

# Sterilization Rate of the Axilla After Neoadjuvant Chemotherapy: The Scope for Conservative Surgery

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**PURPOSE** The role of axillary conservation after neoadjuvant chemotherapy (NACT) is debatable. We routinely carry out complete axillary lymph node dissection (ALND). This study was conducted to understand the pathologic axillary complete response (pAxCR) after NACT.

**MATERIALS AND METHODS** We evaluated a prospective database of patients with breast cancer who underwent surgery after NACT in the year 2017 at our institution. NACT was administered to downstage locally advanced breast cancer or facilitate breast-conservation surgery.

**RESULTS** Of 793 patients who underwent surgery after NACT, 97(12.2%) had cN0 disease, 407 (51.3%) had cN1, 262 (32%) had cN2, and 27 (3.4%) had cN3 at presentation. Eighty-eight patients (11.1%) had cT1-2 primary tumor stage, and 623 patients (78.6%) had cT3-4 primary tumor stage; primary tumor stage details were unavailable for 82 patients (10.3%). The median age was 46 years (range, 21-74 years). On histopathology, the overall pAxCR rate was 52.8%. In the cN1 and cN2 settings, 58.7% and 36.6% of patients achieved ypNO status, respectively. The overall pathologic complete response rate was 22.64% (161 of 711 patients). On univariable analysis, cN stage, histologic grade, hormone receptor status, NACT duration, and lymphovascular invasion were significantly associated with pAxCR ( $P < .001$ ). On logistic regression, prechemotherapy cN status (odds ratio [OR], 3.08; 95% CI, 2.18 to 4.37;  $P < .001$ ), estrogen and progesterone receptor status (OR, 0.34; 95% CI, 0.3 to 0.4;  $P < .001$ ), and administration of both chemotherapy regimens preoperatively (OR, 0.66; 95% CI, 0.45 to 0.97;  $P < .05$ ) predicted pAxCR.

**CONCLUSION** At least half of patients with cN1 and a third of patients with cN2 breast cancer who develop pAxCR may be suitable candidates for axillary conservation. A careful postchemotherapy assessment followed by a conservative axillary procedure may be an alternative to ALND, but this needs to be studied prospectively.

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## INTRODUCTION

Breast cancer is the most common cancer in India.<sup>1</sup> The stage at presentation of breast cancer is higher in developing countries, with 30%-40% of patients presenting with locally advanced breast cancer (LABC).<sup>2</sup> Neoadjuvant chemotherapy (NACT) is used to downstage LABC and to downsize the primary tumor to allow breast-conserving surgery (BCS) in early breast cancer. There is increasing evidence for the use of preoperative chemotherapy, especially in patients with triple-negative and human epidermal growth factor receptor 2 (HER2)-positive breast cancer, to allow for risk-adapted postoperative adjuvant therapy planning based on pathologic complete response (pCR).<sup>3,4</sup> It is essential to stage the axilla appropriately in patients undergoing NACT to prognosticate and to determine appropriate second-line chemotherapy regimens. Currently, it is standard of care to offer an

axillary staging procedure such as sentinel node biopsy (SNB) in a clinicoradiologic node-negative axilla in the early breast cancer setting. Large randomized controlled trials have proven the safety of SNB over a complete axillary lymph node dissection (ALND) in a node-negative axilla with an acceptable false-negative rate (FNR) of up to 10%, showing no detriment on disease-free survival while avoiding the adverse effects of ALND.<sup>5,6</sup> The low axillary sampling (LAS) procedure has been validated at our center in early breast cancer in up-front operated patients and has been found to have an FNR of 10.5%, similar to that of SNB.<sup>7</sup> In the event of a positive axillary staging procedure, it is necessary to clear axillary lymph nodes (ALNs) at least up to level II to be of therapeutic value.<sup>8</sup> In a previous study, we documented a level III node-positive rate of 27.3% in a node-positive axilla at our institution.<sup>9</sup> Hence, our institutional practice is to

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## CONTEXT

### Key Objective

Our aim was to assess the rate of patients with a pathologic axillary complete response (pAxCR) after neoadjuvant chemotherapy (NACT) in breast cancer, a subgroup possibly eligible for axillary-conservation surgery.

