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ORIGINAL RESEARCH

Preoperative Prognostic Factors of Colorectal Cancer in Patients from Central China: A Retrospective Observational Study

Qilin Fan[1,2,*], Min Jin[2–4,*], Jun Fan[5], Feng Wen[1], Weitian Xu[1], Hongli Liu[2–4]

[1]Department of Gastroenterology, General Hospital of Central Theater Command, Wuhan, Hubei, People's Republic of China; [2]Hubei Province Key Laboratory of Precision Radiation Oncology, Wuhan, Hubei, People's Republic of China; [3]Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; [4]Institute of Radiation Oncology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; [5]Department of Pathology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China

*These authors contributed equally to this work

Correspondence: Hongli Liu, Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China, Email hongli_liu@hust.edu.cn; Weitian Xu, Department of Gastroenterology, General Hospital of Central Theater Command, Wuhan, Hubei, People's Republic of China, Email xuweitian456@126.com

Purpose: This study aimed to investigate the clinicopathological characteristics and identify prognostic factors influencing overall survival (OS) in colorectal cancer (CRC) patients from central China.

Patients and Methods: We conducted a retrospective analysis of clinicopathologic data obtainable at the preoperative decision point from 1452 patients with pathologically confirmed CRC who underwent surgical resection between January 2015 and December 2017 at the Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, in central China. Associations between clinicopathological variables and OS were evaluated using independent sample tests, Kaplan–Meier survival analysis, and Log rank tests. A Cox proportional hazards model was employed to identify independent predictors of OS.

Results: Of 1452 patients, 58.9% were male and 41.1% female (ratio 1.43:1). Multivariate logistic regression identified age, tumor differentiation, preoperative CEA, and metastasis as independent mortality predictors (all $P \leq 0.01$; Table 1). A univariate analysis of this predominantly rectal-cancer cohort (51.9%) revealed that numerous clinicopathological variables, including age, tumor size, grade, tumor deposits, perineural and vascular invasion, nodal status, surgical margins, clinical stage, primary site, preoperative CEA, treatment modality, distant metastasis, and recurrence, were each significantly associated with overall survival (Table 2). In the overall cohort, age ≥75 years (OR = 3.812), poor differentiation (OR = 2.590), elevated CEA (OR = 4.594), and liver metastasis (OR = 4.370) were independently associated with higher mortality (all $P \leq 0.045$; Table 3). Subgroup analyses (Table 4) showed that in colon cancer, age ≥75 years (OR = 4.961, $P = 0.001$) and metastasis (OR = 37.029, $P < 0.001$) increased mortality risk. In rectal cancer, lymph node involvement (1–3 nodes: OR = 2.968, $P = 0.004$; 4–6: OR = 4.771, $P = 0.001$; ≥7: OR = 11.131, $P < 0.001$) and metastasis (OR = 1.292, $P < 0.001$) were independent risk factors, while elevated CEA was not significant ($P = 0.065$).

Conclusion: In this large cohort, mortality risk in CRC is independently associated with age, differentiation, CEA, and metastasis—with distinct risk patterns between colon and rectal cancers—highlighting the importance of primary tumor location in prognostic assessment.

Keywords: colorectal cancer, clinicopathological features, survival analysis, prognosis

Introduction

Colorectal cancer (CRC) continues to pose a substantial global health burden, maintaining its position as the third most commonly diagnosed malignancy and the second leading cause of cancer-related mortality worldwide.[1] The most recent GLOBOCAN 2022 estimates indicate approximately 1.93 million new cases and over 900,000 deaths annually, reflecting the persistent challenge this disease represents.[2] While incidence rates have stabilized or even declined in some Western countries due to effective screening programs, China is experiencing a concerning rise in CRC burden. According to the

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latest data from the National Cancer Center of China, CRC has now become the second most frequently diagnosed cancer and ranks fourth in cancer-related mortality, with estimated annual incidence exceeding 560,000 cases.[3,4]

The management of CRC has evolved into a highly sophisticated, stage-dependent approach. Early-stage lesions are increasingly managed through advanced endoscopic techniques including endoscopic mucosal resection and submucosal dissection, achieving excellent oncological outcomes with minimal invasiveness. For locally advanced disease, surgical resection with systematic lymph node dissection remains fundamental to curative treatment strategies. The surgical approach has progressively shifted from conventional open procedures to minimally invasive techniques, with laparoscopic and robotic surgeries demonstrating comparable oncological efficacy while offering enhanced postoperative recovery.[5] Contemporary patient outcomes are determined by a complex interplay of tumor biology, pathological characteristics, treatment response, and host factors.

Recently, our team systematically delineated the clinicopathological features and prognostic value of KRAS, NRAS, and BRAF gene mutations based on a colorectal cancer cohort from the same medical center during 2015–2017.[6] That study revealed the impact of molecular heterogeneity on prognosis. However, in clinical practice, particularly when formulating preoperative treatment strategies (such as decisions regarding neoadjuvant therapy), genetic testing results may not be immediately available or routinely performed. Therefore, utilizing readily accessible preoperative clinical and laboratory indicators for rapid and effective risk stratification bears indispensable practical significance. This study aims to address this gap by focusing on evaluating the impact of preoperative obtainable factors on the overall survival of colorectal cancer patients, thereby providing evidence from a central Chinese population for the preoperative assessment framework.

The TNM staging system, currently in its 9th edition, continues to serve as the cornerstone for CRC prognosis and therapeutic decision-making.[7] However, recognized limitations of this anatomical-based classification have stimulated extensive research into complementary prognostic biomarkers. Multiple factors beyond TNM staging have demonstrated prognostic significance, including patient demographics, tumor morphological characteristics, serum biomarkers such as carcinoembryonic antigen (CEA), histopathological features (lymphovascular invasion, perineural infiltration, tumor budding), and molecular alterations including KRAS/NRAS/BRAF mutations and microsatellite instability status.[8–10] The prognostic implications of specific molecular markers remain partially controversial. While KRAS and NRAS mutations are well-established predictors of resistance to anti-EGFR therapies in metastatic CRC,[11,12] their independent prognostic value continues to be debated, with some studies demonstrating association with poorer survival while others, including large Chinese cohorts, showing limited independent prognostic significance.[13,14] Similarly, BRAF V600E mutations are generally associated with aggressive clinical behavior and poor outcomes, though their prognostic impact may vary across different ethnic populations.[15,16]

The timing of prognostic factor assessment represents a critical consideration in CRC research. Most traditional studies have focused on post-surgical pathological and molecular findings. However, in the contemporary era of multimodal CRC management incorporating neoadjuvant therapies, these postoperative parameters may be confounded by treatment effects. Consequently, the identification and validation of pre-operative prognostic factors carries significant clinical relevance, as these parameters are available at initial diagnosis to guide primary treatment decisions, surgical planning, and patient counseling.

