular variations. Right-sided colon cancers often display MSI-H and mucinous adenocarcinoma, whereas left-sided colon and rectal cancers are more commonly linked to microsatellite stability (MSS) and chromosomal instability (CIN) [23]. These differences affect not only prognosis but also responsiveness to chemotherapy and targeted therapies [24].

The main advantage of postoperative chemotherapy is that it significantly reduces recurrence and metastasis risk in high-risk patients, extending their survival [13]. Standardized adjuvant chemotherapy regimens effectively control tumor progression, especially for CEA-positive, multiple metastases, and T4-stage patients [25, 26]. EOCRC patients receive more intensive adjuvant therapy than LOCRC patients [14], potentially leading to further benefits. However, chemotherapy-related long-term toxicities may significantly decrease younger patients' quality of life [27]. Additionally, chemotherapy efficacy may be limited in patients with certain molecular characteristics, causing heterogeneous treatment responses [28]. Accurately predicting EOCRC patients' postoperative survival prognosis and developing individualized treatment plans based on patient characteristics remains a major clinical challenge.

A dynamic survival prediction model integrating multiple variables was developed, facilitating follow-up management at various intervals. An intuitive scoring system enhances clinical applicability. Validation via C-index and calibration curves confirmed the model's superior predictive performance and reliability. High-risk patients, such as those with CEA positivity, stage IV disease, or metastasis, can be identified for optimized adjuvant therapy, while low-risk patients may avoid unnecessary treatment escalation.

Limitations

However, certain limitations remain, providing directions for future optimization studies. First, despite the SEER database's extensive coverage, it lacks detailed treatment information, such as chemotherapy regimens, duration, dosage, and targeted therapies, which may affect the model's predictive accuracy. Second, the SEER database does not include molecular biomarkers (e.g., KRAS and BRAF mutations and MSI status), critical to colorectal cancer aggressiveness and treatment sensitivity. Future efforts should incorporate these variables into model development.

Conclusion

This study identified independent prognostic factors for post-operative chemotherapy in EOCRC patients using the SEER database and constructed and validated a survival

