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Original Article

A Survey of Practice Patterns for Clinical Nodal Staging Prior to Neoadjuvant Chemotherapy in Breast Cancer

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Abstract

Background: The importance of clinical staging in breast cancer has increased owing to the wide use of neoadjuvant systemic therapy (NST). This study aimed to investigate the current practice patterns regarding clinical nodal staging in breast cancer in real-world settings.

Materials and Methods: A web-based survey was administered to board-certified oncologists in Korea, including breast surgical, medical, and radiation oncologists, from January to April 2022. The survey included 19 general questions and 4 case-based questions.

Results: In total, 122 oncologists (45 radiation, 44 surgical, and 33 medical oncologists) completed the survey. Among them, 108 (88%) responded that clinical staging before NST was primarily performed by breast surgeons. All the respondents referred to imaging studies during nodal staging. Overall, 64 (52.5%) responders determined the stage strictly based on the radiology reports, whereas 58 (47.5%) made their own decision while noting radiology reports. Of those who made their own decisions, 88% referred to the number or size of the suspicious node. Of the 75 respondents involved in prescribing regimens for neoadjuvant chemotherapy, 58 (77.3%) responded that the reimbursement regulations in the selection of NST regimens affected nodal staging in clinical practice. In the case-based questions, high variability was observed among the clinicians in the same cases.

Conclusions: Diverse assessments by specialists owing to the lack of a clear, harmonized staging system for the clinical nodal staging of breast cancer can lead to diverse practice patterns. Thus, practical, harmonized, and objective methods for clinical nodal staging and for the outcomes of post-NST response are warranted for appropriate treatment decisions and accurate outcome evaluation.

Key words: neoadjuvant therapy; breast cancer; staging; surgery; chemotherapy; radiotherapy.

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Implications for Practice

After using neoadjuvant systemic therapy (NST) in breast cancer, the clinical stage was used more frequently than before and became as important as pathological staging before the NST era. However, the criteria for clinical and pathological nodal staging are different in breast cancer staging, thereby rendering it difficult to decide the optimal treatment. This study investigated the current practice patterns regarding clinical nodal staging in breast cancer in a real-world setting by administering a survey to board-certified oncologists. The findings showed diverse assessments among specialists, which lead to diverse practice patterns. These results can help clinicians acknowledge the current situations regarding breast cancer staging and provide a momentum for discussions to improve diagnosis, treatment strategy, and proper outcome evaluation of breast cancer.

Introduction

Historically, chemotherapy, radiation therapy, endocrine therapy, and targeted therapy were performed following an upfront surgery for breast cancer. Recently, the use of neoadjuvant systemic therapy (NST) in breast cancer has increased based on studies, including the landmark National Surgical Bowel and Breast Project (NSABP) B-18 and B-27 trials.[1,2]

Before the use of NST, the nodal stage was mostly pathologically determined after upfront surgery, and it affected all treatment processes. Whether a patient receives chemotherapy and with which regimen is determined according to their nodal stage.[3] The pathological nodal stage also plays an important role in determining the extent of axillary surgery. Recent trials reported that the sentinel lymph node biopsy (SLNB) alone shows comparable outcomes to those of axillary lymph node dissection in patients with breast cancer with a low burden of axillary metastasis.[4-6] Additionally, adjuvant radiotherapy has been administered to patients based on pathological staging.[7,8] Moreover, radiation fields in terms of regional nodal irradiation are influenced by the presence or number of positive nodes after surgery.[9,10] These issues remain debatable in each area, especially in detailed clinical situations.

After the use of NST, the clinical stage was used more frequently than before and became as important as pathological staging before the NST era. The clinical nodal stage plays an important role in determining whether to apply NST as well as in deciding its regimen and assessing NST response. Presently, it is considered safe to perform SLNB for patients who were initially lymph node-positive but have no suspicious lymph nodes after NST.[11] Regarding radiation therapy after NST, it is recommended to determine the field and dose based on the maximal disease stage before NST and after surgery.[3] As downstaging is frequently achieved after NST, radiation therapy is performed based on the clinical stage before NST in most cases.[12,13]

This strategy of determining the treatment plan based on the clinical stage in patients with NST presupposes that the concept or prognostic impact of the clinical and pathological stages is consistent. However, the criteria for clinical and pathological nodal staging are different in the American Joint Committee on Cancer (AJCC) breast cancer staging, thereby rendering it difficult to decide the optimal treatment. Therefore, this study aimed to investigate how specialists determine the clinical nodal staging before NST and the factors that clinicians should consider in assessing clinical nodal staging.

