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Is Routine Axillary Imaging Necessary in Clinically Node-Negative Patients Undergoing Neoadjuvant Chemotherapy?

Andrea V. Barrio, MD^{1,*}, Anita Mamtani, MD^{1,*}, Anne Eaton, MS², Sandra Brennan, MD³, Michelle Stempel, MPH¹, and Monica Morrow, MD¹

¹Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY

²Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY

³Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY

Abstract

Background—National Comprehensive Cancer Network guidelines recommend axillary imaging prior to neoadjuvant chemotherapy (NAC) in breast cancer patients who are clinically node negative (cN0) by physical exam; however, the benefit of this approach remains uncertain. The purpose of this study was to determine whether abnormal axillary imaging pre-NAC predicts nodal metastases post-NAC (ypN+) in cN0 patients.

Methods—cN0 patients undergoing NAC followed by axillary surgery were identified. Rates of ypN+ were compared among patients with abnormal pre-treatment axillary imaging vs. normal or no pre-treatment imaging using Fisher's exact test.

Results—From 05/2008–03/2016, 402 eligible cN0 patients were identified. Median age was 49.5 years; median tumor size was 4cm. 38% were ER+/HER2-, 30% HER2+, and 32% triple negative. All had pre-NAC mammograms, 40% axillary ultrasound, 83% MRI, and 51% PET. Abnormal nodes on imaging were seen in 208 patients (52%); 128 had pre-NAC node biopsy, and 75 were positive. Overall, 28% (n=111) of patients were ypN+ after NAC. Although the incidence of ypN+ was significantly higher in patients with abnormal nodes on pre-NAC imaging (p=0.001), 54% did not require ALND post-NAC. Among patients with normal nodes on pre-NAC imaging, 20% were ypN+ post-NAC.

Conclusions—Half of patients with abnormal nodes on pre-NAC imaging did not require ALND post-NAC, while 20% of those with normal pre-NAC nodes had disease post-NAC, indicating that in cN0 patients already selected for NAC, axillary imaging pre-NAC does not predict the need for axillary surgery post-NAC with sufficient accuracy to be clinically useful.

Corresponding author: Andrea V. Barrio, MD, Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, 300 East 66th Street, New York, NY 10065, (T) 646-888-5117, (F) 646-888-4921, (E) barrioa@mskcc.org.

*Denotes shared first authorship

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Keywords

neoadjuvant chemotherapy; clinically node-negative; axillary lymph node dissection

INTRODUCTION

Axillary ultrasound (US) with selective needle biopsy of suspicious axillary nodes in newly diagnosed breast cancer patients has been used for preoperative staging of the axilla for many years.¹ In clinically node-negative (cN0) patients, Holwitt et al demonstrated that axillary US plus biopsy identified unsuspected nodal disease in 28%, obviating the need for sentinel node biopsy (SNB).² Following publication of the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial, the routine practice of axillary US in cN0 patients undergoing primary surgery was called into question³, as Z0011 demonstrated that axillary lymph node dissection (ALND) could be safely omitted in cN0 patients undergoing breast-conserving surgery with one or two positive sentinel nodes (SNs).⁴

In patients receiving neoadjuvant chemotherapy (NAC), the use of axillary US to stage the axilla pre-treatment in cN0 patients is controversial. Current National Comprehensive Cancer Network (NCCN) guidelines recommend consideration of axillary imaging with biopsy of any suspicious nodes prior to NAC in breast cancer patients found to be cN0 by physical exam alone.⁵ One of the arguments supporting pre-NAC axillary imaging is improved selection for ALND post-NAC. However, one of the major benefits of NAC is axillary downstaging, with nodal pathologic complete response rates of 21% to 97%, depending on tumor subtype^{6,7}; therefore, a decision to perform post-NAC ALND based on the finding of subclinical nodal metastases pre-NAC may result in unnecessary axillary surgery. The purpose of our study was to determine whether abnormal axillary imaging pre-NAC in cN0 patients was predictive of the presence of nodal metastases post-NAC.