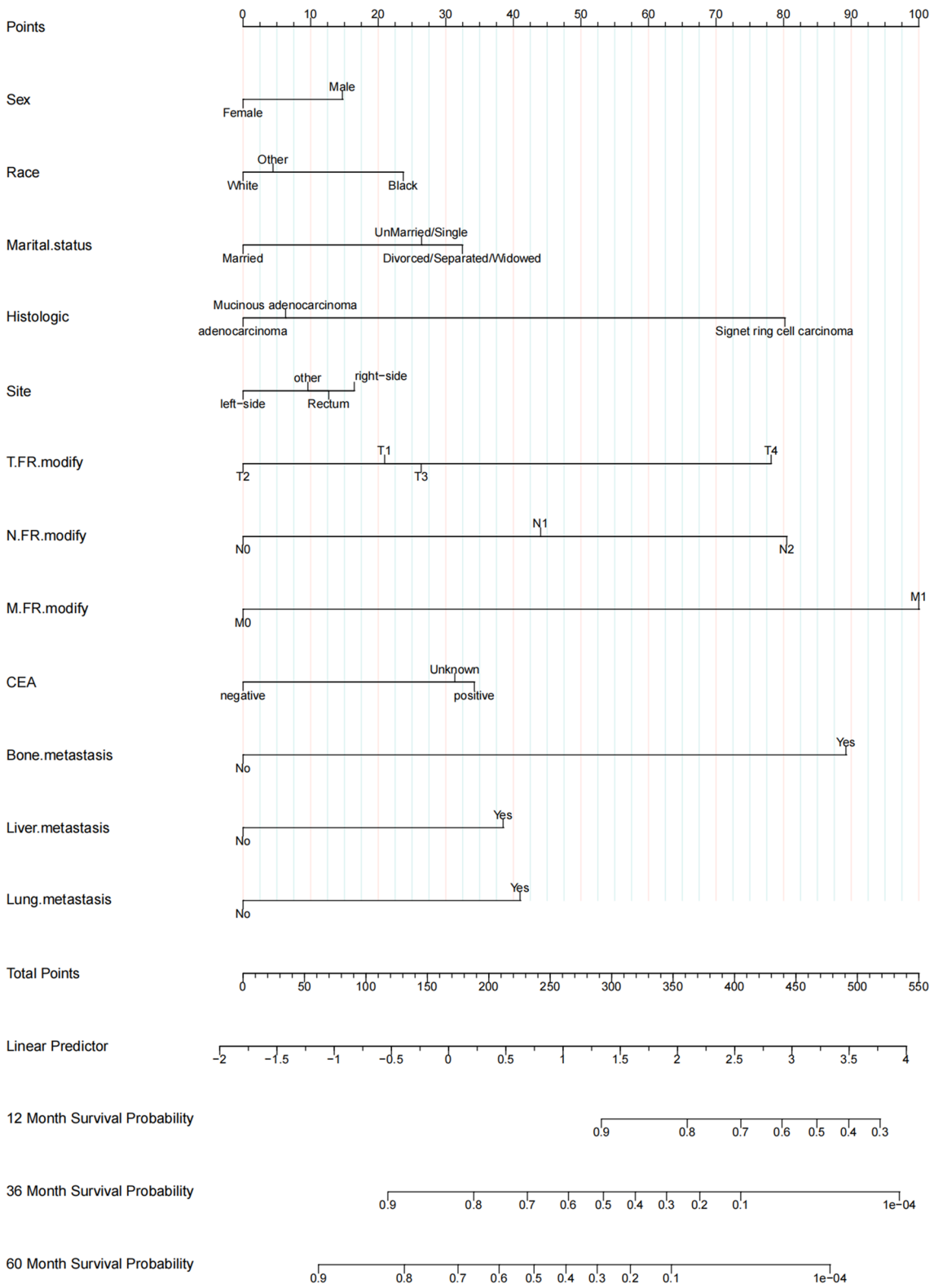

Fig. 2 Nomogram for predicting 1-, 3-, and 5-year OS in patients with EOCRC

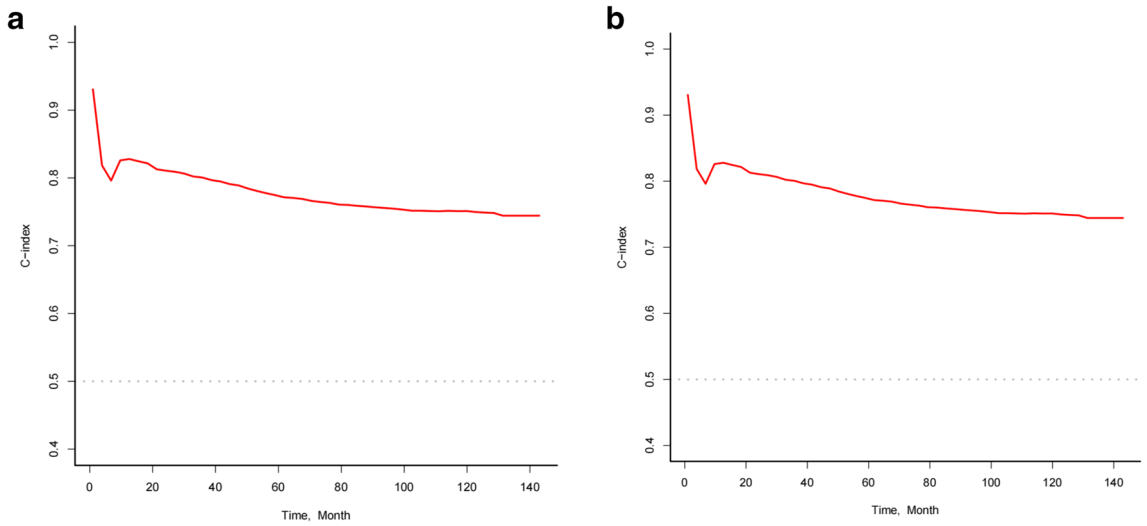

Fig. 3 **a** C-index for training group. **b** C-index for validation group