Methods and Materials

A web-based survey was administered to board-certified oncologists, including breast surgical, medical, and radiation oncologists dedicated to breast cancer, from January to April 2022. The invitation with the survey link and the consent form were sent via email from each society: the Korean Radiation Oncology Group (KROG), Korean Breast Cancer Study Group (KBCSG), and Korean Cancer Study Group (KCSG). The survey included 19 general questions about the respondents, examination, and their assessment approaches and 4 case-based questions. The survey details are provided in Supplementary Data 1. This study was approved by the Institutional Review Board of Seoul National University Hospital (No. 2105-185-1222). Participation in this study was completely voluntary and responses were reported anonymously unless the participant desired to volunteer identifying information. In cases where identifying information was volunteered, responses were immediately de-identified for subsequent analysis.

Most of the analyses were descriptive. A comparison of the specialties of the respondents was performed using chi-square test. Statistical analysis was performed using MedCalc (version 19.6.1, MedCalc Software, Mariakerke, Belgium) and Stata 16.1 (StataCorp LLC, USA). A *P*-value of <.05 was considered statistically significant.

Results

Demographics of the Respondents

In total, 123 oncologists participated in the survey, of whom, one radiation oncologist dropped out in the middle of the survey by answering that they are not involved in the staging process at all. Thus, 122 oncologists completed the survey. Radiation oncologists constituted the highest proportion of the respondents (n = 45, 37%), followed by surgeons (n = 44, 36%), and medical oncologists (n = 33, 27%). The median number of years of experience as a specialist was 12 years, and 65.6% of respondents treated >10 first-visit patients with breast cancer monthly. Detailed data regarding the demographics of the respondents and the responses regarding initial examinations for assessing the clinical nodal stage are presented in Table 1. Of the 122 respondents, 108 (88.5%) responded that clinical staging was performed primarily by surgeons, and 9 (7.4%) responded that a multidisciplinary team approach was followed.

Questions Regarding Frequencies of Physical Examination and Axillary Lymph Node Biopsy

When asked about the physical examination during the initial staging, 93 (76.2%) respondents stated that they participated in the physical examination process. Of those, 22 (23.7%) did not routinely perform physical examinations or performed them in <80% of cases. Additionally, 62.2% of radiation oncologists and 15.2% medical oncologists did not routinely

Table 1. Respondent demographics and responses on approaches to assessing clinical nodal stage in breast cancer.

