Original Article

Prediction of axillary nodal burden using preoperative magnetic resonance imaging scoring in patients with clinically node-negative breast cancer: a retrospective cohort study

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Background: Axillary lymph node metastasis (ALNM) is a significant predictor of overall patient survival; thus, precise evaluation of ALNM is essential for staging breast cancer, informing multimodal treatment strategies, and ensuring optimal patient care. This study aimed to establish a magnetic resonance imaging (MRI) scoring system for predicting extensive axillary nodal metastasis in patients with clinically node-negative breast cancer derived from preoperative breast and axillary MRI.

Methods: This study included 226 patients with clinically node-negative breast cancer who underwent preoperative breast and axillary MRI between January 1, 2010 and December 31, 2020 at King Chulalongkorn Memorial Hospital. Their clinical, radiological, and pathological features were retrospectively reviewed. MRI characteristics of breast tumors and axillary lymph nodes (LNs) were assessed. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and Cohen's Kappa coefficient of the scoring system were evaluated. The receiver operating characteristic curve was used to determine the cutoff value for the MRI scoring system to differentiate extensive ALNM from nonextensive ALNM.

Results: Of the 226 patients, 144 had cancer-free axilla, 51 had 1–2 positive metastatic LNs, and 31 had ≥3 positive metastatic LNs. Moreover, only 60 could be evaluated for the apparent diffusion coefficient (ADC) value of LNs because of size limitations. The cutoff value for the MRI scoring system with ADC was 14 (NPV =87.1% with moderately acceptable discrimination), and the cutoff value without ADC was 8 (sensitivity =77.4%; specificity =81%; PPV =39.3%; NPV =95.8% with moderately acceptable discrimination).

Conclusions: The MRI scoring system using breast and axillary LN characteristics from preoperative MRI may help predict extensive ALNM and aid axillary nodal treatment selection.

Keywords: Axillary nodal metastases; breast cancer; magnetic resonance imaging (MRI); diffusion-weighted imaging (DWI); axillary nodal burden

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Introduction

Background

Breast cancer is the most common cancer among women, accounting for 12.5% of all new annual cancer cases worldwide (1). Axillary lymph node metastasis (ALNM) strongly predicts overall patient survival and recurrence; therefore, an accurate assessment of ALNM is crucial in staging breast cancer (2).

Rational and knowledge gap

Since the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial was published, clinical paradigms for axilla treatment have been changed to a less aggressive approach. This trial demonstrated that sentinel lymph node biopsy (SLNB) without axillary lymph node (LN) dissection is appropriate in selected patients with clinically node-negative cancer having 1–2 nodal metastases at SLNB and undergoing breast-conserving surgery (3). Thus, the preoperative assessment of axillary nodal burden is essential to guide multidisciplinary treatment decisions and provide optimal patient treatment (4,5). Currently, there are several methods for assessing axillary nodal burden, such as ultrasound and positron emission tomography/computed tomography (PET/CT) (2,6-8). However, these methods continue to possess constraints. For instance, ultrasound exhibits variable sensitivity and specificity and is dependent on the operator (2), while magnetic resonance imaging (MRI) is a high-resolution imaging technique characterized by high sensitivity and a substantial negative predictive value (NPV), capable of evaluating LNs across all three levels (9-14). Diffusion-weighted imaging (DWI) is a technique that helps improve the identification of ALNM (15-18). However, the individual evaluation of LNs may not be stratified into extensive and nonextensive groups.

Highlight box

Key findings

- The magnetic resonance imaging (MRI) scoring system uses breast and axillary lymph node (LN) characteristics from preoperative MRI and could predict extensive axillary lymph node metastasis (ALNM) and aid axillary nodal treatment selection.

What is known and what is new?

- The preoperative assessment of the axillary nodal burden is essential to guide multidisciplinary treatment decisions and provide optimal patient treatment. However, the individual evaluation of LNs might not be stratified into extensive and nonextensive groups.
- The MRI scoring system based on preoperative breast MRI may help to predict extensive ALNM in patients with clinically node-negative breast cancer.

