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RESEARCH

Development and validation of cancer-specific survival prediction nomogram for patients with T4 stage colon cancer after surgical resection: a population-based study

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Abstract

Purpose The increasing incidence of colorectal cancer has coincided with a rise in T4 stage colon cancer (CC), yet research on its prognosis remains limited. This study aimed to identify risk factors and develop a nomogram to predict cancer-specific survival (CSS), optimizing treatment strategies for different subgroups.

Methods Using data from the from the Surveillance, Epidemiology, and End Results (SEER) database, we identified risk factors in T4 stage CC patients and created a nomogram to predict CSS. Patients were divided into low- and high-risk groups, and the nomogram was validated. Propensity score matching was used to evaluate the benefits of various therapies across subgroups.

Results Independent risk factors, including T stage, N stage, tumor grade, age, and therapy sequence, were identified through Cox regression analyses and incorporated into the nomogram. The nomogram outperformed the American Joint Committee on Cancer (AJCC) 7th staging system, with a Concordance-index of 0.77 in both training and validation sets. The receiver operating characteristic curves showed area under the curve values of 0.81, 0.77, and 0.75 for 1-, 3-, and 5-year CSS, respectively. Calibration plots confirmed strong alignment between predicted and actual outcomes, and decision curve analysis highlighted the nomogram's superior clinical utility. Chemotherapy significantly improved CSS, while radiation did not. Adjuvant therapy was particularly beneficial in high-risk groups.

Conclusion This study offered a thorough prognostic analysis of T4 stage colon cancer patients and developed nomograms for predicting CSS. Subgroup analyses highlight the potential benefits of various treatment options.

Keywords Colon cancer · Surveillance, Epidemiology, and End Results · T4 stage · Nomogram · Adjuvant therapy

Introduction

The colorectal cancer (CRC) ranks as the second leading cause of cancer-related mortality and the third most prevalent cancer globally. In 2022, there were more than 1.8 million new diagnoses and 881,899 fatalities attributed to the disease [1]. Advances in imaging technology have led to a marked rise in the detection of T4 stage colon cancer (CC) in recent years [2]. Typically, the T4 stage tumor invade deeply into the colon wall, extending into pericolonic tissues and regional lymph nodes, indicating a higher tumor burden and more extensive infiltration [3]. The deeper invasion of these tumors is associated with a poorer prognosis and an elevated risk of both local and distant recurrence [4]. Unlike T1-3 stages, T4 stage is widely regarded as a critical prognostic factor for CC, adversely affecting survival outcomes [5]. The National Comprehensive Cancer Network (NCCN) guidelines advocate for adjuvant chemotherapy in patients with T4 stage CC (without distant metastasis) following curative resection [6]. However, notable variability in clinical outcomes has been observed among patients with T4 stage CC undergoing similar treatments, with survival rates ranging from 15 to 75% [7]. Moreover, recent studies

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indicated that certain patients with T4 stage CC might benefit from neoadjuvant therapy [8]. Additionally, proximal and distal CC exhibited distinct clinical, pathological, biological, and prognostic characteristics due to their different embryologic origins and gut microbiota, influencing their responses to adjuvant therapy [9]. These findings indicate that the existing TNM staging system may not adequately convey prognostic information or the benefits of different therapy options. Therefore, new strategies are essential for better prognostic assessment, enabling personalized therapy and improved survival outcomes for patients with T4 stage CC.

While previous studies showed that survival rates for CRC correlated with factors such as primary tumor site, N stage, and lymphatic invasion, there is currently a lack of appropriate predictive guidelines for the survival of T4 stage CRC patients [10–12]. Furthermore, analyses of various treatment options across different risk groups based on predictive nomograms in T4 stage CC remain limited [13, 14]. Compared with overall survival, cancer-specific survival (CSS) is more closely related to the cancer and may better guide treatment decisions.

This study aimed to leverage data from the Surveillance, Epidemiology, and End Results (SEER) database to identify prognostic factors and create a nomogram for predicting CSS in patients with T4 stage CC. Additionally, we sought to compare various treatment options across subgroups to determine the most effective therapy for T4 stage CC patients.

Methods

Database source and patients selection

This retrospective cohort study analyzed clinicopathological data from CC patients in the SEER database between January 1, 2010, and December 31, 2017, using SEER*Stat 8.4.0.1 software. Data collected included age, race, tumor grade, sex, histological grade, 7th AJCC stages (T, N, M), tumor size, regional nodes examined, treatment sequence (surgery before, after, or without chemoradiotherapy), preoperative carcinoembryonic antigen (CEA) levels, perineural invasion, tumor deposits, and radiotherapy and chemotherapy information. The grade is assessed through pathologic examination or the tumor's differentiation level, with a lower grade indicating a higher differentiation degree. Tumor deposits are defined as microscopic or macroscopic tumor nodules found in the lymphatic drainage area of the primary tumor. The absence of tumor deposits is documented as negative, and similarly, the lack of perineural invasion by the tumor is also recorded as negative. CEA positive is defined as when the serum CEA level exceeds 5 ng/mL.

Inclusion criteria were: (I) patients with primary T4N0-2M0 stage CC; (II) those with CC as the sole primary malignancy; and (III) patients who underwent surgical treatment with complete pathological specimen examination postoperatively. Exclusion criteria included: (I) patients with multiple primary tumors; (II) those reported solely through autopsy or death certificates; (III) patients with incomplete data on any inclusion criteria; (IV) patients under 18 years; and (V) those with zero survival months. Ultimately, 5,942 patients met the criteria, randomized in a 7:3 ratio into a training set of 4,159 patients and a validation set of 1,783 patients (Fig. 1). The validation set was used for internal validation of the nomogram. The primary endpoint was CSS, calculated as the duration from diagnosis to death attributed to cancer or last follow-up. This study utilized publicly available data from the SEER database, with all patient data de-identified prior to collection, thus exempting it from ethics committee approval or informed consent. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study adhered to the TRIPODAI checklist.

Propensity score-matching (PSM)

To mitigate bias and confounding factors between low-risk and high-risk groups among T4 stage CC patients, we used the method of PSM. It accounted for age, sex, race, T stage, N stage, primary tumor site, tumor grade, tumor size, CEA level, perineural invasion, and tumor deposits. Logistic regression was utilized to calculate propensity scores. T4 stage CC patients, regardless of therapy type (including radiation, chemotherapy, and treatment sequence), were matched in a 1:1 ratio using PSM. The PSM analysis was executed utilizing the matching package of R software, employing the 1:1 nearest neighbor matching approach to ensure balanced comparison groups. We compared clinicopathological variables before and after PSM using the chi-squared test to evaluate the effectiveness of the matching process.

