Breast Cancer: Targets and Therapy

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ORIGINAL RESEARCH

Clinical Prognostic Value of C-Reactive Protein-Albumin-Lymphocyte Index (CALLY) in Patients with Stage III Breast Cancer

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Objective: To investigate the relationship between the C-reactive protein-albumin-lymphocyte index (CALLY) and clinicopathological characteristics, as well as its prognostic value in stage III breast cancer patients.

Methods: A retrospective analysis was conducted on the clinicopathological data of 187 stage III breast cancer patients who were treated in our hospital from 2010 to 2015. The optimal cut-off value for CALLY index was determined by ROC curve. Chi-square tests and Fisher's exact tests were used for intergroup analysis. Survival curves were plotted using Kaplan-Meier method, and comparisons between groups were made using Log Rank test. Univariate and multivariate analyses were performed using the COX regression model. A nomogram prediction model was constructed based on the results of multivariate analysis and validated using the concordance index (C-index), calibration curves, and decision curve analysis (DCA).

Results: According to ROC curve, the optimal cut-off value for CALLY was determined to be 0.10, dividing the patients into a low CALLY group (54 patients) and a high CALLY group (133 patients). CALLY was identified as a potential independent prognostic factor for stage III breast cancer patients. Patients with high CALLY values had longer survival time than those with low CALLY values (DFS: $\chi^2 = 9.109$, $P = 0.0025$; OS: $\chi^2 = 5.637$, $P = 0.0176$). The C-indices for the nomograms predicting DFS and OS were 0.692 (95% *CI*: 0.541–0.811) and 0.730 (95% *CI*: 0.586–0.838), respectively. The calibration curves showed excellent calibration performance for predicting 1-year and 3-year DFS and OS. Decision curve analysis revealed that the nomogram model had better clinical performance than the CALLY model in predicting 3-year, 5-year, and 10-year DFS and OS.

Conclusion: CALLY index is a potential independent prognostic factor for stage III breast cancer patients. It provides new insights and methods for clinical diagnosis and treatment of breast cancer.

Keywords: breast cancer, CALLY, albumin, C-reactive protein, prognosis, nomogram

Introduction

Breast cancer is the most common malignant tumor among women in China, occurring predominantly in the breast glandular epithelial tissue.[1] Its incidence and mortality rates are increasing annually, posing a significant threat to women's physical and mental health. In recent years, with the rapid development of medical equipment and technology, the prevention and treatment of breast cancer have gradually improved. However, some newly diagnosed breast cancer patients are already in the advanced stage.[2] The severe disease invasion and continuous clinical treatment lead to more physical symptoms and psychological symptoms in patients, significantly reducing the quality of life of breast cancer patients.[3] Increased evidence indicates that systemic inflammation, immune response, and nutritional status play important roles in the occurrence and development of malignant tumors.[4] Based on peripheral blood immune-inflammatory markers, such as the neutrophil-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, C-reactive protein

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(CRP), and albumin, have been proven to have prognostic significance for malignant tumors.[5] The C-reactive protein-albumin-lymphocyte index (CALLY) includes C-reactive protein, albumin, and lymphocyte count, reflecting inflammation, nutritional status, and immune capacity, respectively.[6] Studies have shown that CALLY index has recently been investigated as a prognostic factor in various gastrointestinal (GIS) and genitourinary system (GUS) cancers,[7–9] CALLY index provides a more comprehensive assessment of tumor prognosis and may be superior to single markers in prognostic stratification.[10] However, the relationship between CALLY index and the clinicopathological features and prognosis of stage III breast cancer is not clear. This study aims to investigate the relationship between CALLY index and clinicopathological features and to assess the prognostic value of CALLY index in breast cancer patients, providing a reference for the treatment of breast cancer.

Materials and Methods

Patients and Study Design

A total of 187 stage III breast cancer patients who visited the National Cancer Center/Cancer Hospital/Chinese Academy of Medical Sciences and Peking Union Medical College from 2010 to 2015 were selected as the study subjects, with ages ranging from 26 to 79 years, and a median age of 52 years. The body mass index (BMI) ranged from 17.93 to 37.58, with a median value of 24.65. All patients and their families signed informed consent forms. All procedures involving patient participation in this study were in accordance with the ethical standards of our hospital's ethics committee and the 1964 Helsinki Declaration and its subsequent amendments. The ethics number is NCC2023C-445.

Inclusion and Exclusion Criteria

Inclusion Criteria: 1) Patients met the pathological diagnostic criteria for breast cancer, with TNM staging at stage III; 2) Complete clinical pathological data and follow-up information; 3) No preoperative anti-tumor treatment. Exclusion criteria: 1) Combined with other malignant tumors such as liver cancer or ovarian cancer, or with other metastases; 2) Combined with acute or chronic infections, or with hypertension, diabetes, heart disease, and other conditions that are difficult to tolerate; 3) Poor patient compliance, withdrawal from the study midway.

Methods

The C-reactive protein-albumin-lymphocyte index (CALLY) is composed of three factors: C-reactive protein (CRP), albumin, and lymphocyte count. The calculation method for CALLY is: (albumin × lymphocyte)/CRP. The unit for albumin is g/L, for CRP is mg/L, and for lymphocyte count is 10^9^/L. The optimal cut-off value for CALLY was determined to be 0.10 based on the ROC curve (area under the curve AUC=0.604, 95% CI: 0.429–0.809).

Follow-Up

All patients received postoperative follow-up after surgical treatment, including outpatient and telephone follow-up. Disease-free survival (DFS) is defined as the time from the end of surgery to the occurrence of recurrence or metastasis.[11] Overall survival (OS) is defined as the time from the end of surgery to death or the last follow-up.[12] The last follow-up date was December 15, 2024.

