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The success of sentinel lymph node biopsy after neoadjuvant therapy: A single institution review

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ABSTRACT

Background: The appropriate management of the axilla among women undergoing neoadjuvant therapy is in evolution.
Method: A retrospective review of a prospective database of women with breast cancer who underwent neoadjuvant systemic therapy using endocrine/chemotherapy (NE/CT) from 2002 to 2015 was performed.
Results: We reviewed 253 women: triple negative breast cancer (30%), ER+HER2- (44%) breast cancer and HER2+ (25%) disease. The mean age was 55 years (SD = 12). 197 patients were analyzed based on their axillary disease. 33 patients (35%) who had clinical N1-3 disease prior to neoadjuvant therapy had no axillary metastases at definitive surgery. There were no significant differences in overall survival or local/regional recurrence between patients who underwent axillary lymph node dissection (ALND), sentinel lymph node biopsy (SLNB), or SLNB+ALND ($p = 0.05061$ and $p = 0.33$).
Conclusion: SLNB is a viable technique in patients with breast cancer undergoing NE/CT. Patients with pre-neoadjuvant therapy proven axillary disease may be a candidate for SLNB as opposed to planned ALND with good multidisciplinary review of their response and localization of previously positive lymph nodes.

1. Introduction

The management of the axilla in women with breast cancer undergoing neoadjuvant therapy is evolving, the current standard of care being an axillary dissection. In clinically node-negative patients, the role of SLN biopsy has been established by NSABP B-27 and multiple meta-analyses that sentinel lymph node identification and false-negative rates (FNR) after neoadjuvant chemotherapy are comparable to patients who received surgery first.[1–3] However, despite these prior studies and analysis the question remains regarding the use of sentinel lymph node (SLN) biopsy in patients with node positive disease.

Multiple studies have examined expanding the use of SLN biopsy in this population with variable results, and in 2013 the American College of Surgeons Oncology Group Z1071 Clinical Trial published their results of a prospective trial of women with node-positive breast cancer who underwent neoadjuvant chemotherapy therapy prior to definitive surgery. All patients had cytologically or histologically proven axillary lymph node metastases, prior to initiation of neoadjuvant chemotherapy. After completion of neoadjuvant chemotherapy, all patients underwent sentinel lymph node biopsy with concomitant axillary lymph node dissection. The objective of their study was to determine if the false-negative rate of sentinel lymph node biopsy in patients with cN1 who at least 2 sentinel lymph nodes identified was greater than 10%. The study demonstrated a FNR of 12.6% in patients with clinical N1 disease with biopsy of 2 or more SLN.[4]

Subsequent analysis of Z1071 found dual agent mapping with both blue dye and radiolabeled colloid was the only significant

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factor affecting identification of a sentinel lymph node, as well as improving the false negative rate.[4,5] Further analysis found use of axillary ultrasound to identify patients as candidates for SLN biopsy would have reduced the false negative rate to 9.8%, positing this as a potentially acceptable level.[6]

Prior to Z1071, multiple studies had reported the variable reliability of SLN biopsy in this population, with FNRs of 2.4–33%.[1,7–15] Subsequent analysis of the Z1071 trial, as well as the SENTINA trial and Sentinel Node Biopsy Following Neoadjuvant chemotherapy (SN FNAC) study have found more acceptable FNR's of 9.1%, 8.6% and 4.9% respectively with identification of at least 3 sentinel lymph nodes and the use of dual agent mapping.[4,10,16] As such our practice has changed to favor SLN biopsy in selected patients who have undergone NE/CT. Given the lack of evidence for axillary dissection improving survival in these patients, but a part of the local/regional control of the disease, we reviewed our experience in this patient population.

These conflicting false-negative rates may be related to differences in technique and procedures of localizing pre-NE/CT positive lymph node disease, in addition to the procedure of sentinel lymph node biopsy. Since 2013 our practice has shifted to primarily performing sentinel lymph node biopsy in this population of NE/CT women if there is no post-therapy evidence of new or residual axillary disease. We examined our experience as a retrospective cohort from 2002 to 2015, specifically analyzing our patient cohort before and after 2013 as an adjunct to review the implications of our practice change on recurrent axillary disease.

