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Is Preoperative Axillary Imaging Beneficial in Identifying Clinically Node-Negative Patients Requiring Axillary Lymph Node Dissection?

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Abstract

Background—ACOSOG Z0011 results support the omission of axillary lymph node dissection (ALND) in women with <3 positive sentinel lymph nodes (SLNs) undergoing breast-conserving surgery (BCS) and radiation therapy. We sought to determine if abnormal axillary imaging is predictive of the need for ALND in this population.

Study Design—Patients with cT1-2N0 breast cancer by physical examination undergoing BCS were managed according to Z0011 criteria independent of axillary imaging. Patient characteristics and rates of ALND were compared among those with and without abnormal LNs detected by mammogram, ultrasound (US), or MRI. All available axillary imaging was reviewed by one breast radiologist.

Results—Between 8/2010–12/2013, 3253 breast cancer patients were treated with BCS and SLN biopsy; 425 patients met Z0011 criteria (cT1-2N0) and had nodal metastasis on SLN biopsy. Clinicopathologic features were: median patient age 58 years; median tumor size 1.8cm; 85% ductal histology; 89% estrogen receptor positive. All women had a mammogram, 242 had axillary US, 172 had MRI. Abnormal LNs were seen on 7%, 25%, and 30% of mammograms, US, and MRIs, respectively. While abnormal LNs on mammogram or US were associated with a significant increase in ALND and a non-significant trend was seen with MRI, 68–73% of women with abnormal axillary imaging did not require ALND.

Conclusions—Among clinically node negative patients with abnormal axillary imaging, 71% did not meet criteria for ALND and were spared further surgical morbidity. Abnormal nodes on

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US, MRI, or mammogram in clinically node-negative patients are not reliable indicators of the need for ALND.

Keywords

breast cancer; axillary lymph node dissection; sentinel lymph node biopsy; axillary imaging; ACOSOG Z0011

INTRODUCTION

Sentinel lymph node biopsy (SLNB) alone is the standard axillary management of clinically and pathologically node-negative breast cancer patients.[1-3] SLNB has subsequently evolved into the primary surgical management for select patients with low-volume axillary disease.[4-6] The American College of Surgeons Oncology Group (ACOSOG) Z0011 study was practice changing and established the safety of SLNB alone for axillary management in women with clinical T1-2N0 invasive breast carcinoma with 1–2 positive sentinel lymph nodes (SLNs) undergoing breast-conserving surgery (BCS) with whole breast radiation. This randomized controlled trial of SLNB alone versus completion axillary lymph node dissection (ALND) reported no difference in overall survival, disease-free survival, or locoregional recurrence between arms, with rates of axillary recurrence <1% in both surgical arms.[6, 7] A subsequent single-institution experience of prospectively accrued patients meeting ACOSOG Z011 criteria found that among SLN positive patients, 84% were able to avoid an ALND and the associated morbidity.[8]

While the ACOSOG Z0011 trial identified clinically node-negative patients by physical exam alone, some have suggested that axillary imaging with or without needle biopsy may be beneficial to allocate high-risk node-positive patients directly to ALND[9-13], omitting SLNB and the possible need for two-step axillary surgery. However, when managing patients according to ACOSOG Z0011, preoperative axillary imaging is only beneficial if it accurately discriminates between patients with metastases in 1 or 2 axillary nodes and those with involvement of 3 or more nodes or gross extracapsular extension (matted nodes) who require ALND. In this study, we sought to determine if abnormal preoperative axillary imaging is associated with the need for ALND in women managed according to ACOSOG Z0011 criteria.

