Breast Cancer: Targets and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

A Prognostic Nutritional Index-Based Nomogram to Predict Breast Cancer Metastasis: A Retrospective Cohort Validation

Zhimin Chen[1,*], Honglan Gao[1,*], Mingwen Cheng[2], Chenglin Song[3]

[1]Department of Clinical Nutrition, The Yancheng Clinical College of Xuzhou Medical University, The First People's Hospital of Yancheng, Yancheng, Jiangsu, 224000, People's Republic of China; [2]Department of Public Health, Yancheng Center for Disease Control and Prevention, Yancheng, Jiangsu, 224000, People's Republic of China; [3]Department of Clinical Nutrition, The Second People's Hospital of Lianyungang, Lianyungang Second People's Hospital Affiliated to Kangda College of Nanjing Medical University, Lianyungang, Jiangsu, 222006, People's Republic of China

*These authors contributed equally to this work

Correspondence: Chenglin Song, Department of Clinical Nutrition, The Second People's Hospital of Lianyungang, Lianyungang Second People's Hospital Affiliated to Kangda College of Nanjing Medical University, No. 41, Hailian East Road, Lianyungang, Jiangsu, 222006, People's Republic of China, Email songchenglin@lygey.com

Background: The prognostic nutritional index (PNI) is significantly associated with the prognosis of breast cancer (BC). However, the relationship between PNI and BC metastasis has not yet been thoroughly studied. This study aims to explore the role of PNI in BC metastasis and develop a predictive nomogram model.

Methods: A retrospective cohort of 311 BC patients was analyzed. The restricted cubic spline (RCS) was utilized to explore the nonlinear relationships between PNI, geriatric nutritional risk index (GNRI), neutrophil percentage-to-albumin ratio (NPAR), hemoglobin, albumin, lymphocyte, and platelet (HALP) ratio and BC metastasis. Multivariate logistic regression analysis was conducted to identify the influencing factors of BC metastasis. A nomogram model was established and internally validated. The performance and clinical applicability of the model were assessed through the area under the receiver operating characteristic (ROC) curve (AUC), calibration curve, Hosmer-Lemeshow test, and decision curve analysis (DCA).

Results: RCS analysis demonstrated nonlinear associations between PNI and HALP with BC metastasis (P for nonlinear < 0.05). PNI and other factors such as T and N stage etc. were identified as independent influencing factors for BC metastasis. The nomogram based on these factors demonstrated strong predictive ability, with the AUCs of 0.85 (95% confidence interval [CI] 0.79, 0.91) and 0.82 (95% CI 0.71, 0.93) in the training and validation set, respectively. The calibration curve, Hosmer-Lemeshow test, and DCA further confirmed its clinical utility.

Conclusion: PNI is an independent predictor of BC metastasis. This PNI-based nomogram provides a practical and user-friendly tool for assessing BC metastasis risk.

Keywords: prognostic nutritional index, breast cancer, metastasis, nomogram

Introduction

Breast cancer (BC) is the most commonly diagnosed malignancy and the leading cause of cancer-related deaths, accounting for approximately 24.5% of all cancer diagnoses globally among women.[1] Despite advances in early diagnosis and treatment, BC metastasis continues to account for the majority of cancer-related deaths and poor outcomes.[2] It is reported that metastases are culpable for approximately 90% of cancer-associated deaths.[3] The primary sites of BC metastasis include bone, lung, liver, and brain, exhibiting a tendency to spread to different organs, a phenomenon known as metastatic heterogeneity, which may be one of the reasons for the failure of BC treatments.[4] Therefore, Understanding the factors that drive BC metastasis and developing effective predictive models to assess metastasis risk are crucial for improving patient outcomes.

Received: 15 February 2025
Accepted: 31 May 2025
Published: 10 June 2025

In previous studies, traditional predictors such as lymph node status, hormone receptor expression, and microRNA have been widely studied.[5,6] However, these factors are limited by practical challenges, such as the complexity of detection, in predicting BC metastasis risk. Recently, the relationship between clinically accessible indicators and cancer prognosis has attracted extensive attention. For example, the prognostic nutritional index (PNI), derived from albumin levels and lymphocyte counts (albumin[g/L] + 5×lymphocytes[$\times 10^9$/L]), serves as a validated biomarker integrating nutritional and immunological profiles.[7] Studies have shown that PNI is closely associated with the prognosis of breast cancer.[8–10] However, previous studies have primarily concluded that a high pre-treatment prognostic nutritional index (PNI) is associated with longer disease-free survival, overall survival, or an increased rate of pathological complete response in breast cancer.[11–14] Currently, there is few research that considers distant metastasis of breast cancer as a primary clinical outcome to analyze the relationship between PNI and metastasis.

In addition to the PNI, nutritional and inflammatory markers such as the geriatric nutritional risk index (GNRI), the neutrophil percentage-to-albumin ratio (NPAR), and the hemoglobin, albumin, lymphocyte, and platelet (HALP) ratio have also attracted widespread attention. These indices have also demonstrated prognostic potential in various malignancies.[15–17] They reflect the multifaceted interactions among cancer progression, systemic inflammation, and condition of nutrition. Although these markers have gradually been incorporated into predictive models for cancer prognosis, such as recurrence or survival,[18–21] there remains a lack of comprehensive models that integrate these markers with other clinical variables to accurately and practically predict BC metastasis.

This study investigates the clinical relevance of four readily accessible biomarkers - PNI, GNRI, NPAR, HALP - in predicting breast cancer metastasis. Leveraging their unique combination of nutritional and inflammatory profiles, we are the first to develop the comprehensive nomogram model that synergistically integrates these biomarkers with key clinical parameters. The resulting tool provides clinicians with an intuitive, evidence-based platform for individualized metastasis risk stratification, enabling timely therapeutic interventions.

Methods

Study Population

This retrospective study included 311 patients with primary breast cancer admitted to the First People's Hospital of Yancheng between March 2015 and December 2023. The final cohort comprised 81 patients with BC metastasis and 230 without metastasis. Inclusion criteria: (1) age > 18 years, (2) female, (3) histopathologically confirmed breast cancer, (4) confirmed metastatic sites (bone, lung, liver, or brain), and diagnosed through imaging or pathological histology, (5) complete clinical and histopathological records. Exclusion criteria: (1) patients with other malignancies, (2) patients with heart, liver, kidney and other organ failure or severe infectious diseases, (3) incomplete clinical data records.

Data Collection

We collected relevant patient information from the electronic medical record system, including age, height, weight, marital status, histological grade, estrogen receptor (ER) status, progesterone receptor (PR) status, human epidermal growth factor receptor 2 (HER2) status, Ki - 67 index, T stage, N stage, molecular subtype, chronic disease history (hypertension, diabetes, and hyperlipemia), treatment regimens, Karnofsky Performance Status (KPS) score, and blood test data. Among them, marital status refers to married and divorced status, with divorced status including divorce, separation, and widowhood. Baseline hematological parameters were obtained within 24 hours of admission through standardized complete blood count (CBC) analysis and biochemical profiling, including white blood cell count (WBC), red blood cell count (RBC), lymphocytes, hemoglobin, albumin, etc.

The formulas for calculating PNI, GNRI, NPAR, and HALP were as follows: PNI = albumin (g/L) + 5 * lymphocyte count(10^9/L);[22] GNRI =[1.489 * albumin (g/L)] +[41.7 *(present weight/ideal body weight)]; ideal body weight was calculated[23] for men: ideal body weight (men) = height (cm) − 100 − ((height (cm) − 150)/4), and for women: ideal body weight (women) = height (cm) − 100 − ((height (cm) − 150)/2.5). NPAR= (neutrophil percentage * 1000/ albumin (g/L));[24] HALP = hemoglobin (g/L) × albumin (g/L) × lymphocyte count (10^9/L)/ platelets (10^9/L).[25]

Statistical Analysis

Normal continuous variables were expressed as mean ± standard deviation (SD), and the independent sample *t*-test was used for comparison between groups. Non-normal continuous variables were expressed as median and interquartile range (IQR), and the non-parametric test was used for comparison between groups. Categorical variables were expressed as frequency and percentage (%), and the chi-square test or Fisher's exact test was used for comparison.

