Original Article

The value of microvascular Doppler ultrasound technique, qualitative or quantitative shear-wave elastography of breast lesions for predicting axillary nodal burden in patients with breast cancer

Bin Wang[1#^], Juan Yang[1#], Yu-Long Tang[2], Yu-Yuan Chen[1], Jia Luo[1], Xin-Wu Cui[3], Christoph F. Dietrich[4], Ai-Jiao Yi[1]

[1]Department of Medical Ultrasound, Yueyang Central Hospital, Yueyang, China; [2]Department of Thyroid Surgery, The Second Xiangya Hospital of Central South University, Changsha, China; [3]Department of Medical Ultrasound, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [4]Department Allgemeine Innere Medizin, Kliniken Hirslanden Beau Site, Salem und Permanence, Bern, Switzerland

Contributions: (I) Conception and design: B Wang, AJ Yi, XW Cui; (II) Administrative support: B Wang, AJ Yi; (III) Provision of study materials or patients: J Yang, YY Chen; (IV) Collection and assembly of data: J Yang, J Luo; (V) Data analysis and interpretation: YL Tang, CF Dietrich; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Xin-Wu Cui, MD, PhD. Department of Medical Ultrasound, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, No. 1095, Jiefang Avenue, Wuhan 430030, China. Email: cuixinwu@live.cn; Ai-Jiao Yi, MD. Department of Medical Ultrasound, Yueyang Central Hospital, No. 39 Dongmaoling Road, Yueyang 414000, China. Email: 938186822@163.com.

Background: The status of the axillary lymph node (ALN) in patients with breast cancer can critically inform clinical decision-making and prognosis. Preoperative evaluation of limited nodal burden (0–2 metastatic ALNs) and high nodal burden (≥3 metastatic ALNs) is vital for individual treatment in patients with breast cancer. Thus, this study aimed to evaluate the value of Angio-PLUS (AP; Aixplorer, SuperSonic Imagine) and the qualitative and quantitative shear-wave elastography (SWE) of breast lesions to predict limited or high axillary nodal burden and to develop a model for predicting limited or high axillary nodal burden.

Methods: From March 2020 to November 2022, a total of 232 consecutive patients with breast cancer comprising 232 breast lesions were enrolled retrospectively from Yueyang Central Hospital. The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), accuracy, and area under the receiver operating characteristic curve (AUC) of AP, qualitative SWE, quantitative SWE, and the predictive model for evaluating limited or high axillary nodal burden were compared.

Results: There was no significant difference in AP patterns between the limited nodal burden group and high nodal burden group. The best cutoff values of Emin (the minimal value of the first Q-box), Emean (the mean value of the first Q-box), Emax (the maximum value of the first Q-box), Eratio (ratio of the first Q-Box and the second Q-Box) and standard deviation for predicting limited or high nodal burden were 80.85 KPa, 133.45 KPa, 153.40 KPa, 9.95, and 19.25 KPa, respectively. The Emax had the highest AUC, and its sensitivity, specificity, PPV, NPV, accuracy, and AUC were 71.64%, 56.36%, 40.00%, 83.04%, 60.78%, and 0.640 [95% confidence interval (CI): 0.575–0.702], respectively. The sensitivity, specificity, PPV, NPV, accuracy, and AUC of seven color patterns for qualitative SWE were 71.64%, 74.55%, 53.33%, 86.62%,

^ ORCID: 0000-0002-6296-541X.

73.71%, and 0.731 (95% CI: 0.669–0.787), respectively, which was significantly higher than all the other quantitative SWE parameters. ALN evaluation in ultrasound and qualitative SWE were independent risk factors for predicting limited or high nodal burden according to a binary logistics regression analysis. The AUC of the predictive model based on independent risk factors was 0.820 (95% CI: 0.765–0.867), which was significantly higher than that of the other independent risk factors.

Conclusions: The seven color patterns in the qualitative SWE of breast lesions were valuable for predicting limited or high nodal burden for patients with breast cancer. Compared with quantitative SWE, qualitative SWE exhibited a better diagnostic performance. Breast lesions present no findings, vertical stripes, and spot patterns were important indicators for limited nodal burden. The predictive model developed in this study could be a simple, noninvasive, and convenient method for predicting limited or high nodal burden, which would be beneficial for clinical decision-making and individual treatment to improve prognosis.

Keywords: Angio-PLUS (AP); shear-wave elastography (SWE); breast cancer; axillary lymph node metastasis (ALNM); nodal burden

Submitted Apr 04, 2023. Accepted for publication Oct 19, 2023. Published online Nov 24, 2023.
doi: 10.21037/qims-23-445
View this article at: https://dx.doi.org/10.21037/qims-23-445

Introduction

Breast cancer is the most common cancer in women and causes serious health problems (1). The state of the axillary lymph node (ALN) in patients with breast cancer can help inform clinical decision-making and prognosis (2). In the American College of Surgeons Oncology Group Z0011 (ACOSOG Z0011) randomized clinical trial (3), 10 years of follow-up indicated no worse local control, disease-free survival, or overall survival in women with elimination of ALN dissection (ALND) who had 1 or 2 metastatic sentinel nodes and clinical T1 or T2 tumors receiving lumpectomy with whole-breast irradiation and systemic therapy. Thus, preoperative evaluation of limited nodal burden (0–2 metastatic ALNs) and high nodal burden (≥3 metastatic ALNs) is vital for individual treatment in patients with breast cancer.

Ultrasound is a noninvasive, convenient, and nonradioactive method for evaluating ALN status; however, the pooled sensitivity and specificity for predicting axillary nodal burden have been reported to be only 66% and 73%, respectively (4), which is unsatisfactory for clinical work.

Elastography is a useful ultrasonic technique, which can quantitatively and qualitatively evaluate tissue stiffness and improve the diagnostic performance in differentiating benign from malignant breast lesions (5). According to the type of compressing force applied, elastography can be classified as stain elastography (SE) and shear-wave elastography (SWE). A previous study reported that SE could be a supplementary method in predict ALN metastasis (ALNM) in patients with breast cancer (6). However, a high dependence on operators and lack of quantitative measurements remain the major limitations of SE.

