Preoperative lymphocyte-albumin-monocyte index as an inflammation- and nutrition-based predictor of overall survival in triple-negative breast cancer: A retrospective cohort study

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Abstract. Serum albumin (ALB) and the lymphocyte-to-monocyte ratio (LMR) are established inflammation- and nutrition-related biomarkers associated with tumor progression. Their combined prognostic value in triple-negative breast cancer (TNBC) has not been fully defined. Therefore, the present study aimed to develop and demonstrate a lymphocyte-albumin-monocyte index (LANI) that integrates ALB and LMR for prognostic assessment in TNBC. A retrospective cohort of 166 surgically treated patients with TNBC was analyzed and divided into training (n=116) and validation (n=50) cohorts. Receiver operating characteristic analysis yielded optimal thresholds of 39.35 g/l for ALB and 2.526 for LMR, which were rounded to clinical cutoffs of 40 g/l and 2.97. Patients were categorized into three LANI groups, namely LANI=0 (ALB <40 g/l and LMR <2.97), LANI=1 (either indicator above the cutoff) and LANI=2 (both indicators above the cutoff). Multivariate Cox analysis demonstrated that tumor stage, histologic grade and LANI were independent predictors of overall survival, with a LANI value of 2 indicating markedly reduced mortality risk (hazard ratio=0.03; 95% CI: 0.002-0.46; P=0.012). A nomogram incorporating these factors showed strong discrimination, good calibration and a meaningful clinical net benefit across both cohorts. Overall, the LANI provides a simple, reproducible and cost-effective biomarker that enhances prognostic stratification and supports individualized management in TNBC.

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Introduction

Triple-negative breast cancer (TNBC) represents an aggressive molecular subtype of breast cancer, accounting for 15-20% of all cases (1,2). Despite advances in comprehensive treatment strategies, TNBC remains characterized by early relapse and a high propensity for distant metastasis (3-5). Owing to the absence of estrogen receptor (ER), progesterone receptor (PR) and HER2, patients receive limited benefits from endocrine or targeted therapies and have been shown to experience markedly worse overall survival (OS) compared with other breast cancer molecular subtypes, particularly hormone receptor-positive and HER2-positive disease (6-8). Although initially chemosensitive, TNBC frequently develops drug resistance, contributing to early relapse, distant metastasis and reduced disease-free survival and OS (9). Current prognostic systems based on tumor size, lymph node status and histologic grade insufficiently capture the biological heterogeneity of TNBC or the important influence of host-related factors (10,11). Growing evidence has indicated that systemic host responses, particularly immune and nutritional status, serve central roles in tumor progression and treatment response (12,13). Thus, biomarkers integrating host immunity and nutrition may offer more accurate prognostic insight within TNBC management.

Systemic inflammation and nutritional deficiency are key determinants of cancer initiation, progression and survival (14). Chronic inflammation promotes immune evasion, angiogenesis and epithelial-mesenchymal transition through cytokine-mediated pathways including IL-6/STAT3, TNF-α/NF-κB and TGF-β (15-17). Concurrently, malnutrition impairs immune competence, leading to compromised T-cell activation, macrophage dysfunction and weakened antitumor responses (18,19). Composite indices reflecting inflammation or nutrition, such as the modified Glasgow prognostic score (mGPS), prognostic nutritional index (PNI), systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), have shown prognostic utility in a number of

malignancies, including TNBC (20-23). Elevated NLR independently predicted shorter disease-free survival in early-stage TNBC (24), while a meta-analysis of 819 patients showed that a high PLR was associated with a worse overall and disease-free survival, although effect sizes and cut-off values varied markedly across studies (25). SII demonstrated prognostic value in both recurrent/metastatic TNBC (n=62) (26) and a large neoadjuvant cohort of 422 patients, whereby postoperative SII remained an independent predictor of OS (27). Composite markers combining inflammatory and nutritional domains have also been explored. For example, the Naples Prognostic Score (NPS) outperformed PNI, NLR, PLR and controlling nutritional status (CONUT) in a cohort of 223 postoperative patients with TNBC (28). However, the majority of TNBC-specific analyses remain constrained by modest sample sizes (frequently <100 patients) (26,29,30) and inconsistent findings across cohorts. For example, PLR has only exhibited OS values considered to be borderline statistically significant before sensitivity adjustment, with numerous neoadjuvant studies having reported that SII, system inflammation response index (SIRI) and PLR were not consistently associated with treatment response or long-term outcomes. Given that the majority of indices quantify inflammatory activation or nutritional reserve in isolation, these values fail to capture bidirectional interactions, which are particularly relevant in TNBC, whereby systemic inflammation, lymphocyte depletion and metabolic fragility often coexist. These limitations highlight the need for a simple integrative biomarker capable of concurrently reflecting inflammatory-immune activity and nutritional status to improve preoperative risk stratification in TNBC.

To address this gap, the present study has developed the lymphocyte-albumin-monocyte index (LANI), a novel biomarker combining serum albumin (ALB) and the lymphocyte-to-monocyte ratio (LMR). Both parameters are routinely measured and inexpensive, supporting feasibility for clinical use. ALB reflects protein nutritional status, as well as the inflammatory response of the host, as hypoalbuminemia is associated with cytokine-driven catabolism, impaired hepatic synthesis and poor tolerance to treatment (31,32). LMR represents the balance between antitumor immunity and tumor-promoting inflammation, as lymphocytes mediate cytotoxic surveillance (33), whereas monocytes can differentiate into tumor-associated macrophages that foster invasion and immune escape (34). In TNBC, accumulating evidence has demonstrated the pronounced coexistence of immune suppression and metabolic exhaustion. Clinically, patients with TNBC frequently exhibit elevated systemic inflammatory activation and impaired lymphocyte-mediated immunity. High NLR has been repeatedly associated with reduced disease-free and OS in early-stage and neoadjuvant TNBC cohorts (35-37), while SII has been identified as an independent adverse prognostic factor in recurrent/metastatic TNBC and in pre-surgery assessments of patients who have undergone neoadjuvant treatment (38). Beyond peripheral inflammation, studies assessing tumor-infiltrating lymphocytes have revealed that increased NLR is associated with lower tumor-infiltrating lymphocyte (TIL) density and an unfavorable CD8/Foxp3 ratio, reflecting a shift toward an immunosuppressive microenvironment (26,39). These findings collectively indicate that TNBC is characterized by both systemic lymphocyte depletion and heightened myeloid-driven inflammatory activity, features that contribute to immune dysfunction and metabolic vulnerability. Existing single-dimension inflammatory or nutritional markers capture only certain aspects of this biology and are therefore insufficient to reflect the dual immune-metabolic disturbance typical of TNBC.

The present study aimed to evaluate the prognostic importance of preoperative LANI in surgically treated TNBC and develop a LANI-based nomogram for individualized survival prediction. A retrospective cohort of 166 patients was analyzed to assess the association between preoperative LANI and long-term OS. Kaplan-Meier curves and multivariate Cox models were applied to determine its prognostic value and a nomogram incorporating LANI, tumor (T) stage and histologic grade was constructed for personalized prediction. Model performance was examined using time-dependent receiver operating characteristic (ROC) curves, calibration plots, Brier scores and decision curve analysis (DCA). Overall, LANI, in addition to its statistical performance, relies on two inexpensive, readily available parameters, highlighting its potential as a practical biomarker for preoperative risk assessment, treatment planning and longitudinal monitoring in TNBC.

