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Characteristics of regional lymph node metastasis in breast cancer and construction of a nomogram model based on ultrasonographic analysis: a retrospective study

Meidi Zhu^{1†}, Zipeng Xu^{2†}, Jing Hu^{3†}, Lingling Hua¹, Yu Zou¹, Fei Qin^{4,5*} and Chaobo Chen^{2*}

Abstract

Objective The ultrasonographic characteristics of lymph node metastasis in breast cancer patients were retrospectively analyzed, and a predictive nomogram model was constructed to provide an imaging basis for better clinical evaluation.

Methods B-mode ultrasound was used to retrospectively analyze the imaging characteristics of regional lymph nodes and tumors. Pathological examination confirmed the presence of lymph node metastasis in breast cancer patients. Univariable and multivariable logistic regression analyses were performed to analyze the risk factors for lymph node metastasis. LASSO regression analysis was performed to screen noninvasive indicators, and a nomogram prediction model was constructed for breast cancer patients with lymph node metastasis.

Results A total of 187 breast cancer patients were enrolled, including 74 patients with lymph node metastasis in the positive group and 113 patients without lymph node metastasis in the negative group. Multivariate analysis revealed that pathological type (OR=4.58, 95% Cl: 1.44-14.6, p=0.01), tumor diameter (OR=1.37, 95% Cl: 1.07-1.74, p=0.012), spiculated margins (OR=7.92, 95% Cl: 3.03-20.67, p<0.001), mixed echo of the breast tumor (OR=37.09, 95% Cl: 3.49-394.1, p=0.003), and unclear lymphatic hilum structure (OR=16.07, 95% Cl: 2.41-107.02, p=0.004) were independent risk factors for lymph node metastasis. A nomogram model was constructed for predicting breast cancer with lymph node metastasis, incorporating three significantly correlated indicators identified through LASSO regression analysis, namely, tumor spiculated margins, cortical thickness of lymph nodes, and unclear lymphatic hilum structure. The receiver operating characteristic (ROC) curve revealed that the area under the curve (AUC) was 0.717 (95% Cl, 0.614–0.820) for the training set and 0.817 (95% Cl, 0.738–0.890) for the validation set. The Hosmer–Lemeshow test results

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for the training set and the validation set were p = 0.9148 and p = 0.1648, respectively. The prediction nomogram has good diagnostic performance.

Conclusions B-mode ultrasound is helpful in the preoperative assessment of breast cancer patients with lymph node metastasis. The predictive nomogram model, which is based on logistic regression and LASSO regression analysis, is clinically safe, reliable, and highly practical.

Keywords B-mode ultrasound, Breast cancer, Lymph node metastasis, Nomogram, LASSO regression analysis

Introduction

Breast cancer is the most common malignant tumor in women [1]. Preoperative assessment of regional lymph nodes, especially the pathological properties of axillary and sentinel lymph nodes, is crucial for determining whether lymph node dissection should be performed [2]. Lymph node metastasis is a risk factor affecting the prognosis of patients with breast cancer [3]. Preoperative assessment of regional lymph nodes, especially the pathological properties of axillary and sentinel lymph nodes, is crucial for determining whether lymph node dissection should be performed. Studies have shown that breast cancer patients with negative sentinel lymph nodes do not need axillary lymph node dissection, which does not affect patients' postoperative recurrence or survival [4]. However, axillary lymph node dissection may cause many complications, including lymphedema, numbness, paresthesia, and limited arm movement [5]. Patients with positive axillary lymph nodes can choose neoadjuvant chemotherapy before surgical treatment. According to a previous study, neoadjuvant chemotherapy can eradicate axillary lymph node disease in approximately 40-65% of HER2-positive breast cancer patients [6]. If lymph nodes become negative after neoadjuvant chemotherapy, axillary lymph node dissection may not be necessary [6, 7]. Therefore, clarifying the pathological properties of regional lymph nodes in breast cancer patients before surgery is highly important for clinical treatment strategies and surgical planning strategies.

Ultrasound-guided puncture biopsy and surgical treatment for lymph node biopsy are the most effective methods to obtain pathology [8]. Although the methods for obtaining lymph node pathology through puncture biopsy have been widely used in clinical practice, they are invasive and may cause certain complications, including hemorrhage, lymphatic leakage, infection, and hematoma, affecting clinical treatment [9].

