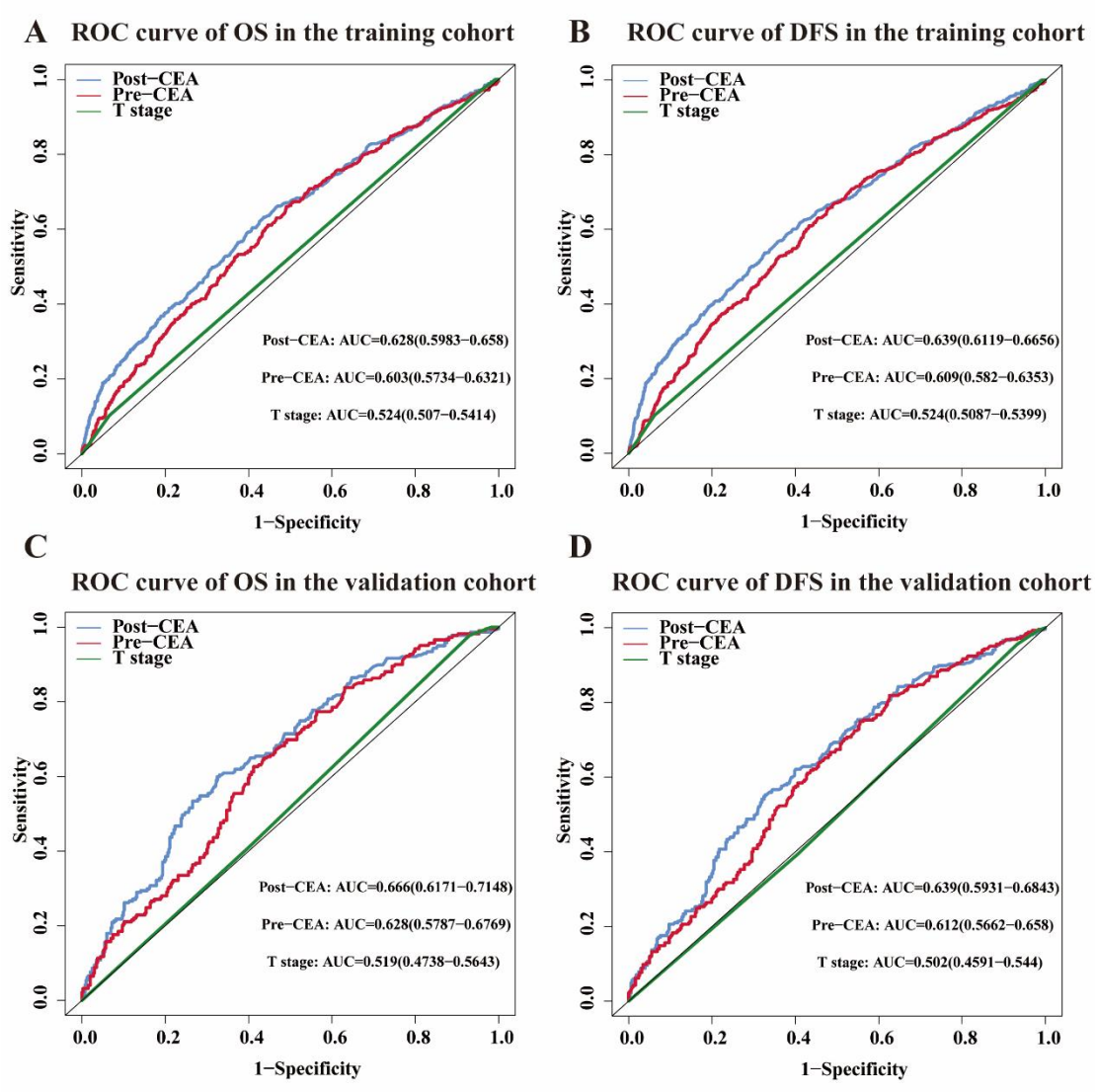
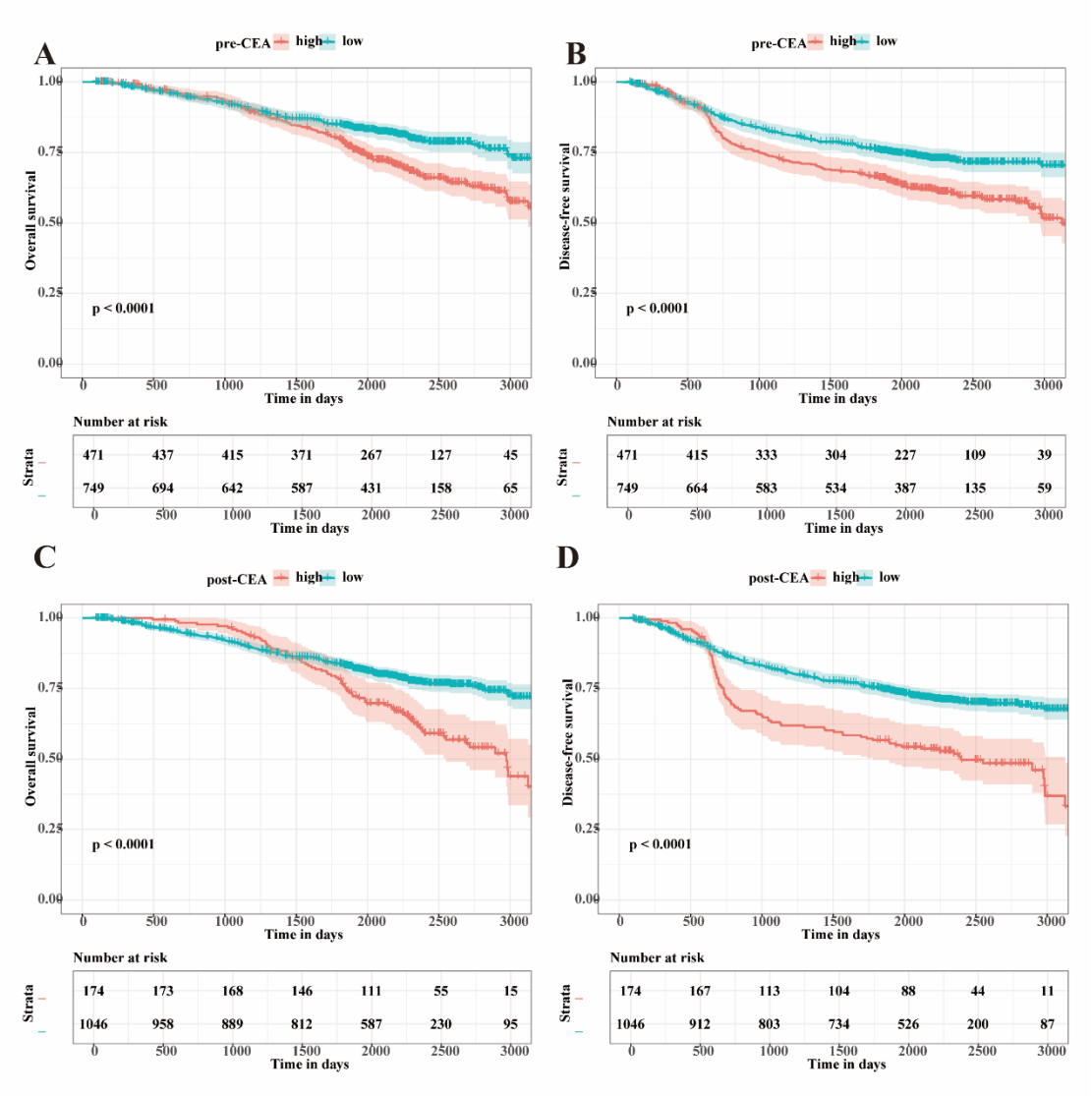