### Knowledge Generated

Our cohort of patients with breast cancer predominantly had larger tumors and higher axillary nodal burden. Response rates varied based on the prechemotherapy axillary nodal stage (cN1 v cN2), hormone receptor status (positive v negative), and duration of NACT (administration of the entire chemotherapy regimen preoperatively v sandwich surgery between 2 regimens). In our study, 58.7% of cN1 patients and 36.6% of cN2 patients developed pAxCR, and these patients may be suitable candidates for axillary conservation.

### Relevance

In the setting of patients presenting with locally advanced breast cancer in low- to middle-income countries, this assessment of response rates forms the basis for feasibility of future prospective axillary-conservation procedures after NACT.

routinely clear up to level III in patients with node-positive breast cancer.

There is controversy surrounding the treatment of the postchemotherapy axilla, especially after NACT has rendered the previously positive ALN clinically undetectable.<sup>10</sup> Hence, a complete ALND is usually carried out in this setting, but it is associated with a significant risk of complications such as lymphedema, paresthesia, axillary web syndrome, and shoulder dysfunction.<sup>11</sup> Three recent studies have assessed the feasibility of SNB in the post-NACT setting.<sup>12-14</sup> Each study failed to meet the primary end point of demonstrating an FNR < 10%, a value deemed acceptable by previous SNB studies in up-front breast cancer surgery. Hence, the applicability of SNB in the post-NACT setting is unproven in view of the lack of noninferiority studies with survival as an end point. We conducted this study to understand the rate of clinically node-positive patients rendered pathologically node negative after NACT. This can provide insight into which patients might benefit from a more conservative approach to the axilla after chemotherapy.

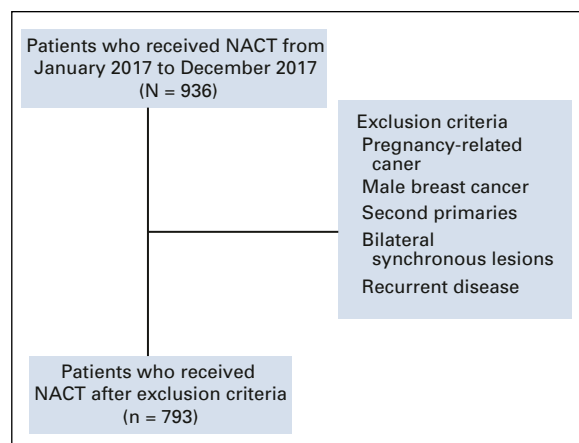
## MATERIALS AND METHODS

This study reviewed our prospectively maintained database of 936 consecutive patients with nonmetastatic breast cancer who underwent surgery after NACT at a single high-volume oncology institution, Tata Memorial Centre, Mumbai, between January and December 2017. Patients with pregnancy-related cancer, second primary breast cancers, male breast cancer, bilateral synchronous lesions, and recurrent disease were excluded (Fig 1). In total, 793 patients were eligible and were included in the study. The clinical stage was evaluated by physical examination, mammography, ultrasound of the abdomen and pelvis, and magnetic resonance imaging (MRI) when appropriate. The clinical lymph node staging followed the American Joint Committee on Cancer staging system for breast cancer (eighth edition).<sup>15</sup> An ALN that was single, hard, and mobile

was considered cN1, a node that was > 3 cm and/or matted was considered cN2, and an ipsilateral supraclavicular lymph node that was hard on palpation was considered cN3. The assignment of node status to the axilla, before and after NACT, was done by clinical examination alone. The ypNO classification was assigned if there was no ALN disease identified on final histopathology. NACT was administered either to downstage LABC or to facilitate BCS in early breast cancer. Patients were evaluated by a multidisciplinary team and underwent modified radical mastectomy or BCS based on patient choice and disease characteristics and as per the decision of the Breast Cancer Disease Management Group. All patients underwent removal of level I to III ALNs, along with the interpectoral nodes. Details of patients' histopathologic records were retrieved from the electronic medical records.