What is the implication, and what should change now?

- The proposed preoperative MRI scoring system may help identify patients with extensive nodal metastasis in clinically node-negative breast cancer. This could assist clinicians and surgeons in considering less invasive axillary nodal treatment strategies to potentially reduce morbidity.

Objective

This study aimed to establish an MRI scoring system based on preoperative breast MRI to predict extensive ALNM in patients with clinically node-negative breast cancer. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-379/rc).

Methods

Study population

The study was approved by the ethics committee of the Faculty of Medicine, Chulalongkorn University (No. 0878/2022), and the requirement for informed consent was waived because of the retrospective nature of the study and confidentiality obligation on the patient's identity. The study was conducted in accordance with the Declaration of Helsinki (revised in 2013). Information on patients who underwent breast MRI between January 1, 2010 and December 31, 2020 at King Chulalongkorn Memorial Hospital was initially retrieved (n=1,793). The Hospital Information System, Radiological Information System, and Picture Archiving and Communication System (PACS) were used to obtain data. The exclusion criteria were as follows: performing MRI for purposes other than preoperative breast cancer evaluation, final pathology showing no invasive primary breast cancer, unavailable axillary pathological data after MRI examination, palpable ALN, and receiving neoadjuvant chemotherapy or ipsilateral breast/axillary surgery for breast cancer before MRI examination. Finally, 226 patients with invasive primary breast cancer with nonpalpable ALNs were included in this study (*Figure 1*).

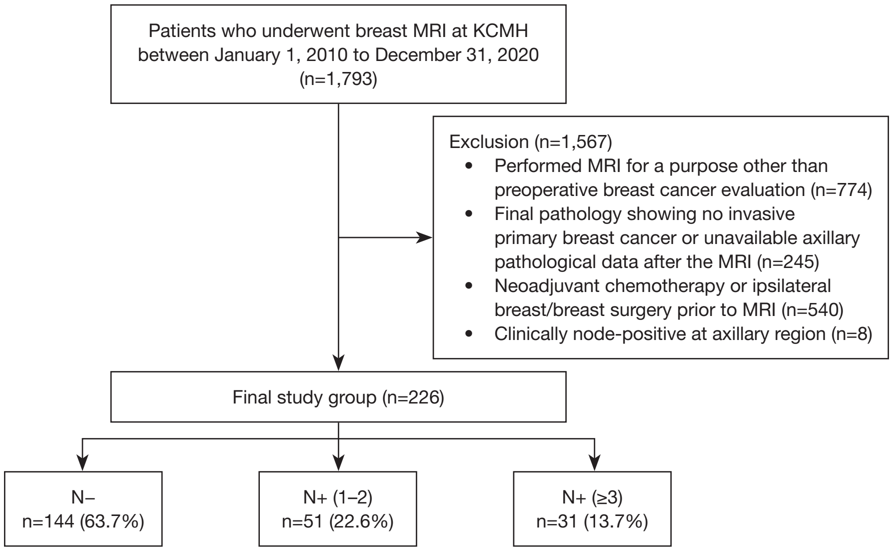

Figure 1 Flowchart of the study population. MRI, magnetic resonance imaging; KCMH, King Chulalongkorn Memorial Hospital; N, number of axillary nodal metastasis.

Table 1 Data collection

Clinical data
• Age
• Family history of breast cancer
• Symptom at presentation
• BRCA status
Radiological data
• Breast tumor: size, margin
• LN: level, number of suspicious LNs, shape, margin, symmetry, cortical morphologic changes (cortical thickness, thickening, SI, enhancement), fatty hilum, short diameter, long-to-short axis ratio, SI on DWI, mean ADC, ADC LN/tumor ratio
Histopathological data
• Staging (T, N)
• Histologic type
• Grade of tumor
• Molecular subtype
• Surgical method

BRCA, breast cancer gene; LN, lymph node; SI, signal intensity; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient; T, tumor size; N, node involvement.