METHODS

Following institutional review board approval, cN0 stage I–III breast cancer patients undergoing NAC between May 2008 and March 2016 were identified from a prospectively maintained database. Patients were staged as cN0 by physical examination. All patients had a pre-treatment mammogram. Axillary ultrasound, breast magnetic resonance imaging (MRI), and positron emission tomography (PET) were performed selectively at the discretion of the treating physician(s). Information regarding the presence of abnormal axillary nodes by imaging and performance of pre-NAC lymph node biopsy was obtained by chart review. Axillary lymph nodes were considered abnormal on mammogram when enlarged, dense or observed to have loss of the fatty hilum. On ultrasound or MRI, nodes were abnormal if they had abnormal nodal morphology, including loss of fatty hilum and/or cortical thickening, eccentric cortical bulge, or cortical blood flow, regardless of nodal size. On PET, nodes were abnormal if they had increased fluorodeoxyglucose (FDG) uptake and elevated standardized uptake value (SUV), without a defined SUV threshold. The choice for biopsy of abnormal nodes seen on pre-NAC imaging in cN0 patients was made by the treating physician.

Patient and tumor characteristics were recorded from the medical record. All patients had primary breast surgery and axillary surgery with either SNB or ALND. SNB was performed with isosulfan blue dye, technetium-99m sulfur colloid, or a combination of both. ALND was performed for any positive SN; in patients with negative nodes, ALND was also performed for failed mapping, cT4 disease at presentation, or intraoperative suspicion of nodal disease.

SNs were serially sectioned at 2 mm intervals along the major axis of the lymph node at the time of gross examination. A single hematoxylin and eosin (H&E) stained section was prepared from each block. Immunohistochemistry was not routinely performed for lymph node evaluation post-NAC.

Clinical variables were summarized using frequency and percentage for categorical covariates, and median and range for continuous covariates, and compared by imaging and pre-NAC biopsy result using Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Rates of nodal metastases post-NAC (ypN+) and ALND were compared among patients with abnormal pre-treatment axillary imaging vs. normal or no pre-treatment imaging using Fisher's exact test and the Wilcoxon rank-sum test. A multivariable logistic regression model was fit to assess the effect of abnormal axillary imaging on rates of ypN+ and ALND post-NAC after adjusting for clinical tumor size, histology, and receptor status. All statistical analysis was done in R 3.1.1 (R Foundation, Vienna, Austria), and p-values < 0.05 were considered significant.

RESULTS

Between May 2008 and March 2016, 402 cN0 patients received NAC followed by axillary surgery. Table 1 describes the clinical characteristics of the study cohort. Median age was 49.5 years and median clinical tumor size was 4 cm. Thirty percent of patients had HER2 positive tumors and 32% had triple-negative (TN) tumors.

All patients had a pre-NAC mammogram. Axillary US was performed in 162 (40%), breast MRI in 332 (83%), and PET scan in 205 (51%). Abnormal nodes were seen in 208 patients (52%) by any imaging modality; specifically abnormal nodes were seen on 12% of mammograms (n = 46), 81% of ultrasounds (n = 131), 46% of MRIs (n = 154), and 51% of PET scans (n = 104). The clinicopathologic characteristics of patients with and without abnormal nodes by imaging are described in Table 2. Patients with abnormal nodes on imaging had larger tumors (4 vs. 3.5 cm, p = 0.002) and were more likely to have ductal histology (92% vs. 86%, p = 0.048); otherwise, the groups did not differ. When comparing patients who had abnormal nodes imaged by axillary US (n = 131) to those with a normal axillary US (n = 31) or no axillary US (n = 240), clinicopathologic characteristics did not significantly differ between groups (Table 3).

Lymph node biopsy prior to NAC was performed in 128 patients; 75 were positive for tumor cells, 51 were negative, and 2 were non-diagnostic. The remaining patients did not have a node biopsy. When comparing patients with and without a positive pre-NAC lymph node

biopsy, age, clinical tumor size, receptor status, histology, and clinical T stage did not differ ($p = \text{NS}$).

