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Establishment and clinical application of a prognostic index for inflammatory status in triple-negative breast cancer patients undergoing neoadjuvant therapy using machine learning

Hao Sun[1†], Jian Liang[1†], Shuanglong Xue[1], Xiaoyan Zhang[1], Mingqiang Ding[1], Jingna Zhu[1], Abiyasi Nanding[2], Tianyi Liu[3], Ge Lou[3], Yue Gao[1], Yingjie Li[4] and Lei Zhong[1*]

Abstract

Objective This study aims to establish a new prognostic index using machine learning models to predict the clinical outcomes of triple-negative breast cancer (TNBC) patients receiving neoadjuvant therapy.

Methods In this study, we collected data from the electronic medical records system of Harbin Medical University Cancer Hospital to establish a training set of 501 breast cancer patients who received neoadjuvant therapy from January 2017 to December 2021. Additionally, we collected data from Harbin Medical University Affiliated Cancer Hospital, Harbin Medical University Affiliated Second Hospital, and Harbin Medical University Affiliated Sixth Hospital to establish a validation set of 1533 patients during the same period. All patients underwent blood tests, and the following inflammatory and immune indices were calculated for each patient: neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammatory index (SII), systemic inflammatory response index (SIRI), and advanced lung cancer inflammation index (ALI). The observed outcomes included Disease-free survival (DFS) and overall survival (OS). Survival analysis was performed using Kaplan–Meier survival curves, Cox survival analysis, propensity score matching analysis (PSM), and a nomogram to comprehensively investigate the impact of inflammatory status on patient survival.

Results The training set comprised 501 patients with a mean age of 48.63 (9.41) years, while the validation set comprised 1533 patients with a mean age of 49.01 (9.51) years. The formula for ANLR established through Lasso regression analysis on the training set is: ANLR index = NLR − 0.04 × ALB (g/L). In both the training and validation sets, ANLR was significantly associated with patient DFS and OS (all $P < 0.05$). Additionally, ANLR was found to be an independent prognostic factor in this study. PSM analysis further confirmed its significant correlation with patient

†Hao Sun and Jian Liang contributed equally to this work.

*Correspondence:
Lei Zhong
zhonglei@hrbmu.edu.cn

Full list of author information is available at the end of the article

DFS and OS (76 cases vs. 76 cases, $\chi2 = 2.179$, $P = 0.001$ and $\chi2 = 2.063$, $P = 0.002$). The nomogram containing ANLR also demonstrated high prognostic value. The C-index for the nomogram in the training set was 0.742 (0.619–0.886) for DFS and 0.758 (0.607–0.821) for OS, while in the validation set, the C-index was 0.733 (0.655–0.791) for DFS and 0.714 (0.634-0.800) for OS.

Conclusion ANLR was associated with the prognosis of TNBC patients receiving neoadjuvant therapy and could identify high-risk postoperative patients.

Keywords Triple-negative breast cancer, Neoadjuvant therapy, Inflammation status, Machine learning, Prognosis

Introduction

In recent decades, significant progress has been made in the research and treatment of breast cancer, particularly for hormone receptor-positive (HR^+) and human epidermal growth factor receptor 2-positive ($HER2^+$) breast cancer [1]. With the widespread application of targeted therapies, hormonal treatments, and personalized medicine, patient survival rates have markedly improved, and breast cancer is increasingly viewed as a chronic disease that can be managed long-term [2]. However, triple-negative breast cancer (TNBC) remains a highly aggressive subtype, lacking the expression of estrogen receptors (ER), progesterone receptors (PR), and HER2, rendering traditional endocrine therapies and HER2-targeted treatments ineffective [3]. Even with effective treatment, TNBC patients face a high risk of recurrence and distant metastasis, with prognoses significantly poorer than those of other breast cancer subtypes [4]. A further challenge is that TNBC patients frequently present with early occult metastases—meaning that at the time of diagnosis, tumor cells have already spread to other sites but have not yet manifested clinical symptoms or been detected by conventional imaging techniques [5]. This hidden metastasis complicates treatment and can lead to poor prognoses due to recurrence or metastasis after treatment completion [6]. TNBC accounts for approximately 15–20% of all breast cancers, making it a critical area in need of breakthroughs in treatment [7]. Therefore, exploring novel therapeutic strategies is of significant clinical and public health importance for improving patient outcomes and quality of life.

Neoadjuvant therapy has emerged as a crucial approach in managing early-stage TNBC, aiming to reduce tumor size and enhance surgical outcomes [8]. Despite advancements in treatment modalities, TNBC remains a formidable subtype with limited options, underscoring the urgent need for robust prognostic markers that can guide clinical decision-making and tailor therapy [9]. Recent studies have elucidated the significant role of inflammation in cancer progression, with various inflammatory markers showing associations with clinical outcomes in breast cancer [10]. Indices such as the neutrophil-to-lymphocyte ratio (NLR) and the systemic immune-inflammatory index (SII) have shown promise in predicting prognosis [11–13]. However, these markers are based on prior research and may not fully align with the rapid advancements in treatment approaches. Thus, establishing new inflammatory markers specifically for TNBC patients undergoing neoadjuvant therapy is of great significance.

In the context of big data and advanced analytics, machine learning presents an innovative opportunity to analyze complex datasets and develop predictive models. This study aims to establish a novel prognostic index that incorporates inflammatory status using machine learning techniques. By leveraging electronic medical records and inflammatory indices, this research seeks to identify high-risk patients among those undergoing neoadjuvant therapy, ultimately contributing to more personalized treatment approaches and improved patient outcomes.

Patients and materials

Patients

In this study, we collected data from the electronic medical records system of Harbin Medical University Cancer Hospital to establish a training set of 501 breast cancer patients who received neoadjuvant therapy from January 2017 to December 2021. Additionally, we collected data from Harbin Medical University Affiliated Cancer Hospital, Harbin Medical University Affiliated Second Hospital, and Harbin Medical University Affiliated Sixth Hospital to establish a validation set of 1533 patients during the same period. All patients were confirmed by pathology to be negative for ER, PR, and HER2, and underwent comprehensive surgical resection. The exclusion criteria for this study included incomplete clinical data, concurrent other tumors, the presence of acute or chronic inflammatory diseases, and loss to follow-up. This study was approved by the Ethics Committee of Sixth Affiliated Hospital of Harbin Medical University (LC2024-052).

