Original Article

Nomogram for predicting preoperative axillary lymph node status in male breast carcinoma: a SEER population-based study

Wenxin Chen[1,2]^, Hebing Wang[1,2], Binglin Yang[1,2], Maoquan Zhang[1,2], Jicheng Chen[1,2]

[1]Department of Breast Surgery, Affiliated Sanming First Hospital of Fujian Medical University, Sanming, China; [2]Department of Breast Surgery, The School of Clinical Medicine, Fujian Medical University, Fuzhou, China

Contributions: (I) Conception and design: W Chen; (II) Administrative support: W Chen; (III) Provision of study materials or patients: W Chen; (IV) Collection and assembly of data: W Chen, H Wang, B Yang; (V) Data analysis and interpretation: W Chen, M Zhang, J Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Wenxin Chen. Department of Breast Surgery, Affiliated Sanming First Hospital of Fujian Medical University, Sanming 365001, China. Email: fjsmcwx@fjmu.edu.cn.

Background: Sentinel lymph node biopsy (SLNB) has been recommended as a replacement for axillary lymph node dissection (ALND) in male breast carcinoma (MBC) with clinical axillary lymph node-negative (ALN-negative) as in the case of female. However, the morbidity after SLNB may also have short-term or long-term complications. To avoid unnecessary surgery, building a model which is able to assess the risk of lymph node metastasis is vitally significant.

Methods: A retrospective review of the clinical and pathology data were carried out for patients diagnosed with MBC between 2010 and 2018 from the Surveillance, Epidemiology, and End Results (SEER) database. The cohort was divided into training and validation cohorts. A logistic regression model was used to construct the nomogram in the training cohort and then verified in the validation cohort. The receiver operating characteristic (ROC) curve, C-index, and calibration were used to evaluate the predictive ability of the nomogram.

Results: Overall, 2,610 patients diagnosed with MBC were included in the study, of which 1,740 were in the training cohort and 870 were in the validation cohort. Logistic regression analysis indicated age at diagnosis, tumor location, tumor stage, pathological type, and histologic grade, were significantly related to axillary lymph node metastasis (ALNM). The area under the curve (AUC) of the nomogram was 0.846 (95% CI: 0.825–0.867) and C-index was 0.848 (95% CI: 0.807–0.889), demonstrating a notable prediction performance. The calibration curve for the nomogram was plotted and the slope was close to 1. The prognostic value of the nomogram was further validated in the validation cohort, with an AUC of 0.848 (95% CI: 0.819–0.877).

Conclusions: A nomogram to predict ALNM was successfully established, especially for those who were of advanced age at diagnosis, had small tumor size, displayed low malignancy, and showed clinical ALN-negative, to avoid unnecessary axillary operation. The quality of life for patients is enhanced without conceding the overall survival rate.

Keywords: Male breast carcinoma (MBC); nomogram; axillary lymph node (ALN); Surveillance, Epidemiology, and End Results database (SEER database)

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^ ORCID: 0000-0002-5122-1933.

Introduction

Male breast carcinoma (MBC) is a rare disease that accounts for less than 1% of all cancers in men (1) and about less than 1% of all breast carcinoma (2). Due to its rarity, the limited information available regarding the prognosis of this disease, treatment, and epidemiology have been extrapolated from the protocols for breast carcinoma in women (3). Axillary lymph node (ALN) status is a key step in breast carcinoma because nodal status has been the standard of care to estimate prognosis and to guide the decision-making process for a systemic treatment plan. Many predictors of axillary lymph node metastasis (ALNM) have been previously suggested in female breast carcinoma (FBC) including age at diagnosis, tumor size, tumor location, pathological type, histologic grade, estrogen receptor (ER) status, progesterone receptor (PR) status, and HER2 status (4-7).

