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

Jarin Noronha, MS, MCh; Shalaka Joshi, MS, MCh, MRes; Rohini Hawaldar, MSc; Nita Nair, DNB, MCh; Vaibhav Vanmali, BCom, PDCR; Vani Parmar, MS; Tanuja Shet, MD; and Rajendra Badwe, MS

Abstract

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 ypN0 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.

JCO Global Oncol 6:1184-1191. © 2020 by American Society of Clinical Oncology

Introduction

Breast cancer is the most common cancer in India. The stage at presentation of breast cancer is higher in developing countries, with 30%-40% of patients presenting with locally advanced breast cancer (LABC). 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). 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.

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. 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. In a previous study, we documented a level III node-positive rate of 27.3% in a node-positive axilla at our institution. Hence, our institutional practice is to...
KEY POINTS
- Patients with node-positive breast cancer 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. 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. Three recent studies have assessed the feasibility of SNB in the post-NACT setting.
- 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.
- 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.
- 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.
- 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.

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). 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 test.
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 $P \leq 0.05$. 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/m² plus cyclophosphamide 600 mg/m² or epirubicin 90 mg/m² plus cyclophosphamide 600 mg/m²) every 3 weeks for 4 cycles, 23% of patients received anthracycline plus cyclophosphamide every 3 weeks for 4 cycles followed by paclitaxel 80 mg/m² every week for 12 cycles or paclitaxel 175 mg/m² every 3 weeks for 4 cycles, 5.7% (HER2-positive patients) received anthracycline plus cyclophosphamide every 3 weeks followed by paclitaxel 80 mg/m² every week for 12 cycles or paclitaxel 175 mg/m² every 3 weeks for 4 cycles, 5.7% (HER2-positive patients) received anthracycline plus cyclophosphamide every 3 weeks followed by paclitaxel 80 mg/m² with trastuzumab 4 mg/m² loading dose followed by 2 mg/m² 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)*     |     |
| Not known                      | 5              | 0.6 |
| Postchemotherapy ypT group^a   |                |     |
| 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) |     |

TABLE 2. Downstaging of Prechemotherapy cN Status After Chemotherapy

| Prechemotherapy cN Status (No. of patients)^a | Postchemotherapy cN Status | ypN Status (No. of patients) |
|-----------------------------------------------|----------------------------|------------------------------|
|                                               | cN0 | cN+ | Total | ypN0 | ypN+ | Total |
| cN0                                           | 2   | 2   | 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   |

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.

^aValues are numbers and percentages, unless otherwise indicated.

^bEighty-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.

^cThe chemotherapy doses were as follows: doxorubicin, 60 mg/m²; epirubicin, 90 mg/m²; cyclophosphamide, 600 mg/m²; paclitaxel, 175 mg/m² if given every 3 weeks, 80 mg/m² if given weekly; trastuzumab, 4 mg/m² loading dose followed by 2 mg/m² 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+ 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. cCR 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 taxanes, 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
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.16 The axillary response rate in node-positive patients is approximately 40%-65%.17-19 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.20 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.21,22 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.23 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.24

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.25 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.26 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%.10 However, in prechemotherapy node-positive patients, the value of performing a postchemotherapy SNB is undefined. Our cohort of patients predominantly consisted of patients with

| Variable                                      | pAxCR | No pAxCR | pAxCR Rate (%) | P  |
|-----------------------------------------------|-------|----------|----------------|----|
| Biologic subtype (n = 758)<sup>a</sup>        |       |          |                |    |
| HR positive/HER2 negative                     | 88    | 151      | 36.8           | <.0001 |
| 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.
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.27

The SENTINA study27a 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 benefited 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).28-30

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.31,32 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

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

| Clinicopathologic Feature | Univariable Analysis (χ²/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.
morbidity associated with axillary surgery. However, SNB studies in the post-NACT setting have failed to meet the primary end point of FNR < 10%. 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. 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. 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 postchemotherapy setting.

In the postchemotherapy setting, at least half of cN1 and a third of cN2 patients are rendered ypNO 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.

AFFILIATIONS
1 Department of Surgical Oncology, Breast Services, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India
2 Clinical Research Secretariat, Tata Memorial Centre, Mumbai, India
3 Department of Pathology, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India
CORRESPONDING AUTHOR
Shalaka Joshi, MCh, MRes, Tata Memorial Hospital, Dr E Borges Rd, Mumbai, India 400012; e-mail: drjoshishalaka@gmail.com.

EQUAL CONTRIBUTION
*J.N. and S.J. contributed equally to this work.

PRIOR PRESENTATION
Presented in part at the 39th Congress of the European Society of Surgical Oncologists, Rotterdam, the Netherlands, October 9-11, 2019.