SNB alone was performed in 254 patients, 77 had an SNB followed by ALND, and 71 had ALND alone. In the 331 patients who had an SNB attempted, dual tracer mapping was used in 93%, and 330 (99.7%) successfully mapped; the median number of SNs removed was 4 (range 1–14). In the 148 patients treated with ALND, the median number of nodes removed was 17 (range 1–46).

Among patients who had an SNB procedure ($n = 330$), there was no difference in the median number of SNs removed between patients with and without abnormal nodes on imaging (4 vs. 4, respectively; $p = 1.0$) or with and without a positive pre-NAC LN biopsy (3 vs. 4, respectively; $p = 0.83$).

After the completion of NAC, 111 patients (28%) had nodal metastases (ypN+) with a median of 2 positive nodes (range 1–16). Breast pathologic complete response, defined as the absence of invasive disease in the breast (in situ allowed), was observed in 35% of 402 patients. The incidence of histologically positive nodes post-treatment was higher in patients with abnormal vs. normal nodes by axillary US (40% vs. 23%, $p = 0.1$), MRI (34% vs. 17%, $p < 0.001$) and PET (42% vs. 21%, $p < 0.001$), although the difference did not reach statistical significance in the axillary US group (Table 4). Patients with and without abnormal nodes on imaging had a similar median number of positive nodes post-NAC: 2.5 vs. 2, respectively ($p = 0.83$). Among patients with abnormal nodes seen by any imaging modality ($n = 208$), 65% had histologically negative nodes post-NAC and 54% did not receive an ALND. For patients with normal nodes on imaging pre-NAC, 20% were ypN+ post-NAC and 27% had an ALND (Table 4).

On multivariable logistic regression analysis, adjusting for clinical tumor size, histology, and receptor status, factors significantly associated with ypN+ were abnormal nodes on imaging (odds ratio [OR] 2.95, 95% confidence interval [CI] 1.77 to 5.01; $p < 0.001$), non-ductal histology (OR 2.93, 95% CI 1.44 to 6.02; $p = 0.003$) and estrogen receptor positive receptor status (OR 3.94, 95% CI 2.22 to 7.18; $p < 0.001$) (Table 5).

DISCUSSION

It is well established that clinically node-negative breast cancer patients may harbor microscopic disease in the axillary lymph nodes, with a frequency of nodal metastases ranging from 10% to 88% depending on tumor type, tumor size, multifocality, receptor status, and patient age.⁸ However, in cN0 patients selected for NAC based on other tumor characteristics, the role of pre-treatment axillary imaging to identify occult disease in the axilla that may be downstaged with chemotherapy remains uncertain. Randomized trials and institutional experiences have shown that the incidence of nodal positivity is lower in patients treated with NAC compared to those undergoing initial surgery. Among 1493 patients with T1–3, N0–1 operable breast cancer enrolled in National Surgical Adjuvant Breast and Bowel Project (NSABP) B-18, the incidence of pathologically negative nodes was 58% in patients randomized to preoperative therapy compared to 42% in those receiving

postoperative therapy ($p < 0.0001$).⁹ Similarly, Hunt et al demonstrated a lower incidence of SN positivity among patients receiving NAC ($n = 575$) compared to those having surgery first ($n = 3171$), which resulted in significantly fewer ALNDs being performed in patients presenting with T2 (27.2% vs. 40.6%, $p < 0.0001$) and T3 disease (45.1% vs. 65.7%, $p = 0.045$). This study also demonstrated no increase in regional recurrence rates in patients undergoing axillary staging after NAC, confirming the safety of this approach.¹⁰ In patients receiving NAC, it is the post-treatment status of the nodes, not the pre-treatment status, which determines surgical management. In cN0 patients already selected for NAC, axillary imaging with identification of suspicious nodes would only be useful if the imaging study consistently identified patients more likely to have nodal metastases after NAC.

