A model for the early identification of sentinel lymph node metastasis in patients with breast cancer based on contrast-enhanced ultrasound and clinical features

JUAN XU and JUNZHI LI

Department of Interventional Ultrasound, Cangzhou Central Hospital, Cangzhou, Hebei 061000, P.R. China

Received February 14, 2022; Accepted August 25, 2022

DOI: 10.3892/ol.2022.13498

Abstract. The present study was designed to establish a model for the early identification of sentinel lymph node (SLN) metastasis in patients with breast cancer (BC). The SLN metastasis predictive model was established with a retrospective training set of 365 patients with BC and was re-evaluated using a prospective validation set of 402 patients with BC. The multivariable analysis indicated that the tumor diameter [odds ratio (OR), 1.189; 95% confidence interval (CI), 1.124-1.257; P<0.001], menopause (OR, 1.011; 95% CI, 0.603-1.436; P<0.001), estrogen receptor (ER) expression (OR, 3.199; 95% CI, 1.077-6.567; P=0.043) and contrast-enhanced ultrasoundography (CEUS) type (OR, 10.563; 95% CI, 6.890-28.372; P<0.001) were independent predictors of SLN status in patients with BC. The SLN metastasis predictive model was as follows: (0.173 x tumor diameter)-(4.490 x menopause) + (2.322 x ER) + (5.445 x CEUS type)-1.9521. In the training set, the model was highly sensitive (83.6%) and specific (94.3%) for the early identification of SLN metastasis. Similarly, in the validation set, the model was highly sensitive (70.4%) and specific (89.5%) for the early identification of SLN metastasis in patients with BC. Overall, in the present study, a model was successfully established to predict SLN metastasis in patients with BC that includes tumor diameter, menopausal status, ER expression and CEUS detection.

Introduction

Breast cancer (BC) is one of the most common malignant tumors. There are ~2.2 million new cases of BC and >680,000 deaths due to BC in the world every year (1). In China, 420,000 new cases of BC and 120,000 deaths from BC are registered per year (2,3). Recently, the survival rate of patients with BC has been significantly improved, with the cancer becoming one of the solid tumors with the best curative effect following the development of comprehensive BC treatments. However, there are still >100,000 BC-associated deaths in China annually, mainly due to recurrence and distant metastasis (4,5).

Axillary lymph nodes (ALNs) are an important prognostic factor for patients with BC, and ALN dissection (ALND) has been widely used in clinical practice as a diagnostic criterion to determine whether the ALNs are involved (6,7). However, its large surgical range can easily cause complications, such as lymphedema, hematoma formation, and restricted mobility (8,9). The sentinel lymph nodes (SLNs) are the first station or group of lymph nodes for drainage. As a barrier to prevent tumor cells from spreading from the lymphatic tract, the clinical significance of SLN has attracted increasing attention (10). Moreover, SLN biopsy (SLNB) is the standard procedure for axillary staging in patients with clinically node-negative (cN0) BC. However, the positive rate of cancer detection in SLNs in patients with cN0 stage BC receiving SLNB is between 20.5 and 25.5% (11,12). Nevertheless, identifying non-invasive and suitable SLNB candidates can be challenging. Although some studies have proposed non-invasive or minimally invasive methods to determine SLN metastasis in patients with BC, such as MRI (13,14), cytokeratin 19 mRNA detection in peripheral blood (15) and Ras association domain family 1 isoform A methylation detection in tissues (16), there is no consensus on the use or recommendation of these approaches in the National Comprehensive Cancer Network guidelines due to lack of evidence (17).