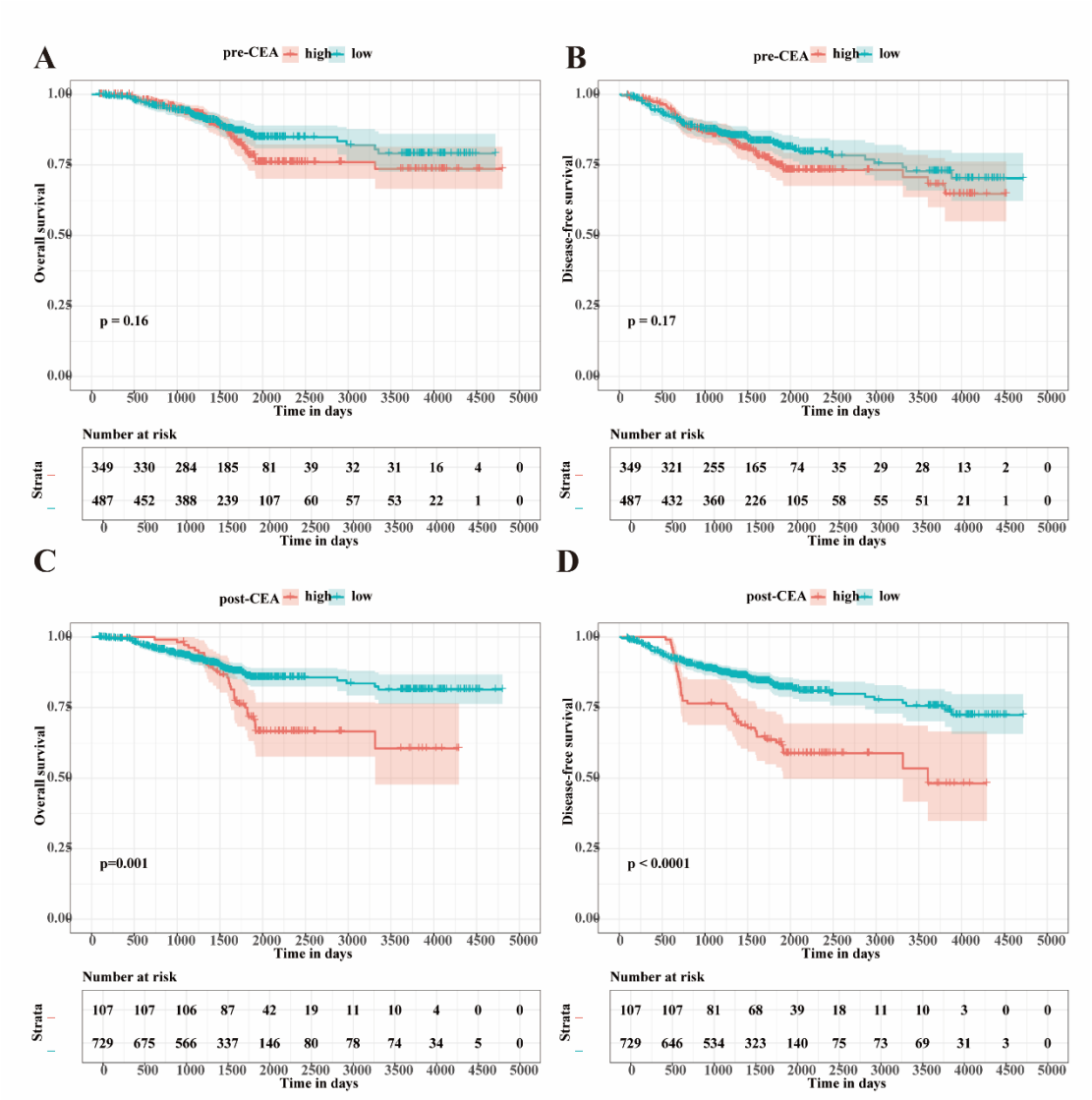
Supplementary Figure 1 Receiver operating characteristic (ROC) curves of overall survival (OS) and disease-free survival (DFS) for T stage and perioperative CEA in the training and validation cohorts.

Figure S1A and S1B ROC curves of OS and DFS for T stage and perioperative CEA in the training cohort;