As a nation experiencing rapidly increasing CRC incidence, China requires more population-specific data, particularly regarding the prognostic significance of pre-operative clinicopathological characteristics.[4,17,18] To address this knowledge gap, we conducted this retrospective cohort study analyzing 1452 CRC patients from central China. The primary objectives were to characterize the clinicopathological profile of CRC in this population and to identify independent pre-operative prognostic factors for overall survival. We anticipate that our findings will contribute valuable insights to inform the development of tailored prevention, treatment, and surveillance strategies for CRC patients in China.

Materials and Methods

Study Population and Data Collection

This retrospective cohort study included 1452 patients with pathologically confirmed colorectal adenocarcinoma who underwent radical resection at the Union Hospital, Tongji Medical College, Huazhong University of Science and

Technology (Central China) between January 2015 and December 2017. The study protocol was approved by the Institutional Ethics Committee (No. 2014-041), and all patients provided written informed consent for their surgical procedures. Patients were selected based on the following criteria: Inclusion criteria: (1) Pathological diagnosis of primary colorectal adenocarcinoma; (2) Underwent curative-intent radical surgery; (3) Had complete clinicopathological and follow-up data. Exclusion criteria: (1) Presence of multiple primary malignancies; (2) Diagnosis of inflammatory bowel disease or hereditary colorectal syndromes (eg, familial adenomatous polyposis, Lynch syndrome); (3) Incomplete medical records.

Clinicopathological data were extracted from electronic medical records, including: age, sex, tumor location, grade of differentiation, preoperative carcinoembryonic antigen (CEA) level, presence of tumor deposits, perineural invasion, vascular invasion, lymph node metastasis, surgical margin status, and clinical stage according to the AJCC 8th edition. Tumor location was classified as right-sided colon (cecum to splenic flexure) or left-sided (descending colon to rectum).[19,20]

Surgical and Treatment Strategy

All surgical procedures were performed based on the patient's performance status, tumor location, and disease stage. The surgical approach (open or laparoscopic) was determined by the attending surgeon. The principles of complete mesocolic excision (for colon cancer) and total mesorectal excision (for rectal cancer) were adhered to. A diverting loop ileostomy was routinely created for patients undergoing low or ultralow anterior resection. The overall management strategy for each patient was discussed and decided by a multidisciplinary team comprising gastrointestinal surgeons, medical oncologists, and radiation oncologists.

Follow-up

Postoperative follow-up was conducted in accordance with the National Comprehensive Cancer Network (NCCN) guidelines. Patients were followed up every 3 months for the first year and every 6 months thereafter. Follow-up assessments were performed through outpatient clinic visits or telephone interviews. The primary endpoint was overall survival (OS), defined as the time from the date of pathological diagnosis to the date of death from any cause or the last follow-up. The final follow-up date for this study was January 24, 2019.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics version 22.0. Normally distributed continuous data were compared using independent sample *t*-tests, while categorical variables were presented as numbers (percentages) and compared using the chi-square test. Overall survival rates were estimated using the Kaplan-Meier method, and differences between groups were compared with the Log rank test. Univariate and multivariate analyses were performed using the Cox proportional hazards regression model to identify independent prognostic factors. The primary objective of this study was to identify prognostic factors available at the preoperative decision-making point. However, to comprehensively evaluate the prognostic landscape and to determine whether definitive pathological findings provide independent information beyond the preoperative assessment, we also included key postoperative pathological variables (eg, tumor differentiation grade, lymph node status) in our multivariate Cox regression model This approach allows us to validate the preoperative clinical judgment and to distinguish factors known preoperatively from those that add prognostic value after surgery, while the study's core remains centered on preoperatively ascertainable information. All statistical tests were two-sided, and a P-value of less than 0.05 was considered statistically significant.

Results

Patient Demographics and Clinicopathologic Characteristics

A total of 1452 patients with pathologically confirmed colorectal cancer were included in this study. The cohort consisted of 855 men (58.9%) and 597 women (41.1%), with a median age of 58 years (range, 13–92 years). The demographic and clinicopathological characteristics of the entire cohort are summarized in Table 1 and illustrated in Figure 1 and Table 2.

Table 1 Multivariate Analysis of the Prognostic Significance of Age, Differentiation, Neurological Invasion, Vascular Tumor Embolus, Clinical Stages, CEA, and Metastasis in CRC Patients

Characteristics	P	HR	95% CI
Age	0.002*	1.276	1.096–1.487
Differentiation	0.010*	1.094	1.021–1.172
Neurological Invasion	0.254	1.193	0.881–1.615
Vascular tumor embolus	0.672	0.938	0.696–1.263
Clinical stages	0.389	0.958	0.870–1.056
CEA	0.001*	1.072	1.029–1.117
Metastasis	<0.01*	25.779	16.758–39.656

Note: *P<0.05.
Abbreviations: HR, Hazard Ratio; CI, confidence interval.