Noninvasive examination methods, including B-mode ultrasound, mammography, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography/CT (PET/CT), and PET/MRI, are used in the clinic to identify the morphological characteristics of regional lymph nodes in breast cancer patients, and each of these noninvasive examination approaches has its own characteristics [10–12]. Recently, reports have shown

that PET/MRI has better diagnostic ability for lymph node metastasis than contrast-enhanced CT. However, PET/MRI has not been widely used due to its high cost and long detection time [13]. At present, B-mode ultrasound is the most widely used method for detecting regional lymph nodes in patients with breast cancer because of its advantages of convenience, rapidity, and intuitiveness, and it has been widely promoted in clinical practice [14]. However, a prediction nomogram model of lymph node metastasis in breast cancer patients has not been established on the basis of B-mode ultrasound.

Herein, we retrospectively collected information from patients diagnosed with breast cancer in our hospital between January 2020 and December 2023. To analyze the morphological characteristics of the breast cancer lesions and lymph nodes in these patients via ultrasound images combined with the pathological results of the lymph nodes, a novel prediction nomogram model was constructed and validated, aiming to provide an imaging basis for better clinical evaluation of lymph node metastasis, which may benefit more patients with breast cancer.

Method

Study design and patients

The present retrospective cohort study included patients with breast cancer admitted to Xishan People's Hospital of Wuxi City between January 2020 and December 2023. Lymph node metastasis, including axillary lymph nodes and sentinel lymph nodes, was confirmed by pathological examination. Breast cancer patients with regional lymph node metastasis were classified into the positive group, and patients without lymph node metastasis were classified into the negative group.

The inclusion criteria were as follows: (1) breast cancer patients with lymph node metastasis (positive group) and without metastasis nonmetastatic (negative group), (2) aged 18–75 years, (3) underwent B-mode ultrasound examination preoperatively, and (4) underwent radical surgery for breast cancer and sentinel lymph node biopsy or lymph node biopsy combined with pathological examination.

The exclusion criteria were as follows: (1) patients without breast cancer, (2) no preoperative B-mode ultrasound evaluation of axillary lymph nodes, (3) nonsurgical treatment for breast cancer patients, and (4) recurrent breast

cancer. The study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Xishan People's Hospital of Wuxi City (No. xs2024ky037). The requirement for informed consent was waived.

Ultrasound examination and analysis

Breast tumor and regional lymph node ultrasound examinations were performed on all patients before surgery. The examinations were conducted by two experienced breast sonographers via the Voluson™ E10 Ultrasound System (GE HealthCare, USA). In this study, all image analyses were independently performed by two physicians who have more than 5 years of diagnostic experience in breast ultrasound. The characteristics of the breast lesions on the ultrasound phantoms were analyzed, including the breast tumor location (inner side or outside), growth pattern (vertical or horizontal), tumor diameter, echo (low or mixture or high), internal echo (heterogeneity or homogeneity), margin (unsmooth or smooth), form (irregular or regular), spiculated margins (no or yes), corner edge (no or yes), hyperechoic halo (no or yes), rear echo attenuation (no or yes), calcification (no or yes), and blood supply (less or moderate or abundant). The characteristics of regional lymph nodes on ultrasound phantoms were analyzed, including lymph node morphology (irregular or regular), lymph node growth pattern (vertical or horizontal), echoes inside the lymph nodes (inhomogeneity or homogeneity), cortical thickness (thicken or normal), and lymphatic hilum structure (unclear or clear).

Pathological features

The pathological features of the patients included pathological type (ductal carcinoma in situ or invasive cancer), diameter, and immunohistochemical analyses [estrogen receptor (ER), progesterone receptor (PR), HER2, human epidermal growth factor receptor (HER2), and antigen Kiel 67 (Ki67)].

Hematological indicators

Hematological indicators, including leukocytes, neutrophils, lymphocytes, monocytes, platelets, the neutrophillymphocyte ratio (NLR), the platelet-lymphocyte ratio (PLR), the systemic immune-inflammation index (SII), the lymphocyte-monocyte ratio (LMR), carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), and carbohydrate antigen 153 (CA153), were collected and analyzed.