### Statistical Analysis

Baseline clinicopathologic characteristics of the cohort were reported as numbers and percentages. Univariable analysis was performed using Pearson  $\chi^2$  or Fisher's exact



**FIG 1.** Flowchart of study population. NACT, neoadjuvant chemotherapy.

**TABLE 1.** Clinicopathologic and Treatment Characteristics of Patients

Characteristic	No. of Patients (N = 793) <sup>a</sup>	%
Median age, years (range)	46 (21-74)	
Menopausal status		
Premenopausal	449	56.6
Postmenopausal	265	33.4
Posthysterectomy	79	10
Surgery performed		
Breast-conserving surgery	352	44.4
Modified radical mastectomy	441	55.6
Prechemotherapy clinical T stage		
T1-2	88	11.1
T3-4	623	78.6
Not known <sup>b</sup>	82	10.3
Median tumor size, cm (range)	6 (2-22)	
Prechemotherapy clinical N stage		
N0	97	12.2
N1	407	51.3
N2	262	32
N3	27	3.4
Histologic grade		
Low (MRB 1, 2)	63	7.9
High (MRB 3)	730	92.1
Lymphovascular invasion <sup>b</sup>		
Present	241	59.3
Absent	470	30.4
Not known <sup>b</sup>	82	10.3
Molecular subtype		
HR+/HER2- (luminal A/B1)	239	30.1
HR+/HER2+ (luminal B2)	141	17.8
HR-/HER2+ (HER2 enriched)	113	14.2
HR-/HER2- (TNBC)	265	33.4
Not known	35	4.4
Type of neoadjuvant chemotherapy <sup>c</sup>		
AC/EC every 3 weeks for 4 cycles + P every week for 12 cycles or every 3 weeks for 4 cycles	182	23
AC/EC every 3 weeks for 4 cycles + P and Tr every 3 weeks for 4 cycles or every week for 12 cycles	45	5.7
AC/EC every 3 weeks for 4 cycles	443	55.9
Weekly P with or without Tr for 12 cycles	99	12.5
Other	24	3
Postchemotherapy cN group		
N0	513	64.7
N1	248	31.3
N2	27	3.4

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test to look for an association between pCR in the axilla and other clinicopathologic variables. Multivariable analysis was done by logistic regression to identify independent predictors of complete response in the axilla. A test was statistically significant if the 2-sided  $P \leq .05$ . Data were analyzed using SPSS version 21.0 for Windows (SPSS, Chicago, IL).

## RESULTS

Of the 793 patients who underwent an ALND after NACT, the median age at presentation was 46 years (range, 21-74 years), with 56.6% patients being premenopausal before NACT. The relevant baseline characteristics before and after NACT are listed in Table 1. A total of 55.6% of patients underwent modified radical mastectomy as a result of either patient preference or a higher stage at presentation. Our cohort consisted predominantly of patients with cT3-4 lesions (78.6%). Because 82 patients had excision biopsy performed elsewhere before presenting to us, cT size, pT size, and tumor lymphovascular invasion (LVI) status were not available. Triple-negative breast cancer (TNBC) and luminal A tumors formed the largest 2 groups of patients, with 33.4% and 30.1% of patients in each group, respectively. A molecular subtype could not be assigned in 35 patients because of lack of proper fixation of the primary tumor in patients who had an excision biopsy for diagnosis elsewhere. On histologic evaluation, 92.1% of patients had high-grade disease.

Although most patients were clinically N1 or N2 at presentation (51.3% and 32%, respectively), a majority of patients (64.7%) were clinically N0 after NACT. The majority of patients in this study received anthracycline-based NACT. Chemotherapy regimens included the following: 55.9% of patients received anthracycline plus cyclophosphamide (doxorubicin 60 mg/m<sup>2</sup> plus cyclophosphamide 600 mg/m<sup>2</sup> or epirubicin 90 mg/m<sup>2</sup> plus cyclophosphamide 600 mg/m<sup>2</sup>) every 3 weeks for 4 cycles, 23% of patients received anthracycline plus cyclophosphamide every 3 weeks for 4 cycles followed by paclitaxel 80 mg/m<sup>2</sup> every week for 12 cycles or paclitaxel 175 mg/m<sup>2</sup> every 3 weeks for 4 cycles, 5.7% (HER2-positive patients) received anthracycline plus cyclophosphamide every 3 weeks for 4 cycles followed by paclitaxel 80 mg/m<sup>2</sup> with trastuzumab 4 mg/m<sup>2</sup> loading dose followed by 2 mg/m<sup>2</sup> every week for 12 cycles, 12.5% received paclitaxel plus trastuzumab every week for 12 cycles, and 3% of patients received other regimens. Only 58.6% of patients with HER2-positive tumors (immunohistochemistry 3+ or fluorescence in situ hybridization positive) received preoperative trastuzumab because of financial constraints.