Statistics analysis

The Mann–Whitney U test was used to evaluate differences in continuous variables, while categorical data were analyzed using the chi-squared test. Odds ratios (OR) and 95% confidence intervals (CI) were determined through univariate and multivariate Cox regression analyses. Independent prognostic factors with *P*-values below 0.05 in the multivariate Cox model were incorporated into a nomogram, creating a visual tool for predicting 1-year, 3-year, and 5-year survival rates. Hazard ratios (HR) and their 95% CIs were reported for all findings. The optimal cutoff for tumor size was established using the X-tile software (version 3.6.1, Yale University, New Haven, Connecticut). Model performance

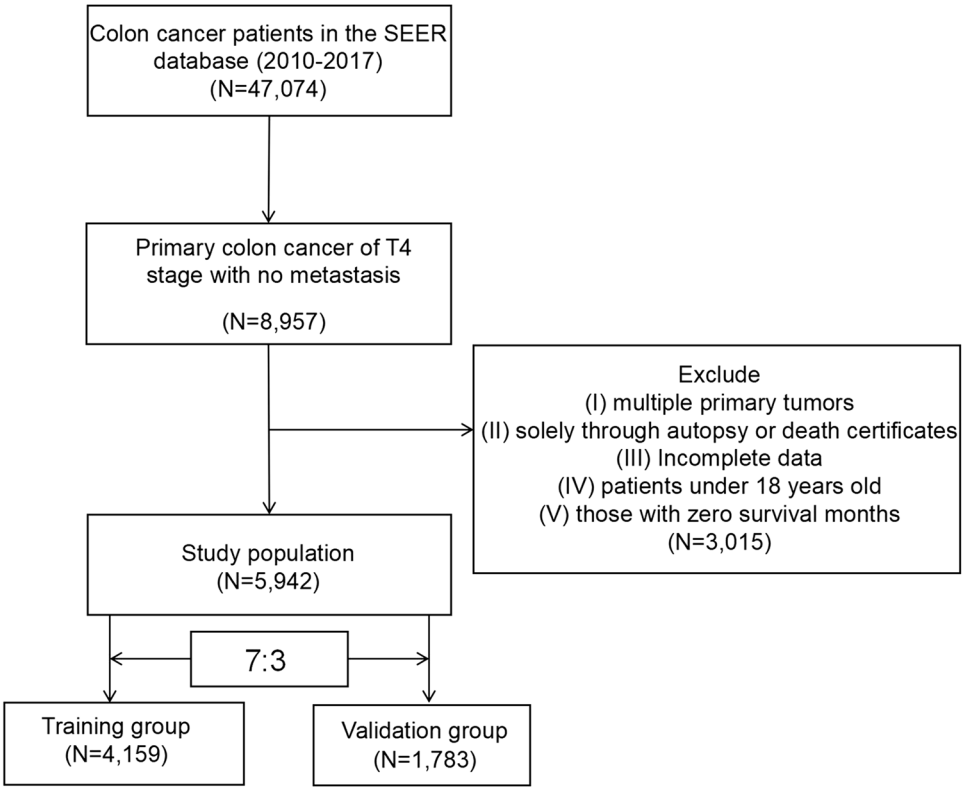


Fig. 1 The selection of patient in the study. SEER, Surveillance, Epidemiology, and End Results

was assessed using the concordance index (C-index) and receiver operating characteristic (ROC) curves, with the area under the curve (AUC) calculated. Calibration plots were utilized to compare predicted and actual survival at 1, 3, and 5 years. The clinical utility of the prediction model was evaluated using decision curve analysis (DCA). Finally, the training set was categorized into two risk groups according to their total points. The Kaplan–Meier method, along with the log-rank test, was utilized to assess differences in CSS between the various subgroups. Statistical analyses were conducted using SPSS 22.0 (International Business Machines Corporation, Armonk, New York) and R version 4.2.0 software.

Results

Basic characteristics of the patients

Our study included a total of 5,942 patients diagnosed with T4 stage CC, divided into a training set of 4,159 patients and a validation set of 1,783 patients. The demographic and clinical characteristics of patients with T4 stage CC in both the training and validation cohorts are presented in Table 1. The patient cohort exhibited a median age of 65 years, accompanied by a median survival of 39 months. In the complete patient cohort, all individuals underwent radical surgery, with the majority (87.33%) undergoing sufficient regional nodes examination. Chemotherapy was administered to a total of 3,661 patients (61.61%), whereas radiotherapy was provided to 281 patients (4.73%). Additionally, only 101 patients (1.70%) received neoadjuvant therapy before surgery, while 3,569 patients (60.06%) underwent adjuvant therapy following their surgeries. Additionally, the Mann–Whitney U and chi-squared tests indicated no significant differences in feature distributions between the training and validation sets.

Prognostic factors for CSS

To identify prognostic indicators for CSS, we conducted univariate and multivariate Cox regression analyses within the training set (Table 2). These analyses revealed several risk factors for predicting CSS, including age at diagnosis, tumor histology, T stage, N stage, tumor grade, CEA level, perineural invasion, tumor deposits, tumor site, treatment sequence, and regional node examination.

Specifically, the T4b stage (HR: 1.20; 95% CI: 1.08–1.33), N1 stage (HR: 1.61; 95% CI: 1.41–1.83), N2 stage (HR: 2.76; 95% CI: 2.41–3.17), poor tumor grade (HR: 1.49; 95% CI: 1.34–1.65), older age (HR: 1.71; 95% CI: 1.54–1.90), tumor histology (HR: 1.30; 95% CI: 1.15–1.47), positive CEA levels (HR: 1.40; 95% CI: 1.27–1.54), tumor deposits (HR: 1.36; 95% CI: 1.22–1.53), right side tumors