SWE can quantitatively and qualitatively evaluate the stiffness of breast lesions, which has generally been considered to be a more reproducible and objective method. Some studies found that quantitative SWE parameters were useful for predicting ANLM and high nodal burden (7,8). However, the optimal cutoff values for different quantitative SWE parameters and the best quantitative parameters varied across these studies. Qualitative SWE is helpful for differentiating between benign and malignant breast lesions (9,10); however, to the best of our knowledge, no studies have reported on the associations between qualitative SWE and limited or high nodal burden.

Angio-PLUS (AP) is a novel microvascular Doppler ultrasound technique (Aixplorer, SuperSonic Imagine, Aix-en-Provence, France), which can detect more microvessels as compared with classical color Doppler flow imaging (CDFI) (11). The morphologic and distribution of vascularity in AP differ between benign and malignant breast lesions (10).

Limited or high nodal burden is difficult to evaluate under the use of conventional ultrasound alone, but use of AP, qualitative SWE, and quantitative SWE of breast lesions could be a supplementary method for predicting limited or high nodal burden. To evaluate the value of AP, qualitative SWE, and quantitative SWE in predicting limited or high axillary nodal burden of breast lesions, we attempted to compare the diagnostic performance of AP, quantitative SWE, and qualitative SWE in predicting limited and high nodal burden in patients with breast cancer and to develop a model for predicting axillary nodal burden for surgeons and patients. We present this article in accordance with the STARD reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-445/rc).

Methods

Patients

From March 2020 to November 2022, a total of 232 consecutive patients with breast cancer comprising 232 breast lesions were retrospectively enrolled from Yueyang Central Hospital. The inclusion criteria were as follows: (I) patients over the age of 18 years; (II) pathological results of all breast lesions confirmed as breast cancer via surgery; (III) and B-mode ultrasound (BMUS), AP, quantitative SWE, and qualitative SWE examinations applied to all breast lesions. The exclusion criteria were listed as follows: (I) breast lesions with unclear or indeterminate pathological results and (II) patients who had received previously invasive examinations or therapies, including biopsies or neoadjuvant chemotherapy. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The medical ethics committee of the Yueyang Central Hospital approved the study and waived the requirement for written informed consent due to the retrospective nature of its design.

Ultrasound examinations

An Aixplorer ultrasound system (SuperSonic Imagine) was used in this study. BMUS, AP, and SWE examinations were performed with a L15-4 or L10-5 linear array transducer.

BMUS examinations

For BMUS examinations, the patients were placed in a supine position with the breast fully exposed. Suspicious breast lesions were evaluated based on the BMUS features of the 2013 edition of the Breast Imaging Reporting and Data System (BI-RADS) (12), which includes shape, margin, orientation, echo pattern, and calcification. All breast lesions were classified as BI-RADS category 3 (probably benign), 4a (low suspicion for malignancy), 4b (moderate suspicion for malignancy), 4c (high suspicion for malignancy), or 5 (highly suggestive of malignancy).

AP examinations

For the AP examinations, all breast lesions were dynamically scanned with the AP to observe the richest and most typical vascularity. The color velocity scale was adjusted to 4 to 6 cm/s, with color gain settings adjusted suitably, until the background noise was suppressed. To obtain satisfactory AP images, as slight as possible pressure was applied on the breast, and the patients were asked to hold their breath for several seconds while the AP examinations were performed.

SWE examinations

SWE examinations were performed by the transducer with as slight as possible pressure as possible. SWE was conducted according to standard recommendations. The sampling frame included the entire breast lesion and surrounding normal tissue. The stiffness range of the color map was 0–180 KPa (blue to red). The quantitative SWE measurement of the breast lesions and surrounding normal tissue were obtained via the region of interest (ROI) with Q-Box. The first Q-Box, 2×2 mm^2 in size, was placed in the hardest part of breast lesions, and Emin (the minimal value of the first Q-box), Emean (the mean value of the first Q-box), Emax (the maximum value of the first Q-box), and standard deviation (SD) were obtained automatically. The second Q-Box with the same size was placed in the surrounding normal breast tissue as a comparison. The Eratio was defined as the ratio of the first Q-Box and the second Q-Box, which could be calculated automatically with the ultrasound system.

Imaging analysis

Two radiologists who had approximately 5 years of experience in breast ultrasound with AP and SWE, analyzed the images while being blinded to the final surgical pathological results. When there were different opinions, a third radiologist evaluated the breast lesions to reach a consensus. The final surgical pathology evaluation was regarded as the gold standard.

We classified vascular morphology and distribution features in the AP of breast lesions into the five following patterns (10): (I) nonvascular pattern, characterized by a lack of blood vessels inside the breast lesion; (II) linear or curvilinear pattern, characterized by a single or few straight or slight curved vessels without crossing inside the breast lesion; (III) tree-like pattern, characterized by proportioned microvessels branching inside the breast lesion; (IV) root hair-like pattern, characterized by a twist and chaotic arrangement with irregular vessels dominating the breast lesion and fewer than two enlarged and twisted vessels around the breast lesion; and (V) crab claw-like pattern, characterized by radial vessels, with small speculated vessels commonly seen around the breast lesion.

The qualitative SWE features of breast lesions were classified into the seven following patterns (9): (I) no findings, in which there was no change in the hue around the lesion at the margin or inside the lesion (homogeneously blue); (II) vertical stripe pattern, in which color could seen at the breast lesion's margin or inside the lesion that differed from the color around the lesion, with a different color extending beyond the lesion and continuing vertically in cords on the cutaneous side and/or the thoracic wall; (III) spot pattern, in which there were colored areas above and/or below the breast lesion; (IV) rim of stiffness pattern, in which a localized colored area was present at the breast lesion's margin, appearing as a continuous closed circle, with a less than 25% lack of SWE signal inside the breast lesions; (V) colored lesion pattern, in which there were heterogeneously colored areas inside the lesion; (VI) void center pattern, in which the SWE signal was lacking inside the breast lesion, with the rest of the SWE box being filled normally; and (VII) horseshoe pattern, in which a localized colored area was present at the breast lesion's margin, appearing as an open circle, with a less than 25% lack of SWE signal inside the breast lesions.