Data collection and follow-up

On the day before treatment, blood samples were collected from patients and relevant blood and biochemical parameters were tested. Regular telephone follow-ups were conducted to determine disease-free survival (DFS) and overall survival (OS) over a follow-up period of 60 months. DFS was defined as the time from treatment

initiation or diagnosis to disease progression, while OS was defined as the time from treatment initiation or diagnosis to patient death. Evidence of disease progression was determined through rigorous imaging and pathological examinations.

Inflammatory status

To more accurately assess patients' inflammatory status, we calculated the NLR, platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), SII and systemic inflammation response index (SIRI) based on blood parameters. The calculation formulas are provided in Supplementary Table 1.

Statistical analysis

Statistical analyses were performed using R (version 4.3.1) and SPSS (version 25). Baseline characteristics were summarized as means ± standard deviations (SDs) for continuous variables and frequencies with percentages for categorical variables. Independent sample t-tests and Chi-square tests were used for correlation analyses. Kaplan–Meier survival curves and log-rank tests were applied to compare survival probabilities across ANLR groups, providing visual and statistical assessments of its association with survival outcomes. Cox proportional hazards regression identified independent prognostic factors and estimated hazard ratios (HRs). LASSO regression was used to construct a refined ANLR-based prognostic indicator by selecting the most predictive inflammatory indices while addressing potential multicollinearity. LASSO was chosen for its efficiency in variable selection and its ability to develop concise, interpretable models suitable for clinical application. A prognostic model and nomograms were then developed to further quantify and visualize the prognostic significance of the new ANLR indicator. Decision curve analysis (DCA) evaluated the clinical utility of the model. To minimize confounding factors, propensity score matching (PSM) was performed, and survival analyses were repeated in the matched cohort to validate the reliability and robustness of the new ANLR indicator as a prognostic marker.

Table 1 Patients' characteristics

	Training set	Validation set	*P*
Items	***n*** **= 501**	***n*** **= 1533**	
Age (years), mean (SD)	48.63(9.41)	49.01(9.51)	0.439
BMI (Kg/m^2), mean (SD)	25.23(4.87)	24.05(5.06)	0.534
Menopause, n (%)			0.550
Yes	276(55.1)	821(53.6)	
No	225(44.9)	712(46.4)	
Family history, n (%)			0.737
Yes	37(7.4)	142(9.3)	
No	464(92.6)	1391(90.7)	
Blood type, n (%)			0.981
A	117(23.4)	361(23.5)	
B	164(32.7)	495(32.3)	
AB	63(12.6)	185(12.1)	
O	157(31.3)	492(32.1)	
Tumor site, n (%)			0.387
Right	233(46.5)	679(44.3)	
Left	268(53.5)	854(55.7)	
LNP, n (%)			0.800
Positive	326(65.1)	1007(65.7)	
Negative	175(34.9)	526(34.3)	
Tumor size, n (%)			0.093
< 30 mm	181(36.1)	614(40.1)	
30–50 mm	219(43.7)	637(41.6)	
> 50 mm	101(20.2)	282(18.4)	
Histological Grading, n (%)			0.614
Grade I	110(22.0)	296(19.3)	
Grade II	333(66.5)	1080(70.5)	
Grade III	58(11.5)	157(10.2)	
TNM stage, n (%)			0.614
II	265(52.9)	771(50.3)	
III	236(47.1)	762(49.7)	

SD: standard deviation; BMI: body mass index; LNP: lymph node positivity

Results

Patient characteristics

The training set comprised 501 patients with an average age of 48.63 (9.41) years, while the validation set consisted of 1,533 patients with an average age of 49.01 (9.51) years. Among them, 1,097 patients (53.9%) were menopause, and 179 patients (8.8%) had a family history. A total of 1,063 patients (52.3%) were classified as TNM stage II, and 998 patients (49.1%) were classified as TNM stage III. There were no significant differences in all pathological parameters between the two groups of patients (all $P > 0.05$), as shown in Table 1.

Construction of risk index

All blood parameters were included in the Lasso regression model for analysis, with the regularization strength λ systematically adjusted to optimize variable selection (Fig. 1A, B). As λ increased, less significant parameters were excluded, leaving only the most predictive factors. When λ = 0.001, only ALB and NLR remained significant, indicating their strong contribution to the model. Based on the Lasso regression coefficients, the ANLR index was constructed as follows: ANLR index = NLR − 0.04 × ALB (g/L).

The prognostic value of ANLR index

The ANLR index achieved a maximum Youden index of approximately 0.247 when calculated using an ROC curve focused on mortality, with an optimal cutoff value of 1.05 (Fig. 2).

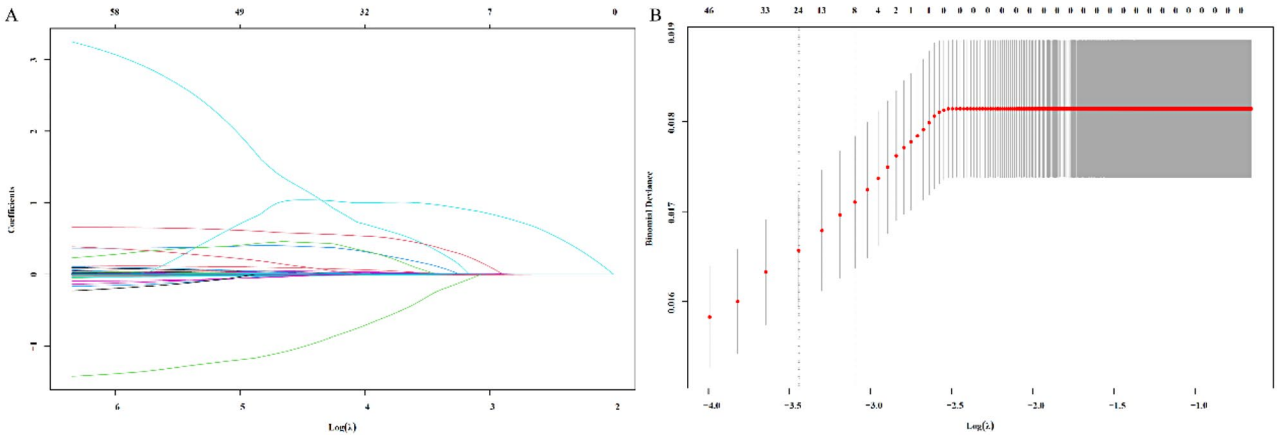

Fig. 1 Establishment of the Lasso model (**A**) and calculation of the optimal λ value (**B**)

