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RESEARCH

Predicting sentinel lymph node metastasis in breast cancer: a study based on the SEER database

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Abstract

Background Sentinel lymph node biopsy (SLNB), a standard surgical procedure for clinically axillary-negative breast cancer patients, significantly reduces complications compared with axillary lymph node dissection, but it is still a relatively invasive procedure with some complications, affecting patient's quality of life. To identify patients who might benefit from avoiding SLNB, this study aimed to develop a nomogram for predicting sentinel lymph node metastasis (SLNM) in breast cancer patients using the SEER database. Methods: We identified breast cancer patients whose 1–5 lymph nodes were examined in the SEER database as those who underwent SLNB. Patients were randomly assigned to the training and validation cohorts at a 3:1 ratio. Univariate and multivariate logistic regression were used to evaluate the relationships between SLNM and patients' clinicopathological characteristics. A nomogram was constructed, and its performance was validated via ROC curves, calibration curves, and decision curve analysis. Results: Age, race, primary site, T stage, M stage, histological grade, pathological type, estrogen receptor status, and progesterone receptor status are independent predictive factors for SLNM in patients with breast cancer. We successfully developed a predictive nomogram for sentinel lymph node status, with AUC values of 0.711 and 0.700 for the training and validation cohorts, respectively. Conclusion: Our study successfully established an SLNM nomogram that provides richer predictive information. The model exhibits good clinical efficacy and serves as a reference value for populations potentially exempt from SLNB.

Keywords Breast cancer · Sentinel lymph node metastasis · Sentinel lymph node biopsy · Risk factors · Predictive model · Nomogram · SEER database

Introduction

Breast cancer is the most common malignant tumor currently affecting women's health worldwide [1]. Establishing a predictive model for patients with breast cancer can provide a crucial reference for individualized clinical diagnosis and treatment decisions, such as the determination of surgical approaches and the development of adjuvant treatment plans. A nomogram is a visual predictive tool. It quantifies the risk of clinical events on the basis of various risk factors and generates numerical probabilities of clinical events [2]. Nomograms are among the most common forms used in studies of breast cancer LNM/prognosis prediction models.

Sentinel lymph node biopsy (SLNB), a landmark advance in breast surgery in the 1990s, has become the most common and important method for assessing axillary lymph node (ALN) status in patients with cN0 breast cancer, following refinements from trials such as NSABP-32, MILAN, and

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ALMANAC [3–6]. The results of SLNB often guide the decision to perform axillary lymph node dissection (ALND) [7–10]. Compared with ALND, SLNB has avoided many unnecessary axillary injuries in patients and has made significant contributions to reducing postoperative pain, arm swelling, activity impairment, muscle weakness, and other complications. However, studies have shown that SLNB, which is still a relatively invasive clinical procedure, has few but persistent complications, affecting the quality of life of some postoperative patients [11, 12]. Therefore, other potentially wider-reaching lymph node biopsy methods, such as targeted axillary dissection (TAD) [13, 14] and marking the axillary node with a radioactive iodine seed (MARI) [15], are being increasingly considered. Research suggests that these more targeted axillary lymph node assessment methods may further reduce surgical complications without compromising accurate ALN evaluation under specific conditions [16].

In fact, the evolving landscape of systemic treatment for breast cancer has also significantly impacted the surgical approaches to ALN assessment. In the pre-targeted therapy era, ALND was deemed essential not only for staging but also for local control, as adjuvant chemotherapy and endocrine therapy provided limited systemic protection [17]. The advent of HER2-directed therapies (e.g., trastuzumab) in the early 2000s marked a paradigm shift, enabling systemic eradication of micrometastases and reducing reliance on extensive nodal surgery [18]. More recently, immunotherapy (e.g., pembrolizumab in triple-negative breast cancer) and antibody–drug conjugates (e.g., trastuzumab deruxtecan) have further diminished the prognostic weight of nodal status by achieving unprecedented pathological complete response rates and metastatic burden reduction [19–21]. These advancements underscore a critical trend: As systemic therapies improve, the necessity of invasive nodal staging diminishes for select patients. For instance, some prospective randomized trials are exploring the possibility of omitting SLNB in patients with early breast cancer [22, 23]. The SOUND trial [22] is one of the important studies that has received widespread attention. The results revealed that there were no statistically significant differences in distant disease-free survival, DFS, OS, the axillary metastasis rate, or the distant metastasis rate between SLNB group and no axillary surgery group. Therefore, the conclusion was reached that "omitting axillary surgery is not inferior to SLNB for specific conditions of breast cancer patients." In the future, the publication of more related research results, including the BOOG 2013–08 trial [24], will provide more medical evidence for omitting SLNB.

Materials and methods

Database

We conducted research on the SEER database. The SEER database deleted all the breast cancer lymph node surgery information in 2011, lacked readily available SLNB/ALND information. To address this issue in the SEER database, we utilized the research findings of Bilimoria et al. [25]. This study extracted patient information from the National Cancer Database (NCDB) for 97,314 patients in the SLNB-alone group and the SLNB-with-completion ALND group. The median number of lymph nodes examined was 3 (interquartile range, 25) for the former group and 13 (918) for the latter. On the basis of these data, if the number of examined lymph nodes was ≤ 5, the patient was considered to have undergone SLNB alone. Many other studies have also used this conclusion as a reference [26–28].

Patients

Our retrospective analysis was conducted on 117,895 breast cancer patients from the SEER (Stat 8.4.2) database between January 2010 and December 2015. The inclusion criteria were as follows: (1) 1–5 lymph node examinations; (2) primary breast cancer; and (3) American Joint Committee on Cancer (AJCC) 7th edition T stage T1-T3 breast cancer. The exclusion criteria were as follows: (1) bilateral breast cancer; (2) neoadjuvant therapy; (3) histological grade IV; (4) AJCC 7th M stage cM0(i+); and (5) incomplete clinicopathological data. The lymph node status was determined on the basis of the "Regional nodes positive 1988" field in the SEER database.

We extracted the following clinicopathological information from the SEER database: age, race, sex, primary site, laterality, T stage, M stage, histological grade, pathological type, breast cancer subtype, ER status, PR status, human epidermal growth factor receptor 2 (HER2) status, and lymph node metastasis status.