The majority of tumors were located in the rectum (754 patients, 51.9%), followed by the left colon (325 patients, 22.4%) and the right colon (296 patients, 20.4%). Tumor location was not specified in 77 patients (5.3%). The mean tumor diameter was 4.36 cm, with most tumors (1007 patients, 69.4%) measuring between 2 cm and 5 cm. Histopathological examination confirmed all lesions as adenocarcinoma. Most tumors were moderately differentiated (1027 patients, 70.7%), while 79 (5.4%) and 213 (14.7%) were well and poorly differentiated, respectively. Tumor deposits were present in 185 patients (12.7%). Perineural invasion and vascular invasion were identified in 311 (21.4%) and 255 (17.5%) patients, respectively. The surgical margins were negative in the vast majority of cases (1431 patients, 98.5%). According to the AJCC 8th edition staging system, the distribution was as follows: Stage I, 196 patients (13.5%); Stage II, 440 (30.3%); Stage III, 491 (33.8%); and Stage IV, 172 (11.8%). Preoperative carcinoembryonic antigen (CEA) levels were elevated in 156 patients (10.7%) and within the normal range in 641 (44.1%). Regarding treatment modalities, 685 patients (47.2%) received adjuvant chemotherapy. A smaller proportion underwent neoadjuvant chemotherapy (16 patients, 1.1%) or chemoradiation (66 patients, 4.5%) (Table 2).

Prognostic Factors Affecting Overall Survival in the Entire Cohort

The mean follow-up duration for the cohort was 22.5 months (range: 0.2–48.3 months). During the follow-up period, 27 patients (1.9%) were lost to contact. At the last follow-up, 144 patients (9.9%) had died, 141 (9.7%) were alive with disease, and 1167 (80.4%) were alive without evidence of disease (Table 2).

Univariate analysis identified several clinicopathological variables significantly associated with overall survival (OS), including age ($P < 0.001$), Tumor size ($P < 0.001$), grade of differentiation ($P < 0.001$), Tumor deposit ($P < 0.001$), Neurological invasion ($P < 0.001$), Vascular tumor emboli ($P < 0.001$), lymph node invasion ($P < 0.001$), Surgical Margin ($P < 0.001$), clinical stage ($P < 0.001$), Primary site ($P < 0.001$), preoperative CEA levels ($P < 0.001$), treatment modality ($P < 0.001$), distant metastasis ($P < 0.001$) and Recurrence ($P < 0.001$) (Table 2). However, multivariate Cox regression analysis demonstrated that only age (Hazard Ratio [HR] = 1.276, 95% CI: 1.096–1.487, $P = 0.002$), grade of differentiation (HR = 1.094, 95% CI: 1.021–1.172, $P = 0.010$), preoperative CEA levels (HR = 1.072, 95% CI: 1.029–1.117, $P = 0.001$), and distant metastasis (HR = 25.779, 95% CI: 16.758–39.656, $P < 0.001$) were independent predictors of mortality (Table 1).

Survival Analysis

Kaplan-Meier survival curves further illustrated the relationship between OS and significant clinicopathologic features (Figure 2). Patients aged ≥75 years exhibited significantly poorer OS compared to younger age groups ($P < 0.01$). Similarly, OS was significantly lower in patients with poorly differentiated tumors compared to those with well-differentiated tumors ($P = 0.045$), and in patients with elevated preoperative CEA levels compared to those with normal levels ($P < 0.01$). Moreover, the presence of liver, bone, or abdominal metastasis was associated with significantly worse survival outcomes ($P < 0.01$, $P = 0.020$, and $P = 0.003$, respectively) (Table 3).

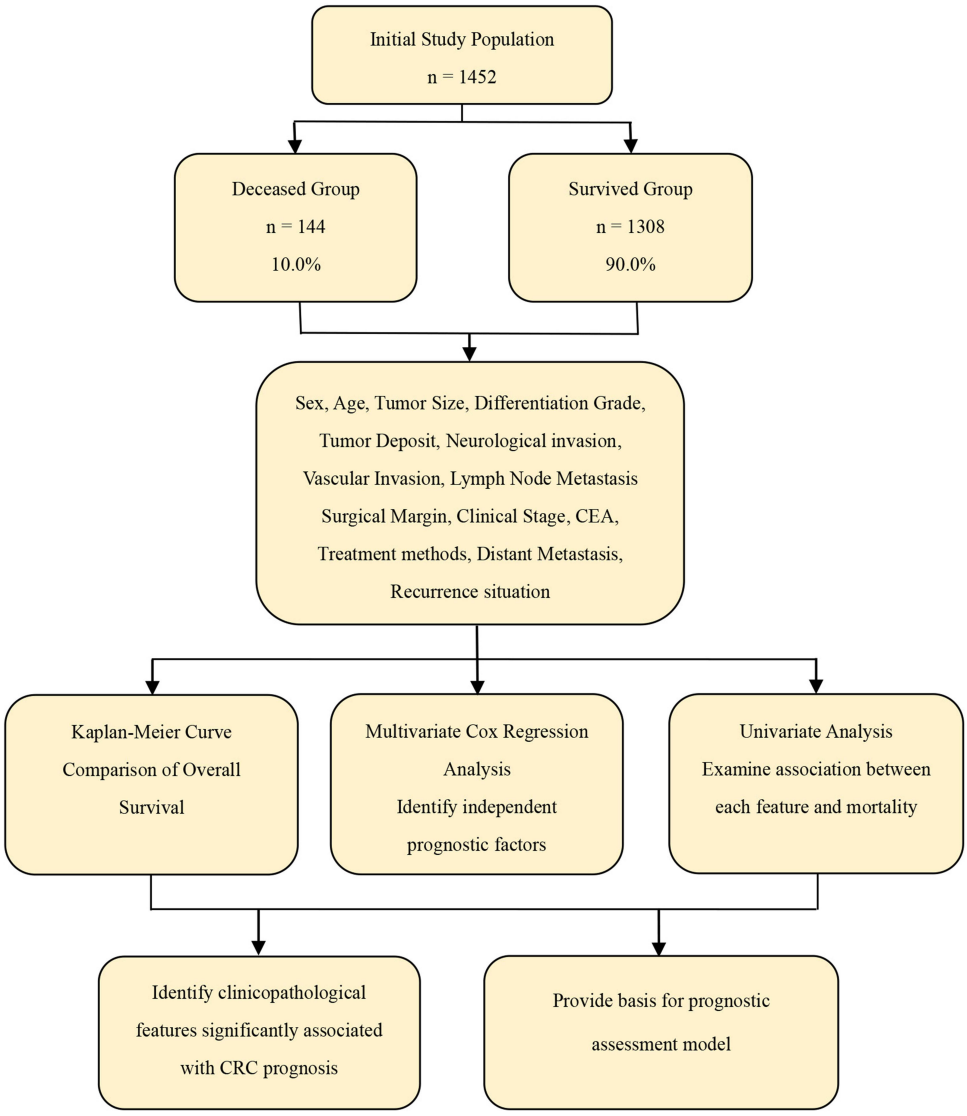

Figure 1 Flowchart of patient selection and study design. The diagram illustrates the process of screening, inclusion, exclusion, and stratification of colorectal cancer patients in this retrospective cohort study. Arrows indicate the direction of patient flow.