Patients and methods

Study population. A total of 166 female patients with TNBC treated at the Affiliated Cancer Hospital of Xinjiang Medical University (Urumqi, China) between January 2018 and December 2019, were included in the present retrospective cohort study. Inclusion criteria ensured patients: i) Were newly diagnosed with primary TNBC without prior anticancer treatment; ii) had available preoperative baseline peripheral blood tests; iii) had undergone curative-intent surgery with axillary evaluation; iv) exhibited postoperative pathological confirmation of invasive carcinoma; v) had complete clinicopathological staging data; and vi) had undergone standardized adjuvant therapy and follow-up according to institutional protocols. Exclusion criteria included the presence of bilateral or multifocal breast cancer, pregnancy or lactation, missing baseline hematological data, prior breast cancer or breast surgery, concomitant malignancies or the absence of definitive postoperative pathology. Patients who had received neoadjuvant therapy were excluded to ensure comparability of baseline laboratory parameters. According to institutional perioperative assessment standards, candidates for curative surgery generally did not present with uncontrolled severe hepatic or renal dysfunction, overt systemic infections or hematologic disorders that could markedly alter ALB or leukocyte-derived indices. All baseline hematological parameters, including serum ALB and leukocyte subsets, were obtained from routine peripheral blood tests performed within 7 days prior to surgery. These measurements were collected at the time of first hospital admission as part of standard preoperative evaluation. No longitudinal or post-treatment measurements of these indices were incorporated into the present analysis. The present study was reviewed and approved by The Ethics Committee of the Affiliated Cancer Hospital of Xinjiang Medical University (approval no. K-2024056) and conducted in accordance with

the Declaration of Helsinki. Written informed consent was obtained from all participants. All eligible patients were consecutively enrolled to minimize selection bias.

Data collection. Clinical and laboratory data were extracted from the electronic medical records. Variables included baseline characteristics (age, BMI, menopausal status, smoking and alcohol history), hematological parameters (ALB, lymphocyte, monocyte, neutrophil and platelet counts), pathological features [T stage, lymph node (N) stage, American Joint Committee on Cancer (AJCC) stage, histologic grade and Ki-67] as well as survival outcomes. LMR was calculated as lymphocyte count divided by monocyte count. The LANI score was derived using prespecified thresholds for ALB and LMR (ALB, 40 g/l; LMR, 2.97): LANI=0 when ALB <40 g/l and LMR <2.97; LANI=1 when either ALB ≥40 g/l or LMR ≥2.97l; and LANI=2 when both ALB ≥40 g/l and LMR ≥2.97. OS was defined as the interval from surgery to mortality (from any cause) or last follow-up (December 2024). Furthermore, due to the retrospective design, a number of factors that can directly influence ALB and lymphocyte/monocyte counts, such as hepatic or renal dysfunction, acute or chronic infections, autoimmune or inflammatory diseases or corticosteroid use, were not systematically documented and therefore could not be adjusted for, leaving potential residual confounding factors.

Statistical analysis. All analyses were performed using SPSS (version 29.0.2; IBM Corp.) and R software (version 4.4.2; Posit Software, PBC). Baseline characteristics were summarized as counts and percentages for categorical variables and as means ± SD or medians with interquartile range (IQR) for continuous variables. Group comparisons used the χ^2 or Fisher's exact test for categorical variables, an unpaired (independent samples) Student's t-test for normally distributed continuous variables (two-group comparisons). The Wilcoxon rank-sum test was used for non-normally distributed variables.

ROC curve analysis was applied to determine the optimal cut-off values for ALB and LMR using the Youden index, yielding 39.35 g/l and 2.526, respectively. To ensure practical clinical applicability, the ROC-derived cut-offs (39.35 g/l for ALB and 2.526 for LMR) were converted to clinically interpretable thresholds. Routine laboratory reports do not provide three-decimal precision and statistically optimized values with excessive granularity are not used in real-world decision-making. Therefore, the ALB cut-off was rounded to 40.0 g/l, consistent with thresholds commonly adopted in breast cancer prognostic studies (40,41). For LMR, the ROC-derived value was converted to 2.97, which most closely preserved the distributional characteristics of the original value while remaining compatible with clinically reportable formats. These refined thresholds were therefore used to construct the LANI score. To examine whether this rounding influenced prognostic performance, a sensitivity analysis was conducted comparing Cox regression and time-dependent ROC results obtained using the raw ROC cut-offs compared with the rounded clinical cut-offs, demonstrating minimal differences in predictive accuracy between the two approaches.

Restricted cubic spline (RCS) models were fitted to evaluate potential non-linear associations of ALB and LMR with OS. Kaplan-Meier survival curves were generated and compared using the log-rank test. Univariate Cox analyses were first performed to screen candidate prognostic variables (P<0.05). However, because T stage, N stage and AJCC stage exhibited notable multicollinearity, given that AJCC stage is derived from T and N, simultaneous inclusion of these variables in the multivariable Cox model resulted in unstable estimates. Therefore, to avoid overadjustment and preserve model stability, only T stage was retained among these tumor burden indicators. This decision was supported by both statistical considerations [more stable hazard ratios (HR) with narrower CIs] and clinical interpretability (T stage representing the core component of anatomical tumor extent). Thus, the final multivariate model included T stage, histologic grade and LANI, representing three complementary dimensions of prognosis, namely tumor burden, biological aggressiveness and host inflammatory-nutritional status, respectively. HRs and 95% CIs were calculated using the Wald method. A prognostic nomogram was constructed based on these variables. Model discrimination and calibration were assessed using time-dependent ROC curves, Brier scores and calibration plots for 1-, 3- and 5-year OS. DCA was used to evaluate clinical net benefit. Internal validation was conducted in the predefined validation cohort. All statistical tests were two-sided, with P<0.05 being considered to indicate a statistically significant difference.

Results

Clinicopathological characteristics of the study cohort. Within the present study, 166 patients with TNBC were included, all of whom underwent curative-intent surgery with axillary evaluation as clinically indicated, comprising 116 in the training cohort and 50 in the validation cohort. Among them, 12.7% were >45 years, 31.3% were aged 45-59 years, 44.6% were aged 60-74 years and 11.4% were aged ≥75 years. BMI distribution showed 4.2% underweight, 42.8% normal, 38.0% overweight and 15.1% obese. With regard to tumor characteristics, 16.9, 61.4, 18.1 and 3.6% were T1, T2, T3 and T4 stages, respectively. Nodal status showed 47.0% N0, 25.3% N1, 17.5% N2 and 10.2% N3 stages. AJCC staging included 10.2% exhibiting stage I, 57.8% stage II and 31.9% stage III. Histologic grade comprised 18.1% grade (G) 1, 59.0% G2 and 22.9% G3. High Ki-67 expression (>30%) was observed in 45.8% of tumors. No significant differences were observed between the training and validation cohorts (all P>0.05; Table I).

Association of ALB and LMR with clinicopathological features. Within the training cohort, low ALB levels (<40.0 g/l) were significantly associated with advanced N stage (P=0.0301), higher AJCC stage (P=0.0221) and poor histologic grade (P=0.0022). Similarly, low LMR levels (<2.97) were significantly associated with a higher T stage (P=0.0051). However, no significant associations were found between ALB or LMR and age, BMI, pathological subtype or Ki-67 expression (all P>0.05; Table II). Notably, a brief examination of these associations revealed that patients with decreased ALB tended to present with more extensive nodal involvement and a more advanced T stage, whereas patients with lower LMR were more likely to exhibit larger primary tumors (a higher T stage). These associations underscore how both ALB and LMR reflect underlying tumor burden

Table I. Baseline clinicopathological characteristics of patients with triple-negative breast cancer in the overall (n=166), training (n=116) and validation (n=50) cohorts.