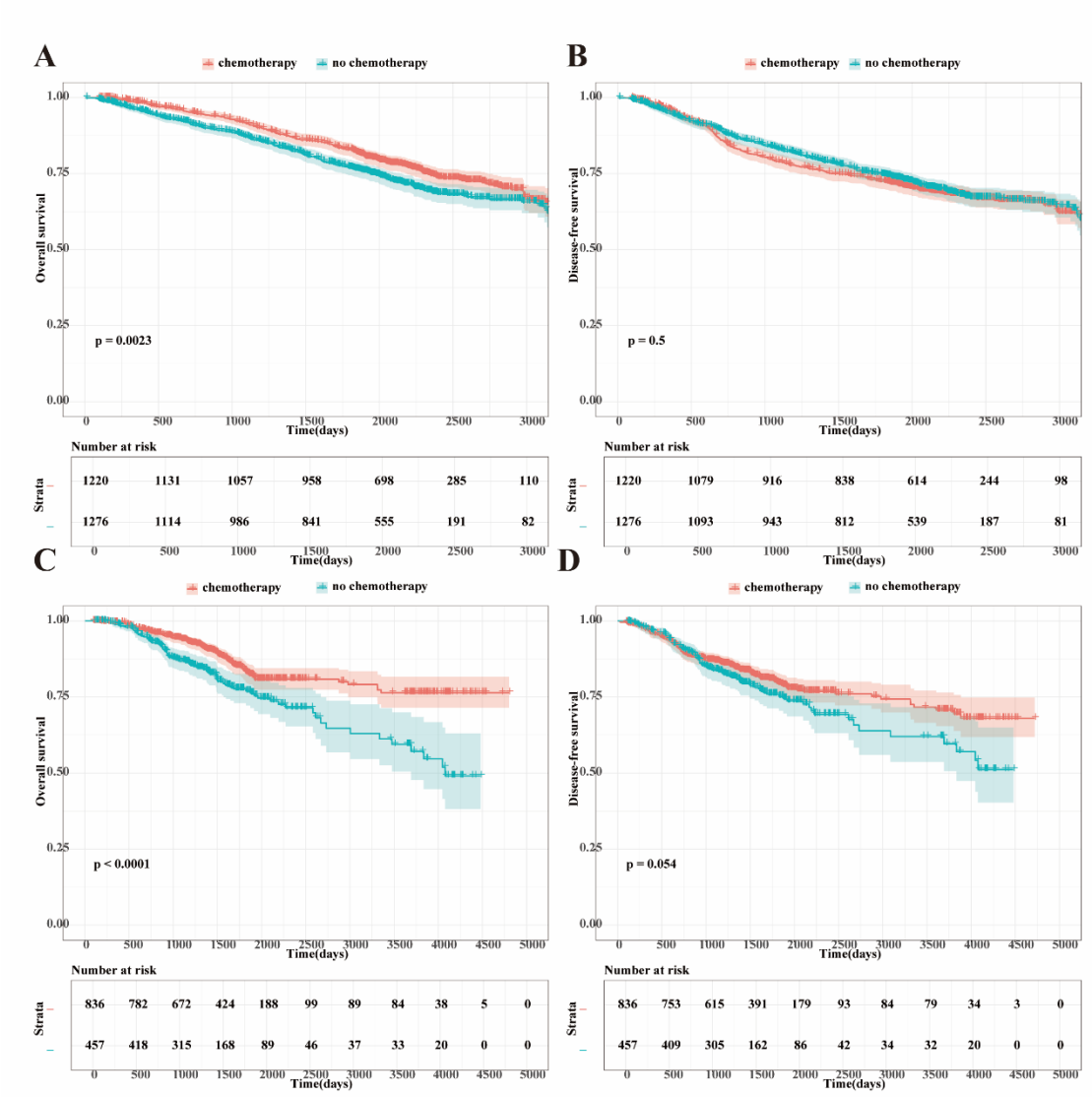
Figure S1C and S1D ROC curves of OS and DFS for T stage and perioperative CEA in the validation cohort; AUC: area under the curve.



Supplementary Figure 2 Kaplan–Meier survival analysis of overall survival (OS) and disease-free survival (DFS) based on perioperative CEA for patients with adjuvant chemotherapy in the training cohort.



Supplementary Figure 3 Kaplan–Meier survival analysis of overall survival (OS) and disease-free survival (DFS) based on perioperative CEA for patients with adjuvant chemotherapy in the validation cohort.

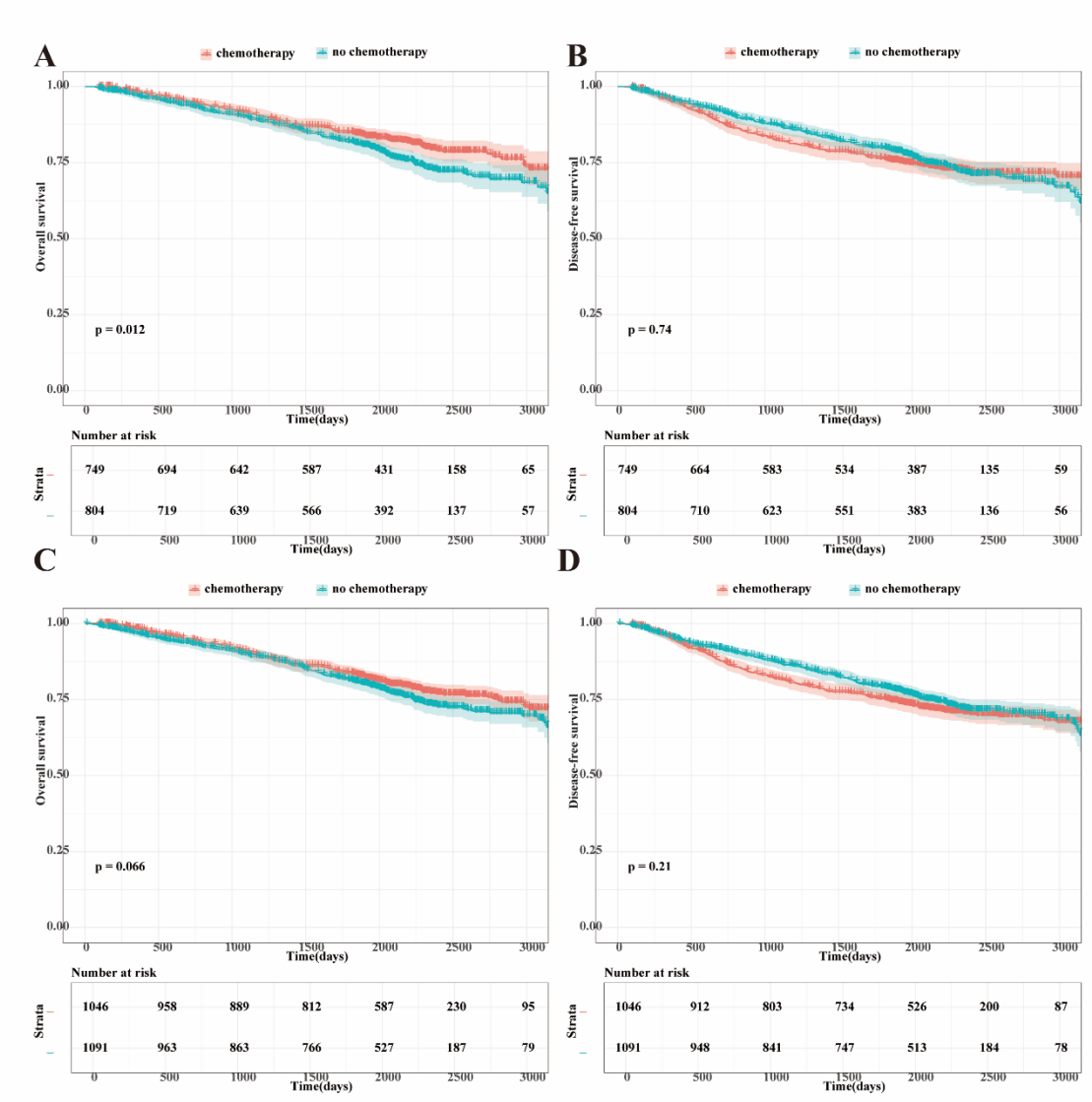


Supplementary Figure 4 Adjuvant chemotherapy significantly prolonged overall survival (OS) but not disease-free survival (DFS) in patients with stage II and III CRC.