METHODS

Following Memorial Sloan Kettering Cancer Center (MSKCC) institutional review board approval, consecutive, prospectively accrued patients meeting ACOSOG Z0011 criteria, defined as clinical T1-2N0 invasive breast carcinoma, undergoing BCS and SLNB with a positive SLN between 8/2010–12/2013 were identified. During this time period at our institution, women staged as clinically node negative by physical examination alone were managed according to ACOSOG Z0011 criteria without the routine use of preoperative axillary imaging. Although some patients had axillary ultrasound prior to presentation at MSKCC and others underwent breast MRI at the surgeons' discretion, regardless of the axillary imaging results, this cohort of clinically node-negative patients was managed with an SLNB and completion ALND based on SLN pathology. Patients not meeting clinical

criteria for ACOSOG Z11 (T3-4 tumors, palpable adenopathy, undergoing mastectomy) and patients undergoing neoadjuvant chemotherapy were excluded. Patient and breast tumor characteristics were recorded. All preoperative axillary imaging by mammogram, ultrasound, or MRI was identified by chart review. Although mammography and MRI are not performed for dedicated axillary evaluation, these studies were included because when abnormal axillary nodes are visualized, this information is included in the radiology report. All available images were reviewed by one breast radiologist with 32 years experience who was blinded to the need for ALND at the time of review, but who was aware that the study population consisted of node-positive patients. Results for images not available for review were abstracted from the radiology report. For each imaging modality, the presence of abnormal axillary lymph nodes and the number of abnormal axillary lymph nodes were documented. Axillary lymph nodes were considered abnormal on ultrasound (US) or MRI when there was abnormal nodal morphology including loss of fatty hilum and/or cortical thickening, or irregularity regardless of nodal size. Enhancement of normal nodes is routinely identified on MRI and was therefore not considered in nodal evaluation. Lymph nodes seen on mammogram were called abnormal when enlarged, dense, or with loss of the fatty hilum. Preoperative axillary lymph node needle biopsy results were collected. Axillary surgical management and final pathology was recorded, including the total number of SLNs removed, SLN metastasis size, whether completion ALND was performed, and the total number of positive axillary lymph nodes. Indication for ALND was either >2 positive SLNs or gross extracapsular extension/matted nodes. Associations were assessed using a two-sample t-test for continuous variables and the chi-square test for categorical variables. A multivariable logistic regression model was fit to assess the effect of abnormal axillary imaging on subsequent ALND after adjusting for age, tumor size on imaging, and the number of lymph nodes removed at SLNB. These covariates were chosen based on univariate findings and our knowledge of clinical factors. Similar models were built for all imaging modalities alone as well as for any abnormal axillary imaging by US or MRI combined. Tests with p-values <.05 were considered to be statistically significant.

RESULTS

Between 8/2010–12/2013, 3253 breast cancer patients were treated with BCS and SLNB; 424 patients (1 bilateral cancer) met ACOSOG Z0011 criteria and had axillary nodal metastasis on SLNB for a total of 425 cases. Study population clinicopathologic features included: median age of 58 years; median tumor size 1.8cm; 85% ductal histology; and 89% estrogen receptor (ER) positive. All patients had a preoperative mammogram, 242 had axillary ultrasound, and 172 had breast MRI. Women having axillary US were younger (56 versus 62 years, p=0.002) and had larger tumors (1.9 versus 1.6 cm, p=0.01). Women having MRI were also younger (54 versus 61 years, p<0.0001). Table 1 compares the clinicopathologic features of women with and without axillary US, and those with and without MRI.

81% of ultrasound images (n=195), 94% of MRI images (n=163), and 92% of mammogram images (n=392) were available for study review. Table 2 summarizes axillary imaging results. Abnormal nodes were seen on 7%, 25%, and 30% of mammograms, US, and MRIs, respectively. Of 61 axillary ultrasounds with abnormal lymph nodes seen, 1–2 abnormal

lymph nodes were seen in 58, and 3 had >2 abnormal lymph nodes. Of 52 MRI studies with abnormal axillary lymph nodes, 45 had 1–2 abnormal lymph nodes and 7 had >2 abnormal lymph nodes. Matted nodes were not observed on any imaging study.

