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Research Article

Development of a Nomogram to Predict Metastasis of Axillary Lymph Node in Breast Cancer

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Abstract

For patients with breast cancer, an alter native to unreliable imaging methods and un necessary debilitating invasive procedures is required that might predict the status of axillary lymph nodes and risk of metastasis. This retrospective study developed a nomogram model for such evaluation, based on readily available clinical variables. The records of 1730 women patients with breast cancer were reviewed. Patients were apportioned to either a training (model building) or test group (validation). Clinical variables and his to pathological parameters were compiled. Categorical and continuous variables were identified using the chi-squared and Student's t-test, respectively. Factors associated with positive lymph nodes were identified using logistic regression, and a nomogram was developed. The discriminative ability and accuracy of the models was evaluated via Receiver Operating Characteristic (ROC) curve analysis. Data contributing to the development of the nomogram included surgery type, chemotherapy status before surgery, histology, number of checked lymph nodes, and tumor size. The areas under the ROC curve of the training and testing groups were 0.79 and 0.74, respectively. The nomogram developed herein is of great potential value for predicting the metastasis of lymph nodes in patients with breast cancer, and warrants clinical verification.

Keywords: Breast cancer; Lymph node; Nomogram; Logistic regression; Impact factor

Abbreviations

BCS: Breast Conserving Surgery; DCIS: Ductal Carcinoma In Situ; IDC: Infiltrating Ductal Carcinoma; ILC: Invasive Lobular Carcinoma; ALN: Axillary Lymph Node; MRM: Modified Radical Mastectomy; SE: Standard Error

Introduction

Breast cancer is the most common cancer in women, and the leading cause of cancer-related mortality [1]. In China, the standard treatment for breast cancer is modified radical mastectomy with Axillary Lymph Node (ALN) dissection [2]. However, after ALN dissection a series of complications are inevitable. The intra operative injury to blood vessels and lymphatic vessels, and postoperative scar hyperplasia, can lead to lymphedema of the affected limb. Because of the recalcitrant nature of these complications and harm to patients' quality of life, great care should be taken during the ALN dissection. Especially, accurate ALN assessment is required for breast cancer staging and prognosis [3]. Identifying sentinel lymph nodes and estimating the risk of metastasis is important for therapy and follow-up [4].

The main alternative to ALN dissection in node-negative patients currently is sentinel lymph node biopsy, but it is an invasive examination, time consuming and expensive. A small percentage of patients who undergo sentinel lymph node biopsy [5,6], ALN status is most commonly assessed through ultra sound examination. This and other imaging methods vary in accuracy and are less satisfactory; these include digital mammography, computed tomography, and magnetic resonance imaging [7,8]. Agliata et al. [9] investigated contrast-enhanced ultrasonography for ALN evaluation, but reported false positive results for malignancy in areas of necrosis that may only be due to an inflammatory condition. Thus, with the current imaging technology, it remains very difficult to identify sentinel lymph nodes before surgery and prevent unnecessary dissection. An alternative solution, such as interpreting accurately and simultaneously the import of appropriate biomarkers, would be desirable.

Estrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal growth Receptor 2 (HER2) are biomarkers that are widely used in clinics [10]. Ki-67 and P53 are also routinely biomarkers of breast cancer may help predict the ALN status and quantify risk when evaluation tested [5]. We hypothesized that a nomogram that incorporated these parameters can predict the ALN status of the individual patient [6]. The retrospective study developed a nomogram model, based on readily available clinical variables of patients with breast cancer who have under gone surgery.

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Materials and Methods

The independent Ethics Committee Review Board of Guangzhou First People's Hospital approved the study protocol. Patients provided informed consent before surgery.

Study design and population

The population of this retrospective study comprised 1730 women with histologically confirmed breast cancer, who underwent surgery from 1 January 1998 to 31 December 2015 at Guangzhou First People's Hospital. Women with any of the following were excluded from this analysis, prior diagnosis of breast cancer or other cancers, stage T4 cancer, distant metastasis, or unknown T-stage, missing histological or surgery information or survival time <3 months.

Patients were sorted by surgery date which was from 1 January 1998 to 31 December 2015, two of every three sorted patients were included in the training set. The remaining patients were included in the testing set for model validation.