Construction and validation of the nomogram

Using R Foundation, 4.2.2, patients were randomly assigned to the training and validation cohorts at a 3:1 ratio for the development and validation of a nomogram. We ultimately identified 9 significant predictive factors suitable for inclusion in the nomogram: age, race, primary site, T stage, M stage, histological grade, pathological type, ER status, and PR status. We assessed the sensitivity and specificity of the predictive model via the area under the receiver operating characteristic (ROC) curve (AUC), visualized the model

calibration through 1000 bootstrap repetitions of the calibration curve, and evaluated the clinical applicability of the nomogram via decision curve analysis (DCA).

Statistical analyses

We used chi-square tests to organize detailed patient baseline information, summarizing the relationships between various influencing factors and sentinel lymph node status. We used univariate logistic regression analysis to verify the correlation, preliminarily excluding factors with no statistically significant impact on SLNM. Then, via multivariate logistic regression, we calculated odds ratios (ORs) to identify significant predictive factors independently associated with SLNM in our study population. ORs are presented with 95% CIs. We also performed Omnibus tests and Hosmer–Lemeshow tests to assess preliminary model goodness-of-fit.

Statistical analyses were performed via IBM SPSS (version 26.0) statistical software. All tests were two sided, and $P < 0.05$ was deemed significant. Random population grouping and the creation of a nomogram were performed via the R Foundation, 4.2.2 and other packages (car, rms, pROC, Hmisc, and rmda).

Results

Exploratory results of scientific grouping of pathology type

We first extracted the pathological type classification field "Site record–rare tumors" from the SEER database, which was not mentioned in previous studies. This field, which is based on the Surveillance of Rare Cancer in Europe (RARECARE), categorizes breast cancer into 7 main types (Table 1). We performed univariate analysis of each pathological classification. The results revealed that the SLNM rate for Paget's disease was the highest, at 19.4%, which was higher than those of invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC). We decided to combine the "Site record-rare tumors" field and the commonly used "ICD-O-3 Hist/behav" field into a new classification method. While retaining the meaningful classification method of the former, we established additional screening criteria: 1) screening out clinically known special types of cancers that are extremely easy or difficult to metastasize through the lymphatic system and 2) screening out special pathological types with large-sample sizes and significantly different SLNM rates than established subgroups. Finally, the predictive factor "pathological type" in this study was divided into 7 subgroups: IDC, ILC, IDC mixed with ILC, mucinous carcinoma, Paget's disease, IMPC, and other types.

Exploratory results of the scientific grouping of age

We grouped age by 5-year intervals. On the basis of the definition of the International Young Breast Cancer Expert Group (BCY) [29, 30], we divided the population under 40 years of age into one group. Owing to the small-sample size (469) for individuals ≥ 90 years old, we did not further subdivide this age group. On this basis, we created a trend graph (Fig. 1). The age of 80 years is a turning point where the curve trend changes significantly. A greater age but still < 80 years is correlated with a lower SLNM rate, which aligns with our clinical experience. However, in those over 80 years of age, the trend reversed, contradicting our clinical experience. Moreover, within the 40–79 age range, the maximum slope of the curve occurs at 60 years, indicating a significant difference between the 40–59 and 60–79 age groups. Therefore, this study divided patients into four groups according to age: < 40, 40–59, 60–79, and ≥ 80 years.

Patient characteristics

From 20,102,015, this study ultimately included 117,895 breast cancer patients, who were randomly divided into a training cohort (88,422 patients) and a validation cohort (29,473 patients). The detailed clinicopathological characteristics are presented in Table 2.

Table 1 The univariate analysis of the field "Site record–rare tumors" by lymph node status

	LN negative	LN positive	Total
19.1 Inv carcinoma of no special type-NST	88,587 (87.3%)	12,893 (12.7%)	101,480
19.2 Invasive lobular carcinoma of breast	8796 (86%)	1437 (14%)	10,233
19.3 Mammary Paget's disease of breast	112 (80.6%)	27 (19.4%)	139
19.4 Special types of adenocarcinoma of breast	4655 (95.9%)	200 (4.1%)	4855
19.5 Metaplastic carcinoma of breast	447 (94.7%)	25 (5.3%)	472
19.6 Salivary gland type tumor of breast	95 (99%)	1 (1%)	96
19.7 Other epithelial tumors of breast	484 (89.8%)	55 (10.2%)	539
56.5 Neuroendocrine carcinoma of other sites	36 (85.7%)	6 (14.3%)	42
69 Not classified	38 (97.4%)	1 (2.6%)	39

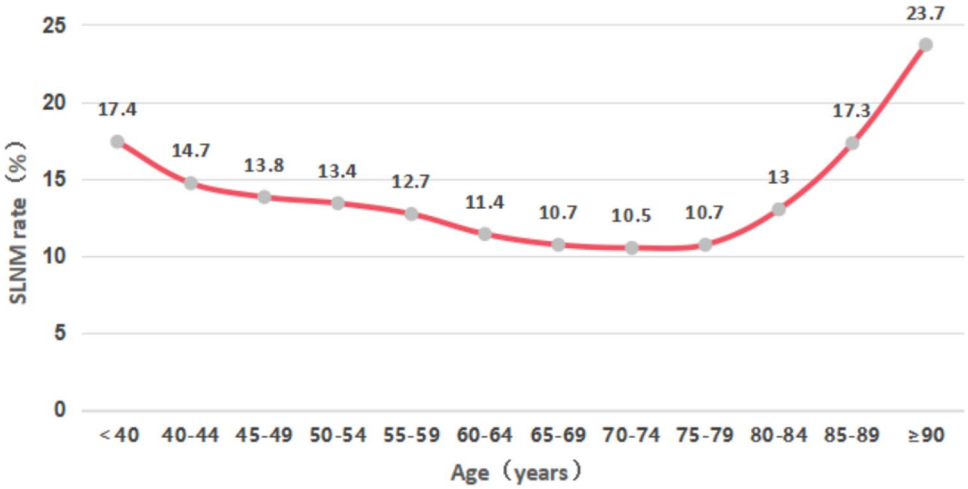

Fig. 1 Trend graph of SLNM rate by age

14,645 breast cancer patients (12.4%) had positive sentinel lymph nodes. The SLNM rate in patients ≥ 80 years old was 14.9%, which was higher than that in the 40–59 and 60–79 age groups and lower than the < 40-year-old group. Japanese patients had the lowest SLNM rate, followed by Chinese patients. "Other" races were similar to "White," while Black patients had the highest rate. Only 584 were male, and their SLNM rate was higher than that of females. The inner quadrant of the breast had a lower overall SLNM rate. The outer quadrants had higher rates, and the axillary tail showing even higher rates. The central part, including the nipple, had the highest percentage. The larger the tumor diameter is, the higher the SLNM rate. In addition, M1 patients had a significantly higher SLNM rate than did M0 patients. A lower tumor histological grade was associated with lower SLNM rates. Among pathology types, mucinous carcinoma had the lowest SLNM rate, IMPC had the highest rate. Among subtypes, triple-negative breast cancer (TNBC) had the lowest SLNM rate, followed by luminal A, HER2-enriched, and luminal B subtypes. ER-positive, PR-positive, and HER2-positive patients had a higher SLNM rate than did negative patients. Laterality was the only factor without a statistically significant difference, with similar rates for the left and right sides.