Construction and validation of the nomogram model

Variables with a p value less than 0.05 in the univariable analyses were included in the multivariable analysis. Least absolute shrinkage and selection operator (LASSO) logistic regression analyses were performed to

screen noninvasive indicators of lymph node metastasis, and these indicators were included in the construction of the nomogram. The samples were randomly divided into a training set and a testing set via R4.0.3, ensuring that there were no significant differences in the features between the two groups. Binary logistic regression analysis was performed on the training set via the lrm function to construct a diagnostic model and generate a nomogram, which was then validated using the testing set. The pROC package was used to plot ROC curves, calculate the area under the curve (AUC), and evaluate the sensitivity and specificity of the diagnostic model. The goodness-of-fit of the diagnostic model was assessed through the Hosmer-Lemeshow test. Decision curves were employed to examine the accuracy of the diagnostic model.

Statistical analysis

SPSS 22.0 (IBM, Armonk, NY, USA) and R4.0.3 statistical software were used for data analysis. The continuous data are expressed as the means±standard deviations and were analyzed via Student's t test or the Shapiro normality test. Categorical data are presented as frequencies and scores, and they were analyzed via the chi-square test or Fisher's exact test. The median is expressed using 25% and 75% quantiles), and the Wilcoxon test was used to compare these two groups. A p value less than 0.05 was considered statistically significant.

Results

Patient characteristics

A total of 378 patients were diagnosed with breast cancer at Xishan People's Hospital of Wuxi City from January 2020 to December 2023. Of these, 187 were included in this study on the basis of the exclusion and inclusion criteria. A total of 74 patients were assigned to the positive group, and the remaining 113 patients were assigned to the negative group according to the pathological analysis (Fig. 1).

The clinicopathological features of the breast cancer patients are shown in Table 1. There were no significant differences in terms of biomarkers, including ER, PR, and HER2, between the positive group and the negative group (p>0.05). However, there were obvious differences in the Ki67 biomarker levels (p<0.05) between these two groups. Furthermore, pathological analysis revealed significant differences in the pathological type and diameter of the breast cancer specimens (p<0.05). Univariate analysis revealed that pathological type (OR=4.23, 95% CI: 1.083-16.336, p=0.011), diameter (OR=1.32, 95% CI: 1.05-1.65, p=0.017), and Ki67 levels (OR=1.01, 95% CI: 1.00-1.03, p=0.045) were associated with lymph node metastasis in breast cancer patients (positive group). The multivariate results indicated that pathological type

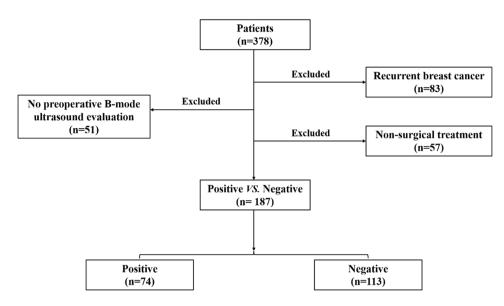


Fig. 1 Study flow diagram

Table 1 Characteristics of breast cancer based on pathological analysis in all patients

Items	Positive (n=74)	Negative $(n=113)$	<i>P</i> value	
Pathological type			0.007	
Ductal carcinoma in situ	4 (5.41%)	22 (19.47%)		
Invasive cancer	70 (94.59%)	91 (80.53%)		
Diameter	2.5 (2,3.5)	2 (1.5,3)	0.037	
Biomarker				
ER*			0.691	
Positive	55 (74.32%)	81 (71.68%)		
Negative	19 (25.68%)	32 (28.32%)		
PR*			0.514	
Positive	37 (50%)	62 (54.87%)		
Negative	37 (50%)	51 (45.13%)		
Her2*			0.306	
Positive	9 (12.16%)	20 (17.7%)		
Negative	65 (87.84%)	93 (82.3%)		
Ki67*	35 (20,50)	25 (15,40)	0.044	
Items	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Pathological type	4.23(1.39,12.84)	0.011	4.58(1.44,14.6)	0.01
Diameter	1.32(1.05,1.65)	0.017	1.37(1.07,1.74)	0.012
Ki67	1.01(1.00,1.03)	0.045	1.01(1.00,1.03)	0.156

^{*}ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor; Ki67, Antigen Kiel 67; OR, odd ratio

(OR=4.58, 95% CI: 1.44–14.6, p=0.01) and diameter (OR=1.37, 95% CI: 1.07–1.74, p=0.012) were independent factors associated with lymph node metastasis in breast cancer patients.