Figure S4A and S4B Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients who did or did not receive adjuvant chemotherapy in the training cohort;

Figure S4C and S4D Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients who did or did not receive

adjuvant chemotherapy in the validation cohort.

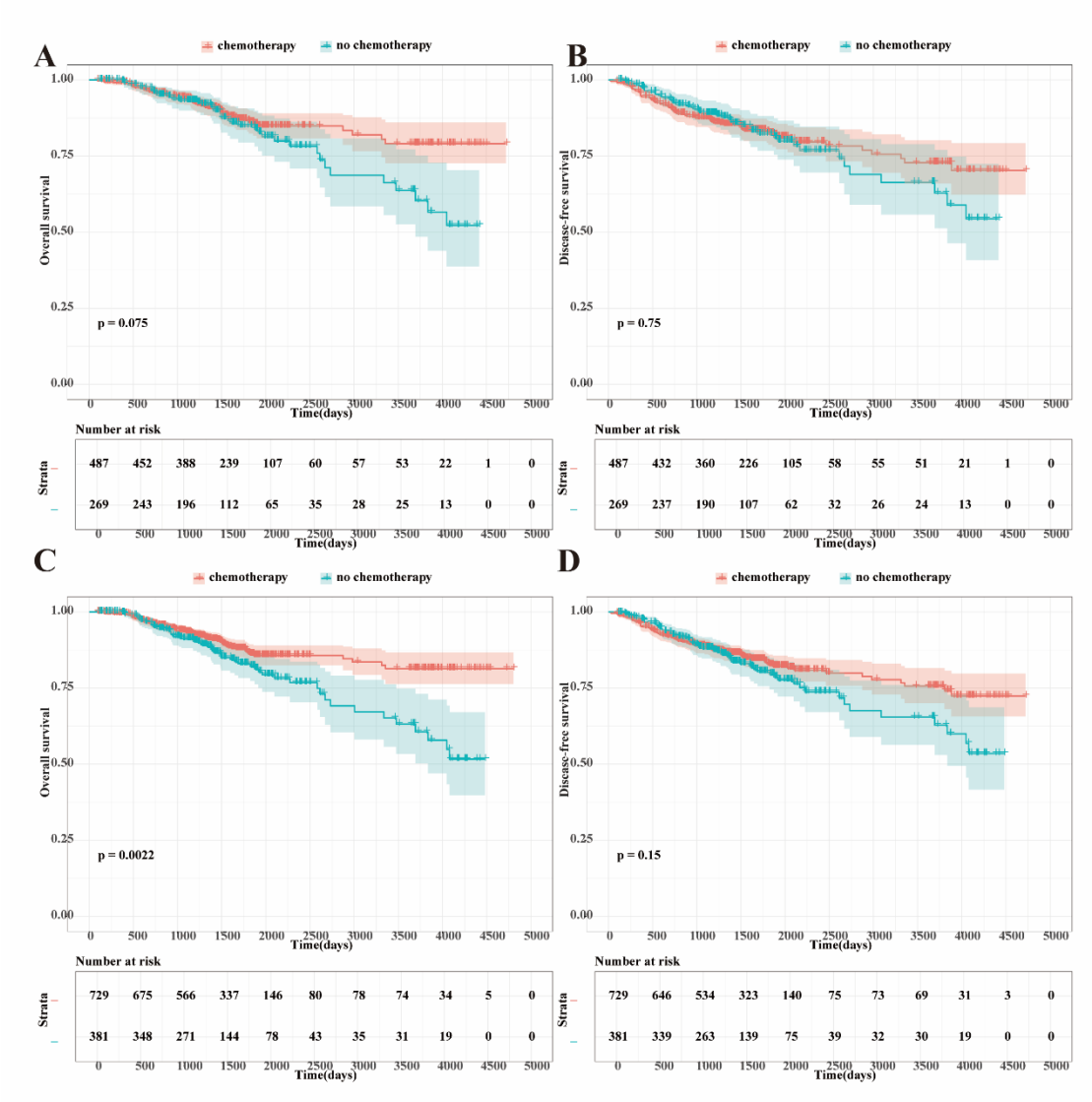


Supplementary Figure 5 Adjuvant chemotherapy cannot improve the prognosis of patients with stage II and III CRC with normal perioperative CEA in the training cohort.

Figure S5A and S5B Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients with normal pre-CEA who did or did not receive adjuvant chemotherapy;