The receiver operating characteristic curve (ROC) was used to determine the optimal cut-off values of PNI, GNRI, NPAR, and HALP. The restricted cubic spline (RCS) curve was used to analyze the linear relationship between PNI, GNRI, NPAR, HALP and breast cancer. Multimodel logistic regression analysis was used to evaluate the association between indicators such as PNI and BC metastasis. Statistically significant factors were incorporated into the nomogram to predict the risk of BC metastasis. Internal validation was performed by randomly splitting the dataset into a training set and a validation set at a ratio of 7:3. The receiver operating characteristic curve (ROC), area under the curve (AUC), Hosmer-Lemeshow test, and calibration curve were used to evaluate the accuracy of the model. The decision curve analysis (DCA) was used to evaluate the clinical utility of the nomogram. All statistical analyses were performed using R software (version 4.4.0), and $P < 0.05$ was considered statistically significant.

Results

Baseline Characteristics

As shown in the flowchart in Figure 1, a total of 311 breast cancer patients were enrolled in this study. 81 patients with BC metastasis and 230 patients without BC metastasis were included. The average age of these patients was 53.69 ± 9.90 years old.

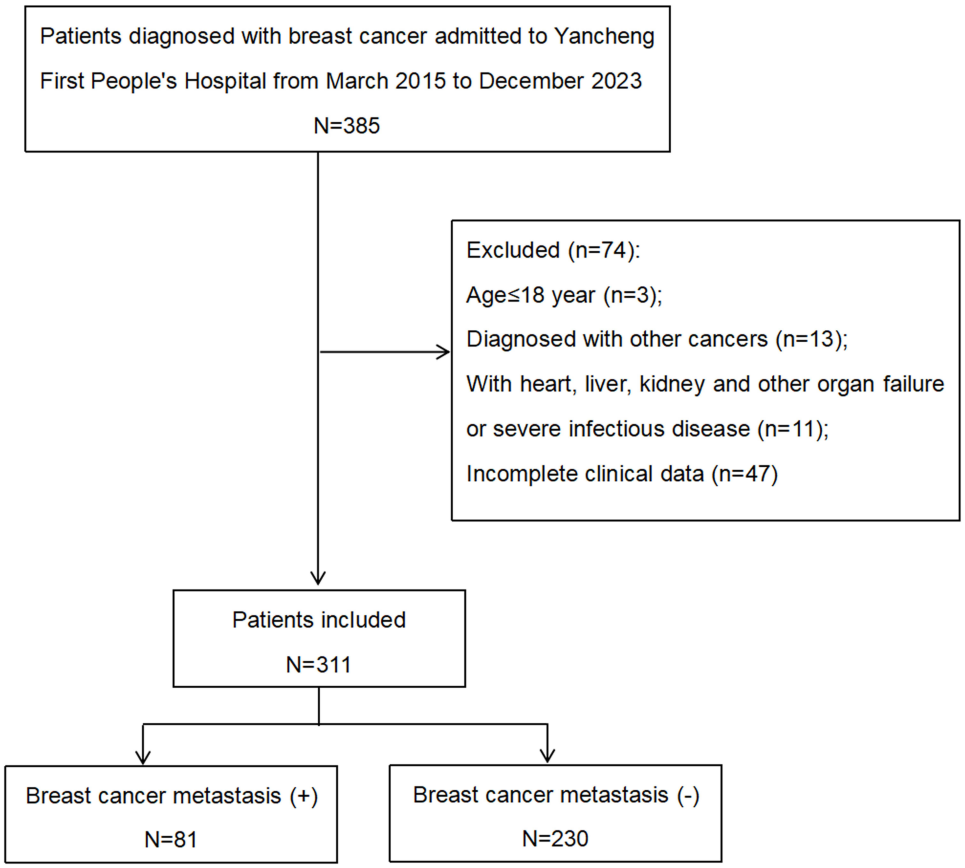

Figure 1 The flow diagram of sample selection in the study.

https://doi.org/10.2147/BCTT.S523001

As presented in Table 1, there were statistically significant differences (P<0.05) in marital status, histological grade, PR status, T stage, N stage, surgery, endocrinotherapy, immunotherapy, hemoglobin, albumin, prealbumin, RBC, PNI, GNRI, and NPAR between the non-metastatic patients and the BC patients with metastasis.

Table 1 Baseline Characteristics of the Study Population

Variables	Overall (n = 311)	Metastasis(-) (n = 230)	Metastasis(+) (n = 81)	*P* value
Age (years), mean±SD	53.69 ± 9.90	53.73 ± 9.82	53.57 ± 10.19	0.896
BMI (kg/m^2), mean±SD	24.59 ± 3.40	24.65 ± 3.51	24.43 ± 3.08	0.612
Marital status, n(%)				**0.022**
Divorced	42 (13.50)	25 (10.87)	17 (20.99)	
Married	269 (86.50)	205 (89.13)	64 (79.01)	
Histological grade, n(%)				**<0.001**
I	17 (5.48)	16 (6.99)	1 (1.23)	
II	124 (40.00)	111 (48.47)	13 (16.05)	
III	169 (54.52)	102 (44.54)	67 (82.72)	
ER status, n(%)				0.256
Negative	118 (37.94)	83 (36.09)	35 (43.21)	
Positive	193 (62.06)	147 (63.91)	46 (56.79)	
PR status, n(%)				**0.031**
Negative	156 (50.16)	107 (46.52)	49 (60.49)	
Positive	155 (49.84)	123 (53.48)	32 (39.51)	
HER2 status, n(%)				0.109
Negative	180 (57.88)	127 (55.22)	53 (65.43)	
Positive	131 (42.12)	103 (44.78)	28 (34.57)	
Ki67 score, n(%)				0.232
<30	89 (28.62)	70 (30.43)	19 (23.46)	
≥30	222 (71.38)	160 (69.57)	62 (76.54)	
T stage, n(%)				**<0.001**
T1	115 (36.98)	104 (45.22)	11 (13.58)	
T2	147 (47.27)	115 (50.00)	32 (39.51)	
T3	38 (12.22)	10 (4.35)	28 (34.57)	
T4	11 (3.54)	1 (0.43)	10 (12.35)	
N stage, n(%)				**<0.001**
N0	98 (31.51)	89 (38.70)	9 (11.11)	
N1	105 (33.76)	83 (36.09)	22 (27.16)	
N2	47 (15.11)	38 (16.52)	9 (11.11)	
N3	61 (19.61)	20 (8.70)	41 (50.62)	
Molecular subtypes, n(%)				0.061
TNBC	54 (17.36)	35 (15.22)	19 (23.46)	
HER2 enriched	75 (24.12)	63 (27.39)	12 (14.81)	
Luminal A	83 (26.69)	63 (27.39)	20 (24.69)	
Luminal B HER2-	68 (21.86)	50 (21.74)	18 (22.22)	
Luminal B HER2+	31 (9.97)	19 (8.26)	12 (14.81)	
Hypertension, n(%)				0.982
No	257 (82.64)	190 (82.61)	67 (82.72)	
Yes	54 (17.36)	40 (17.39)	14 (17.28)	
Diabetes, n(%)				0.604
No	281 (90.35)	209 (90.87)	72 (88.89)	
Yes	30 (9.65)	21 (9.13)	9 (11.11)	

(*Continued*)

Table 1 (Continued).