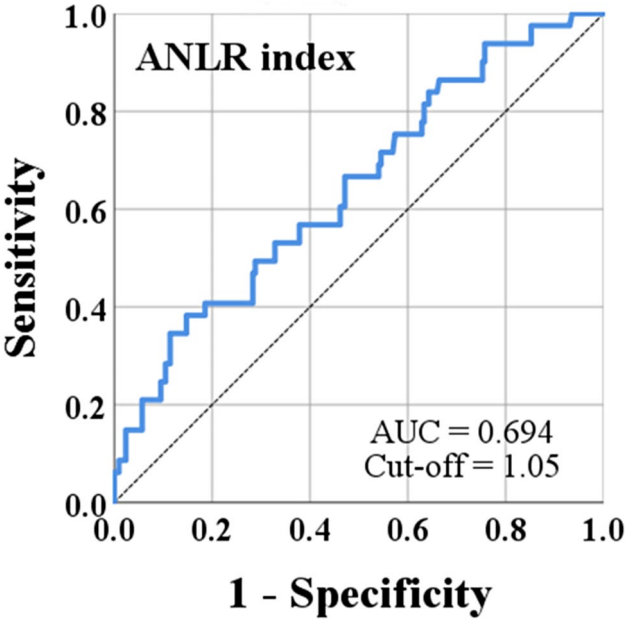

Fig. 2 The ROC curve of ANLR

Table 2 The AUC of ANLR and classical inflammatory markers

Items	AUC	95%CI
ANLR	0.694	0.607–0.772
NLR	0.657	0.534–0.691
PLR	0.639	0.555–0.723
LMR	0.648	0,549-0.716
SII	0.601	0.533–0.744
SIRI	0.635	0.528–0.692

AUC: Area under the curve; CI: Confidence interval; ANLR: Alb and Neutrophil-Lymphocyte Ratio; NLR: Neutrophil-Lymphocyte Ratio; PLR: Platelet-Lymphocyte Ratio; LMR: Lymphocyte-Monocyte Ratio; SII: Systemic Immune-Inflammation Index; SIRI: Systemic Inflammation Response Index

Furthermore, compared with other classical inflammatory markers, ANLR exhibited the highest AUC of 0.694 (Table 2).

Survival analysis of ANLR index

Survival analysis in training set

The timeROC analysis for ANLR showed that the 3-, 4-, and 5-year AUCs for DFS were 0.657, 0.713, and 0.692, and for OS were 0.643, 0.707, and 0.679, respectively (Fig. 3A, B). Patients with higher ANLR had significantly shorter DFS (408 cases vs. 93 cases, $\chi^2=3.735$, $P<0.001$) and OS (408 cases vs. 93 cases, $\chi^2=4.117$, $P<0.001$, Fig. 3C, D).

Survival analysis in test set

In the validation set, timeROC analysis for ANLR revealed 3-, 4-, and 5-year AUCs of 0.696, 0.717, and 0.693 for DFS, and 0.684, 0.719, and 0.692 for OS (Fig. 4A, B). Patients with higher ANLR values exhibited significantly shorter DFS and OS (1239 cases vs. 294 cases, $\chi^2=3.889$, $P<0.001$ and $\chi^2=4.746$, $P<0.001$, Fig. 4C, D). The risk analysis of ANLR index also revealed significant differences between high-risk and low-risk groups (Fig. 4E, F).

Cox survival analysis

In the validation set, univariate analysis revealed that tumor size, lymph node positivity (LNP), histological grading, TNM stage, and ANLR index were all associated with DFS and OS (all $P<0.05$). Further multivariate analysis identified LNP (HR=1.544, $P<0.001$ and HR=1.995, $P<0.001$), TNM stage (HR=2.582, $P<0.001$ and HR=2.796, $P<0.001$) and ANLR (HR=3.551, $P<0.001$ and HR=3.798, $P<0.001$) as independent prognostic factors for both DFS and OS (Tables 3 and 4).