### Response Rates in the Axilla and Primary Tumor

On histopathologic evaluation, the overall pathologic axillary complete response (pAxCR) rate was 52.8% (419 of 793 patients). In the cN1 and cN2 setting, 58.7% of patients (239 of 407) and 36.6% of patients (96 of 262) achieved

**TABLE 1.** Clinicopathologic and Treatment Characteristics of Patients (Continued)

Characteristic	No. of Patients (N = 793) <sup>a</sup>	%
Not known	5	0.6
Postchemotherapy ypT group <sup>b</sup>		
T1-2	628	79.2
T3-4	83	10.5
Not known	82	10.3
Mean postchemotherapy tumor size, cm (range)	2.48 (0-16.5)	
Postchemotherapy ypN group		
N0	419	52.8
N1 (1-3 ALNs positive)	177	22.3
N2 (4-10 ALNs positive)	131	16.5
N3 (> 10 ALNs positive)	66	8.3
Axillary sterilization/pAxCR		
Overall	419	52.8
cN1	239	58.7
cN2	96	36.6

Abbreviations: AC, doxorubicin and cyclophosphamide; ALN, axillary lymph node; EC, epirubicin and cyclophosphamide; HER2, human epidermal growth factor receptor; HR, hormone receptor; MRB, Modified Richardson Bloom score; P, paclitaxel; pAxCR, pathologic axillary complete response; TNBC, triple-negative breast cancer; Tr, trastuzumab.

<sup>a</sup>Values are numbers and percentages, unless otherwise indicated.

<sup>b</sup>Eighty-two patients had diagnostic excision biopsy done elsewhere; hence, the exact pT size and presence of lymphovascular invasion in the primary tumor could not be ascertained in these patients.

<sup>c</sup>The chemotherapy doses were as follows: doxorubicin, 60 mg/m<sup>2</sup>; epirubicin, 90 mg/m<sup>2</sup>; cyclophosphamide, 600 mg/m<sup>2</sup>; paclitaxel, 175 mg/m<sup>2</sup> if given every 3 weeks, 80 mg/m<sup>2</sup> if given weekly; trastuzumab, 4 mg/m<sup>2</sup> loading dose followed by 2 mg/m<sup>2</sup> weekly.

pAxCR status, respectively (Table 2). Although 83.3% of patients were clinically node positive before chemotherapy, 64.7% were clinically node negative after chemotherapy. Thus, only 11.9% of patients were clinically node negative but were found to harbor ALN metastases on histology. However, 32.4% of patients (89 of 275) who remained cN+

**TABLE 2.** Downstaging of Prechemotherapy cN Status After Chemotherapy

Prechemotherapy cN Status	Postchemotherapy cN Status (No. of patients) <sup>a</sup>			ypN Status (No. of patients)		
	cN0	cN+	Total	ypN0	ypN+	Total
cN0	2	0	2	73	24	97
cN1	275	129	404	239	168	407
cN2	114	146	260	96	166	262
cN3	1	0	1	11	16	27
Total	392	275	667	419	374	793

<sup>a</sup>Postchemotherapy cN status was available for 667 patients.

after NACT had negative nodes on histopathology, confirming the fallacy of clinical examination of the axilla. The median number of ALNs dissected was 16 (range, 0-47), whereas the median number of positive ALNs was 4 (range, 1-32). Postchemotherapy distribution of pathologic N staging was ypN0 in 52.8% of patients, ypN1 (1-3 positive ALNs) in 22.3%, ypN2 (4-10 positive ALNs) in 16.5%, and ypN3 (> 10 positive ALNs) in 8.3%. The clinical and pathological downstaging of prechemotherapy axillary lymph node status is further explained in Table 2.