Statistical analysis

Statistics analysis was performed using MedCalc software 19.4 (MedCalc Software, Ostend, Belgium) and SPSS 23.0 (IBM Corp., Armonk, NY, USA). We used the mean and SDs for quantitative variables and the chi-squared or Fisher exact tests for categorical variables. A receiver operating characteristic (ROC) curve was drawn for predicting limited and high nodal burden based on the quantitative SWE parameters of each breast lesion. The optimal cutoff value was calculated with the Youden index (maximum of sensitivity + specificity − 1). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and area under the receiver operating characteristic curve (AUC) of BMUS, AP, qualitative SWE, quantitative SWE, and the predictive model were evaluated and compared. A P value of <0.05 was considered statistically significant.

Results

Of the 232 enrolled breast lesions, 165 (71.1%) were confirmed to have a limited nodal burden, including 133 (57.3%) with negative for ALNM and 32 (13.8%) with 1 or 2 ALNMs. Moreover, 67 (28.9%) breast lesions were confirmed to have high nodal burden (*Figure 1*). All patients were divided into a limited nodal burden group and a high nodal burden group. The general information of patients, BMUS features of breast lesions, and ALN evaluation in ultrasound are listed in *Table 1*. There were significant differences in tumor size, margin, and ALN evaluation in ultrasound between the limited nodal burden group and the high nodal burden group, while there was no significant difference in the other general information and BMUS features between the limited nodal burden group and the high nodal burden group.

Comparison of the AP, qualitative SWE, and quantitative SWE between the limited nodal burden group and high nodal burden group

There was no significant difference in AP patterns between the limited nodal burden group and high nodal burden group, while qualitative SWE and quantitative SWE were significantly different between the limited nodal burden group and high nodal burden group. Moreover, all breast lesions with no findings, with spot pattern, or with vertical stripes were considered to be limited nodal burden (*Table 2*).

Diagnostic performance of qualitative SWE for predicting limited and high nodal burden

The diagnostic criteria of qualitative SWE for predicting limited and high nodal burden are listed as follows: when breast lesions only manifested one of the seven color patterns, including no finding, spot pattern, vertical stripes, stiffness pattern, colored lesion pattern, void center pattern, or horseshoe pattern, they were regarded as limited nodal burden; when breast lesions manifested a combination of two patterns, including rim of stiffness pattern, colored lesion pattern, void center pattern, or horseshoe pattern, they were regarded as high nodal burden, and the sensitivity, specificity, PPV, NPV, accuracy and AUC were

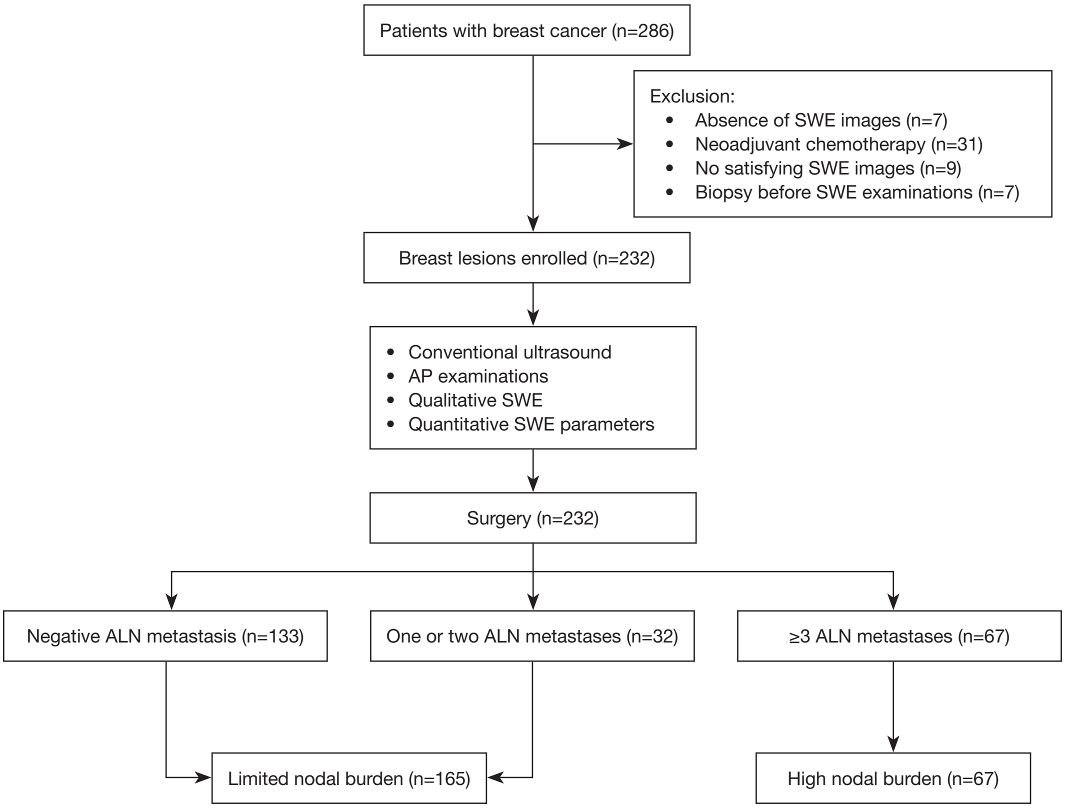

Figure 1 The flowchart of this study. SWE, shear-wave elastography; AP, Angio-PLUS; ALN, axillary lymph node.