AUTHOR CONTRIBUTIONS
Conception and design: Jinar Noronha, Shalaka Joshi, Rajendra Badwe
Administrative support: Rohini Hawaldar, Vaibhav Vannali

REFERENCES
1. Bray F, Ferlay J, Soerjomataram I, et al: Global cancer statistics 2018. GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68:394-424, 2018
2. Nair N, Seth T, Parmar V, et al: Breast cancer in a tertiary cancer center in India: An audit, with outcome analysis. Indian J Cancer 55:16-22, 2018
3. von Minckwitz G, Huang CS, Mano MS, et al: Trastuzumab emtansine for residual invasive HER2-positive breast cancer. N Engl J Med 380:617-628, 2019
4. Masuda N, Lee SJ, Ohtani S, et al: Adjuvant capecitabine for breast cancer after preoperative chemotherapy. N Engl J Med 376:2147-2159, 2017
5. Krag DN, Anderson SJ, Julian TB, et al: Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer. Overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol 11:927-933, 2010
6. Mansel RE, Fallowfield L, Kissin M, et al: Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: The ALMANAC trial. J Natl Cancer Inst 98:599-609, 2016
7. Parmar V, Hawaldar R, Nair NS, et al: Sentinel node biopsy versus low axillary sampling in women with clinically node negative operable breast cancer. Breast 22:1081-1086, 2013
8. National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology Breast Cancer (Version 3.2018). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
30. You S, Kang DK, Jung YS, et al: Evaluation of lymph node status after neoadjuvant chemotherapy in breast cancer patients: Comparison of diagnostic methods.

29. Kubota M, Inoue K, Koh S, et al: Role of ultrasonography in treatment selection. Breast Cancer 10:188-197, 2003

28. Hyun SJ, Kim E-K, Moon HJ, et al: Preoperative axillary lymph node evaluation in breast cancer patients by breast magnetic resonance imaging (MRI). Can breast MRI exclude advanced nodal disease? Eur Radiol 26:3865-3873, 2016

27a. Kuehn T, Bauerfeind I, Fehm T, et al: Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): A prospective, multicentre cohort study. Lancet Oncol 14:609-618, 2013

27. Fleming CA, McCarthy K, Ryan C, et al: Evaluation of discordance in primary tumor and lymph node response after neoadjuvant therapy in breast cancer. Clin Breast Cancer 18:445-451, 2018

26. Cavalcante FP, Millen EC, Zerwes FP, et al: Role of axillary surgery after neoadjuvant chemotherapy. JCO Glob Oncol 6:238-241, 2020

25. Giuliano AE, Ballman KV, McCall L, et al: Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: The ACOSOG Z0011 (Alliance) randomized clinical trial. JAMA 318:918-926, 2017

24. Specht MC, Fey JV, Borgen PI, et al: Is the clinically positive axilla in breast cancer really a contraindication to sentinel lymph node biopsy? J Am Coll Surg 200:10-14, 2005

23. Voogd AC, Coebergh JW, Repelaer van Driel OJ, et al: The risk of nodal metastases in breast cancer patients with clinically negative lymph nodes: A population-based analysis. Breast Cancer Res Treat 62:63-69, 2000

22. Ménard S, Fortis S, Castiglioni F, et al: HER2 as a prognostic factor in breast cancer. Oncology 61:67-72, 2001 (suppl 2)

21. Kaplan HG, Malmgren JA: Impact of triple negative phenotype on breast cancer prognosis. Breast J 14:456-463, 2008

20. Choi HJ, Ryu JM, Kim I, et al: Prediction of axillary pathologic response with breast pathologic complete response after neoadjuvant chemotherapy. Breast Cancer Res Treat 176:591-596, 2016

19. L-Tweigeri TA, AlSayed A, Alawadi S, et al: A multicenter prospective phase II trial of neoadjuvant epirubicin, cyclophosphamide, and 5-fluorouracil (FEC100) followed by cisplatin-docetaxel with or without trastuzumab in locally advanced breast cancer. Cancer Chemother Pharmacol 77:147-153, 2016

18. Zhang GC, Zhang YF, Xu FP, et al: Axillary-lymph node status, adjusted for pathologic complete response in breast and axilla after neoadjuvant chemotherapy, predicts differential disease-free survival in breast cancer. Curr Oncol 20:e180-e192, 2013

17. Sikov WM, Berry DA, Perou CM, et al: Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide on pathologic complete response rates in stage II to III triple-negative breast cancer: CALGB 40603 (Alliance). J Clin Oncol 33:13-21, 2015

16. Tadros AB, Poirier B, Basik M, et al: Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: The SN FNAC study. J Clin Oncol 33:258-264, 2015

15. Amin MB, Edge S, Greene F, et al (eds): AJCC Cancer Staging Manual (ed 8). New York, NY, Springer, 2017

14. Boileau JF, Poirier B, Basik M, et al: Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: The SN FNAC study. J Clin Oncol 33:258-264, 2015

13. Boughey JC, Suman VJ, Mittenfost EA, et al: Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: The ACOSOG Z1071 (Alliance) clinical trial. JAMA 310:1455-1461, 2013

12. Kuehn T, Bauerfeind I, Fehm T, et al: Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): A prospective, multicentre cohort study. Lancet Oncol 14:609-618, 2013

11. Swenson KK, Nissen MJ, Geronsky C, et al: Comparison of side effects between sentinel lymph node and axillary lymph node dissection for breast cancer. Ann Surg Oncol 9:745-753, 2002

10. Pilewskie M, Morrow M: Axillary nodal management following neoadjuvant chemotherapy: A review. JAMA Oncol 3:549-555, 2017

9. Joshi S, Noronha J, Hawaldar R, et al: Merits of level III axillary dissection in node-positive breast cancer: A prospective, single-institution study from India. J Glob Oncol 5:1-8, 2019

8. Currey A, Patten CR, Bergom C, et al: Management of the axilla after neo-adjuvant chemotherapy for breast cancer: Sentinel node biopsy and radiotherapy considerations. Breast J 24:902-910, 2018