Variables	Overall (n = 311)	Metastasis(-) (n = 230)	Metastasis(+) (n = 81)	*P* value
Hyperlipemia, n(%)				0.917
No	293 (94.21)	216 (93.91)	77 (95.06)	
Yes	18 (5.79)	14 (6.09)	4 (4.94)	
Surgery, n(%)				**<0.001**
No	13 (4.18)	1 (0.43)	12 (14.81)	
Yes	298 (95.82)	229 (99.57)	69 (85.19)	
Chemotherapy, n(%)				0.545
No	24 (7.72)	19 (8.26)	5 (6.17)	
Yes	287 (92.28)	211 (91.74)	76 (93.83)	
Radiotherapy, n(%)				0.913
No	136 (43.73)	101 (43.91)	35 (43.21)	
Yes	175 (56.27)	129 (56.09)	46 (56.79)	
Endocrinotherapy, n(%)				**<0.001**
No	218 (70.10)	176 (76.52)	42 (51.85)	
Yes	93 (29.90)	54 (23.48)	39 (48.15)	
Immunotherapy, n(%)				**<0.001**
No	183 (58.84)	151 (65.65)	32 (39.51)	
Yes	128 (41.16)	79 (34.35)	49 (60.49)	
KPS score, mean±SD	83.49 ± 6.87	83.78 ± 6.27	82.65 ± 8.33	0.204
Hemoglobin (g/L), mean±SD	116.96 ± 15.85	118.67 ± 13.30	112.11 ± 20.84	**0.009**
Platelet (10^9/L), mean±SD	196.76 ± 80.65	194.57 ± 75.34	202.95 ± 94.34	0.422
Total protein (g/L), mean±SD	67.71 ± 6.40	67.67 ± 6.31	67.80 ± 6.71	0.885
Albumin (g/L), mean±SD	39.96 ± 3.86	40.35 ± 3.64	38.87 ± 4.27	**0.006**
Prealbumin (g/L), mean±SD	226.50 ± 49.05	233.96 ± 41.02	205.31 ± 62.38	**<0.001**
TG (mmol/L), mean±SD	1.98 ± 1.19	1.98 ± 1.20	1.98 ± 1.18	0.988
TC (mmol/L), mean±SD	5.05 ± 1.04	5.07 ± 1.05	5.01 ± 1.02	0.666
HDL-C (mmol/L), mean±SD	1.20 ± 0.27	1.21 ± 0.25	1.18 ± 0.31	0.322
LDL-C (mmol/L), mean±SD	3.11 ± 0.75	3.11 ± 0.75	3.13 ± 0.74	0.850
FPG (mmol/L), mean±SD	5.59 ± 1.61	5.51 ± 1.61	5.82 ± 1.60	0.138
WBC (10^9/L), median (IQR)	4.63 (3.70, 6.00)	4.65 (3.71, 5.88)	4.55 (3.61, 6.29)	0.989
Neutrophil (10^9/L), median (IQR)	2.61 (2.02, 3.67)	2.64 (2.03, 3.54)	2.59 (1.93, 4.08)	0.655
Neutrophil percentage (%), median (IQR)	0.59 (0.51, 0.67)	0.58 (0.50, 0.66)	0.60 (0.51, 0.74)	0.149
Lymphocyte (10^9/L), median (IQR)	1.26 (0.95, 1.66)	1.28 (0.98, 1.68)	1.23 (0.83, 1.63)	0.109
Lymphocyte percentage (%), median (IQR)	0.29 (0.21, 0.36)	0.30 (0.22, 0.36)	0.28 (0.18, 0.37)	0.254
Monocyte (10^9/L), median (IQR)	0.38 (0.27, 0.49)	0.39 (0.28, 0.48)	0.36 (0.26, 0.49)	0.380
Monocyte percentage (%), median (IQR)	0.08 (0.06, 0.10)	0.09 (0.06, 0.10)	0.08 (0.06, 0.10)	0.158
RBC (10^9/L), median (IQR)	3.97 (3.57, 4.28)	4.01 (3.65, 4.31)	3.78 (3.23, 4.20)	**<0.001**
PNI	46.65 ± 4.99	47.19 ± 4.57	45.12 ± 5.80	**0.004**
GNRI	106.36 ± 8.46	107.03 ± 8.41	104.44 ± 8.37	**0.017**
NPAR	14.97 ± 3.99	14.57 ± 3.70	16.10 ± 4.56	**0.008**
HALP	37.17 ± 22.62	38.21 ± 21.26	34.21 ± 26.02	0.172

Note: Bold values indicate $P < 0.05$.

Abbreviations: BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; KPS, karnofsky performance status; TNBC, triple-negative breast cancer; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; WBC, white blood cell count; RBC, red blood cell count; PNI, prognostic nutritional index; GNRI, geriatric nutritional risk index; NPAR, neutrophil percentage-to-albumin ratio; HALP, hemoglobin, albumin, lymphocyte, and platelet ratio.

Influencing Factors of Breast Cancer Metastasis

As shown in Figure 2, we used restricted cubic spline (RCS) curves to analyze the nonlinear relationships between PNI, GNRI, NPAR, HALP and BC metastasis. After adjusting for age, BMI, marital status, histological grade, hypertension,

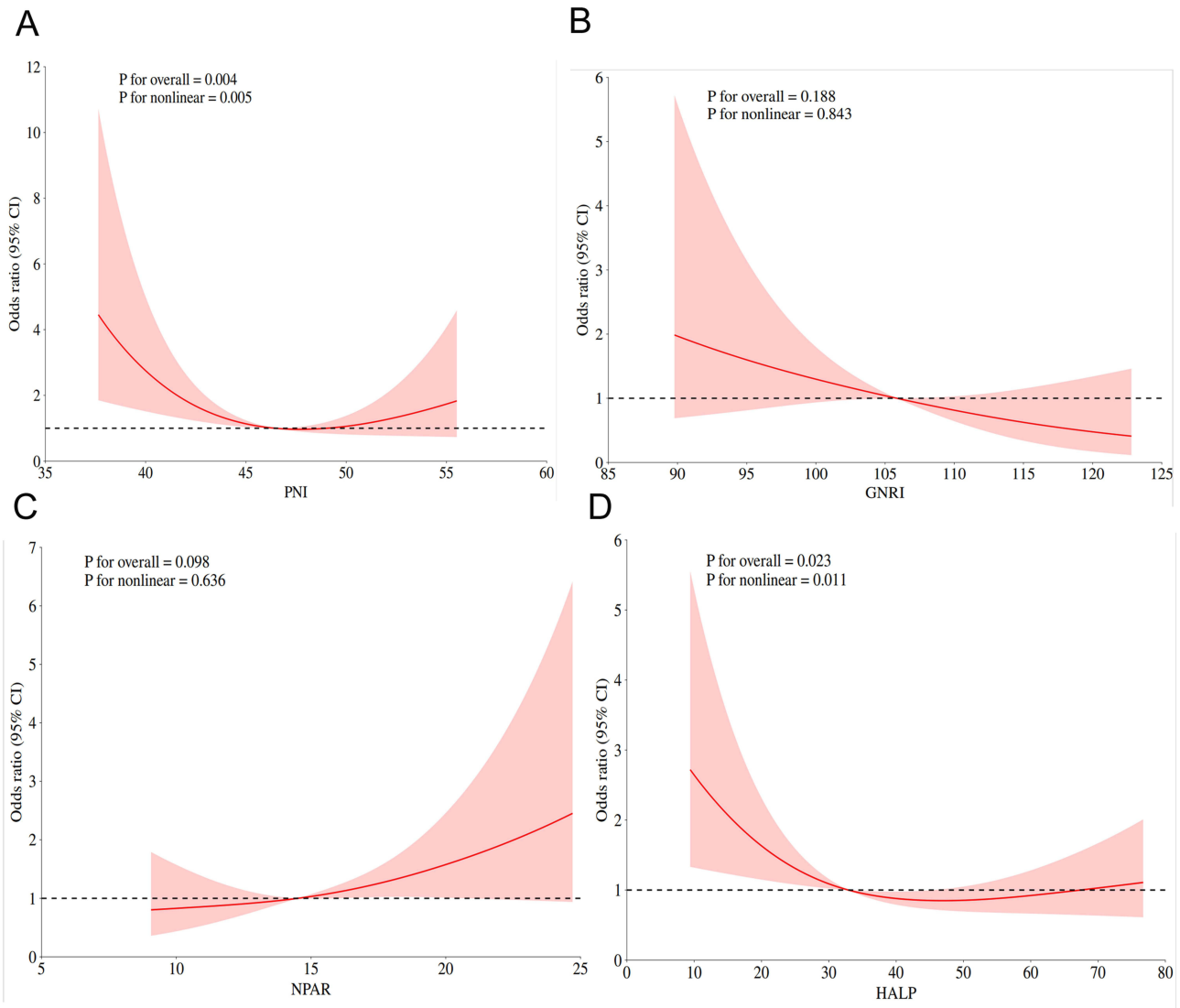

Figure 2 Restricted cubic spline curves for analyzing the nonlinear relationships between BC metastasis and PNI (**A**), GNRI (**B**), NPAR (**C**), HALP (**D**).

diabetes, hyperlipidemia, and KPS score, PNI and HALP were nonlinearly correlated with BC metastasis (P for overall association < 0.05, P for nonlinear < 0.05) (Figure 2A–D). However, there was no linear correlation between GNRI, NPAR and BC metastasis (P for overall association > 0.05, P for nonlinear > 0.05) (Figure 2B and C).