However, there are only a few predictive models for ALNM in MBC. Vaysse *et al.* (8) used two nomograms (validated in the female population) to demonstrate that the predictive factor of ALNM in FBC was not applicable to MBC. The possibility of building a prediction model of ALNM in MBC is hypothesized; of which can help identify patients with low risk of ALN involvement so as to improve the quality of life with no adverse effects on the survival rate. To verify the hypothesis, this study of applying the data from the Surveillance, Epidemiology, and End Results (SEER) database was conducted to explore the relationship between clinicopathologic features and ALN status. We present the following article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2516/rc).

Highlight box

Key findings

- A model to predict ALNM was successfully established in MBC.

What is known and what is new?

- Many predictors of ALNM have been previously suggested in FBC.
- It can also predict ALNM by the preoperative clinical features in MBC.

What is the implication, and what should change now?

- This nomogram could serve as an acceptable and adoptable clinical tool in preoperative evaluation in MBC, especially for those who were clinically and radiologically node-negative to avoid an SLNB procedure safely. This can enhance the quality of life for patients without conceding the overall survival rate.

Methods

Data were obtained from (SEER) (www.seer.cancer.gov) with the following search parameters. Incidence: SEER Research Data, 18 Registries, November 2020 Sub (2000 to 2018). The ethical approval of this study was exempted by the Ethics Committee of Affiliated Sanming First Hospital of Fujian Medical University as the data were from the publicly accessible database, SEER. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

A total of 2,610 male patients were selected according to the following inclusion and exclusion criteria between 2010 and 2018 in the investigation. Patients were included when meeting the following criteria: (I) male patients; (II) patients were diagnosed with primary breast cancer [International Classification of Diseases for Oncology, Third Edition (ICD-O-3)]; (III) patients aged 18 years old or above at diagnosis. Patients with the following criteria were excluded: (I) unknown clinical information including tumor size, American Joint Committee on Cancer (AJCC) stage, Tumor location (primary site-labeled), Pathological type, Histologic grade, estrogen receptor (ER) status, progesterone receptor (PR) status, and HER2 status; (II) regional nodes examined positive; (III) with metastatic or synchronous tumors.

The selected patients were randomly assigned in a 2:1 ratio to a training cohort and a validation cohort. The training cohort was used to construct the predictive risk model, and the validation cohort was applied to internal validation.

Variables including age at diagnosis, tumor location, AJCC tumor node metastasis (TNM) stage, AJCC T status, AJCC N status, pathological type, histologic grade, ER status, PR status, and HER2 status were gathered from the SEER database. Age was classified into four groups: '≤50', '51–60', '61–70', '71–80', and '>80'. Tumor location was classified as central portion of breast (Central), upper outer quadrant (UOQ), lower outer quadrant (LOQ), lower inner quadrant (LIQ), and upper inner quadrant (UIQ), nipple, overlapping lesion of breast (Overlapping), axillary tail of breast and Breast NOS (other). The pathological type was classified as invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), adenocarcinomas (ADENOCA), Paget's disease (Paget), and others. ER, PR and HER2 were all classified as positive and negative (note: the SEER database began collecting HER-2 information in 2010). Histologic grade was classified as grades I, II, and III. AJCC TNM Stage was classified as stages I, II, and III.

AJCC Tumor Status was classified as T1, T2, T3, and T4. AJCC Lymph Node Status was classified as positive and negative. The molecular subtype was classified as Luminal A, Luminal B, HER2+, and triple-negative (TN).

Statistical analysis

Baseline characteristics between the training cohort and the validation cohort were identified by using Pearson's Chi-square or Fisher's exact tests for categorical variables and Student's *t*-test for quantitative variables. Using the clinical and pathological data of the training cohort, a univariate logistic regression analysis was performed to explore ALNM-related variables. To identify factors that were associated with ALN involvement, binary logistic regression analysis was used for multivariable analysis. Odds ratios (OR) were presented with 95% CI. A logistic regression model was used to structure the nomogram. The receiver operating characteristic (ROC) curve, the area under the curve (AUC), and the concordance index (C-index) were used to distinguish the effect of the prediction ability of the model. Calibration was assessed graphically by plotting the relationship between actual (observed) probabilities and predicted probabilities in both cohorts. Internal validation of performance was estimated with the bootstrapping method (1,000 replications). To further evaluate the clinical value of the model, certain cut-off values were considered for predicting the risk in patients in the validation cohort and the corresponding accuracy and the false-negative rate of the cut-off values were calculated to assess the screening indicators of patients with low ALNM risk. Statistical analyses were conducted using SPSS for Windows (version 26.0, SPSS Inc., Chicago, IL, USA) and the R programming language and environment version 3.4.1. A two-tailed P value <0.05 was considered statistically significant.