	Radiation oncologists (n = 45)	Surgical oncologists (n = 44)	Medical oncologists (n = 33)	*P*-values
First-visit patients with breast cancer per month				
0-10	12 (26.7%)	21 (47.7%)	9 (27.3%)	.4078
11-30	22 (48.9%)	16 (36.4%)	18 (54.6%)	
30-50	5 (11.1%)	4 (9.1%)	3 (9.1%)	
>50	6 (13.3%)	3 (6.8%)	3 (9.1%)	
Department that performs clinical staging before NST				
Surgery	30 (66.7%)	31 (70.5%)	15 (45.5%)	.2052
Medical oncology	2 (4.4%)	1 (2.3%)	3 (9.1%)	
Radiation oncology	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Decisions are made through multidisciplinary care	1 (2.2%)	4 (9.1%)	4 (12.1%)	
>Two departments	12 (26.7%)	8 (18.2%)	11 (33.3%)	
Timing of considering/evaluating clinical nodal staging				
Before NST	8 (17.8%)	40 (90.9%)	32 (97.0%)	<.0001
Before surgery	1 (2.2%)	4 (9.1%)	1 (3.0%)	
Before radiation therapy	36 (80.0%)	0 (0.0%)	0 (0.0%)	
Tests performed basically when determining clinical nodal staging before NST (multiple choice available)				
Physical exam	34 (75.6%)	39 (88.6%)	28 (84.9%)	.9094
Mammography	36 (80.0%)	40 (90.9%)	27 (81.8%)	
Ultrasonography	44 (97.8%)	44 (100.0%)	31 (93.9%)	
CT	36 (80.0%)	33 (75.0%)	28 (84.9%)	
MRI	41 (91.1%)	41 (93.2%)	31 (93.9%)	
PET	15 (33.3%)	5 (11.4%)	10 (30.3%)	
Axillary lymph node biopsy	28 (62.2%)	26 (59.1%)	21 (63.6%)	
Participation in physical examination				
Strictly perform in accordance with AJCC staging				
Imaging results are reflected in staging	7 (15.6%)	25 (56.8%)	16 (48.5%)	<.0001
Imaging results are not reflected in staging	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Performed >80%	3 (6.7%)	11 (25.0%)	9 (25.0%)	
Performed <80%	4 (8.9%)	4 (9.1%)	3 (9.1%)	
Do not perform routinely	5 (11.1%)	3 (6.8%)	3 (9.1%)	
Do not participate in physical examination	23 (51.1%)	0 (0.0%)	2 (6.1%)	
Others	3 (6.7%)	1 (6.7%)	0 (0.0%)	
Frequency of performing LN biopsy before NST				.185
All cases	9 (20.0%)	18 (40.9%)	13 (39.4%)	
≥80% in suspected LNs	7 (15.6%)	7 (15.8%)	8 (24.2%)	
50%-80% in suspected LNs	10 (22.2%)	4 (9.1%)	4 (12.1%)	
<50% in suspected LNs	11 (24.4%)	9 (20.5%)	4 (12.1%)	
No biopsy performed	5 (11.1%)	2 (4.5%)	0 (0.0%)	
Others	**3 (6.7%)**	**4 (9.1%)**	**4 (12.1%)**	
Compliance with AJCC criteria cN staging when performing physical examination				
Yes	18 (40.0%)	34 (77.3%)	23 (69.7%)	<.0001
No	0 (0.0%)	9 (20.5%)	3 (9.1%)	
Reflect the number of lymph nodes in staging	0 (0.0%)	8 (18.2%)	3 (9.1%)	
Do not reflect the number of lymph nodes in staging	0 (0.0%)	1 (2.3%)	0 (0.0%)	
Do not participate in physical examination	27 (60.0%)	1 (2.3%)	7 (21.2%)	

Abbreviations: AJCC, American Joint Committee on Cancer; CT, computed tomography; LN, lymph node; MR, magnetic resonance imaging; NST, neoadjuvant systemic therapy; PET, positron emission tomography.

perform physical examinations. Regarding the frequency of axillary lymph node biopsy, 62% of respondents stated that they regularly performed biopsies for suspicious axillary lymph nodes and 65% responded that they performed an axillary biopsy in at least 50% of cases.

Questions Regarding Imaging Examinations and Interpretation

The most frequently performed initial imaging study was ultrasonography (98%), followed by magnetic resonance imaging (MRI) (93%). All respondents stated that they referred to imaging studies during the nodal staging process, with 52% strictly adhering to the radiology reports and 48% making their decisions based on the radiology reports. Of those making their decisions based on the radiology reports, 88% referred to the number or size of the suspicious node.

Furthermore, the survey contained questions regarding the challenging situations when the findings are discordant among the different examinations. In cases where physical examination and imaging results are discordant, nearly half of the respondents (49.2%) stated that they would assess the clinical nodal stage according to the higher stage, and 41% stated that they would refer to the imaging results. When asked regarding cases where lymph node biopsy results of suspected lymph node metastasis on imaging were negative, 69% stated that they would determine them as node-positive.

Effect of Reimbursement Regulation on Nodal Staging

When the respondents were asked if they are involved in prescribing NST and whether the reimbursement regulations affect the assessment of nodal staging, 75 of them stated that they were involved in prescribing NST regimens and 58 (77%) stated that the reimbursement regulations in the selection of NST regimens affect nodal staging in practice.