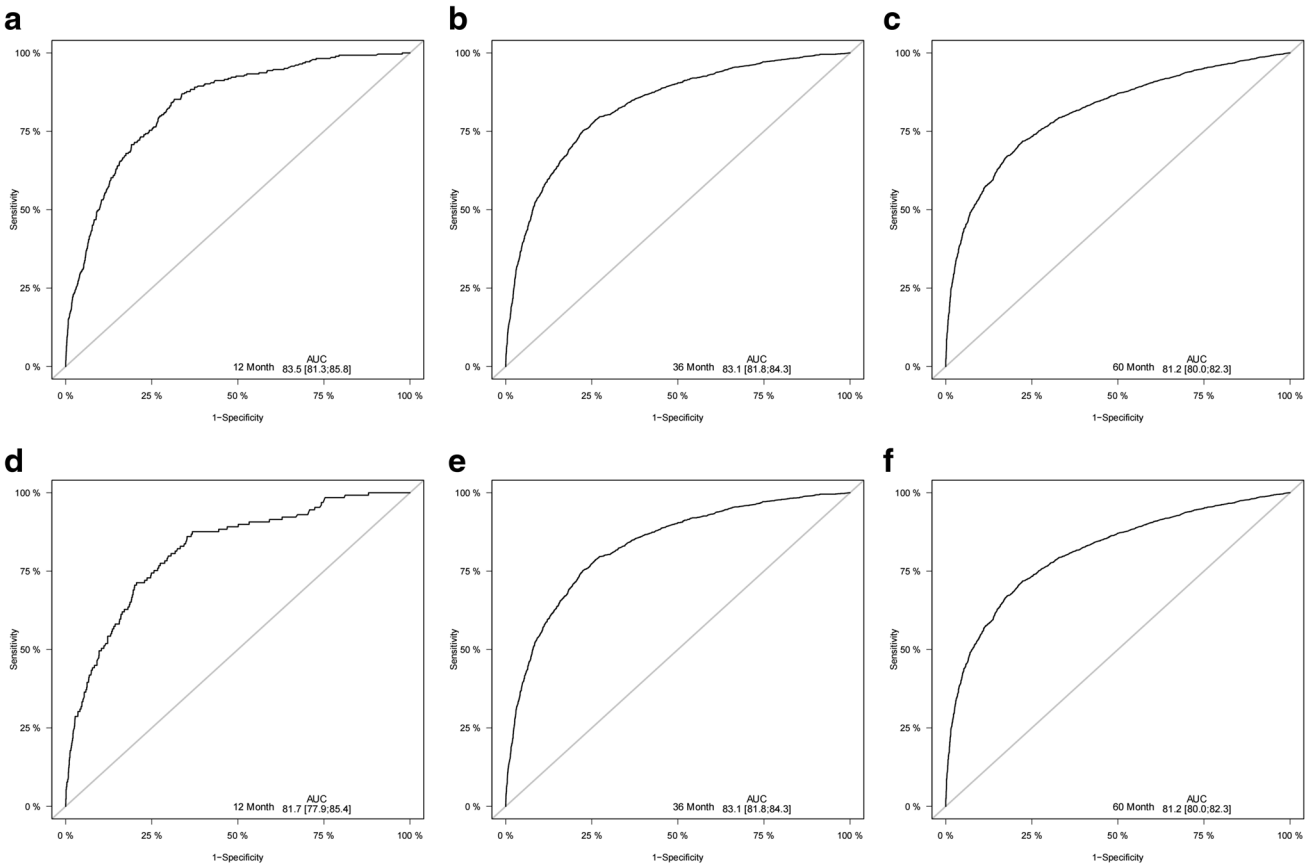

Fig. 4 The receiver operating characteristic (ROC) curves of Nomograms. **a–c** ROC curves of the training group for 1, 3, and 5 years. **d–f** The ROC curves of the validation group for 1, 3, 5 years