Contrast-enhanced ultrasound (CEUS) is a technology that enhances the echo of the backscatter using a contrast agent to improve the resolution, sensitivity and specificity of ultrasound diagnosis. CEUS can directly reflect the blood perfusion of diseased and normal tissues, show the new abnormal blood vessels that appear when the tumor rapidly progresses and play an important role in the qualitative diagnosis of tumors (18,19). Recently, a number of studies demonstrated that CEUS could be used to non-invasively predict SLN metastasis in patients with early stage BC (20,21), but it was rarely included in previous SLN metastasis prediction models (22). Hence, in the present study, a model was built to predict SLN metastasis based on CEUS and the basic clinical features of patients with BC.
Patients and methods

Patients. First, the data of 365 patients with BC (all female) hospitalized in the Cangzhou Central Hospital (Cangzhou, China) between January 2017 and December 2018 were retrospectively collected. These 365 patients comprised the training set (the population used to build the model; age range, 24–83 years; mean age, 52.07 years) and were divided into the SLN-negative (no-metastasis; n=255) and SLN-positive (metastasis; n=110) groups based on pathological results. Next, the data of 402 patients with BC (all female) hospitalized in the Cangzhou Central Hospital between January 2019 and April 2021 were prospectively collected (age range, 23.79 years; mean age, 51.43 years). These 402 patients were used as the prospective validation set to verify the SLN status predictive model established using the training set. Similarly, they were divided into SLN-negative (no-metastasis; n=287) and SLN-positive (metastasis; n=115) groups based on pathological results.

All recruited patients with BC (including patients in the validation and training sets) met the following criteria. The inclusion criteria were: i) Female sex; ii) no previous history of other malignancies; iii) a pathological diagnosis of BC; iv) cancer cells that have not metastasized to distant organs; v) the first diagnosis of BC; and vi) a clear SLN status. The exclusion criteria were: i) male sex; ii) radiotherapy and chemotherapy received before surgery; iii) allergy to ultrasound contrast agents; iv) pregnancy or breastfeeding; v) a previous history of axillary surgery; and vi) severe heart or lung disease. This study was approved by the Ethics Committee of the Cangzhou Central Hospital, and clinical diagnoses and treatments complied with the Helsinki Declaration.

Data collection. The age and menopause data of the patients with BC were extracted from electronic medical records. Laboratory tests included those for pathological type, tumor diameter, histological grade, CEUS detection, and expression of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) and Ki-67. SLNB was used to identify SLN+/- status.

Establishment of CEUS scoring system. According to the CEUS performance, the patients with BC were divided into four categories: Complete uniform enhancement (type I), uniform enhancement of the periphery and medulla (type II), uneven enhancement (type III) and no enhancement of the periphery and/or medulla (type IV). In the training and prospective validation sets, most patients with SLN-negative BC were type I, followed by type II. By contrast, most patients with SLN-positive BC were type IV, followed by type III.

Statistical analysis. In the present study, SPSS19.0 software (IBM Corp.) was used for statistical analysis. Univariate binary regression analysis was used for univariate analysis of categorical data, and unconditional logistic regression was used for the multivariate analysis, and the relative risk is expressed as odds ratio (OR) and 95% confidence intervals (CIs). Additionally, receiver operating characteristic (ROC) curves were used to evaluate the predictive value of the SLN status predictive model in the patients with BC. The areas under the ROC curves (AUCs) were used to estimate the predictive accuracy. The cut-off value was defined at the maximum of the sum of sensitivity and specificity. P<0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics of patients with BC in the training set. The baseline characteristics of the patients with BC in the training set are presented in Table I. Patients with SLN-negative and -positive BC significantly differed regarding the pathological type, tumor diameter, menopause, ER expression, PR expression and CEUS type. Namely, compared with the SLN-negative BC group, the SLN-positive BC group had a higher proportion of infiltration, a larger tumor diameter, a higher proportion of postmenopausal patients, a higher proportion of ER-positive patients and a higher proportion of PR-positive patients. Meanwhile, they did not differ in age, histological grade, HER2 expression and Ki-67 expression (P>0.05).