Correlation between ultrasonographic characteristics and lymph node metastasis

The ultrasonographic characteristics of breast cancers and lymph nodes were summarized and analyzed. Compared with patients in the negative group, those in the positive group had larger tumor diameters, higher

mixture echo proportions, and spiculated margin proportions (p<0.05, Table 2). Moreover, a greater proportion of the lymph nodes in the positive group had an irregular morphology, more inhomogeneity inside the lymph node echoes, cortical thickening, and unclear lymphatic hilum structure (p<0.05, Table 2).

Univariable and multivariable analyses for all patients

Univariate logistic regression analysis was subsequently performed. The diameter, mixed echo, and spiculated margins of the breast tumor, together with irregular **Table 2** Ultrasonographic characteristics of breast cancers and lymph nodes

Items	Positive (n=74)	Negative (<i>n</i> = 113)	<i>P</i> value
Breast tumor location			
Inner side	20 (27.03%)	40 (35.4%)	0.23
outside	54 (72.97%)	73 (64.6%)	
Growth pattern			0.615
Vertical	6 (8.11%)	7 (6.19%)	
Horizontal	68 (91.89%)	106 (93.81%)	
Tumor diameter	23 (19,30)	20 (15,27)	0.011
Echo			0.016
Low	68 (91.89%)	111 (98.23%)	
Mixture	6 (8.11%)	1 (0.88%)	
High	0 (0%)	1 (0.88%)	
Internal echo			0.998
Heterogeneity	51 (68.92%)	78 (69.03%)	
Homogeneity	23 (31.08%)	35 (30.97%)	
Margin			0.407
Unsmooth	67 (90.54%)	106 (93.81%)	
Smooth	7 (9.46%)	7 (6.19%)	
Form			0.682
Irregular	64 (86.49%)	100 (88.5%)	
Regular	10 (13.51%)	13 (11.5%)	
Spiculated margins			0.003
No	23 (31.08%)	60 (53.1%)	
Yes	51 (68.92%)	53 (46.9%)	
Corner edge			0.305
No	58 (78.38%)	81 (71.68%)	
Yes	16 (21.62%)	32 (28.32%)	
Hyperechoic halo	,	,	0.657
No	66 (89.19%)	103 (91.15%)	
Yes	8 (10.81%)	10 (8.85%)	
Rear echo attenuation	- (· - · · - · /	(-1.5.)	0.325
No	61 (82.43%)	99 (87.61%)	
Yes	13 (17.57%)	14 (12.39%)	
Calcification	.5 (17.5776)	(.2.337.6)	0.363
No	31 (41.89%)	55 (48.67%)	0.505
Yes	43 (58.11%)	58 (51.33%)	
Blood supply	13 (36.1170)	30 (31.3370)	0.817
Less	59 (79.73%)	91 (80.53%)	0.017
Moderate	4 (5.41%)	8 (7.08%)	
Abundant	11 (14.86%)	14 (12.39%)	
Lymph node morphology	11 (14.00%)	14 (12.3570)	
Irregular	11 (14.86%)	2 (1.77%)	0.001
Regular	63 (85.14%)	111 (98.23%)	0.001
Lymph node growth pattern	03 (03.1470)	111 (50.2370)	0.396
Vertical	1 (1.35%)	0 (0%)	0.590
Horizontal			
	73 (98.65%)	113 (100%)	0.001
Echoes inside lymph nodes	11 (14 000/)	2 (1 770/)	0.001
Inhomogeneity	11 (14.86%)	2 (1.77%)	
Homogeneity	63 (85.14%)	111 (98.23%)	-0.004
Cortical thickness	20 (40 5 40/)	7 (6 100/)	< 0.001
Thicken	30 (40.54%)	7 (6.19%)	
Normal	44 (59.46%)	106 (93.81%)	
Lymphatic hilum structure	00 (04 055)	2 (2 (55))	< 0.001
Unclear	23 (31.08%)	3 (2.65%)	
Clear	51 (68.92%)	110 (97.35%)	

Table 3 Univariable and multivariable analyses for ultrasonographic characteristics with lymph node metastasis