Case-Based Questions

Following the general questions regarding the assessment of clinical nodal staging in breast cancer, 4 subsequent questions asked about the nodal stage that the respondents would determine in different clinical situations. Table 2 shows the case descriptions and representative images. The respondents were asked to choose clinical N0, N1, or N2 based on the provided descriptions and images. The first case asked about the impact of the imaging study. In this case, the node was not palpable and negative on biopsy but highly suspicious on MRI. In this case, 57.4% selected N0 and 40.2% selected N1. The second and third cases asked about the impact of the number of nodes on imaging. In the second case, the node was not palpable, but 2 borderline lymph nodes were observed on sonography with a positive biopsy result. Most of the participants (94.3%) selected N1, whereas 4.9% selected N2. In the third case, multiple suspicious nodes were observed on imaging, but no tumor was detected on biopsy. Notably, large variability was observed in this case, and more than half (56.6%) of the respondents selected N2, reflecting that many clinicians assessed clinical nodal staging based on the number of nodes on imaging. The last case asked about the assessment when the biopsy results could not be provided. In this case, the nodes were not palpable, and the imaging result revealed borderline or indeterminate findings. In this case, 55.7% and 35.3% of the respondents selected N0 and N1, respectively. The summaries of the responses with further details on the specialties of the respondents are shown in Fig. 1. None of the differences in the percentage of responses between the specialties were statistically significant.

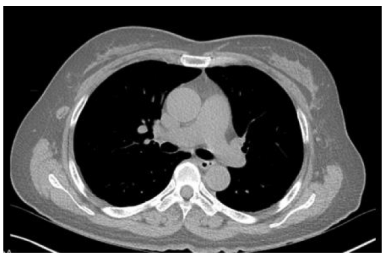
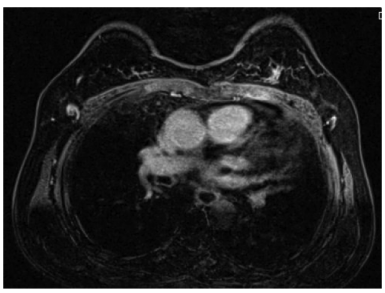
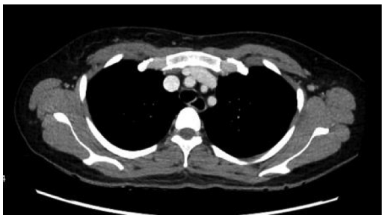
Discussion

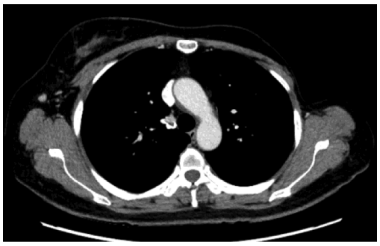
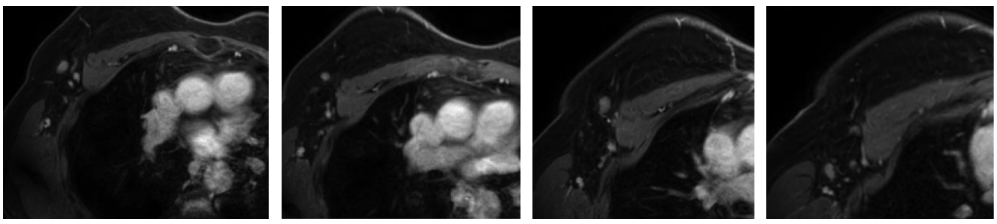
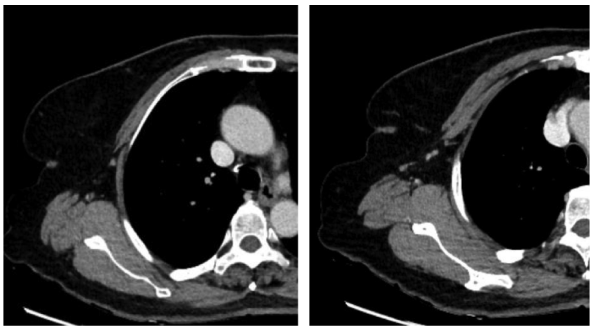
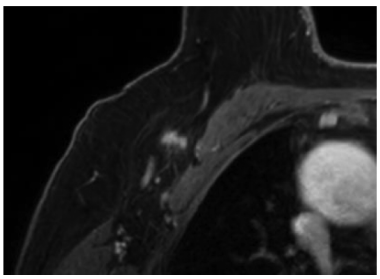
Herein, we showed that large variability exists among specialists in breast cancer regarding methods and criteria in assessing the clinical nodal stage before NST for breast cancer. The responses of these specialists also indicated that they mostly relied on imaging studies rather than physical examinations, with the vast majority referring to the size and/or number of nodes in the imaging studies.