Data collection

The following data were collected: age; tumor size and stage; histology; number of lymph nodes checked; number of positive lymph nodes; and the biomarkers ER, PR, HER2, Ki-67, and P53. Hematoxylin and Eosin (H&E) stain and immunohistochemistry were performed with paraffin embedded tumor tissues. Immunohistochemistry in two-step was performed following the operating instructions of the kit to examine the expression of HER2, P53, ER, PR and Ki-67. The kit is from MXB Biotechnologies Corporation in Fuzhou, China. Percent expression values of ER and PR were categorized by 0,1,2,3. HER2 and P53 were categorized by negative and positive, Ki-67 was score by percentage of tumor cells. Each specimen was examined independently by 2 experienced pathologists.

Statistical analysis

General analytic strategy: Generally, data were analyzed using SAS (Version 9.2, SAS institute, Cary, NC) and State (Version 15.0, State Corp., College station, TX) software. Two-sided P-values <0.05 were considered statistically significant.

Identification of candidate variables: The clinical and biological variables of the training and testing groups were compared using the chi-squared test for categorical variables and Student's t-test for continuous variables.

In the training group, the association between each variable and lymph node positiveness was assessed using univariate logistic regression analyses. Variables with skewed distribution were transformed into normality using the Box-Cox method. Variables were selected that were significant in both the categorical and continuous analyses for continuous variables. The bootstrap resembling method was performed to verify the results internally, 1000 bootstrap samples were produced. The number of times with a P-value <0.05 was recorded. Variables that appeared significant for the prediction of lymph node status were analyzed in a stepwise selection and model development (below).

Stepwise selection and model construction: Stepwise selection was conducted using multivariate logistic regression to identify possible factors related to lymph node positiveness. Multiple imputations were used to process the missing data in the training group, and 10 variables were generated by Stata's MI (multiple imputations) package. The average value of the training group was used as the value of the missing data of the test group. Any variable that was selected in 10 imputed datasets was used to build the final model.

Nomogram and model validation: To visualize our predictive model graphically in nomogram, the nomolog package of the State software was used. A Receiver Operating Characteristic (ROC) curve was constructed to evaluate the discriminant ability and accuracy of the models. The areas under the ROC curve (AUCs) of the model were calculated respectively in the training and test groups.

Results

Characteristics of study population

Among the 1730 patients with breast cancer, the mean age of patients was 52.05 ± 12.05 years , the lymph nodes of 819 (47.3%) patients were metastatic and 911 (52.7%) were negative.

The training and test groups consisted of 1153 and 577 patients, respectively (Table 1). The 2 groups were statistically comparable except for tumor size, T stage, and ER levels (P=0.0043, 0.0149, and 0.0064, respectively). In the training group, the rate of patients in T3 stage was greater than that of the test group, while the rates in T1 and T2 were lower.

The percentages of patients with ER negative and ER2+ in training group were larger than those in testing group. The percentages of patients with ER1+ and ER3+ in training group were less than those in testing group (Table 1).

Univariate analysis in the training group

In the univariate analysis, tumor size, surgery type, histology, number of checked lymph nodes, chemotherapy before surgery, T stage, PR, P53, and Ki-67 status were significantly associated with ALN metastasis (Table 2).

Stepwise selection and final model construction

Ten imputation datasets were generated from the training set. For each, stepwise selection was performed, step-by-step, to determine the best variables to include in the multivariate logistic regression. Five variables were selected which were significant in all of the 10 imputed datasets as follows: surgery type; chemotherapy before surgery; histology; number of checked lymph nodes; and tumor size. A nomogram was established based on the results of the multivariate logistic analysis (Table 3) (Figure 1).

Validation of the model

For the training group, the Area Under Curve (AUC) of Receiver Operating Characteristics (ROC) curve was calculated as 0.79 (95% CI: 0.75-0.83) (Figure 2). When applied to the test group, this model was discriminating with an AUC of 0.74 (95% CI: 0.69-0.79).

Discussion

In this retrospective study of the clinical data of 1730 women patients with breast cancer, a nomogram model was developed to predict the metastatic status of ALNs. This model was well established in the training group and verified in the test group, with AUCs of 0.79 and 0.74, respectively, indicating great performance and stability to differentiate positive and negative lymph nodes.