In our study, 111 (28%) cN0 patients had histologically positive nodes after NAC. Although patients with abnormal nodes on pre-treatment imaging had a higher incidence of nodal positivity post-NAC (35% vs. 20%, $p = 0.001$), ALND was avoided in the majority of patients, irrespective of pre-treatment imaging findings (ALND rate: 46% abnormal nodes vs. 27% normal nodes). Importantly, patients with normal nodes on pre-treatment imaging still had a substantial incidence of nodal positivity post-NAC (20%), suggesting that pre-treatment axillary imaging does not reliably predict the need for ALND following systemic therapy. These findings are consistent with the known false-negative rate of preoperative axillary evaluation with axillary US, MRI, and PET, with documented false-negative rates of 25%¹¹, 35%¹², and 79%¹³, respectively, and explains why approximately 20% of patients in our study with normal nodes on imaging pre-NAC were histologically node positive post-NAC.

Another possible explanation for the poor correlation between pre-treatment axillary imaging and nodal positivity post-NAC is that the status of the axilla post-NAC in cN0 patients is influenced by both the initial nodal status and the response of the tumor to chemotherapy. In our study, although abnormal axillary imaging was a predictor of nodal positivity post-NAC (OR = 2.95, $p < 0.001$), additional predictors of residual positive nodes post-NAC were non-ductal histology (OR = 2.93, $p = 0.003$) and estrogen receptor positivity (OR = 3.94, $p < 0.001$), with hormone receptor status being the strongest predictor of nodal disease. The finding that patients with ductal histology were more likely to have abnormal nodes on pre-NAC imaging ($p = 0.048$) and yet less likely to harbor positive nodes post-NAC supports existing data that lobular cancers are less responsive to NAC with a higher disease burden post-treatment than ductal cancers, in large part due to their strong estrogen receptor positivity.^{14,15}

Overall, patients with estrogen receptor positive tumors not only have a higher rate of nodal metastases at presentation compared to those with estrogen receptor negative tumors^{8,16}, they also have a significantly lower rate of nodal pCR compared to patients with triple-negative or HER2 positive breast cancers.^{6,7} Although not directly evaluated in our study, the higher likelihood of nodal metastases in estrogen receptor positive patients after NAC suggests that in the clinically node-negative subset of patients who meet Z0011 eligibility criteria at presentation, consideration of initial surgery as a more likely approach to avoiding ALND is appropriate. In aggregate, the findings in our study support the concept that tumor

subtype, not pre-treatment imaging findings, is the most important predictor of nodal metastases and ALND post-NAC.

One argument in favor of pre-NAC axillary imaging is that identification of positive axillary nodes in cN0 patients pre-NAC may influence recommendations for radiation post-NAC, particularly in patients undergoing mastectomy. In women with positive nodes treated with initial surgery, postmastectomy radiation therapy reduces locoregional recurrence and improves overall survival, particularly in women with 4 or more positive nodes.¹⁷ However, initial nodal status is less important in patients receiving NAC, as the post-treatment status of the axilla is the primary determinant of locoregional recurrence. In a review of NSABP B-18 and NSABP B-27, studies which did not allow the use of postmastectomy radiotherapy, Mamounas et al demonstrated a low incidence of locoregional recurrence (< 10%) in patients who achieved a nodal pathologic complete response with NAC, regardless of clinical nodal status at presentation¹⁸, suggesting that identification of nodal disease with axillary imaging in cN0 patients pre-NAC should not substantially alter treatment decisions.

This study is limited by the retrospective nature of the axillary imaging review; re-review of imaging may have identified additional patients with suspicious axillary imaging, which could influence the association with pathological nodal status post-NAC. However, in clinical practice, imaging is traditionally read by a single radiologist without re-review, and therefore the reported data reflect the association more likely to be observed in everyday practice. Furthermore, although we found no difference in the clinical characteristics of patients with and without abnormal nodes, it is possible that the finding of abnormal axillary imaging influenced the decision for preoperative chemotherapy, particularly in patients with T1 disease, suggesting a small clinical benefit to preoperative imaging in selected patients.