Figure S5C and S5D Kaplan–Meier curves of overall survival (OS) and

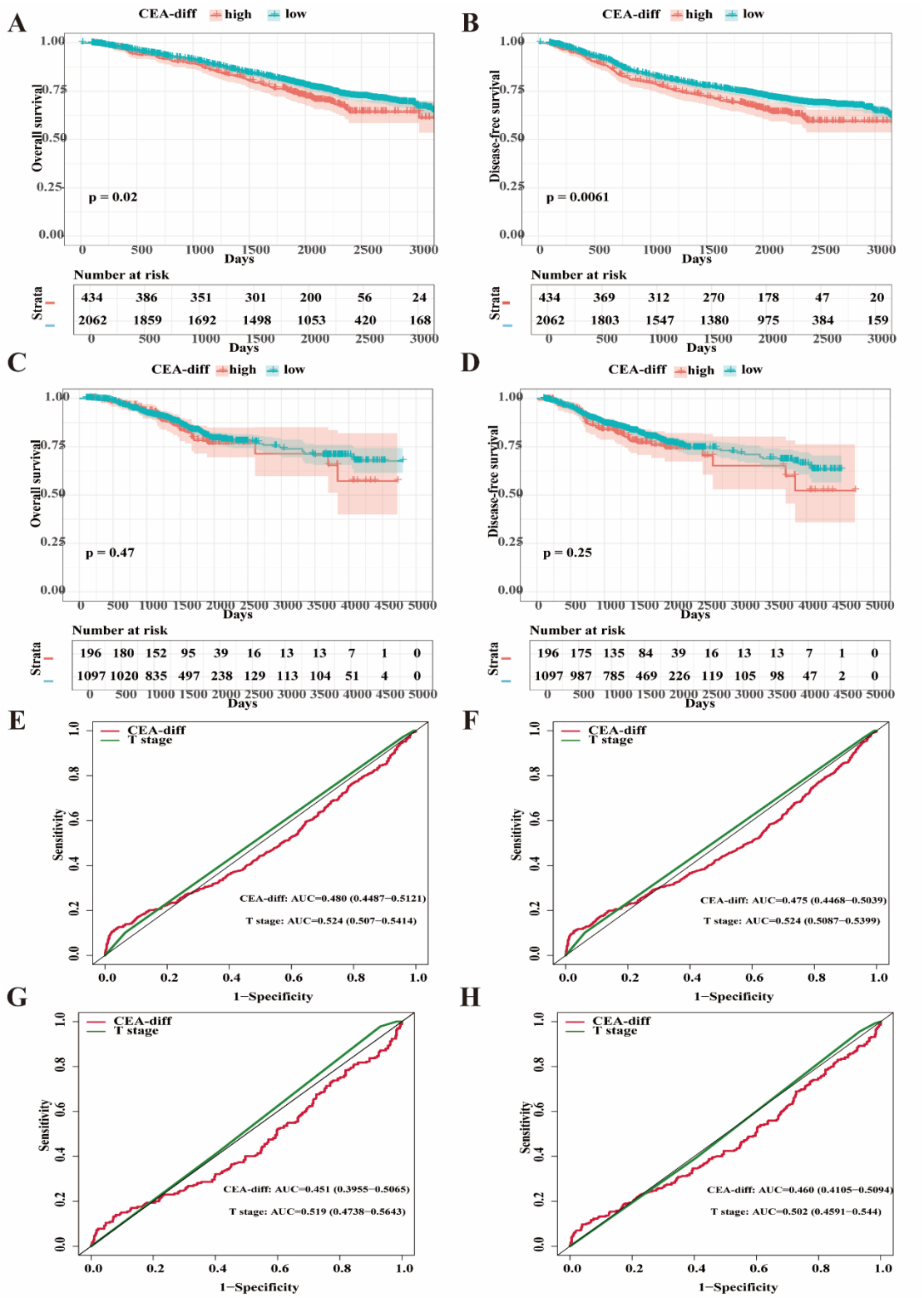
disease-free survival (DFS) for patients with normal post-CEA who did or did not receive adjuvant chemotherapy.



Supplementary Figure 6 Adjuvant chemotherapy cannot improve the prognosis of patients with stage II and III CRC with normal perioperative CEA in the validation cohort.

Figure S6A and S6B Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients with normal pre-CEA who did or did not receive adjuvant chemotherapy;

Figure S6C and S6D Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients with normal post-CEA who did or did not receive adjuvant chemotherapy.



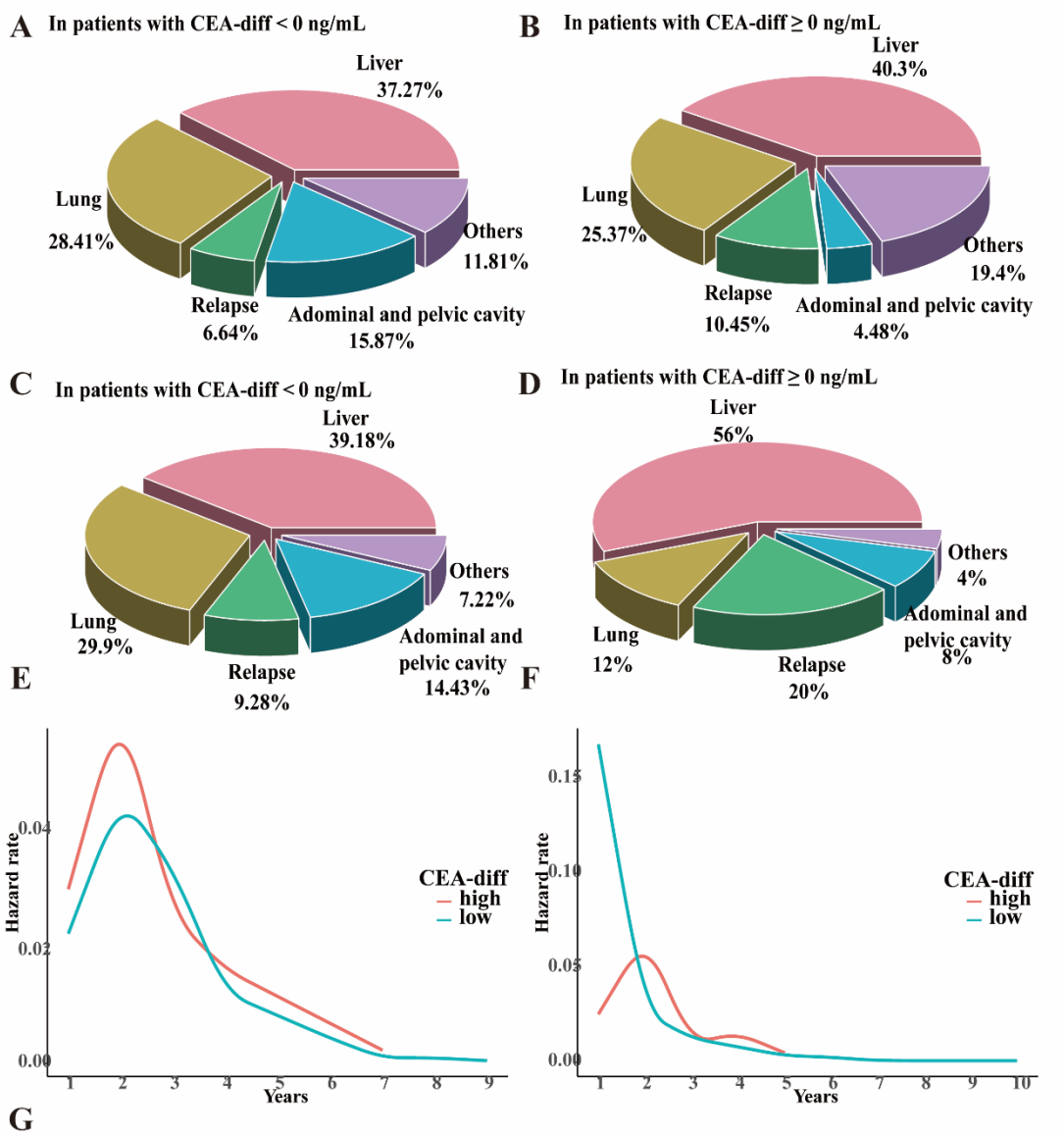
Supplementary Figure 7 Potential for assessing the prognosis of patients based on dynamic changes in CEA.