Baseline characteristics of patients with BC in the prospective validation set. The baseline characteristics of patients with BC in the prospective validation set are shown in Table II. Similar to the training set, patients with SLN-negative and -positive BC were significantly different regarding the pathological type, tumor diameter, menopause, ER expression, PR expression, Ki-67 expression, and CEUS type (P<0.05). Namely, compared with the SLN-negative BC group, the SLN-positive BC group had a higher proportion of infiltration, a larger tumor diameter, a higher proportion of postmenopausal patients, a higher proportion of ER-positive patients, a higher proportion of PR-positive patients and a higher proportion of Ki-67-positive patients. Meanwhile, they did not differ in age, histological grade or HER2 expression (P>0.05).

Establishment of the SLN status predictive model. According to the results in Tables I and II, pathological type, tumor diameter (≤2, 2–3, and ≥3 were assigned as 1, 2, and 3, respectively), age (≤40, 40–50, 50–60 and ≥60 years were assigned as 1, 2, 3, and 4, respectively), ER (negative and positive were assigned as 1 and 2, respectively), PR (negative and positive were assigned as 1 and 2, respectively), Ki-67 (negative and positive were assigned as 1 and 2, respectively) and CEUS type (types I, II, III and IV were assigned as 1, 2, 3 and 4, respectively) were included into the multivariate analysis to establish the predictive model for SLN status. The model was as follows: (0.173 x tumor diameter)–(4.490 x menopause) + (2.322 x ER) + (5.445 x CEUS type). Moreover, the independent predictors of SLN status in patients with BC included tumor diameter (OR, 1.189; 95% CI, 1.124–1.257; P<0.001), menopause (OR, 1.011; 95% CI, 0.603–1.436; P<0.001), ER expression (OR, 3.199; 95% CI, 1.077–6.567; P=0.043) and CEUS type (OR, 10.563; 95% CI, 6.890–28.372; P<0.001) (Table III). Overall, the model could be used to predict the SLN status of patients with BC. According to SNL status using SLNB, the sensitivity and specificity of the model for diagnosing SLN status could then be calculated (Fig. 1). The clinical data (tumor diameter, menopause, ER and CEUS type) of one patient with BC were substituted into the aforementioned formula (model) to obtain a value, and if
the value was >0, SLN positivity was predicted, otherwise an SLN-negative status was predicted. In the training set, the AUC, sensitivity and specificity were 0.899, 83.6 and 94.3%, respectively (Fig. 1A). In the prospective validation set, the AUC, sensitivity and specificity were 0.826, 70.4 and 89.5%, respectively (Fig. 1B).

**Discussion**

SLNB is a minimally invasive detection method that can accurately determine the pathological status of the ALNs in patients with early stage BC, preventing ALN-negative patients from undergoing ALND, thereby reducing the incidence of postoperative complications and improving the quality of life of patients after surgery (23,24). Nevertheless, SLNB still has postoperative complications, such as a 0-7% incidence of lymphedema and a 20% incidence of upper limb numbness (25,26). Furthermore, the radionuclide labeling, blue dye injection and fluorescent dye methods used in SLNB are not only invasive, but also have a low diagnostic accuracy rate due to the difficulty of lymph node puncture (27,28). Moreover, performing SLNB for all patients with wastes limited medical resources and increases the financial burden on the patients. By contrast, SLN status is not only necessary for the staging of patients with BC, but SLN burden also has a strong effect on the outcome of invasive patients with

### Table I. Baseline characteristics of SLN-negative (n=255) and -positive (n=110) patients with breast cancer in the training set (n=365).