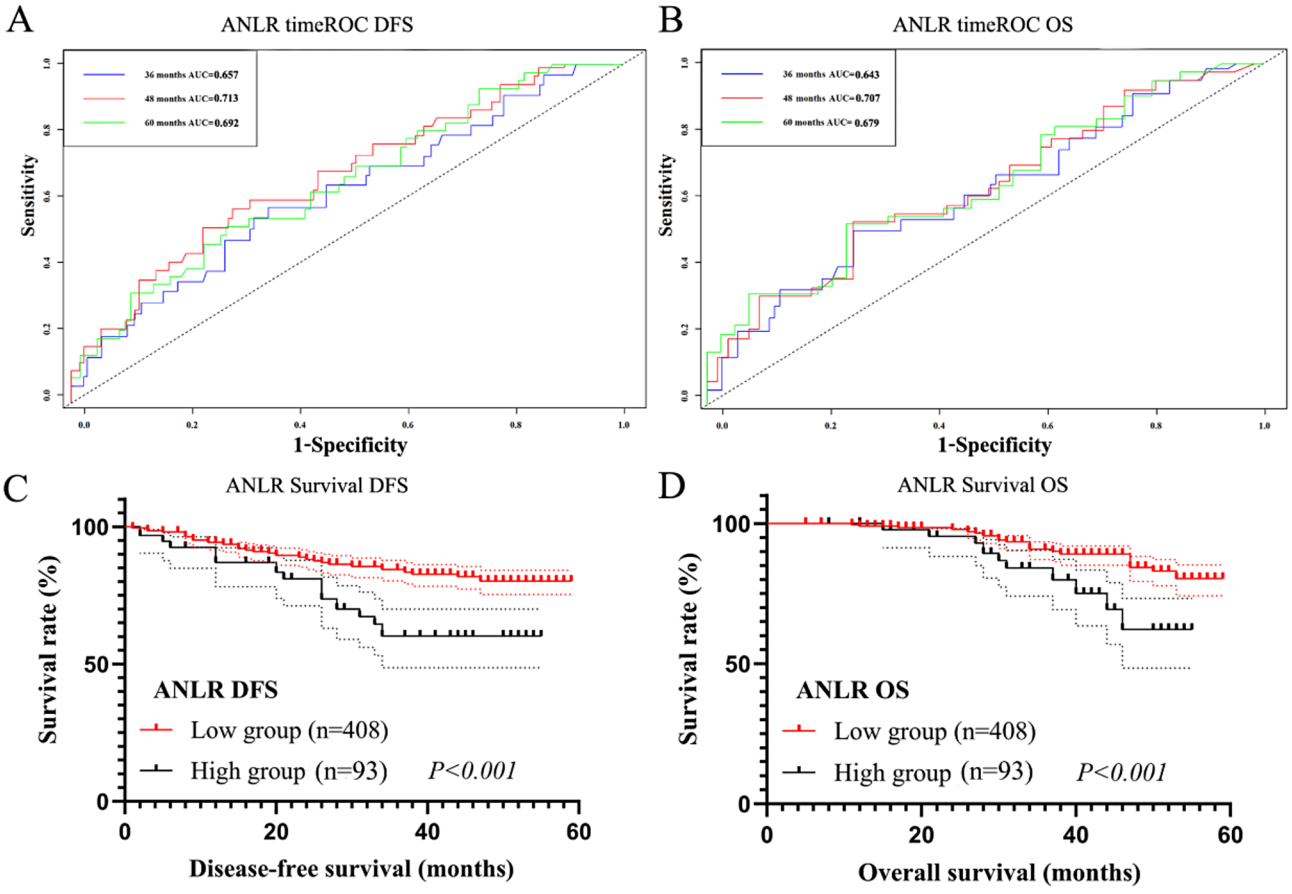

Fig. 3 Survival analysis in Training set. (**A**) The timeROC of ANLR in DFS; (**B**) The timeROC of ANLR in OS; (**C**) The survival curve of ANLR in DFS; (**D**) The survival curve of ANLR in OS

Propensity score matching analysis for ANLR

In the validation set, correlation analysis showed that the ANLR index was significantly associated with age, BMI, family history, PLN, tumor size, histological grading, and TNM stage (all $P<0.05$). Based on these correlation analysis results, we selected variables with significant statistical associations for PSM. A 1:1 nearest-neighbor matching method without replacement was applied to ensure that patients with similar prognostic characteristics were paired. Through this matching process, a total of 152 patients were included, with 76 in the high ANLR group and 76 in the low ANLR group. After matching, there were no significant differences in baseline clinical characteristics between the two ANLR groups (all $P>0.05$, Table 5), confirming the balance and comparability of the matched cohorts. This rigorous matching process ensures that the observed prognostic differences are primarily attributable to the ANLR index.

After PSM, the 3-, 4-, and 5-year AUCs for DFS of ANLR were 0.647, 0.672, and 0.666, respectively, and for OS were 0.668, 0.655, and 0.653, respectively (Fig. 5A, B). Higher ANLR remained associated with shorter DFS and OS (76 cases vs. 76 cases, $\chi^2=2.179$, $P=0.001$ and $\chi^2=2.063$, $P=0.002$, Fig. 5C, D).

Comparison of prognostic value of ANLR in different periods

By collecting the levels of ALB, NEU, and LYM the day before surgery, the preoperative ANLR index (pANLR) was calculated. The timeROC curve analysis showed that the AUC of ANLR for both DFS and OS was higher than that of pANLR at all stages (Fig. 6).

Construction of nomograms

The Schoenfeld residual plots indicated that both TNM stage and the ANLR index met the proportional hazards assumption (all $P>0.05$, Fig. 7A, B). The nomograms incorporating TNM stage and the ANLR index were developed in the training set (Fig. 7C, D). The C-index for the nomogram in the training set was 0.742 (0.619–0.886) for DFS and 0.758 (0.607–0.821) for OS, while in the validation set, the C-index was 0.733 (0.655–0.791) for DFS and 0.714 (0.634-0.800) for OS. Calibration curves based on the validation set demonstrated good agreement of the nomogram (Fig. 7E, F).