	Cohort			
Characteristic	Overall, n (%)	Training, n (%)	Validation, n (%)	P-value
Age, years				0.886
<45	21 (12.7)	16 (13.8)	5 (10.0)	
45-59	52 (31.3)	37 (31.9)	15 (30.0)	
60-74	74 (44.6)	50 (43.1)	24 (48.0)	
≥75	19 (11.4)	13 (11.2)	6 (12.0)	
BMI, kg/m^2				0.325
<18.5	7 (4.2)	3 (2.6)	4 (8.0)	
>28	25 (15.1)	18 (15.5)	7 (14.0)	
18.5-24	71 (42.8)	53 (45.7)	18 (36.0)	
24-28	63 (38.0)	42 (36.2)	21 (42.0)	
T stage				0.337
T1	28 (16.9)	19 (16.4)	9 (18.0)	
T2	102 (61.4)	68 (58.6)	34 (68.0)	
T3	30 (18.1)	25 (21.6)	5 (10.0)	
T4	6 (3.6)	4 (3.4)	2 (4.0)	
N stage				0.832
N0	78 (47.0)	57 (49.1)	21 (42.0)	
N1	42 (25.3)	29 (25.0)	13 (26.0)	
N2	29 (17.5)	19 (16.4)	10 (20.0)	
N3	17 (10.2)	11 (9.5)	6 (12.0)	
AJCC stage				0.757
I	17 (10.2)	12 (10.3)	5 (10.0)	
II	96 (57.8)	69 (59.5)	27 (54.0)	
III	53 (31.9)	35 (30.2)	18 (36.0)	
Histologic grade				0.355
G1	30 (18.1)	24 (20.7)	6 (12.0)	
G2	98 (59.0)	65 (56.0)	33 (66.0)	
G3	38 (22.9)	27 (23.3)	11 (22.0)	
Ki-67				0.762
>30%	76 (45.8)	54 (46.6)	22 (44.0)	
≤30%	90 (54.2)	62 (53.4)	28 (56.0)	

P-values calculated using χ^2 tests or Fisher's exact tests as appropriate. T stage, tumor stage; N stage, lymph node stage; AJCC, American Joint Committee on Cancer.

and systemic inflammatory-nutritional status, providing a biological rationale for their integration into the LANI score. These findings suggest that decreased ALB and LMR are associated with tumor progression and adverse pathological characteristics in patients with TNBC.

Determination of optimal cut-off values for ALB and LMR. ROC curve analysis identified 39.35 g/l as the optimal cut-off value for ALB [area under the curve (AUC)=0.757] and 2.526 for LMR (AUC=0.634), indicating the prognostic predictive ability of these indices in patients with TNBC (Fig. 1A). RCS analysis further demonstrated a continuous association between decreasing ALB, lower LMR levels and an elevated OS risk, demonstrating their prognostic significance (Fig. 1B and C). For improved clinical interpretability and applicability, the present ROC-derived cut-off values (39.35 g/l and 2.526) were rounded to the nearest conventional clinical thresholds (40.0 g/l and 2.97, respectively) for subsequent LANI model construction. Collectively, these findings highlight the prognostic relevance of ALB and LMR in patients with TNBC. To further enhance predictive accuracy, these markers were integrated into the LANI model for comprehensive prognostic evaluation.

Development and prognostic value of the LANI model. To improve prognostic stratification in TNBC management, the LANI model was developed using the rounded clinical

Table II. Association between ALB and LMR levels and clinicopathological features in patients with triple-negative breast cancer.

	ALB				LMR			
Characteristic	Overall (n=116)	<40.0 (n=42)	≥40.0 (n=74)	P-value	Overall (n=116)	<2.97 (n=33)	≥2.97 (n=83)	P-value
Age, years				>0.999[a]				0.364[a]
<45	16 (13.8)	6 (14.3)	10 (13.5)		16 (13.8)	5 (15.2)	11 (13.3)	
≥75	13 (11.2)	5 (11.9)	8 (10.8)		13 (11.2)	6 l(18.2)	7 (8.4)	
45-59	37 (31.9)	13 (31.0)	24 (32.4)		37 (31.9)	11 (33.3)	26 (31.3)	
60-74	50 (43.1)	18 (42.9)	32 (43.2)		50 (43.1)	11 (33.3)	39 (47.0)	
BMI, kg/m^2				0.552[a]				0.651[a]
<18.5	3 (2.6)	2 (4.8)	1 (1.4)		3 (2.6)	1 (3.0)	2 (2.4)	
>28	18 (15.5)	6 (14.3)	12 (16.2)		18 (15.5)	3 (9.1)	15 (18.1)	
18.5-24	53 (45.7)	21 (50.0)	32 (43.2)		53 (45.7)	17 (51.5)	36 (43.4)	
24-28	42 (36.2)	13 (31.0)	29 (39.2)		42 (36.2)	12 (36.4)	30 (36.1)	
Pathology				0.918[b]				0.259[b]
Invasive ductal carcinoma	89 (76.7)	32 (76.2)	57 (77.0)		89 (76.7)	23 (69.7)	66 (79.5)	
Invasive lobular carcinoma	27 (23.3)	10 (23.8)	17 (23.0)		27 (23.3)	10 (30.3)	17 (20.5)	
T stage				0.357[a]				0.005[a]
T1	19 (16.4)	7 (16.7)	12 (16.2)		19 (16.4)	6 (18.2)	13 (15.7)	
T2	68 (58.6)	25 (59.5)	43 (58.1)		68 (58.6)	20 (60.6)	48 (57.8)	
T3	25 (21.6)	7 (16.7)	18 (24.3)		25 (21.6)	3 (9.1)	22 (26.5)	
T4	4 (3.4)	3 (7.1)	1 (1.4)		4 (3.4)	4 (12.1)	0 (0.0)	
N stage				0.030[a]				0.647[a]
N0	57 (49.1)	15 (35.7)	42 (56.8)		57 (49.1)	14 (42.4)	43 (51.8)	
N1	29 (25.0)	11 (26.2)	18 (24.3)		29 (25.0)	8 (24.2)	21 (25.3)	
N2	19 (16.4)	8 (19.0)	11 (14.9)		19 (16.4)	7 (21.2)	12 (14.5)	
N3	11 (9.5)	8 (19.0)	3 (4.1)		11 (9.5)	4 (12.1)	7 (8.4)	
AJCC stage				0.022[a]				0.111[a]
I	12 (10.3)	6 (14.3)	6 (8.1)		12 (10.3)	4 (12.1)	8 (9.6)	
II	69 (59.5)	18 (42.9)	51 (68.9)		69 (59.5)	15 (45.5)	54 (65.1)	
III	35 (30.2)	18 (42.9)	17 (23.0)		35 (30.2)	14 (42.4)	21 (25.3)	
Histologic grade				0.002[b]				0.271[b]
G1	24 (20.7)	4 (9.5)	20 (27.0)		24 (20.7)	6 (18.2)	18 (21.7)	
G2	65 (56.0)	21 (50.0)	44 (59.5)		65 (56.0)	16 (48.5)	49 (59.0)	
G3	27 (23.3)	17 (40.5)	10 (13.5)		27 (23.3)	11 (33.3)	16 (19.3)	
Ki-67				0.862[b]				0.499[b]
>30%	54 (46.6)	20 (47.6)	34 (45.9)		54 (46.6)	17 (51.5)	37 (44.6)	
≤30%	62 (53.4)	22 (52.4)	40 (54.1)		62 (53.4)	16 (48.5)	46 (55.4)	