Statistical Analysis

All statistical analyses were performed using SPSS Statistics 22.0 software (IBM) and R language (http://www.R-project.org/, version 4.2.2). Descriptive statistical methods were used to analyze the clinicopathological features of stage III breast cancer. Numerical variables were analyzed using chi-square tests or Fisher's exact tests. Survival curves were plotted using the Kaplan-Meier method, and comparisons between groups were made using the Log Rank test. Univariate analysis was first performed on the included variables, and then potential independent variables were selected based on the results of univariate analysis to establish a multivariate COX proportional hazards regression model. The optimal cut-off value for CALLY was determined by the ROC curve. A nomogram prediction model was constructed based on the results of multivariate analysis

and internally validated using the concordance index (C-index), calibration curves, and decision curve analysis (DCA). A P value of < 0.05 was considered statistically significant.

Results

General Situation

A total of 187 stage III breast cancer patients were included in this study, all of whom were female. According to the ROC curve, the optimal cut-off value for CALLY index was determined, dividing the patients into two groups: the low group with 54 patients and the high group with 133 patients. The clinical pathological data of the breast cancer patients were shown in Table 1. All patients underwent surgical treatment, including 177 cases of total mastectomy and 10 cases of breast-conserving surgery. According to pathological types, there were 13 cases of Luminal A type, 18 cases of

Table 1 The Clinical Pathological Characteristics by CALLY

Parameter	Level	Overall (Low Group+High Group)	Low Group	High Group	*P*
n		187	54	133	
Age	<52	81 (43.3)	21 (38.9)	60 (45.1)	0.538
	≥52	106 (56.7)	33 (61.1)	73 (54.9)	
Marital status	Married	183 (97.9)	53 (98.1)	130 (97.7)	1.000
	Unmarried	4 (2.1)	1 (1.9)	3 (2.3)	
BMI	<24.65	89 (47.6)	26 (48.1)	63 (47.4)	1.000
	≥24.65	98 (52.4)	28 (51.9)	70 (52.6)	
Family history	No	141 (75.4)	42 (77.8)	99 (74.4)	0.769
	Yes	46 (24.6)	12 (22.2)	34 (25.6)	
Menarche age	<14	58 (31.0)	14 (25.9)	44 (33.1)	0.433
	≥14	129 (69.0)	40 (74.1)	89 (66.9)	
Menopause	No	103 (55.1)	26 (48.1)	77 (57.9)	0.293
	Yes	84 (44.9)	28 (51.9)	56 (42.1)	
Albumin	<44.1	111 (59.4)	35 (64.8)	76 (57.1)	0.422
	≥44.1	76 (40.6)	19 (35.2)	57 (42.9)	
Lymphocyte	<1.68	98 (52.4)	36 (66.7)	62 (46.6)	0.020
	≥1.68	89 (47.6)	18 (33.3)	71 (53.4)	
C-reactive protein	<0.30	102 (54.5)	0 (0.0)	102 (76.7)	<0.001
	≥0.30	85 (45.5)	54 (100.0)	31 (23.3)	
CA125	<12.32	106 (56.7)	23 (42.6)	83 (62.4)	0.021
	≥12.32	81 (43.3)	31 (57.4)	50 (37.6)	
CA153	<11.33	105 (56.1)	28 (51.9)	77 (57.9)	0.554
	≥11.33	82 (43.9)	26 (48.1)	56 (42.1)	
CEA	<1.87	92 (49.2)	21 (38.9)	71 (53.4)	0.102
	≥1.87	95 (50.8)	33 (61.1)	62 (46.6)	
Neutrophil	<3.23	111 (59.4)	30 (55.6)	81 (60.9)	0.610
	≥3.23	76 (40.6)	24 (44.4)	52 (39.1)	
Monocytes	<0.30	115 (61.5)	36 (66.7)	79 (59.4)	0.447
	≥0.30	72 (38.5)	18 (33.3)	54 (40.6)	
Type of surgery	Mastectomy	177 (94.7)	51 (94.4)	126 (94.7)	1.000
	Breast-conserving surgery	10 (5.3)	3 (5.6)	7 (5.3)	
Tumor size	<2	52 (27.8)	10 (18.5)	42 (31.6)	0.104
	≥2	135 (72.2)	44 (81.5)	91 (68.4)	
Total lymph nodes	<22	88 (47.1)	25 (46.3)	63 (47.4)	1.000
	≥22	99 (52.9)	29 (53.7)	70 (52.6)	

(*Continued*)

Table 1 (Continued).