Subgroup Analysis by Primary Tumor Location

To assess whether risk factors for postoperative mortality differ by tumor location, we performed multivariate logistic regression analyses stratified by colon cancer (n = 698) and rectal cancer (n = 754) subgroups (Table 4).

In colon cancer, after adjustment for all covariates, age ≥ 75 years (OR = 4.961, 95% CI: 1.874–13.130, P = 0.001) and presence of metastasis (OR = 37.029, 95% CI: 20.17–67.98, P < 0.001) were the strongest independent predictors of increased mortality. Additionally, elevated preoperative CEA (OR = 6.067, 95% CI: 2.954–12.458, P < 0.001), advanced

Table 2 Clinicopathological Features of Patients with CRC and Their Correlation with Mortality

Characteristics	Overall (n=1452)	Survival (n=1308)	Mortality (n=144)	P-value	OR	95% CI
Gender				0.567	0.902	0.634–1.284
Male	855 (58.9%)	767	88	NE	NE	NE
Female	597 (41.1%)	541	56	NE	NE	NE

(*Continued*)

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Table 2 (Continued).

Characteristics	Overall (n=1452)	Survival (n=1308)	Mortality (n=144)	P-value	OR	95% CI
Age (year)				<0.001*	1.654	1.336–2.047
≤44	166 (11.4%)	154	12	Ref.	Ref.	Ref.
45–54	399 (27.5%)	376	23	0.512	0.785	0.381–1.617
55–64	441 (30.4%)	400	41	0.422	1.315	0.673–2.570
65–74	329 (22.7%)	290	39	0.114	1.726	0.878–3.393
≥75	117 (8.0%)	88	29	<0.001*	4.229	2.055–8.705
Tumor size				<0.001*	NE	NE
d<2cm	86 (5.9%)	77	9	Ref.	Ref.	Ref.
2cm≤d<5cm	1007 (69.4%)	910	97	0.802	0.912	0.443–1.876
5cm≤d	325 (22.4%)	292	33	0.932	0.967	0.444–2.106
Unknown	34 (2.3%)	29	5	0.516	1.475	0.456–4.770
Differentiation				<0.001*	1.146	1.029–1.275
Well	79 (5.4%)	74	5	Ref.	Ref.	Ref.
Moderate	1027 (70.7%)	948	79	0.660	1.233	0.485–3.139
Poor	213 (14.7%)	174	39	0.015*	3.317	1.258–8.750
Unknown	133 (9.2%)	112	21	0.050	2.775	1.002–7.684
Tumor deposit				<0.001*	NE	NE
Absent	1095 (75.4%)	1015	80	Ref.	Ref.	Ref.
Present	185 (12.7%)	146	39	<0.001*	3.366	2.212–5.123
Unknown	172 (11.9%)	147	25	0.002*	2.173	1.342–3.516
Neurological invasion				<0.001*	NE	NE
Absent	1104 (76.0%)	1005	99	Ref.	Ref.	Ref.
Present	311 (21.4%)	269	42	0.019*	1.585	1.078–2.330
Unknown	37 (2.5%)	34	3	0.857	0.857	0.270–2.969
Vascular tumor emboli				<0.001*	NE	NE
Absent	1155 (79.5%)	1057	98	Ref.	Ref.	Ref.
Present	255 (17.5%)	212	43	<0.001*	2.188	1.485–3.224
Unknown	42 (2.9%)	39	3	0.759	0.83	0.252–2.734
Lymph node invasion				<0.001*	NE	NE
0	762 (52.5%)	723	39	Ref.	Ref.	Ref.
1–3	364 (25.1%)	323	41	<0.001*	2.353	1.489–3.719
4–6	125 (8.6%)	107	18	<0.001*	3.119	1.721–5.650
≥7	127 (8.7%)	94	33	<0.001*	6.508	3.904–10.848
Unknown	74 (5.1%)	61	13	<0.001*	3.951	2.002–7.798
Surgical Margin				<0.001*	NE	NE
Uninvolved	1431 (98.5%)	1292	139	Ref.	Ref.	Ref.
Involved	17 (1.2%)	13	4	0.069	2.86	0.920–8.891
Unknown	4 (0.3%)	3	1	0.329	3.098	0.320–29.988
Clinical stages				<0.001*	NE	NE
Stage I	196 (13.5%)	192	4	Ref.	Ref.	Ref.
Stage II	440 (30.3%)	418	22	0.092	2.526	0.859–7.431
Stage III	491 (33.8%)	437	54	0.001*	5.931	2.118–16.608
Stage IV	172 (11.8%)	127	45	<0.001*	17.008	5.970–48.45
Unknown	153 (10.5%)	134	19	0.001*	6.806	2.264–20.457
Primary site				<0.001*	NE	NE
Right colon	296 (20.4%)	267	29	Ref.	Ref.	Ref.
Left colon	325 (22.4%)	285	40	0.321	0.774	0.466–1.284
Rectal cancer	754 (51.9%)	691	63	0.044*	0.650	0.427–0.988
Unknown	77 (5.3%)	65	12	0.442	1.315	0.654–2.646

(*Continued*)

Table 2 (Continued).