The mean postchemotherapy pathologic tumor size was 2.48 cm (range, 0-16.5 cm). Complete response at the primary tumor site was seen in 25.45% of patients (181 of 711), of whom 88.9% (161 of 181 patients) also had pAxCR. pCR was considered when no invasive disease was found in the primary site as well as lymph nodes. Thus, overall pCR was seen in 22.64% of patients (161 of 711, excluding the 82 patients who had had diagnostic excision biopsy before starting chemotherapy). Five hundred thirty (74.55%) of 711 patients had residual disease at the primary site, of whom only 211 patients (39.8%) had pAxCR (*P* < .0001). Responses at the primary tumor site and in the axilla were not correlated. The pAxCR rates according to molecular subtype were 36.8%, 44.7%, 64.5%, and 66.8% in patients with hormone receptor (HR)-positive and HER2-negative disease, HR- and HER2-positive disease, HR-negative and HER2-positive disease, and TNBC, respectively (*P* < .0001; Table 3). The pAxCR rate was significantly influenced by the type of chemotherapy used and duration of NACT. pAxCR rates were 44.6%, 63.6%, 59.8%, and 72.7% with anthracyclines, anthracyclines and taxanes with trastuzumab, anthracyclines and taxane and trastuzumab, respectively (*P* < .0001). However, within the HER2-positive subset, the pAxCR rate was significantly higher for 12 cycles of weekly paclitaxel and trastuzumab (72.7%) compared with AC/EC administered every 3 weeks for 4 cycles (30%; *P* < .0001). Thus, the response was not solely dependent on the duration of chemotherapy but also on the regimen of NACT used.

**Univariable and Multivariable Analysis of Factors Affecting pAxCR**

On univariable analysis, cN stage, histologic grade, HR status, NACT duration, and LVI were factors that significantly correlated with pAxCR (*P* < .001). On logistic regression, prechemotherapy cN status (odds ratio [OR], 3.08; 95% CI, 2.18 to 4.37; *P* < .001), HR status (OR, 0.34; 95% CI, 0.3 to 0.4; *P* < .001), and administration of both chemotherapy regimens preoperatively (OR, 0.66; 95% CI, 0.45 to 0.97; *P* < .05) were factors that predicted pAxCR (Table 4).

**DISCUSSION**

Predicting response in the axilla after NACT is vital to determine prognosis, consider axillary conservation, and improve patient outcomes. We observed an overall pAxCR

**TABLE 3.** Correlation of Molecular Subtype, Type of Chemotherapy Used, and pCR in Primary Tumor With pAxCR

Variable	No. of Patients		pAxCR Rate (%)	P
	pAxCR	No pAxCR		
Biologic subtype (n = 758) <sup>a</sup>				<.0001
HR positive/HER2 negative	88	151	36.8	
HR positive/HER2 positive	63	78	44.7	
HR negative/HER2 positive	73	40	64.5	
TNBC	177	88	66.8	
Type of chemotherapy used (n = 769) <sup>b</sup>				<.001
AC/EC	198	246	44.6	
AC/EC plus paclitaxel and trastuzumab	28	16	63.6	
AC/EC plus paclitaxel	109	73	59.8	
Paclitaxel and trastuzumab	72	27	72.7	
Breast response (n = 711) <sup>c</sup>				<.0001
Breast primary pCR	161	20		
Residual breast disease	211	319		

Abbreviations: AC, doxorubicin and cyclophosphamide; EC, epirubicin and cyclophosphamide; HER2, human epidermal growth factor receptor; HR, hormone receptor; pAxCR, pathologic axillary complete response; pCR, pathologic complete response; TNBC, triple-negative breast cancer.

<sup>a</sup>Thirty-five patients did not have a complete triple immunohistochemistry assessment as a result of fixation issues.

<sup>b</sup>Twenty-four patients had other preoperative chemotherapy regimens.