There have been several previous models reported to predict the ALN status, with AUCs ranging from 0.70 to 0.79 [11-13]. The first predictive model for lymph node status was developed a decade ago by Bevilacqua, et al. [7] with an AUC of 0.75. This nomogram

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Table 1: Characteristics of the training and test groups.

	Missing, n		Training	Testing	*P*
Age, y	0	<50	583 (50.56)	285 (49.39)	0.646
		≥50	570 (49.44)	292 (50.61)	
Location	0	Left	557 (50.04)	286 (49.57)	0.852
		Right	576 (49.96)	291 (50.43)	
Surgery type	0	MRM	1028 (89.25)	502 (87.00)	0.333
		BCS	57 (4.94)	28 (4.83)	
		Resection	36 (3.12)	25 (4.33)	
		Biopsy	31 (2.69)	22 (3.81)	
Histology	0	DCIS	59 (5.12)	31 (5.37)	0.638
		IDC	896 (77.71)	442 (76.60)	
		ILC	91 (7.89)	51 (8.84)	
		Mixed	45 (4.86)	34 (5.89)	
		Others	51 (4.42)	19 (3.29)	
Tumor size	0		2.67 ± 1.37	2.93 ± 1.83	0.004
T-stage	0	T1	394 (34.17)	195 (33.8)	0.015
		T2	681 (59.06)	320 (55.46)	
		T3	78 (6.76)	62 (10.75)	
N-stage	82	N0	600 (54.15)	290 (53.70)	0.297
		N1	289 (26.08)	157 (29.07)	
		N2	131 (11.82)	62 (11.48)	
		N3	88 (7.94)	31 (5.74)	
Checked LNs, n	0		11.88 ± 6.79	11.60 ± 6.28	0.405
Metastatic LNs, n	0		2.46 ± 5.12	2.07 ± 4.24	0.107
LNs, n	0	Present	538 (46.66)	281 (48.70)	0.423
		Not present	615 (53.34)	296 (51.3)	
ER	174	0	345 (33.01)	195 (38.16)	0.006
		1	134 (12.82)	43 (8.41)	
		2	106 (10.14)	67 (13.11)	
		3	460 (44.02)	206 (40.31)	
PR	175	0	405 (38.79)	216 (42.27)	0.421
		1	201 (19.25)	103 (20.16)	
		2	151 (14.46)	67 (13.11)	
		3	287 (27.49)	125 (24.46)	
Molecular subtype	195	Luminal A	226 (21.94)	115 (22.77)	0.237
		Luminal B	512 (49.71)	225 (44.55)	
		HER2	107 (20.19)	115 (22.77)	
		Triple negative	84 (8.16)	50 (9.90)	
HER2	207	Positive	723 (70.06)	341 (68.06)	0.427
		Negative	309 (29.94)	160 (31.94)	
Ki-67 (%)	526		38.49 ± 28.25	38.23 ± 27.12	0.878
P53	803	Positive	73 (11.97)	35 (11.04)	0.677
		Negative	537 (88.03)	282 (88.96)	

Data reported as n (%), unless indicated otherwise.

Abbreviations: BCS: Breast Conserving Surgery; DCIS: Ductal Carcinoma in Situ; IDC: Infiltrating Ductal Carcinoma; ILC: Invasive Lobular Carcinoma; LN: Lymph Node; MRM: Modified Radical Mastectomy.

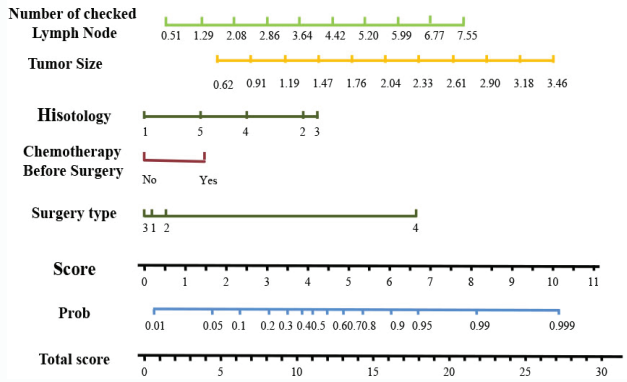

Figure 1: Nomogram for predicting the risk of ALN metastasis. The nomogram has 8 rows. The upper 5 rows are the scores corresponding to each variable. For each patient, a vertical line is drawn between the variable value and the corresponding score line, and then a score is assigned to each variable based on clinical pathology characteristics, to obtain a total score (row 8). The risk of ALN can be predicted according to the total scores (row 7).