Univariate logistic regression analysis

The ORs of each subgroup obtained from the univariate logistic regression analysis (Table 3) were consistent with the ratio of SLNM rates between subgroups from the chi-square test, successfully validating the correlation between each influencing factor and SLNM. Laterality, which does not affect SLNM (P = 0.489), was first excluded. Age, race, sex, primary site, T stage, M stage, histological grade, pathological type, subtype, ER status, PR status, and HER2 status were statistically significantly predictive of positive lymph nodes (P < 0.001).

Multivariate logistic regression analysis

The factors screened by univariate analysis were included in multivariate logistic regression analysis to further screen independent predictive factors associated with SLNM. The training cohort results (Table 4) revealed that sex and HER2 status had p values of 0.479 and 0.227, indicating that these factors are not independent predictors of SLNM and were excluded from the final predictive model. Moreover, we excluded breast cancer subtypes as confounding factors for ER status, PR status, and HER2 status. The remaining factors had $p < 0.001$ in the training cohort. Therefore, this study ultimately identified 9 independent predictive factors influencing SLNM: age, race, primary site, T stage, M stage, histological grade, pathological type, ER status, and PR status. Importantly, T2, T3, M1, and IMPC had significantly higher OR values than did the other factors, suggesting that T stage, M stage, and pathological type play more prominent roles in influencing SLNM rates. In addition, Omnibus tests and Hosmer–Lemeshow tests were performed to evaluate the model. The Hosmer–Lemeshow test performed well on both the training cohort ($p = 0.172$) and the total population ($p = 0.192$), indicating good model fit. The results of the Omnibus test (P < 0.001) showed that the entire model is effective and accurately predicts SLNM.

Construction and validation of the nomogram

On the basis of the results of multivariate analysis, we developed a nomogram (Fig. 2) to predict SLNM in patients with breast cancer. By summing the scores of each factor, we can predict the probability of SLNM in every specific patient. Overall, Japanese and Chinese patients with no distant

Table 2 Clinicopathologic characteristics of the cohort by lymph node status

	Whole cohort				Training cohort			
	LN negative	LN positive	Total	*P*	LN negative	LN positive	Total	*P*
All	103,250(87.6%)	14,645(12.4%)	117,895		77,426(87.6%)	10,996(12.4%)	88,422	
Age				< 0.001				< 0.001
< 40	3331(82.6%)	701(17.4%)	4032		2472(82.3%)	533(17.7%)	3005	
40–59	42,503(86.5%)	6610(13.5%)	49,113		31,892(86.5%)	4966(13.5%)	36,858	
60–79	50,879(89.2%)	6192(10.8%)	57,071		38,157(89.2%)	4631(10.8%)	42,788	
≥ 80	6537(85.1%)	1142(14.9%)	7679		4905(85.0%)	866(15.0%)	5771	
Race				< 0.001				< 0.001
Chinese	1676(88.6%)	215(11.4%)	1891		1233(88.5%)	161(11.5%)	1394	
Japanese	1327(92.5%)	107(7.5%)	1434		1010(92.0%)	88(8.0%)	1098	
White	83,580(87.6%)	11,795(12.4%)	95,375		62,668(87.6%)	8833(12.4%)	71,501	
Black	9340(85.9%)	1537(14.1%)	10,877		6986(85.7%)	1167(14.3%)	8153	
Others	7327(88.1%)	991(11.9%)	8318		5529(88.1%)	747(11.9%)	6276	
Sex				< 0.001				< 0.001
Female	102,778(87.6%)	14,533(12.4%)	117,311		77,080(87.6%)	10,915(12.4%)	87,995	
Male	472(80.8%)	112(19.2%)	584		346(81.0%)	81(19.0%)	427	
Site				< 0.001				< 0.001
Central	4576(81.6%)	1029(18.4%)	5605		3414(82.1%)	746(17.9%)	4160	
Up-In	16,816(91.5%)	1559(8.5%)	18,375		12,657(91.6%)	1165(8.4%)	13,822	
Low-In	7078(89.3%)	852(10.7%)	7930		75,302(89.1%)	647(10.9%)	5949	
Up-Out	39,246(86,5%)	6115(13.5%)	45,361		29,359(86,4%)	4605(13.6%)	33,964	
Low-Out	8644(86.2%)	1382(13.8%)	10,026		6519(86.1%)	1054(13.9%)	7573	
Tail	420(83.7%)	82(16.3%)	502		307(84.1%)	58(15.9%)	365	
Overlap	26,470(88.0%)	3626(12.0%)	30,096		19,868(88.0%)	2721(12.0%)	22,589	
Laterality				0.489				0.71
Left	52,832(87.6%)	7449(12.4%)	60,281		39,592(87.6%)	5602(12.4%)	45,194	
Right	50,418(87.5%)	7196(12.5%)	57,614		37,834(87.5%)	5394(12.5%)	43,228	
T stage				< 0.001				< 0.001
T1mic	1344(98.0%)	28(2.0%)	1372		1023(98.0%)	21(2.0%)	1044	
T1a	9960(97.4%)	269(2.6%)	10,229		7452(97.4%)	199(2.6%)	7651	
T1b	26,310(94.2%)	1616(5.8%)	27,926		18,720(94.3%)	1182(5.7%)	20,902	
T1c	42,740(87.6%)	6062(12.4%)	48,802		32,059(87.7%)	4515(12.3%)	36,574	
T2	21,497(78.4%)	5922(21.6%)	27,419		16,122(78.2%)	4505(21.8%)	20,627	
T3	1399(65.2%)	748(34.8%)	2147		1050(64.7%)	574(35.3%)	1624	
M stage				< 0.001				< 0.001
M0	103,122(87.8%)	14,299(12.2%)	117,421		77,324(87.8%)	10,745(12.2%)	88,069	
M1	128(27.0%)	346(73.0%)	474		102(28.9%)	251(71.1%)	474	
Grade				< 0.001				< 0.001
I	31,256(91.4%)	2944(8.6%)	34,200		23,438(91.5%)	2180(8.5%)	25,618	
II	46,156(86.5%)	7231(13.5%)	53,387		34,646(86.4%)	5453(13.6%)	40,099	
III	25,838(85.3%)	4470(14.7%)	30,308		19,342(85.2%)	3363(14.8%)	22,705	
Pathology				< 0.001				< 0.001
IDC	82,953(87.6%)	11,795(12.4%)	94,748		62,167(87.5%)	8855(12.5%)	71,022	
ILC	8796(86.0%)	1437(14.0%)	10,233		6652(86.0%)	1087(14.0%)	7739	
IDC&ILC	5320(84.2%)	996(15.8%)	6316		3990(84.1%)	757(15.9%)	4747	
Mucinous	2558(96.9%)	82(3.1%)	2640		1923(97.3%)	82(2.7%)	1976	
Paget	112(80.6%)	27(19.4%)	139		82(82.0%)	18(18.0%)	100	
IMPC	314(75.5%)	102(24.5%)	416		246(78.1%)	69(21.9%)	315	
Others	3197(93.9%)	206(6.1%)	3403		2366(93.8%)	157(6.2%)	2523	