Assessing nodal status before chemotherapy is crucial for determining axillary management and radiation treatment or its field after NST as well as NST determination, regimen selection, and response evaluation.[14] According to the AJCC 8th staging criteria, the clinical nodal stage is primarily determined via physical examination.[15] The findings of imaging studies and biopsies can be used for nodal staging; however, clear criteria, such as number or size of the nodes, do not exist. However, in real-world practices, several factors, such as size, shape, enhancement, or number of nodes, are considered while determining the clinical nodal stage via imaging studies. The National Comprehensive Cancer Network (NCCN) guidelines in breast cancer recommend considering the number of nodes before NST in deciding axillary management.[3]

For these reasons, the clinical nodal stage is evaluated based on mammography, ultrasonography, computed tomography, and MRI in actual clinical environments. Additionally, it is determined by arbitrary judgment without clear criteria. Moreover, there is no gold standard of imaging for evaluating the nodal status as these imaging techniques show variable sensitivity and specificity.[16] This may lead to errors in interpretation or affect the reliability of results when conducting future clinical stage-based studies and establishing treatment guidelines; thus, applying more consistent and clinically useful criteria reflecting real-world situations is essential. All respondents in this study referred to imaging studies, and nearly 90% of those who make their assessments based on radiology reports referred to the number or size of nodes, which are not included in the current staging system. Furthermore, the complexity of the assessment due to the discrepancies in physical examinations, imaging studies, and biopsy results without a gold standard evaluation method was shown. Most examinations, including physical examination and imaging studies, report high specificity in their performance; however, the sensitivity remained unsatisfactory. The survey results revealed that ultrasonography is the most commonly performed imaging study. It shows a high specificity of >90%; however, its sensitivity could be as low as 48.8% as it is operator-dependent.[17] The sensitivity of MRI varies among studies and is generally higher than that of other modalities, while some studies with conventional MRI reported low sensitivity (as low as 48%).[18] Novel modalities such as ultrasmall superparamagnetic iron oxide-enhanced T2-weighted MRI

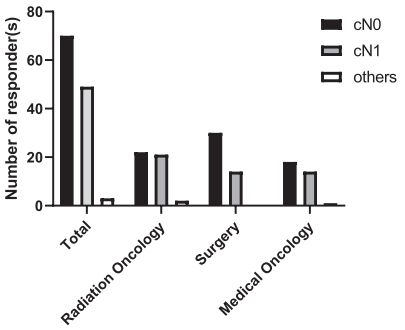
Table 2. Case description.

Case	Case description
Case 1	F/54, right breast cancer (IDC), cT2N■M0, luminal B, nuclear grade 3, histologic grade III, ER/PR/HER-2 3%/-/-, ki-67 60% * Axillary node: not palpable * Breast ultrasonography with Doppler: unifocal breast cancer, right lower outer quadrant (C6), low suspicious LN in the right axilla * Chest CT: No mention on axillary LN  * Breast MRI: unifocal breast cancer, right lower outer quadrant (C6), highly suspicious LN in the right axilla  * Axillary LN needle Bx: lymph node, "axillary, right, level I." Needle biopsy: lymphoid tissue with no tumor
Case 2	F/42, left breast cancer (IDC), cT1N■M0, HER2, nuclear grade 3, histologic grade III, ER/PR/HER-2 5%/-/3+, ki-67 7% * Axillary node: not palpable * Breast ultrasonography with Doppler: 2 borderline LNs in the left axilla, level I, L3 * Chest CT: left breast cancer with left axillary LN metastasis  * Axillary LN needle Bx: metastatic carcinoma, clinically from breast