Characteristics	Overall (n=1452)	Survival (n=1308)	Mortality (n=144)	P-value	OR	95% CI
CEA				<0.001*	NE	NE
Normal	641 (44.1%)	611	30	Ref.	Ref.	Ref.
High	156 (10.7%)	128	28	<0.001*	4.455	2.573–7.715
Unknown	655 (45.1%)	569	86	<0.001*	3.078	2.001–4.737
Treatment				0.010*	NE	NE
Neoadjuvant chemotherapy	16(1.1%)	12	2	Ref.	Ref.	Ref.
Chemoradiation	66 (4.5%)	62	4	0.385	0.452	0.075–2.715
Radiotherapy	2 (0.1%)	1	1	0.225	7	0.302–162.204
Chemotherapy	685 (47.2%)	639	46	0.374	0.504	0.111–2.285
Unknown	683 (47.0%)	592	91	0.924	1.076	0.241–4.812
Metastasis				<0.001*	28.660	15.546–52.837
Absent	1289 (88.8%)	1187	102	Ref.	Ref.	Ref.
Liver	67 (4.16%)	44	23	<0.010*	4.151	2.101–8.200
Lung	27 (1.85%)	22	5	0.262	2.247	0.546–9.245
Bone	14 (0.96%)	10	4	0.001*	6.858	2.135–22.030
Abdomen	21 (1.44%)	15	6	0.313	2.074	0.503–8.547
Pelvic cavity	17 (1.17%)	15	2	0.622	1.647	0.227–11.948
Other	2 (0.13%)	2	0	0.969	0.000	0.000–1.090E+181
Multiple	13 (0.89%)	11	2	0.375	2.454	0.338–17.801
Unknown	2 (0.13%)	2	0	0.969	0.000	0.000–1.090E+181
Recurrence				<0.001*	NE	NE
Absent	1171 (80.6%)	1067	104	Ref.	Ref.	Ref.
Present	45 (3.1%)	37	8	0.048*	2.218	1.006–4.889
Unknown	236 (16.2%)	204	32	0.028*	1.609	1.054–2.458

Notes: Data are presented as n (%) unless otherwise specified. *P < 0.05 was considered statistically significant. OR for Age represents the trend per year increase, derived from univariate logistic regression with age as a continuous variable. Left colon includes descending colon and sigmoid colon; right colon includes cecum, ascending colon, and transverse colon. Metastasis indicates metachronous lesions detected during follow-up; "Other" includes kidney and chest metastases; "Multiple" indicates ≥2 metastatic sites. P-values for categorical variables were calculated using Chi-square test or Fisher's exact test, as appropriate. All ORs and 95% CIs were derived from univariate logistic regression models. Reference groups were selected based on clinical relevance and sample size.
Abbreviations: OR, odds ratio; CI, confidence interval; Ref., reference; NE, not estimable due to sparse data.

lymph node involvement (≥7 positive nodes: OR = 2.639, 95% CI: 1.147–6.069, P = 0.022), neural invasion (OR = 1.822, 95% CI: 1.101–3.016, P = 0.020), vascular tumor emboli (OR = 2.731, 95% CI: 1.624–4.594, P < 0.001), and clinical stage III (OR = 19.525, 95% CI: 2.548–149.599, P = 0.004) were also independently associated with higher mortality. Tumor differentiation grade, tumor deposit, and other clinical stages did not remain significant in this subgroup (all P > 0.05) (Table 4).

In rectal cancer, a distinct risk pattern emerged. Lymph node involvement showed a strong, graded association with mortality: compared with node-negative patients, those with 1–3 positive nodes (OR = 2.968, 95% CI: 1.409–6.250, P = 0.004), 4–6 nodes (OR = 4.771, 95% CI: 1.948–11.684, P = 0.001), and ≥7 nodes (OR = 11.131, 95% CI: 5.273–23.501, P < 0.001) had progressively higher odds of death. Metastasis (OR = 1.292, 95% CI: 1.095–1.526, P < 0.001), poor tumor differentiation (OR = 4.554, 95% CI: 1.009–20.557, P = 0.049), tumor deposit (present: OR = 4.384, 95% CI: 2.372–8.104, P < 0.001; unknown: OR = 3.531, 95% CI: 1.783–6.992, P < 0.001), and advanced clinical stage (stage II: OR = 5.009, 95% CI: 1.482–16.933, P = 0.010; stage III: OR = 14.824, 95% CI: 4.274–51.407, P < 0.001; stage IV: OR = 6.545, 95% CI: 1.716–24.964, P = 0.006) were also independently associated with higher mortality. In contrast, elevated preoperative CEA did not reach statistical significance in rectal cancer (OR = 2.409, 95% CI: 0.947–6.129, P = 0.065). Age, neural invasion, and vascular tumor emboli were not significant predictors in this subgroup (all P > 0.05) (Table 4).