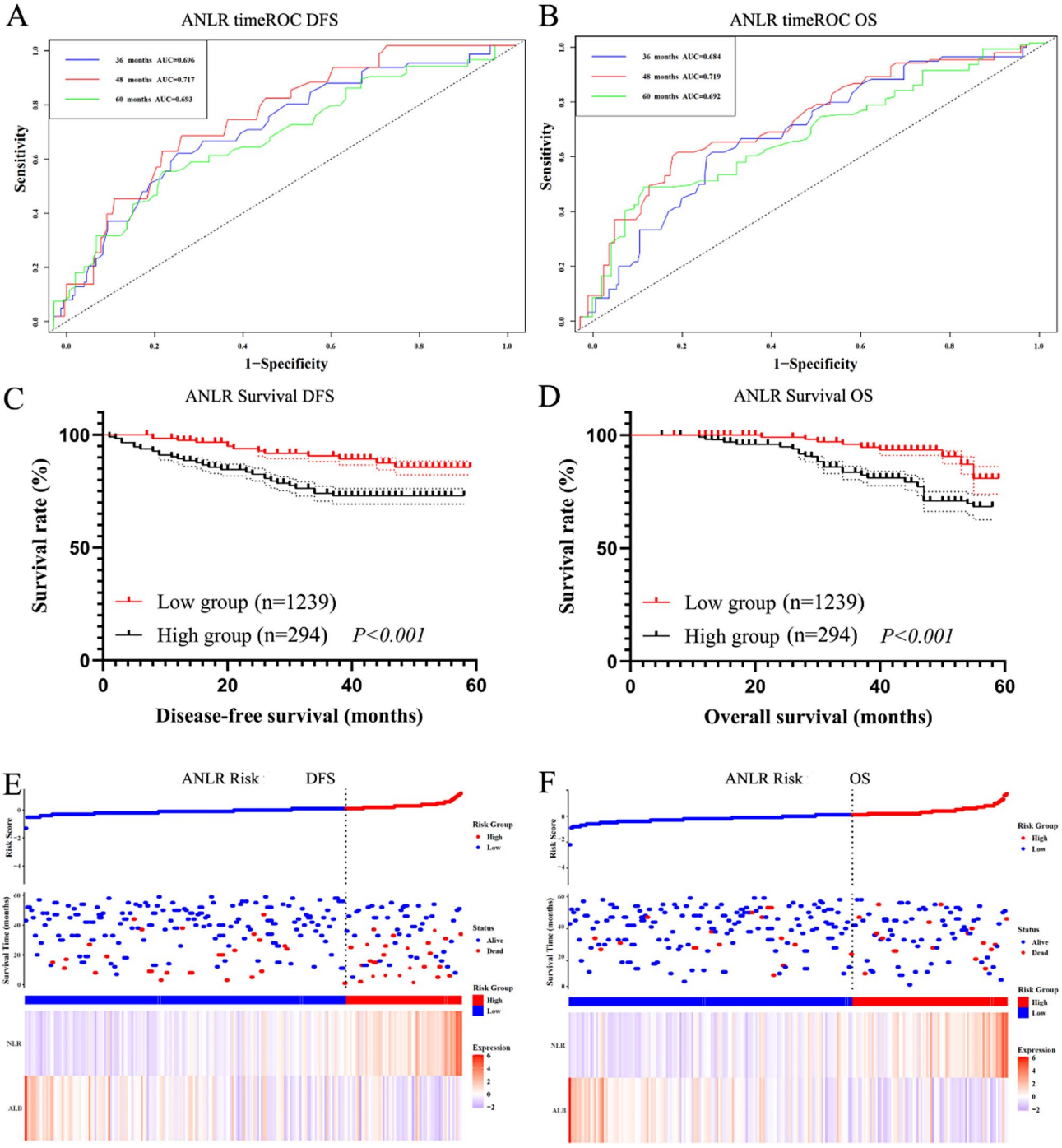

Fig. 4 Survival analysis in Test set. (**A**) The timeROC of ANLR in DFS; (**B**) The timeROC of ANLR in OS; (**C**) The survival curve of ANLR in DFS; (**D**) The survival curve of ANLR in OS; (**E**) The risk analysis of ANLR in DFS; (**F**) The risk analysis of ANLR in OS

Discussion

The association between inflammation and cancer progression is well-documented, with various inflammatory markers reflecting the host's immune response to tumorigenesis [14, 15]. In TNBC, where traditional hormone-targeted therapies are ineffective, understanding the role of inflammation becomes particularly crucial [16]. TNBC is characterized by its aggressive behavior and poor prognosis, making it imperative to identify reliable prognostic indicators that can guide treatment decisions [17].

Research on the impact of inflammatory status on cancer patients has become quite mature. Classic inflammatory markers such as NLR, PLR, LMR, SII, SIRI, and ALI have been found to be associated with the prognosis

Table 3 Univariate Cox analysis of DFS and OS

	DFS		OS	
Items	**HR (95%CI)**	**P**	**HR (95%CI)**	**P**
Age	1.019(1.008–1.030)	< 0.001	1.016(1.004–1.028)	0.010
BMI	1.047(1.034–1.059)	< 0.001	1.037(1.021–1.053)	< 0.001
ANLR				
< 1.05	Ref		Ref	
≥ 1.05	4.134(3.713–4.658)	< 0.001	4.326(3.597–5.016)	< 0.001
Menopause				
Yes	Ref		Ref	
No	0.946(0.821–1.091)	0.449	0.913(0.792–1.052)	0.438
Family history				
Yes	Ref		Ref	
No	1.060(0.752–1.495)	0.739	1.079(0.946–1.114)	0.534
Primary tumor site				
Right	Ref		Ref	
Left	1.012(0.874–1.266)	0.705	1.070(0.915–1.348)	0.653
Tumor size				
< 30 mm	Ref		Ref	
30–50 mm	1.086(0.876–1.077)	0.282	1.008(0.771–1.070)	0.250
> 50 mm	1.681(1.400-2.018)	< 0.001	1.756(14.62–2.110)	< 0.001
LNP				
Negative	Ref		Ref	
Positive	2.160(1.703–2.740)	< 0.001	3.168(2.357–4.260)	< 0.001
Histological Grading				
Grade I	Ref		Ref	
Grade II	1.390(1.017-1.900)	0.039	1.469(1.075–2.008)	0.016
Grade III	1.580(1.198–2.085)	0.001	1.545(1.171–2.038)	0.002
TNM stage				
II	Ref		Ref	
III	3.501(2.008–5.114)	< 0.001	4.595(3.383–5.839)	< 0.001

DFS: Disease-Free Survival; OS: Overall survival; HR: Hazard ratio; BMI: Body mass index; ANLR: Alb and Neutrophil-Lymphocyte Ratio; LNP: lymph node positivity

of various cancers. Melanoma is one of the earliest solid tumors to utilize immune checkpoint inhibitors. Capone and colleagues analyzed the relationship between NLR and its derived marker dNLR with the prognosis of advanced melanoma patients treated with nivolumab. They collected and analyzed data from 97 patients and found that when baseline levels were below a critical threshold, both NLR and dNLR were associated with improved survival rates [18]. Additionally, Mandaliya and his colleagues analyzed the prognostic predictive capabilities of NLR, PLR, LMR, and ALI in advanced non-small cell lung cancer. They collected data from 279 advanced patients over a five-year period for analysis. The results indicated that high baseline NLR, high PLR, low LMR, and low ALI were significantly associated with poor OS. Similar findings were observed across various subgroups, including age [19]. In another study, Guo and colleagues investigated the predictive value of preoperative inflammatory markers for early recurrence after surgery in hepatitis B virus-related hepatocellular carcinoma (HCC). They conducted a retrospective analysis of 162 patients who underwent HCC resection, determining the optimal cutoff values for the NLR, PLR, SIRI, and SII. The results indicated that tumor diameter, tumor differentiation, vascular invasion, and elevated inflammatory markers were associated with an increased risk of early recurrence. The combined index developed in the study demonstrated strong predictive capability (AUC of 0.804), outperforming individual markers [20]. Inflammatory status is also widely used in breast cancer, especially TNBC. In a retrospective study, Nakamoto and colleagues explored the link between systemic immune markers and outcomes of atezolizumab treatment in advanced TNBC patients. Analyzing 36 patients across eight Japanese institutions, they found that low baseline NLR and a decrease in NLR at the second treatment cycle were associated with longer OS, while high baseline absolute lymphocyte count (ALC) and reduced NLR predicted longer time to treatment failure (TTF). The study supports the efficacy and safety of atezolizumab and underscores the predictive value of immune markers in advanced TNBC [21]. Another study conducted by Wang Ping and colleagues in 2019 explored the relationship between the SII and the Breast Imaging Reporting and Data System (BI-RADS)