Case	Case description
Case 3	F/41, right breast cancer (IDC), 1 h, cT3N■, TNBC, nuclear grade 3, histologic grade III, ki-67 60% * Axillary node: single palpable mass with a diameter of 1 cm * Mammography: mass in the right upper center with enlarged axillary LNs * Breast ultrasonography with Doppler: multiple, 5-10 enlarged LNs in the right axilla, level I, likely metastasis, L4 4.8 mm  * Chest CT: 4.5 cm mass in the right breast, consistent with breast cancer, prominent right axillary LN, possible metastasis * Breast MRI: unifocal breast cancer with a high possibility of axillary LN metastasis, right (C5/6), several (4-5) enlarged LNs in the right axilla, level I, possibly metastasis  * Right axilla Bx: lymphoid tissue with no tumor
Case 4	F/68, right breast cancer (IDC), 9 h, cT2N■, luminal B, nuclear grade 3, histologic grade II, ki-67 8% * Axillary node: not palpable * Breast ultrasonography with Doppler: 2 low suspicious borderline LNs in the right axilla, level I * Chest CT: small LNs in the right axilla, level I, indeterminate (approximately 5 mm)  * Breast MRI: several borderline LNs in the right axilla, level I  * Right axilla Bx: not done

Bx, biopsy; CT, computed tomography; ER, estrogen receptor; HER, human epidermal growth factor receptor; IDC, invasive ductal carcinoma; LN, lymph node; MRI, magnetic resonance imaging; PR, progesterone receptor; TNBC, triple-negative breast cancer.

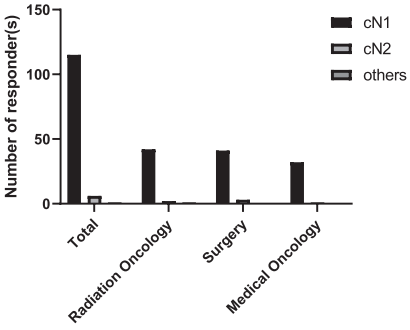
Case 1



	Total (n=122)	Radiation Oncology (n=45)	Surgery (n=44)	Medical Oncology (n=33)
cN0	70 (57.4%)	22 (48.9%)	30 (68.2%)	18 (54.6%)
cN1	49 (40.2%)	21 (46.7%)	14 (31.8%)	14 (42.4%)
others	3 (2.4%)	2 (4.4%)	0	1 (3%)

*others: cN+, re-biopsy, assess as "cN0 or cN1"

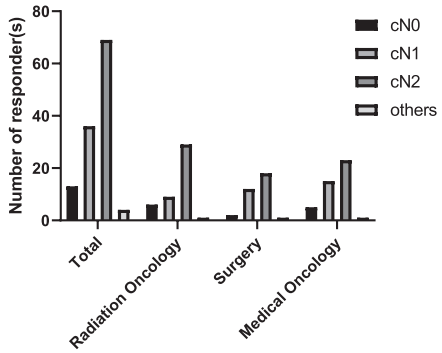
Case 2



	Total (n=122)	Radiation Oncology (n=45)	Surgery (n=44)	Medical Oncology (n=33)
cN1	115 (94.3%)	42 (93.3%)	41 (83.2%)	32 (97.0%)
cN2	6 (4.9%)	2 (4.5%)	3 (6.8%)	1 (3.0%)
others	1 (0.8%)	1 (2.2%)	0	0