Based on the receiver operating characteristic (ROC) curve analysis and the optimal Youden's index, the optimal cut-off values of PNI, GNRI, NPAR and HALP were 43.83, 103.52, 16.67, and 30.38, respectively (Table 2). According to the cut - off value, we divided PNI into two groups (PNI< 43.83 and PNI ≥ 43.83). The relationships between PNI and clinical parameters in BC patients were detailed showed in Table 3. Compared to the low PNI group (PNI< 43.83), there were significant differences in the distribution of age, T stage, N stage, hyperlipidemia, liver metastasis, metastasis, hemoglobin, total protein, albumin, and other blood parameters in the high PNI group (PNI ≥ 43.83).

Multivariate logistic regression analysis was further used to identify the influencing factors of BC metastasis (Table 4). After adjusting for age, BMI, KPS score, hypertension, diabetes, hyperlipidemia, ER, HER2, Ki67, molecular subtypes, WBC, neutrophil, neutrophil percentage, lymphocyte, lymphocyte percentage, monocyte, monocyte percentage, triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and glucose (Model 3), marital status, T stage, N stage, RBC, total protein, and PNI were identified as independent influencing factors for BC metastasis.

Table 2 Receiver Operating Characteristics Analyses of Parameters in Patients with BC Metastasis

Variables	Cut Off Value	AUC (95% CI)	Sensitivity	Specificity
PNI	43.83	0.60 (0.52–0.68)	0.23	0.56
GNRI	103.52	0.59 (0.51–0.66)	0.33	0.49
NPAR	16.67	0.58 (0.50–0.65)	0.78	0.38
HALP	30.38	0.58 (0.51–0.66)	0.38	0.46

Abbreviations: AUC, area under the receiver operating characteristic curve; PNI, prognostic nutritional index; GNRI, geriatric nutritional risk index; NPAR, neutrophil percentage-to-albumin ratio; HALP, hemoglobin, albumin, lymphocyte, and platelet ratio.

Table 3 Relationship Between PNI and Clinical Parameters in BC Patients

Variables	Overall (n = 311)	PNI<43.83 (n = 88)	PNI≥43.83 (n =223)	*P* value
Age (years), mean±SD	53.69 ± 9.90	55.64 ± 10.23	52.92 ± 9.69	**0.029**
BMI (kg/m^2), mean±SD	24.59 ± 3.40	24.60 ± 3.32	24.59 ± 3.44	0.974
Marital status, n(%)				0.745
Divorced	42 (13.50)	11 (12.50)	31 (13.90)	
Married	269 (86.50)	77 (87.50)	192 (86.10)	
Histological grade, n(%)				0.442
I	17 (5.48)	4 (4.55)	13 (5.86)	
II	124 (40.00)	31 (35.23)	93 (41.89)	
III	169 (54.52)	53 (60.23)	116 (52.25)	
ER status, n(%)				0.232
Negative	118 (37.94)	38 (43.18)	80 (35.87)	
Positive	193 (62.06)	50 (56.82)	143 (64.13)	
PR status, n(%)				0.472
Negative	156 (50.16)	47 (53.41)	109 (48.88)	
Positive	155 (49.84)	41 (46.59)	114 (51.12)	
HER2 status, n(%)				0.300
Negative	180 (57.88)	55 (62.50)	125 (56.05)	
Positive	131 (42.12)	33 (37.50)	98 (43.95)	
Ki67 score, n(%)				0.085
<30	89 (28.62)	19 (21.59)	70 (31.39)	
≥30	222 (71.38)	69 (78.41)	153 (68.61)	
T stage, n(%)				**<0.001**
T1	115 (36.98)	24 (27.27)	91 (40.81)	
T2	147 (47.27)	40 (45.45)	107 (47.98)	
T3	38 (12.22)	16 (18.18)	22 (9.87)	
T4	11 (3.54)	8 (9.09)	3 (1.35)	
N stage, n(%)				**0.005**
N0	98 (31.51)	19 (21.59)	79 (35.43)	
N1	105 (33.76)	32 (36.36)	73 (32.74)	
N2	47 (15.11)	10 (11.36)	37 (16.59)	
N3	61 (19.61)	27 (30.68)	34 (15.25)	
Molecular subtypes, n(%)				0.357
TNBC	54 (17.36)	21 (23.86)	33 (14.80)	
HER2 enriched	75 (24.12)	19 (21.59)	56 (25.11)	
Luminal A	83 (26.69)	18 (20.45)	50 (22.42)	
Luminal B HER2-	68 (21.86)	20 (22.73)	63 (28.25)	
Luminal B HER2+	31 (9.97)	10 (11.36)	21 (9.42)	

(*Continued*)

Table 3 (Continued).

Variables	Overall (n = 311)	PNI<43.83 (n = 88)	PNI≥43.83 (n =223)	*P* value
Hypertension, n(%)				0.671
No	257 (82.64)	74 (84.09)	183 (82.06)	
Yes	54 (17.36)	14 (15.91)	40 (17.94)	
Diabetes, n(%)				0.827
No	281 (90.35)	79 (89.77)	202 (90.58)	
Yes	30 (9.65)	9 (10.23)	21 (9.42)	
Hyperlipemia, n(%)				**0.027**
No	293 (94.21)	87 (98.86)	206 (92.38)	
Yes	18 (5.79)	1 (1.14)	17 (7.62)	
Bone metastasis, n(%)				0.187
No	261 (83.92)	70 (79.55)	191 (85.65)	
Yes	50 (16.08)	18 (20.45)	32 (14.35)	
Lung metastasis, n(%)				0.057
No	278 (89.39)	74 (84.09)	204 (91.48)	
Yes	33 (10.61)	14 (15.91)	19 (8.52)	
Liver metastasis, n(%)				**0.003**
No	292 (93.89)	77 (87.50)	215 (96.41)	
Yes	19 (6.11)	11 (12.50)	8 (3.59)	
Brain metastasis, n(%)				0.168
No	292 (93.89)	80 (90.91)	212 (95.07)	
Yes	19 (6.11)	8 (9.09)	11 (4.93)	
BC metastasis, n(%)				**<0.001**
No	230 (73.95)	52 (59.09)	178 (79.82)	
Yes	81 (26.05)	36 (40.91)	45 (20.18)	
KPS score, mean±SD	83.49 ± 6.87	83.78 ± 6.27	82.65 ± 8.33	0.204
Hemoglobin (g/L), mean±SD	116.96 ± 15.85	106.30 ± 18.12	121.17 ± 12.61	**<0.001**
Platelet (10^9/L), mean±SD	196.76 ± 80.65	188.34 ± 96.79	200.08 ± 73.29	0.306
Total protein (g/L), mean±SD	67.71 ± 6.40	62.85 ± 4.85	69.62 ± 5.92	**<0.001**
Albumin (g/L), mean±SD	39.96 ± 3.86	36.15 ± 2.62	41.47 ± 3.17	**<0.001**
Prealbumin (g/L), mean±SD	226.50 ± 49.05	196.90 ± 57.77	238.18 ± 39.58	**<0.001**
TG (mmol/L), mean±SD	1.98 ± 1.19	1.91 ± 1.25	2.01 ± 1.17	0.526
TC (mmol/L), mean±SD	5.05 ± 1.04	4.87 ± 0.91	5.12 ± 1.08	0.051
HDL-C (mmol/L), mean±SD	1.20 ± 0.27	1.14 ± 0.26	1.23 ± 0.26	**0.010**
LDL-C (mmol/L), mean±SD	3.11 ± 0.75	2.96 ± 0.64	3.17 ± 0.78	**0.017**
FPG (mmol/L), mean±SD	5.59 ± 1.61	5.61 ± 2.33	5.58 ± 1.23	0.881
WBC (10^9/L), median (IQR)	4.63 (3.70, 6.00)	3.96 (2.73, 6.01)	4.84 (3.98, 5.99)	**<0.001**
Neutrophil (10^9/L), median (IQR)	2.61 (2.02, 3.67)	2.43 (1.48, 4.12)	2.65 (2.10, 3.57)	0.211
Neutrophil percentage (%), median (IQR)	0.59 (0.51, 0.67)	0.63 (0.53, 0.73)	0.57 (0.50, 0.64)	**<0.001**
Lymphocyte (10^9/L), median (IQR)	1.26 (0.95, 1.66)	0.89 (0.69, 1.17)	1.44 (1.11, 1.83)	**<0.001**
Lymphocyte percentage (%), median (IQR)	0.29 (0.21, 0.36)	0.24 (0.15, 0.32)	0.31 (0.24, 0.37)	**<0.001**
Monocyte (10^9/L), median (IQR)	0.38 (0.27, 0.49)	0.33 (0.24, 0.49)	0.39 (0.29, 0.48)	**0.032**
Monocyte percentage (%), median (IQR)	0.08 (0.06, 0.10)	0.09 (0.06, 0.11)	0.08 (0.06, 0.10)	0.380
RBC (10^9/L), median (IQR)	3.97 (3.57, 4.28)	3.55 (3.21, 3.95)	4.06 (3.79, 4.35)	**<0.001**