| Characteristics               | Total patients, n | SLN, n (%) | OR         | 95% CI       | P-value<sup>a</sup> |
|-------------------------------|-------------------|------------|------------|--------------|----------------------|
|                               |                   | Negative   | Positive   |              |                      |
| Pathological type             |                   |            |            |              |                      |
| Non-infiltration              | 58                | 54 (93.10) | 4 (6.90)   | 7.199        | 2.510-20.193         | <0.001 |
| Infiltration                  | 307               | 201 (65.47)| 106 (34.53)|             |                      |        |
| Tumor diameter, cm ≤2         | 133               | 107 (80.45)| 26 (19.55) | 2.336        | 1.409-3.872          | 0.001  |
| >2                            | 232               | 148 (63.79)| 84 (36.21) |             |                      |        |
| Age, years ≤50                | 230               | 158 (68.70)| 72 (31.30) | 0.860        | 0.539-1.372          | 0.526  |
| >50                           | 135               | 97 (71.85) | 38 (28.15) |             |                      |        |
| Menopause                     |                   |            |            |              |                      |
| Yes                           | 228               | 146 (64.03)| 82 (35.97) | 0.457        | 0.279-0.751          | 0.002  |
| No                            | 137               | 109 (79.56)| 28 (20.44) |             |                      |        |
| Histological grade            |                   |            |            |              |                      |
| I+II                          | 288               | 202 (70.14)| 86 (29.86) | 1.064        | 0.617-1.833          | 0.824  |
| III                           | 77                | 53 (68.83) | 24 (31.17) |             |                      |        |
| ER negative                   | 113               | 92 (81.42) | 21 (18.58) | 2.009        | 1.167-3.458          | 0.012  |
| Positive                      | 252               | 163 (64.68)| 89 (35.32) |             |                      |        |
| PR negative                   | 136               | 108 (79.41)| 28 (20.59) | 2.152        | 1.311-3.532          | 0.002  |
| Positive                      | 229               | 147 (64.19)| 82 (35.81) |             |                      |        |
| HER2 negative                 | 257               | 185 (71.98)| 72 (28.02) | 1.395        | 0.863-2.253          | 0.174  |
| Positive                      | 108               | 70 (64.81) | 38 (35.19) |             |                      |        |
| Ki-67 negative                | 71                | 55 (77.46) | 16 (22.54) | 1.616        | 0.879-2.968          | 0.122  |
| Positive                      | 294               | 200 (68.03)| 94 (31.97) |             |                      |        |
| CEUS type                     |                   |            |            |              |                      |
| I+II                          | 223               | 213 (95.52)| 10 (4.48)  | 50.714       | 24.454-105.176       | <0.001 |
| III+IV                        | 142               | 42 (29.58)| 100 (70.42)|             |                      |        |

<sup>a</sup>P-values indicate differences between SLN-negative and SLN-positive patients with breast cancer. P<0.05 was considered to indicate a statistically significant difference. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; CEUS, contrast-enhanced ultrasonography; OR, odds ratio; CI, confidence interval.
Therefore, the establishment of a model that can predict SLN metastasis is of great significance to patients with BC. However, the clinicopathological characteristics of SLN-positive patients are similar to those of SLN-negative patients, which limits the ability to predict lymph node metastasis before surgery (30). In the present study, besides the clinicopathological characteristics of BC patients, CEUS was introduced to establish an SLN metastasis prediction model for patients with BC. In CEUS detection, the contrast agent is percutaneously injected and can conveniently pass through the lymphatic endothelial cell space and enter lymphatic vessels.

Table II. Baseline characteristics of SLN-negative (n=287) and -positive (n=115) patients with breast cancer in the prospective validation set (n=402).