Data collection

Clinical and histopathological data, including age, family history of breast cancer, symptoms at presentation, breast cancer gene (BRCA) status, stage (T, N), histological type, tumor grade, molecular subtype, and surgical methods, were obtained from the medical records and retrospectively reviewed (*Table 1*).

The radiological data were reviewed via the PACS. The MRI images were obtained using a 1.5-Tesla MRI system

Table 2 MRI scoring system

MRI characteristics	Score
Breast tumor size	
≤2 cm	0
>2 to ≤5 cm	1
> 5 cm or chest wall/skin involvement	2
Breast tumor margin	
Circumscribed	0
Spiculate/indistinct	1
Number of suspicious LNs†	
0 node	0
1–2 nodes	1
≥3 nodes	2
LN shape	
Oval	0
Round	1
Irregular	2
LN margin	
Circumscribed	0
Spiculate/indistinct	1
Symmetry of LN	
Symmetry	0
Asymmetry	1
Cortical thickness of LN	
<3 mm	0
≥3 mm	1
Cortical thickening of LN	
Symmetrical	0
Asymmetrical	1
Fatty hilum	
Presence	0
Loss of fatty hilum	1
Cortex signal intensity	
Homogeneous	0
Heterogeneous	1
Short diameter of LN	
<10 mm	0
≥10 mm	1
Long-to-short diameter ratio	
≥2	0
<2	1
LN enhancement	
Homogeneous	0
Rim/heterogeneous	1
Mean ADC value	
>0.904×10^{-3} mm^2/sec‡	0
≤0.904×10^{-3} mm^2/sec	1
ADC ratio (ADC LN/ADC breast lesion)	
>1.097×10^{-3} mm^2/sec§	0
≤1.097×10^{-3} mm^2/sec	1
The signal intensity of LN on DWI	
Low	0
High	1

Table 2 *(continued)*

A previous study (14) demonstrated that breast tumor size and margin, LN SD, LN LD/SD, LN margin, LN hilum, LN symmetry, and cortical thickening are associated with ALNM. †, other previous studies (12,19) revealed that ≥3 suspicious axillary LNs on US/MRI correlated with ≥3 metastatic axillary LNs; ‡, another previous study (15) showed that the cutoff ADC value at 0.904×10^{-3} mm^2/sec resulted in 87.0% sensitivity, 88.9% specificity, and 91.8% accuracy in diagnosing ALNM; §, another previous study (20) demonstrated that the cutoff value at 1.097×10^{-3} mm^2/sec resulted in 84.44% sensitivity, 88.24% specificity, a positive predictive value of 90.48%, a negative predictive value of 81.08%, and 86.08% accuracy in ALNM detection. MRI, magnetic resonance imaging; LNs, lymph nodes; ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; SD, short diameter; LD, long diameter; ALNM, axillary lymph node metastasis; US, ultrasound.

with a dedicated breast coil and intravenous paramagnetic contrast. Apparent diffusion coefficient (ADC) maps were automatically created with b values of 0 and 800. The characteristics of breast tumors and axillary LNs were independently reviewed by two researchers. All clinical and histopathological data were blinded during the review to avoid bias. Any disagreement between the two researchers was resolved by consensus.