Parameter	Level	Overall (Low Group+High Group)	Low Group	High Group	*P*
Positive lymph nodes	<2	67 (35.8)	15 (27.8)	52 (39.1)	0.195
	≥2	120 (64.2)	39 (72.2)	81 (60.9)	
Molecular subtype	Luminal A	13 (7.0)	5 (9.3)	8 (6.0)	0.403
	Luminal B HER2+	18 (9.6)	2 (3.7)	16 (12.0)	
	Luminal B HER2-	94 (50.3)	30 (55.6)	64 (48.1)	
	HER2 enriched	30 (16.0)	9 (16.7)	21 (15.8)	
	Triple negative	32 (17.1)	8 (14.8)	24 (18.0)	
Estrogen receptor	Negative	65 (34.8)	18 (33.3)	47 (35.3)	0.927
	Positive	122 (65.2)	36 (66.7)	86 (64.7)	
Progesterone receptor	Negative	72 (38.5)	17 (31.5)	55 (41.4)	0.275
	Positive	115 (61.5)	37 (68.5)	78 (58.6)	
HER2	Negative	139 (74.3)	43 (79.6)	96 (72.2)	0.383
	Positive	48 (25.7)	11 (20.4)	37 (27.8)	
Ki67	<14%	99 (52.9)	30 (55.6)	69 (51.9)	0.768
	≥14%	88 (47.1)	24 (44.4)	64 (48.1)	
Postoperative chemotherapy	No	41 (21.9)	9 (16.7)	32 (24.1)	0.362
	Yes	146 (78.1)	45 (83.3)	101 (75.9)	
Postoperative radiotherapy	No	46 (24.6)	10 (18.5)	36 (27.1)	0.297
	Yes	141 (75.4)	44 (81.5)	97 (72.9)	
Postoperative endocrine therapy	No	84 (44.9)	22 (40.7)	62 (46.6)	0.569
	Yes	103 (55.1)	32 (59.3)	71 (53.4)	
Postoperative targeted therapy	No	174 (93.0)	51 (94.4)	123 (92.5)	0.872
	Yes	13 (7.0)	3 (5.6)	10 (7.5)	

Luminal B HER2-positive type, 94 cases of Luminal B HER2-negative type, 30 cases of HER2 over expression type, and 32 cases of triple-negative type. After surgical treatment, 146 patients received postoperative chemotherapy, 141 patients received postoperative radiotherapy, 103 patients received endocrine therapy, and 13 patients received targeted therapy. CALLY index was associated with lymphocyte count (L), C-reactive protein (CRP), and carbohydrate antigen 125 (CA125). The differences between the two groups were statistically significant ($P < 0.05$) (Table 1).

Relationship Between CALLY and Postoperative Survival in Breast Cancer Patients

Based on CALLY index, the breast cancer patients included were divided into two groups. The low CALLY group had 54 patients with a mean DFS of 29.27 months and a mean OS of 67.47 months. The high CALLY group had 133 patients with a mean DFS of 38.03 months and a mean OS of 76.89 months. According to the Log-Rank comparison of survival curves between the two groups, the high CALLY group had significantly longer survival times than the low CALLY group, with statistically significant differences (DFS: $\chi^2 = 9.109$, $P = 0.0025$; OS: $\chi^2 = 5.637$, $P = 0.0176$). The survival curves are shown in Figure 1A and B.

COX Regression Analysis of Prognostic Factors for Breast Cancer Patients

Univariate analysis showed that age, menopausal status, albumin, C-reactive protein, lymphocyte count, CALLY index, carbohydrate antigen 153 (CA153), estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and postoperative endocrine therapy were significant variables for disease-free survival (DFS). These variables were then included in the multivariate analysis, and it was found that albumin, C-reactive protein, lymphocyte count, CALLY index, and CA153 were potential independent prognostic factors for DFS (Table 2). Univariate analysis also showed that age, menopausal status, albumin, C-reactive protein, lymphocyte count, CALLY index, CA153, carcinoembryonic antigen (CEA), total lymph node count (TLN), estrogen receptor