[a]Fisher's exact test; [b]χ^2 test. ALB, albumin; LMR, lymphocyte-to-monocyte ratio; T stage, tumor stage; N stage, lymph node stage; AJCC, American Joint Committee on Cancer.

cut-offs for ALB and LMR (Table III). Patients were categorized into three groups: LANI=0 (ALB <40.0 g/l and LMR <2.97), LANI=1 (either ALB ≥40.0 g/l or LMR ≥2.97) and LANI=2 (ALB ≥40.0 g/l and LMR ≥2.97). To illustrate the distribution of events across LANI strata, survival outcomes were summarized in both cohorts. Within the training cohort (n=116), 18 mortalities occurred. According to the Cox regression dataset, 17/59 (28.8%) mortalities were observed in the LANI ≤1 group, whereas only 1/57 (1.8%) mortalities occurred in the LANI=2 group (Table IV). Within the validation cohort (n=50), 7 mortalities were observed during follow-up. The lower mortality rate consistently observed in the LANI=2

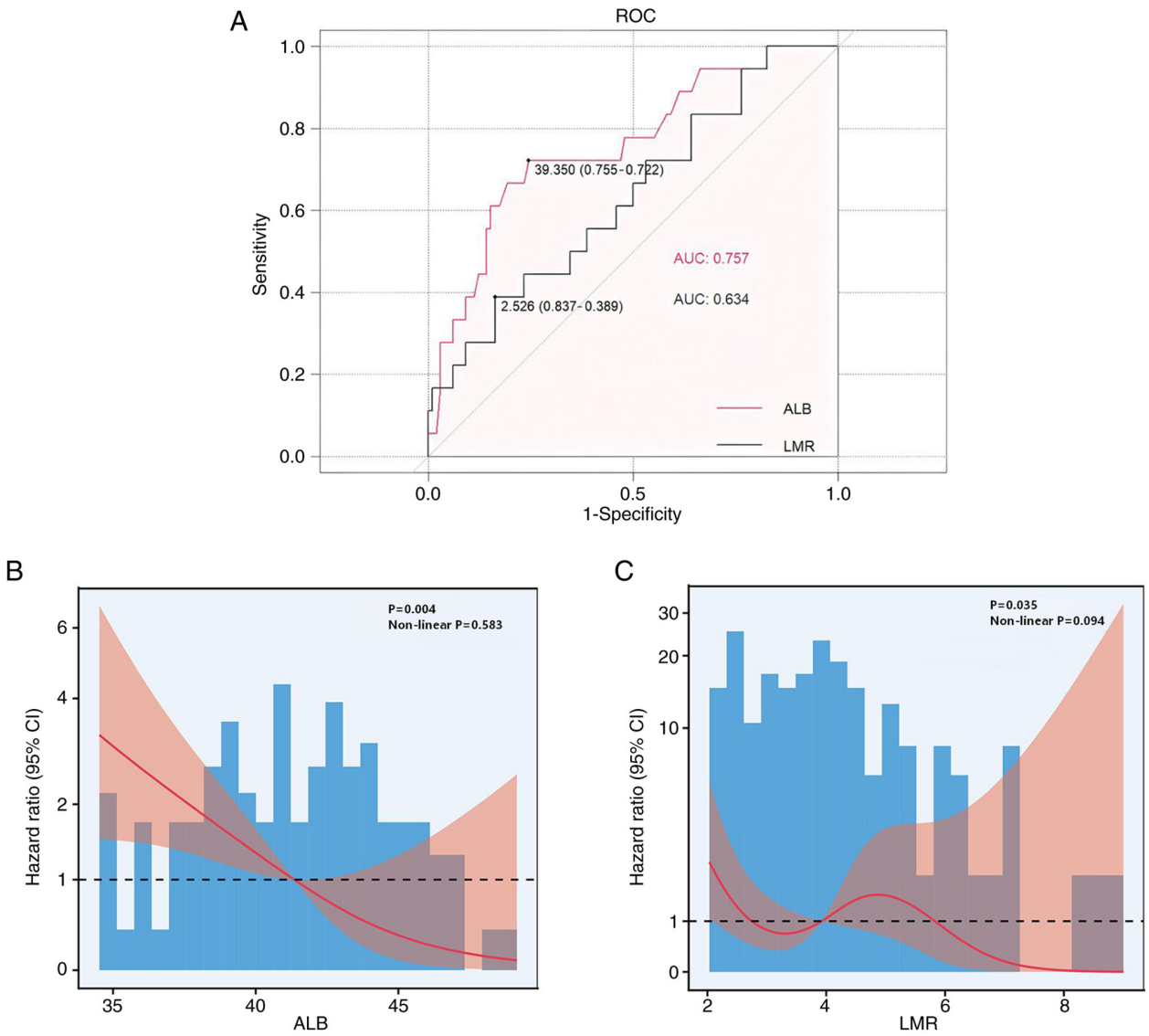

Figure 1. Prognostic relevance of ALB and LMR in patients with triple-negative breast cancer. (A) ROC curve analysis for serum ALB and LMR, showing their predictive accuracy for OS, with optimal cut-off values of 39.35 g/l for ALB (AUC=0.757) and 2.526 for LMR (AUC=0.634). These ROC-derived cut-offs closely approximated the prespecified clinical thresholds for ALB and LMR (40.0 g/l and 2.97, respectively) used in the LANI classification to enhance clinical applicability. RCS plots illustrating the continuous relationship between (B) ALB, (C) LMR and OS risk. ALB, albumin; LMR, lymphocyte-to-monocyte ratio; ROC, receiver operating curve; AUC, area under the curve; LANI, lymphocyte-albumin-monocyte index; OS, overall survival.

group across both cohorts supports its protective effect and may explain the wide CI exhibited by this group, which reflects a limited number of events rather than model instability. ROC curve analysis demonstrated that LANI achieved a higher discriminatory ability for OS compared with either ALB or LMR alone (AUC=0.792; Fig. 2A). Kaplan-Meier analysis further exhibited significantly longer OS for patients in LANI=2 compared with those of LANI ≤1 (log-rank P<0.001; Fig. 2B).

Within the univariate Cox analysis, a higher T stage, N stage, histologic grade and lower ALB value were all associated with worse survival. Furthermore, within the multivariate model including T stage, histologic grade and LANI, T3 (HR=4.12; 95% CI: 1.10-15.48; P=0.036), T4 (HR=24.23; 95% CI: 2.30-255.54; P=0.008), G3 histologic grade (HR=2.76; 95% CI: 1.41-5.40; P=0.003) and LANI (HR=0.03; 95% CI: 0.002-0.46; P=0.012) remained independent prognostic factors for OS (Table IV). Sensitivity analyses demonstrated the robustness of LANI. Cox models based on raw ROC-derived cut-offs and rounded clinical thresholds yielded comparable

Table III. Development of the LANI prognostic model based on ALB and LMR levels in patients with triple-negative breast cancer.

LANI	Levels	No. patients
0	ALB <40.0 and LMR <2.97	16
1	ALB ≥40.0 or LMR ≥2.97	43
2	ALB ≥40.0 and LMR ≥2.97	57

LANI, lymphocyte-albumin-monocyte index; ALB, albumin; LMR, lymphocyte-to-monocyte ratio.

Table IV. Univariate and multivariate Cox regression analyses of clinicopathological factors associated with overall survival in patients with triple-negative breast cancer.