Items	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	<i>P</i> value
Tumor diameter	1.03(1.01,1.06)	0.017	1.02[0.99,1.06]	0.256
Echo				
Low	ref		ref	
Mixture	9.79(1.15,83.11)	0.036	37.09[3.49,394.1]	0.003
High	0(0, Inf)	0.987	0[0, Inf]	0.989
Spiculated margins	2.51(1.36,4.65)	0.003	7.92[3.03,20.67]	< 0.001
Lymph node morphology	9.69(2.08,45.11)	0.004	1.55[0.18,13.73]	0.694
Echoes inside lymph nodes	9.69(2.08,45.11)	0.004	0.47[0.05,4.34]	0.504
Cortical thickness	10.32(4.22,25.26)	< 0.001	3.96[0.96,16.4]	0.058
Lymphatic hilum structure	16.54(4.75,57.61)	< 0.001	16.07[2.41,107.02]	0.004

OR, odds ratio

Table 4 Expression of hematological indicators based on lymph node properties

Items	Positive (n = 74)	Negative $(n=113)$	P value	
Leukocyte	6.04 ± 1.72	5.85 ± 1.64	0.463	
Neutrophils	3.5 (2.63,4.46)	3.25 (2.57,4.05)	0.327	
Lymphocytes	1.79 (1.43,2.08)	1.76 (1.4,2.25)	0.839	
Monocytes	0.42 (0.35,0.53)	0.44 (0.35,0.51)	0.724	
Platelets	218.5 (168,264.5)	208 (167,242)	0.151	
NLR	1.89 (1.4,2.56)	1.84 (1.33,2.59)	0.687	
PLR	118.82 (96.57,157.94)	117.31 (90.05,156.25)	0.499	
SII	434.54 (264.61,604.98)	390.5 (266.7,535.04)	0.307	
LMR	4.34 (3.26,5.22)	4.38 (3.16,5.36)	0.928	
CEA	2.45 (1.72,3.52)	1.97 (1.2,3.27)	0.031	
CA125	10.6 (8.3,14.85)	10 (7.4,13.9)	0.151	
CA153	10.46 (7.73,17.45)	9.33 (7,15.5)	0.049	
Items	Univariate analysis			
	OR (95% CI)	P value		
CEA	1.09(0.95,1.24)	0.231		
CA153	1(0.99,1.01)	0.72		

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; LMR, lymphocyte-to-monocyte ratio; CEA, carcinoembryonic antigen; CA125, carbohydrate antigen 125; CA153, carbohydrate antigen 153

lymph node morphology, cortical thickness, and unclear lymphatic hilum structure, were risk factors for lymph node metastasis in patients with breast cancer (p<0.05, Table 3). Multivariate logistic regression analysis suggested that spiculated margins and mixed echoes of the breast tumor, combined with unclear lymphatic hilum structure, were independent risk factors for lymph node metastasis in patients with breast cancer (p<0.05, Table 3).

Correlations between hematological indicators and lymph node metastasis in patients with breast cancer

The correlations between hematological indicators and lymph node metastasis in breast cancer patients were analyzed. There were no significant differences in the locations of leukocytes, neutrophils, lymphocytes, monocytes, platelets, the neutrophil-to-lymphocyte ratio

(NLR), the platelet-to-lymphocyte ratio (PLR), the systemic immune-inflammation index (SII), the lymphocyte-to-monocyte ratio (LMR), or carbohydrate antigen 125 (CA125) (all p>0.05, Table 4) between the positive and negative groups. Moreover, there were significant differences in carcinoembryonic antigen (CEA) and carbohydrate antigen 153 (CA153) levels (p<0.05, Table 4). However, univariate logistic regression analysis indicated that CEA and CA153 were not independent factors associated with lymph node metastasis in all breast cancer patients (p>0.05, Table 4).

Validation of noninvasive indicators for screening lymph node metastasis in breast cancer patients via LASSO regression analysis

Independent risk factors (p<0.1) for preoperative characteristics in patients with breast cancer and lymph nodes via B-mode ultrasound were further analyzed. LASSO logistic regression analysis was performed to select three significantly correlated indicators with nonzero coefficients, including tumor spiculated margins, cortical thickness of the lymph node, and unclear lymphatic hilum structure, with coefficients of 0.06, 0.76, and 0.41, respectively (Fig. 2).