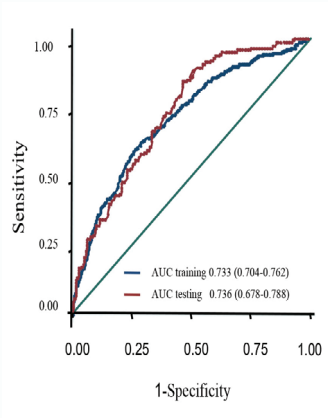

Figure 2: ROC curves of the model constructed from the training group and applied to the test group.

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Table 2: Univariate analysis for biological variables associated with ALNs metastasis.

OR (95% C.I.)	P	Bootstrap %*		
Surgery type	MRM	1		
	BCS	0.786 (0.457-1.353)	0.0176	
	Tumor resection	0.447 (0.213-0.936)	0.0002	
	Biopsy	16.84 (3.998-70.931)	<0.0001	
	Trend		0.0125	71.8
Chemotherapy before surgery	0	0.276 (0.171-0.446)	<0.0001	100
	1	1		
Histology	DCIS	0.177 (0.086-0.364)	0.177	
	IDC	1		
	ILC	1.049 (0.682-1.615)	0.0001	
	Mixed	0.428 (0.239-0.768)	0.6287	
	Other	0.336 (0.177-0.639)	0.1862	
	Trend		0.0453	47.3
Tumor size (Square root transformed)		4.579 (3.226-6.498)	<0.0001	100
T-stage	T1	1		
	T2	1.871 (1.449-2.417)	0.1788	
	T3	5.380 (3.108-9.313)	<0.0001	
	Trend		<0.0001	100
Checked lymph node(Square root transformed)		1.686 (1.476-1.925)	<0.0001	100
PR	0	1		
	1	0.947 (0.675-1.328)	0.4005	
	2	0.788 (0.541-1.148)	0.5379	
	3	0.719 (0.530-0.975)	0.106	
	Trend		0.0243	58.3
Ki-67 (Square root transformed)		1.008 (1.003-1.013)	0.0026	67.5
P53	Positive	1		
	Negative	1.736 (1.024-2.945)	0.0406	52.4

*<0.05

Abbreviations: BCS: Breast Conserving Surgery; DCIS: Ductal Carcinoma in Situ; IDC: Infiltrating Ductal Carcinoma; ILC: Invasive Lobular Carcinoma; ALN: Axillary Lymph Node; MRM: Modified Radical Mastectomy.

Table 3: Multivariate logistic regression for biological variables associated with ALNs metastasis.

OR (95% C.I.)	SE	t	P		
Surgery type	MRM	1			
	BCS	1.151 (0.636-2.084)	0.349	0.46	0.642
	Tumor resection	0.902 (0.387-2.096)	0.388	-0.24	0.81
	Biopsy	12.831 (2.785-59.118)	9.999	3.27	0.0001
Chemotherapy before surgery	0	1	<0.0001		
	1	1.883 (1.120-3.167)	0.499	2.39	0.017
Histology	DCIS	1			
	IDC	5.236 (2.478-11.066)	1.999	4.34	<0.0001
	ILC	6.091 (2.596-14.2889)	2.65	4.15	<0.0001
	Mixed	2.875 (1.112-7.434)	1.394	2.18	0.029
	Other	1.789 (0.653-4.890)	0.92	1.13	0.258
Checked lymph nodes		1.565 (1.356-1.806)	0.115	6.12	<0.0001
Tumor size		3.484 (2.367-5.128)	0.687	6.33	<0.0001

Abbreviations: BCS: Breast Conserving Surgery; DCIS: Ductal Carcinoma in Situ; IDC: Infiltrating Ductal Carcinoma; ILC: Invasive Lobular Carcinoma; ALN: Axillary Lymph Node; MRM: Modified Radical Mastectomy; SE: Standard Error.

was verified by patients in many medical centers with AUCs of 0.78, 0.73, and 0.71, respectively [8]. Our current model can be considered validated, stable, and reliable to predict ALN status.