Characteristic	No. patients	Event (n)	Univariate			Multivariate		
			HR	95% CI	P-value	HR	95% CI	P-value
Age, years								
<45	16	3						
≥75	13	2	0.79	0.13-4.75	0.799	2.84	0.23-34.94	0.415
45-59	37	8	1.21	0.32-4.56	0.78	2.00	0.36-11.02	0.426
60-74	50	5	0.51	0.12-2.14	0.36	1.24	0.17-8.94	0.831
BMI, kg/m^2								
<18.5	3	0						
>28	18	3	3.21	0.44-6.35	0.132	3.99	0.48-36.92	0.841
18.5-24	53	9	0.77	0.31-2.56	0.671	0.66	0.25-1.72	0.394
24-28	42	6	1.22	0.36-4.99	0.865	1.65	0.28-9.63	0.578
T stage								
T1	19	1						
T2	68	12	3.50	0.46-26.93	0.229	7.53	0.54-104.87	0.133
T3	25	2	10.56	1.94-57.26	0.015	4.12	1.10-15.48	0.036
T4	4	3	22.81	2.35-221.19	0.007	24.23	2.30-255.54	0.008
N stage								
N0	57	2						
N1	29	5	5.22	1.01-26.92	0.048	5.98	0.60-59.47	0.127
N2	19	6	10.94	2.21-54.26	0.003	3.02	0.08-111.19	0.548
N3	11	5	15.81	3.07-81.51	<0.001	1.53	0.02-100.16	0.842
AJCC stage								
I	12	1						
II	69	4	0.67	0.07-5.98	0.719			
III	35	13	5.27	0.69-40.32	0.109			
Histologic grade								
G1	24	3						
G2	65	2	2.41	1.12-5.18	0.024	1.98	1.05-3.72	0.036
G3	27	13	4.64	1.32-16.33	0.017	2.76	1.41-5.40	0.003
Ki-67								
>30%	54	11						
≤30%	62	7	0.53	0.21-1.38	0.196	1.34	0.25-7.06	0.730
ALB								
<40.0	42	13						
≥40.0	74	5	0.18	0.07-0.52	0.001	1.73	0.23-12.77	0.591
LMR								
<2.97	33	8						
≥2.97	83	10	0.46	0.18-1.17	0.105	3.19	0.47-21.55	0.234
LANI								
≤1	59	17						
2	57	1	0.05	0.01-0.39	0.004	0.03	0.002-0.46	0.012

HRs and 95% CIs were estimated using the Wald method. All P-values were two-sided. The N stage was not retained in the multivariable model due to collinearity with the T stage. Wide confidence intervals (for example, for T4 and N3) and estimates for grade 2 tumors reflect a limited numbers of events rather than model instability. HR, hazard ratio; ALB, albumin; LMR, lymphocyte-to-monocyte ratio; LANI, lymphocyte-albumin-monocyte index; T stage, tumor stage; N stage, lymph node stage; AJCC, American Joint Committee on Cancer.

estimates, indicating that rounding the cut-offs did not notably compromise model performance (data not shown).

Nomogram construction and calibration. A prognostic nomogram incorporating T stage, histologic grade and LANI was

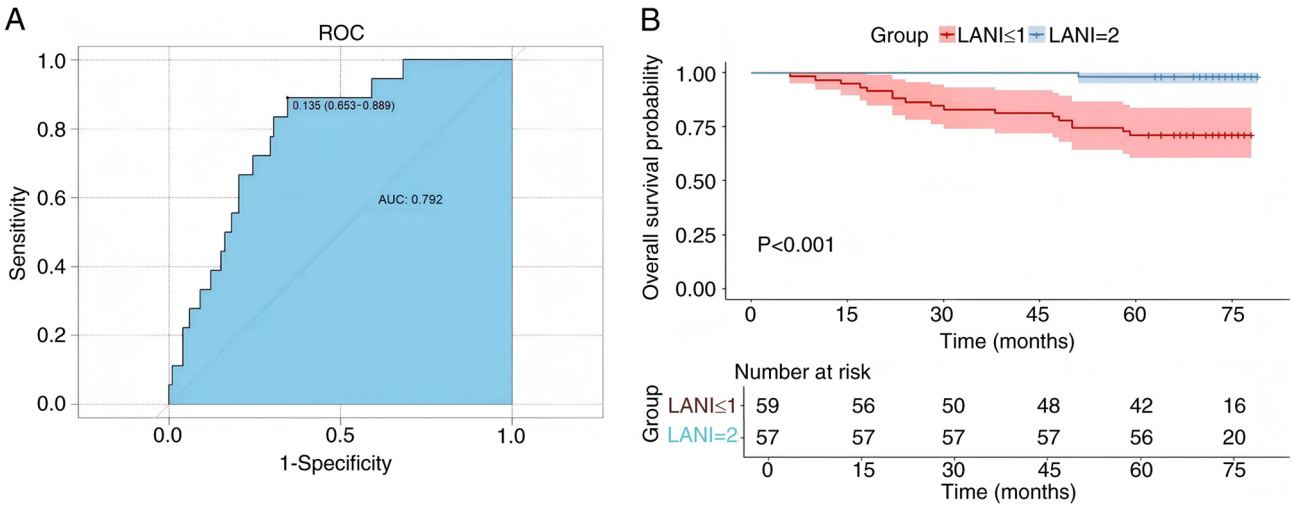

Figure 2. Development and validation of the LANI prognostic model in patients with triple-negative breast cancer. (A) ROC curve analysis evaluating the predictive performance of the LANI model for OS. The LANI model achieved the highest AUC (0.792), indicating improved prognostic accuracy. (B) Kaplan-Meier survival curves stratified by LANI scores, showing that patients with LANI=2 exhibited significantly improved OS compared with those with LANI ≤1 (log-rank P<0.001). Numbers at risk are also shown (LANI ≤1, n=59; LANI=2, n=57). LANI, lymphocyte-albumin-monocyte index; ROC, receiver operating curve; AUC, area under the curve; OS, overall survival.

constructed to predict 1-, 3- and 5-year OS in patients with TNBC (Fig. 3A). Brier score analyses demonstrated a good predictive performance by the model, with values of 1.6, 5.7 and 7.7 for 1-, 3- and 5-year OS in the training cohort and 5.2, 9.3 and 12.7 in the validation cohort (Fig. 3B-G). The relatively low Brier scores across different time points indicated stable model accuracy. In addition, calibration plots comparing predicted and observed OS revealed a close concordance, particularly at 1 and 3 years, suggesting a good calibration performance by the nomogram (Fig. 3H). These findings demonstrate that the nomogram based on LANI and clinicopathological factors provides reliable individualized prognostic predictions for patients with TNBC.

Clinical utility of the nomogram. DCA was applied to assess the net clinical benefit of the LANI-based nomogram in patients with TNBC (Fig. 4A-F). Within the training cohort, the nomogram consistently outperformed the treat-all and treat-none strategies across a range of threshold probabilities for 1-, 3- and 5-year OS, with the most pronounced benefit observed between 5-45% for 3-year OS and up to 70% for 5-year OS. Within the validation cohort, the nomogram similarly demonstrated a higher net benefit compared with the treat-all and treat-none strategies across a clinically relevant range of threshold probabilities (Fig. 4D-F). These findings suggest that the nomogram may provide good value in guiding individualized clinical decisions, especially for medium- to long-term prognostic assessment. Collectively, the DCA results highlight the robustness and translational potential of the LANI-based nomogram as a reliable tool for risk stratification in TNBC.