Generation of a nomogram via LASSO regression analysis

R4.0.3 was subsequently used to divide the whole dataset into a training set and a validation set. There was no significant difference between the two groups (p>0.05, Table 5). Based on the results of LASSO regression analysis, tumor spiculated margins, cortical thickness of the lymph node, and unclear lymphatic hilum structure were included in the prediction nomogram model (Fig. 3A). The receiver operating characteristic (ROC) curve revealed that the area under the curve (AUC) was 0.717 (0.614–0.820) for the training set (Fig. 3B) and 0.817 (0.738–0.890) for the validation set (Fig. 3C), indicating good diagnostic performance. The calibration chart shows the consistency between the predicted

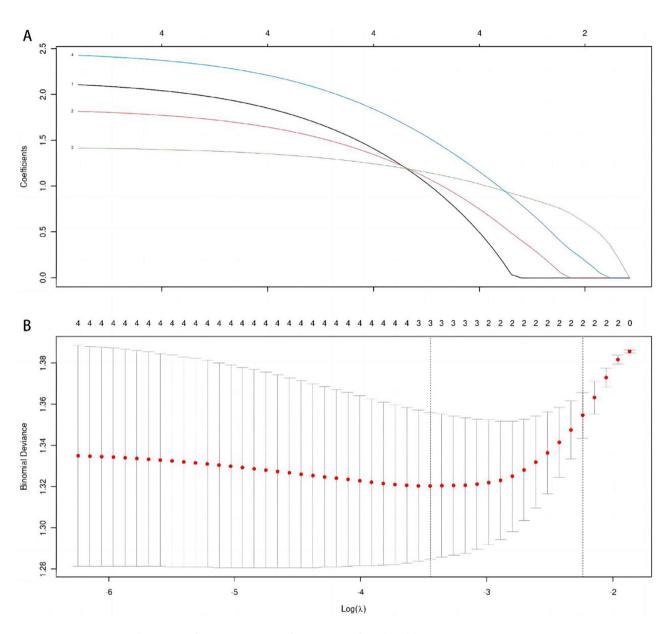


Fig. 2 LASSO regression analysis. (A) Log (λ) and regression coefficients. (B) Log (λ) and model error

and actual nomograms in the training set and validation set (Fig. 3D-E). Moreover, the Hosmer–Lemeshow test yielded p=0.9148 for the training set and p=0.1648 for the validation set. The p values were all greater than 0.05, indicating that there was no pronounced difference between the predicted value of the nomogram and the actual nomogram. Finally, clinical decision curves were generated, which revealed that the model was far from extreme curves in both the training set and the validation set, suggesting that the constructed prediction nomogram model is safe, reliable, and.

Discussion

From 1989 to 2000, the mortality rate of breast cancer decreased by approximately 43%; although the incidence rate increased annually, the rate of decline in mortality also decreased [15]. Early screening, diagnosis, and treatment of breast cancer play important roles. Breast cancer with lymph node metastasis is a risk factor for recurrence and long-term survival [2, 3]. Therefore, early differentiation of regional lymph node characteristics is highly important for diagnosing and treating breast cancer.

The present study retrospectively analyzed the B-mode ultrasound imaging characteristics of relevant lymph node properties in patients diagnosed with breast cancer, analyzed related risk factors, and constructed a new prediction nomogram model. Multivariate logistic

Table 5 Comparison of features between the training set and validation set

Items (Variable)	Total	Train set	Valid set	Р
	(n = 187)	(n = 93)	(n = 94)	value
Tumor spiculated				0.423
margin, n (%)				
No	83 (44.39)	44 (47.31)	39 (41.49)	
Yes	104 (55.61)	49 (52.69)	55 (58.51)	
Lymph cortical				0.106
thickness, n (%)				
Normal	150 (80.21)	79 (84.95)	71 (75.53)	
Thicken	37 (19.79)	14 (15.05)	23 (24.47)	
Lymphatic hilum				0.097
structure, n (%)				
Clear	161 (86.1)	84 (90.32)	77 (81.91)	
Unclear	26 (13.9)	9 (9.68)	17 (18.09)	

regression analysis suggested that spiculated margins, mixed echoes of the breast tumor, and unclear lymphatic hilum structure are independent risk factors for lymph node metastasis in patients with breast cancer. However, hematological indicators, such as CEA, CA125, and CA153, are not independent factors associated with lymph node metastasis. The LASSO method, which is a popular and robust high-dimensional predictive regression method [16], identified three risk factors, including tumor spiculated margins, cortical thickness of the lymph node, and unclear lymphatic hilum structure. For the first time, the present study constructed and validated a novel prediction nomogram model by combining the characteristics of B-mode ultrasound images with pathological properties, providing a basis for the diagnosis and treatment of breast cancer to help evaluate its preoperative clinical value.