Table 1 General information and conventional ultrasound features of breast lesions

Characteristic	Limited nodal burden (0–2 metastatic ALNs) (n=165)	High nodal burden (≥3 metastatic ALNs) (n=67)	χ^2	P
Age (years)				
Range 1				
<50	73	31	0.709	0.779
≥50	92	36		
Range 2				
<40	26	9	0.201	0.654
≥40	139	58		
Left/right breast				
Left	94	41	0.350	0.554
Right	71	26		

Table 1 *(continued)*

Table 1 *(continued)*

Characteristic	Limited nodal burden (0–2 metastatic ALNs) (n=165)	High nodal burden (≥3 metastatic ALNs) (n=67)	χ^2	P
Location				
Upper outer quadrant	97	44	–	0.614
Lower outer quadrant	17	8		
Lower inner quadrant	11	4		
Upper inner quadrant	39	10		
Posterior papilla	1	1		
Size				
<20 mm	73	18	6.036	0.014
≥20 mm	92	49		
Depth				
<10 mm	138	50	2.517	0.113
≥10 mm	27	17		
Shape				
Oval or round	16	6	0.031	0.861
Irregular	149	61		
Orientation				
Parallel	118	55	2.810	0.094
Not parallel	47	12		
Margin				
Circumscribed	79	21	5.313	0.021
Indistinct, angular, microlobulated, or spiculated	86	46		
Calcification				
Absence	101	40	0.046	0.831
Presence	64	27		
Echo pattern				
Solid	158	67	–	0.197
Complex cystic and solid	7	0		
Mass/non-mass-like lesions				
Mass	140	61	1.580	0.209
Non-mass-like	25	6		
ALN evaluation in US				
Negative	102	20	19.53	<0.001
Positive	63	47		

ALN, axillary lymph node; US, ultrasound.

Table 2 Comparison of AP, qualitative SWE, and quantitative SWE between the limited nodal burden group and high nodal burden group

Variables	Limited nodal burden (0–2 metastatic ALNs) (n=165)	High nodal burden (≥3 metastatic ALNs) (n=67)	P
AP			
Non-vascular pattern	7	1	0.812
Linear or curvilinear pattern	53	22	
Tree-like pattern	1	0	
A root hair-like pattern	22	7	
A crab claw-like pattern	82	37	
Qualitative SWE			
No finding	8	0	<0.001
Spot pattern	1	0	
Vertical stripes pattern	7	0	
Void center pattern	9	4	
Horseshoe pattern	15	2	
Rim of stiffness pattern	36	3	
Colored lesion pattern	47	10	
Combination of 2 patterns	42	48	
Quantitative SWE			
Emin (KPa)	54.44±46.86	70.61±53.70	0.023
Emean (KPa)	107.14±64.13	146.93±68.38	<0.001
Emax (KPa)	148.73±82.79	198.63±81.33	<0.001
Eratio	9.31±7.20	13.60±11.22	0.001
SD (KPa)	23.82±17.69	33.40±19.87	<0.001

Quantitative variables are expressed as the mean ± SD, while qualitative variables are expressed as frequencies. AP, Angio-PLUS; SWE, shear-wave elastography; ALN, axillary lymph node; Emin, the minimal value of the first Q-box; Emean, the mean value of the first Q-box; Emax, the maximum value of the first Q-box; Eratio, ratio of the first Q-Box and the second Q-Box; SD, standard deviation.

71.64%, 74.55%, 53.33%, 86.62%, 73.71%, and 0.731 [95% confidence interval (CI): 0.669–0.787], respectively (*Table 3*).

Diagnostic performance of quantitative SWE for predicting limited and high nodal burden

The best cutoff values of Emin, Eman, Emax, Eratio, and SD for predicting limited or high nodal burden were 80.85 KPa, 133.45 KPa, 153.40 KPa, 9.95, and 19.25 KPa, respectively. The diagnostic performance of all quantitative parameters are shown in *Table 3*. The Emax had the highest AUC, and its sensitivity, specificity, PPV, NPV, accuracy, and AUC were 71.64%, 56.36%, 40.00%, 83.04%, 60.78%, and 0.640 (95% CI: 0.575–0.702), respectively. However, there was no significant difference among Emin, Eman, Emax, Eratio, or SD for predicting limited or high nodal burden.

Comparison of diagnostic performance between qualitative and quantitative SWE for predicting limited and high nodal burden

Compared with all quantitative SWE parameters for predicting limited or high nodal burden, qualitative SWE had better diagnostic performance. When breast lesions manifested no findings, spot pattern, or vertical stripes, the patients had limited nodal burden, which was an important indicator for predicting limited nodal burden (*Figure 2*). When breast lesions manifested the rim of stiffness pattern, colored lesion pattern, void center pattern, or

Table 3 Comparison of the diagnostic performance between qualitative and quantitative SWE for predicting limited and high nodal burden

Variable	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC (95% CI)	P*
Qualitative SWE							
1 of 7 color patterns *vs.* Combination of 2 malignant patterns	71.64%	74.55%	53.33%	86.62%	73.71%	0.731 (0.669–0.787)	–
Quantitative SWE							
Emin (<80.85 *vs.*≥80.85 KPa)	44.78%	75.76%	42.86%	77.16%	66.84%	0.603 (0.537–0.666)	0.005
Emean (<133.45 *vs.*≥133.45 KPa)	56.72%	69.70%	43.18%	79.86%	65.95%	0.632 (0.566–0.694)	0.015
Emax (<153.40 *vs.*≥153.40 KPa)	71.64%	56.36%	40.00%	83.04%	60.78%	0.640 (0.575–0.702)	0.021
Eratio (<9.95 *vs.*≥9.95)	59.70%	66.67%	42.11%	80.29%	64.66%	0.632 (0.566–0.694)	0.019
SD (<19.25 *vs.* ≥19.25 KPa)	74.63%	47.27%	36.50%	82.11%	55.17%	0.609 (0.543–0.673)	0.002

*, comparison of diagnostic performance between qualitative SWE and all quantitative SWE parameters. SWE, shear-wave elastography; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the receiver operating characteristic curve; CI, confidence interval; Emin, the minimal value of the first Q-box; Emean, the mean value of the first Q-box; Emax, the maximum value of the first Q-box; Eratio, ratio of the first Q-Box and the second Q-Box; SD, standard deviation.

horseshoe pattern, 84.92% (107/126) of these patients had limited nodal burden. When breast lesions manifested a combination of two patterns, including rim of stiffness pattern, colored lesion pattern, void center pattern, or horseshoe pattern, the percentage of high nodal burden was significantly increased, reaching 53.33% (48/90) (*Figure 3*).