Of the 425 node-positive patients in this study, 300 (71%) had macrometastases (tumor deposits >2mm in size) and 121 (29%) had micrometastases detected by hematoxylin and eosin staining. Women with abnormal axillary imaging by US or MRI had significantly more SLNs removed than those with normal axillary imaging or no imaging performed. The median number of SLNs removed was 3 when axillary US or MRI was negative or not performed compared to 5 for those with an abnormal axillary US, (p=0.0003); and 4 when abnormal LNs were seen on MRI, p=0.04).

Only 71 patients (17%) underwent ALND, while 354 (83%) had 1–2 positive SLNs and were managed with SLNB alone. Indications for ALND were >2 positive sentinel lymph nodes in 53 patients and presence of extracapsular extension in 18 patients. Table 3 summarizes rates of ALND among women with normal and abnormal axillary lymph nodes seen on mammogram, ultrasound, and MRI. 12–15% of women with no abnormal lymph nodes seen on axillary imaging underwent ALND, while 27–32% of women with any abnormal lymph nodes seen on axillary imaging underwent ALND. Women with abnormal lymph nodes seen on mammogram or axillary US were significantly more likely to require ALND (rate of ALND for no abnormal nodes versus any abnormal nodes on mammogram: 15% versus 32%, p=0.016; rate of ALND for women with no axillary US performed, no abnormal nodes seen on US or any abnormal nodes on US: 17%, 12%, and 30%, respectively; p=0.005). ALND was numerically more frequent when abnormal nodes were seen on MRI, but this difference was not statistically significant (p=0.09). Among 10 patients with >2 abnormal lymph nodes on US or MRI, only 2 required ALND. When both axillary US and MRI demonstrated abnormal axillary nodes (n=24), the rate of ALND was 13%. Overall, ALND was performed in 16% of patients who had a preoperative mammogram only, 12% of those who had an US and/or MRI which did not demonstrate abnormal axillary nodes, and 34% of those with abnormal axillary nodes by MRI or US (p<0.0001).

On multivariable logistic regression analysis controlling for age, imaging tumor size, number of lymph nodes removed at SLNB, and axillary imaging results, factors significantly associated with ALND included larger tumor size, increasing number of lymph nodes removed at SLNB, and abnormal lymph nodes seen on mammogram (odds ratio [OR] 2.6, 95% confidence interval [CI] 1.1–6.18, p=0.03) or US (OR 2.7, 95% CI 1.27–5.88, p=0.03). Abnormal axillary lymph nodes on MRI were not significantly associated with the need for ALND (OR 1.8, 95% CI 0.78–4.38, p=0.38) (Table 4).

Preoperative axillary LN needle biopsy was performed in 18 women (7 negative/inadequate biopsies, 11 positive for nodal metastasis). Among women with a negative lymph node biopsy, 14% (1/7) required completion ALND, and among women with a positive lymph node biopsy, 45% (5/11) required ALND (p=0.03).

DISCUSSION

Changes in the approach to axillary management have led to controversy regarding the appropriate extent of preoperative axillary imaging evaluation. As reported in 2 large meta-analyses, preoperative axillary US and selective needle biopsy correctly identifies approximately 50%–55% of node-positive patients.[14, 15] However, the clinical utility of preoperative axillary evaluation has changed in the ACOSOG Z0011 era as, increasingly, a select group of node-positive breast cancer patients are safely managed with SLNB alone.[16] For physicians who apply Z0011 criteria to omit ALND, axillary imaging is only useful if it accurately discriminates between patients with ≥3 involved nodes or gross extracapsular extension and those with a lesser nodal disease burden. In our study of a contemporary group of early breast cancer patients managed according to ACOSOG Z0011 criteria, axillary imaging did not reliably identify women requiring ALND. Although 25–30% of patients had abnormal lymph nodes identified by US or MRI, 70–73% of these patients had only 1–2 positive SLNs and were spared the morbidity of ALND. Similarly, 68% of patients with abnormal nodes seen on mammogram did not require ALND. As anticipated, more women with abnormal axillary imaging required ALND than in the group with normal or no axillary imaging performed. However, the performance of routine ALND for all women with abnormal axillary imaging to avoid a second operation in approximately one-third of patients does not outweigh the harm of exposing two-thirds of these women to well-documented increased morbidity of ALND compared to sentinel node biopsy alone.[17, 18]