Table 2 (continued)

	Whole cohort				Training cohort			
	LN negative	LN positive	Total	*P*	LN negative	LN positive	Total	*P*
Subtype				< 0.001				< 0.001
Luminal A	81,916(87.4%)	11,792(12.6%)	93,708		61,427(87.4%)	18,827(12.6%)	70,254	
Luminal B	8568(86.3%)	1358(13.7%)	9926		6442(86.2%)	1032(13.8%)	7474	
HER2-enrich	3020(86.5%)	472(13.5%)	3492		2283(86.5%)	357(13.5%)	2640	
TNBC	9746(90.5%)	1023(9.5%)	10,769		7274(90.3%)	780(9.7%)	8054	
ER				< 0.001				< 0.001
Negative	13,634(89.5%)	1597(10.5%)	15,231		10,223(89.4%)	1211(10.6%)	12,434	
Positive	89,616(87.3%)	13,048(12.7%)	102,664		67,203(87.3%)	9785(12.7%)	76,988	
PR				< 0.001				< 0.001
Negative	23,435(89.2%)	2848(10.8%)	26,283		17,503(89.0%)	2164(11.0%)	19,667	
Positive	79,815(87.1%)	11,797(12.9%)	91,612		59,923(87.2%)	10,996(12.8%)	68,755	
HER2				< 0.001				< 0.001
Negative	91,662(87.7%)	12,815(12.3%)	104,477		68,701(87.7%)	9607(12.3%)	78,308	
Positive	11,588(86,4%)	1830(13.6%)	13,418		8725(86,3%)	1389(13.7%)	10,114	

	Validation cohort			
	LN negative	LN positive	Total	*P*
All	25,824 (87.6%)	3649 (12.4%)	29,473	
Age				< 0.001
< 40	859(83.6%)	168(16.4%)	1027	
40–59	10,611(86.6%)	1644(13.4%)	12,255	
60–79	12,722(89.1%)	1561(10.9%)	14,283	
≥ 80	1632(85.5%)	276(14.5%)	1908	
Race				0.001
Chinese	443(89.1%)	54(10.9%)	497	
Japanese	317(94.3%)	19(5.7%)	336	
White	20,912(97.6%)	2962(12.4%)	23,874	
Black	2354(86.4%)	370(13.6%)	2724	
Others	1798(88.1%)	244(11.9%)	2042	
Sex				0.005
Female	25,698(87.7%)	3618(12.3%)	29,316	
Male	126(80.3%)	31(19.7%)	157	
Site				< 0.001
Central	1162(80.4%)	283(19.6%)	1145	
Up-In	4159(91.3%)	394(8.7%)	4553	
Low-In	1776(89.7%)	205(10.3%)	1981	
Up-Out	9887(86.8%)	1510(13.2%)	11,397	
Low-Out	2125(86.6%)	328(13.4%)	2453	
Tail	113(82.5%)	24(17.5%)	137	
Overlap	6602(87.9%)	905(12.1%)	7507	
Laterality				0.46
Left	13,240(87.8%)	1847(12.2%)	15,087	
Right	12,584(87.5%)	1802(12.5%)	14,386	
T stage				< 0.001
T1mic	321(97.9%)	7(2.1%)	328	
T1a	2508(97.3%)	70(2.7%)	2578	
T1b	6590(93.8%)	434(6.2%)	7024	
T1c	10,681(87.3%)	1547(12.7%)	12,228	

Table 2 (continued)

	Validation cohort			
	LN negative	LN positive	Total	*P*
T2	5375(79.1%)	1417(20/9%)	6792	
T3	349(66.7%)	174(33.3%)	523	
M stage				< 0.001
M0	25,798(87.9%)	3554(12.1%)	29,352	
M1	26(21.5%)	95(78.5%)	121	
Grade				< 0.001
I	7818(91.1%)	764(8.9%)	8582	
II	11,510(86.6%)	1778(13.4%)	13,288	
III	6496(85.4%)	1107(14.6%)	7603	
Pathology				< 0.001
IDC	20,786(87.6%)	2940(12.4%)	23,726	
ILC	2144(86.0%)	350(14.0%)	2494	
IDC&ILC	1330(84.8%)	239(15.2%)	1569	
Mucinous	635(95.6%)	29(4.4%)	664	
Paget	30(76.9%)	9(23.1%)	39	
IMPC	68(67.3%)	33(32.7%)	101	
Others	831(94.4%)	49(5.6%)	880	
Subtype				< 0.001
Luminal A	20,489(87.4%)	2965(12.6%)	23,454	
Luminal B	2126(86.7%)	326(13.3%)	2452	
HER2-enrich	737(86.5%)	115(13.5%)	852	
TNBC	2472(91.0%)	243(9.0%)	2715	
ER				< 0.001
Negative	3411(89.8%)	386(10.2%)	3797	
Positive	22,413(87.3%)	3263(12.7%)	25,676	
PR				< 0.001
Negative	5932(89.7%)	684(10.3%)	6616	
Positive	19,892(87.0%)	2965(13.0%)	22,857	
HER2				0.073
Negative	22,961(87.7%)	3208(12.3%)	26,169	
Positive	2863(86,7%)	441(13.3%)	3304	

metastasis and T1mic, grade 1, and mucinous tumors in the central position of the breast had a lower risk of SLNM, whereas Black patients with distant metastasis and T3, grade 2&3, and IMPC tumors were more likely to have SLNM.