Note: Bold values indicate $P < 0.05$.

Abbreviations: BC, breast cancer; BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; KPS, karnofsky performance status; TNBC, triple-negative breast cancer; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; WBC, white blood cell count; RBC, red blood cell count; PNI, prognostic nutritional index.

Table 4 Multivariate Logistic Regression Analyses of Factors Associated with BC Metastasis

Variables	Model 1		Model 2		Model 3	
	OR(95% CI)	*P* value	OR(95% CI)	*P* value	OR(95% CI)	*P* value
Marital status, n(%)						
Divorced	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Married	0.46 (0.23 ~ 0.90)	**0.024**	0.34 (0.12 ~ 0.91)	**0.032**	0.16 (0.05 ~ 0.53)	**0.003**
Histological grade						
I	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
II	1.87 (0.23 ~ 15.31)	0.558	0.91 (0.09 ~ 9.74)	0.941	0.68 (0.06 ~ 8.46)	0.768
III	10.51 (1.36 ~ 81.12)	**0.024**	3.70 (0.37 ~ 36.90)	0.265	4.36 (0.38 ~ 50.14)	0.237
PR status						
Negative	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Positive	0.57 (0.34 ~ 0.95)	**0.032**	0.88 (0.43 ~ 1.80)	0.719	0.50 (0.13 ~ 2.00)	0.329
T stage						
T1	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
T2	2.63 (1.26 ~ 5.48)	**0.010**	1.95 (0.83 ~ 4.60)	0.126	2.49 (0.92 ~ 6.76)	0.073
T3	26.47 (10.21 ~ 68.63)	**<0.001**	9.38 (3.01 ~ 29.20)	**<0.001**	11.38 (2.78 ~ 46.51)	**<0.001**
T4	94.55 (11.05 ~ 809.29)	**<0.001**	9.95 (0.94 ~ 105.50)	0.056	37.08 (2.06 ~ 668.80)	**0.014**
N stage						
N0	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
N1	2.62 (1.14 ~ 6.02)	**0.023**	1.51 (0.58 ~ 3.94)	0.399	1.43 (0.46 ~ 4.47)	0.540
N2	2.34 (0.86 ~ 6.36)	0.095	1.60 (0.52 ~ 4.93)	0.409	2.47 (0.62 ~ 9.73)	0.198
N3	20.27 (8.50 ~ 48.35)	**<0.001**	4.56 (1.57 ~ 13.27)	**0.005**	6.30 (1.71 ~ 23.18)	**0.006**
RBC	0.39 (0.25 ~ 0.62)	**<0.001**	0.26 (0.07 ~ 1.01)	0.052	0.11 (0.02 ~ 0.62)	**0.012**
Hemoglobin	0.97 (0.96 ~ 0.99)	**0.002**	1.03 (0.98 ~ 1.09)	0.236	1.05 (0.99 ~ 1.12)	0.117
Total protein	1.00 (0.96 ~ 1.04)	0.884	1.10 (1.01 ~ 1.21)	**0.037**	1.16 (1.03 ~ 1.30)	**0.011**
Albumin	0.90 (0.84 ~ 0.97)	**0.003**	0.98 (0.81 ~ 1.18)	0.851	1.03 (0.82 ~ 1.30)	0.793
Prealbumin	0.99 (0.98 ~ 0.99)	**<0.001**	0.99 (0.99 ~ 1.00)	0.155	0.99 (0.98 ~ 1.00)	0.054
PNI						
<43.83	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥43.83	0.37 (0.21 ~ 0.62)	**<0.001**	0.66 (0.23 ~ 1.88)	0.439	0.19 (0.04 ~ 0.88)	**0.034**
GNRI						
<103.52	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥103.52	0.47 (0.28 ~ 0.79)	**0.004**	0.39 (0.13 ~ 1.14)	0.086	0.37 (0.10 ~ 1.33)	0.128
NPAR						
<16.67	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥16.67	2.23 (1.29 ~ 3.86)	**0.004**	0.86 (0.34 ~ 2.14)	0.741	0.50 (0.11 ~ 2.39)	0.388
HALP						
<30.38	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
≥30.38	0.51 (0.31 ~ 0.85)	**0.010**	0.75 (0.34 ~ 1.63)	0.463	0.48 (0.13 ~ 1.74)	0.266

Notes: Model 1: unadjusted; Model 2: adjusted for age, BMI; Model 3: adjusted for age, BMI, KPS score, hypertension, diabetes, hyperlipemia, ER, HER2, Ki67, molecular subtypes, WBC, neutrophil, neutrophil percentage, lymphocyte, lymphocyte percentage, monocyte, monocyte percentage, triglyceride, total cholesterol, HDL-C, LDL-C, glucose. Bold values indicate $P < 0.05$.

Abbreviations: BC, breast cancer; OR, odds ratio; CI, confidence interval; PR, progesterone receptor; RBC, red blood cell count; PNI, prognostic nutritional index; GNRI, geriatric nutritional risk index; NPAR, neutrophil percentage-to-albumin ratio; HALP, hemoglobin, albumin, lymphocyte, and platelet ratio.

Patients with high PNI (PNI ≥ 43.83) had a significantly lower probability of BC metastasis compared to those with low PNI (PNI < 43.83) (adjusted OR 0.19, 95% CI 0.04, 0.88, P = 0.034). Patients with a higher T stage, N stage, and total protein were more likely to experience BC metastasis (adjusted OR for T3 was 11.38, 95% CI 2.78, 46.51, P < 0.001; adjusted OR for T4 was 37.08, 95% CI 2.06, 668.80, P = 0.014; adjusted OR for N3 was 6.30, 95% CI 1.71, 23.18, P = 0.006; adjusted OR for total protein was 1.16, 95% CI 1.03, 1.30, P = 0.011). Married patients had a lower probability of BC metastasis than those who were divorced (including divorced, widowed, and separated) (adjusted OR 0.16, 95% CI 0.05, 0.53, P = 0.003). The higher the RBC, the lower the risk of BC metastasis (adjusted OR 0.11, 95% CI 0.02, 0.62, P = 0.012).

Establishment and Verification of a Clinical Prediction Model for Breast Cancer Metastasis

We incorporated the independent influencing factors, namely marital status, T stage, N stage, RBC, total protein, and PNI, into the construction of a nomogram model for BC metastasis (Figure 3). Each variable was assigned a score ranging from 0 to 100. The scores corresponding to each variable were summed up to calculate the total score, and the risk of BC metastasis was located on the nomogram according to the total score level. Through this approach, the likelihood of BC metastasis can be evaluated more effectively and intuitively. For example, total scores ≥240 on the nomogram correspond to a 90% probability of BC metastasis (scale range: 0–350).