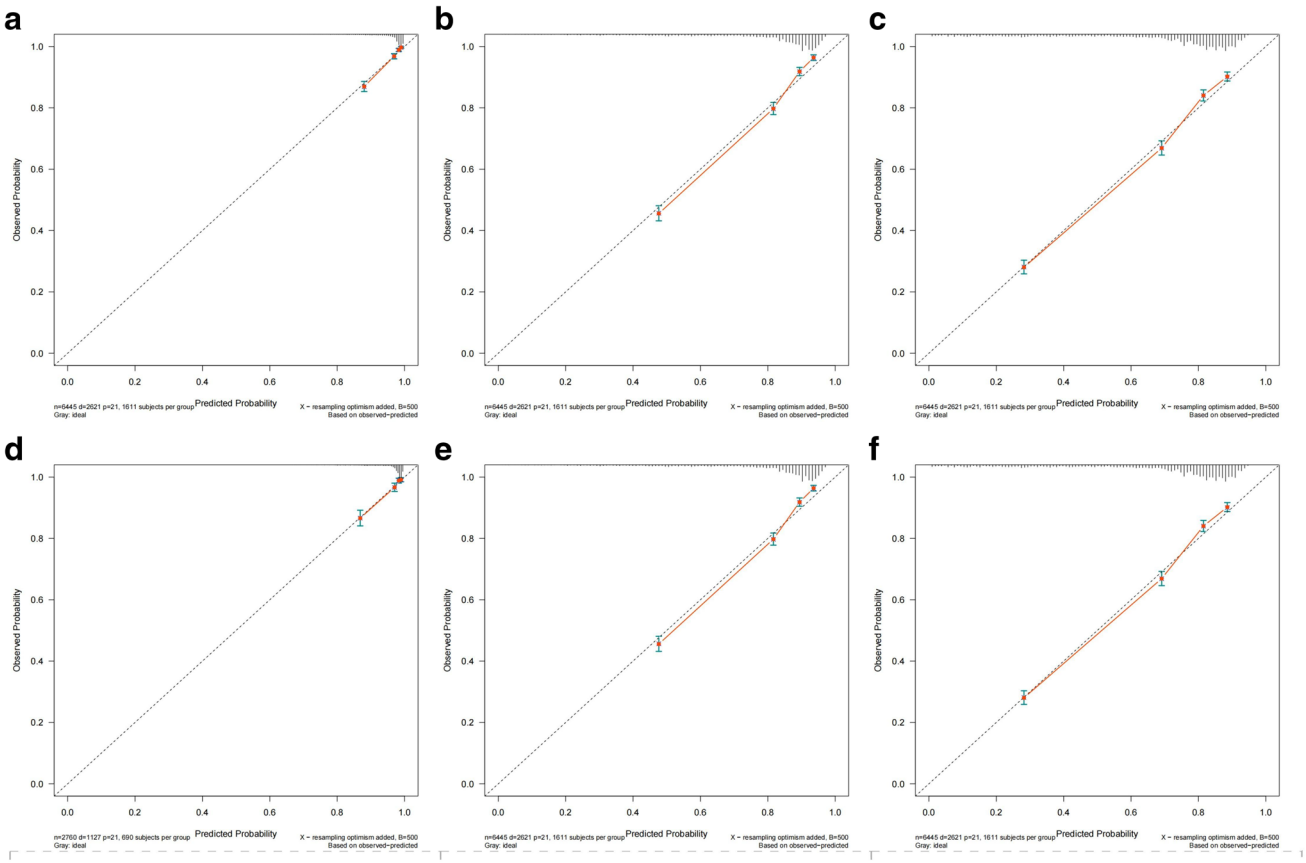

Fig. 5 Calibration curves for Nomograms. **a–c** Calibration curves for 1-, 3-, and 5-year OS in the Nomogram prediction training group.. **d–f** Calibration curves for 1-, 3-, and 5-year OS in the Nomogram prediction validation group

prediction model. The model demonstrates good accuracy and potential clinical applicability.

Supplementary information The online version contains supplementary material available at https://doi.org/10.1007/s00384-025-04853-6.

Acknowledgements The authors would like to acknowledge the reviewers for their helpful comments on this paper.

Author contributions All authors contributed to the research design. Study design: ZG.T and YX.Z, statistical analysis: ZG.T and X.Y, manuscript writing: ZG.T and GJ.Z, study guidance and supervision: ZG.T, all authors participated in writing and approved the submission of the manuscript for publication.

Funding None.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval and consent to participate Not applicable. This article does not include any research involving human participants or animals conducted by the authors.

Competing interests The authors declare no competing interests.