| Characteristics          | Total patients, n | SLN, n (%) | OR     | 95% CI       | P-value
|--------------------------|-------------------|------------|--------|--------------|--------
| Pathological type        | 333               | 224 (67.27)| 109 (32.73) | 4.514 | 2.016-10.104 | <0.001 |
| Non-infiltration         | 69                | 63 (91.30) | 6 (8.70) |              |        |
| Infiltration             |                   |            |         |              |        |
| Tumor diameter, cm       |                   |            |         |              |        |
| ≤2                       | 150               | 123 (82.00)| 27 (18.00) | 1.825 | 1.279-2.606 | 0.001 |
| >2 to <3                 | 165               | 108 (65.45)| 57 (34.55) |              |        |
| ≥3                       | 87                | 56 (64.37) | 31 (35.63) |              |        |
| Age, years               |                   |            |         |              |        |
| ≤40                      | 80                | 58 (72.50) | 22 (27.50) | 1.084 | 0.910-1.291 | 0.804 |
| 40-50                    | 172               | 126 (73.26)| 46 (26.74) |              |        |
| 50-60                    | 93                | 63 (67.74) | 30 (32.26) |              |        |
| ≥60                      | 57                | 40 (70.18) | 17 (29.82) |              |        |
| Menopause                |                   |            |         |              |        |
| Yes                      | 254               | 167 (65.75)| 87 (34.25) | 0.769 | 0.667-0.887 | 0.001 |
| No                       | 148               | 120 (81.08)| 28 (18.92) |              |        |
| Histological grade       |                   |            |         |              |        |
| I                        | 13                | 10 (76.92) | 3 (23.08) | 0.929 | 0.836-1.033 | 0.768 |
| II                       | 300               | 211 (70.33)| 89 (29.67) |              |        |
| III                      | 89                | 66 (74.16) | 23 (25.84) |              |        |
| ER                       |                   |            |         |              |        |
| Negative                 | 126               | 105 (83.33)| 21 (16.67) | 2.003 | 1.322-3.036 | <0.001 |
| Positive                 | 276               | 182 (65.94)| 94 (34.06) |              |        |
| PR                       |                   |            |         |              |        |
| Negative                 | 150               | 121 (80.67)| 29 (19.33) | 1.672 | 1.187-2.355 | 0.002 |
| Positive                 | 252               | 166 (65.87)| 86 (34.13) |              |        |
| HER2                     |                   |            |         |              |        |
| Negative                 | 263               | 190 (72.24)| 73 (27.76) | 1.043 | 0.887-1.226 | 0.604 |
| Positive                 | 139               | 97 (69.78) | 42 (30.22) |              |        |
| Ki-67                    |                   |            |         |              |        |
| Negative                 | 79                | 63 (79.75) | 16 (20.25) | 1.578 | 0.953-2.612 | 0.043 |
| Positive                 | 323               | 224 (69.35)| 99 (30.65) |              |        |
| CEUS type                |                   |            |         |              |        |
| I                        | 163               | 159 (97.55)| 4 (2.45)  | 3.531 | 2.534-4.920 | <0.001 |
| II                       | 82                | 68 (82.93)| 14 (17.07) |              |        |
| III                      | 102               | 45 (44.12)| 57 (55.88) |              |        |
| IV                       | 55                | 15 (27.27)| 40 (72.73) |              |        |

P-values indicate differences between SLN-negative and SLN-positive patients with breast cancer. P<0.05 was considered to indicate a statistically significant difference. ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; CEUS, contrast-enhanced ultrasonography; OR, odds ratio; CI, confidence interval.
through a series of related processes, such as endocytosis and exocytosis, and finally gathers in the lymph nodes of the drainage area. Moreover, CEUS has proved to be helpful for the diagnosis of SLN metastasis (31,32). Previous studies have divided the mode of SLN transcutaneous CEUS enhancement into uniform, uneven and no enhancement (32,33). The uniform enhancement is characterized as benign, and the uneven and non-enhancement as malignant. However, this classification method has very low specificity in the diagnosis of SLN metastasis (52‑78%) (32,33). This might be related to the fact that some benign lymph nodes can also show uneven enhancement. Therefore, uneven enhancement cannot be simply diagnosed as a metastatic lymph node. The present study first established the CEUS classification standard based on the CEUS performance of 365 patients with BC in the training set: Completely uniform enhancement (type I), uniform enhancement of the periphery and medulla (type II), uneven enhancement (type III), and no enhancement of the periphery and (or) medulla (type IV).

In both the retrospective training and prospective validation sets, it was found that most patients with SLN-negative BC were classified as type I, followed by type II, and that most patients with SLN-positive BC were classified as type IV, followed by type III. Considering the associations between SLN metastasis and clinical characteristics, pathological type, tumor diameter, age, ER expression, PR expression, Ki‑67 expression and CEUS type were included into the multiple regression analysis. Hence, a simple model was established to predict SLN metastasis in patients with BC, including tumor diameter, menopause, ER expression and CEUS type. In the training and validation sets, the AUCs were 0.899 and 0.826.