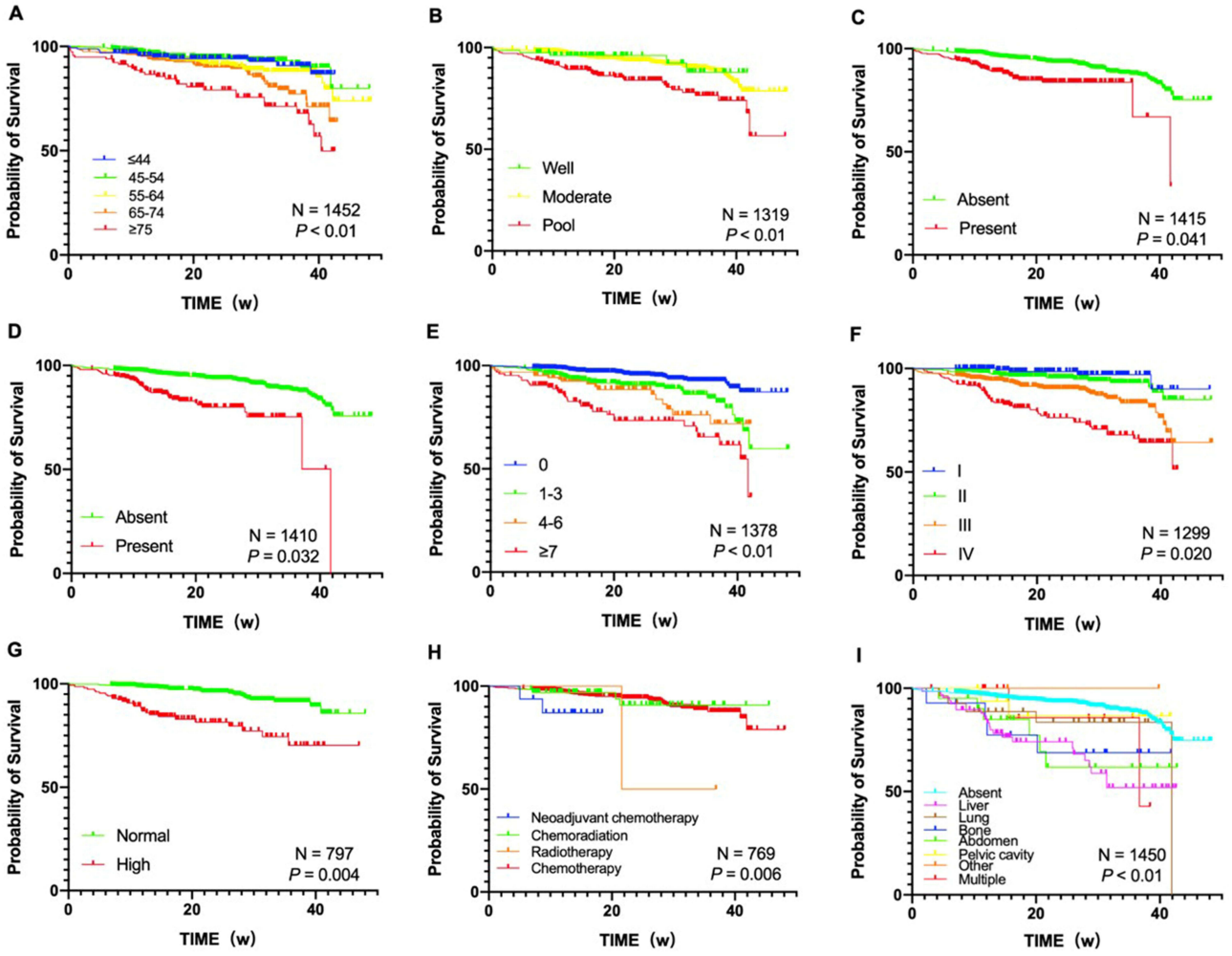

Figure 2 The relationship between overall survival and clinicopathologic features. Kaplan-Meier curves showing the impact of age (**A**), grade of differentiation (**B**), neural invasion (**C**), vascular tumor emboli (**D**), lymph node invasion (**E**), clinical stage of the disease (**F**), preoperative CEA level (**G**), treatments (**H**), and metastasis (**I**) on the overall survival of study patients. TIME means the weeks from diagnosis to the last follow-up or death.

These subgroup analyses reveal distinct prognostic profiles between colon and rectal cancers: while metastasis consistently predicts higher mortality in both sites, advanced age and elevated CEA dominate in colon cancer, whereas lymph node burden, poor differentiation, and tumor deposit are more prominent in rectal cancer (Table 4).

Table 3 Colorectal Cancer Mortality According to Different Groups in CRC Patients

	P	OR	95% CI
Age group			
≤44	Ref.	Ref.	Ref.
45–54	0.796	0.912	0.453–1.834
55–64	0.334	1.274	0.722–2.615
65–74	0.035*	2.011	1.052–3.844
≥75	<0.01*	3.812	1.944–7.475

(*Continued*)

Table 3 (Continued).

	P	OR	95% CI
Differentiation			
Well	Ref.	Ref.	Ref.
Moderate	0.820	1.111	0.450–2.743
Pool	0.045*	2.590	1.020–6.577
Unknown	0.055	2.602	0.981–6.902
CEA			
Normal	Ref.	Ref.	Ref.
High	<0.01*	4.594	2.743–7.693
Unknown	<0.01*	2489	1.641–3.776
Metastasis			
Absent	Ref.	Ref.	Ref.
Liver	<0.01*	4.370	2.777–6.878
Lung	0.082	2.221	0.905–5.454
Bone	0.020*	3.287	1.209–8.933
Abdomen	0.003*	3.523	1.545–8.032
Pelvic cavity	0.945	1.051	0.259–4.268
Other	0.965	0.000	0.000–8.034E+171
Multiple	0.230	2.358	0.581–9.565
Unknown	0.975	0.000	0.000–4.325E+250

Notes: Within each variable, the first category served as the reference group. OR and p-value for each category reflect the comparison with the reference category within the same variable. *P < 0.05.
Abbreviations: OR, odds ratio; CI, confidence interval; Ref., reference.

Table 4 Subgroup Analysis of Patients with Colon Cancer and Rectal Cancer

	Colon Cancer			Rectal Cancer		
	P-value	OR	95% CI	P-value	OR	95% CI
Age	<0.001*	NE	NE	<0.001*	NE	NE
≤44	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
45–54	0.558	1.349	0.496–3.670	0.131	0.444	0.155–1.272
55–64	0.174	1.915	0.751–4.885	0.765	0.864	0.330–2.258
65–74	0.058	2.492	0.969–6.413	0.792	1.139	0.498–3.166
≥75	0.001*	4.961	1.874–13.130	0.075	0.075	0.432–3.007
Grade of differentiation	<0.001*	NE	NE	<0.001*	NE	NE
Well	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Moderate	0.970	0.976	0.286–3.330	0.525	1.603	0.374–6.869
Poor	0.166	2.462	0.688–8.809	0.049	4.554	1.009–20.557
Unknown	0.081	3.181	0.866–11.691	0.634	1.527	0.267–8.737
Tumor deposit	<0.001*	NE	NE	<0.001*	NE	NE
Absent	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Present	<0.001*	2.844	1.579–5.124	<0.001*	4.384	2.372–8.104
Unknown	0.323	1.421	0.708–2.852	<0.001*	3.531	1.783–6.992
Neural invasion	<0.001*	NE	NE	<0.001*	NE	NE
Absent	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Present	0.020	1.822	1.101–3.016	0.455	1.262	0.686–2.322
Unknown	0.254	2.118	0.584–7.679	0.986	0	0-Inf

(*Continued*)

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Table 4 (Continued).