Figure S7A and S7B Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the training cohort with different levels of CEA difference (CEA-diff);

Figure S7C and S7D Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the validation cohort with different levels of CEA difference (CEA-diff);

Figure S7E and S7F Receiver operating characteristic (ROC) curves of overall survival (OS) and disease-free survival (DFS) for T stage and CEA difference (CEA-diff) in the training cohort;

Figure S7G and S7H Receiver operating characteristic (ROC) curves of overall survival (OS) and disease-free survival (DFS) for T stage and CEA difference (CEA-diff) in the validation cohort; AUC: area under the curve.



Level	Recurrence or metastasis rate in training cohort (%)	Recurrence or metastasis rate in validation cohort (%)
CEA-diff≥0 ng/ml	15.44	12.24
CEA-diff<0 ng/ml	12.9	8.84

Supplementary Figure 8 Recurrence and metastasis pattern based on dynamic changes in CEA.

Figure S8A Relative frequencies of recurrence or metastasis sites for

patients in the training cohort with CEA difference (CEA-diff) < 0 ng/mL;

Figure S8B Relative frequencies of recurrence or metastasis sites for patients in the training cohort with CEA difference (CEA-diff) ≥ 0 ng/mL;

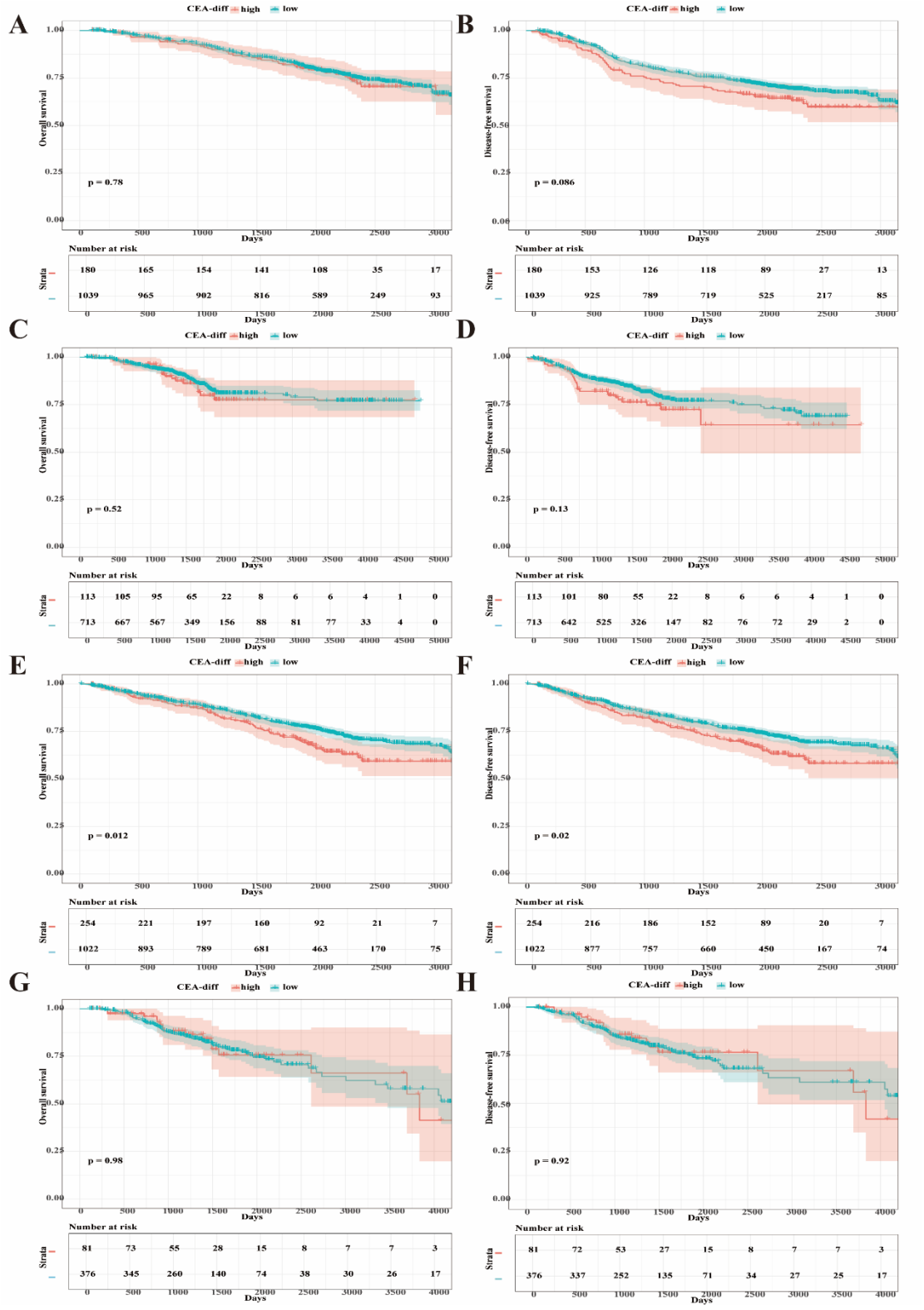
Figure S8C Relative frequencies of recurrence or metastasis sites for patients in the validation cohort with CEA difference (CEA-diff) < 0 ng/mL;

Figure S8D Relative frequencies of recurrence or metastasis sites for patients in the validation cohort with CEA difference (CEA-diff) ≥ 0 ng/mL;

Figure S8E Annual recurrence or metastasis hazard rates for patients based on CEA difference (CEA-diff) in the training cohort;

Figure S8F Annual recurrence or metastasis hazard rates for patients based on CEA difference (CEA-diff) in the validation cohort;

Figure S8G Annual recurrence or metastasis rates for patients based on CEA difference (CEA-diff).