The most suspicious LN for metastasis or the largest LN in the ipsilateral axilla was chosen to assess our MRI scoring system's imaging characteristics and score (*Table 2*). Regions

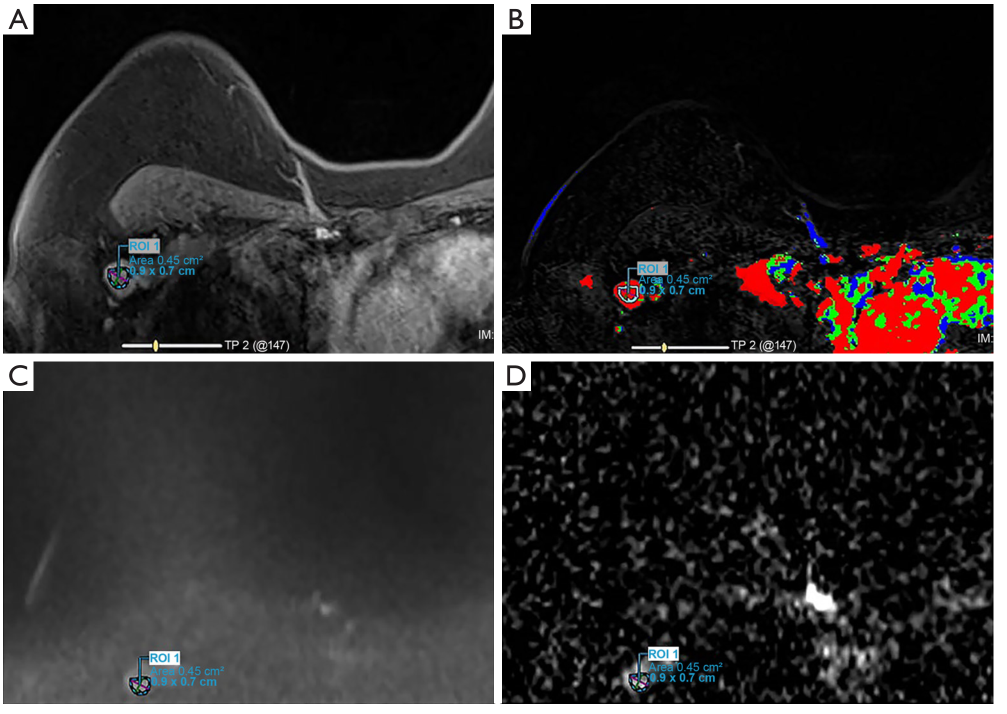

Figure 2 A 50-year-old patient with IDC: (A) contrast-enhanced T1-weighted image, (B) color-coded dynamic contrast material enhanced image, (C) DWI at b =800, and (D) ADC map showing the manually drawn ROI of the largest right axillary node. ROI, region of interest; IDC, invasive ductal carcinoma; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient.

of interest (ROIs) were manually drawn on LNs with a short diameter (SD) >5 mm on axial DWI images (at b value =800 s/mm^2). The ROIs were marked as slightly smaller than the actual size of the nodes/primary breast tumors and included the most considerable solid portion possible. The identified ROIs were then copied and pasted onto the corresponding ADC map for quantitative analysis (*Figure 2*). The ADC values of the axillary LNs were averaged from three measurements. The results are presented as the mean ADC value. The ADC values of the primary breast tumors were also obtained. The ADC LN/tumor ratio was then calculated.

Statistical analysis

All statistical analyses were performed using Statistical Package for the Social Sciences (version 28.0; IBM Corp., Armonk, NY, USA) and STATA. All continuous variables are presented as means and standard deviations. All categorical variables are presented as frequencies and percentages and were analyzed using the chi-square test. P values <0.05 were used to denote statistical significance.

The diagnostic performance of the MRI scoring system for predicting extensive ALNM was evaluated via validity (sensitivity and specificity), efficiency [positive predictive value (PPV) and NPV], and reliability (Cohen's Kappa statistics). The receiver operating characteristic (ROC) curve was drawn, and the area under the ROC curve was used to determine the cutoff value of this MRI scoring system for differentiating between extensive and nonextensive ALNM. Extensive nodal metastasis was defined as ≥3 metastatic nodes. We aimed for the predictions to demonstrate high sensitivity and NPV, confirming that the patients do not have a significant nodal burden. We employed the threshold of approximately 80% for AUC and 90% for sensitivity.