The AUCs for the training and validation cohorts (Fig. 3) were 0.711 (95% CI: 0.706–0.716) and 0.700 (95% CI: 0.691–0.708), respectively, indicating good discriminatory ability of the nomogram in differentiating sentinel lymph node status. Moreover, we performed 1000 bootstrap repetitions on the training and validation cohorts to obtain two calibration curves (Fig. 4). The calibration curves showed good agreement between the actual SLNM rate and the predicted rate, suggesting good calibration of the nomogram. The DCA results (Fig. 5) also showed that this nomogram is a reliable clinical tool for predicting SLNM in breast cancer patients.

Discussion

In this study, we developed a predictive nomogram to assess the probability of SLNM in breast cancer patients. Nine significant predictive factors with independent effects were ultimately identified. ROC curves, calibration curves, and clinical decision analysis of both the training and validation cohorts demonstrated that this nomogram has high sensitivity and specificity in predicting SLNM in patients with breast cancer and is a reliable clinical tool.

Age is one of the key objects explored in this study. On the basis of practical clinical experience, older patients tend to have a lower SLNM rate. However, our study data revealed that this pattern only exists in patients under 80 years of age. In patients over 80 years old, a greater age was associated with a higher SLNM rate, which is a novel

Table 3 The results of the univariate logistic regression analysis

	OR	95%CI	P		OR	95%CI	P		OR	95%CI	P
Age			< 0.001	T stage			< 0.001	Subtype			< 0.001
< 40	1.729	1.587–1.884		T1mic	Reference	Reference		Luminal A	1.371	1.282–1.467	
40–59	1.278	1.231–1.326		T1a	1.296	0.875–1.921	0.196	Luminal B	1.51	1.385–1.646	
60–79	Reference	Reference		T1b	2.948	2.021–4.301		HER2-enrich	1.489	1.325–1.673	
≥ 80	1.435	1.341–1.537		T1c	6.808	4.678–9.908		TNBC	Reference	Reference	
Race			< 0.001	T2	13.223	9.085–19.246		ER			< 0.001
Chinese	1.591	1.248–2.208		T3	25.664	17.470–37.702		Negative	Reference	Reference	
Japanese	Reference	Reference		M stage			< 0.001	Positive	1.243	1.177–1.313	
White	1.75	1.436–2.133		M0	Reference	Reference		PR			< 0.001
Black	2.041	1.664–2.503		M1	19.494	15.905–23.895		Negative	Reference	Reference	
Others	1.3677	1.363–2.605		Pathology			< 0.001	Positive	1.216	1.165–1.270	
Sex			< 0.001	IDC	4.436	3.557–5531		HER2			< 0.001
Female	Reference	Reference		ILC	5.096	3.692–6.51		Negative	Reference	Reference	
Male	1.678	1.365–2.064		IDC&ILC	5.84	4.640–7.351		Positive	1.13	1.072–1.191	
Site			< 0.001	Mucinous	Reference	Reference		Laterality			0.489
Central	2.426	2.227–2.641		Paget	7.52	4.680–12.084		Left	Reference	Reference	
Up-In	Reference	Reference		IMPC	10.133	7.407–13.864		Right	1.012	0.978–1.048	
Low-In	1.298	1.189–1.418		Others	2.01	1.548–2.610					
Up–Out	1.681	1.585–1.782		Grade			< 0.001				
Low-Out	1.725	1.597–1.862		I	Reference	Reference					
Tail	2.106	1.653–2.683		II	1.663	1.590–1.740					
Overlap	1.478	1.388–1.573		III	1.837	1.748–1.930					

Table 4 Multivariate logistic regression analysis of possible variables in predicting SLNM in training cohorts

	OR	95%CI	*P*		OR	95%CI	*P*		OR	95%CI	*P*
Age			< 0.001	Up–Out	1.728	1.612–1.852		Mucinous	Reference	Reference	
< 40	1.387	1.25–1.539		Low-Out	1.717	1.567–1.882		Paget	8.517	4.628–15.671	
40–59	1.211	1.158–1.266		Tail	2.233	1.658–3.008		IMPC	11.001	7.428–16.293	
60–79	Reference	Reference		Overlap	1.472	1.367–1.585		Others	2.804	2.031–3.87	
≥ 80	1.253	1.154–1.36		T stage			< 0.001	Grade			< 0.001
Race			< 0.001	T1mic	Reference	Reference		I	Reference	Reference	
Chinese	1.392	1.051–1.843		T1a	1.303	0.827–2.055		II	1.268	1.2–1.34	
Japanese	Reference	Reference		T1b	2.917	1.884–4.515		III	1.245	1.163–1.332	
White	1.569	1.253–1.964		T1c	6.654	4.311–10.271		ER			< 0.001
Black	1.775	1.406–2.242		T2	13.047	8.45–20.143		Negative	Reference	Reference	
Others	1.396	1.101–1.77		T3	25.035	16.024–39.113		Positive	1.365	1.249–1.492	
Sex			0.479	M stage				PR			< 0.001
Female	Reference	Reference		M0	Reference	Reference		Negative	Reference	Reference	
Male	0.91	0.702–1.18		M1	10.746	8.429–13.7		Positive	1.282	1.196–1.374	
Site			< 0.001	Pathology			< 0.001	HER2			0.227
central	2.291	2.062–2.544		IDC	5.741	4.352–7.574		Negative	Reference	Reference	
Up-In	Reference	Reference		ILC	4.903	3.692–6.51		Positive	1.041	0.975–1.112	
Low-In	1.417	1.277–1.573		IDC&ILC	6.181	4.638–8.239					