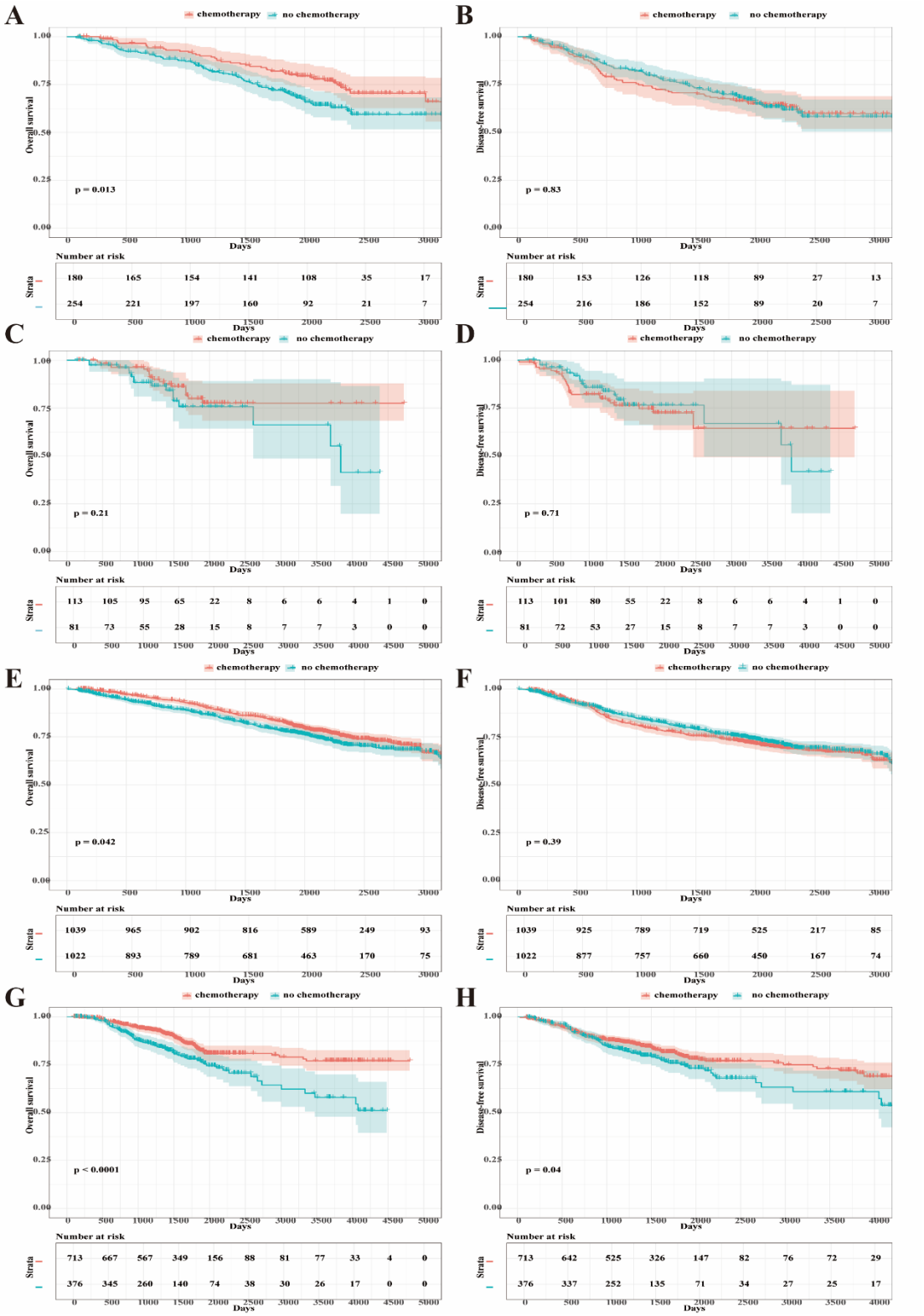
Supplementary Figure 9 Kaplan–Meier survival analysis of overall survival (OS) and disease-free survival (DFS) based on dynamic changes in CEA for patients with or without adjuvant chemotherapy.

Figure S9A and S9B Kaplan–Meier survival analysis of overall survival (OS) and disease-free survival (DFS) based on CEA difference (CEA-diff) for patients with adjuvant chemotherapy in the training cohort;

Figure S9C and S9D Kaplan–Meier survival analysis of overall survival (OS) and disease-free survival (DFS) based on CEA difference (CEA-diff) for patients with adjuvant chemotherapy in the validation cohort;

Figure S9E and S9F Kaplan–Meier survival analysis of overall survival (OS) and disease-free survival (DFS) based on CEA difference (CEA-diff) for patients without adjuvant chemotherapy in the training cohort;

Figure S9G and S9H Kaplan–Meier survival analysis of overall survival (OS) and disease-free survival (DFS) based on CEA difference (CEA-diff) for patients without adjuvant chemotherapy in the validation cohort.



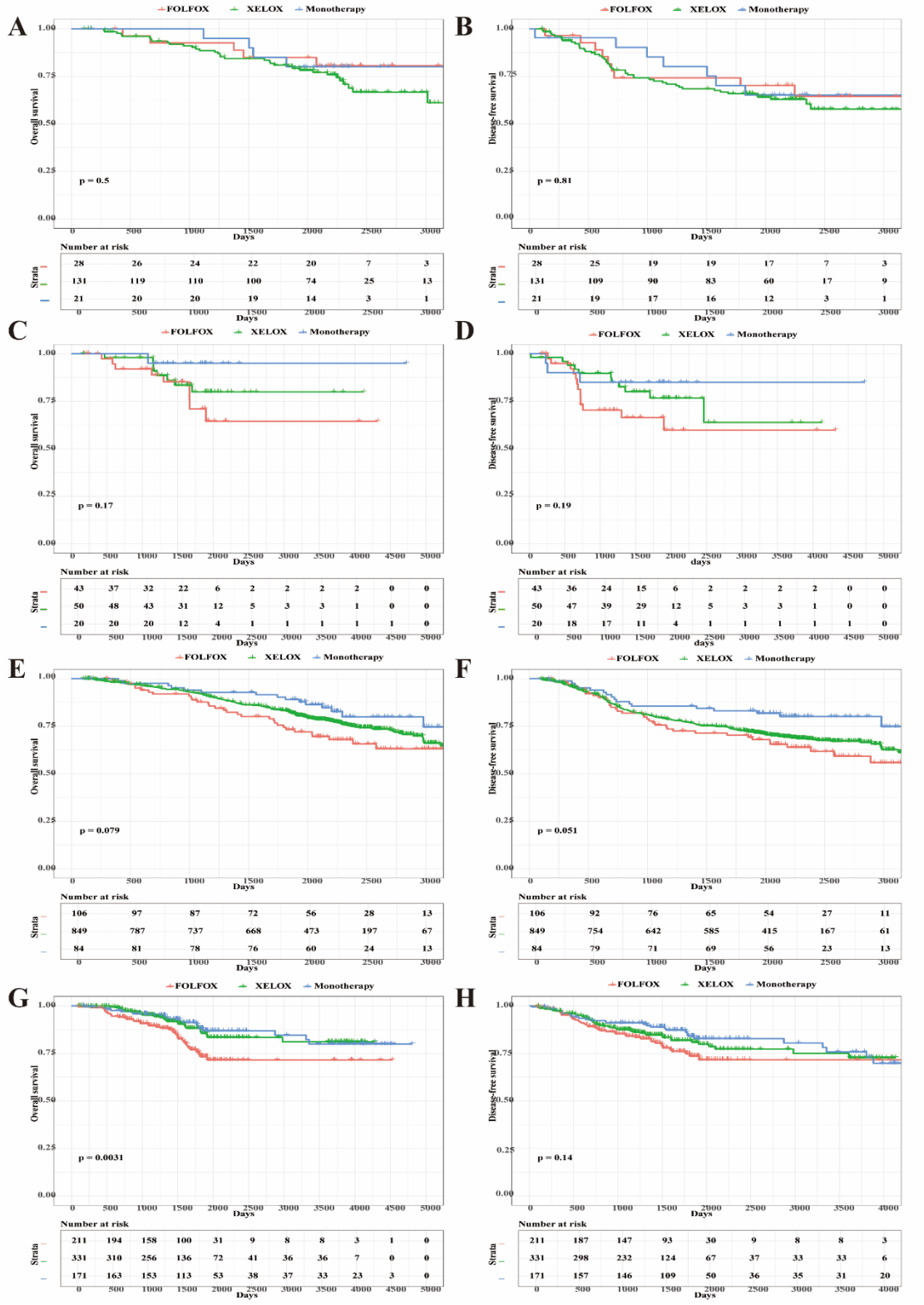
Supplementary Figure 10 Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients who with or without adjuvant chemotherapy.