Results

Comparison of clinicopathological characteristics between the training cohort and the validation cohort

Based on the inclusion criteria, A total of 2,610 patients who had well-documented patient data were identified for analysis. According to the ratio of 2:1, 1,740 were included in the training cohort and 870 were included in the validation cohort. The clinical and pathological data of the patients between the two groups did not differ significantly (P>0.05) (*Table 1*).

Univariate logistic regression analysis of ALNM in the training cohort

Univariate logistic regression analysis was used to probe ALNM-related variables (*Table 2*) and showed that age, tumor location, tumor stage, pathological type, histologic grade, ER, PR, Her-2, and molecular subtypes were related to MBC ALNM (P<0.05).

Multivariate logistic regression analysis of ALNM in the training group

After adjusting the significant variables from the univariate analysis, the multivariate analysis found that age at diagnosis, tumor location, tumor stage, pathological type, and histologic grade stayed as independent predictive factors of ALNM (*Table 3*).

Establishment of a prediction model for ALNM

A nomogram to predict ALNM was developed in the training cohort (*Figure 1*). The nomogram that incorporated the following independent predictors was shown to be associated with ALNM including age, pathological type, tumor location, histologic grade, and tumor stage. The weights of each variable in the nomogram corresponded to different points. Points for the following factors were added to the total points, which corresponded to the linear predictors and risk predictors of ALNM: age, histological (pathological type), Site (tumor location), Grade (histologic grade), and T-stage (tumor stage).

ROC curves of the training cohort are plotted in *Figure 2A*. AUC was 0.846 (95% CI: 0.825–0.867). The nomogram verified excellent accuracy for predicting ALN, with an unadjusted C-index of 0.848 (95% CI: 0.807–0.889). To test the prediction efficiency of the nomogram, 1,000 bootstrap resamplings were executed for verification through the calibration chart in the training cohort (*Figure 2B*). The calibration curve displayed a marked effect of the nomogram. These results testified that the nomogram was a suitable predictor of ALNM.

The predictive ability of nomograms in the validation cohort

This nomogram was prospectively used for patients in the validation cohort. It depicted the ROC curve (*Figure 2C*), and the AUC value calculated was 0.848 (95% CI: 0.819–0.877), indicating a good predictive ability. The nomogram

Table 1 Comparison of the descriptive characteristics between the training cohort and the validation cohort