In conclusion, in a cohort of cN0 patients receiving NAC, half of patients with abnormal nodes on pre-NAC imaging did not require ALND post-NAC, while 20% of those with normal pre-NAC nodes had disease post-NAC, indicating that in cN0 patients already selected for preoperative chemotherapy, axillary imaging pre-NAC does not predict the need for axillary surgery post-NAC with sufficient accuracy to be clinically useful.

References

1. Houssami N, Ciatto S, Turner RM, Cody HS 3rd, Macaskill P. Preoperative ultrasound-guided needle biopsy of axillary nodes in invasive breast cancer: meta-analysis of its accuracy and utility in staging the axilla. *Ann Surg*. 2011; 254(2):243–51. [PubMed: 21597359]
2. Holwitt DM, Gillanders WE, Aft RL, Eberlein TJ, Margenthaler JA. Sentinel lymph node biopsy in patients with multicentric/multifocal breast cancer: low false-negative rate and lack of axillary recurrence. *Am J Surg*. 2008; 196(4):562–5. [PubMed: 18760396]
3. Pilewskie M, Jochelson M, Gooch JC, Patil S, Stempel M, Morrow M. Is Preoperative Axillary Imaging Beneficial in Identifying Clinically Node-Negative Patients Requiring Axillary Lymph Node Dissection? *J Am Coll Surg*. 2016; 222(2):138–45. [PubMed: 26711795]
4. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. *Jama*. 2011; 305(6):569–75. [PubMed: 21304082]
5. Gradishar WJ, Anderson BO, Blair SL, Burstein HJ, Cyr A, Elias AD, et al. Breast cancer version 3.2014. *J Natl Compr Canc Netw*. 2014; 12(4):542–90. [PubMed: 24717572]

6. Boughey JC, McCall LM, Ballman KV, Mittendorf EA, Ahrendt GM, Wilke LG, et al. Tumor biology correlates with rates of breast-conserving surgery and pathologic complete response after neoadjuvant chemotherapy for breast cancer: findings from the ACOSOG Z1071 (Alliance) Prospective Multicenter Clinical Trial. *Ann Surg*. 2014; 260(4):608–14. discussion 14–6. [PubMed: 25203877]
7. Mamtani A, Barrio AV, King TA, Van Zee KJ, Plitas G, Pilewskie M, et al. How Often Does Neoadjuvant Chemotherapy Avoid Axillary Dissection in Patients With Histologically Confirmed Nodal Metastases? Results of a Prospective Study. *Ann Surg Oncol*. 2016
8. Bevilacqua JL, Kattan MW, Fey JV, Cody HS 3rd, Borgen PI, Van Zee KJ. Doctor, what are my chances of having a positive sentinel node? A validated nomogram for risk estimation. *J Clin Oncol*. 2007; 25(24):3670–9. [PubMed: 17664461]
9. Rastogi P, Anderson SJ, Bear HD, Geyer CE, Kahlenberg MS, Robidoux A, et al. Preoperative chemotherapy: updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. *J Clin Oncol*. 2008; 26(5):778–85. [PubMed: 18258986]
10. Hunt KK, Yi M, Mittendorf EA, Guerrero C, Babiera GV, Bedrosian I, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy is accurate and reduces the need for axillary dissection in breast cancer patients. *Ann Surg*. 2009; 250(4):558–66. [PubMed: 19730235]
11. Diepstraten SC, Sever AR, Buckens CF, Veldhuis WB, van Dalen T, van den Bosch MA, et al. Value of preoperative ultrasound-guided axillary lymph node biopsy for preventing completion axillary lymph node dissection in breast cancer: a systematic review and meta-analysis. *Ann Surg Oncol*. 2014; 21(1):51–9. [PubMed: 24008555]
12. Javid S, Segara D, Lotfi P, Raza S, Golshan M. Can breast MRI predict axillary lymph node metastasis in women undergoing neoadjuvant chemotherapy. *Ann Surg Oncol*. 2010; 17(7):1841–6. [PubMed: 20143266]
13. Jeong YJ, Kang DY, Yoon HJ, Son HJ. Additional value of F-18 FDG PET/CT for initial staging in breast cancer with clinically negative axillary nodes. *Breast Cancer Res Treat*. 2014; 145(1):137–42. [PubMed: 24682676]
14. Cristofanilli M, Gonzalez-Angulo A, Sneige N, Kau SW, Broglio K, Theriault RL, et al. Invasive lobular carcinoma classic type: response to primary chemotherapy and survival outcomes. *J Clin Oncol*. 2005; 23(1):41–8. [PubMed: 15625359]
15. Lips EH, Mulder L, de Ronde JJ, Mandjes IA, Vincent A, Vrancken Peeters MT, et al. Neoadjuvant chemotherapy in ER+ HER2- breast cancer: response prediction based on immunohistochemical and molecular characteristics. *Breast Cancer Res Treat*. 2012; 131(3):827–36. [PubMed: 21472434]
16. Wiechmann L, Sampson M, Stempel M, Jacks LM, Patil SM, King T, et al. Presenting features of breast cancer differ by molecular subtype. *Ann Surg Oncol*. 2009; 16(10):2705–10. [PubMed: 19593632]
17. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans V, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005; 366(9503):2087–106. [PubMed: 16360786]
18. Mamounas EP, Anderson SJ, Dignam JJ, Bear HD, Julian TB, Geyer CE Jr, et al. Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27. *J Clin Oncol*. 2012; 30(32):3960–6. [PubMed: 23032615]