Table 5 summarizes studies evaluating the ability of axillary imaging to predict nodal disease burden. These studies encompass heterogeneous patient populations, including patients with T3-4 tumors, multicentric carcinoma, and clinically node-positive disease who do not meet ACOSOG Z0011 eligibility criteria. For women with a negative axillary US, the likelihood of a heavy nodal disease burden, defined as either pN2-3 or >2 positive nodes, was uniformly low, ranging from 0%–12%. For women with a suspicious axillary US, the rate of heavy nodal disease burden varied from 8%–31%. Importantly, aside from the current study, all node-positive patients were treated with ALND and therefore the reported results reflect the total number of positive lymph nodes, not the number of positive SLNs, potentially leading to an underestimation of the number of women who would be spared ALND when managed according to ACOSOG Z0011 criteria.

Hieken et al[9] reported on the ability of axillary imaging to identify the presence of >2 positive lymph nodes on final pathology in 988 consecutive breast cancer patients; 92% of women had axillary US and 51% MRI. Axillary US was abnormal in 263 (29%), and MRI was abnormal in 168 (33%). Final pathology revealed >2 lymph nodes containing metastases in 13.5% of women who had one abnormal node on axillary US compared to 30.8% in women with multiple abnormal nodes on US. Similarly, 15.1% of women with one abnormal node seen on MRI had >2 positive lymph nodes compared to 32.6% with multiple suspicious nodes seen on MRI. Similar to our results, even among women with >2 abnormal lymph nodes seen on preoperative imaging, the majority (67%–69%) had only 1–2 positive nodes on final pathology. Their study differed from ours in that clinical nodal status was unknown, and the reference point for number of involved nodes for the majority of women was the axillary dissection pathology, not the number of positive sentinel nodes, potentially

overestimating the number of women requiring axillary dissection. In spite of this, the authors concluded that axillary imaging was of value in selecting patients for immediate axillary dissection, although such an approach would result in overtreatment of approximately 70% of women with multiple abnormal nodes on US or MRI.

Conversely, in a study by Abe et al[19], the presence of multiple abnormal lymph nodes on axillary imaging was associated with a high likelihood of having pN2-3 disease. Of 559 patients with invasive carcinoma, 181 had abnormal lymph nodes on axillary US and 28% had pN2-3 disease on final pathology compared to 3% of those with a negative axillary US. The number of highly suspicious nodes seen on US was related to the positive predictive value for identifying pN2-3 disease (82% among patients with ≥2 highly suspicious lymph nodes on US, 91% for those with ≥3 highly suspicious lymph nodes on US).

The ability of MRI alone to predict heavy nodal disease burden was evaluated by Mortellaro et al.[20] In a cohort of 56 patients with early breast cancer who underwent MRI, 8 were found to have at least one node with no fatty hilum. In this small group, the presence of ≥1 axillary lymph nodes with no fatty hilum on MRI (correlation coefficient 0.28, p=0.035) and the number of nodes with no fatty hilum (correlation coefficient 0.27, p=0.02) were both significantly associated with having ≥2 positive nodes on final pathology. In our study, 172 women had MRI imaging, and the presence of an abnormal node seen on MRI was not a significant predictor of the need for ALND (13% of patients with negative MRI, 27% of patients with abnormal nodes on MRI, p=0.085). The wide variation in identification of patients with pN2-3 disease when >2 suspicious nodes were seen (32%–82%) in these studies likely reflects the heterogeneity of the study populations. In contrast, in a population limited to those meeting ACOSOG Z0011 eligibility criteria, we found only 10 patients with >2 abnormal lymph nodes on axillary imaging, and only 2 of these required ALND. Our results are unlikely to reflect poor sensitivity of axillary imaging since only 55 of the 324 patients who had an axillary US or an MRI were found to have >2 positive sentinel nodes.