Characteristics	Training (n=1,740)	Validation (n=870)	P value
Age at diagnosis (years), mean ± SD	67.57±11.70	67.64±12.03	0.895
Age (years), n (%)			0.542
≤50	137 (7.9)	79 (9.1)	
51–60	336 (19.3)	147 (16.9)	
61–70	539 (31.0)	269 (30.9)	
71–80	456 (26.2)	233 (26.8)	
>80	272 (15.6)	142 (16.3)	
Tumor location[#], n (%)			0.716
Central	744 (42.8)	403 (46.3)	
UIQ	82 (4.7)	35 (4.0)	
LIQ	32 (1.8)	14 (1.6)	
UOQ	222 (12.8)	100 (11.5)	
LOQ	65 (3.7)	35 (4.0)	
Nipple	79 (4.5)	39 (4.5)	
Others	228 (13.1)	100 (11.5)	
Overlapping	288 (16.6)	144 (16.6)	
Tumor stage, n (%)			0.808
T1	866 (49.8)	421 (48.4)	
T2	704 (40.5)	360 (41.4)	
T3	47 (2.7)	21 (2.4)	
T4	123 (7.1)	68 (7.8)	
Pathological type, n (%)			0.334
IDC	1,582 (90.9)	789 (90.7)	
ILC	14 (0.8)	8 (0.9)	
ADENO-CA	92 (5.3)	39 (4.5)	
Paget	20 (1.1)	8 (0.9)	
Others*	32 (1.8)	26 (3.0)	
Histologic grade, n (%)			0.613
I	251 (14.4)	124 (14.3)	
II	936 (53.8)	453 (52.1)	
III	553 (31.8)	293 (33.7)	
ER, n (%)			0.620
Positive	1,707 (98.1)	851 (97.8)	
Negative	33 (1.9)	19 (2.2)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	Training (n=1,740)	Validation (n=870)	P value
PR, n (%)			0.724
Positive	1,595 (91.7)	801 (92.1)	
Negative	145 (8.3)	69 (7.9)	
HER2 receptor status, n (%)			0.899
Positive	215 (12.4)	106 (12.2)	
Negative	1,525 (87.6)	764 (87.8)	
AJCC stage, n (%)			0.930
I	837 (48.1)	412 (47.4)	
II	626 (36.0)	319 (36.7)	
III	277 (15.9)	129 (16.0)	
Lymph node status, n (%)			0.976
Negative	1,179 (67.8)	590 (67.8)	
Positive	561 (32.2)	280 (32.2)	
Molecular subtype, n (%)			0.730
Luminal A	1,502 (86.3)	748 (86.0)	
Luminal B	209 (12.0)	104 (12.0)	
HER2+	6 (0.3)	2 (0.2)	
TN	23 (1.3)	16 (1.8)	

[#], tumor location: in cases of multifocal tumors or unifocal tumors that involved more than 1 quadrant, the tumor location was classified in the following order of location priority: central portion of breast, UOQ, LOQ, LIQ, and UIQ, nipple, overlapping lesion of breast (overlapping), Axillary tail of breast and Breast NOS (other). *, others: metaplastic carcinoma, medullary carcinoma, unspecified malignant neoplasms except for CNS, papillary carcinoma, infiltrating micropapillary carcinoma, tubular carcinoma, etc. (https://seer.cancer.gov/tools/solidtumor/Breast_STM.pdf). UIQ, upper inner quadrant; LIQ, lower inner quadrant; UOQ, upper outer quadrant; LOQ, lower outer quadrant; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ADENO-CA, adenocarcinomas; ER, estrogen receptor; PR, progesterone receptor; TN, triple-negative; AJCC, American Joint Committee on Cancer; CNS, central nervous system.

was internally verified using the bootstrap (1,000 bootstrap resamples) validation method. Good calibration was observed for the probability of ALNM in the validation cohort (*Figure 2D*). To further evaluate the clinical value of the model under different risks of ALNM. We select 14 cut-offs according to the Jordan index. The number of patients, the number of patients with ALNM, sensitivity, specificity, accuracy, and negative predictive value of ALNM were calculated under different predicted risk values (*Table 4*). As can be seen from the table, this model is more accurate in predicting patients with negative ALN. There were 204 cases with a predicted risk of <10%, and only 14 (6.9%) had ALNM, indicating that the model was more accurate in predicting patients with a lower risk of ALNM. The reason for this result is related to the study design. Both the training cohort and the validation group were patients with clinically negative ALN, resulting in a more accurate prediction of negative lymph nodes and a poorer prediction of positive lymph nodes.

Discussion

Sentinel lymph node biopsy (SLNB) has been recommended as a replacement for axillary dissection in MBC with clinical ALN-negative, as with the case in women (9). However, the morbidity after SLN biopsy is not negligible, short-term or long-term complications such as upper limb edema, numbness, and shoulder pain may also occur in FBC