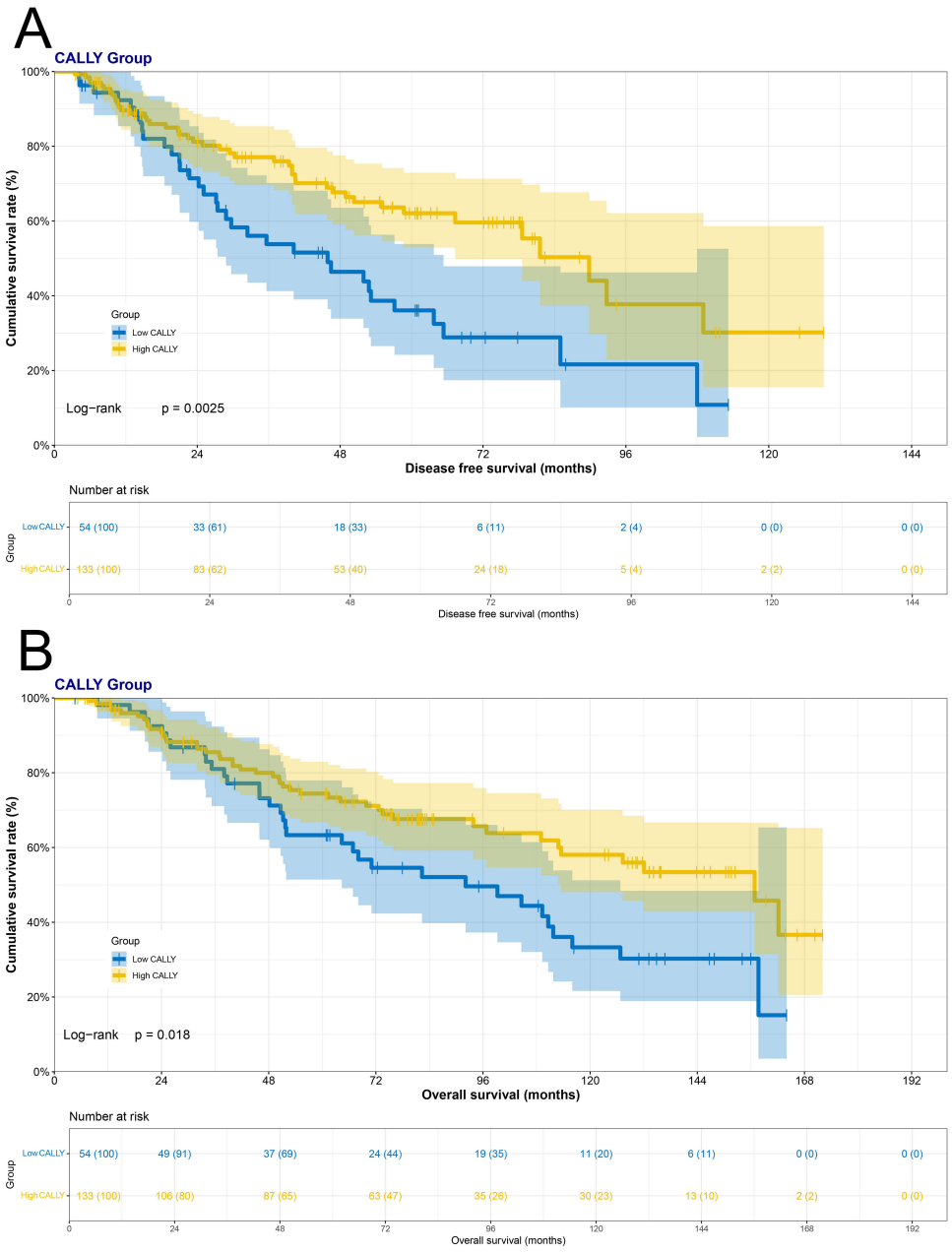

Figure 1 Disease-free survival (DFS) (**A**) and overall survival (OS) (**B**) curves for stage III breast cancer patients with different CALLY values.

(ER), progesterone receptor (PR), HER2, and postoperative endocrine therapy were significant variables for overall survival (OS). These variables were further included in the multivariate analysis, and it was found that albumin, C-reactive protein, lymphocyte count, CALLY index, CA153, TLN, and estrogen receptor (ER) were potential independent prognostic factors for OS (Table 3).

Construction and Validation of the Nomogram

Based on the multivariate COX regression model analysis for DFS and OS, the prognostic independent factors for DFS (albumin, C-reactive protein, lymphocyte count, CALLY index, CA153) and OS (albumin, C-reactive protein, lymphocyte count, CALLY index, CA153, TLN, ER) were included in the nomogram construction (Figure 2). The C-index for the nomogram predicting DFS was 0.692 (95% CI: 0.541–0.811), and for OS was 0.730 (95% CI: 0.586–0.838). The calibration curves showed a significant correlation between the predicted values and the actual observed values at 1-year,

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Table 2 Survival Analyses Based on Univariate and Multivariate Analyses for DFS in Stage III Breast Cancer Patients

Characteristics	Level	Univariate			Multivariate		
		HR	95% CI	P	HR	95% CI	P
Age	<52	1 (Ref.)		0.034	1 (Ref.)		0.135
	≥52	1.670	1.040–2.683		2.097	0.794–5.543	
BMI	<24.65	1 (Ref.)		0.546			
	≥24.65	1.149	0.733–1.800				
Family history	No	1 (Ref.)		0.291			
	Yes	0.748	0.436–1.282				
Menopause	No	1 (Ref.)		0.016	1 (Ref.)		0.682
	Yes	1.743	1.109–2.742		0.826	0.331–2.062	
Type of surgery	Mastectomy	1 (Ref.)		0.330			
	Breast-conserving surgery	0.563	0.177–1.789				
Albumin	<44.1	1 (Ref.)		0.005	1 (Ref.)		0.024
	≥44.1	0.490	0.298–0.806		0.530	0.306–0.919	
C-reactive protein	<0.30	1 (Ref.)		0.001	1 (Ref.)		0.010
	≥0.30	2.217	1.397–3.518		1.853	1.156–2.972	
Lymphocyte	<1.68	1 (Ref.)		0.005	1 (Ref.)		0.005
	≥1.68	0.515	0.323–0.820		0.299	0.128–0.696	
Monocytes	<0.30	1 (Ref.)		0.967			
	≥0.30	0.990	0.616–1.591				
Neutrophil	<3.23	1 (Ref.)		0.270			
	≥3.23	0.770	0.485–1.225				
CALLY index	Low	1 (Ref.)		0.003	1 (Ref.)		0.019
	High	0.505	0.321–0.794		0.572	0.359–0.912	
CA125	<12.32	1 (Ref.)		0.359			
	≥12.32	1.394	0.685–2.837				
CA153	<11.33	1 (Ref.)		0.021	1 (Ref.)		0.049
	≥11.33	1.699	1.082–2.670		2.179	1.002–4.737	
CEA	<1.87	1 (Ref.)		0.115			
	≥1.87	1.527	0.901–2.587				
Tumor size	<2	1 (Ref.)		0.088			
	≥2	1.599	0.932–2.743				
Total lymph nodes	<22	1 (Ref.)		0.378			
	≥22	1.280	0.740–2.215				
Positive lymph nodes	<2	1 (Ref.)		0.065			
	≥2	1.596	0.971–2.622				
Estrogen receptor	Negative	1 (Ref.)		0.000	1 (Ref.)		0.418
	Positive	0.444	0.282–0.700		0.585	0.160–2.139	
Progesterone receptor	Negative	1 (Ref.)		0.023	1 (Ref.)		0.749
	Positive	0.590	0.375–0.928		0.839	0.285–2.467	
HER2	Negative	1 (Ref.)		0.008	1 (Ref.)		0.625
	Positive	1.941	1.190–3.168		1.260	0.500–3.176	
Ki67	<14%	1 (Ref.)		0.341			
	≥14%	2.094	0.458–9.580				
Postoperative chemotherapy	No	1 (Ref.)		0.470			
	Yes	0.629	0.179–2.209				
Postoperative endocrine therapy	No	1 (Ref.)		0.017	1 (Ref.)		0.682
	Yes	0.572	0.361–0.904		0.793	0.262–2.404	
Postoperative radiotherapy	No	1 (Ref.)		0.982			
	Yes	0.994	0.569–1.736				
Postoperative targeted therapy	No	1 (Ref.)		0.292			
	Yes	0.260	0.021–3.190				