*others: cN+

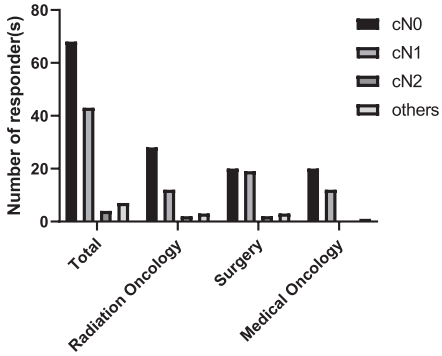
Case 3



	Total (n=122)	Radiation Oncology (n=45)	Surgery (n=44)	Medical Oncology (n=33)
cN0	13 (10.7%)	6 (13.3%)	5 (11.4%)	2 (6%)
cN1	36 (29.5%)	9 (20%)	15 (34.1%)	12 (36.4%)
cN2	69 (56.5%)	29 (64.5%)	23 (52.3%)	18 (54.6%)
others	4 (3.3%)	1 (2.2%)	1 (2.2%)	1 (3%)

*others: cN+, assess as "cN0 or cN1", check subtype of the tumor

Case 4



	Total (n=122)	Radiation Oncology (n=45)	Surgery (n=44)	Medical Oncology (n=33)
cN0	68 (55.7%)	28 (62.2%)	20 (45.5%)	20 (60.6%)
cN1	43 (35.3%)	12 (26.7%)	19 (43.2%)	12 (36.4%)
cN2	4 (3.3%)	2 (4.4%)	2 (4.5%)	0
others	7 (5.7%)	3 (6.7%)	3 (6.8%)	1 (3.0%)

*others: cN+, cNx, perform biopsy, check subtype of the tumor

Figure 1. Number and percentage of responder(s) that selected N0, N1, or N2 based on the provided descriptions and images.

can achieve high sensitivity and specificity of up to 100% and 95%, respectively. However, it is not widely used currently.[19]

Under these circumstances, clinical trials apply various criteria for axillary lymph node positivity in breast cancer.[20-22] Moreover, some early data regarding the outcomes of NST for breast cancer lack criteria for determining node positivity or separating clinical N1 or N2.[23-25] Considering that those studies provide important information for deciding treatments regarding NST in breast cancer, vague criteria might cause confusion.

We included 4 cases to demonstrate the diversity in the assessment of node positivity by the clinicians and its possible impact on clinical consequences. Case 1 included a nonpalpable, biopsy-negative, but highly suspicious axillary node on MRI. In this case, nearly 60% of respondents selected N0 and 40% selected N1, signifying that 40% of respondents rely on radiology reports even when the biopsy results are negative. Additionally, this indicates that if a patient receives a total mastectomy, they will not be recommended to receive postoperative radiotherapy by 57% of specialists and will be recommended to receive whole chest wall with or without regional nodal irradiation by 40% of specialists.

Furthermore, numerous cases akin to case 3 can be observed in real-world settings, that is, multiple suspicious nodes on imaging but negative biopsy. Notably, a large variability exists in the responses for this case, with more than half the respondents selecting N2, probably based on the number of nodes. This also signifies that patients can be treated in diverse ways at the clinician's discretion. In this case, radiation oncologists tended to select N0 or N2 rather than N1, with the rate of N2 being the highest, indicating that the specialists tended to consider the number of nodes and biopsy results, possibly because the radiation field may differ between N1 and N2 cases, as reported by studies involving the upfront surgery era with nodal staging based on pathology.[3]

Recently designed clinical trials, including NSABP B-51, require pathological confirmation of the axillary node via fine needle aspiration or core biopsy.[26,27] The process qualifies to be enrolled in the node-positive group in a clinical trial. However, clinical decisions in daily practice could differ from those in the clinical trial, and pathological confirmation could not be performed in some cases. Because of the waiting time for biopsy, 25.4% of respondents stated that they performed a biopsy before NST in <50% of cases. Additionally, 69% responded that pathologically negative cases would be considered node-positive if an imaging study showed a positive finding. Another surprising result from this survey was that 77% of those involved in prescribing NST responded that the reimbursement system affected their clinical nodal staging. This implies that the reimbursement system could also provide discordance among specialists regarding the clinical nodal stage.