Table III. Multivariate analysis of CEUS, clinical features and sentinel lymph node status.

| Variables        | Coefficient | S.E. | Wals  | P-value | OR    | 95% CI       |
|------------------|-------------|------|-------|---------|-------|--------------|
| Pathological type| 1.048       | 0.568| 3.402 | 0.065   | 2.851 | 0.936-8.677 |
| Tumor diameter   | 0.173       | 0.028| 36.805| <0.001  | 1.189 | 1.124-1.257 |
| Age              | -0.062      | 0.022| 2.650 | 0.056   | 0.940 | 0.900-0.982 |
| Menopause        | -4.490      | 0.599| 56.287| <0.001  | 1.011 | 0.603-1.436 |
| ER               | 2.322       | 1.147| 4.099 | 0.043   | 3.199 | 1.077-6.567 |
| PR               | -4.845      | 1.545| 3.838 | 0.062   | 0.008 | 0.000-0.162 |
| Ki-67            | -1.289      | 1.093| 1.390 | 0.238   | 0.276 | 0.032-2.348 |
| CEUS type        | 5.445       | 0.619| 77.484| <0.001  | 10.563| 6.890-28.372 |
| Constant value   | -1.952      | 0.948| 1.009 | 0.315   | 0.386 |              |

ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; CEUS, contrast-enhanced ultrasonography; OR, odds ratio; CI, confidence interval; S.E. standard error; Wals, a χ² value.

Figure 1. ROC curves of the sentinel lymph node status predictive model in (A) the training set and (B) the prospective validation set. AUC, area under the ROC curve; ROC, receiver operating characteristic.
respectively, which suggested that this model had high accuracy in predicting SLN metastasis in patients with BC (34,35). At the same time, the model also had high sensitivity and specificity in diagnosing SLN metastasis in training and validation sets.

However, since the clinical data of the training set was retrospectively analyzed when building the model, invasive tests (CEUS) were included, indicating that the model can not work under non-invasive conditions. Meanwhile, in the retrospective and prospective validation sets, the sensitivity of the model was not high (83.6 and 70.4%, respectively). Nevertheless, a predictive model can be gradually revised as the sample size increases in the future. Overall, in the present study, a model was established to predict SLN metastasis in patients with BC based on tumor diameter, menopausal status, ER expression and CEUS detection. However, one limitation of the present study was that it did not have a test set. In the future, larger scale clinical data in patients with BC, including tumor diameter, menopausal status, ER expression and CEUS detection, could be applied from other studies to evaluate the model. In addition, a nomogram was not constructed for relapse in the patients with BC (36), which makes the results of this study difficult to understand for non-specialists.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Authors’ contributions