Results

Patients' demographic and pathological characteristics

The patients' characteristics are summarized in *Table 3*. The mean age of the patients was 51.9±10.4 years and ranged from 27 to 81 years. The ALNs were derived from SLNB and axillary LN dissection. Of the 226 enrolled patients, 19 had a positive family history of breast cancer, of whom

Table 3 Baseline patient characteristics

Baseline characteristics	Pathological lymph node status		P value
	Nonextensive node metastasis, n (%)	Extensive node metastasis, n (%)	
Family history of breast cancer			0.75
Negative	178 (91.3)	29 (93.5)	
Positive	17 (8.7)	2 (6.5)	
Symptom at presentation			0.38
Asymptomatic	59 (30.3)	7 (22.6)	
Symptomatic	136 (69.7)	24 (77.4)	
Histologic type			0.29
IDC	163 (83.6)	25 (80.6)	
ILC	16 (8.2)	5 (16.1)	
Others	16 (8.2)	1 (3.2)	
Tumor grade			0.38
Grade 1	35 (17.9)	2 (6.5)	
Grade 2	87 (44.6)	14 (45.2)	
Grade 3	63 (32.3)	13 (41.9)	
Not evaluated	10 (5.1)	2 (6.5)	
Molecular subtype			0.32
Luminal A	48 (24.6)	5 (16.1)	
Luminal B	98 (50.3)	22 (71.0)	
HER2 enriched	24 (12.3)	2 (6.5)	
Triple-negative	24 (12.3)	2 (6.5)	
Not evaluated	1 (0.5)	0 (0.0)	

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2.

2 had extensive nodal metastasis. Of the 195 patients with nonextensive nodal metastasis, 136 (69.7%) had symptoms at presentation, whereas 24 of the 31 patients with extensive nodal metastasis (77.4%) had symptoms at presentation. The most common histological type in the nonextensive and extensive nodal metastasis groups was invasive ductal carcinoma (IDC), accounting for 83.6% and 80.6%, respectively. The frequency of tumor grades in the nonextensive and extensive nodal metastasis groups was sorted in descending order as follows: grade 2, grade 3, and grade 1. Of the 195 patients with nonextensive nodal metastasis, 98 (50.3%) were luminal B, 48 (24.6%) were luminal A, 24 (12.3%) were HER2-enriched, and 24 (12.3%) were triple-negative molecular subtype.

Patients' MRI characteristics

Table 4 shows the MRI characteristics of the axillary LNs and primary breast tumors in the nonextensive and extensive nodal metastasis groups. Of the 195 patients with nonextensive nodal metastasis, 75.4% showed no suspicious LN on MRI, 21.0% showed 1–2 questionable LNs, and 3.6% had ≥3 suspicious LNs, whereas of the 31 patients with extensive nodal metastasis, 48.4% had ≥3 suspicious LNs, 29.0% had 1–2 suspicious LNs, and 22.6% showed no suspicious LNs. The circumscribed margin was the most common in the nonextensive and extensive nodal metastasis groups (94.9% *vs.* 61.3%, respectively). The number, shape, and margin of axillary LNs are significant

Table 4 Axillary node and primary breast tumor MRI characteristics in nonextensive and extensive nodal metastasis patients