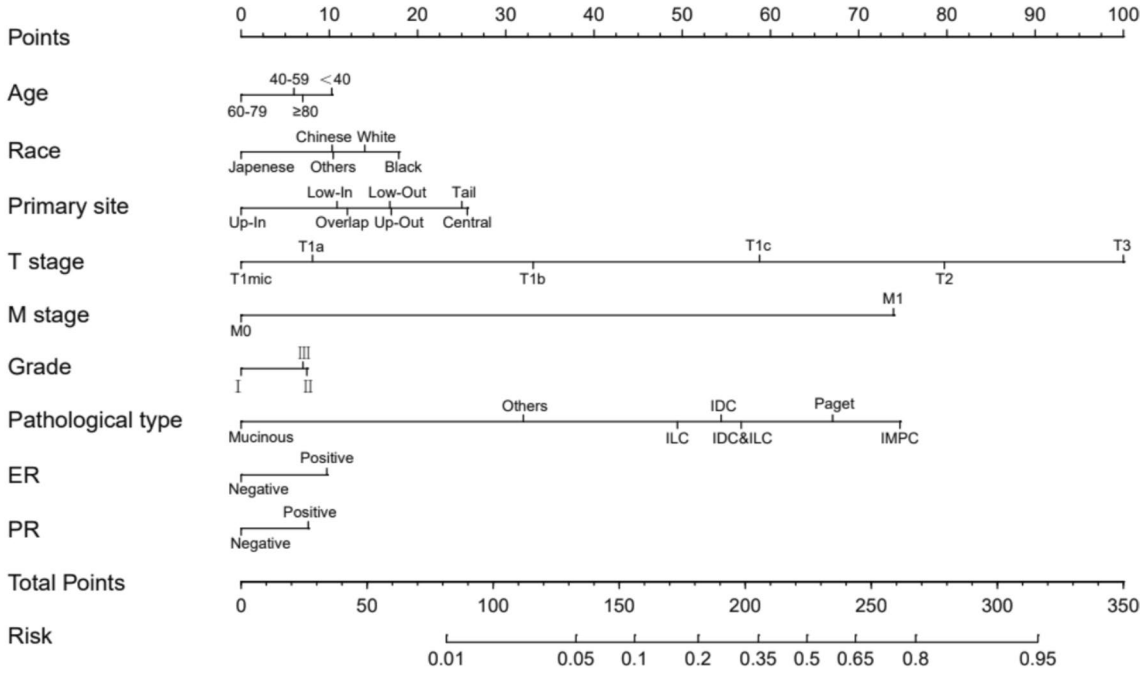

Fig. 2 Nomogram predicting the probability of SLNM

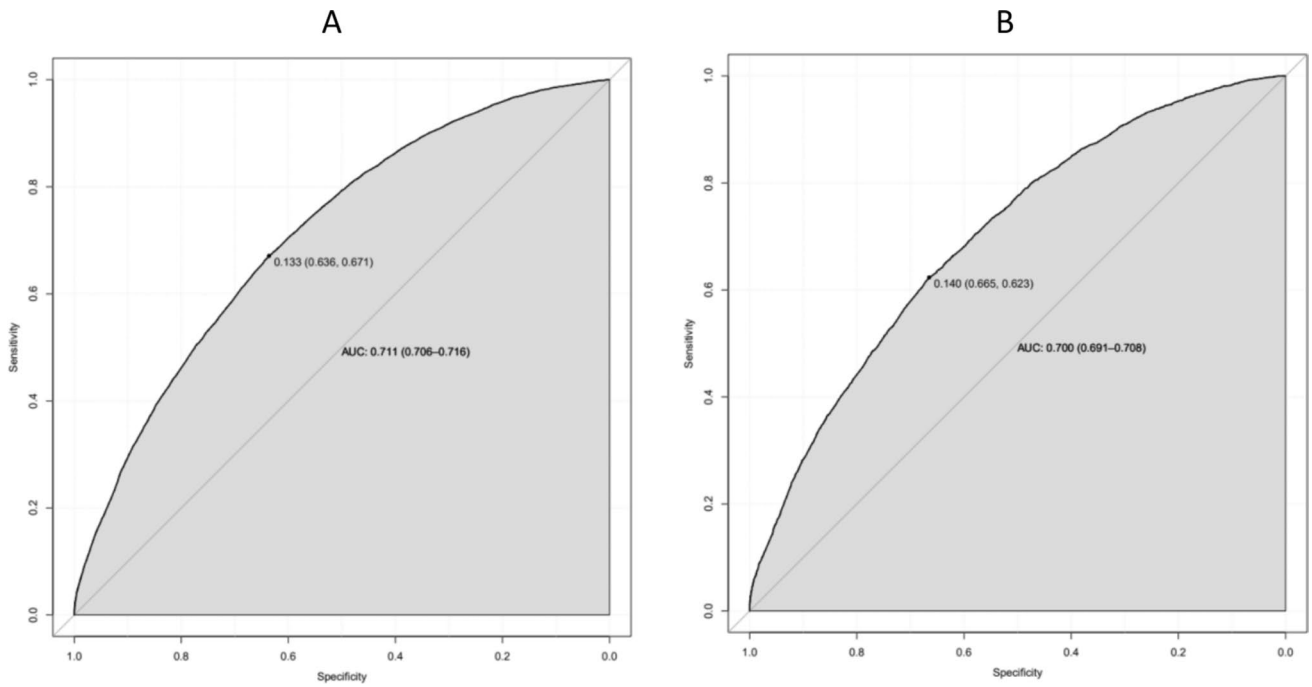

Fig. 3 ROC curves of the nomogram for the probability of SLNM. **A** training cohort; **B** validation cohort

finding. Although we cannot enumerate all previous prediction model studies on the relationship between age and LNM, the results of all single-center studies reviewed thus far support this clinical experience [31–37]. We believe that this is related mainly to the absolute shortage of patients aged ≥ 80 years; for this reason, few studies have categorized the population aged ≥ 80 years as a separate group. In fact, according to the findings of our study, previous studies' age-grouping methods essentially mixed the lowest SLNM rate group (60–79 years old) with the ≥ 80-year-old group.