JX was responsible for the conception and design of the study. JX and JL performed the experiments, analyzed the data and confirm the authenticity of all the raw data. Both authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Cangzhou Central Hospital Ethics Committee (Cangzhou, China). All patients provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Siegel RL, Miller KD and Jemal A: Cancer statistics, 2020. CA Cancer J Clin 70: 7-30, 2020.
2. Wong IO, Schooling CM, Cowling BJ and Leung GM: Breast cancer incidence and mortality in a transitioning Chinese population: Current and future trends. Br J Cancer 112: 167-170, 2015.
3. Jian W, Shao K, Qin Q, Wang X, Song S and Wang X: Clinical and genetic characterization of hereditary breast cancer in a Chinese population. Hered Cancer Clin Pract 15: 19, 2017.
4. Liao Y, Li D, Zhang N, Xia C, Zheng R, Zeng H, Zhang S, Wang J and Chen W: Application of sandwich spatial estimation method in cancer mapping: A case study for breast cancer mortality in the Chinese mainland, 2005. Stat Methods Med Res 28: 3609-3626, 2019.
5. Wang Z, Bao J, Yu C, Wang J and Li C: Secular trends of breast cancer in China, South Korea, Japan and the United States: Application of the age-period-cohort analysis. Int J Environ Res Public Health 12: 15409-15418, 2015.
6. Zhang Y, Li J, Fan Y, Li X, Qiu J, Zhu M and Li H: Risk factors for axillary lymph node metastases in clinical stage T1-2N0M0 breast cancer patients. Medicine (Baltimore) 98: e17481, 2019.
7. Hennigs A, Riedel F, Felitt M, Köpke M, Rezai M, Nitz U, Moderow M, Golatta M, Söhn C and Heil J: Evolution of the use of completion axillary lymph node dissection in patients with T1/2N0M0 breast cancer and tumour-involved sentinel lymph nodes undergoing mastectomy: A cohort study. Ann Surg Oncol 26: 2435-2443, 2019.
8. Talelamps P, Sanidas E, Christoudoulakis M, Askoxylakis J, Melissas J and Tsiftsis DD: Sealants after axillary lymph node dissection for breast cancer: Good intentions but bad results. Am J Surg 198: 55-58, 2009.
9. Madsen RJ, Esmonde NO, Ramsey KL and Hansen JE: Axillary lymph node dissection is a risk factor for major complications after immediate breast reconstruction. Ann Plast Surg 77: 513-516, 2016.
10. Euscher E: Pathology of sentinel lymph nodes: Historical perspective and current applications in gynecologic cancer. Int J Gynecol Cancer 30: 394-401, 2020.
11. Malter W, Hellmich M, Badian M, Kirn V, Mullmann P and Krämer S: Factors predictive of sentinel lymph node involvement in primary breast cancer. Anticancer Res 38: 3657-3662, 2018.
12. Chen X, He Y, Wang J, Luo L, Fan Z, Li J, Xie Y, Wang T and Ouyang T: Feasibility of using negative ultrasonography results of axillary lymph nodes to predict sentinel lymph node metastasis in breast cancer patients. Cancer Med 7: 3066-3072, 2018 (Epub ahead of print).
13. Liu C, Ding J, Spuhler K, Gao Y, Serrano Sosa M, Moriarty M, Hussain S, He X, Liang C and Huang C: Preoperative prediction of sentinel lymph node metastasis in breast cancer by radiomic signatures from dynamic contrast-enhanced MRI. J Magn Reson Imaging 49: 131-140, 2019.
14. Dong Y, Feng Q, Yang W, Lu Z, Deng C, Zhang L, Lian Z, Liu J, Luo X, Pei S, et al: Preoperative prediction of sentinel lymph node metastasis in breast cancer based on radiomics of T2-weighted fat-suppression and diffusion-weighted MRI. Eur Radiol 28: 582-591, 2018.
15. Visser M, Jiwa M, Horstman A, Brink AA, Pol RP, van Diest P, Snijders PJ and Meijer CJ: Intra-operative rapid diagnostic method based on CK19 mRNA expression for the detection of lymph node metastases in breast cancer. Int J Cancer 122: 2562-2567, 2008.
16. Abe M, Kagara N, Miyake T, Tanei T, Naoi Y, Shimoda M, Shimazu K, Kim SJ and Noguchi S: Highly sensitive detection of sentinel lymph node metastasis of breast cancer by digital PCR for RASSF1A methylation. Oncol Rep 42: 2382-2389, 2019.