To verify the robustness and clinical utility of the nomogram model, we randomly splitted the dataset into a training set and a validation set at a ratio of 7:3. The AUC of the prediction model in the training set was 0.85 (95% CI 0.79, 0.91), and that in the validation set was 0.82 (95% CI 0.71, 0.93) (Figure 4). The calibration curves of the training set and the validation set indicated that the predictive probability of the model matched the actual probability of the disease. The

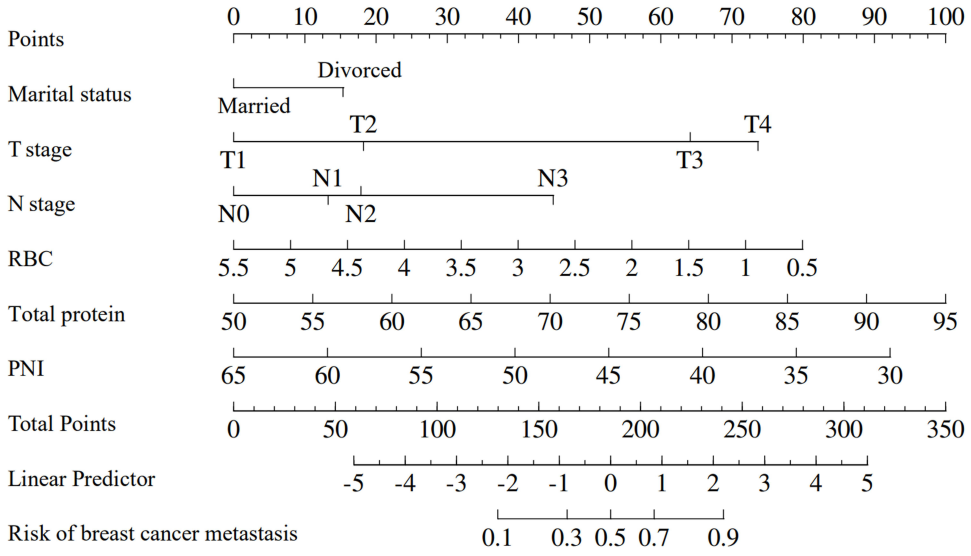

Figure 3 The nomogram for predicting the risk of BC metastasis.

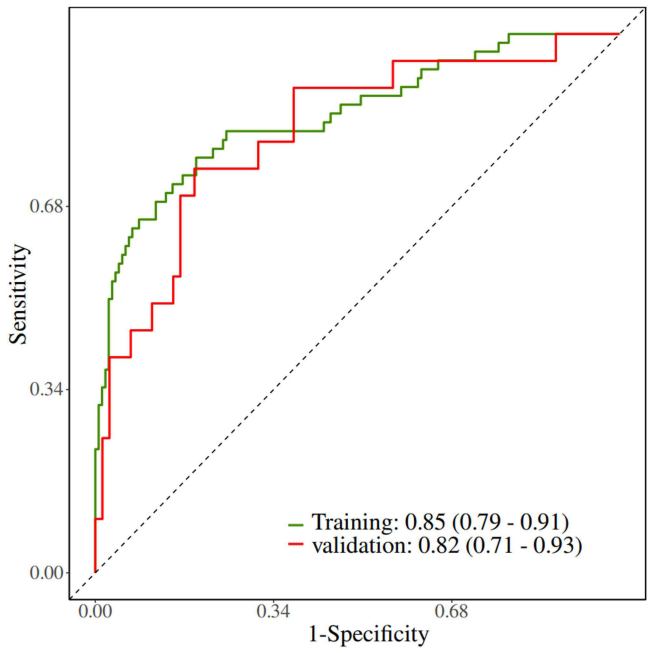

Figure 4 The AUC of the nomogram for predicting BC metastasis in the training and validation set.

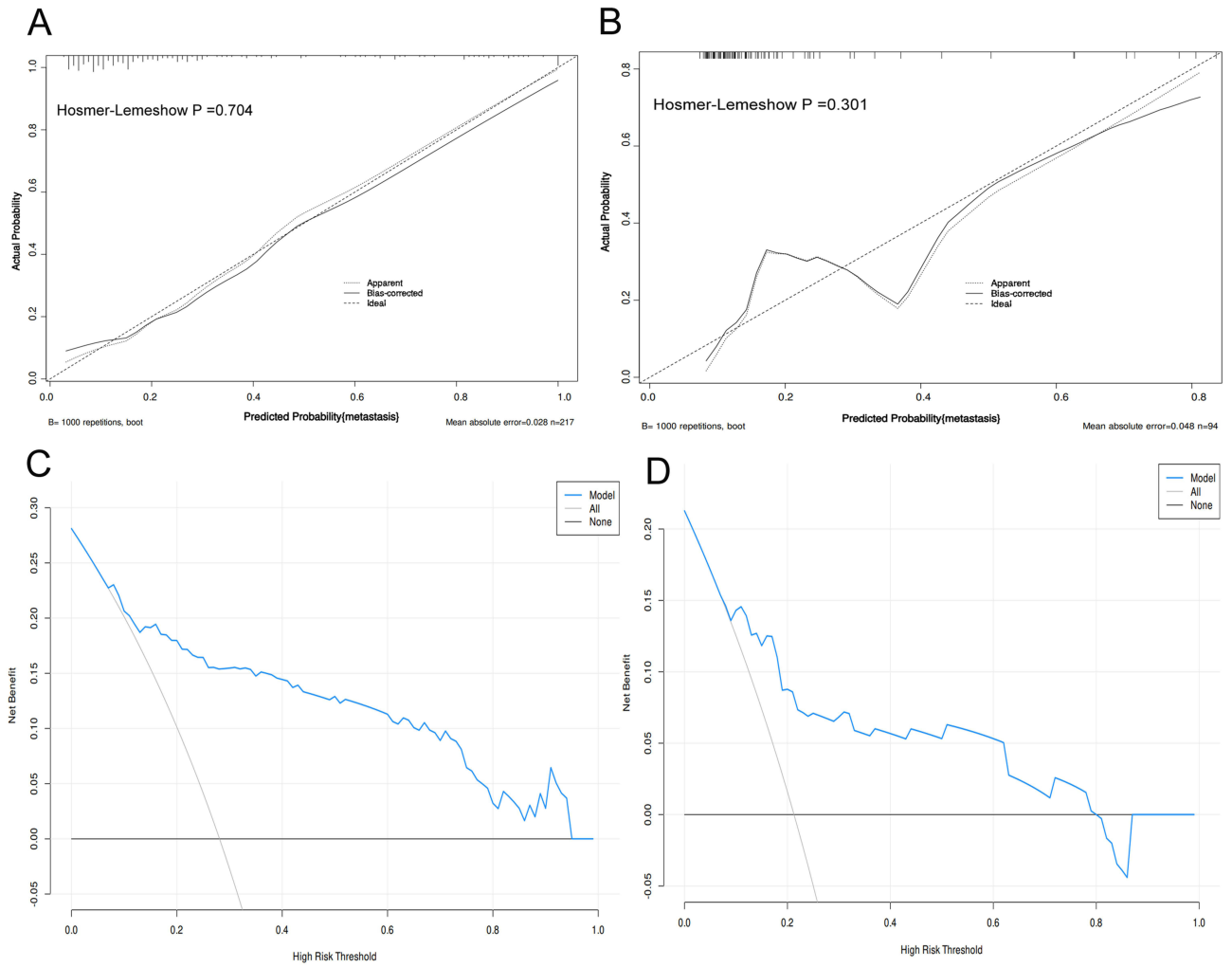

Figure 5 Calibration curves, Hosmer-Lemeshow test and decision curve analysis of the nomogram in the training set and the validation set. Calibration curves and Hosmer-Lemeshow test in the training set (**A**) and the validation set (**B**); decision curve analysis in the training set (**C**) and the validation set (**D**).