Table 1 Baseline characteristics of patients in training and test sets

	Total	Training set	Test set	*P* value
	N = 2,501	*N* = 1,750	*N* = 751	
Age, *n* (%):				0.078
< 60 years	1,079 (43.14)	735 (42.00)	344 (45.81)	
≥ 60 years	1,422 (56.86)	1,015 (58.00)	407 (54.19)	
Sex, *n* (%):				0.103
Female	1,064 (42.54)	726 (41.49)	338 (45.01)	
Male	1,437 (57.46)	1,024 (58.51)	413 (54.99)	
Race, *n* (%):				0.811
White	2,041 (81.61)	1,426 (81.49)	615 (81.89)	
Others	460 (18.39)	324 (18.51)	136 (18.11)	
Grade, *n* (%):				0.671
I/II	2,300 (91.96)	1,612 (92.11)	688 (91.61)	
III/IV	201 (8.04)	138 (7.89)	63 (8.39)	
Histology, *n* (%):				0.285
Adenocarcinoma	2,442 (97.64)	1,705 (97.43)	737 (98.14)	
Others	59 (2.36)	45 (2.57)	14 (1.86)	
T stage, *n* (%):				0.365
T1	1,171 (46.82)	809 (46.23)	362 (48.20)	
T2	1,330 (53.18)	941 (53.77)	389 (51.80)	
Surgery options, *n*(%)				0.136
Local resection	550 (21.99)	399 (22.80)	151 (20.11)	
Radical resection	1,951 (78.01)	1,351 (77.20)	600 (79.89)	
Radiation, *n* (%):				0.921
No	1,925 (76.97)	1,346 (76.91)	579 (77.10)	
Yes	576 (23.03)	404 (23.09)	172 (22.90)	
Chemotherapy, *n* (%):				0.972
No	1,926 (77.01)	1,348 (77.03)	578 (76.96)	
Yes	575 (22.99)	402 (22.97)	173 (23.04)	
Treatment sequence:				0.876
Only surgery	1,925 (76.97)	1,347 (76.97)	578 (76.96)	
Adjuvant therapy	165 (6.60)	118 (6.74)	47 (6.26)	
Neoadjuvant therapy	411 (16.43)	285 (16.29)	126 (16.78)	
CEA[a], *n* (%):				0.892
Negative	1,985 (79.37)	1,387 (79.26)	598 (79.63)	
Positive	516 (20.63)	363 (20.74)	153 (20.37)	
Perineural invasion, *n* (%):				0.681
No	2,443 (97.68)	1,708 (97.60)	735 (97.87)	
Yes	58 (2.32)	42 (2.40)	16 (2.13)	
Tumor size, *n* (%)				0.852
< 18 mm	889 (35.55)	620 (35.43)	269 (35.82)	
≥ 18 mm	1,612 (64.45)	1,130 (64.57)	482 (64.18)	

a, carcinoembryonic antigen

(HR: 1.11; 95% CI: 1.01–1.24), and perineural invasion (HR: 1.27; 95% CI: 1.14–1.42) were all associated with poorer CSS. Conversely, adequate regional node examination (HR: 0.68; 95% CI: 0.60–0.78), adjuvant therapy (HR: 0.43; 95% CI: 0.39–0.48), and neoadjuvant therapy (HR: 0.58; 95% CI: 0.39–0.87) were linked to improved CSS prognosis. Furthermore, given that right-sided tumors are recognized as a risk factor, we compared the clinical features of T4 stage CC patients between left-sided and right-sided cases (Table S1). Patients with left-sided tumors exhibited better survival outcomes compared to those with right-sided tumors. The left-sided group was characterized by a younger age, a higher proportion of males, better tumor grade, more cases of adenocarcinoma, fewer cases of lymph

Table 2 Univariate and multivariate Cox analysis for cancer-specific survival of patients in the training set

Characteristics	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P*-value	Hazard ratio (95% CI)	*P*-value
Age (year)				
< 60	Ref		Ref	
≥ 60	2.12 (1.92 ~ 2.34)	< 0.001*	1.71 (1.54 ~ 1.90)	< 0.001*
Sex				
Female	Ref			
Male	0.90 (0.82 ~ 0.99)	0.029*	0.97 (0.86 ~ 1.09)	0.592
Race				
White	Ref			
Others	0.97 (0.86 ~ 1.09)	0.590		
Tumor Site				
Left	Ref		Ref	
Transverse colon	1.12 (0.94 ~ 1.33)	0.204		
Right	1.34 (1.21 ~ 1.48)	< 0.001*	1.11 (1.01 ~ 1.24)	0.046*
Grade				
Well and moderate	Ref		Ref	
Poor and undifferentiated	1.85 (1.68 ~ 2.04)	< 0.001*	1.49 (1.34 ~ 1.65)	< 0.001*
Histology				
Adenocarcinoma	Ref		Ref	
Others	1.37 (1.21 ~ 1.55)	< 0.001*	1.30 (1.15 ~ 1.47)	< 0.001*
T stage				
T4a	Ref		Ref	
T4b	1.06 (0.96 ~ 1.17)	< 0.001*	1.20 (1.08 ~ 1.33)	0.002*
N stage				
N0	Ref		Ref	
N1	1.41 (1.24 ~ 1.59)	< 0.001*	1.61 (1.41 ~ 1.83)	< 0.001*
N2	2.45 (2.18 ~ 2.76)	< 0.001*	2.76 (2.41 ~ 3.17)	< 0.001*
Regional nodes examined				
< 12	Ref		Ref	
≥ 12	0.67 (0.59 ~ 0.77)	< 0.001*	0.68 (0.60 ~ 0.78)	< 0.001*
Radiation				
No	Ref			
Yes	0.73 (0.58 ~ 0.93)	0.011*	1.13 (0.88 ~ 1.45)	0.352
Chemotherapy				
No/unknown	Ref		Ref	
Yes	0.50 (0.45 ~ 0.55)	< 0.001*	1.97 (0.28 ~ 14.13)	0.499
Treatment sequence				
Only surgery	Ref		Ref	
adjuvant	0.49 (0.45 ~ 0.54)	< 0.001*	0.43 (0.39 ~ 0.48)	< 0.001*
neoadjuvant	0.57 (0.38 ~ 0.85)	< 0.006*	0.58 (0.39 ~ 0.87)	0.042*
CEA [a]				
Negative	Ref		Ref	
Positive	1.56 (1.42 ~ 1.72)	< 0.001*	1.40 (1.27 ~ 1.54)	0.008*
Perineural invasion				
No	Ref		Ref	
Yes	1.54 (1.39 ~ 1.71)	< 0.001*	1.27 (1.14 ~ 1.42)	< 0.001*
Tumor deposits				
No	Ref		Ref	
Yes	1.83 (1.65 ~ 2.03)	< 0.001*	1.36 (1.22 ~ 1.53)	< 0.001*

Table 2 (continued)

Characteristics	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P*-value	Hazard ratio (95% CI)	*P*-value
Tumor size (mm)				
< 38	Ref		Ref	
≥ 38	1.15 (1.02 ~ 1.30)	< 0.018*	1.12 (0.99 ~ 1.27)	0.078

a, CEA, carcinoembryonic antigen

node metastasis, a greater likelihood of receiving chemoradiotherapy, and smaller tumor size, although they had fewer regional nodes examined. In addition, a comparative analysis of CSS across three distinct tumor locations was conducted (Figure S1). The findings revealed that the left-sided group exhibited superior CSS compared with the right and transverse groups. However, no significant disparities were observed between the right-sided and the transverse groups.