While there is a lack of consensus on the need for axillary dissection based on abnormal axillary imaging, there appears to be more enthusiasm for performing immediate axillary dissection when metastases are diagnosed by image-guided needle biopsy.[21, 22] In our small cohort of 11 women with a positive lymph node needle biopsy, 45% required ALND while 55% were managed with SLNB alone.

Our study highlights that in a population of patients meeting ACOSOG Z0011 criteria with a negative axillary physical examination, the overall risk of heavy nodal disease burden is low and the majority of women with abnormal axillary imaging do not require ALND. In our clinical practice, we do not routinely perform axillary US in clinically node-negative patients. In patients who have had an axillary US done elsewhere which demonstrates abnormal nodes, and in those found to have abnormal axillary nodes on MRI done to evaluate the breast, preoperative needle biopsy is performed only if >3 abnormal nodes are visualized or matted nodes are present. In the absence of these uncommon features, management is not changed by the imaging findings and the axilla is staged with sentinel node biopsy, with ALND reserved for patients with metastases in >3 sentinel nodes or gross extracapsular extension.

Limitations of this study include the retrospective nature of the axillary imaging review, with 6%, 8%, and 19% of MRI, mammogram, and US images, respectively, unavailable. On imaging review, the breast radiologist was not blinded to the study results, as all included patients were known to be node positive. Additionally, axillary imaging was not performed on all patients treated during this time period and the indications for axillary imaging are unknown. However, these factors bias the study in favor of axillary imaging, since it is likely that patients selected for axillary imaging would be those felt to be at higher risk for nodal metastases, a supposition supported by the younger age and larger tumor size in patients undergoing axillary US. Bias introduced by the retrospective radiology review is also likely to favor axillary imaging since subtle abnormalities are more likely to be called abnormal in patients known to have nodal metastases. Strengths of the study include a large consecutive cohort of women treated according to ACOSOG Z0011 criteria based on clinical nodal exam alone, irrespective of axillary imaging results, with the need for axillary dissection determined based on the number of involved sentinel nodes, not total nodal involvement at axillary dissection.

In summary, in a population of patients meeting ACOSOG Z0011 criteria, axillary imaging did not reliably identify patients with >2 positive SLNs, who should undergo ALND without determination of the number of involved sentinel nodes. If all patients in our study with abnormal axillary imaging were triaged to ALND, 68%–73% would have been overtreated and subjected to unnecessary surgical morbidity. Our findings suggest that for patients meeting Z0011 criteria, axillary imaging is not an effective use of resources.

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Abbreviations and Acronyms

SLNB	sentinel lymph node biopsy
ACOSOG	American College of Surgeons Oncology Group
SLNs	sentinel lymph nodes
BCS	breast-conserving surgery
ALND	axillary lymph node dissection
MSKCC	Memorial Sloan Kettering Cancer Center
US	ultrasound
ER	estrogen receptor
OR	odds ratio
CI	confidence interval

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Table 1

Comparison of Clinicopathologic Features of Women With and Without Axillary Ultrasound and Women With and Without MRI