MRI characteristics	Pathological LN status		P value
	Nonextensive node metastasis, n (%)	Extensive node metastasis, n (%)	
LN			
Number of suspicious LNs			<0.001
0	147 (75.4)	7 (22.6)	
1–2	41 (21.0)	9 (29.0)	
≥3	7 (3.6)	15 (48.4)	
Shape			<0.001
Oval	172 (88.2)	13 (41.9)	
Round	19 (9.7)	11 (35.5)	
Irregular	4 (2.1)	7 (22.6)	
Margin			<0.001
Circumscribed	185 (94.9)	19 (61.3)	
Spiculated, indistinct	10 (5.1)	12 (38.7)	
LN symmetry in both axillae			<0.001
Symmetry	158 (81.0)	7 (22.6)	
Asymmetry	37 (19.0)	24 (77.4)	
Cortical thickness			<0.001
<3 mm	147 (75.4)	6 (19.4)	
≥3 mm	48 (24.6)	25 (80.6)	
Cortical thickening			<0.001
Symmetrical	151 (77.4)	9 (29.0)	
Asymmetrical	44 (22.6)	22 (71.0)	
Fatty hilum			<0.001
Presence	179 (91.8)	13 (41.9)	
Absence	16 (8.2)	18 (58.1)	
Cortex signal intensity			<0.001
Homogeneous	183 (93.8)	16 (51.6)	
Heterogeneous	12 (6.2)	15 (48.4)	
Short diameter			<0.001
<10 mm	182 (93.3)	17 (54.8)	
≥10 mm	13 (6.7)	14 (45.2)	
Long-to-short diameter ratio			<0.001
≥2	136 (69.7)	9 (29.0)	
<2	59 (30.3)	22 (71.0)	

Table 4 *(continued)*

Table 4 *(continued)*

MRI characteristics	Pathological LN status		P value
	Nonextensive node metastasis, n (%)	Extensive node metastasis, n (%)	
SI on DWI			0.18
Low	64 (32.8)	5 (16.1)	
High	120 (61.5)	24 (77.4)	
Not evaluated	11 (5.6)	2 (6.5)	
Mean ADC value			>0.99
>0.904×10^{-3} mm^2/sec	5 (12.8)	2 (9.5)	
≤0.904×10^{-3} mm^2/sec	34 (87.2)	19 (90.5)	
Breast lesion			
Size			<0.001
≤2 cm	88 (45.1)	5 (16.1)	
>2 to ≤5 cm	95 (48.7)	16 (51.6)	
>5 cm or chest wall/skin involvement	12 (6.2)	10 (32.3)	
Margin			0.37
Circumscribed	10 (5.1)	0 (0.0)	
Spiculated, indistinct	185 (94.9)	31 (100.0)	

MRI, magnetic resonance imaging; LN, lymph node; SI, signal intensity; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient.

in differentiating axillary nodal burden (P<0.001). LN asymmetry in both axillae, ≥3 mm cortical thickening, asymmetrical cortical thickening, and the absence of fatty hilum were found more frequently in the extensive nodal metastasis group (P<0.001), accounting for approximately 77.4%, 80.6%, 71.0%, and 58.1%, respectively. In contrast, these characteristics were found in the nonextensive nodal metastasis group at approximately 19.0%, 24.6%, 22.6%, and 8.2%, respectively. Moreover, 93.3% of patients with nonextensive nodal metastasis had LNs with SDs <10 mm, whereas approximately 54.8% had LNs with SDs <10 mm. Furthermore, most patients with extensive nodal metastasis (71.0%) showed <2 long diameter (LD)/SD ratio, whereas most patients with nonextensive nodal metastasis (69.7%) showed ≥2 LD/SD ratio. No statistically significant difference in signal intensity (SI) on DWI was observed between the nonextensive and extensive nodal metastasis groups (P=0.18).

Most nonextensive and extensive nodal metastasis groups had spiculated or indistinct breast lesions (100% *vs.* 94.9%, respectively). The sizes of the breast lesions in the nonextensive nodal metastasis group were >2–5 cm in 48.7%, ≤2 cm in 45.1%, and >5 cm/chest wall or skin involvement in 6.2%. The sizes of the breast lesions in the extensive nodal metastasis group were >2–5 cm in 51.6%, >5 cm/chest wall or skin involvement in 32.3%, and ≤2 cm in 16.1%.