P values of the Hosmer-Lemeshow test were 0.704 and 0.301 respectively in the training and validation set, suggesting no differences between the predicted probability and the actual probability of the model (Figure 5A and B). The decision curves showed that the model had high clinical utility in both the training set and the validation set (Figure 5C and D).

Discussion

This study identified PNI as an independent predictor of breast cancer metastasis and developed a nomogram model incorporating PNI, marital status, T stage, N stage, RBC, and total protein. The AUC values for the training and validation sets were 0.85 and 0.82, respectively, indicating strong predictive performance. Furthermore, the calibration curves and Hosmer-Lemeshow test results confirmed the model's reliability in predicting observed outcomes, while decision curve analysis demonstrated high net benefit across a range of threshold probabilities. Collectively, these metrics highlight the model's potential as a practical, evidence-based tool for risk stratification in clinical settings.

The prognostic nutritional index (PNI), calculated from serum albumin levels and lymphocyte counts, reflects a patient's immune and nutritional status, which are critical determinants of cancer progression and metastasis.[26,27] Research by Xiang et al has found that low serum albumin level is associated with poor overall survival (OS) in patients with metastatic breast cancer and served as a prognostic factor.[28] Previous studies have shown that lymphocyte count can prevent tumor progression by activating the host immune response.[29] Low PNI reflects the presence of malnutrition or impaired immune function in patients. This condition may weaken the body's immune surveillance, increasing the

potential for tumor immune evasion and metastasis.[10] PNI has been reported as independent predictors of prognosis in various cancers, including gastric, colorectal, and lung cancers.[30–32] In the context of breast cancer, existing studies have demonstrated the prognostic value of PNI in predicting disease-free survival and overall survival, as well as its utility in guiding treatment strategies.[33,34] For example, Qu et al have confirmed that PNI is positively correlated with pathological complete response rate in breast cancer patients.[14] Furthermore, systematic reviews have also highlighted the predictive ability of the PNI for the prognosis of breast cancer patients.[8] This study further expands the application of PNI in assessing the risk of metastasis in breast cancer. It clarifies the non-linear relationship between PNI and breast cancer metastasis. By incorporating PNI into a predictive model, the actual clinical risk stratification has been improved. Additionally, dynamic monitoring of PNI may also assist in guiding nutritional support and immunomodulatory therapy, thereby improving patient prognosis.

In addition to PNI, other nutritional and inflammatory indices, including HALP, also showed nonlinear association with BC metastasis in our analysis. Our results align with previous studies, which have identified HALP as a reliable prognostic indicator for various malignancies.[17,35] However, in the final logistic regression model, HALP, GNRI, and NPAR were not associated with BC metastasis, with PNI emerging as the stronger independent predictor. It is well known that cancer-related inflammation promotes tumor growth, invasion, and metastasis, while malnutrition may exacerbate these processes by weakening immune surveillance and promoting inflammation.[36,37] The clinical advantage of PNI may lie in its biological foundation, which is closely related to the dual functions of immune surveillance and nutritional support within the tumor microenvironment. Other indicators may be limited by their definitions or the sample size, failing to account for multiple mechanisms.

The nomogram model developed in this study integrates PNI along with other independent predictive factors, such as marital status, T stage, N stage, RBC, and total protein, providing a personalized risk prediction tool for BC metastasis. The inclusion of marital status in the model may appear unconventional. However, previous studies have demonstrated that marital status is an independent prognostic indicator for survival in patients with breast cancer.[38,39] Marital status may influence cancer prognosis through mechanisms including infection, immune response regulation, social support and treatment adherence.[40–42] Although the biological basis of this association remains unclear, its inclusion underscores the multifactorial nature of breast cancer metastasis.

Despite these advantages, this study has several limitations. Firstly, while retrospective design allows for quick and effective analysis of existing clinical data, it may introduce selection bias, thereby limiting the generalizability of the findings and the exploration of causal relationships. Prospective studies are needed in the future to confirm the predictive value of PNI. Secondly, the relatively small sample size may affect the extrapolation of the results. Larger-scale, multicenter studies and external validation are required to further conform these findings. Lastly, although this study focused on objective and easily accessible laboratory parameters, other potentially relevant biomarkers, such as C-reactive protein or interleukin-6, were not included. Incorporating these biomarkers could further enhance the model's accuracy and provide additional insights into the biological mechanisms driving BC metastasis.

Conclusions

In conclusion, this study identifies PNI as an independent predictor of BC metastasis and introduces a novel PNI-based nomogram model with significant predictive accuracy and clinical applicability. By integrating nutritional, inflammatory, and clinical factors into a user-friendly tool, this model enables personalized risk assessment and enhances clinical decision-making. Given the limitations of our retrospective design and sample size, future studies should validate these findings in large-scale prospective multicenter cohorts and explore interventions targeting nutritional and inflammatory pathways to mitigate metastasis risk (such as protocolized albumin support and lymphocyte-boosting diets for PNI < 43.83). Compared to traditional prediction models like TNM stage, this PNI-based nomogram model may be more advantageous in improving the prognosis of breast cancer patients.

Data Sharing Statement

The original data presented in this paper is available from the corresponding author upon request. The data is not publicly available due to privacy and ethical restrictions.

Ethics Approval and Consent Participate

This study followed the Declaration of Helsinki. The ethical review process and informed consent procedures were approved by the Ethics Committee of Yancheng First People's Hospital (Jiangsu, China) (ethics number: 2025-K-035). Since this study was retrospective and the data were anonymous, the ethics committee agreed to waive the requirement for written informed consent.

Acknowledgments

We express our gratitude to all participants and colleagues who actively contributed to the study.

Funding

This research received no external funding.