Table 3 Survival Analyses Based on Univariate and Multivariate Analyses for OS in Stage III Breast Cancer Patients

Characteristics	Level	Univariate			Multivariate		
		HR	95% CI	P	HR	95% CI	P
Age	<52	1 (Ref.)		0.005	1 (Ref.)		0.172
	≥52	1.969	1.228–3.155		1.740	0.786–3.852	
BMI	<24.65	1 (Ref.)		0.933			
	≥24.65	0.981	0.625–1.540				
Family history	No	1 (Ref.)		0.447			
	Yes	0.811	0.473–1.391				
Menopause	No	1 (Ref.)		0.004	1 (Ref.)		0.952
	Yes	1.922	1.225–3.016		1.026	0.440–2.391	
Type of surgery	Mastectomy	1 (Ref.)		0.232			
	Breast-conserving surgery	0.494	0.156–1.569				
Albumin	<44.1	1 (Ref.)		0.005	1 (Ref.)		0.002
	≥44.1	0.500	0.308–0.811		0.427	0.247–0.735	
C-reactive protein	<0.30	1 (Ref.)		0.000	1 (Ref.)		0.005
	≥0.30	2.282	1.438–3.621		3.215	1.434–7.207	
Lymphocyte	<1.68	1 (Ref.)		0.009	1 (Ref.)		0.028
	≥1.68	0.538	0.337–0.859		0.478	0.248–0.923	
Monocytes	<0.30	1 (Ref.)		0.638			
	≥0.30	0.893	0.559–1.428				
Neutrophil	<3.23	1 (Ref.)		0.590			
	≥3.23	0.882	0.559–1.392				
CALLY index	Low	1 (Ref.)		0.019	1 (Ref.)		0.035
	High	0.582	0.370–0.915		0.444	0.209–0.945	
CA125	<12.32	1 (Ref.)		0.235			
	≥12.32	1.590	0.740–3.414				
CA153	<11.33	1 (Ref.)		0.008	1 (Ref.)		0.004
	≥11.33	1.842	1.170–2.898		2.816	1.383–5.735	
CEA	<1.87	1 (Ref.)		0.024	1 (Ref.)		0.956
	≥1.87	1.690	1.071–2.667		1.020	0.515–2.020	
Tumor size	<2	1 (Ref.)		0.210			
	≥2	1.412	0.823–2.422				
Total lymph nodes	<22	1 (Ref.)		0.002	1 (Ref.)		0.001
	≥22	2.519	1.386–4.580		2.546	1.480–4.378	
Positive lymph nodes	<2	1 (Ref.)		0.145			
	≥2	2.074	0.778–5.523				
Estrogen receptor	Negative	1 (Ref.)		0.000	1 (Ref.)		0.001
	Positive	0.393	0.247–0.624		0.383	0.219–0.670	
Progesterone receptor	Negative	1 (Ref.)		0.030	1 (Ref.)		0.178
	Positive	0.606	0.386–0.953		0.512	0.193–1.356	
HER2	Negative	1 (Ref.)		0.042	1 (Ref.)		0.219
	Positive	1.649	1.017–2.674		1.835	0.697–4.831	
Ki67	<14%	1 (Ref.)		0.260			
	≥14%	2.338	0.533–10.246				
Postoperative chemotherapy	No	1 (Ref.)		0.135			
	Yes	0.325	0.074–1.419				
Postoperative endocrine therapy	No	1 (Ref.)		0.007	1 (Ref.)		0.971
	Yes	0.535	0.340–0.842		0.981	0.359–2.684	
Postoperative radiotherapy	No	1 (Ref.)		0.889			
	Yes	0.961	0.553–1.672				
Postoperative targeted therapy	No	1 (Ref.)		0.322			
	Yes	0.601	0.219–1.648				