After analyzing the MRI characteristics of the LNs and breast lesions according to the ROC and Kappa statistics, the cutoff value for the MRI scoring system with available LN ADC value to predict extensive nodal metastasis was 14 (total 60 patients), showing sensitivity, specificity, PPV, and NPV of approximately 81%, 69.2%, 58.6%, and 87.1%, respectively. The ROC area was 0.751 [95% confidence interval (CI): 0.638–0.864], representing acceptable discrimination. The Kappa value was 0.461 (95% CI: 0.244–0.679), indicating moderate agreement (*Figure 3*).

The cutoff value for the MRI scoring system without the ADC value to predict extensive nodal metastasis was 8 (total 226 patients), showing sensitivity, specificity, PPV, and NPV of approximately 77.4%, 81%, 39.3%, and 95.8%, respectively. The ROC area was 0.792 (95% CI:

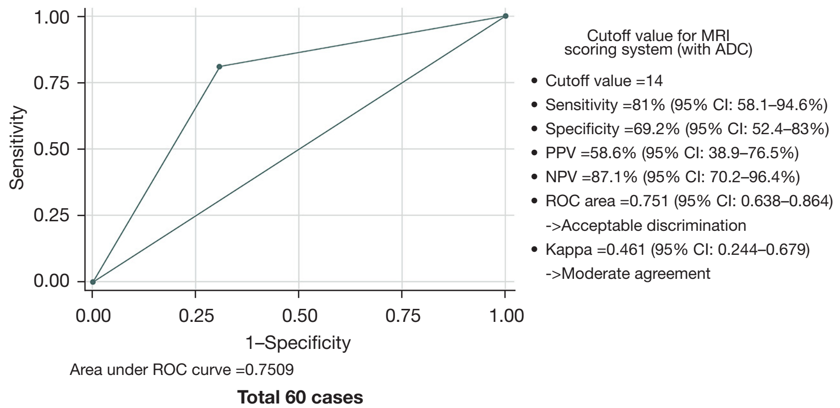

Figure 3 ROC curve and cutoff value of the MRI scoring system with ADC value. MRI, magnetic resonance imaging; ADC, apparent diffusion coefficient; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operating characteristic; Kappa, Cohen's Kappa coefficient.

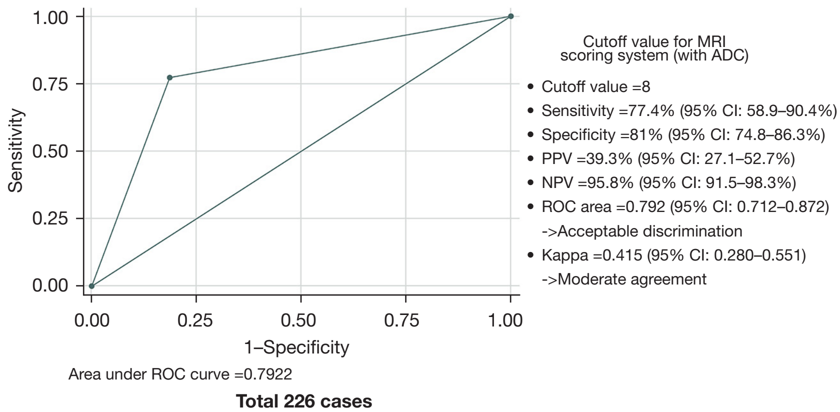

Figure 4 ROC curve and cutoff value of the MRI scoring system without ADC value. MRI, magnetic resonance imaging; ADC, apparent diffusion coefficient; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operating characteristic; Kappa, Cohen's Kappa coefficient.

0.712–0.872), representing acceptable discrimination. The Kappa value was 0.415 (95% CI: 0.280–0.551), indicating moderate agreement (*Figure 4*).

Discussion

In patients with breast cancer, the preoperative evaluation of the axillary nodal status is essential for prognosis prediction and development of management strategies. Since the publication of ACOSOG Z0011, axillary nodal management in patients with nonextensive nodal metastasis has become less invasive.