	Colon Cancer			Rectal Cancer		
	P-value	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**
Vascular tumor emboli	<0.001*	NE	NE	<0.001*	NE	NE
Absent	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Present	<0.001*	2.731	1.624–4.594	0.077	1.705	0.945–3.077
Unknown	0.349	1.832	0.517–6.495	0.985	0	0-Inf
Lymph node invasion	<0.001*	NE	NE	<0.001*	NE	NE
0	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1–3	0.051	1.815	0.997–3.305	0.004	2.968	1.409–6.250
4–6	0.200	1.741	0.745–4.065	0.001	4.771	1.948–11.684
≥7	0.022	2.639	1.147–6.069	<0.001	11.131	5.273–23.501
Unknown	<0.001*	5.461	2.288–13.035	0.168	2.499	0.679–9.190
Metastasis	<0.001*	37.029	20.17–67.980	<0.001*	1.292	1.095–1.526
CEA	<0.001*	NE	NE	<0.001*	NE	NE
Normal	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
High	<0.001	6.067	2.954–12.458	0.065	2.409	0.947–6.129
Unknown	0.002	2.626	1.430–4.822	<0.001*	3.527	1.912–6.506
Clinical stage	<0.001*	NE	NE	<0.001*	NE	NE
Normal	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
I	0.256	3.268	0.423–25.232	0.526	1.574	0.387–6.401
II	0.059	6.957	0.926–52.276	0.010	5.009	1.482–16.933
III	0.004	19.525	2.548–149.599	<0.001*	14.824	4.274–51.407
IV	0.067	7.059	0.874–56.983	0.006	6.545	1.716–24.964

Notes: *P < 0.05. This table presents results from separate multivariate logistic regression for colon and rectal cancer subgroups. The reference category for each variable is indicated. Blank cells for colon cancer (CEA, Stage) and some rectal cancer variables in the original table were due to a formatting error; the complete analysis is now shown above. For variables with extremely wide confidence intervals (eg, OR ~ 0), the point estimate should be interpreted with caution.

Abbreviations: OR, odds ratio; CI, confidence interval; Ref., reference category.

Discussion

The findings of this study, which establish a preoperative clinical prognostic model, are complementary to our earlier molecular analysis of a partially overlapping cohort from the same center.[6] While the prior work elucidated the role of specific gene mutations, the current work provides a practical, immediately applicable tool based on readily accessible clinical parameters. Together, these studies offer a more holistic, two-dimensional (clinical and molecular) view of prognosis in CRC patients from Central China, each addressing different clinical questions and decision points in the patient care pathway.

Our findings align with and extend the current understanding of prognostic factors in colorectal cancer. The identification of advanced age, poor tumor differentiation, elevated preoperative CEA levels, and distant metastasis as independent predictors of poor survival is consistent with multiple contemporary studies. A recent large-scale multicenter analysis by Zhang et al involving over 12,000 Chinese CRC patients similarly confirmed that age ≥75 years and poor differentiation remained significant prognostic factors even after adjusting for modern treatment modalities.[21] Furthermore, our results regarding the prognostic value of preoperative CEA align with emerging evidence suggesting that integrating serial CEA measurements with other biomarkers enhances early detection of recurrence and improves risk stratification.[22]

While the individual prognostic factors identified in our study - advanced age, poor tumor differentiation, elevated preoperative CEA, and metastasis - are indeed recognized in the broader literature, the primary novelty and clinical utility of this work lie in their systematic validation and integration within a large, well-defined preoperative cohort from Central China. In the era of precision medicine, confirming the applicability and quantifying the weight of established factors in specific populations and clinical scenarios (here, preoperative decision-making) is a fundamental and necessary

contribution. This study provides a practical, immediately applicable clinical risk model using readily available parameters, addressing a direct need in settings where routine genetic testing may not be feasible at the initial diagnostic point. We acknowledge that incorporating molecular data (eg, KRAS, NRAS, BRAF, MSI status) would provide deeper biological insights As noted, our team has explored such molecular profiles in a related cohort.[6] The logical and critical next step, as suggested, is to integrate the robust clinical model presented here with molecular biomarkers in future studies to construct a multi-dimensional prognostic framework, further advancing personalized management for CRC patients in our region.

The discussion surrounding tumor laterality in CRC prognosis continues to evolve. In our central Chinese cohort, approximately 74.3% of tumors originated from the left side, consistent with general epidemiological patterns. Notably, we found no significant association between tumor laterality and overall survival, a finding supported by a recent Japanese multicenter study of stage I–III colon cancer that reported comparable 5-year disease-free survival rates between left- and right-sided tumors (89.4% vs 88.6%).[23] However, the relationship appears more complex when considering molecular subtypes and specific clinical scenarios. A 2024 analysis of the SEER database by Thompson et al revealed that while there was no overall mortality difference by tumor side, right-sided stage II tumors demonstrated lower mortality risk, whereas right-sided stage III tumors carried significantly higher risk.[24] In metastatic settings, emerging evidence suggests that the prognostic impact of tumor location may be modulated by specific treatment approaches. The Australian study by Price et al demonstrated that left-sided primary tumors were generally associated with longer survival in metastatic CRC, except among patients who underwent complete resection of liver metastases, where the survival difference disappeared.[25] These nuanced findings highlight the importance of considering both tumor biology and treatment context when evaluating the prognostic significance of tumor location.

Several limitations warrant consideration when interpreting our results. First, the retrospective, single-center design inherently carries risks of selection bias and limits generalizability to other populations. Second, this study was designed to focus on preoperative clinical factors and therefore did not incorporate molecular profiling data such as KRAS/NRAS/BRAF status. It is important to note that the molecular characteristics of a subset of this patient population have been previously reported by our group.[6] Third, the median follow-up time of approximately 22 months is relatively short; while suitable for assessing early outcomes, it may not fully capture long-term survival patterns, potentially influencing the survival rates observed. Future studies with extended follow-up are needed. Additionally, we lacked systematic data on patient comorbidities, which are known to significantly influence overall survival outcomes. Future prospective, multi-center studies incorporating comprehensive molecular profiling, detailed treatment records, and comorbidity assessments are essential to validate and extend our findings. Recent advancements in multi-omics approaches and artificial intelligence-based prognostic models offer promising avenues for developing more accurate, individualized risk prediction tools.[26]

Despite these limitations, our study provides valuable real-world evidence from a substantial cohort of CRC patients in central China. The identification of robust preoperative prognostic factors enables improved risk stratification at diagnosis, facilitating more personalized treatment planning and patient counseling. As precision medicine continues to transform oncology, integrating these clinicopathological factors with molecular biomarkers will be essential for optimizing outcomes in CRC patients.