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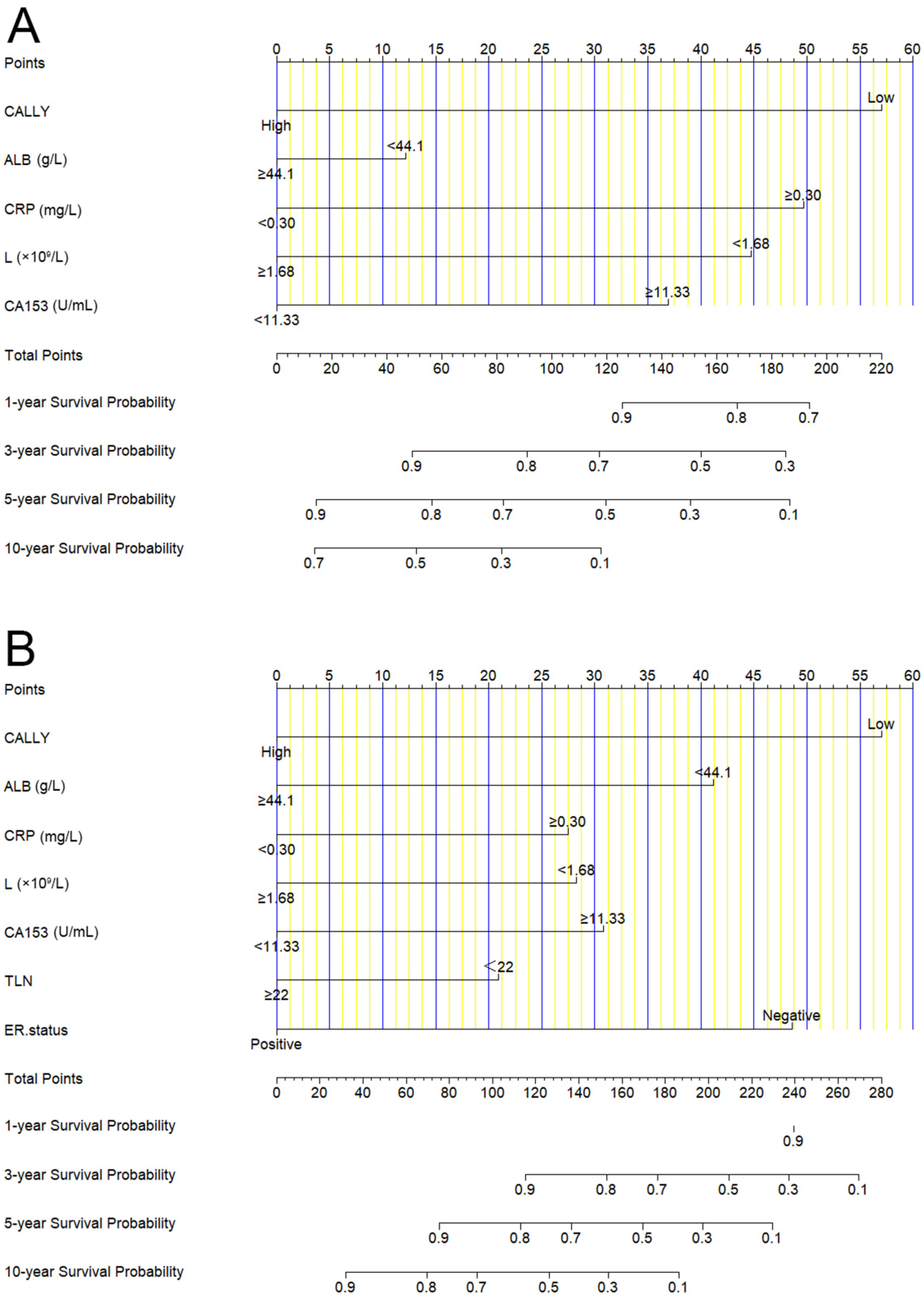

Figure 2 Nomogram for predicting disease-free survival (DFS) (**A**) and overall survival (OS) (**B**) in stage III breast cancer patients.

3-year, 5-year, and 10-year time points, with particularly excellent calibration performance for 1-year and 3-year DFS and OS (Figure 3). Decision curve analysis showed that the nomogram model had better clinical performance than the CALLY model in predicting 3-year, 5-year, and 10-year DFS and OS (Figure 4).