Development and validation of a prognostic nomogram

Using the multivariate analysis results from the training set, we created a nomogram to predict CSS in T4 stage CC patients (Fig. 2). Each variable was assigned a score from 0 to 100 based on its impact on model accuracy. By summing the scores for each patient, we derived a total point value to estimate the likelihood of 1-year, 3-year, and 5-year CSS. Notably, higher scores indicated worse prognoses. In the training set, the nomogram showed a C-index of 0.77 (95% CI: 0.74–0.79), significantly higher than the 7th AJCC staging system (C-index 0.61, 95% CI: 0.59–0.62). ROC analysis showed AUC values of 0.81, 0.77, and 0.75 for 1-year, 3-year, and 5-year CSS, respectively (Figure S2A-S2C). Calibration plots for 1-year, 3-year, and 5-year CSS confirmed good agreement between predicted and observed outcomes (Figure S3A-S3C). DCA curves indicated superior clinical utility compared to the 7th AJCC staging system (Figure S4A). Validation in the independent validation set showed a C-index of 0.77 (95% CI: 0.73–0.80), with AUC values of 0.81, 0.77, and 0.77 for 1-year, 3-year, and 5-year CSS, respectively (Figure S2A-S2C). Calibration plots (Figure S3D-S3F) and DCA (Figure S4B) in the testing set confirmed similar findings to the training set, demonstrating improved clinical utility over the 7th AJCC staging system.

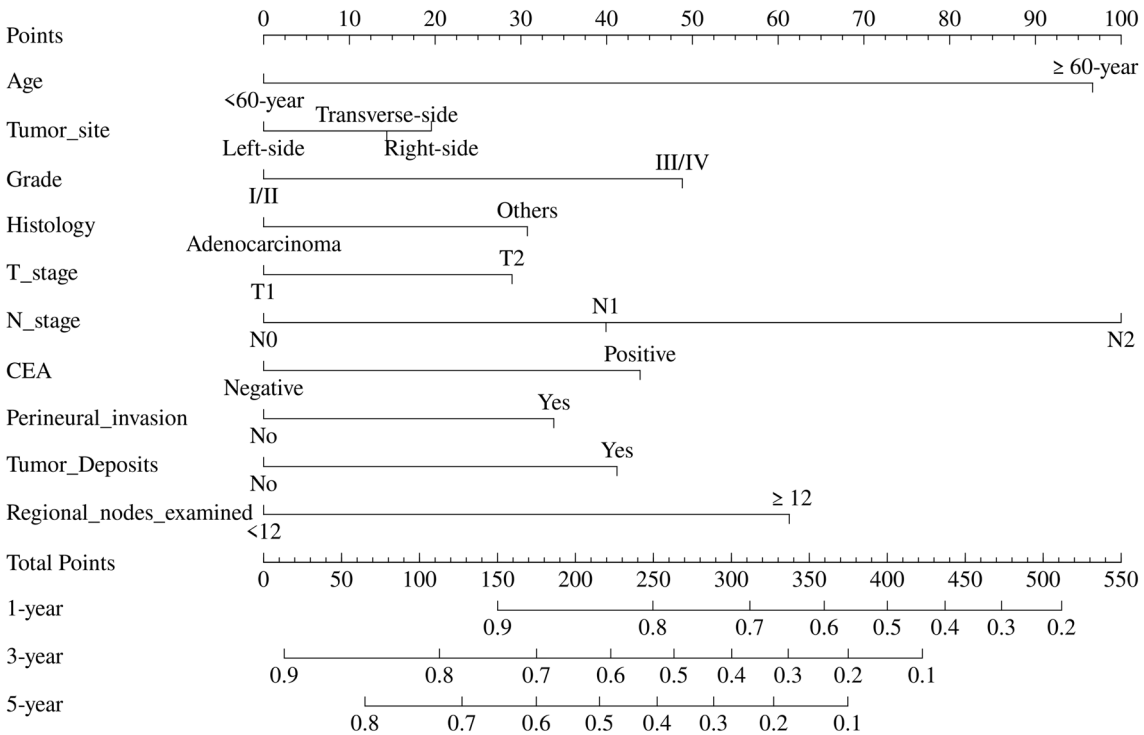


Fig. 2 A nomogram to predict CSS in T4 stage CC patients. CSS, cancer-specific survival; CC, colon cancer