Conclusions

In conclusion, this study establishes that poor tumor differentiation, elevated preoperative CEA levels, distant metastasis, and advanced age (≥75 years) serve as significant indicators of unfavorable prognosis in Chinese colorectal cancer patients. These findings highlight the importance of preoperative assessment and tailored treatment strategies based on specific clinicopathological features. To build upon this foundation, future research should focus on integrating this clinical prognostic model with molecular biomarkers and validating it in prospective, multi-center settings to develop more comprehensive tools for personalized patient management.

Ethical Approval

This study was approved by the Institutional Review Board/Ethics Committee of Tongji Medical College of Huazhong University of Science and Technology (Approval No.2014-041]). This study complies with the Declaration of Helsinki. Due to the retrospective nature of the study and the use of anonymized data, the requirement for informed consent was waived by the ethics committee.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229–263. doi:10.3322/caac.21834
2. Xi Y, Xu P. Global colorectal cancer burden in 2020 and projections to 2040. *Transl Oncol*. 2021;14(10):101174. doi:10.1016/j.tranon.2021.101174
3. Zheng R, Zhang S, Zeng H, et al. Cancer incidence and mortality in China, 2022. *J Natl Cancer Cent*. 2024;4(1):47–53. doi:10.1016/j.jncc.2024.01.006
4. Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2022. *CA Cancer J Clin*. 2025;75(1):12–49.
5. Park JS, Kang H, Park SY, et al. Long-term oncologic outcomes after laparoscopic vs open surgery for patients with colorectal cancer: 10-year follow-up of a randomized clinical trial. *JAMA Surg*. 2024;159(2):155–163.
6. Chang XN, Shang FM, Jiang HY, et al. Clinicopathological features and prognostic value of KRAS/NRAS/BRAF mutations in colorectal cancer patients of central China. *Curr Med Sci*. 2021;41(1):118–126. doi:10.1007/s11596-021-2326-1
7. Brierley JD, Gospodarowicz MK, Wittekind C, et al. *TNM Classification of Malignant Tumours*. 9th ed. Wiley-Blackwell; 2024.
8. Argilés G, Tabernero J, Labianca R, et al. Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2023;34(6):522–538.
9. Benson AB, Venook AP, Al-Hawary MM, et al. Colon cancer, version 3.2024: NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2024;22(2):135–169.
10. Wang X, Liu J, Yang J, et al. Comprehensive molecular characterization of Chinese colorectal cancer patients. *Nat Commun*. 2023;14(1):5132. doi:10.1038/s41467-023-40830-9
11. Van Cutsem E, Cervantes A, Adam R, et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. *Ann Oncol*. 2023;34(4):358–387. doi:10.1016/j.annonc.2022.12.013
12. Xie YH, Chen YX, Fang JY. Comprehensive review of targeted therapy for colorectal cancer. *Signal Transduct Target Ther*. 2023;8(1):120. doi:10.1038/s41392-023-01327-5
13. Li J, Ma X, Chakrabarti J, et al. KRAS mutation and prognosis in colorectal cancer: a multi-center cohort study from China. *Oncogene*. 2024;43(5):612–623.
14. Wang Z, Wang X, Ying J, et al. Molecular profiling and its prognostic value in Chinese colorectal cancer patients: results from a prospective, multicenter study. *Lancet Reg Health West Pac*. 2023;41:100892.
15. Loree JM, Kopetz S. Current companion diagnostics in advanced colorectal cancer. *J Clin Oncol*. 2023;41(12):1359–1369. doi:10.1200/JCO.22.01013
16. Gholami S, Moghbeli M, Kiani J, et al. Clinicopathological and molecular features of colorectal cancer in Middle Eastern populations: a multi-center study. *Oncologist*. 2023;28(4):345–356.
17. Jin K, Ren C, Liu Y, et al. Temporal trends in the incidence and mortality of colorectal cancer in China, 2020–2030: a Bayesian age-period-cohort analysis. *Lancet Public Health*. 2023;8(12):e943–e953. doi:10.1016/S2468-2667(23)00211-6

18. Dilek ON, Kahraman DİA, Kahraman G, et al. Carcinoembryonic antigen in the diagnosis, treatment, and follow-up of focal liver lesions. *World J Gastrointest Surg*. 2024;16(4):999–1007. doi:10.4240/wjgs.v16.i4.999
19. Hong Z, Wang T, Wang W, et al. Proteomic profiling and tumor microenvironment characterization reveal molecular and immunological hallmarks of left-sided and right-sided colon cancer tumorigenesis. *J Proteome Res*. 2023;22(9):2973–2984. doi:10.1021/acs.jproteome.3c00302
20. Idrissi MB, El Bouhaddouti H, Mouaqit O, et al. Left-sided colon cancer and right-sided colon cancer: are they the same cancer or two different entities? *Cureus*. 2023;15(4):e37563. doi:10.7759/cureus.37563
21. Zhang H, Wang R, Li X, et al. Prognostic significance of clinicopathological factors in Chinese colorectal cancer patients: a multicenter retrospective analysis. *J Gastrointest Oncol*. 2024;15(2):567–578.
22. Chen L, Liu Y, Wang J. Dynamic CEA monitoring and its prognostic value in colorectal cancer management. *Cancer Biomarkers*. 2024;39(3):215–225.
23. Tanaka K, Yamaguchi T, Shimada Y. Tumor laterality and survival in stage I-III colon cancer: a multicenter Japanese cohort study. *Ann Surg Oncol*. 2023;30(7):4123–4131. doi:10.1245/s10434-023-13367-w
24. Thompson E, Miller K, White R. Stage-dependent prognostic significance of tumor location in colorectal cancer: a SEER database analysis. *Am J Cancer Res*. 2024;14(1):245–256.
25. Price T, Wong R, Shapiro J. The impact of primary tumor location on survival in metastatic colorectal cancer: an Australian multicenter study. *Eur J Cancer*. 2023;182:112–121.
26. Wang S, Zhang X, Li H. Artificial intelligence in colorectal cancer prognosis: a systematic review. *Nat Commun*. 2024;15(1):2345.