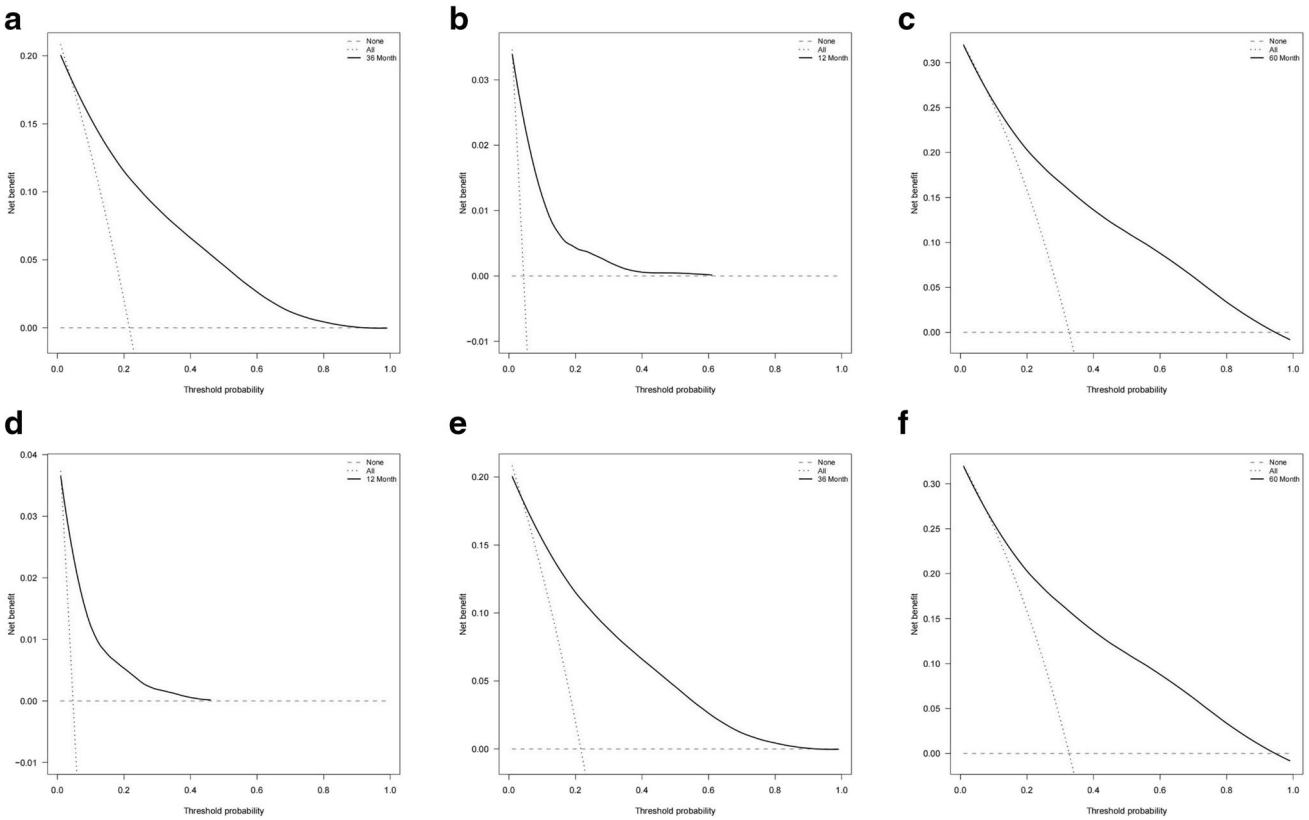

Fig. 6 Decision analysis curves (DCA) for Nomogram. **a–c** DCA curves for 1, 3, and 5 years for training groups. **d–f** DCA curves for 1, 3, and 5 years for validation groups