Multivariate analysis of general information, BMUS features, and SWE for predicting limited and high nodal burden

Based on the univariate analysis of general information as well as the BMUS, qualitative SWE, and quantitative SWE findings between the limited nodal burden group and high nodal burden group, size, margin, ALN evaluation in ultrasound, qualitative SWE patterns, and quantitative SWE parameters were found to be significantly different between the limited nodal burden group and high nodal burden group. According to the binary logistics regression analysis, ALN evaluation in ultrasound and qualitative SWE were independent risk factors for predicting limited or high nodal burden (*Table 4*). The following predictive model was constructed based on binary logistics regression analysis: Logit (P) = −5.409 + 1.908 × ALN evaluation in ultrasound + 2.377 × qualitative SWE.

Comparison of diagnostic performance between independent risk factors and predictive model

ROC analysis was performed to evaluate the independent risk factors and the predictive model. The AUC of the predictive model was 0.820 (95% CI: 0.765–0.867) (*Table 5*), which was significantly higher than that of the other independent risk factors (*Figure 4*).

Discussion

Our study found the seven color patterns of qualitative SWE were useful for predicting limited and high nodal burden. Compared with all the quantitative SWE parameters, qualitative SWE had better diagnostic performance. Breast lesions that manifested no finding, spots pattern, or vertical stripes were important indicators for predicting limited nodal burden, with an accuracy of 100% in this study. Moreover, a predictive model was established for predicting limited or high nodal burden in patients with breast cancer. The model had the best AUC (0.820; 95% CI: 0.765–0.867) compared with using qualitative SWE or ALN evaluation in the use of ultrasound alone.

The ALNM status of breast cancer is important for clinical decision-making and prognosis of patients. Conventional ultrasound evaluation of ALN is mainly based on the aspect ratio, absence of fat gates, heterogeneous cortical thickening, and peripheral or mixed blood flow type (13,14), but previous studies (15-17) have reported conventional ultrasound to be insufficient for the preoperative evaluation of ALNM, with the sensitivity ranging from 35% to 82% and the specificity ranging from 73% to 97.9%. The sensitivity and specificity for predicting high nodal burden in this study were 70.15% and 61.82%,

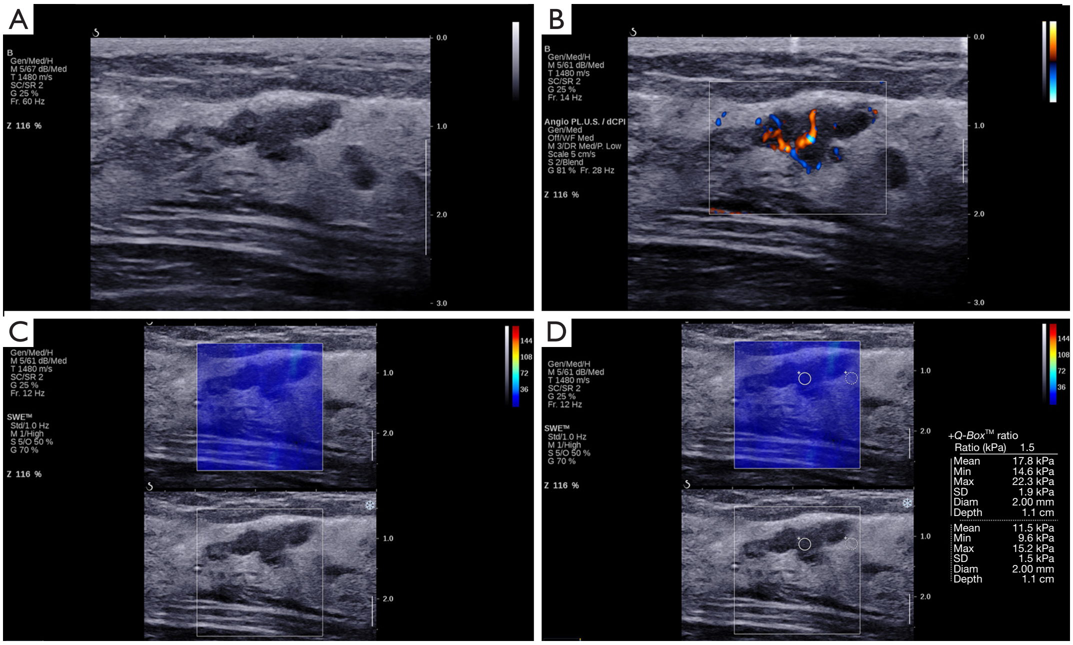

Figure 2 A 44-year-old woman with breast lesion in left breast. The pathology of this breast lesion was high-grade ductal carcinoma *in situ* combined with invasive ductal carcinoma. The final surgical pathology indicated negative lymph node metastasis in the axilla. (A) Conventional ultrasound revealed a 16 mm × 7 mm irregular, hypoechoic lesion, which was categorized as BI-RADS 4a. (B) The morphologic and distribution of vascularity in AP was a linear pattern. (C) Qualitative SWE patterns: no findings. (D) The Emin, Emean, Emax, SD, and Eratio were 14.5 KPa, 17.8 KPa, 22.3 KPa, 1.9 KPa, and 1.5, respectively. Qualitative SWE predicted negative lymph node metastasis in the axilla. The snowflake symbols represent the freeze of SWE examination. The solid line circle represents the first Q-box, and the dashed line circle represents the second Q-box. SWE, shear-wave elastography; dCPI, direction color power imaging; SD, standard deviation; BI-RADS, Breast Imaging Reporting and Data System; AP, Angio-PLUS; Emin, the minimal value of the first Q-box; Emean, the mean value of the first Q-box; Emax, the maximum value of the first Q-box; Eratio, ratio of the first Q-Box and the second Q-Box.

respectively, which was consistent with previous research. Thus, using conventional ultrasound alone to evaluate limited or high nodal was unsatisfactory.