In the present study, tumor size was the most important factor in lymph node assessment, although tumor histology was also significantly associated. Our results are in accord with many previous reports, in which these two factors were recognized as independent predictors [14-16].

In this study, associations among immune-histo-chemical pathology variables were evaluated, all of which are available in routine clinical practice for patients with breast cancer. The value of ER and PR levels for the prediction of lymph node status differs from previous reports. Some research showed a low risk of metastasis in ALNs when tumors tested negative for ER or PR, but others found no predictive value [17,18]. In our study, in the univariate analysis the ER and HER2 levels were not significantly associated with lymph node status, and PR positivity was a protective factor in metastatic lymph nodes. However, the multivariate analysis did not indicate that these were independent factors of ALN status. Taking ER, PR, and HER2 together, Reyal, et al. [9] reported that molecular subtypes were an informative risk factor of metastatic lymph nodes. In our present study, molecular subtype had no significant value, according to the multivariate analysis.

The proliferation marker Ki-67 [19] has been suggested as a promising biomarker of cancer, which provides a quick method to evaluate the percentage of proliferating cells within a tumor. Huang et al. [20] suggested that Ki-67 had a significant influence on recurrence. Similar to the result of Xi Jin's [21], Ki-67 is a dependent factor in risk of lymph node, which was consistent with our current research. P53 is over expressed in breast cancer tissues. With the increasing of its expression, the tumor tissue is worse differentiation, higher malignancy and worse prognosis [22]. We found the two markers were risk factors for lymph node in breast cancer in university analysis, but significant differences were not found in multi-factors analysis. More data should be analyzed in future research.

For the final analysis, 5 variables were selected to develop the nomogram surgery type, chemotherapy before surgery, histology, number of checked lymph nodes, and tumor size. Other investigators have reported variables that have great value for predicting ALN status [14,23,24]. Bevilacqua [23] conducted a study of 4608 patients with breast cancer to build a nomogram that included age; tumor histology, location, size, ER and PR. According to the research of Xie, et al. [14], tumor size, menopausal status, ER, PR, HER2, and two other genes (nm-23 and Kiss-1) were efficient predictors of lymph node status. Viale, et al. [24] found that reliable predictors of lymph node metastasis were peritumoral vascular invasion and tumor size and

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multimodality. Some significant variables in our results are similar to those of the above studies. In addition, other variables investigated in the present study may have potential reference value for predicting lymph node metastasis in breast cancer: surgery type, chemotherapy before surgery, and number of checked lymph nodes.

There are some limitations in current study. Firstly, the model was only confirmed in our hospital's test group, so there may be selection bias and more institutions are needed to verify it. Secondly, the immune-histo-chemical markers considered important in breast cancer have changed during the past 10 years, and the data may now be considered incomplete. This may affect the validity of the model. In particular, new genomic data regarding breast cancer have been reported, and therefore more biomarkers should be used in further research. Finally, the nomogram was obtained by retrospective analysis of past data, and it requires prospective validation for clinical practice.

In conclusion, we developed and verified a novel nomogram, which is useful to assess the probability of lymph node metastasis in patients with breast cancer. Patients should be more attention because of different of surgery type and histology. Because of large tumor size, more number of checked lymph nodes, chemotherapy status before surgery was risk variables for metastasis in lymph node, decisions should be chosen before treatments.