Internal validation of the LANI model. To further demonstrate the robustness of the LANI model, internal validation was performed using the predefined validation cohort. Model discrimination remained robust in the validation cohort (Fig. 2). Kaplan-Meier analysis demonstrated that patients with LANI=2 exhibited a significantly longer OS compared with those of LANI ≤1 (log-rank P<0.001; Fig. 2B), consistent with findings from the training cohort. These validation results reinforced the stability and generalizability of the LANI-based nomogram across independent subsets. Calibration analyses (Fig. 3B-H) showed close agreement between predicted and observed outcomes, supporting the calibration accuracy of the model. In addition, DCA (Fig. 4D-F) demonstrated a consistently higher net clinical benefit of the LANI-based nomogram compared with the treat-all or treat-none strategies. Collectively, these results support the feasibility of integrating the LANI score into individualized prognostic assessments and clinical decision-making for patients with TNBC.

Discussion

Within the present study, the LANI model, an integrative biomarker combining serum ALB and the LMR, was developed. Furthermore, its strong prognostic value in TNBC was demonstrated. Among 166 surgically treated patients, those with LANI=2 (ALB ≥40.0 g/l and LMR ≥2.97) consistently showed the most favorable OS. Multivariate Cox regression demonstrated LANI as an independent protective factor, whereas higher T stage (T3-T4) and poor histologic differentiation (G3) were adverse prognostic indicators. A prognostic nomogram incorporating LANI, T stage and histologic grade achieved robust discrimination, reliable calibration and clear clinical net benefits, highlighting its translational potential. The LANI thresholds were derived from ROC-based cut-off values and rounded to commonly used clinical reference points to enhance interpretability without impairing predictive performance.

Beyond statistical performance, the biological foundation of LANI provides a coherent mechanistic explanation for its prognostic relevance in TNBC. In this cohort, low serum ALB was significantly associated with higher nodal burden, a more advanced AJCC stage and worse histologic differentiation, whereas a reduced LMR was associated with deeper primary tumor invasion. These clinical patterns suggest that an

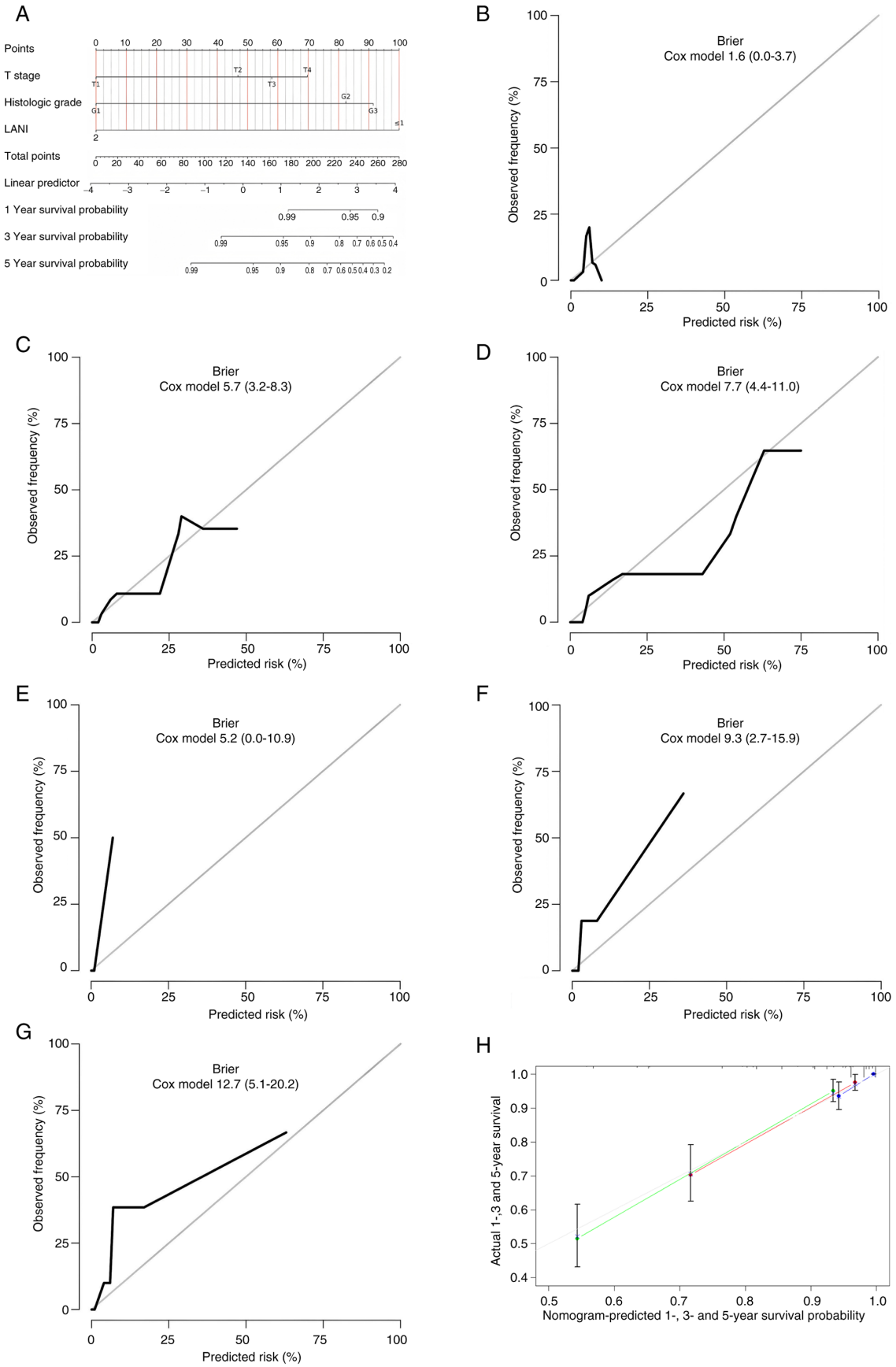

Figure 3. Construction and calibration of the prognostic nomogram for patients with triple-negative breast cancer. (A) Nomogram integrating T stage, histologic grade and LANI to predict 1-, 3- and 5-year overall survival. (B) Brier score-based calibration plot at 1 year. (C) Brier score-based calibration plot at 3 years. (D) Brier score-based calibration plot at 5 years. (E) Brier score-based calibration plot at 1 year in the validation cohort. (F) Brier score-based calibration plot at 3 years in the validation cohort. (G) Brier score-based calibration plot at 5 years in the validation cohort. (H) Calibration curve comparing predicted and observed survival probabilities, revealing a close concordance between predicted and observed survival, suggesting good calibration performance of the model. T stage, tumor stage; LANI, lymphocyte-albumin-monocyte index.