2. Materials and methods

We performed a retrospective review of a prospectively collected database of women with breast cancer who underwent NE/CT prior to definitive breast surgery. We analyzed patient factors, tumor factors, and specifically axillary staging procedures performed in this cohort. N-stage was determined by clinical examination, radiologic testing, or biopsy-proven metastases, on a case-by-case basis. The neoadjuvant endocrine or chemotherapy regimen was determined at the discretion of the patients' medical oncologist, and the axillary staging procedure was decided in multidisciplinary conference.

Descriptive statistics were analyzed by axillary procedure performed, either axillary lymph node dissection (ALND), SLN biopsy, or SLN biopsy + completion axillary lymph node dissection (CALND). Pathologic complete response (pCR) was analyzed only in patients with a clinical N-stage of >0, and defined as absence of residual invasive disease in the axillary lymph nodes, after having clinical evidence of pre-NE/CT nodal disease. Patient demographics and tumor characteristics were compared between categories by analysis of variance (ANOVA) for continuous variables or chi-square tests for categorical variables. Time to local/regional recurrence was defined as the time from primary surgery date to the date of first local or regional recurrence. Recurrence-free survival (RFS) included time from primary surgery date to the date of first recurrence (local or regional) or death from any cause. Overall survival (OS) was calculated as the time from primary surgery date to date of death from any cause. Patients without a recurrence or death event at last follow-up were considered censored for RFS and OS analyses. Event curves were estimated by the Kaplan-Meier method and compared between axillary procedure groups by the log-rank test. Two-sided p-value <0.05 were considered statistically significant.

3. Results

3.1. Patient factors (Table 1)

From 2002 to 2015 we identified 253 patients with breast cancer who underwent NE/CT and definitive breast surgery. Patients with inflammatory breast cancer, stage IV disease, or who had no axillary staging procedure performed, were excluded (Fig. 1). Analysis was conducted on the remaining 198 patients. The mean age was 54 years (range 22–88). 53% of patients were post-menopausal (n = 106). The majority of patients were Caucasian (80%, n = 157), followed by Hispanic (7.7%, n = 15), and African American (3.6%, n = 7). Mean BMI was 26.9 (standard deviation 5.7). Median follow up time was 2.4 years (standard deviation 2.1 years).

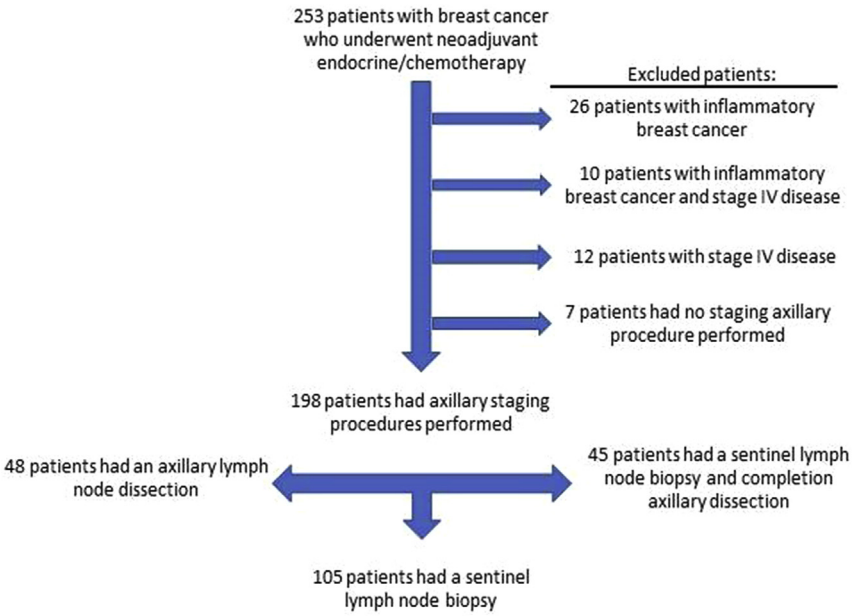

Fig. 1. Consort diagram of neoadjuvant patients.

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