References

1. Siegel RL, Wagle NS, Cercek A, Smith RA, Jemal A (2023) Colorectal cancer statistics, 2023. CA: a cancer journal for clinicians 73(3):233–254. https://doi.org/10.3322/caac.21772
2. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F (2017) Global patterns and trends in colorectal cancer incidence and mortality. Gut 66(4):683–691. https://doi.org/10.1136/gutjnl-2015-310912
3. Patel SG, Karlitz JJ, Yen T, Lieu CH, Boland CR (2022) The rising tide of early-onset colorectal cancer: a comprehensive review of epidemiology, clinical features, biology, risk factors, prevention, and early detection. The lancet Gastroenterology & hepatology 7(3):262–274. https://doi.org/10.1016/S2468-1253(21)00426-X
4. Dwyer AJ, Murphy CC, Boland CR, Garcia R, Hampel H, Limburg P, Lowery J, Zauber AG, Waring S, Worrall S, Perea J, Siegel R, Lee J, Molmenti C, Sears CL, Buckhaults P, Hayes R, Hussan H, de Miranda N, Palles C, … Ahnen D (2019) A summary of the fight colorectal cancer working meeting: exploring risk factors and etiology of sporadic early-age onset colorectal cancer. Gastroenterology 157(2):280–288. https://doi.org/10.1053/j.gastro.2019.04.049
5. Stoffel EM, Murphy CC (2020) Epidemiology and mechanisms of the increasing incidence of colon and rectal cancers in young adults. Gastroenterology 158(2):341–353. https://doi.org/10.1053/j.gastro.2019.07.055
6. Chang DT, Pai RK, Rybicki LA, Dimaio MA, Limaye M, Jayachandran P, Koong AC, Kunz PA, Fisher GA, Ford JM, Welton M, Shelton A, Ma L, Arber DA, Pai RK (2012) Clinicopathologic and molecular features of sporadic early-onset colorectal adenocarcinoma: an adenocarcinoma with frequent signet ring cell differentiation, rectal and sigmoid involvement, and adverse morphologic features. Mod Pathol 25(8):1128–1139. https://doi.org/10.1038/modpathol.2012.61
7. Willauer AN, Liu Y, Pereira AAL, Lam M, Morris JS, Raghav KPS, Morris VK, Menter D, Broaddus R, Meric-Bernstam F, Hayes-Jordan A, Huh W, Overman MJ, Kopetz S, Loree JM (2019) Clinical and molecular characterization of early-onset colorectal cancer. Cancer 125(12):2002–2010. https://doi.org/10.1002/cncr.31994
8. Song M, Hu FB, Spiegelman D, Chan AT, Wu K, Ogino S, Fuchs CS, Willett WC, Giovannucci EL (2016) Long-term status and change of body fat distribution, and risk of colorectal cancer: a prospective cohort study. Int J Epidemiol 45(3):871–883. https://doi.org/10.1093/ije/dyv177
9. Liang PS, Chen TY, Giovannucci E (2009) Cigarette smoking and colorectal cancer incidence and mortality: systematic review and meta-analysis. Int J Cancer 124(10):2406–2415. https://doi.org/10.1002/ijc.24191
10. Chan GHJ, Chee CE (2019) Making sense of adjuvant chemotherapy in colorectal cancer. Journal of gastrointestinal oncology 10(6):1183–1192. https://doi.org/10.21037/jgo.2019.06.03