Table 4 Multivariate Cox analysis of DFS and OS

	DFS		OS	
Items	**HR (95%CI)**	**P**	**HR (95%CI)**	**P**
Age	1.002(0.994–1.010)	0.563	1.004(0.996–1.012)	0.338
BMI	1.005(0.975–1.014)	0.589	1.006(0.974–1.014)	0.554
ANLR				
< 1.05	Ref		Ref	
≥ 1.05	3.551(2.547–4.982)	< 0.001	3.798(2.987–4.679)	< 0.001
Tumor size				
< 30 mm	Ref		Ref	
30–50 mm	1.057(0.898–1.255)	0.523	1.185(0.787–1.332)	0.222
> 50 mm	1.139(0.850–1.525)	0.383	1.360(0.997–1.959)	0.063
LNP				
Negative	Ref		Ref	
Positive	1.544(1.238–2.421)	< 0.001	1.995(1.595–2.496)	< 0.001
Histological Grading				
Grade I	Ref		Ref	
Grade II	1.389(0.926–2.083)	0.147	1.120(0.835–1.501)	0.450
Grade III	1.164(0.783–1.852)	0.253	1.055(0.878–1.517)	0.737
TNM stage				
II	Ref		Ref	
III	2.582(1.771–4.674)	< 0.001	2.796(1.555–4.021)	< 0.001

DFS: Disease-Free Survival; OS: Overall survival; HR: Hazard ratio; BMI: Body mass index; ANLR: Alb and Neutrophil-Lymphocyte Ratio; LNP: lymph node positivity

classification with the prognosis of 215 patients with TNBC. The results showed that low SII was associated with better survival rates: the median OS for patients with low SII was 60.9 months, while for those with high SII it was 40.3 months (HR=3.78, $P<0.001$); the median DFS was 22.4 months and 14.4 months, respectively (HR=3.16, $P<0.001$). Patients with BI-RADS 5 classification also had shorter survival times. Multivariable analysis indicated that high SII is an independent predictor of poor prognosis (OS: HR=2.96, $P<0.001$; DFS: HR=2.85, $P=0.005$). The study concluded that pre-treatment SII and BI-RADS 5 are important prognostic indicators for TNBC patients, suggesting the need for further research on the potential role of SII in clinical decision-making [22]. These studies highlight the significant potential of inflammatory status in TNBC.

In this study, we established a novel inflammatory marker, ANLR, composed of ALB and the NLR, through a grouped analysis of 2,034 TNBC patients receiving neoadjuvant therapy. ANLR was not only significantly associated with patient prognosis but also demonstrated a higher prognostic value compared to other classical inflammatory markers such as SII and PLR. Furthermore, ANLR served as an independent prognostic factor for both DFS and OS, showing predictive power comparable to TNM staging and outperforming other inflammatory markers in multivariable analysis. Notably, ANLR has also shown greater prognostic value in studies focusing on TNBC compared to other inflammatory markers reported in previous research [23–25]. Subsequent PSM analysis further validated ANLR's substantial prognostic value by minimizing potential confounding factors, highlighting its significant advantage and clinical relevance in this patient cohort. These findings underscore the potential of ANLR as a reliable and practical tool for personalized prognostic assessment in TNBC.

ANLR is a novel inflammatory biomarker whose mechanism for predicting prognosis can be analyzed through the specific roles and interactions of its components. Firstly, albumin plays a crucial physiological role in plasma, including maintaining oncotic pressure and transporting nutrients and medications [26–28]. A decrease in albumin levels is often associated with chronic inflammation, malnutrition, and tumor-related cachexia [29]. Particularly in cancer patients, low albumin levels indicate systemic inflammation and a reduced ability to combat tumors [30]. Research has demonstrated that low albumin levels correlate with poor prognosis in cancer patients, highlighting a weakened anti-tumor response [31, 32]. Thus, albumin not only reflects a patient's nutritional status but is also closely linked to overall health and quality of life [33]. Secondly, the NLR serves as an indicator of the body's inflammatory state and provides insights into the tumor microenvironment [34, 35]. An increase in neutrophils generally reflects the body's response to tumor cells,

Table 5 Propensity score matching analysis

	Before PSM			After PSM		
	Low ANLR	High ANLR		Low ANLR	High ANLR	
Items	***n*** **= 1239**	***n*** **= 294**	***P***	***n*** **= 76**	***n*** **= 76**	***P***
Age (years), mean (SD)	50.64(9.19)	49.18(9.14)	0.016	49.37(9.08)	49.45(9.24)	0.717
BMI (Kg/m^2), mean (SD)	25.27(5.32)	24.15(3.69)	0.001	24.44(4.26)	24.28(3.72)	0.608
Menopause, n (%)			0.864			0.138
Yes	114(9.2)	28(9.5)		7(9.2)	9(11.8)	
No	1125(90.8)	266(90.5)		69(90.8)	67(88.2)	
Family history, n (%)			< 0.001			0.351
Yes	565(45.6)	184(62.6)		37(48.7)	36(47.4)	
No	674(54.4)	110(37.4)		39(51.3)	40(52.6)	
Blood type, n (%)			0.136			0.762
A	483(39.0)	101(34.4)		28(36.8)	29(38.2)	
B	319(25.7)	68(23.1)		18(23.7)	17(22.4)	
AB	115(9.3)	35(11.9)		7(9.2)	8(10.5)	
O	322(26.0)	90(30.6)		23(30.3)	22(28.9)	
Tumor site, n (%)			0.063			0.209
Right	574(46.3)	105(35.7)		34(44.7)	32(42.1)	
Left	665(53.7)	189(64.3)		42(55.3)	44(57.9)	
PLN, n (%)			0.002			0.091
Positive	748(60.4)	206(70.1)		51(67.1)	49(64.3)	
Negative	491(39.6)	88(29.9)		25(32.9)	27(35.7)	
Tumor size, n (%)			< 0.001			0.155
< 30 mm	531(42.9)	83(28.2)		24(31.6)	22(28.9)	
30–50 mm	526(42.5)	111(37.8)		31(40.8)	31(40.8)	
> 50 mm	182(14.6)	100(34.0)		21(27.6)	23(30.3)	
Histological Grading, n (%)			< 0.001			0.537
Grade I	263(21.2)	33(11.2)		12(15.8)	11(14.5)	
Grade II	864(69.7)	216(73.5)		57(75.0)	57(75.0)	
Grade III	112(9.1)	45(15.3)		7(9.2)	8(10.5)	
TNM stage, n (%)			< 0.001			0.766
II	668(53.9)	103(35.0)		40(52.6)	39(51.3)	
III	571(46.1)	191(65.0)		36(47.4)	37(48.7)	

PSM: Propensity score matching; ANLR: Alb and Neutrophil-Lymphocyte Ratio; BMI: Body mass index; LNP: lymph node positivity

while lymphocytes are key components of the immune response [36, 37]. Elevated NLR signifies an enhanced inflammatory response, which is often associated with increased risks of tumor progression, metastasis, and recurrence [38]. In cancer patients, a high NLR is frequently linked to poorer survival rates and prognosis, indicating a state of immune suppression within the tumor microenvironment [39, 40]. By combining albumin with NLR, ANLR enables a comprehensive assessment of both inflammatory and nutritional statuses. This holistic approach allows ANLR to reflect not only the body's inflammatory response but also overall health and anti-tumor capacity. Consequently, ANLR serves as a more effective prognostic indicator for TNBC patients.