Synopsis

The benefit of axillary imaging in cN0 breast cancer patients selected for NAC is uncertain. Here we find that pre-treatment axillary imaging does not predict nodal metastases post-NAC with sufficient accuracy to be clinically useful in this patient population.

TABLE 1

Clinicopathologic characteristics of study cohort

Participant characteristics		N = 402	
		Median	Range
Age, yrs		49.5	23–81
Clinical tumor size, cm		4.0	1.1–10.0
		N	%
Histology	Ductal	358	89
	Lobular or mixed	40	10
	Other§	4	1
Lymphovascular invasion		115	29
Receptor status	ER+/HER2--	151	38
	HER2+	122	30
	Triple negative	129	32
cT	T1	24	6
	T2	260	65
	T3	80	20
	T4	38	9

§ Metaplastic (n = 2), neuroendocrine (n = 2)

ER, estrogen receptor; cT, clinical T stage

TABLE 2

Clinicopathologic features of patients with and without abnormal nodes on pre-NAC imaging

Participant characteristics	Normal nodes N = 194	Abnormal nodes N = 208	P-value
Age at diagnosis, median, yrs (range)	50 (26–78)	49 (23–81)	0.67
Clinical tumor size, median, cm (range)	3.5 (1.1–10.0)	4.0 (1.1–10)	0.002
Histology, n (%)			0.048
Ductal	167 (86%)	191 (92%)	
Lobular or mixed	26 (13%)	14 (7%)	
Other	1 (1%)	3 (1%)	
Receptor status, n (%)			0.48
ER+/HER2-	78 (40%)	73 (35%)	
HER2+	64 (29%)	66 (32%)	
ER-/HER2-	60 (31%)	69 (33%)	
Lymphovascular invasion, n (%)	55 (28%)	60 (29%)	1
Clinical T stage, n (%)			0.213
T1	16 (8%)	8 (4%)	
T2	127 (65%)	133(64%)	
T3	35 (18%)	45 (22%)	
T4	16 (8%)	22 (11%)	

ER, estrogen receptor

TABLE 3

Clinical characteristics of patients with abnormal axillary ultrasound versus normal or not done