Figure S10A and S10B Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the training cohort with CEA difference (CEA-diff) ≥ 0 ng/mL who did or did not receive adjuvant chemotherapy;

Figure S10C and S10D Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the validation cohort with CEA difference (CEA-diff) ≥ 0 ng/mL who did or did not receive adjuvant chemotherapy;

Figure S10E and S10F Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the training cohort with CEA difference (CEA-diff) < 0 ng/mL who did or did not receive adjuvant chemotherapy;

Figure S10G and S10H Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the validation cohort with CEA difference (CEA-diff) < 0 ng/mL who did or did not receive adjuvant chemotherapy.



Supplementary Figure 11 Potential of dynamic changes of CEA in guiding the selection of adjuvant chemotherapy strategies.

Figure S11A and S11B Kaplan–Meier curves of overall survival (OS) and

disease-free survival (DFS) for patients in the training cohort with CEA difference (CEA-diff) ≥ 0 ng/mL after receiving different adjuvant chemotherapy strategies;

Figure S11C and S11D Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the validation cohort with CEA difference (CEA-diff) ≥ 0 ng/mL after receiving different adjuvant chemotherapy strategies;

Figure S11E and S11F Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the training cohort with CEA difference (CEA-diff) < 0 ng/mL after receiving different adjuvant chemotherapy strategies;

Figure S11G and S11H Kaplan–Meier curves of overall survival (OS) and disease-free survival (DFS) for patients in the validation cohort with CEA difference (CEA-diff) < 0 ng/mL after receiving different adjuvant chemotherapy strategies.

Supplementary Table 1 Univariate Cox regression analysis of perioperative CEA for overall survival (OS) and disease-free survival (DFS) in training cohort.

	Factors	Categorical variable				Continuous variable			
		HR	95% CI		P value	HR	95% CI		P value
			Lower	Upper			Lower	Upper	
OS	Pre-CEA	1.605	1.368	1.882	＜0.001	1.003	1.002	1.004	＜0.001
	Post-CEA	2.338	1.949	2.805	＜0.001	1.001	1.001	1.001	＜0.001
DFS	Pre-CEA	1.587	1.371	1.838	＜0.001	1.003	1.002	1.004	＜0.001
	Post-CEA	2.406	2.031	2.85	＜0.001	1.001	1.001	1.002	＜0.001

Categorical variable: CEA was defined as a categorical variable and the cutoff value is 5ng/mL; Continuous variable: CEA was defined as a continuous variable; CI: confidence interval.

Supplementary Table 2 Univariate Cox regression analysis of perioperative CEA for overall survival (OS) and disease-free survival (DFS) in validation cohort.

	Factors	Categorical variable				Continuous variable			
		HR	95% CI		P value	HR	95% CI		P value
			Lower	Upper			Lower	Upper	
OS	Pre-CEA	1.59	1.206	2.095	0.00101	1.003	1.002	1.004	＜0.001
	Post-CEA	2.388	1.771	3.22	＜0.001	1.002	1.001	1.003	0.000534
DFS	Pre-CEA	1.445	1.13	1.849	0.00338	1.003	1.001	1.004	＜0.001
	Post-CEA	2.396	1.826	3.143	＜0.001	1.001	1.001	1.002	0.000731

Categorical variable: CEA was defined as a categorical variable and the cutoff value is 5ng/ml; Continuous variable: CEA was defined as a continuous variable; CI: confidence interval.

Supplementary Table 3 Confirmatory analysis

	Overall survival			Disease-free survival		
Variables	**HR**	**95% CI**	**P value**	**HR**	**95% CI**	**P value**
Age	1.0335	1.0261-1.041	＜0.001	1.023	1.0164-1.0297	＜0.001
Height	1.0015	0.9964-1.0065	0.5704	1.0011	0.9966-1.0057	0.6188
Ileus	1.3878	1.1511-1.6732	＜0.001	1.4859	1.2524-1.763	＜0.001
Diabetes	-	-	-	1.4767	1.2104-1.8014	＜0.001

Differentiation (moderate)	0.5686	0.4109-0.7867	＜0.001	0.6433	0.4775-0.8665	0.0037
Differentiation (poor)	0.7503	0.5224-1.0775	0.1197	0.8333	0.5979-1.1613	0.2815
Mucinous carcinoma	1.2054	1.0088-1.4404	0.0397	1.1564	0.9805-1.3639	0.0844
Left colon (Ref=Rectum)	0.7831	0.6608-0.9282	0.0048	0.8137	0.6968-0.9502	0.0092

Right colon (Ref=Rectum)	0.7964	0.6622-0.9579	0.0157	0.813	0.6855-0.9643	0.0174
Perineural invasion	1.4806	1.2519-1.7512	＜0.001	1.4163	1.2139-1.6525	＜0.001
Vascular cancer embolus	1.4833	1.2116-1.8159	＜0.001	1.342	1.1075-1.6261	0.0027
AJCC stage	1.7236	1.4865-1.9985	＜0.001	1.711	1.4951-1.9581	＜0.001
Post-CEA	1.0009	1.0005-1.0012	＜0.001	1.0008	1.0002-1.0013	0.005

Cohorts	1.0398	0.8653-1.2494	0.6772	1.0007	1.0003-1.0011	＜0.001