Factor	No axillary US (n=183)	Axillary US (n=242)	p Value	No MRI (n=253)	MRI (n=172)	p Value
Age, y, median (range)	61.6 (30.6–92.1)	55.6 (28.2–85.0)	0.002	61.8 (31.5–92.1)	53.2 (28.2–83.4)	<.0001
Preoperative tumor size by imaging, cm, median (range)	1.6 (0.08–5.8)	1.8 (0.4–6.0)	0.006	1.6 (0.08–6.0)	1.8 (0.4–5.8)	0.58
Abnormal lymph nodes seen on mammogram, n (%)	6 (3)	25 (10)	0.006	18 (7)	13 (8)	0.86
Final pathologic tumor size, cm, median (range)	1.6 (0.4–5.2)	1.9 (0.1–5.2)	0.009	1.8 (0.1–4.9)	1.8 (0.3–5.2)	0.87
Tumor histology, n (%)			0.33			0.91
Ductal	151 (83)	211 (87)		216 (85)	146 (85)	
Lobular	23 (13)	20 (8)		26 (10)	17 (10)	
Other	9 (5)	11 (5)		11 (4)	9 (5)	
Nuclear grade, n (%)			0.06			0.13
1	20 (11)	12 (5)		14 (6)	18 (10)	
2	97 (53)	130 (54)		137 (54)	90 (52)	
3	61 (33)	92 (38)		96 (38)	57 (33)	
NA	5 (3)	8 (3)		6 (2)	7 (4)	
Multifocal tumor, n (%)	24 (13)	32 (13)	0.96	31 (12)	25 (15)	0.48
LVI present, n (%)	106 (58)	144 (60)	0.74	149 (59)	101 (59)	0.97
ER status, n (%)			0.41			0.86
Positive	165 (90)	212 (88)		225 (89)	152 (88)	
Negative	18 (10)	30 (12)		28 (11)	20 (12)	
PR status, n (%)			0.40			0.73
Positive	154 (84)	196 (81)		207 (82)	143 (83)	
Negative	29 (16)	46 (19)		46 (18)	29 (17)	
HER2-neu status, n (%)*			0.10			0.54
Positive	38 (21)	67 (28)		60 (24)	45 (26)	
Negative	144 (79)	173 (72)		192 (76)	125 (74)	
SLN microscopic ECE, n	170	204	0.015	222	152	0.19
Present, n (%)	66 (39)	55 (27)		66 (30)	55 (36)	
Absent, n (%)	104 (61)	149 (73)		156 (70)	97 (64)	

US, ultrasound; NA, not available; LVI, lymphovascular invasion; ER, estrogen receptor; PR, progesterone receptor; SLN, sentinel lymph node; ECE, extracapsular extension.

* Data missing for 3 patients.

Table 2

Ipsilateral Axillary Imaging Findings

	Mammogram	Axillary ultrasound	MRI
Total n	425	242	172
No abnormal LNs seen, n (%)	394 (93)	181 (75)	120 (70)
Abnormal LNs seen, n (%)	31* (7)	61 (25)	52 (30)
Number of abnormal lymph nodes seen, n (%)			
1	21 (5)	46 (19)	32 (19)
2	9 (2)†	12 (5)	13 (8)
> 2		3 (1)	7 (4)

LN, lymph node.

*Data on number of abnormal lymph nodes missing for one mammogram.

†Includes imaging with >1 abnormal lymph nodes.

Table 3

Need for Axillary Lymph Node Dissection among Women With and Without Abnormal Axillary Imaging

Imaging modality	n	ALND required	No ALND	p Value
Individual axillary imaging results				
Mammogram				0.016
No abnormal LNs	391	61 (15%)	333 (85%)	
Any abnormal LNs	31	10 (32%)	21 (68%)	
Axillary US				0.005
Not done	183	31 (17%)	151 (83%)	
No abnormal LNs	181	21 (12%)	160 (88%)	
Any abnormal LNs	61	18 (30%)	43 (70%)	
MRI				0.085
Not done	253	40 (16%)	212 (84%)	
No abnormal LNs	120	16 (13%	104 (87%)	
Any abnormal LNs	52	14 (27%)	38 (73%)	
Combined axillary imaging results				
Mammogram only*	101	16 (16%)	85 (84%)	<0.0001
Negative axillary imaging by US and/or MRI	254	31 (12%)	223 (88%)	
Abnormal axillary imaging by US and/or MRI	70	24 (34%)	46 (66%)	

ALND, axillary lymph node dissection; LN, lymph node; US, ultrasound.