11. Biller LH, Schrag D (2021) Diagnosis and treatment of metastatic colorectal cancer: a review. JAMA 325(7):669–685. https://doi.org/10.1001/jama.2021.0106
12. Spaander MCW, Zauber AG, Syngal S, Blaser MJ, Sung JJ, You YN, Kuipers EJ (2023) Young-onset colorectal cancer. Nat Rev Dis Primers 9(1):21. https://doi.org/10.1038/s41572-023-00432-7
13. Kolarich A, George TJ Jr, Hughes SJ, Delitto D, Allegra CJ, Hall WA, Chang GJ, Tan SA, Shaw CM, Iqbal A (2018) Rectal cancer patients younger than 50 years lack a survival benefit from NCCN guideline-directed treatment for stage II and III disease. Cancer 124(17):3510–3519. https://doi.org/10.1002/cncr.31527
14. Eng C, Jácome AA, Agarwal R, Hayat MH, Byndloss MX, Holowatyj AN, Bailey C, Lieu CH (2022) A comprehensive framework for early-onset colorectal cancer research. Lancet Oncol 23(3):e116–e128. https://doi.org/10.1016/S1470-2045(21)00588-X
15. Ganesh K, Stadler ZK, Cercek A, Mendelsohn RB, Shia J, Segal NH, Diaz LA Jr (2019) Immunotherapy in colorectal cancer: rationale, challenges and potential. Nat Rev Gastroenterol Hepatol 16(6):361–375. https://doi.org/10.1038/s41575-019-0126-x
16. Castro-Espin C, Agudo A (2022) The role of diet in prognosis among cancer survivors: a systematic review and meta-analysis of dietary patterns and diet interventions. Nutrients 14(2):348. https://doi.org/10.3390/nu14020348
17. Okamoto K, Ozawa T, Nozawa H, Sasaki K, Murono K, Emoto S, Yamauchi S, Sugihara K, Ishihara S (2024) Prognosis of early-onset vs. late-onset stage II/III colorectal cancer patients with adjuvant chemotherapy: a multicenter propensity score matched study. International journal of clinical oncology 29(11):1721–1729. https://doi.org/10.1007/s10147-024-02601-4
18. Coughlin SS (2020) Social determinants of colorectal cancer risk, stage, and survival: a systematic review. Int J Colorectal Dis 35(6):985–995. https://doi.org/10.1007/s00384-020-03585-z
19. Vuik FER, Nieuwenburg SAV, Nagtegaal ID, Kuipers EJ, Spaander MCW (2021) Clinicopathological characteristics of early onset colorectal cancer. In: Alimentary pharmacology & therapeutics, vol 54. Issues 11–12. Wiley. pp 1463–1471. https://doi.org/10.1111/apt.16638
20. Catalano V, Bergamo F, Cremolini C, Vincenzi B, Negri F, Giordani P, Santini D, Sarti D, Torresi U, Bisonni R, Silva R, Rocchi M, Lonardi S, Falcone A, Mattioli R, Graziano F (2018) Optimizing the use of first-line chemotherapy in metastatic colorectal cancer patients with mucinous histology. A multicenter, retrospective, combined analysis on 897 patients. In: Annals of oncology, vol 29. Elsevier BV, p v97. https://doi.org/10.1093/annonc/mdy150.014
21. Fernández-Ponce C, Geribaldi-Doldán N, Sánchez-Gomar I, Quiroz RN, Ibarra LA, Escorcia LG, Fernández-Cisnal R, Martinez GA, García-Cózar F, Quiroz EN (2021) The role of glycosyltransferases in colorectal cancer. Int J Mol Sci 22(11):5822. https://doi.org/10.3390/ijms22115822
22. Hall C, Clarke L, Pal A, Buchwald P, Eglinton T, Wakeman C, Frizelle F (2019) A review of the role of carcinoembryonic antigen in clinical practice. Annals of coloproctology 35(6):294–305. https://doi.org/10.3393/ac.2019.11.13
23. Zhong M, Wu B (2021) Zhongguo yi xue ke xue yuan xue bao. Acta Academiae Medicinae Sinicae 43(6):980–985. https://doi.org/10.3881/j.issn.1000-503X.12867
24. Tom CM, Mankarious MM, Jeganathan NA, Deutsch M, Koltun WA, Berg AS, Scow JS (2023) Characteristics and outcomes of right- versus left-sided early-onset colorectal cancer. Dis Colon Rectum 66(4):498–510. https://doi.org/10.1097/DCR.0000000000002273
25. Akdeniz N, Kaplan MA, Uncu D, İnanç M, Kaya S, Dane F, Küçüköner M, Demirci A, Bilici M, Durnalı AG, Koral L, Şendur MAN, Erol C, Türkmen E, Ölmez ÖF, Açıkgöz Ö, Laçin Ş, Şahinli H, Urakçı Z, Işıkdoğan A (2021) The comparison of FOLFOX regimens with different doses of 5-FU for the adjuvant treatment of colorectal cancer: a multicenter study. Int J Colorectal Dis 36(6):1311–1319. https://doi.org/10.1007/s00384-021-03888-9
26. Mei WJ, Wang XZ, Li YF, Sun YM, Yang CK, Lin JZ, Wu ZG, Zhang R, Wang W, Li Y, Zhuang YZ, Lei J, Wan XB, Ren YK, Cheng Y, Li WL, Wang ZQ, Xu DB, Mo XW, Ju HX, … Ding PR (2023) Neoadjuvant chemotherapy with CAPOX versus chemoradiation for locally advanced rectal cancer with uninvolved mesorectal fascia (CONVERT): initial results of a phase III trial. Ann Surg 277(4):557–564. https://doi.org/10.1097/SLA.0000000000005780
27. Teng C, Cohen J, Egger S, Blinman PL, Vardy JL (2022) Systematic review of long-term chemotherapy-induced peripheral neuropathy (CIPN) following adjuvant oxaliplatin for colorectal cancer. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 30(1):33–47. https://doi.org/10.1007/s00520-021-06502-4
28. Cutshaw G, Joshi N, Wen X, Quam E, Bogatcheva G, Hassan N, Uthaman S, Waite J, Sarkar S, Singh B, Bardhan R (2024) Metabolic response to small molecule therapy in colorectal cancer tracked with Raman spectroscopy and metabolomics. Angewandte Chemie (International ed. in English) 63(43):e202410919. https://doi.org/10.1002/anie.202410919