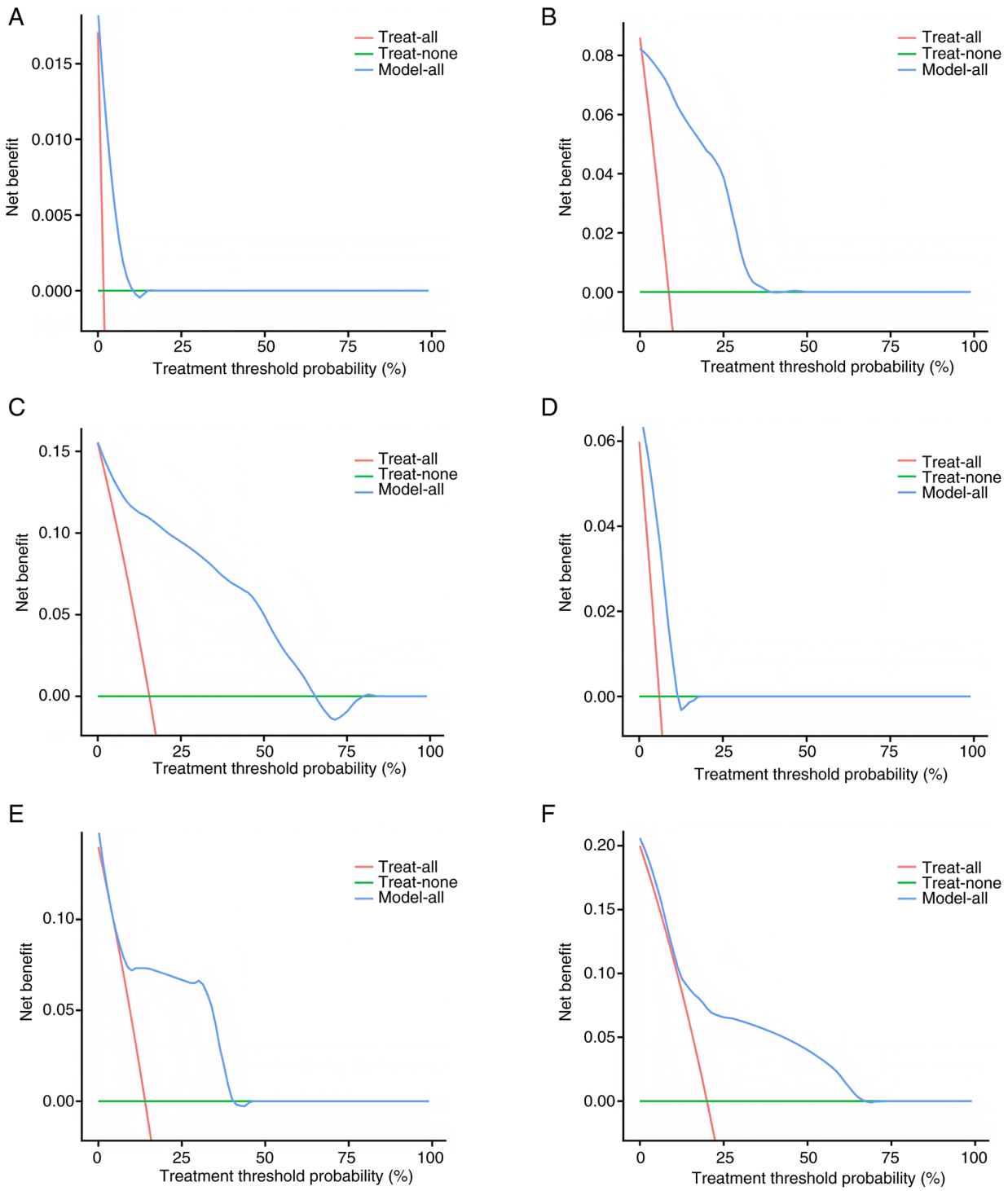

Figure 4. DCA of the LANI-based nomogram in patients with triple-negative breast cancer. (A) DCA for 1-year OS in the training cohort. (B) DCA for 3-year OS in the training cohort. (C) DCA for 5-year OS in the training cohort. (D) DCA for 1-year OS in the validation cohort. (E) DCA for 3-year OS in the validation cohort. (F) DCA for 5-year OS in the validation cohort. Blue curves represent the nomogram incorporating LANI, T stage and histologic grade, compared with the treat-all (red) and treat-none (green) strategies. Across clinically relevant thresholds, the nomogram consistently yielded greater net benefit, underscoring its potential clinical applicability in risk stratification. DCA, decision curve analysis; LANI, lymphocyte-albumin-monocyte index; T stage, tumor stage; OS, overall survival.

unfavorable LANI profile reflects not only anatomical tumor advancement but also a profoundly perturbed host milieu characterized by chronic inflammation, metabolic stress and compromised antitumor immunity.

Serum ALB is a sensitive indicator of protein-energy reserve and inflammatory-metabolic load, whereby in aggressive breast cancer types, proinflammatory cytokines, such as IL-6 and TNF-α, are frequently elevated and activate STAT3 and NF-κB signaling in hepatocytes, shifting protein synthesis toward acute-phase reactants at the expense of ALB production (42-44). This negative acute-phase response accelerates proteolysis, amplifies oxidative stress and sustains a systemic catabolic state,

consistent with studies showing that ALB-related inflammatory ratios, such as the neutrophil percentage-to-ALB ratio (NPAR), reflect systemic inflammation and distant metastatic potential in breast cancer (45-47). Meanwhile, the LMR captures the balance between lymphocyte-mediated antitumor immunity and monocyte/macrophage-driven protumor inflammation. Accumulating evidence has shown that breast cancer cells promote monocyte differentiation into M2-polarized tumor-associated macrophages through exosomal long non-coding RNAs, the MIR4435-2HG/ubiquitin-conjugating enzyme E2 N axis and the leupaxin/histone deacetylase 6/early growth response 2 pathway, accompanied by upregulation of IL-10, VEGF and TGF-β, thereby facilitating angiogenesis, epithelial-mesenchymal transition and immune escape (48-50). Integration of these findings with the present results suggests LANI effectively unifies two key biological axes, protein-energy reserve and immune-cell homeostasis, into a condensed surrogate of the host immunometabolic state, providing a robust mechanistic basis for its association with TNBC clinical outcomes.

Growing evidence has indicated that inflammatory-nutritional composite indices exhibit improved prognostic discrimination compared with single inflammatory markers in breast cancer. For example, in a postoperative TNBC cohort (n=223), the NPS demonstrated higher AUCs and C-indices compared with PNI, NLR, PLR and CONUT for both OS and breast cancer-specific survival, underscoring the value of integrating immune and nutritional dimensions (28). In a neoadjuvant TNBC population, Zhu *et al* (30) showed that a multiparametric model incorporating IL-6, PLR, SII and Ki-67 exhibited improved stratification of disease-free survival compared with any single indicator. Consistently, Sun *et al* (38) introduced the ALB-corrected NLR ratio (NLR-0.04 x ALB), reporting C-indices of 0.74-0.76 for disease-free survival and OS in both the training and validation cohorts, outperforming traditional inflammation-based parameters. Furthermore, a large neoadjuvant study demonstrated that pretreatment and posttreatment NLR markedly contributed to OS prediction, with the constructed nomogram reaching a C-index of ~0.76, further supporting the rationale for embedding inflammatory markers into composite prognostic models (51).

Based upon these breast cancer-specific findings, the present study introduced a simple TNBC-focused composite index (LANI) that integrates serum ALB and the LMR into a single prognostic measure and to the best of our knowledge, this was applied for the first time in tumor prognostic research. In the present cohort, preoperative LANI achieved an AUC of 0.792 for OS, outperforming ALB alone (AUC=0.757) and the LMR alone (AUC=0.634). Previous breast cancer studies have shown that commonly used inflammatory or inflammatory-nutritional markers, such as NLR, SII, and SIRI, typically yield AUC values between 0.58-0.63, whereas composite scores such as NPS, PLR or NLR-based prognostic models frequently fall between 0.60-0.70 (28,52,53). Within this framework, the AUC=0.792 of LANI lies toward the upper end of the performance spectrum reported for similar indices and reflects a comparatively strong discriminatory ability in the TNBC setting. Although isolated studies have described higher AUCs, such as an NLR AUC=0.827 in an overall breast cancer population (54), these findings were influenced by differences in study population and the incorporation of tumor markers, limiting direct comparison. Collectively, these observations position LANI as a high-performing, biologically grounded inflammatory-nutritional index with potential utility for prognostic refinement in TNBC.