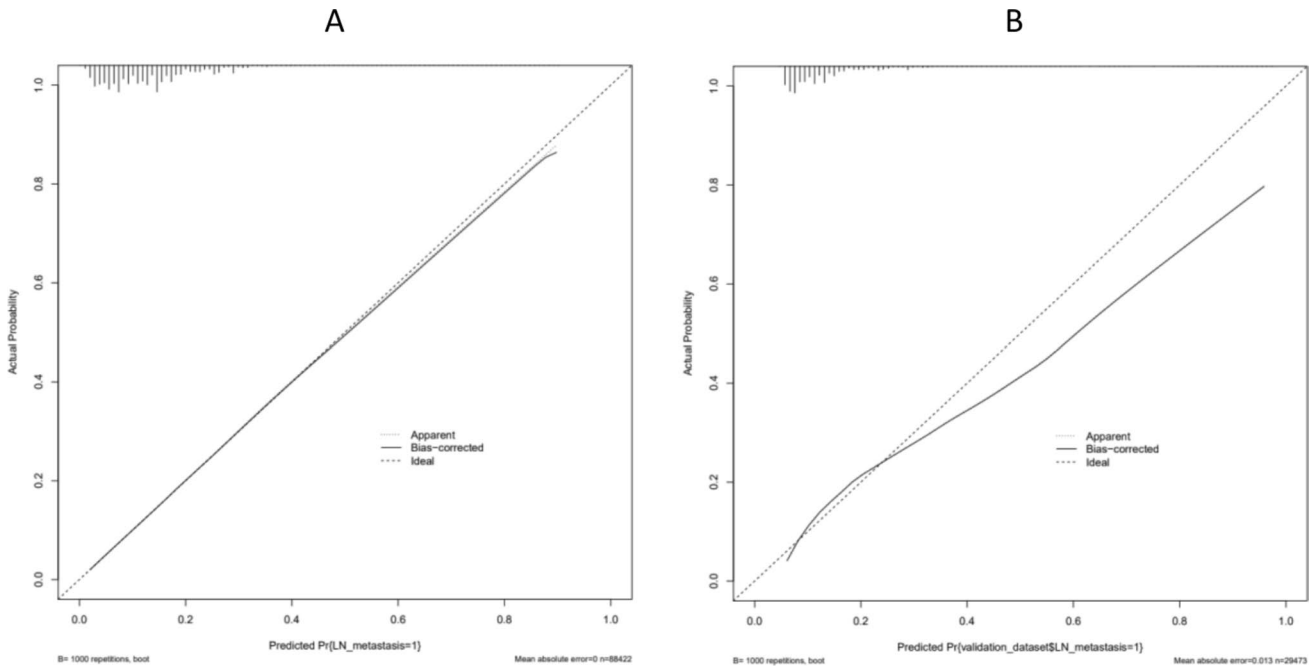

Fig. 4 Calibration curves of the nomogram for the probability of SLNM. **A** training cohort; **B** validation cohort

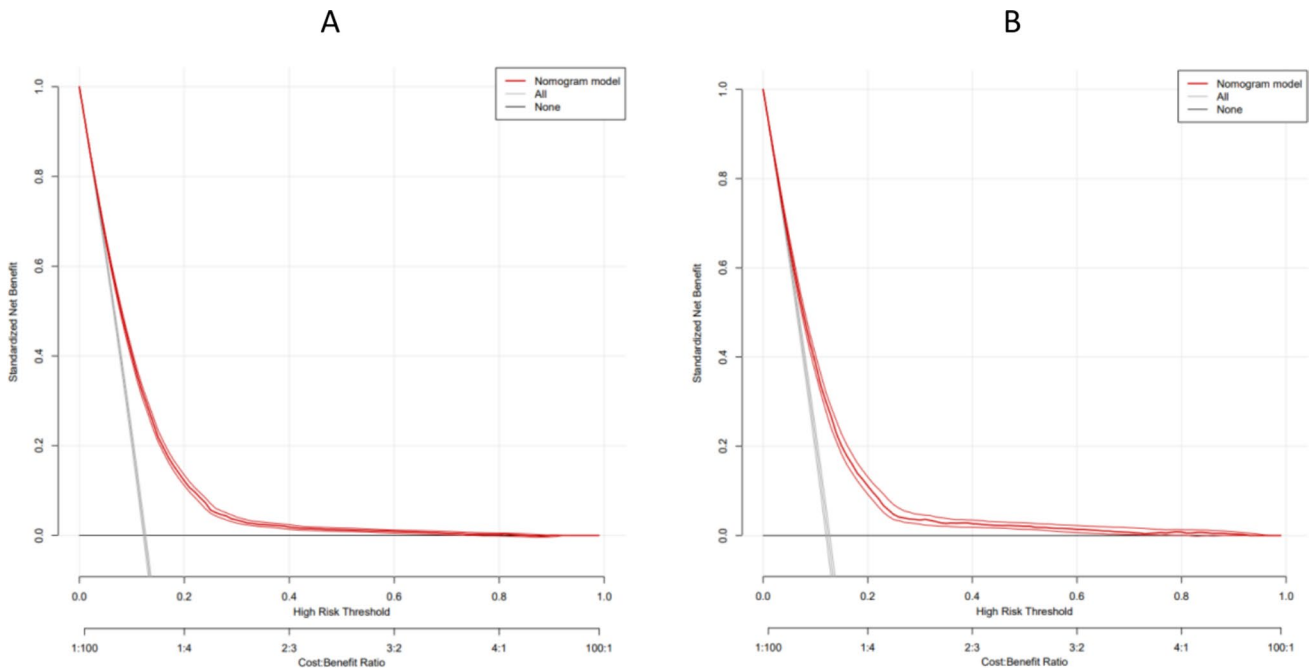

Fig. 5 DCA of the nomogram for the probability of SLNM (bootstrap 1000 repetitions). **A** training cohort; **B** validation cohort

This naturally diluted the unique characteristics of the ≥ 80 age group, indicating that previous research underestimates the importance of the ≥ 80 age group. Therefore, it is necessary to conduct more systematic research on this population to fully explore the authenticity of the newly discovered pattern and its underlying reasons. This will become one of our key future research directions. On the basis of the patient baseline information statistically derived from this study, we can preliminarily analyze the possible reasons for this new finding: 1. Patients ≥ 80 years old have characteristics

such as relatively larger tumors, a greater proportion of distant metastasis, and lower tumor differentiation. 2. This may also be related to the fact that elderly patients are less likely to detect the disease promptly, and by the time they seek medical attention, breast cancer may have significantly progressed. We similarly explored the scientific grouping of pathological types and ultimately categorized them into 7 types. The results revealed that mucinous adenocarcinoma was the least likely to metastasize via sentinel lymph nodes. The characteristics of mucinous adenocarcinoma, including lower histological grade, better differentiation, and lower LNM rates, have also been confirmed in multiple studies [36, 38, 39]. Compared with the most common pathological type "IDC," Paget's disease [40] and IMPC [31, 41] are considered to have a high tendency for LNM, requiring greater clinical vigilance to avoid overlooking such lymphatic progression. Moreover, we found that the pathological type of IDC mixed with ILC had a significantly higher SLNM rate than did pure IDC and pure ILC. No previous research has focused on a detailed study of this type, which will also be a key focus of our future research.