Table 2 Univariate analysis for factors associated with ALNM

Variables	OR	95% CI	P value
Age (years)			<0.001
≤50	1 (ref)		
51–60	0.896	0.601–1.337	0.592
61–70	0.572	0.390–0.838	0.004
71–80	0.452	0.304–0.670	<0.001
>80	0.335	0.215–0.522	<0.001
Tumor location			<0.001
Central	1 (ref)		
UIQ	0.380	0.216–0.668	0.001
LIQ	0.361	0.147–0.888	0.027
UOQ	0.528	0.377–0.740	<0.001
LOQ	0.600	0.3411–1.053	0.075
Nipple	0.859	0.530–1.395	0.540
Other	0.723	0.527–0.991	0.044
Overlapping	0.551	0.408–0.745	<0.001
Tumor stage			<0.001
T1	1 (ref)		
T2	6.065	4.703–7.823	<0.001
T3	24.513	12.099–49.667	<0.001
T4	53.929	30.248–96.150	<0.001
Pathological type			0.002
IDC	1 (ref)		
ILC	0.801	0.250–2.565	0.708
ADENO-CA	0.359	0.201–0.641	0.001
Paget	2.002	0.828–4.840	0.123
Other	0.462	0.189–1.129	0.090
Histologic grade			<0.001
I	1 (ref)		
II	3.065	1.977–4.752	<0.001
III	10.642	6.815–16.617	<0.001
ER			
ER+	1 (ref)		
ER–	2.271	1.139–4.530	0.020
PR			
PR+	1 (ref)		
PR–	1.541	1.089–2.181	0.015
HER2			
HER2+	1 (ref)		
HER2–	0.544	0.407–0.727	<0.001
Molecular subtype			<0.001
LMA	1 (ref)		
LMB	1.809	1.348–2.429	<0.001
HER2	4.602	0.840–25.216	0.079
TN	1.770	0.771–4.066	0.178

ALNM, axillary lymph node metastasis; OR, odds ratio; CI, confidence interval; UIQ, upper inner quadrant; LIQ, lower inner quadrant; UOQ, upper outer quadrant; LOQ, lower outer quadrant; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ADENO-CA, adenocarcinomas; ER, estrogen receptor; PR, progesterone receptor; TN, triple-negative.

patients with SLNB (10,11). MBC usually has the same common presentation as FBC. Many models for predicting ALNM have been used in women with breast carcinoma (12,13). This study aimed to select patients with low risk of ALNM and to protect them from unnecessary axillary operations as in the case of women.

Most studies about MBC come with only small sample sizes as MBC is rarely seen, in view of this, the SEER database supplies a relatively large sample size for the study. In the study, we obtained 2,610 cases from the SEER database. The results provided evidence that analyzing the clinicopathological features can also be used to assist in the judgment of ALN status in MBC. A nomogram was successfully established for the prediction of ALNM in MBC. Age, pathological type, tumor location, histologic grade, and tumor stage were associated with ALNM. Applying this model to patients in the training cohort and the validation cohort in this study, the performance of the nomogram in these two groups was similar (AUC 0.846 *vs.* 0.848), and the nomogram showed good predictive value in both.

Zavagno *et al.* (14) findings showed that the youngest

Table 3 Multivariate logistic regression analysis for factors associated with ALNM

Variables	OR	95% CI	P value
Age (years)			<0.001
≤50	1 (ref)		
51–60	0.830	0.503–1.368	0.464
61–70	0.441	0.275–0.710	0.001
71–80	0.372	0.228–0.607	<0.001
>80	0.198	0.113–0.347	<0.001
Tumor location			0.001
Central	1 (ref)		
UIQ	0.508	0.264–0.975	0.042
LIQ	0.493	0.183–1.332	0.163
UOQ	0.603	0.400–0.909	0.016
LOQ	0.615	0.305–1.239	0.174
Nipple	0.631	0.328–1.212	0.167
Other	0.522	0.352–0.776	0.001
Overlapping	0.497	0.342–0.722	<0.001
Tumor stage			<0.001
T1	1 (ref)		
T2	5.877	4.463–7.739	<0.001
T3	25.211	11.632–54.643	<0.001
T4	60.418	32.409–112.631	<0.001
Pathological type			0.024
IDC	1 (ref)		
ILC	0.405	0.090–1.832	0.241
ADENO-CA	0.355	0.176–0.716	0.004
Paget	1.512	0.457–4.997	0.498
Other	0.542	0.186–1.577	0.261
Histologic grade			<0.001
I	1 (ref)		
II	2.569	1.555–4.245	<0.001
III	7.240	4.335–12.093	<0.001
Constant	0.126		<0.001

ALNM, axillary lymph node metastasis; OR, odds ratio; CI, confidence interval; UIQ, upper inner quadrant; LIQ, lower inner quadrant; UOQ, upper outer quadrant; LOQ, lower outer quadrant; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ADENO-CA, adenocarcinomas.