Compared to traditional inflammatory biomarkers, ANLR presents several clear advantages. Traditional single inflammatory markers can be influenced by various factors, including infections, comorbid conditions, and physiological states [41, 42]. In contrast, ANLR combines two distinct biological markers, providing a more stable and comprehensive evaluation that mitigates the impact of these external factors. Additionally, the calculation of ANLR is relatively straightforward and easy to implement in clinical practice. Clinicians can derive the necessary data from routine blood tests to quickly compute ANLR and adjust treatment strategies as needed. This ease of use enhances the potential for ANLR to be integrated into standard clinical protocols, offering a valuable tool for predicting outcomes in TNBC patients.

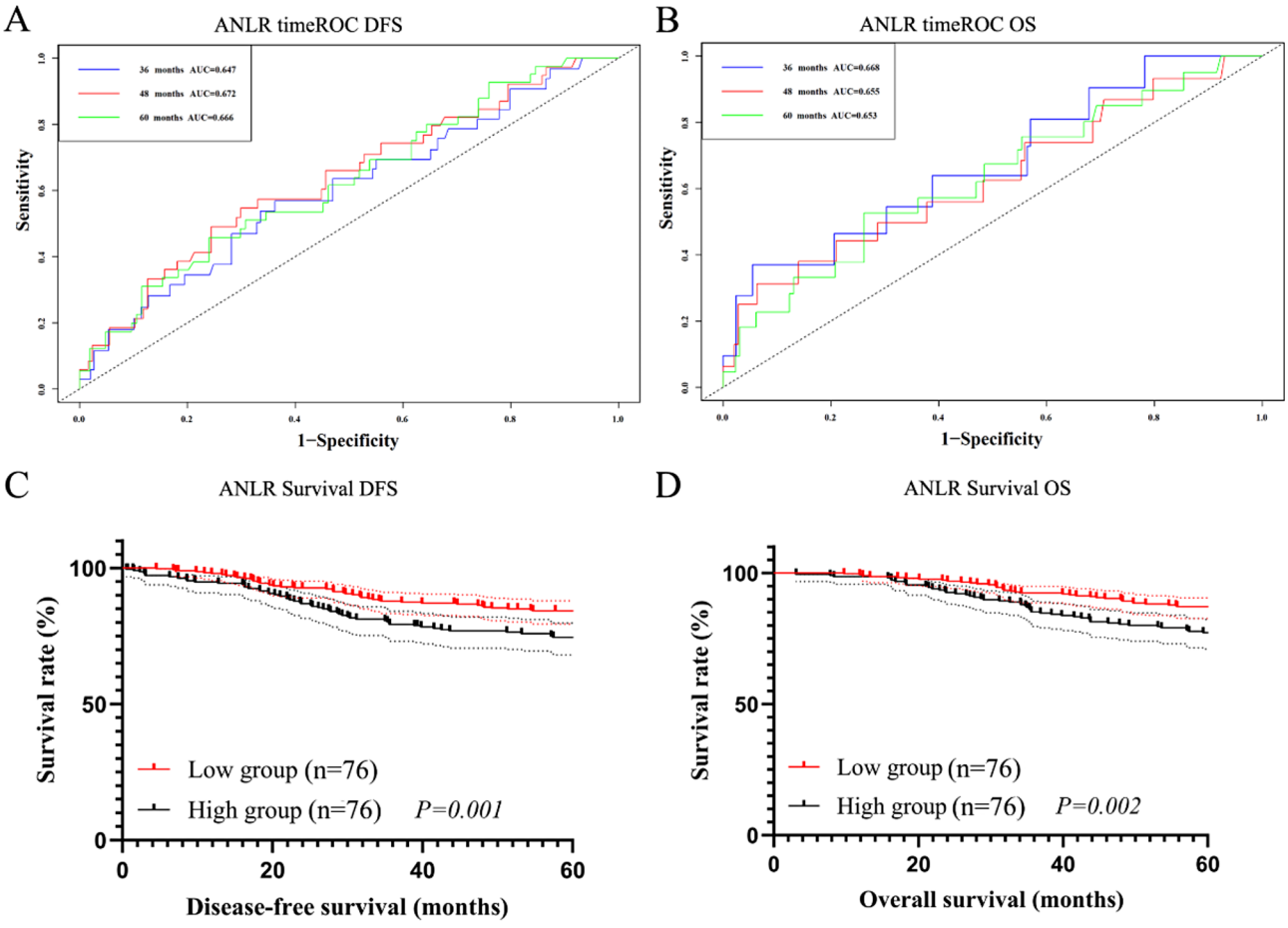

Fig. 5 Survival analysis after PSM. (**A**) The timeROC of ANLR in DFS; (**B**) The timeROC of ANLR in OS; (**C**) The survival curve of ANLR in DFS; (**D**) The survival curve of ANLR in OS

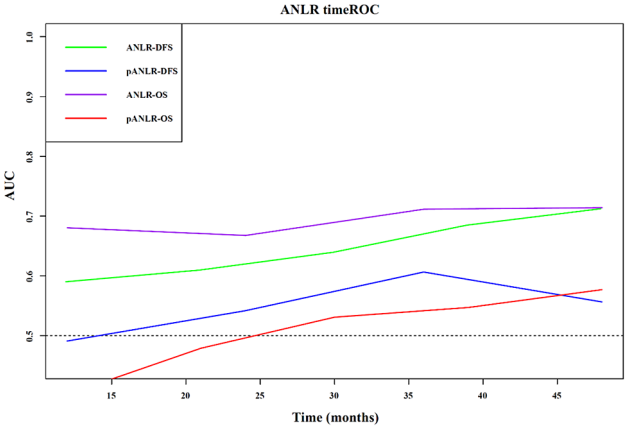

Fig. 6 The timeROC curve of ANLR and pANLR

Despite the promising results, our study is not without limitations. The retrospective nature of the analysis may introduce biases, and the generalizability of our findings should be validated in larger, prospective cohorts. Additionally, while ANLR demonstrated strong prognostic value, further studies are needed to explore its biological mechanisms, particularly how ANLR interacts with tumor microenvironments and immune responses. Furthermore, the study's reliance on a single-center dataset may limit its applicability to broader populations, and potential confounding factors, despite efforts to control them through propensity score matching, cannot be entirely ruled out. Future research should also investigate the integration of ANLR with other novel inflammatory or immune markers to enhance prognostic accuracy.