17. Gradishar WJ, Anderson BO, Abraham J, Cuzick J, Moller T, et al: Breast cancer, version 3.2020, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 18:452-478, 2020.
20. Li C, Yao M, Shao S, Li X, Li G and Wu R: Diagnostic efficacy of contrast-enhanced ultrasound for breast lesions of different sizes: A comparative study with magnetic resonance imaging. Br J Radiol 93: 20190932, 2020.
21. Chen C, Wang Y, Niu J, Liu X, Li Q and Gong X: Domain knowledge powered deep learning for breast cancer diagnosis based on contrast-enhanced ultrasound videos. IEEE Trans Med Imaging 40: 2439-2451, 2021.
22. Wang L, Li J, Qiao J, Guo X, Bian X, Guo L, Liu Z and Lu Z: Establishment of a model for predicting sentinel lymph node metastasis in early breast cancer based on contrast-enhanced ultrasound and clinicopathological features. Gland Surg 10: 1701-1712, 2021.
23. Poordt IGM, Walstra CJEF, Vugts G, Maaskant-Braat AJG, Voogd AC, Schipper RJ and Nieuwenhuijzen GAP; Sentinel Node And Recurrent Breast Cancer (SNARB) study group: Low risk of development of a regional recurrence after an unsuccessful repeat sentinel lymph node biopsy in patients with ipsilateral breast tumor recurrence. Ann Surg Oncol 26: 2417-2427, 2019.
24. Oaks ZA, Goyal S, Liu Y, Hayes KR, Gupta GP, Patel SA and Royce TJ: Sentinel lymph node biopsy (SLNB) versus axillary lymph node dissection in US women with breast cancer and persistently positive lymph nodes following neoadjuvant chemotherapy. Int J Radiat Oncol Biol Phys 108 (Suppl): e24-e25, 2020.
25. Qiu PE, Liu YB and Wang YS: Internal mammary sentinel lymph node biopsy: Abandon or persist? Onco Targets Ther 9: 3879-3882, 2016.
26. Ugras S, Matsen C, Eaton A, Stempel M, Morrow M and Cody HS III: Reoperative sentinel lymph node biopsy is feasible for locally recurrent breast cancer, but is it worthwhile? Ann Surg Oncol 23: 744-748, 2016.
27. Dasgupta P, Youl PH, Pyke C, Aitken JF and Baade PD: Sentinel node biopsy for early breast cancer in Queensland, Australia, during 2008-2012. ANZ J Surg 88: E400-E405, 2018.
28. Goonawardena J, Yong C and Law M: Use of indocyanine green fluorescence compared to radioisotope for sentinel lymph node biopsy in early-stage breast cancer: Systematic review and meta-analysis. Am J Surg 220: 665-676, 2020.
29. Meattini I, Desideri I, Saieva C, Francolini G, Scotti V, Bonomo P, Greto D, Mangoni M, Nori J, Orzalesi L, et al: Impact of sentinel node tumor burden on outcome of invasive breast cancer patients. Eur J Surg Oncol 40: 1195-1202, 2014.
30. Caudle AS, Yi M, Hoffman KE, Mittendorf EA, Babiera GV, Hwang RF, Meric-Bernstam F, Sahin AA and Hunt KK: Impact of identification of internal mammary sentinel lymph node metastasis in breast cancer patients. Ann Surg Oncol 21: 60-65, 2014.
31. Gkegkes ID and Lavazzo C: Contrast enhanced ultrasound (CEU) using microbubbles for sentinel lymph node biopsy in breast cancer: A systematic review. Acta Chir Belg 115: 212-218, 2015.
32. Zhao J, Zhang J, Zhu QL, Jiang YX, Sun Q, Zhou YD, Wang MQ, Meng ZL and Mao XX: The value of contrast-enhanced ultrasound for sentinel lymph node identification and characterisation in pre-operative breast cancer patients: A prospective study. Eur Radiol 28: 1654-1661, 2018.
33. Xie F, Zhang D, Cheng L, Yu L, Yang L, Tong F, Liu H, Wang S and Wang S: Intradermal microbubbles and contrast-enhanced ultrasound (CEUS) is a feasible approach for sentinel lymph node identification in early-stage breast cancer. World J Surg Oncol 13: 319, 2015.
34. Cook NR: Use and misuse of the receiver operating characteristic curve in risk prediction. Circulation 115: 928-935, 2007.
35. Hajian-Tilaki K: Receiver operating characteristic (ROC) curve analysis for medical diagnostic test evaluation. Caspian J Intern Med 4: 627-635, 2013.
36. Iasonos A, Schrag D, Raj GV and Panageas KS: How to build and interpret a nomogram for cancer prognosis. J Clin Oncol 26: 1364-1370, 2008.