In recent years, some studies have examined the value of quantitative SWE and qualitative SWE for evaluating the prognosis of patients with breast cancer. For example, Ventura *et al.* (18) found that quantitative SWE and qualitative SWE had good reproducibility in different operators with various experience and could be promising methods for noninvasively evaluating the prognosis of patients with breast cancer.

Several studies have focused on the prediction of negative or positive ALNM with quantitative SWE in patients with breast cancer. Evans *et al.* (8) reported that mean stiffness on SWE was an independent risk factor for predicting ALNM in women with invasive breast cancer. Wen *et al.* (19) found Emax showed the best diagnostic performance for predicting ALNM among all quantitative SWE parameters, with the optimal cutoff value of Emax being higher than 111.05 KPa yielding an AUC of 0.85. Jiang *et al.* (20) reported that Eratio had the best diagnostic performance among quantitative SWE parameters for diagnosing ALNM and yielded an AUC of 0.845, with an optimal cutoff value of an Eratio higher than 3.9. The best quantitative SWE parameters and the optimal cutoff values for predicting ALNM vary across different studies, which might be related to sample size of enrolled patients, method of quantitative measurement, and operator variability.

Li *et al.* (7) reported that the Emax, Emean, and SD of breast lesions were significantly higher a high nodal burden group compared with a limited nodal burden group, and when the optimal cutoff values of 119.52 KPa for Emax, 97.31 KPa for Emean, and 19.38 KPa for SD were used, the AUCs for predicting high nodal burden were 0.642, 0.635, and 0.646, respectively. In this study, the best cutoff values of all quantitative SWE parameters for predicting high nodal burden

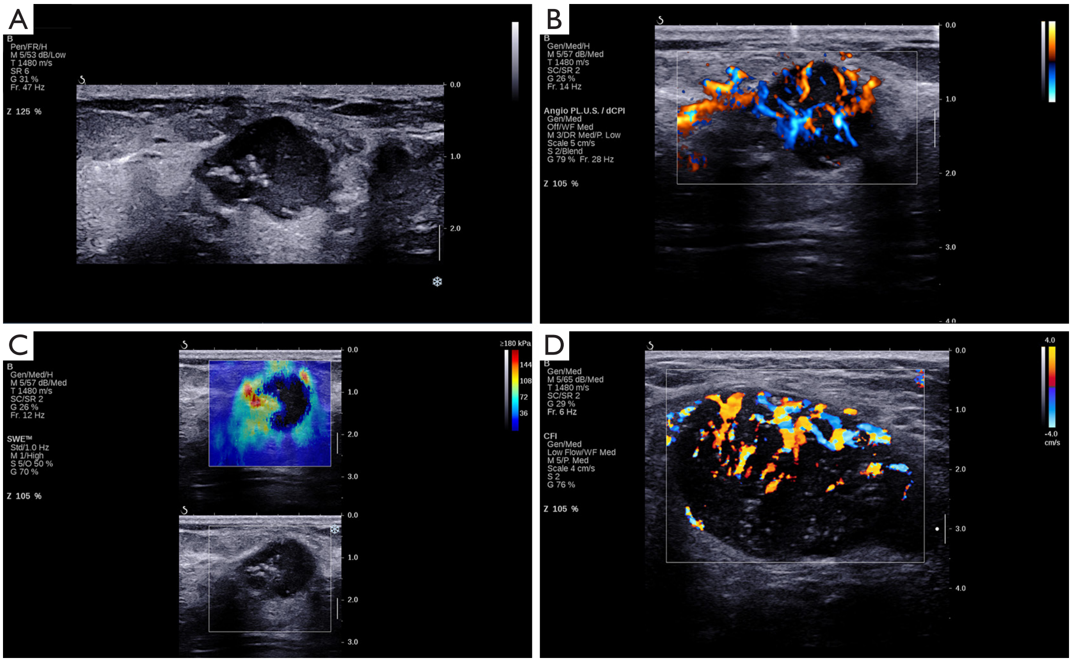

Figure 3 A 46-year-old woman with breast lesions in the left breast. The pathology of this breast lesion was invasive ductal carcinoma (grade 3). The final surgical pathology indicated 4 lymph node metastases in the axilla. (A) Conventional ultrasound revealed a 20 mm × 15 mm irregular, hypoechoic lesion, with scattered calcifications inside the breast lesion, which was categorized as BI-RADS 4c. (B) The morphologic and distribution of vascularity in AP was a crab claw-like pattern. (C) Qualitative SWE patterns: rim of stiffness pattern and void center pattern. Qualitative SWE predicted high nodal burden in the axilla. (D) The axillary lymph node had an aspect ratio >2, absence of fat gates, heterogeneous cortical thickening, scattered calcifications, and peripheral blood flow type, which was considered indicative of axillary lymph node metastasis. The snowflake symbols represent the freeze of SWE examination. SWE, shear-wave elastography; dCPI, direction color power imaging; CFI, color flow imaging; BI-RADS, Breast Imaging Reporting and Data System; AP, Angio-PLUS.