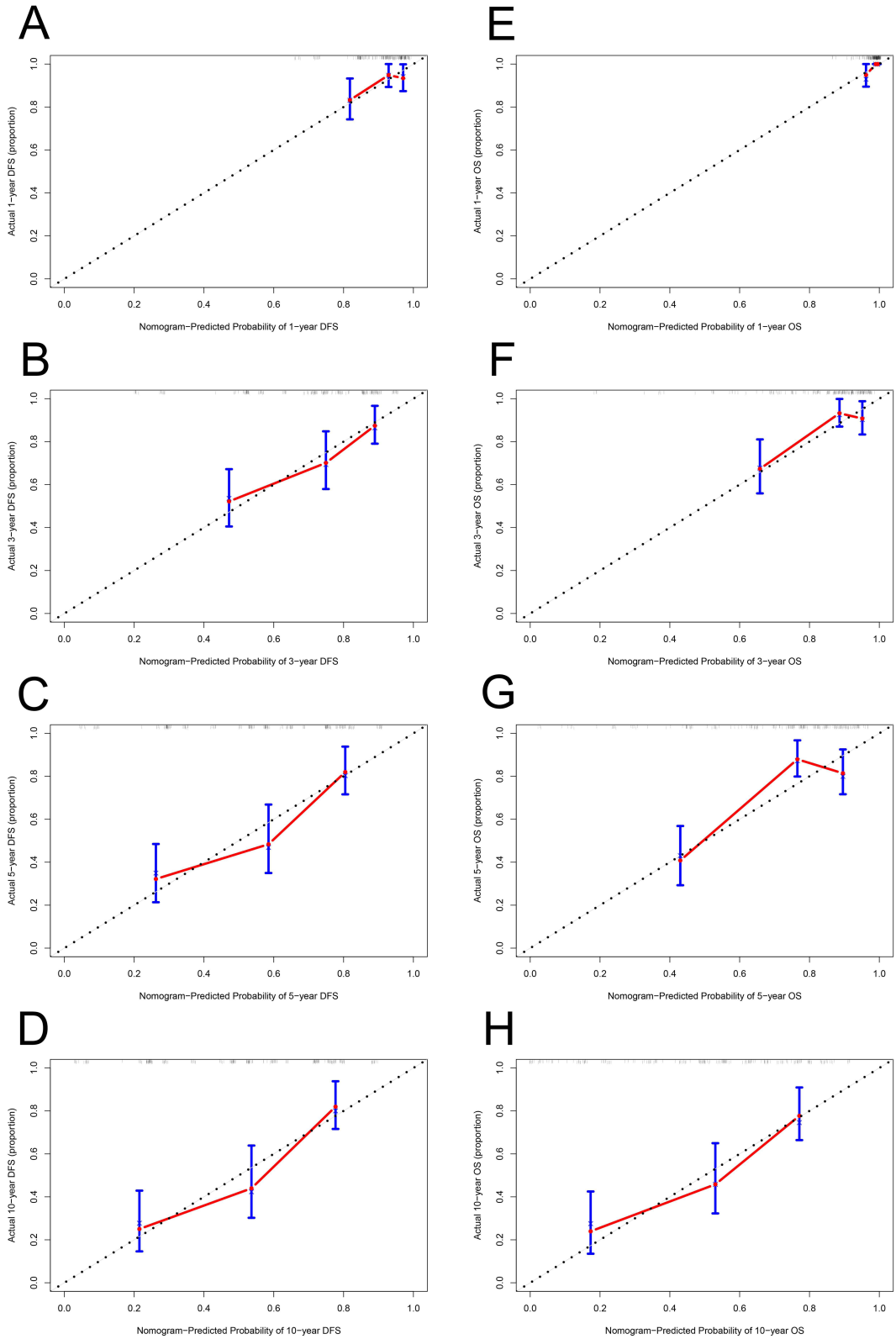

Figure 3 Calibration curves for predicting 1-year, 3-year, 5-year, and 10-year disease-free survival (DFS) (**A**–**D**) and overall survival (OS) (**E**–**H**) in stage III breast cancer patients.

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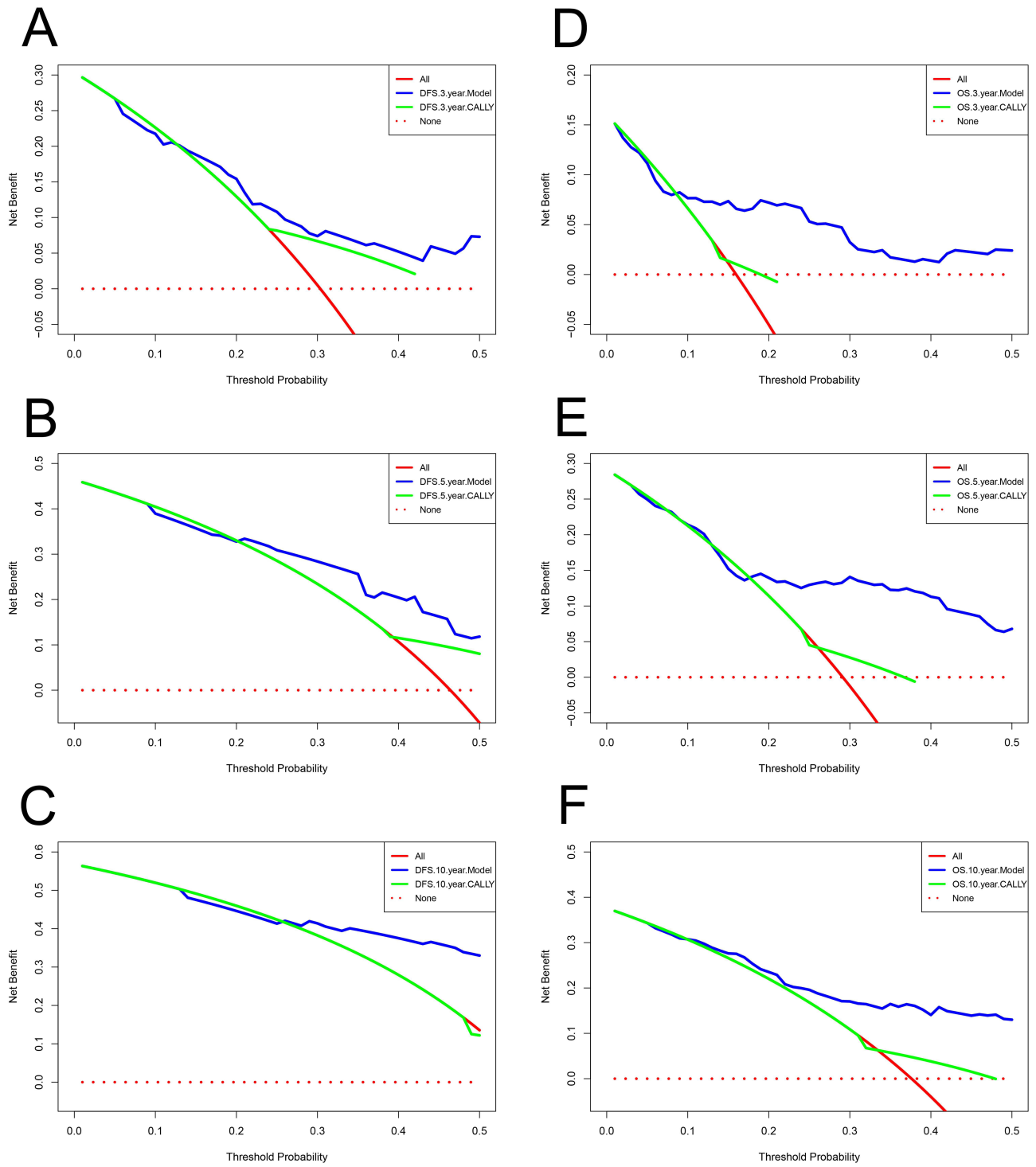

Figure 4 Decision curve analysis for predicting 3-year, 5-year, and 10-year disease-free survival (DFS) (**A**–**C**) and overall survival (OS) (**D**–**F**) in stage III breast cancer patients.