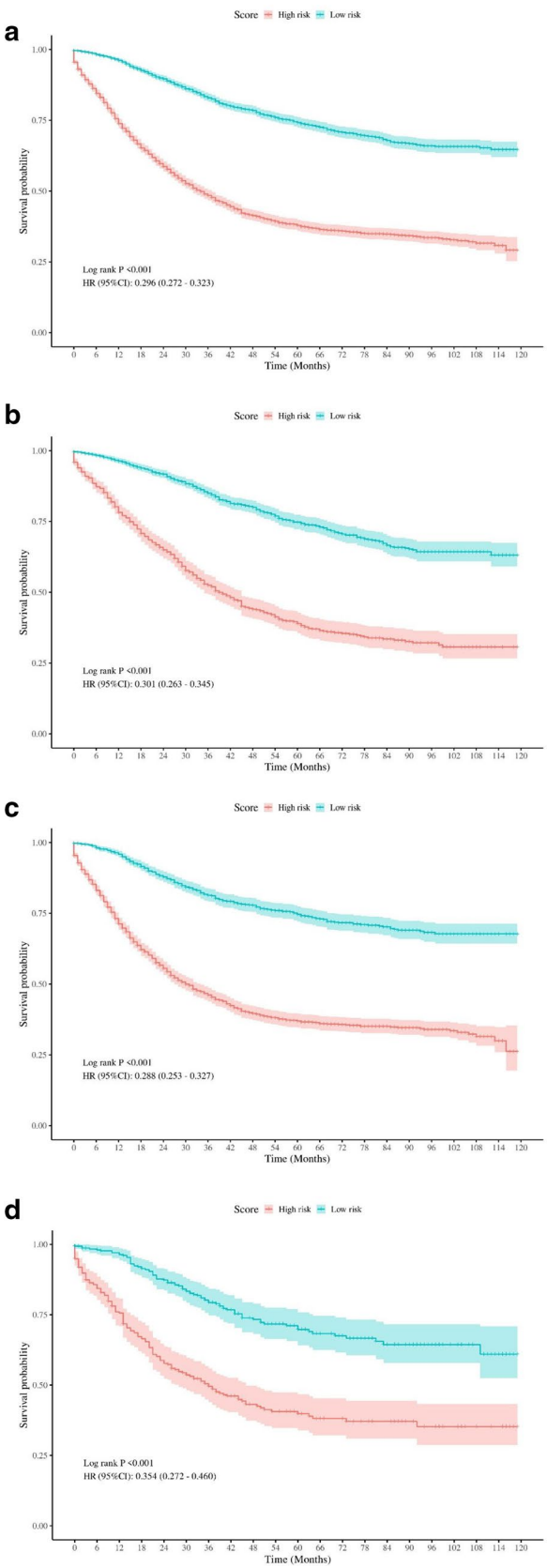


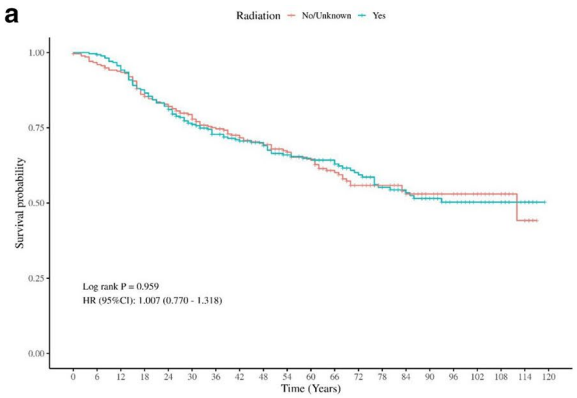
Fig. 3 The Kaplan–Meier survival curves of CSS between the high-risk group and the low-risk group in all (A), left-side colon (B), right-side colon (C) and transverse colon (D) tumor sites. CSS, cancer-specific survival; HR, hazard ratio; CI, confidence interval

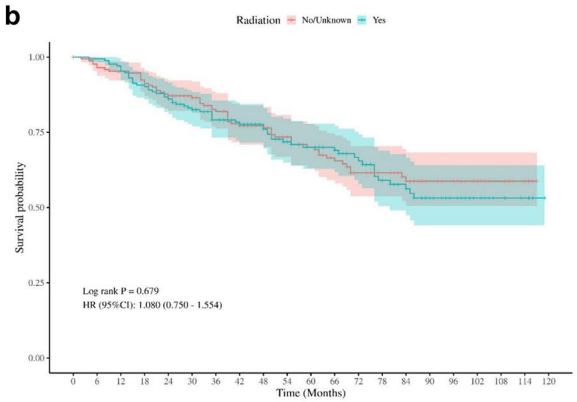
The effects of different treatment options in various subgroups

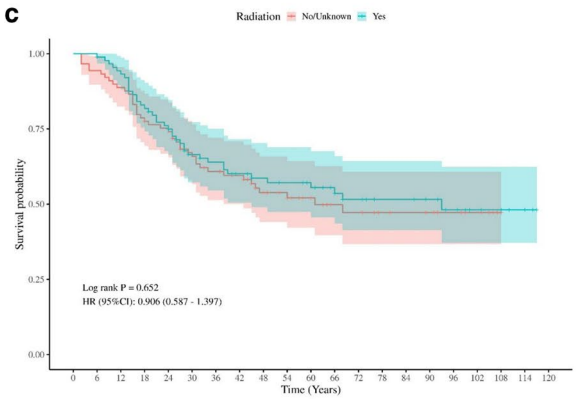
Patients were divided into two subgroups based on their scores in the prediction model: the low-risk group (< 156 points) and the high-risk group (≥ 156 points) in the CSS nomogram. Kaplan–Meier survival curves showed a significant difference in CSS between the two groups in different tumor sites (Fig. 3A-3D). By each process of PSM, most baseline information of the variables was balanced and comparable (see the tables in the supplementary files). After PSM, we evaluated different treatment options in various subgroups. Radiation therapy demonstrated no benefits for T4 stage CC patients across various tumor locations (Fig. 4A-4D). Similarly, radiation provided no advantages in either low-risk or high-risk groups within all tumor sites (Figures S5 and S6). In contrast, chemotherapy significantly enhanced CSS across all tumor site groups (Fig. 5A-5D). Moreover, chemotherapy yielded substantial benefits for both risk groups across all tumor locations (Figures S7 and S8)**.** Adjuvant therapy exhibited significant advantages for T4 stage CC patients when compared to neoadjuvant therapy, particularly within right-sided tumors (Fig. 6A-6D). Additionally, among the high-risk group of T4 stage CC patients, adjuvant therapy showed remarkable benefits; however, there was no significant difference observed in the low-risk group (Figures S9 and S10). Notably, adjuvant treatment in the low-risk left-sided group resulted in a considerable improvement in CSS (Figure S9B). However, due to the grouping method and the database, some subgroups had a small sample size, which affected the results.

Discussion

In contrast to T1-3 stages, T4 stage was identified as a significant risk factor for CC, associated with increased recurrence risk and decreased survival rates [15]. The standard treatment for patients with T4 stage CC is adjuvant chemotherapy following radical resection [6]. However, significant variability in clinical outcomes has been observed among patients with T4 stage CC undergoing similar treatments, with wide differences in survival rates [16]. Additionally, a research indicated that the effects of adjuvant chemotherapy varied significantly depending on the tumor site [17]. However, most published studies on prognostic predictions for CC did not specifically analyze