Table 4 Multivariate analysis of general information, BMUS features, and ALN evaluation in US and SWE for predicting limited and high nodal burden

Intercept and variable	Predictive model		
	β	Odds ratio (95% CI)	P
Intercept	−5.409	–	–
Qualitative SWE	2.377	10.774 (5.141–22.579)	<0.001
ALN evaluation in US	1.908	6.740 (3.138–14.479)	<0.001

BMUS, B-mode ultrasound; ALN, axillary lymph node; US, ultrasound; SWE, shear-wave elastography; CI, confidence interval.

Table 5 The AUC of independent risk factors and the predictive model

Variables	AUC	95% CI	P*
Predictive model	0.820	0.765–0.867	–
Qualitative SWE	0.731	0.669–0.787	<0.001
ALN evaluation in US	0.660	0.595–0.721	<0.001

*, comparison of diagnostic performance between the predictive model and qualitative SWE for axillary lymph node evaluation in ultrasound. AUC, area under the receiver operating characteristic curve; CI, confidence interval; SWE, shear-wave elastography; ALN, axillary lymph node; US, ultrasound.

were 80.85 KPa for Emin, 133.45 KPa for Emean, 153.40 KPa for Emax, 9.95 for Eratio, and 19.25 KPa for SD. However, the AUC of all quantitative SWE parameters ranged from 0.603 to 0.640, which was poor and consistent with that of a previous study (7). Thus, a more effective method to predict limited or high nodal burden needs to be developed.

Qualitative SWE for the differentiation between benign and malignant breast masses has been widely studied. Lin *et al.* (9) proposed seven color patterns for discriminating benign from malignant breast lesions, with benign breast

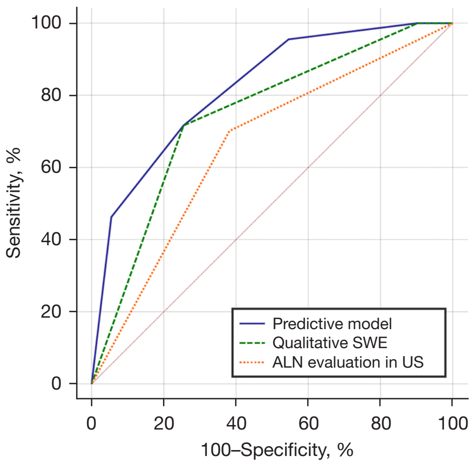

Figure 4 ROC of independent risk factors and the predictive model. SWE, shear-wave elastography; ALN, axillary lymph node; US, ultrasound; ROC, receiver operating characteristic.

lesions always presenting no findings, vertical stripes, or spot pattern and malignant breast lesions mainly presenting rim of stiffness pattern, colored lesion pattern, void center pattern, or horseshoe pattern (10). However, few studies have investigated the value of qualitative SWE in predicting limited or high nodal burden. In this study, breast lesions with limited nodal burden mainly presented one pattern of seven color patterns, while the percentage of high nodal burden was increased in breast lesions presenting a combination of two malignant patterns. Moreover, when breast lesions presented no findings, spot patterns, or vertical stripes in qualitative SWE, all patients (n=16) had a limited nodal burden: one of these patients had one ALNM, and 15 were negative for ALNM. The possible reasons for this might be related to the low stiffness in the tumor and peritumoral tissue, which is indicative of a low degree of breast lesion invasion. Thus, breast lesions presenting no findings, spot pattern, or vertical stripe pattern in qualitative SWE could be an important indicator for predicting limited nodal burden.

When breast lesions presented a combination of two malignant SWE patterns, including void center pattern, rim of stiffness pattern, and horseshoe pattern, the rate of high nodal burden was 53.33%. The rim of stiffness pattern and horseshoe pattern reflect a high degree of stiffness in the peritumoral tissue, indicating peritumoral invasion of breast lesions, which is related to the spreading and ALNM of breast cancer (21). Moreover, void center pattern presents a lack of SWE signal inside the lesion, which might be related to the rapid growth of the tumor with liquefaction of a necrotic lesion inside the tumor or dense collagen deposition around the tumor causing severe attenuation of shear-wave signal, all features which could indicate a high degree of invasion and high nodal burden.

Compared with quantitative SWE parameters, qualitative SWE had better diagnostic performance for predicting limited or high nodal burden, especially for those breast lesions present no findings, spot pattern, or vertical stripes, with an accuracy of 100% for predicting limited nodal burden.

According to the binary logistic regression analysis of general information, conventional ultrasound features, and SWE, a predictive model was established for predicting limited or high nodal burden in patients with breast cancer. The model had best AUC (0.820; 95% CI: 0.765–0.867) compared with qualitative SWE and axillary evaluation in ultrasound. This predictive model may thus serve as a noninvasive, convenient, and simple method for predicting limited or high nodal burden in clinical practice.

There were several limitations in this study. First, we employed a retrospective design, which involved some inevitable bias. Second, the sample size was not large, and multicenter studies with large samples should be performed in the future. Third, the time span of the study was short, and the pathological types of breast lesions might have been limited.

Conclusions

Qualitative SWE of breast lesions was useful for predicting limited or high nodal burden for patients with breast cancer. Compared with quantitative SWE, qualitative SWE had better diagnostic performance. Breast lesions presenting no findings, vertical stripes, and spot pattern were important indicators for limited nodal burden. A predictive model developed in this study could be a noninvasive, simple, and convenient method for predicting limited or high nodal burden, which would be beneficial to clinical decision-making and the individual treatment for improving prognosis.

Acknowledgments

Funding: This work was supported by the National Natural Science Foundation of China (Nos. 82071953 and 21878237), the Science and Technology Department of Hunan Province (No. 2020SK52705), and the General Funding Project of Hunan Provincial Health Commission

(No. B202309029532).

Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-23-445/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-445/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The medical ethics committee of the Yueyang Central Hospital approved the study and waived the requirement for written informed consent due to the retrospective nature of the study.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
2. Park KU, Caudle A. Management of the Axilla in the Patient with Breast Cancer. Surg Clin North Am 2018;98:747-60.
3. Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, Ollila DW, Hansen NM, Whitworth PW, Blumencranz PW, Leitch AM, Saha S, Hunt KK, Morrow M. Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA 2017;318:918-26.
4. Man V, Luk WP, Fung LH, Kwong A. The role of pre-operative axillary ultrasound in assessment of axillary tumor burden in breast cancer patients: a systematic review and meta-analysis. Breast Cancer Res Treat 2022;196:245-54.
5. Săftoiu A, Gilja OH, Sidhu PS, Dietrich CF, Cantisani V, Amy D, et al. The EFSUMB Guidelines and Recommendations for the Clinical Practice of Elastography in Non-Hepatic Applications: Update 2018. Ultraschall Med 2019;40:425-53.
6. Zhao Q, Sun JW, Zhou H, Du LY, Wang XL, Tao L, Jiang ZP, Zhou XL. Erratum to "Preoperative conventional ultrasound and sonoelastography evaluation for predicting axillary lymph node metastasis in patients with malignant breast lesions" Ultrasound Med Biol 44 (2018) 2587-2595. Ultrasound Med Biol 2019;45:2585.
7. Li B, Zhao X, Wang Q, Jing H, Shao H, Zhang L, Cheng W. Prediction of high nodal burden in invasive breast cancer by quantitative shear wave elastography. Quant Imaging Med Surg 2022;12:1336-47.
8. Evans A, Rauchhaus P, Whelehan P, Thomson K, Purdie CA, Jordan LB, Michie CO, Thompson A, Vinnicombe S. Does shear wave ultrasound independently predict axillary lymph node metastasis in women with invasive breast cancer? Breast Cancer Res Treat 2014;143:153-7.
9. Lin X, Chang C, Wu C, Chen Q, Peng Y, Luo B, Tang L, Li J, Zheng J, Zhou R, Cui G, Li A, Wang X, Qian L, Zhang J, Wen C, Gay J, Zhang H, Li A, Chen Y. Confirmed value of shear wave elastography for ultrasound characterization of breast masses using a conservative approach in Chinese women: a large-size prospective multicenter trial. Cancer Manag Res 2018;10:4447-58.
10. Wang B, Chen YY, Yang S, Chen ZW, Luo J, Cui XW, Dietrich CF, Yi AJ. Combined Use of Shear Wave Elastography, Microvascular Doppler Ultrasound Technique, and BI-RADS for the Differentiation of Benign and Malignant Breast Masses. Front Oncol 2022;12:906501.
11. Liu H, Liao Q, Wang Y, Hu Y, Zhu Q, Wang L, Liu Q, Li J, Jiang Y. A new tool for diagnosing parathyroid lesions: angio plus ultrasound imaging. J Thorac Dis 2019;11:4829-34.
12. D'Orsi CJ, Sickles EA, Mendelson EB. ACR BI-RADS Atlas, Breast Imaging Reporting and Data System. Reston, VA, USA: American College of Radiology; 2013.

13. Cheng Y, Li G, Jing H, Yuan S, Zhang L, Cheng W. Effectiveness of Quantitative Shear Wave Elastography for the Prediction of Axillary Lymph Node Metastasis. Evid Based Complement Alternat Med 2022;2022:8769889.
14. Luo C, Lu L, Zhang W, Li X, Zhou P, Ran Z. The Value of Shear Wave Elastography in the Diagnosis of Breast Cancer Axillary Lymph Node Metastasis and Its Correlation With Molecular Classification of Breast Masses. Front Oncol 2022;12:846568.
15. Alkuwari E, Auger M. Accuracy of fine-needle aspiration cytology of axillary lymph nodes in breast cancer patients: a study of 115 cases with cytologic-histologic correlation. Cancer 2008;114:89-93.
16. Balu-Maestro C, Chapellier C, Carrier P, Darcourt J, Ettore F, Raoust I. Role of imaging in the evaluation of axillary nodes and metastatic disease from breast carcinoma. J Radiol 2005;86:1649-57.
17. Sianesi M, Ceci G, Ghirarduzzi A, Del Rio P, Guazzi A, Pisanelli B, Martella E, Ardizzoni A, Di Blasio B, Arcuri MF. Use of axillary ultrasonography in breast cancer: a useful tool to reduce sentinel node procedures. Ann Ital Chir 2009;80:315-8.
18. Ventura C, Baldassarre S, Cerimele F, Pepi L, Marconi E, Ercolani P, Floridi C, Argalia G, Goteri G, Giovagnoni A. 2D shear wave elastography in evaluation of prognostic factors in breast cancer. Radiol Med 2022;127:1221-7.
19. Wen X, Yu X, Tian Y, Liu Z, Cheng W, Li H, Kang J, Wei T, Yuan S, Tian J. Quantitative shear wave elastography in primary invasive breast cancers, based on collagen-S100A4 pathology, indicates axillary lymph node metastasis. Quant Imaging Med Surg 2020;10:624-33.
20. Jiang Y, Wang B, Li JK, Li SY, Niu RL, Fu NQ, Zheng JJ, Liu G, Wang ZL. Collagen fiber features and COL1A1: are they associated with elastic parameters in breast lesions, and can COL1A1 predict axillary lymph node metastasis? BMC Cancer 2022;22:1004.
21. Zhang H, Dong Y, Jia X, Zhang J, Li Z, Chuan Z, et al. Comprehensive Risk System Based on Shear Wave Elastography and BI-RADS Categories in Assessing Axillary Lymph Node Metastasis of Invasive Breast Cancer-A Multicenter Study. Front Oncol 2022;12:830910.

Cite this article as: Wang B, Yang J, Tang YL, Chen YY, Luo J, Cui XW, Dietrich CF, Yi AJ. The value of microvascular Doppler ultrasound technique, qualitative or quantitative shear-wave elastography of breast lesions for predicting axillary nodal burden in patients with breast cancer. Quant Imaging Med Surg 2024;14(1):408-420. doi: 10.21037/qims-23-445