Discussion

Breast cancer is a heterogeneous disease that poses a significant challenge to the health of women worldwide.[13] Studies have shown that inflammation is involved in the occurrence, development, and metastasis of tumors, and the inflammatory microenvironment is an important determinant of the clinical prognosis of breast cancer. The carcinogenic signaling pathways involved can enhance epithelial-mesenchymal transition (EMT) and promote tumor metastasis.[14,15] Systemic

inflammatory responses can be assessed through routine blood markers.[16] When there is an increase in inflammatory cells such as neutrophils in the peripheral blood and a decrease in immune cells such as lymphocytes, malignant tumors are more likely to recur and metastasize.[17–19] Neutrophils promote tumor progression by secreting interleukin-6 and vascular endothelial growth factors, while lymphocytes play a key role in tumor immune surveillance, thereby inhibiting tumor progression and metastasis. Studies have shown that the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein can be used to predict the prognosis of breast cancer.[20,21] What's more, CALLY index with other prognostic parameters in breast cancer and demonstrated its superior predictive value.[22] In recent years, a new composite biological index, CALLY, has also been validated for its prognostic significance in various malignant tumors.[23]

The CALLY index, as a composite indicator reflecting inflammation, nutritional status, and immune response, has potential prognostic significance in stage III breast cancer patients. Our study explored the prognostic value of the CALLY index in these patients and constructed a prognostic nomogram model incorporating the CALLY index. The results showed that patients with a higher CALLY index had longer survival periods than those with a lower CALLY index. This finding provides strong evidence for the application of the CALLY index in the prognostic assessment of breast cancer.

Based on univariate and multivariate analyses, potential independent predictors of disease-free survival (DFS) mainly included albumin, C-reactive protein (CRP), lymphocytes, CALLY index, and CA153. For overall survival (OS), the potential independent predictors also included total lymph node number (TLN) and estrogen receptor (ER) status. We further developed a prognostic nomogram model that included the CALLY index and other indicators. This nomogram model demonstrated higher accuracy in predicting 1-, 3-, 5-, and 10-year survival probabilities compared to single traditional prognostic indicators. The C-index values for predicting DFS and OS in this study were 0.692 and 0.730, respectively, indicating good predictive ability of the nomogram model. Calibration curves and decision curve analysis further validated the accuracy and clinical utility of the nomogram model. The nomogram model showed high calibration effects in predicting 1- and 3-year DFS and OS, and its clinical utility was superior to the CALLY model alone. This provides a more accurate and reliable prognostic assessment tool for breast cancer patients.

CALLY index is composed of three factors: C-reactive protein, albumin, and lymphocyte count.[23] In clinical practice, composite indicators are more accurate than single biomarkers in predicting tumor prognosis.[24,25] Elevated C-reactive protein levels are associated with the release of tumor cytokines and immune suppression, while hypoalbuminemia reflects malnutrition and cachexia, both of which can lead to poor treatment tolerance and shortened survival.[19] As a widely used nutritional indicator, serum albumin levels can reflect the nutritional status and liver function of patients with various malignant tumors.[26,27] Elevated C-reactive protein levels are significantly associated with adverse outcomes such as metastasis and recurrence in breast cancer patients and can serve as a simple tool for risk assessment and prognostic prediction of breast cancer.[28,29] Other studies have shown that low serum albumin levels predict poor prognosis in metastatic breast cancer patients, and nomograms based on albumin have good predictive efficacy for overall survival.[30,31] Lymphocytes play a key role in tumor immune surveillance by inducing cytotoxic death to combat tumor cells and inhibit tumor progression.[32,33] Moreover, lymphopenia indicates impaired anti-tumor immune function, which can further accelerate disease deterioration.[33,34] By integrating these factors, CALLY index comprehensively quantifies the interaction between pro-tumor inflammation, nutritional depletion, and immune dysfunction, all of which collectively drive the progression and metastasis of breast cancer.[35]

The results of this study initially clarify that CALLY index has significant importance in the prognostic assessment and treatment decision-making for stage III breast cancer patients. The further construction of a nomogram can provide more personalized prognostic assessment and treatment recommendations for patients. This helps clinicians to develop more rational treatment plans and improve treatment outcomes. It also helps breast cancer patients to better understand their condition and prognosis, thereby enhancing their treatment confidence and compliance. However, this study also has certain limitations. First, this study is a single-center retrospective study with a relatively small sample size, which may introduce some selection bias. Second, although the calculation method of CALLY index is simple and easy to understand, further validation of its applicability and accuracy in different populations is still needed. Finally, although the constructed nomogram model has good predictive ability, it still needs to be continuously verified in actual clinical applications. In

future research, we will further expand the sample size and conduct multicenter, prospective studies to verify the accuracy and reliability of the CALLY index and the nomogram model in the prognostic assessment of breast cancer.

Conclusion

In summary, the CALLY index, as a composite indicator reflecting inflammation, nutritional status, and immune response, shows significant prognostic value in stage III breast cancer. The application of the nomogram model in combination with CALLY index provides more personalized prognostic assessment and treatment recommendations for breast cancer patients. This finding offers new insights and methods for the clinical diagnosis and treatment of breast cancer.

Ethics Approval and Consent to Participate

This study was approved by the ethics review committee of the Cancer Hospital, Chinese Academy of Medical Sciences (NCC2023C-445). And this study was performed in compliance with the 1964 Declaration of Helsinki and its later amendments. The patients were selected and signed informed consent forms.

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

All authors declare no conflicts of interest.

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