Disclosure

The authors declare no conflicts of interest in this work.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–249. doi:10.3322/caac.21660
2. Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. *Nature*. 2012;490(7418):61–70. doi:10.1038/nature11412.
3. Valastyan S, Weinberg RA. Tumor metastasis: molecular insights and evolving paradigms. *Cell*. 2011;147(2):275–292. doi:10.1016/j.cell.2011.09.024
4. Liang Y, Zhang H, Song X, Yang Q. Metastatic heterogeneity of breast cancer: molecular mechanism and potential therapeutic targets. *Semin Cancer Biol*. 2020;60:14–27. doi:10.1016/j.semcancer.2019.08.012
5. Tirada N, Aujero M, Khorjekar G, et al. Breast cancer tissue markers, genomic profiling, and other prognostic factors: a primer for radiologists. *Radiographics*. 2018;38(7):1902–1920. doi:10.1148/rg.2018180047
6. Wang W, Luo YP. MicroRNAs in breast cancer: oncogene and tumor suppressors with clinical potential. *J Zhejiang Univ Sci B*. 2015;16(1):18–31. doi:10.1631/jzus.B1400184
7. Bullock AF, Greenley SL, McKenzie GAG, Paton LW, Johnson MJ. Relationship between markers of malnutrition and clinical outcomes in older adults with cancer: systematic review, narrative synthesis and meta-analysis. *Eur J Clin Nutr*. 2020;74(11):1519–1535. doi:10.1038/s41430-020-0629-0
8. Peng P, Chen L, Shen Q, Xu Z, Ding X. Prognostic nutritional index (PNI) and controlling nutritional status (CONUT) score for predicting outcomes of breast cancer: a systematic review and meta-analysis. *Pak J Med Sci*. 2023;39(5):1535–1541. doi:10.12669/pjms.39.5.7781
9. Sun L, Liu J, Wang D. Prognostic value of the preoperative prognostic nutritional index and systemic immuno-inflammatory index in Chinese breast cancer patients: a clinical retrospective cohort study. *J Surg Oncol*. 2023;127(6):921–928. doi:10.1002/jso.27210
10. Hu G, Ding Q, Zhong K, Wang S, Huang L. Low pretreatment prognostic nutritional index predicts poor survival in breast cancer patients: a meta-analysis. *PLoS One*. 2023;18(1):e0280669. doi:10.1371/journal.pone.0280669
11. Chen L, Bai P, Kong X, et al. Prognostic nutritional index (PNI) in patients with breast cancer treated with neoadjuvant chemotherapy as a useful prognostic indicator. *Front Cell Dev Biol*. 2021;9:656741. doi:10.3389/fcell.2021.656741
12. Hua X, Long ZQ, Huang X, et al. The value of prognostic nutritional index (PNI) in predicting survival and guiding radiotherapy of patients with T1-2N1 breast cancer. *Front Oncol*. 2020;9:1562. doi:10.3389/fonc.2019.01562
13. Xu T, Zhang SM, Wu HM, et al. Prognostic significance of prognostic nutritional index and systemic immune-inflammation index in patients after curative breast cancer resection: a retrospective cohort study. *BMC Cancer*. 2022;22(1):1128. doi:10.1186/s12885-022-10218-x
14. Qu F, Luo Y, Peng Y, et al. Construction and validation of a prognostic nutritional index-based nomogram for predicting pathological complete response in breast cancer: a two-center study of 1,170 patients. *Front Immunol*. 2024;14:1335546. doi:10.3389/fimmu.2023.1335546
15. Haas M, Lein A, Fuereder T, et al. The geriatric nutritional risk index (GNRI) as a prognostic biomarker for immune checkpoint inhibitor response in recurrent and/or metastatic head and neck cancer. *Nutrients*. 2023;15(4):880. doi:10.3390/nu15040880
16. Li X, Wu M, Chen M, et al. The association between neutrophil-percentage-to-albumin ratio (NPAR) and mortality among individuals with cancer: insights from national health and nutrition examination survey. *Cancer Med*. 2025;14(2):e70527. doi:10.1002/cam4.70527
17. Xu H, Zheng X, Ai J, Yang L. Hemoglobin, albumin, lymphocyte, and platelet (HALP) score and cancer prognosis: a systematic review and meta-analysis of 13,110 patients. *Int Immunopharmacol*. 2023;114:109496. doi:10.1016/j.intimp.2022.109496
18. Lei W, Wang W, Qin S, Yao W. Author correction: predictive value of inflammation and nutritional index in immunotherapy for stage IV non-small cell lung cancer and model construction. *Sci Rep*. 2024;14(1):19518. doi:10.1038/s41598-024-70611-3
19. Wu P, Liu J, Wang X, et al. Development and validation of a nomogram based on geriatric nutritional risk index for predicting prognosis and postoperative complications in surgical patients with upper urinary tract urothelial carcinoma. *J Cancer Res Clin Oncol*. 2023;149(20):18185–18200. doi:10.1007/s00432-023-05462-y
20. Ko CA, Fang KH, Tsai MS, et al. Prognostic value of neutrophil percentage-to-albumin ratio in patients with oral cavity cancer. *Cancers*. 2022;14(19):4892. doi:10.3390/cancers14194892
21. Liu H, Zou Q, Zhang H, Ma X. Development of a prediction model based on hemoglobin, albumin, lymphocyte count, and platelet-score for lymph node metastasis in rectal cancer. *Eur J Cancer Prev*. 2025. doi:10.1097/CEJ.0000000000000954

22. Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. *Nihon Geka Gakkai Zasshi*. 1984;85(9):1001–1005.
23. Bouillanne O, Morineau G, Dupont C, et al. Geriatric nutritional risk index: a new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr*. 2005;82(4):777–783. doi:10.1093/ajcn/82.4.777
24. Lv XN, Shen YQ, Li ZQ, et al. Neutrophil percentage to albumin ratio is associated with stroke-associated pneumonia and poor outcome in patients with spontaneous intracerebral hemorrhage. *Front Immunol*. 2023;14:1173718. doi:10.3389/fimmu.2023.1173718
25. Güç ZG, Alacacıoğlu A, Kalender ME, et al. HALP score and GNRI: simple and easily accessible indexes for predicting prognosis in advanced stage NSCLC patients. The İzmir oncology group (IZOG) study. *Front Nutr*. 2022;9:905292. doi:10.3389/fnut.2022.905292
26. Kulkarni A, Bowers LW. The role of immune dysfunction in obesity-associated cancer risk, progression, and metastasis. *Cell Mol Life Sci*. 2021;78 (7):3423–3442. doi:10.1007/s00018-020-03752-z
27. Saha SK, Lee SB, Won J, et al. Correlation between oxidative stress, nutrition, and cancer initiation. *Int J Mol Sci*. 2017;18(7):1544. doi:10.3390/ijms18071544
28. Xiang M, Zhang H, Tian J, Yuan Y, Xu Z, Chen J. Low serum albumin levels and high neutrophil counts are predictive of a poorer prognosis in patients with metastatic breast cancer. *Oncol Lett*. 2022;24(6):432. doi:10.3892/ol.2022.13552
29. An X, Ding PR, Li YH, et al. Elevated neutrophil to lymphocyte ratio predicts survival in advanced pancreatic cancer. *Biomarkers*. 2010;15 (6):516–522. doi:10.3109/1354750X.2010.491557
30. Jing Y, Ren M, Li X, et al. The effect of systemic immune-inflammatory index (SII) and prognostic nutritional index (PNI) in early gastric cancer. *J Inflamm Res*. 2024;17:10273–10287. doi:10.2147/JIR.S499094
31. Li J, Zhu N, Wang C, et al. Preoperative albumin-to-globulin ratio and prognostic nutritional index predict the prognosis of colorectal cancer: a retrospective study. *Sci Rep*. 2023;13(1):17272. doi:10.1038/s41598-023-43391-5
32. Zhang B, Chen J, Yu H, Li M, Cai M, Chen L. Prognostic nutritional index predicts efficacy and immune-related adverse events of first-line chemoimmunotherapy in patients with extensive-stage small-cell lung cancer. *J Inflamm Res*. 2024;17:1777–1788. doi:10.2147/JIR.S450804
33. Prasetiyo PD, Baskoro BA, Hariyanto TI. The role of nutrition-based index in predicting survival of breast cancer patients: a systematic review and meta-analysis. *Heliyon*. 2023;10(1):e23541. doi:10.1016/j.heliyon.2023.e23541
34. Keskinkilic M, Semiz HS, Polat G, Arayici ME, Yavuzsen T, Oztop I. The Prognostic Indicator in Breast Cancer Treated with CDK4/6 Inhibitors: The Prognostic Nutritional Index. *Future Oncol*; 2023;19(7):517–29. doi:10.2217/fon-2022-1023
35. Zhao Z, Xu L. Prognostic significance of HALP score and combination of peripheral blood multiple indicators in patients with early breast cancer. *Front Oncol*. 2023;13:1253895. doi:10.3389/fonc.2023.1253895
36. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell*. 2010;140(6):883–899. doi:10.1016/j.cell.2010.01.025
37. Flores-Pérez JA, de la Rosa Oliva F, Argenes Y, Meneses-Garcia A. Nutrition, cancer and personalized medicine. *Adv Exp Med Biol*. 2019;1168:157–168. doi:10.1007/978-3-030-24100-1_11
38. Zhu S, Lei C. Association between marital status and all-cause mortality of patients with metastatic breast cancer: a population-based study. *Sci Rep*. 2023;13(1):9067. doi:10.1038/s41598-023-36139-8
39. Lan T, Lu Y, Luo H, et al. Effects of marital status on prognosis in women with infiltrating ductal carcinoma of the breast: a real-world 1: 1 propensity-matched study. *Med Sci Monit*. 2020;26:e923630. doi:10.12659/MSM.923630
40. Kinlen LJ, Gilham C, Ray R, Thomas DB, Peto J. Cohabitation, infection and breast cancer risk. *Int J Cancer*. 2021;148(6):1408–1418. doi:10.1002/ijc.33319
41. Janerich DT, Thompson WD. Reduced breast cancer risk after remarriage: evidence of genetic-immune protection. *Epidemiology*. 1995;6 (3):254–257. doi:10.1097/00001648-199505000-00011
42. Zhang J, Gan L, Wu Z, Yan S, Liu X, Guo W. The influence of marital status on the stage at diagnosis, treatment, and survival of adult patients with gastric cancer: a population-based study. *Oncotarget*. 2017;8(14):22385–22405. doi:10.18632/oncotarget.7399