Key findings

Our study demonstrated that the number of suspicious LNs and other MRI characteristics of the axillary LNs, including shape, margin, symmetry, cortical thickening, LN hilum, LN SD, and LN LD/SD ratio, and breast tumor size and margin, were associated with extensive nodal metastasis.

Strengths and limitations

Vasigh *et al.* and Keelan *et al.* found that ultrasonographic evaluation of the axilla of patients with early-stage, clinically node-negative breast cancer is not sensitive enough to differentiate nonextensive nodal metastasis from extensive nodal metastasis (19,20). Although some studies have demonstrated that extranodal extension in involved axillary nodes is associated with an extensive nodal burden, it is highly invasive (21-24). Therefore, a higher sensitivity modality, such as MRI, was chosen for stratification in this study.

In this study, we encountered several limitations. First, this was a retrospective study conducted at a single institution. Second, the number of patients with extensive nodal metastasis (31 of the 226 patients) and those who had measurable ADC values (60 of the 226 patients) was small, which might affect the reliability of the results; some findings were not statistically significant because of lack of power. This could be because of the exclusion of patients who received neoadjuvant therapy and were clinically nodal-positive. Third, we did not analyze all axillary LNs seen on MRI but chose only one LN per person with the most suspicious characteristics or the largest size. Fourth, we did not perform lesion-by-lesion comparisons between the most suspicious LN on MRI and pathological results. Finally, most patients had IDC histological subtypes; therefore, using this MRI scoring system in patients with other histological subtypes might have limitations.

Comparison with similar research

Similar to Caudle *et al.* and Ha *et al.*, we showed that the number of suspicious LNs could be used to predict extensive nodal metastasis (10,25). Our analysis also demonstrated that other MRI characteristics of the axillary LNs, including shape, margin, symmetry, cortical thickening, LN hilum, LN SD, and LN LD/SD ratio, and breast tumor size and margin, were associated with extensive nodal metastasis, which was similar to the results reported by Li *et al.* (9).

Only a few studies have examined the DWI and ADC values of LNs. They found that these values could be used to discriminate between metastatic and nonmetastatic nodal metastases (17). He *et al.* demonstrated that their MRI scoring system, including SI on DWI and ADC value with a cutoff value of 6, had sensitivity and specificity of approximately 96% and 83%, respectively, for diagnosing metastatic nodes (26). No recent study has used the DWI and ADC values of LNs to discriminate between nonextensive and extensive nodal metastases. Our study included 60 patients with available ADC values but found no significant difference in SI on DWI and mean ADC values between the nonextensive and extensive nodal metastasis groups.

Explanations of the findings

Our study showed that the cutoff values of our MRI scoring system with and without ADC had high sensitivity, specificity, and NPV but had relatively low PPV. Compared with a previous study (27), which showed high NPV (approximately 99.6%) of breast MRI to exclude advanced nodal disease, the cutoff value of our MRI scoring system without ADC value also showed high NPV (approximately 95.8%).

Implications and actions needed

Song *et al.* suggested that patients with low probability scores from their clinical imaging nomogram accompanying negative axillary ultrasonography are candidates for the SLNB omission (28). This result emphasized our MRI scoring system's ability to exclude extensive nodal metastasis, which may help avoid unnecessary axillary surgery. Xu *et al.* (29) revealed that MRI characteristics of breast edema were promising imaging features for predicting axillary nodal burden; therefore, further study with breast edema in the MRI scoring system increase the system accuracy.

Conclusions

The proposed preoperative MRI scoring system may help identify patients with extensive nodal metastasis in clinically node-negative breast cancer. This could assist clinicians and surgeons in considering less invasive axillary nodal treatment strategies to reduce morbidity.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-24-379/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-379/dss

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-379/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-379/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, ensuring that any questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (revised in 2013). The study was approved by the ethics committee of the Faculty of Medicine, Chulalongkorn University (No. 0878/2022). The requirement for informed consent was waived because of the retrospective nature of the study and the confidentiality obligations concerning patient identities.

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