Ultrasound imaging has the characteristics of high spatial resolution, which is more convenient for detecting enlarged lymph nodes than CT and/or MRI, and it is the preferred method to observe the characteristics of lymph node enlargement [12, 17]. MRI has even been used to evaluate axillary lymph node metastasis in breast cancer patients. However, MRI examinations take longer and are more expensive than B-mode ultrasound [18]. B-mode ultrasound is conducive to clinical promotion because of its convenient management, high portability of equipment, low cost, and high spatial resolution [14]. Predicting lymph node metastasis through indicators detected by B-mode ultrasound has significant advantages.

The detection of B-mode ultrasound imaging characteristics has been reported in prediction models of lymph node metastasis in thyroid cancer patients and plays an important role in the preoperative evaluation of thyroid cancer [19]. Similar studies have been reported for hepatocellular carcinoma [20], gastric cancer [21], colorectal cancer [22], and endometrial stromal sarcoma [23]. Multiparameter ultrasound can help distinguish malignant

and benign cervical lymph nodes, as well as assist in selecting follow-up or surgical treatment in primary cases, which is highly important for the prognosis followup of cancer patients [24]. However, a prediction nomogram model related to B-mode ultrasound examination has not been developed. A previous study has indicated that the use of a special ultrasound model (with a 3 mm margin model in the tumor area) can effectively evaluate the status of axillary lymph nodes, which is more accurate than the use of a peritumoral model alone [25]. Another similar study has used ultrasound images to evaluate changes effectively from inside the tumor to the surrounding area around the tumor, and multiple ultrasound parameters have been used to construct a prediction model, which more effectively evaluates the status of axillary lymph nodes in early breast cancer patients and provides a noninvasive strategy for clinical diagnosis and treatment [26]. However, there are few reports on a prediction model of preoperative ultrasound for lymph node metastasis in patients with breast cancer that uses the LASSO analysis method [27]. Although there have been studies on the use of ultrasound and/or radiological imaging to detect breast cancer lymph node metastasis [27, 28] to date, there have been no reports on the gold-standard preoperative ultrasound prediction model for breast cancer patients with lymph node metastasis via the LASSO analysis method. Wang et al. [27]. collected ultrasound images of 755 patients with early breast cancer, and they performed radiomic analysis of the intertumoral and different peritumoral regions to construct a prediction model via the LASSO analysis method. The results of this prediction model suggested that the AUC value of the nomogram were 0.906 (95% CI: 0.882-0.930) and 0.922 (95% CI: 0.894-0.960) in the primary and external validation cohorts, respectively. Another retrospective study, which included 426 B-ultrasound images of early-stage breast cancer patients [28], constructed a radiometric nomogram via LASSO logistic regression and multifactor analysis,, including tumor size, lymph node status, and radiological characteristics, resulting in AUC values of 0.78 and 0.71 in the primary and validation cohorts, respectively [28]. In addition, a retrospective study has analyzed the ultrasound image characteristics of lymph nodes in 176 stage T1-2 breast cancer patients, with AUC values of 0.900 (95% CI: 0.853–0.931) and 0.821 (95% CI: 0.769-0.868) in the training and test sets, respectively [29]. Other researchers have used MRI images to construct a predictive nomogram model based on LASSO logistic regression to predict axillary lymph node metastasis status and disease-free survival, providing an important imaging basis for the diagnosis, treatment strategies, and personalized surgical plans of early breast cancer patients [18]. Compared to the present study, these results are more consistent, but the key