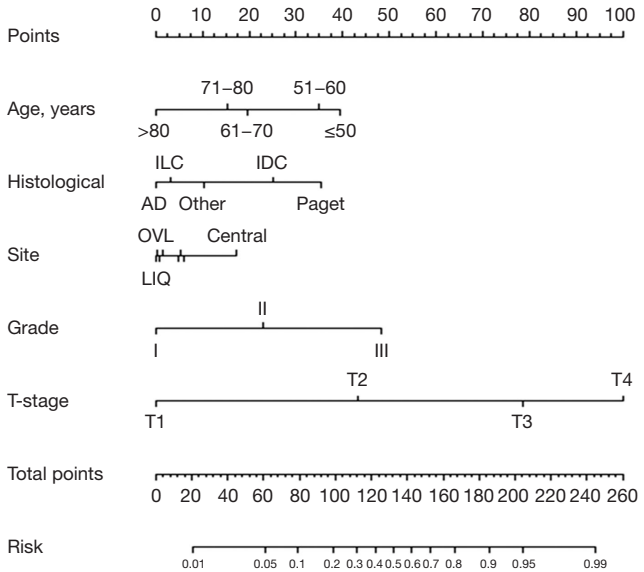

Figure 1 Nomogram for predicting the probability of ALNM. There are a total of 8 rows in the nomogram. The top row shows the point assignment for each variable. The behavioral variables are presented in rows 2 to 6, and the points for each variable correspond with the scale of the top row. The points of the five variables are added to the total points presented on the scale in row 7, which corresponds to the risk predictor of ALNM in row 8. IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LIQ, lower inner quadrant; OVL, Overlapping lesion of breast; AD, adenocarcinomas; ALNM, axillary lymph node metastasis.

patients had the worst prognostic pattern, which improves as age increases, and is the best in patients over 75 years of age by looking at the influence of age on the pathologic and biological features of breast cancer. Many previous studies showed that young age was independently associated with a higher likelihood of one or more positive lymph nodes in FBC (15,16). There are few reports on the influence of age on ALNM in MBC. The research showed that age at diagnosis was an independent prognostic factor for the risk of ALNM in MBC, and the risk decreased with age.

The pathological types of MBC are mainly IDC, lobular carcinoma is rare, and other types, such as adenocarcinoma, papillary carcinoma, and Paget's disease, have also been reported (2). Many researchers (12,15) have found that favorable histotypes (medullary, cribriform, tubular, mucinous) have a significantly lower risk of ALNM than ductal carcinoma in FBC. There is also little research on