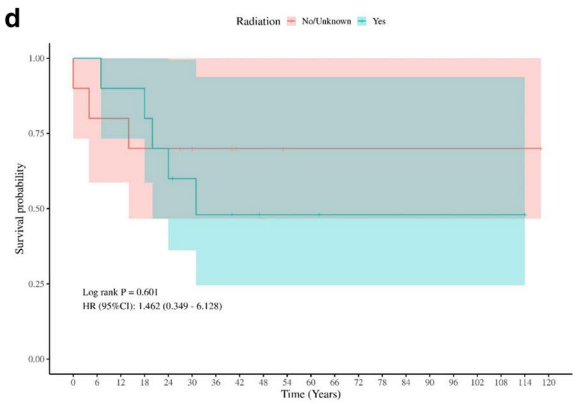
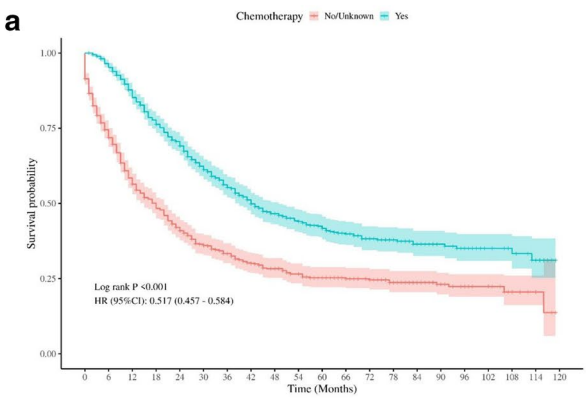
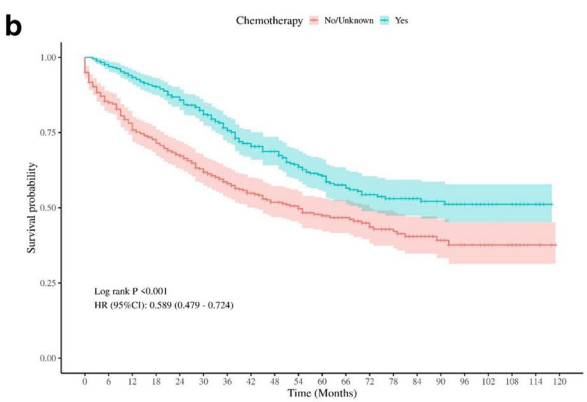
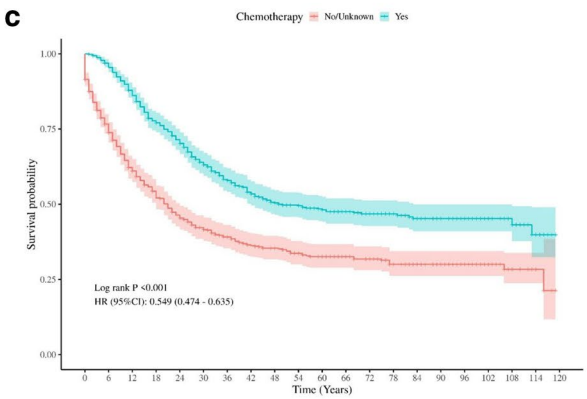


Fig. 4 The Kaplan–Meier survival curves of CSS under radiation therapy in all (A), left-side colon (B), right-side colon (C) and transverse colon (D) tumor sites. CSS, cancer-specific survival; HR, hazard ratio; CI, confidence interval







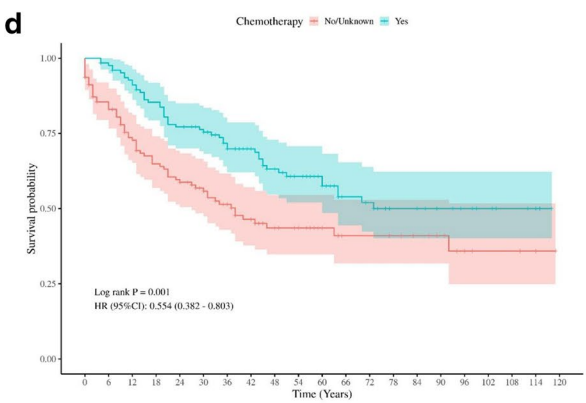


Fig. 5 The Kaplan–Meier survival curves of CSS under chemotherapy in all (A), left-side colon (B), right-side colon (C) and transverse colon (D) tumor sites. CSS, cancer-specific survival; HR, hazard ratio; CI, confidence interval

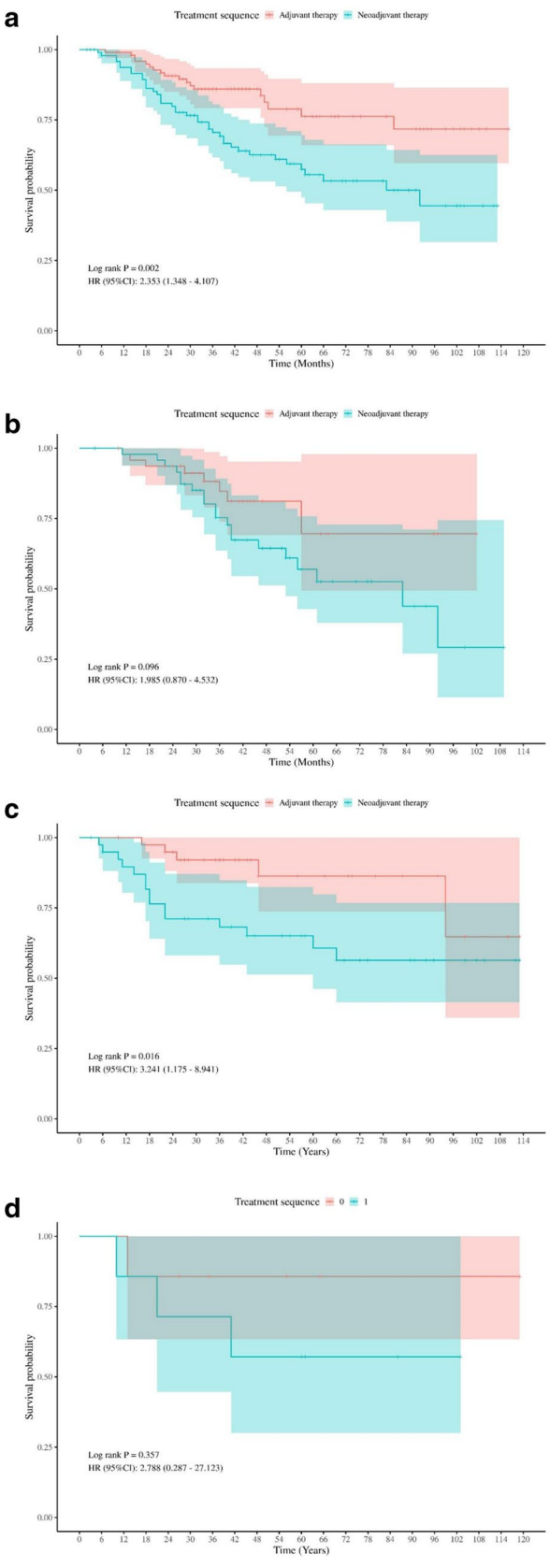


Fig. 6 The Kaplan–Meier survival curves of CSS between adjuvant therapy and neoadjuvant therapy in all (A), left-side colon (B), right-side colon (C) and transverse colon (D) tumor sites. CSS, cancer-specific survival; HR, hazard ratio; CI, confidence interval

T4 stage patients, and there was a notable lack of efficacy analyses for different treatment options across various subgroups [17, 18].