Although neutrophil, lymphocyte, monocyte, platelet and ALB values were available for all patients in the present study, a number of biochemical indicators required for reconstructing mGPS, PNI or CONUT, specifically C-reactive protein, total protein and total cholesterol, were not consistently documented. As the present study was retrospective and relied entirely on electronic medical records, these parameters were only obtained when clinicians suspected inflammatory activity or metabolic-nutritional abnormalities, resulting in marked missingness and precluding reconstruction of those indices. Despite this limitation, the prognostic performance of LANI remained comparable with and in some instances higher than that reported for established inflammatory-nutritional markers, suggesting the potential advantages of integrating immune and nutritional components into a unified index. As LANI was newly introduced in the present study, its prognostic utility has not been evaluated previously in breast cancer or other malignancies. Future prospective TNBC cohorts with complete biochemical datasets will be key in reconstructing established indices and enabling direct, head-to-head comparisons of ROC-based and C-index performances to precisely determine the clinical positioning of LANI.

By jointly incorporating serum ALB and the LMR, LANI consolidates nutritional and immune status into a quantitative surrogate of immunometabolic exhaustion. Patients with LANI=0, defined by concurrent hypoalbuminemia and low LMR, exhibit a high-risk host phenotype marked by chronic inflammation, catabolic metabolic remodeling, lymphocyte depletion and myeloid-dominant immunosuppression. This phenotype aligns with recent studies demonstrating that ALB-based inflammatory ratios and lymphocyte-derived indices (including NPAR and PLR) predict distant metastasis and unfavorable survival in breast cancer (50,55). In TNBC, such immunometabolic exhaustion frequently coexists with an immunosuppressive tumor microenvironment characterized by M2-type macrophage enrichment, insufficient $CD8^+$ T-cell infiltration and elevated expression of checkpoint molecules including programmed cell death protein 1/programmed death-ligand 1, T cell immunoglobulin and mucin domain-containing 3 and lymphocyte activation gene 3, all of which promote immune evasion and diminish therapeutic benefit (56-59). Inflammatory cytokines, tumor-infiltrating lymphocytes and immune checkpoint molecules were not analyzed in the present study, as owing to the retrospective design, such measurements were not part of the routine assessment at the time of patient enrollment. Consequently, long-term archived serum or tissue specimens suitable for multiplex cytokine testing or immune profiling were not consistently available, precluding reliable quantification of these biomarkers. Nevertheless, the clinical patterns observed in the present cohort, including the significantly worse OS in patients with low LANI and its association with more advanced clinicopathological features, are consistent with established translational evidence suggesting that IL-6/TNF-α-driven inflammation, M2 macrophage polarization and $CD8^+$ T-cell dysfunction shape an immunosuppressive TNBC

microenvironment and contribute to adverse outcomes (60). These consistencies suggest that LANI may capture an underlying immunometabolic program integral to tumor aggressiveness and treatment responsiveness. Future investigations should therefore aim to incorporate LANI-stratified immune analyses, including: i) Multiplex immunohistochemistry to assess CD8, CD68 and CD163 expression and characterize TIL density and tumor-associated macrophage polarization; ii) serum multiplex cytokine profiling of IL-6, TNF-α and IL-10; and iii) single-cell or spatial transcriptomic profiling to delineate immunometabolic niches across LANI groups (61-63). Through such integrative approaches, LANI may evolve from a pragmatic clinical index into a translational bridge associating routine hematologic markers with high-dimensional immune-molecular phenotyping, supporting its development as a mechanistically grounded prognostic and potentially predictive biomarker in TNBC.

In addition, a number of methodological considerations should be acknowledged when interpreting the present findings. The present study was retrospective and single-center in design, with a modest sample size and a relatively limited number of outcome events, which inherently restricts the generalizability of the results. Although internal validation supported the stability of the model, the absence of external, multicenter validation precludes a full assessment of its reproducibility and robustness in broader TNBC populations. Furthermore, despite multivariable adjustment, residual confounding cannot be fully excluded, particularly because comorbidities, inflammatory conditions and medication exposures that could influence ALB, lymphocyte or monocyte measurements were not systematically documented. More specifically, serum ALB may be influenced by unrecognized hepatic dysfunction (including steatosis, chronic hepatitis or impaired synthetic capacity), renal protein loss, inflammatory cytokine-driven acute-phase responses, perioperative hemodilution from intravenous fluids, malnutrition, catabolic illness and less commonly, protein-losing enteropathy (64,65). In addition, lymphocyte and monocyte counts may fluctuate with acute or chronic infections, autoimmune or inflammatory disorders, hematologic abnormalities, physiologic stress responses and prior or undocumented exposure to immunosuppressive medications or corticosteroids. Given that such factors were not consistently captured in the present retrospective dataset, their potential confounding effects could not be fully assessed. Furthermore, although G2 tumors exhibited an intermediate risk in the multivariate analysis, the modest effect size and limited number of events necessitate cautious interpretation and further validation in larger cohorts. Similarly, the low HR observed in the LANI=2 subgroup must be viewed in the context of event sparsity, as only a single mortality occurred within this category in each cohort, which inevitably broadened the CIs, reflecting statistical limitations rather than model instability. Despite this, the protective direction of association remained consistent across all cohorts and sensitivity analyses, supporting the biological plausibility of LANI as an indicator of host resilience. The integrated nomogram combining LANI, T stage and histologic grade demonstrated strong discrimination, favorable calibration and meaningful clinical utility, yet these prognostic properties also require validation in larger, more event-rich populations. Collectively, these sources of bias are likely non-differential in nature and would tend to attenuate, rather than exaggerate, the observed associations, suggesting that the estimated effect of LANI may, if anything, be conservative.

Future prospective, large-scale, multicenter studies with standardized documentation of comorbidities, inflammatory and nutritional biomarkers and medication exposures will be key in validating these findings across heterogeneous TNBC populations. Incorporating serial measurements will allow characterization of dynamic immuno-nutritional trajectories throughout the perioperative period and adjuvant therapy. Further integration of LANI with TNBC molecular subtyping, genomic and immunogenomic features and emerging multi-omics signatures, may deepen understanding of the immunometabolic mechanisms underlying host-tumor interactions. Embedding LANI into clinical prediction models or digital decision-support platforms may ultimately enhance individualized risk stratification and guide perioperative and systemic treatment planning within precision oncology frameworks. Overall, LANI represents a simple, accessible and biologically grounded biomarker with promising utility in the preoperative evaluation of TNBC, warranting further validation and clinical translation in future multicenter prospective studies.

In conclusion, the present study demonstrates that the LANI, derived from serum ALB and the LMR, is a reliable and independent predictor of OS in patients with TNBC. LANI reflects the combined influence of nutritional status and systemic immune-inflammatory balance, enabling clearer preoperative risk stratification compared with either component alone. The LANI-based nomogram showed strong discrimination, good calibration and meaningful clinical benefits in both the training and validation cohorts. These findings support LANI as a simple and reproducible tool that may complement conventional pathological parameters and assist individualized perioperative management of TNBC.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

BM contributed to the conception and design of the present study. BZ, KW, MA and FL collected and analyzed data. BZ and KW wrote and revised the manuscript. BZ and FL confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by The Ethics Committee of the Affiliated Cancer Hospital of Xinjiang Medical University (approval no. K-2024056) in accordance with the Declaration of Helsinki. All patients signed a written informed consent form, which included consent to participate in the present study, use of their medical data for research purposes and the publication of anonymized findings.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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