<sup>c</sup>Eighty-two patients had a diagnostic excision biopsy, making response in the primary tumor nonassessable.

rate of 52.8% in patients presenting with relatively advanced-stage tumors. The initial nodal stage (N1 v N2 nodal disease), histologic grade, HR status, presence of LVI in the primary tumor, and duration of NACT were significantly associated with pAxCR. The nodal burden and stage at presentation affect the rate of axillary sterilization. Previous studies have predicted a 100% axillary pCR rate in pre-NACT cN0 axilla when a pCR was achieved in the primary tumor, especially in HER2-positive and TNBC patients.<sup>16</sup> The axillary response rate in node-positive patients is approximately 40%-65%.<sup>17-19</sup> The safety of post-chemotherapy axillary conservative surgery is doubtful in our context of high nodal burden at presentation. HR-positive tumors are known to have a poor response to chemotherapy. We found that the molecular subtype of breast cancer affects the nodal response rate significantly. This kind of differential response has also been observed with pCR rates.<sup>20</sup> Similar to our study, other published studies have shown response rates of > 60% in the poor-prognosis molecular subtypes such as HER2-enriched and triple-negative subsets. Paradoxically, these subtypes of tumors are associated with worse long-term survival outcomes.<sup>21,22</sup> Although the opportunity to de-escalate axillary surgery seems to be greater in molecular subtypes with a poor prognosis after NACT, the safety is questionable until proven in a prospective randomized study.

We found the discrepancy between the clinical and pathologic node-negative rate after NACT to be only

approximately 10%, a rate different than that reported in studies in up-front breast surgery, in which nearly 30% of clinically node-negative patients had positive nodes on pathology.<sup>23</sup> In addition, 32% of palpable nodes were clinically node negative, thus confirming the inaccuracy of physical examination to stage the axilla after NACT. Other studies have similarly determined that a third of cN0 examinations are falsely negative and approximately a third of clinically node-positive examinations are falsely positive, although not in the post-NACT setting.<sup>24</sup>

SNB is an effective procedure in staging the axilla in patients with node-negative breast cancer. If sentinel nodes are positive, then it is advisable to complete the ALND. Recent evidence supporting axilla conservation when 1-2 ALNs are positive can only be applied to low-risk patient groups.<sup>25</sup> With the advent of risk-adapted chemotherapeutic strategies, the use of NACT is increasing, especially for TNBC and HER2-positive breast cancer. Accurate staging of the axilla is necessary when NACT is planned. Previous studies carried out to evaluate the timing of SNB (ie, before or after receiving chemotherapy) acknowledge the pros and cons of each approach.<sup>26</sup> Recent meta-analyses have shown that, in pre-NACT cN0 patients, it is feasible to offer an SNB procedure, with an identification rate of 90%-94% and an FNR of 7%-12%.<sup>10</sup> However, in prechemotherapy node-positive patients, the value of performing a postchemotherapy SNB is undefined. Our cohort of patients predominantly consisted of patients with

**TABLE 4.** Univariable and Multivariable Analysis of Factors Predicting pAxCR

Clinicopathologic Feature	Univariable Analysis ( $\chi^2$ /Fisher's exact)		Logistic Regression (multivariable)		
	pCR (No./Total No.)	P	OR	95% CI	P
Age, years		.54	0.85	0.60 to 1.20	.36
< 50	283/528				
> 50	136/265				
cT stage		.19	1.14	0.81 to 1.62	.43
T1-2	53/88				
T3-4	319/623				
cN stage		<.001	3.08	2.18 to 4.37	<.001
N0-1	312/504				
N2-3	96/262				
Histologic grade		<.001	—	—	—
Low (2)	21/63				
High (3)	398/730				
HR status (ER and/or PR)		<.001	0.34	0.30 to 0.40	<.001
Positive	161/401				
Negative	257/390				
HER2 status		.86	1.37	0.97 to 1.93	.07
Positive	136/255				
Negative	266/505				
Lymphovascular invasion present	53/241	<.001	—	—	—
NACT duration		<.01	0.66	0.45 to 0.97	<.05
Absent	319/470				
All up-front	137/226				
Sandwich surgery	270/543				

NOTE. Histologic grade and presence of lymphovascular invasion were excluded from the logistic regression because of the strong correlation with nodal positivity and confounding effect on the multivariable analysis.