In this study, we analyzed prognostic factors and developed predictive nomograms for CSS in T4 stage CC patients. Consistent with previous research, our analysis of 5,942 T4 stage patients from the SEER database identified T stage, N stage, poor tumor grade, age, tumor histology, elevated CEA levels, tumor deposits, number of regional nodes examined and perineural invasion as independent prognostic factors for CSS. Greater T stage, higher N stage, poorer tumor grade, tumor histology, elderly and elevated CEA levels have been widely recognized as independent risk factors influencing tumor survival in numerous studies [19, 20]. Similarly, a study indicated that adequate lymph node examination was critical to the survival prognosis in stage III CRC patients [21]. Besides, a recent research indicated that tumor deposits correlated with early metastasis and poor prognosis [22]. Furthermore, we identified the tumor site and treatment sequence as independent prognostic factors for CSS in T4 stage CC patients, differing from findings in previous studies [18]. A research reported that the prognosis of right site CC was better than that of left site among patients with stage II CC [23]. However, in our study, compared to the left side, right site was recognized as independent risk factor for CSS in T4 stage CC patients. The possible reason is that left-sided patients had better tumor grade ($P < 0.001$) and less reginal lymph nodes metastasis ($P < 0.001$) compared to right-sided patients with T4 stage CC. We hypothesize that the phenomenon may be associated with microsatellite instability (MSI) in CRC. Previous studies demonstrated that MSI tumors clustered in later-onset CRC, predominantly affecting right-colon locations and exhibiting poorly differentiated histopathology [24, 25]. Furthermore, the phenomenon could potentially be associated with the tumor immune escape mechanisms. CD47-mediated immune regulation appears integral to tumor evasion mechanisms in CC. One study demonstrated that significant CD47/SIRPα axis-driven immunosuppression through phagocytosis inhibition [26]. Additionally, CD47 modulated the tumor microenvironment (TME) by dysregulating cytokine networks, particularly interleukin-10 and tumor growth factor-β signaling, fostering an immune-privileged niche that supports malignant progression in the right-sided CC [27].

A prior study indicated that adjuvant chemotherapy offered no survival benefit for CSS in stage II colorectal

cancer patients [28]. Conversely, our study found that chemotherapy significantly improved CSS in patients with T4 stage CC. The possible reason is that the higher T stage, the more sensitive the tumor is to chemotherapy [29].

Using the predictive nomogram, patients were divided into low-risk and high-risk subgroups. Kaplan–Meier analysis revealed a significant difference in CSS between the two groups across various tumor sites. After PSM in the training group, we found that chemotherapy provided significant benefits for T4 stage CC patients, while radiation therapy showed no advantage. Similar results were shown in different tumor sites. The survival benefit of adjuvant chemotherapy in patients with T4 stage CC was well recognized and aligned with the findings of our study [30]. Radiotherapy is an important treatment for CRC, but its efficacy is hindered by the tumor's low radio-sensitivity and the toxicity to adjacent healthy tissues. Optimal dosage and irradiation range are essential to reduce harm to normal tissues, with modern techniques designed to enhance tumor targeting while safeguarding healthy cells. Consistent with previous studies, our findings indicated that radiation offered no benefits for T4 stage CC patients [31]. One possible explanation is that adjuvant radiotherapy is not commonly employed for T4 stage non-rectal colon adenocarcinoma due to its potential to cause long-term tissue damage and elevate the risk of subsequent malignancies [32]. Additionally, our findings indicated that adjuvant therapy after surgery offered superior CSS compared to neoadjuvant treatment before surge in high-risk T4 stage CC patients. However, some recent researches indicated that neoadjuvant chemotherapy enhanced the chances of negative resection margins in T3-4 stage advanced CC, offering an alternative to initial surgery followed by chemotherapy for locally advanced cases [33, 34]. In contrast, one study revealed neoadjuvant therapy showed no significant benefits in patients with high-risk stage II and III CC [35]. One potential explanation is that the high-risk group may have a higher proportion of deficient mismatch repair (dMMR), who do not derive benefits from neoadjuvant therapy [36]. Furthermore, our sample of patients receiving neoadjuvant therapy was limited, highlighting the need for larger clinical trials to validate these findings.

Understanding CSS is essential for alleviating anxiety and improving quality of life in patients, particularly those with initially poor prognoses. The CSS nomogram allows clinicians to assess mortality risk and design personalized follow-up and monitoring plans. This approach offers valuable insights into the evolving nature of postoperative survival, empowering both patients and clinicians to choose better therapy options.

This study had several limitations. First, the SEER database lacked key biomarker data, including MSI and dMMR status, both of which are vital prognostic markers. Additionally, it provided only basic therapeutic records without details on surgical techniques, chemotherapy regimens, radiation doses, patient health conditions, or socio-economic factors that may influence survival outcomes. These gaps limited the depth of our analysis. Future researches should address these variables to assess their impact better. Moreover, the retrospective design introduced potential selection bias. More prospective cohort studies or randomized controlled trials are required to validate our results and reduce bias. Although the SEER database is widely used in cancer researches, it mainly covers cancer patient data from certain regions in the United States. Therefore, the research results may not fully represent the actual situation of T4 stage CC patients worldwide. Furthermore, medical institutions and treatment teams in different regions may adopt different treatment guidelines and practice standards. Due to uneven distribution of medical resources, differences in socioeconomic status or cultural differences, some patients may not be able to receive the best treatment plan. This inequality in treatment options may lead to poor prognosis for patients, thereby affecting the assessment of treatment effects in the research.

In future studies, the potential impact of other factors on research results can be reduced by expanding the sample size, including patient data from more regions, and adopting more rigorous data collection and processing methods. At the same time, other databases or data sources can also be considered for validation and supplementary analysis to improve the accuracy of the results.

Conclusions

Our study offered a detailed analysis of prognostic factors affecting CSS in T4 stage CC patients by use of data from the SEER database. We developed and validated prediction nomograms for CSS and assessed the impact of various treatment options across different subgroups. Although our model demonstrated encouraging performance in predicting survival outcomes for T4 stage CC patients, further evaluation through multicenter studies is necessary to confirm its clinical applicability.

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Author contribution YX was involved in manuscript review and data collection. ZS was contributing to making tables and figures. ZL was responsible for the writing and revision of the manuscript. TJ focused on data statistics and manuscript review. ZW served as the corresponding author, overseeing the review of the article and providing guidance on the study design. (YX,ZS,ZL have contributed equally to this work.)

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

Declarations

Ethical approval The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Competing interests The authors declare no competing interests.