Recent trials and ongoing clinical trials might change the paradigm of post-NST treatment. From the low recurrence rate following SLNB alone in patients with cN1 breast cancer who achieved cN0 after NST, the post-NST response is used to determine axillary management.[28-30] Trials such as the ASLAN trial (Avoid Sentinel Lymph Node After Neoadjuvant chemotherapy; NCT04993625) and the EUBREAST-01 trial (Omission of SLNB in Triple-negative and HER2-positive Breast Cancer Patients With rCR and pCR in the Breast After NAST; NCT04101851) are recruiting participants according to the pre-NST clinical nodal status to forego SLNB.[31,32] The RAPCHEM study (De-escalation of radiotherapy after primary chemotherapy in cT1-2N1 breast cancer; NCT01279304) showed that de-escalating radiotherapy based on locoregional recurrence risk in cN1 patients is oncologically safe, and the NSABP B-51 will further elucidate the de-escalated radiotherapy approach toward patients with ypN0 after NST.[22,26] The biological subtype of breast cancer is also an important factor that must be considered. The pathological complete response rates from NST differ according to the biological subtypes. Therefore, some suggest that knowing the subtype could help decide treatment approaches after NST.[33,34]

This study has some limitations that should be considered when interpreting the results. First, this study was performed in a single country using unified national health insurance coverage. This might not reflect the circumstances in other clinical settings. Second, although we tried to include the most challenging clinical scenarios in the survey, these scenarios cannot represent every challenging situation faced in the real world. Another potential limitation of this study is that radiation oncologists, who do not routinely participate in initial nodal staging, were the most well-represented group of breast oncologists in our cohort; however, nodal status can be assessed during any stage of treatment, and any discrepancies among physicians involved in the care team—including radiation oncologists—could significantly alter the course of treatment. Lastly, the decision-making policies regarding staging and treatment differ among institutions. Therefore, the results of this survey might not be applicable to real-world practices.

In conclusion, we found significant differences in clinical nodal staging in breast cancer among clinicians because of the absence of a clear staging system. This can lead to diverse practice patterns, and the current version of the NCCN also states the possibility of overtreatment with systemic therapy if the clinical stage is overestimated as well as locoregional undertreatment with radiotherapy if the clinical stage is underestimated.[3] Thus, a detailed consensus guideline on the pre-NST work-up process is warranted. Furthermore, we should consider the possibilities of the transition from considering both the cN and ypN statuses to focusing solely on the ypN status in future treatment decisions according to the results of the upcoming clinical trials.

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Conflict of Interest

Han-Byoel Lee and Wonshik Han are members of the board of directors, and have stock and ownership interests at DCGen, Co., Ltd., outside this work. Han-Byoel Lee received research funding from Devicor Medical Product, Inc., and consulting fees and honoraria from Alvogen, Boryung, Lilly, Novartis, Roche, Takeda, and Celltrion Pharm, outside this work. Seock-Ah Im received research funds through Seoul National University Hospital from AstraZeneca, Pfizer, Eisai, Boryung Phrm, Daichi-Sankyo, and Roche outside of this work, and has an advisory role with AstraZeneca, Hanmi, Pfizer, Eisai, Bertis, Novartis, Daichi-Sankyo, MSD, Lilly, and Roche. Jee Hyun Kim has a consulting/advisory relationship with Eisai, Roche, Eisai, MSD, Yuhan, Daiichi Sankyo, and Everest Medicine, has received research funding from Roche, Ono Pharmaceutical, Eisai, and honoraria from Novartis, Roche, Pfizer, AstraZeneca, Eisai, Lilly, and Sanofi. The other authors indicated no financial relationships.

Author Contributions

Conception/design: H.-B.L., K.-H.L., H.C. Provision of study material or patients: H.-B.L., K.-H.L., Y.B.K., J.Y., J.H.K., Y.H.P., H.k.K., H.-G.M., W.H., D.-W.L., S.-A.I., B.-S.J., J.H.C. Collection and/or assembly of data: H.-B.L., K.-H.L., Y.B.K., J.Y., J.H.K., Y.H.P., J.H.C. Data analysis and interpretation: H.-B.L., K.-H.L., S.H.S., J.H.C. Manuscript writing: H.-B.L., K.-H.L., K.K., J.H.C., K.H.S. Final approval of manuscript: All authors.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary Material

Supplementary material is available at *The Oncologist* online.

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