Abbreviations: ER, estrogen receptor; HER2, human epidermal growth factor receptor; HR, hormone receptor; NACT, neoadjuvant chemotherapy; OR, odds ratio; pAxCR, pathologic axillary complete response; pCR, pathologic complete response; PR, progesterone receptor.

higher nodal burden and with a median clinical tumor size of 6 cm, in whom the feasibility of a conservative axillary procedure has not been studied. We observed poor correlation between primary tumor complete response and pAxCR. Although 52.8% of patients had pAxCR, only 25.5% of patients had a PCR in primary tumor. This may be a result of error in clinical axillary examination and tumor heterogeneity that has been reported between the primary tumor and nodal foci of tumor.<sup>27</sup>

The SENTINA study<sup>27a</sup> of post-NACT SNB used stringent axillary staging criteria with clinical examination, as well as pre- and postchemotherapy ultrasound of the axilla. In our study, adding ultrasound of the axilla to improve clinical axillary staging accuracy would likely have benefitted the 10% of patients with a clinically node-negative axilla who had positive nodes on pathology and the 30% of patients with a clinically palpable node after NACT who were actually node negative on the pathologic report. However, we

did not routinely use ultrasound of the axilla for axillary staging for logistic reasons and relied on clinical examination findings alone. Unfortunately, axillary imaging using ultrasound, MRI, and positron emission tomography still has limited accuracy in the assessment of pAxCR unless combined with a fine-needle aspiration cytology (FNAC).<sup>28-30</sup> Some recently published studies have suggested using ultrasound-guided clip placement in FNAC-proven positive nodes to aid their identification and subsequent removal during surgery after NACT. This has been shown to improve the FNR and accuracy of post-NACT nodal assessment.<sup>31,32</sup> Because of financial constraints, this method is not practically applicable in our setting, and we do not routinely use this strategy at our center.

Predicting responses can help identify appropriate patients in whom aggressive surgery may be avoided. As seen in early breast cancer, axillary treatment de-escalation (SNB or LAS) is effective in reducing lymphedema rates and other

morbidities associated with axillary surgery.<sup>33,34</sup> However, SNB studies in the post-NACT setting have failed to meet the primary end point of FNR < 10%.<sup>12,13</sup> We have recently validated a method of LAS that involves a low-cost axillary intervention in patients with LABC and large operable breast cancer after chemotherapy. Although the SNB identification rate was 87.1% with a median of 5 nodes, the LAS identification rate was 98% with a median of 7 nodes. In addition, 37.4% of SNB-identified nodes were positive, whereas 39.6% of LAS-identified nodes were positive.<sup>35</sup> However, this study included few cN2 patients, and long-term randomized studies with survival end points will be necessary to determine the safety of an axillary-conservation approach in node-positive patients rendered node negative after NACT. Currently, no study has evaluated the feasibility and safety of SNB in cN2 axilla. The role of axillary irradiation as an alternative to surgical ALND in this setting is experimental.<sup>36</sup> In our study, axillary staging was done using

clinical assessment alone. Approximately 60% of patients with HER2-positive tumors received trastuzumab as part of their neoadjuvant therapy, a drug known to affect the rate of pCR in these patients, as a result of financial issues. However, this is one of largest studies performed in a single tertiary cancer institute in India in patients with predominantly LABC. Therefore, the results are still relevant in our setting and allow us to draw meaningful conclusions concerning the feasibility of conservative axillary surgery, such as LAS, in the post-chemotherapy setting.

In the postchemotherapy setting, at least half of cN1 and a third of cN2 patients are rendered ypN0 and may be suitable candidates for conservative surgery of the axilla. Future prospective studies are needed to evaluate alternatives to routine complete ALND, such as LAS and other techniques, especially in the postchemotherapy setting in patients with more advanced disease at presentation.

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## PRIOR PRESENTATION

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**Accountable for all aspects of the work:** All authors

## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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