Regarding race, as most previous studies categorized it into White, Black, and others, we referenced Iqbal J et al.'s earlier study [42] on the basis of the SEER database and additionally screened Chinese and Japanese populations, whose sample sizes were large enough and exhibited significantly different LNM rates than did other races. The results revealed that the SLNM rates for Chinese and Japanese patients were significantly lower than those for Black and White patients. SLNM risk positively correlates with tumor size, as reported in nearly all relevant studies by researchers such as Rivadeneira [43]. This conclusion, along with the conclusion that "M1 patients have a much higher LNM rate than M0 patients," applies in almost all scenarios. Our study also revealed that patients with primary tumors located in the axillary tail and nipple/central regions of the breast were more likely to experience SLNM, requiring attention to these relatively unique primary tumor locations. Research by Gou et al. [44] indicated that the axillary tail is an independent factor contributing to LNM. Another survey revealed that tumors in the central and nipple regions were associated with LNM [45]. With respect to breast cancer subtypes, Reyal et al. [46] reported that the TNBC had the lowest SLNM rate, and the HER2-enriched subtype had the highest SLNM rate. A study based on the SEER database [47] suggested that while the risk of LNM in the TNBC is significantly lower than that in the luminal A subtype, there is no significant difference between the other subtypes. In fact, our univariate logistic regression analysis revealed statistically significant differences in SLNM between subtypes. However, in our multivariate logistic regression analysis, subtype was not considered a significant predictive factor. The above results indicate that there may indeed be differences in SLNM between different breast cancer subtypes, while TNBC is generally considered the least likely to metastasize to lymph nodes. However, when factors with greater influence on SLNM are included in the predictive model, the overall differences between subtypes are further reduced, which is the primary reason for the discrepancy between the univariate and multivariate analysis results for breast cancer subtypes.

Compared with previous studies, our nomogram has several advantages. First, almost all previous prediction model studies for SLNM were small-sample, single-center studies. Owing to limitations in the geographic area and absolute number of people included in these studies, their predictive value is questionable. Although two articles [48, 49] used the National Cancer Database (NCDB) for large-sample prediction model studies, they both limited the enrolled population to ductal carcinoma in situ (DCIS) and did not establish an SLNM model for a broader population. Therefore, on the basis of the conclusions of Bilimoria et al. [25]., we screened the population considered to have undergone SLNB in the SEER database, leveraging the advantages of this database's large, multicenter sample size. This allowed us to build a prediction model for SLNM in a wider population of patients with breast cancer. Compared with previous similar studies, our prediction information is richer, the prediction model is larger, and it can be better applied in clinical practice. Moreover, before conducting clinicopathological feature analysis, we first explored the scientific grouping of each predictive factor. This is a novel approach compared with previous SEER database-based predictive model studies. Taking "pathological type" as an example, most existing SEER database-based studies simply divide it into three categories: IDC, ILC, and others. Reducing the subgroups of a prediction factor often leads to higher AUC values and better model discrimination, which is why few researchers choose grouping methods beyond the "three-category" approach. However, the "site record–rare tumors" field appears to have not been studied previously. On the basis of the clinical value of pathological type, sample size, and significant differences in SLNM rates, we successfully created a new classification method. Similarly, we conducted a scientific exploration of the "age" factor on the basis of the inherent objective relationship between age and SLNM, resulting in an age grouping that was more suitable for this study. We believe that evaluating a predictive model solely on the basis of AUC values is insufficient. Many studies prioritize increasing AUC values, often altering factor groupings to achieve this goal, potentially misclassifying groups with high discrimination into one category, and leading to erroneous conclusions.

This nomogram holds significant potential for clinical translation and optimizing axillary management in breast cancer. By enabling personalized risk stratification (e.g.,

identifying low-risk patients who may safely avoid SLNB), it aligns with global trends toward surgical de-escalation, potentially reducing complications like lymphedema by 15–20% [19, 22]. Its integration with multimodal data—such as imaging (MRI/PET-CT) and targeted therapies (e.g., HER2 blockade)—supports dynamic treatment planning [18], while cost-effectiveness analyses suggest substantial savings in resource-limited settings [21]. Moreover, the nomogram's framework can be augmented with deep learning algorithms trained on radiopathomic data, potentially elevating AUC to > 0.85. [20]

Although the nomogram showed several advantages and significant potential, this study had some limitations. Our study utilized the conclusions of Bilimoria KY et al. to define breast cancer patients with 1–5 lymph nodes examined in the SEER database as patients who underwent SLNB. This approach is similar to a double-edged sword. While this allowed us to successfully establish a predictive model for SLNM in breast cancer patients on the basis of the SEER database, this definition inevitably contains bias. We could not perfectly match the actual SLNB population, which is a major limitation of our study. Moreover, several knowledge gaps remains. First, we could not obtain other important information from the SEER database, such as vascular invasion, despite its proven importance in axillary LNM in some single-center studies [50, 51]. Second, external validation in non-Western populations (e.g., Chinese cohorts) is pending, and the model's generalizability requires further confirmation. Since our nomogram is based on a population of White and Black individuals, efforts are needed to minimize selection bias. Finally, the nomogram's AUC (0.700–0.711) suggests moderate discriminative power. Incorporating predictive factors such as vascular invasion and molecular biomarkers (e.g., circulating tumor DNA or immune characteristics) may improve the accuracy of the model's prediction.

Overall, although SLNB has significantly fewer surgical complications than ALND, trials such as INSEMA (NCT02466737) [52] still demonstrate persistent complications, including pain, lymphedema, and functional impairment, evident within the first month after surgery. Therefore, in clinical practice, we should strive to improve axillary lymph node assessment while ensuring patient quality of life. We developed this nomogram to more accurately predict the individual probability of SLNM, with the goal of tentatively screening patients who were predicted to be SLN (-). This may provide valuable evidence for potential SLNB exemptions, achieving broader benefits. Over the next five years, we anticipate that predictive models will increasingly integrate multiomics data (genomic, radiomic, and clinicopathological) to achieve higher precision. Moreover, artificial intelligence-driven tools could dynamically update risk predictions based on real-world data, enabling adaptive clinical decision-making. Our study serves as a foundational step toward these goals, emphasizing the need for collaborative efforts to validate and refine such models in prospective trials.

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Data availability Publicly available datasets were analyzed in this study. This data can be found here: Surveillance, Epidemiology, and End Results (SEER) database (https://seer.cancer.gov/).

Declarations

Conflict of interest The authors declare no competing interests.

Ethics approval and consent to participate All the procedures followed were in accordance with the Helsinki Declaration and its later amendments. The data released by the SEER database were publicly available and does not require informed patient consent because cancer is a reportable disease in every state in the USA.

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