*Six women had abnormal axillary imaging by mammogram with no additional axillary imaging performed.

Table 4

Multivariable Logistic Regression Models for Axillary Lymph Node Dissection According to Axillary Imaging Results

	Odds Ratio	95% CI	p Value
Mammography			
Age	1.02	0.99–1.04	0.18
Imaging tumor size, cm	1.50	1.14–1.97	0.0039
Total nodes removed at SLNB	1.33	1.20–1.48	<0.0001
No abnormal LNs on mammogram	1.0 (ref)		
Abnormal LNs on mammogram	2.61	1.10–6.18	0.030
Ultrasound			
Age	1.02	0.99–1.04	0.20
Imaging tumor size	1.57	1.19–2.07	0.0014
Total nodes removed at SLNB	1.31	1.18–1.45	<0.0001
No abnormal LNs on US	0.57	0.30–1.07	0.079*
Abnormal LNs on US	1.55	1.27–5.88	0.25*
Axillary US not done	1.0 (ref)		
MRI			
Age	1.01	0.99–1.04	0.29
Imaging tumor size	1.51	1.15–1.99	0.0033
Total nodes removed at SLNB	1.32	1.19–1.46	<0.0001
No abnormal LNs on MRI	0.80	0.40–1.59	0.52
Abnormal LN on MRI	1.47	0.68–3.16	0.33†
MRI not done	1.0 (ref)		
Combined axillary imaging			
Age	1.02	0.99–1.04	0.17
Imaging tumor size	1.56	1.18–2.07	0.0017
Total nodes removed at SLNB	1.30	1.17–1.44	<0.0001
No abnormal LNs on US or MRI	1.0 (ref)		
Abnormal LNs on US or MRI	3.22	1.65–6.29	0.0006
Imaging with mammogram only	1.55	0.76–3.16	0.23‡

LN, lymph node; ALND, axillary lymph node dissection; US, ultrasound.

*p Value for overall type 3 test is 0.0030.

†p Value for overall type 3 test is 0.380.

‡p Value for overall type 3 test is 0.0028.

Table 5

Axillary Ultrasound as a Predictor of Extent of Pathologic Nodal Disease Burden

First author	No. with axillary US	Pathologic nodal status by US results			p Value
		Pathologic nodal status	Negative US, n (%)	Suspicious US, n (%)	
Kwak[23]*	323 SLNB	pN0	129 (88)	127 (72)	0.002
		pN1	17 (12)	35 (20)	
		pN2-3	1 (1)	14 (8)	
Abe[19]	559	pN0	291 (77)	69 (38)	
		pN1	77 (20)	62 (34)	
		pN2-3	10 (3)	50 (28)	
Damera[24]	166	pN0	45 (71)	57 (55)	
		pN1	17 (27)	27 (26)	
		pN2-3	1 (2)	19 (18)	
Hinson[25]	112†	pN0	37 (73)	17 (28)	
		pN1	14 (27)	25 (41)	
		pN2-3	0	19 (31)	
Nori[26]	132	pN0	78 (77)	12 (39)	
		1-2 positive nodes	21 (21)	13 (42)	
		>2 positive nodes	2 (2)	6 (19)	
Current‡	242	pN0	-	-	0.005
		1-2 positive nodes	160 (88)	43 (70)	
		>2 positive nodes	21 (12)	18 (30)	

US, ultrasound; SLNB, sentinel lymph node biopsy.

*Axilla imaged with ultrasound, MRI, and/or PET scan. Abnormal nodes on any imaging modality included.

†US performed on patients identified as being high risk for nodal metastasis based on grade III tumors, size ≥1 cm, or grade II and size ≥1.5 cm.

‡All patients with a positive sentinel lymph node biopsy.