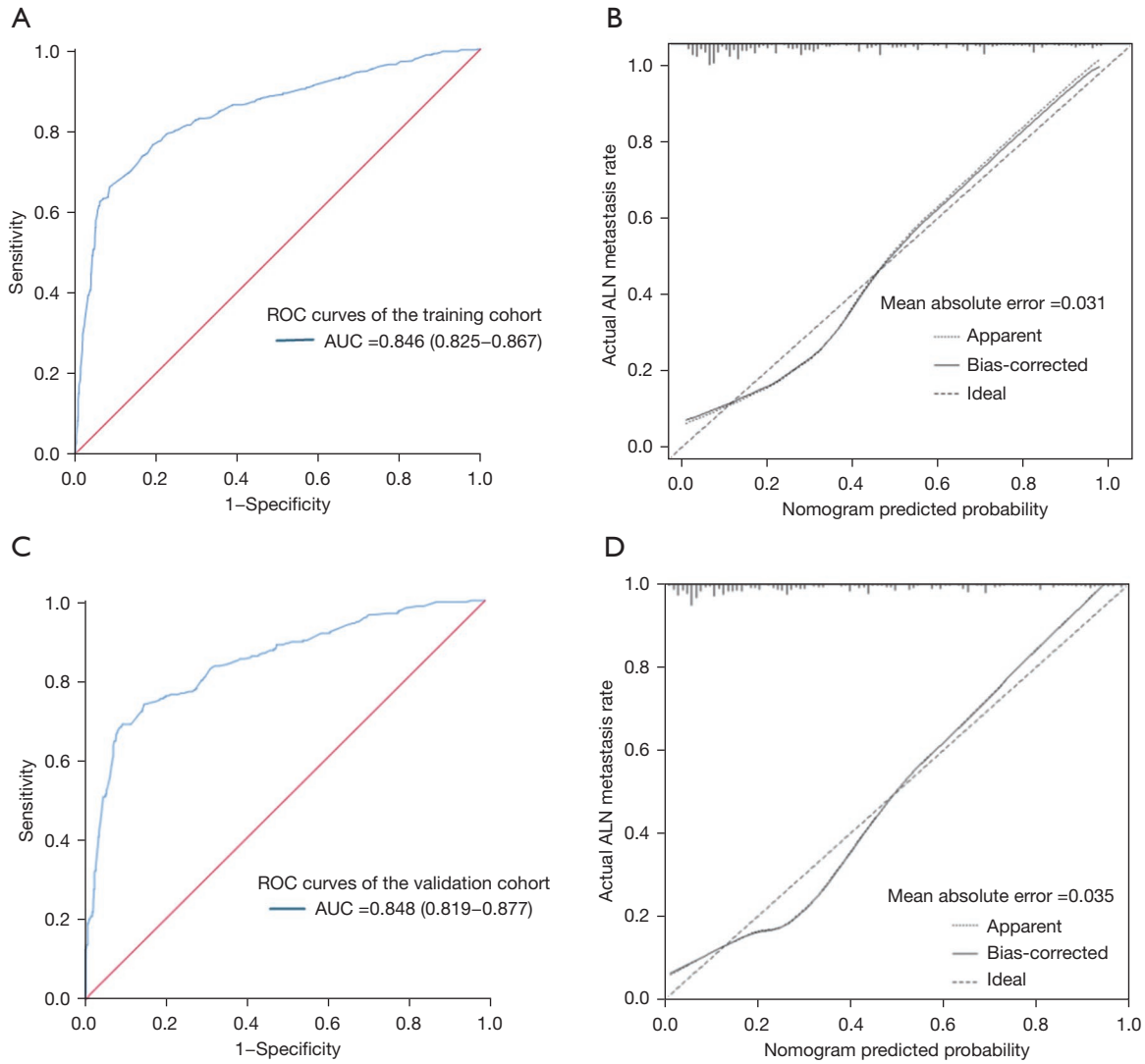

Figure 2 Discrimination and calibration of the nomogram in training and validation cohorts. (A,C) ROC curve for discrimination in the training and validation cohorts. (B,D) Calibration plots of actual (observed) and predicted probabilities for the nomogram in the training and validation cohorts. The x-axis represents the nomogram predicted probability as measured by logistic regression analysis, and the y-axis the actual probability. Vertical lines indicate the frequency distribution of predicted probabilities. The dotted line indicates the ideal reference line where the predicted probabilities match the observed probabilities. The calibration curve indicated excellent calibration of the nomogram. ROC, receiver operating characteristic; AUC, area under the curve.

the relationship between pathological types and ALNM in MBC. The research also found that other pathological types of MBC, such as lobular carcinoma and adenocarcinoma, were less prone to ALNM than IDC. Paget's disease had the highest risk of ALNM in MBC. Due to the lack of other clinical and pathological data provided by the SEER database, the causes were unable to further explore, which may be related to delayed treatment due to the patient's misdiagnosed breast cancer as eczema of the nipple. Another reason may be the abundance of lymphatic vessels in the nipple and areola area, which is more prone to lymph node metastasis.