Participant characteristics	Normal nodes on US N = 31	Abnormal nodes on US N = 131	Not done N = 240	P-value
Age at diagnosis, median, yrs (range)	48 (32–74)	48 (23–81)	51 (26–78)	0.34
Clinical tumor size, median, (range)	4.0 (1.8–10.0)	4.0 (1.1–10)	4.0 (1.1–10)	0.38
Histology, n (%)				0.31
Ductal	29(94%)	118 (90%)	211 (88%)	
Lobular or mixed	2 (6%)	10 (8%)	28 (12%)	
Other	0(0%)	3 (2%)	1 (0.4%)	
Receptor status, n (%)				0.47 [*]
ER+/HER2-	16 (52%)	43 (33%)	92 (38%)	
HER2+	8 (25%)	41 (31%)	73 (31%)	
ER-/HER2-	7 (23%)	47 (36%)	75 (31%)	
Lymphovascular invasion, n (%)	10(32%)	41 (31%)	64 (27%)	0.56
Clinical T stage, n (%)				0.62
T1	1 (3%)	6 (5%)	17 (7%)	
T2	21 (68%)	91(69%)	148 (62%)	
T3	8 (26%)	23 (18%)	49 (20%)	
T4	1 (3%)	11 (8%)	26 (11%)	

*
p-value for ultrasound done versus not done

US, ultrasound; ER, estrogen receptor

TABLE 4

Rates of ypN+ and ALND among cN0 patients with abnormal versus normal or no pre-treatment axillary imaging

Imaging Modality	No. of patients N = 402	No. patients ypN+ N = 111	p-value	ALND N = 148	p-value
Mammogram					
Normal nodes	356	95 (27%)	0.29 *	130 (37%)	0.75 *
Abnormal nodes	46	16 (35%)		18 (39%)	
Axillary ultrasound					
Normal nodes	31	7 (23%)	0.1 *	8 (26%)	0.01 *
Abnormal nodes	131	52 (40%)	0.001 †	68 (52%)	<0.001 †
Not done	240	52 (22%)		72 (30%)	
MRI					
Normal nodes	178	30 (17%)	<0.001 *	42(24%)	<0.001 *
Abnormal nodes	154	53 (34%)	<0.001 †	70 (45%)	<0.001 †
Not done	70	28 (40%)		36 (51%)	
PET					
Normal nodes	101	21 (21%)	<0.001 *	27 (27%)	<0.001 *
Abnormal nodes	104	44 (42%)	<0.001 †	57 (55%)	<0.001 †
Not done	197	46 (23%)		64 (32%)	
Any					
Normal nodes	194	39 (20%)	0.001 *	52 (27%)	<0.001 *
Abnormal nodes	208	72 (35%)		96 (46%)	

* P-value for normal vs. abnormal

† P-value for normal vs. abnormal vs. not done

ypN+, post-treatment nodal metastases; ALND, axillary lymph node dissection; cN0, clinically node negative; PET, positron emission tomography

TABLE 5

Predictors of nodal positivity and ALND after NAC

Variable	ypN+				ALND			
	Odds ratio	95% CI	P-value		Odds ratio	95% CI	P-value	
Clinical tumor size								
Abnormal nodes								
No	1.02	0.89–1.16	0.8		1.09	0.97–1.23	0.16	
Yes	1.0 (ref)		<0.001		1.0 (ref)		<0.001	
	2.95	1.77–5.01			2.89	1.83–4.63		
Histology								
Ductal	1.0 (ref)		0.003		1.0 (ref)		<0.001	
Other	2.93	1.44–6.02			2.25	1.12–4.6		
Receptor status								
ER-/HER2-	Ref		<0.001		1.0 (ref)		<0.001	
ER+/HER2-	3.94	2.22–7.18			3.11	1.83–5.38		
HER2+	0.62	0.29–1.27			0.84	0.46–1.51		

ypN+, post-treatment nodal metastases; ALND, axillary lymph node dissection; CI, confidence interval; ER, estrogen receptor