References

1. Bray F, Laversanne M, Sung H et al (2024) Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 74:229–263
2. Patel SG, Dominitz JA (2024) Screening for colorectal cancer. Ann Intern Med 177:Itc49-itc64
3. Chen M, Chen T (2023) Individualized conditional survival nomograms for stage I-III early onset colorectal cancer patients. Jpn J Clin Oncol 53:115–121
4. Zheng X, Cen W, Zhu J et al (2023) Prognostic value of tumor deposits in stage III colorectal cancer patients with different N stages: a population-based, retrospective cohort study. Ann Surg Oncol 30:8067–8073
5. Bastiaenen VP, Aalbers AGJ, Arjona-Sánchez A et al (2021) Risk of metachronous peritoneal metastases in patients with pT4a versus pT4b colon cancer: an international multicentre cohort study. Eur J Surg Oncol 47:2405–2413
6. Benson AB, Venook AP, Adam M et al (2024) Colon Cancer, Version 3.2024, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 22(2D)
7. Sobrero AF, Puccini A, Shi Q et al (2020) A new prognostic and predictive tool for shared decision making in stage III colon cancer. Eur J Cancer 138:182–188
8. Chalabi M, Verschoor YL, Tan PB et al (2024) Neoadjuvant immunotherapy in locally advanced mismatch repair-deficient colon cancer. N Engl J Med 390:1949–1958
9. Baxter NN, Kennedy EB, Bergsland E et al (2022) Adjuvant therapy for stage II colon cancer: ASCO guideline update. J Clin Oncol 40:892–910
10. Yang Y, Xu P, Zhang C (2023) Construction of the survival nomograms for colon cancer patients of different ages based on the SEER database. J Cancer Res Clin Oncol 149:15395–15406
11. Tian Q-S, Zhang C, Bao Z-J et al (2024) The role of CD47 in immune escape of colon cancer and its correlation with heterogeneity of tumor immune microenvironment. PeerJ 12:e18579
12. Zhao F, Sun Y, Zhao J et al (2024) Clinical characteristics and prognosis analysis of postoperative patients with stage I-III colon cancer based on SEER database. Clin Transl Oncol 26:225–230
13. Qu Z, Wang Y, Guo D et al (2024) Comparison of deep learning models to traditional Cox regression in predicting survival of colon cancer: Based on the SEER database. J Gastroenterol Hepatol 39:1816–1826
14. Ulanja MB, Asafo-Agyei KO, Neelam V et al (2024) Survival trends for left and right sided colon cancer using population-based SEER database: A forty-five-year analysis from 1975 to 2019. Cancer Med 13:e7145
15. Macari D, Kawak S, Raofi V et al (2020) Recurrence pattern and outcomes in T4 colon cancer: a single institution analysis. J Surg Oncol 121:337–341
16. Kesireddy M, Tenner L (2023) Colon cancer survivorship in patients who have received adjuvant chemotherapy. Clin Colorectal Cancer 22:361–374
17. Zeng W, Xu J, Liao Z et al (2024) Construction of a diagnostic nomogram model for predicting the risk of lymph node metastasis in clinical T1 or T2 colon cancer based on the SEER database. Transl Cancer Res 13:1016–1025
18. Zeng H, Xue X, Chen D et al (2024) Conditional survival analysis and real-time prognosis prediction in stage III T3–T4 colon cancer patients after surgical resection: a SEER database analysis. Int J Colorectal Dis 39:54
19. Chen B, Ma Y, Zhou J et al (2023) Predicting survival and prognosis in early-onset locally advanced colon cancer: a retrospective observational study. Int J Colorectal Dis 38:250
20. Shi Y, Wu X, Qu W et al (2023) Construction and validation of a prognostic nomogram for predicting cancer-specific survival in patients with intermediate and advanced colon cancer after receiving surgery and chemotherapy. J Cancer Res Clin Oncol 149:12821–12834
21. Beirat AF, Amarin JZ, Suradi HH et al (2024) Lymph node ratio is a more robust predictor of overall survival than N stage in stage III colorectal adenocarcinoma. Diagn Pathol 19:44
22. Zheng HD, Hu YH, Ye K et al (2023) Development and validation of a nomogram for preoperative prediction of tumor deposits in colorectal cancer. World J Gastroenterol 29:5483–5493
23. Wang S, Xu X, Guan J et al (2020) Better survival of right-sided than left-sided stage II colon cancer: a propensity scores matching analysis based on SEER database. Turk J Gastroenterol 31:805–813
24. Sui Q, Zhang X, Chen C et al (2022) Inflammation promotes resistance to immune checkpoint inhibitors in high microsatellite instability colorectal cancer. Nat Commun 13:7316
25. Chen XY, Li HX, Cheng H et al (2024) Microsatellite instability in colorectal cancer. Indian J Pathol Microbiol
26. Hsieh RC, Krishnan S, Wu RC et al (2022) ATR-mediated CD47 and PD-L1 up-regulation restricts radiotherapy-induced immune priming and abscopal responses in colorectal cancer. Sci Immunol 7:1l9330
27. Huang C, Wang X, Wang Y et al (2024) Sirpα on tumor-associated myeloid cells restrains antitumor immunity in colorectal cancer independent of its interaction with CD47. Nat Cancer 5:500–516
28. Tan C, Wang Q, Yao S (2024) Effects of adjuvant chemotherapy on early-onset stage ii colon cancer at different tumor sites. Am J Clin Oncol 47:253–258
29. Mo S, Ye L, Wang D et al (2023) Early detection of molecular residual disease and risk stratification for stage I to III colorectal cancer via circulating tumor DNA methylation. JAMA Oncol 9:770–778
30. Tan G, Lin C, Huang C et al (2022) Radiosensitivity of colorectal cancer and radiation-induced gut damages are regulated by gasdermin E. Cancer Lett 529:1–10

31. Sebastian NT, Tan Y, Miller ED et al (2020) Surgery with and without adjuvant radiotherapy is associated with similar survival in T4 colon cancer. Colorectal Dis 22:779–789
32. Huang Y, Gu X, Ge K et al (2020) The survival benefit of adjuvant radiotherapy for pathological T4N2M0 colon cancer in the modern chemotherapy era: evidence from the SEER database 2004–2015. Artif Cells Nanomed Biotechnol 48:834–840
33. Cheong CK, Nistala KRY, Ng CH et al (2020) Neoadjuvant therapy in locally advanced colon cancer: a meta-analysis and systematic review. J Gastrointest Oncol 11:847–857
34. Gosavi R, Chia C, Michael M et al (2021) Neoadjuvant chemotherapy in locally advanced colon cancer: a systematic review and meta-analysis. Int J Colorectal Dis 36:2063–2070
35. Karoui M, Gallois C, Piessen G et al (2021) Does neoadjuvant FOLFOX chemotherapy improve the prognosis of high-risk Stage II and III colon cancers? Three years' follow-up results of the PRODIGE 22 phase II randomized multicentre trial. Colorectal Dis 23:1357–1369
36. Morton D, Seymour M, Magill L et al (2023) Preoperative chemotherapy for operable colon cancer: mature results of an international randomized controlled trial. J Clin Oncol 41:1541–1552