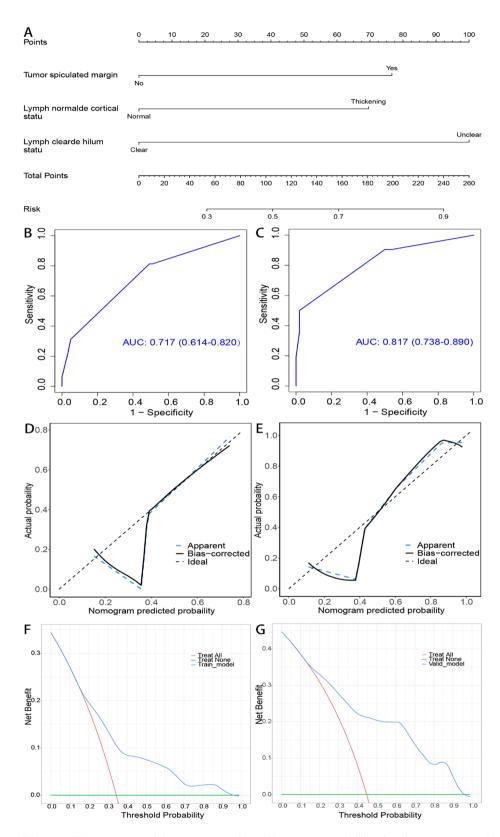


Fig. 3 Nomogram, ROC curve, calibration curve, and decision curve analyses. (A) Nomogram model based on the training group. ROC curve of the nomogram for breast cancer patients with lymph node metastasis in the training group (B) and validation group (C). Calibration curve of the nomogram for breast cancer patients with lymph node metastasis in the training group (D) and validation group (E). Decision curve of the nomogram for breast cancer patients with lymph node metastasis in the training group (F) and validation group (G)

elements selected for constructing the prediction model are different. Furthermore, breast tumor spiculated margins, cortical thickness of the lymph node, and unclear lymphatic hilum structure can be quickly obtained through B-mode ultrasound. According to the present results, the calibration chart and Hosmer-Lemeshow test results revealed that the predictive value of the nomogram was not significantly different from the actual value in the present study. Moreover, the clinical decision curve confirmed that the constructed prediction nomogram model is safe, reliable, and practical. However, the present prediction nomogram model is based on the characteristics of three significantly correlated indicators via B-mode ultrasound images screened by LASSO logistic regression analysis, which is simpler but more convenient to perform.

The new prediction nomogram model has important clinical significance for the early prediction of regional lymph node metastasis in breast cancer patients. This predictive nomogram model may help in the formulation of diagnostic and treatment strategies, thereby benefitting more patients in the future.

On the basis of B-mode ultrasound image analysis, the present study identified the risk factors for lymph node metastasis in patients with breast cancer and developed a new nomogram model that has good diagnostic performance. However, the present study had several limitations. The data from the single medical center and the heterogeneity of patients are limited to residents from Jiangsu Province and/or surrounding areas. Although the sample size is good, there is still a significant difference in disease distribution compared with that of the entire population in China and even around the world. Furthermore, racial heterogeneity could not be included in the study cohort. Therefore, multicenter cooperation may be helpful in remedying these deficiencies. Moreover, the predictive model still lacks clinical practice and validation in more patients, which requires a more rigorous follow-up research strategy in the future to obtain better feedback.

Conclusions

With the incidence rate of breast cancer increasing annually, early screening and diagnosis with effective methods are important means to improve treatment effectiveness. The B-mode ultrasound approach has the advantages of convenience, rapidity, and intuitiveness in detecting regional lymph nodes in breast cancer patients. In this study, a prediction nomogram model was constructed through retrospective analysis of B-mode ultrasound images via LASSO logistic regression analysis, which is clinically safe, reliable, and highly practical, thereby benefitting more patients with breast cancer.

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Author contributions

All authors have read and approved the final manuscript. C.C. and Z.X.: designed the research and drafted the paper. L.H. and Y.Z.: organized the cases, performed research, and reviewed this paper. M.Z.: designed the mathematical methods. J.H. and F.Q.: collected and analyzed the data.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author (Chaobo Chen) upon reasonable request. For any queries, kindly contact bobo19820106@gmail.com.

Declarations

Ethics approval and consent to participate

The need for written informed consent was waived by the Xishan People's Hospital of Wuxi City Ethics Committee because of the retrospective nature of the study (No. xs2024ky037). The study complied with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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