Conclusion

In conclusion, our study demonstrates that the ANLR is a valuable prognostic marker for TNBC patients undergoing neoadjuvant therapy. The ANLR shows strong predictive ability for patient outcomes and can effectively identify high-risk patients postoperatively.

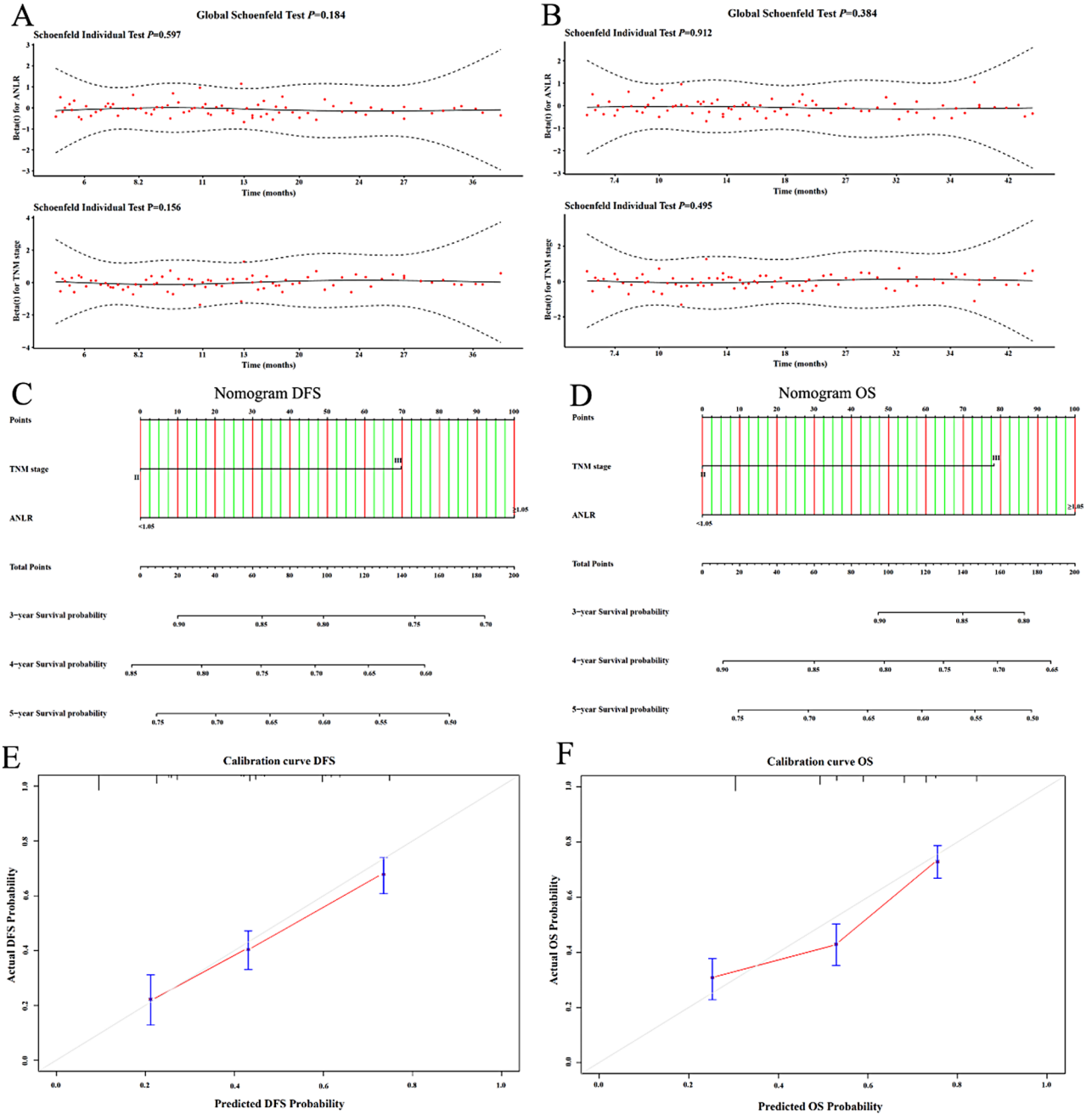

Fig. 7 Construction of nomograms. (**A**) Schoenfeld residual plots of DFS; (**B**) Schoenfeld residual plots of OS; (**C**) Nomogram of DFS; (**D**) Nomogram of OS; (**E** Calibration curve of DFS; (**F**) Calibration curve of OS

Author contributions

Writing-original draft and Writing-review & editing: H.S. and J.L.; Data curation and Investigation: S.X., X.Z., Mingqiang Ding and J.Z.; Methodology and Supervision: A.N., T.L. and G.L., Y.G. and Y.L.; Resources, Funding acquisition, and Project administration: L.Z. All authors have read and agreed to the published version of the manuscript.

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Data availability

The data supporting this study can be provided by the corresponding author upon reasonable request.

Declarations

Ethical approval

This study was conducted in accordance with the Helsinki Declaration and received approval from the ethics committee of Sixth Affiliated Hospital of Harbin Medical University (LC2024-052). All patients signed an "Informed Consent Form for the Secondary Use of Medical History Data/Biological

Specimens". Informed consent was obtained from all individual participants included in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Breast Surgery, Sixth Affiliated Hospital of Harbin Medical University, Harbin 150023, China
[2]Department of Pathology, The Affiliated Cancer Hospital of Harbin Medical University, Harbin 150086, China
[3]Department of Pathology, Second Affiliated Hospital of Harbin Medical University, Harbin 150086, China
[4]Department of Pathology, Sixth Affiliated Hospital of Harbin Medical University, Harbin 150023, China

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