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics. CA Cancer J Clin. 2010;60(5):277-300.
2. Society AC. Breast Cancer Facts & Figures 2017-2018. Atlanta: American Cancer Society; 2017.
3. Liu C, Jiang Y, Gu X, Xu Z, Ai L, Zhang H, et al. Predicting level 2 axillary lymph node metastasis in a Chinese breast cancer population post-neoadjuvant chemotherapy: development and assessment of a new predictive nomogram. Oncotarget. 2017;8(45):79147-56.
4. Qiu SQ, Zeng HC, Zhang F, Chen C, Huang WH, Pleijhuis RG, et al. A nomogram to predict the probability of axillary lymph node metastasis in early breast cancer patients with positive axillary ultrasound. Sci Rep. 2016;6:21196.
5. Ashikaga T, Krag DN, Land SR, Julian TB, Anderson SJ, Brown AM, et al. Morbidity results from the NSABP B-32 trial comparing sentinel lymph node dissection: versus axillary dissection. J Surg Oncol. 2010;102(2):111-8.
6. McLaughlin SA, Wright MJ, Morris KT, Sampson MR, Brockway JP, Hurley KE, et al. Prevalence of lymphedema in women with breast cancer 5 years after sentinel lymph node biopsy or axillary dissection: patient perceptions and precautionary behaviors. J Clin Oncol. 2008;26(32):5220-6.
7. Turnbull L, Brown S, Harvey I, Olivier C, Drew P, Napp V, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomised controlled trial. Lancet. 2010;375(9714):563-71.
8. Ahn SK, Kim MK, Kim J, Lee E, Yoo TK, Lee HB, et al. Can We Skip Intraoperative Evaluation of Sentinel Lymph Nodes? Nomogram Predicting Involvement of Three or More Axillary Lymph Nodes before Breast Cancer Surgery. Cancer Res Treat. 2017;49(4):1088-96.
9. Agliata G, Valeri G, Argalia G, Tarabelli E, Giuseppetti GM. Role of Contrast-Enhanced Sonography in the Evaluation of Axillary Lymph Nodes in Breast Carcinoma: A Monocentric Study. J Ultrasound Med. 2017;36(3):505-11.
10. Xiong Z, Deng G, Huang X, Li X, Xie X, Wang J, et al. Bone metastasis pattern in initial metastatic breast cancer: a population-based study. Cancer Manag Res. 2018;10:287-95.
11. Patani NR, Dwek MV, Douek M. Predictors of axillary lymph node metastasis in breast cancer: a systematic review. Eur J Surg Oncol. 2007;33(4):409-19.
12. Chen JY, Chen JJ, Yang BL, Liu ZB, Huang XY, Liu GY, et al. Predicting sentinel lymph node metastasis in a Chinese breast cancer population: assessment of an existing nomogram and a new predictive nomogram. Breast Cancer Res Treat. 2012;135(3):839-48.
13. Xie F, Yang H, Wang S, Zhou B, Tong F, Yang D, et al. A logistic regression model for predicting axillary lymph node metastases in early breast carcinoma patients. Sensors (Basel). 2012;12(7):9936-50.
14. Greer LT, Rosman M, Charles Mylander W, Liang W, Buras RR, Chagpar AB, et al. A prediction model for the presence of axillary lymph node involvement in women with invasive breast cancer: a focus on older women. Breast J. 2014;20(2):147-53.
15. Klar M, Foeldi M, Markert S, Gitsch G, Stickeler E, Watermann D. Good prediction of the likelihood for sentinel lymph node metastasis by using the MSKCC nomogram in a German breast cancer population. Ann Surg Oncol. 2009;16(5):1136-42.
16. Qiu PF, Liu JJ, Wang YS, Yang GR, Liu YB, Sun X, et al. Risk factors for sentinel lymph node metastasis and validation study of the MSKCC nomogram in breast cancer patients. Jpn J Clin Oncol. 2012;42(11):1002-7.
17. Silverstein MJ, Skinner KA, Lomis TJ. Predicting axillary nodal positivity in 2282 patients with breast carcinoma. World J Surg. 2001;25(6):767-72.
18. H WE. The National Comprehensive Cancer Network (NCCN) has announced important updates. Pharmacoeconomics & Outcomes News. 2008;566:2.
19. Elledge RM, Allred DC. Prognostic and predictive value of p53 and p21 in breast cancer. Breast Cancer Res Treat. 1998;52(1-3):79-98.
20. Zaha DC. Significance of immunohistochemistry in breast cancer. World J Clin Oncol. 2014;5(3):382-92.
21. Balachandran VP, Gonen M, Smith JJ, DeMatteo RP. Nomograms in oncology: more than meets the eye. Lancet Oncol. 2015;16(4):e173-80.
22. Bevilacqua JL, Kattan MW, Fey JV, Cody HS, Borgen PI, Van Zee KJ. Doctor, what are my chances of having a positive sentinel node? A validated nomogram for risk estimation. J Clin Oncol. 2007;25(24):3670-9.
23. Viale G, Zurrida S, Maiorano E, Mazzarol G, Pruneri G, Paganelli G, et al. Predicting the status of axillary sentinel lymph nodes in 4351 patients with invasive breast carcinoma treated in a single institution. Cancer. 2005;103(3):492-500.

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