MBC is mostly manifested as a mass in the areola area, while the male breast is significantly smaller than the female breast. The tumor is close to the skin, nipple, areola, and chest wall. When the tumor occurs, the mammary lymphatic

Table 4 Accuracy of the developed model's prediction in the validation cohort

Case No.	Predicted risk	No. of patients (%)	No. of patients with ALNM	Sensitivity (%)	Specificity (%)	Accuracy (%)	Negative predictive value (%)
1	<0.051	76 (8.74)	2	99.30	87.50	97.37	97.37
2	<0.100	204 (23.45)	14	95.00	67.80	93.14	93.14
3	<0.150	307 (35.29)	30	89.30	53.10	90.23	90.23
4	<0.202	369 (42.41)	39	86.10	44.10	89.43	89.43
5	<0.248	437 (50.23)	54	80.70	35.10	87.64	87.64
6	<0.299	496 (57.01)	62	77.90	26.40	87.50	87.50
7	<0.353	553 (63.56)	71	74.60	18.30	87.16	87.16
8	<0.400	568 (65.29)	76	72.90	16.60	86.62	86.62
9	<0.452	616 (70.80)	90	67.90	10.80	85.39	85.39
10	<0.501	642 (73.79)	94	66.40	7.10	85.36	85.36
11	<0.603	708 (81.38)	144	48.60	4.40	84.46	85.36
12	<0.696	764 (87.82)	189	32.50	2.50	84.16	85.36
13	<0.803	792 (91.03)	213	23.90	1.90	84.22	85.36
14	<0.899	817 (93.91)	230	17.90	0.50	83.72	85.36

ALNM, axillary lymph node metastasis.

drainage system is easily being invaded at early stage and this leads to lymph node metastasis (17). Yang *et al.* (18) confirmed that central location was an independent predictor of ALNM in MBC. Tumors located in the central region are more likely to have ALNM than in other regions. The results also showed that lymph node metastasis was less likely to occur in tumors located elsewhere than in the central region.

The increasing tumor grade is associated with a higher risk for ALNM in FBC. This fact has been confirmed in some studies (16,19). A few studies (18-20) have found that the risk of ALNM increases with histological grade in MBC. It can be seen from the univariate analysis of our research that Grade 3 was associated with a 6.240-fold greater risk for lymphatic metastasis than grade 1, while grade 2 versus grade 1 had a 1.569-fold risk.

The T-stage is an objective performance criterium of the growth time and growth rate of the tumor. T-stage emerged as the most powerful independent predictor of SLNM. This fact has been confirmed in some research in FBC (20,21). Some researchers (22,23) support the opinion that the advanced tumor stage is associated with a higher risk of death in MBC. Due to the low incidence of MBC, the relationship between T-stage and ALNM is also rarely researched. The results showed that T-stage played a crucial role in ALNM in MBC. The risk of ALNM increases significantly with T-stage.

Although the nomogram showed conspicuously accuracy for predicting ALNM, there were still some limitations in the present study. First, the data analysis was based on SEER, with a lack of centralized pathology review, and limited information regarding the surgery. In addition, some important clinical information such as preoperative ultrasound and imaging examination, as well as some immunohistochemical index such as Ki67, was lacking. Second, the use of retrospective data introduced the possibility of selection bias. Third, the vast majority of patients in this study were white, so predictions for non-white patients might be less accurate. Prospective investigations and more in-depth research were needed to help establish the results.

Conclusions

In conclusion, this nomogram can be used as a suitable and applicable clinical tool for preoperative evaluation of MBC, especially for those who are of advanced age at diagnosis, have small tumor size, low malignancy, and are

radiologically node-negative, to avoid the unnecessary axillary operation before sentinel lymph node biopsy. This can enhance the quality of life for patients without conceding the overall survival rate.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work and in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The ethical approval of this study was exempted by the Ethics Committee of Affiliated Sanming First Hospital of Fujian Medical University as the data were from the publicly accessible database, SEER. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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