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Accurate axillary lymph node dissection is feasible after neoadjuvant chemotherapy

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Abstract

BACKGROUND: Recently, lower axillary lymph node retrieval after neoadjuvant chemotherapy was reported. We did not have this experience, and retrospectively analyzed our axillary lymph node dissections (ALNDs).

METHODS: One hundred ninety-one patients who had ALND after neoadjuvant chemotherapy were compared with 192 patients with primary ALND after a positive sentinel node biopsy.

RESULTS: There were no differences in the mean number of nodes retrieved between the neoadjuvant group and the primary surgery group: 16.3 (range 4–38) and 15.8 (range 6–33), respectively ($P = .4$); or in the retrieval of fewer than 10 lymph nodes: 13/191 (7%) and 11/192 (6%) ($P = .7$). The number of cases with retrieval of more than 20 lymph nodes was higher in the neoadjuvant group: 42/191 (22%) versus 26/192 (13%) ($P = .03$). In the neoadjuvant group, 150/191 (79%) patients had residual lymph node metastasis after neoadjuvant chemotherapy.

CONCLUSION: Our results show the feasibility and need to remove enough lymph nodes to provide precise prognostic information and adequate local control.

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The primary site of lymphatic drainage of the breast is the axillary region, and therefore the axillary lymph nodes are often involved in regional metastatic disease in breast cancer. The standard treatment of axillary lymph node me-

tastasis is an axillary lymph node dissection (ALND). With the advent of the sentinel node biopsy procedure, the question has been raised how to treat further lymph node metastasis in case of a positive sentinel node. Awaiting the outcome of large randomized multicenter trials, in which surgery to the axilla will be compared with axillary radiation or no further treatment, ALND will remain the standard of care in patients with proven lymph node metastasis.^{1,2}

Dissection of the axilla and analysis of the axillary lymph nodes have prognostic and therapeutic impacts. In-

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formation about the number or ratio of positive lymph nodes is important for prognostic purposes and helps to determine the need for adjuvant systemic therapy like chemotherapy, endocrine, and targeted biological therapy, and for radiotherapy.^{3,4} From this prognostic perspective, a sufficient number of lymph nodes have to be removed to be predictive that the remaining lymph nodes will be negative. A minimum of 10 nodes have to be retrieved to achieve 90% probability that the remaining lymph nodes are not involved.⁵ For therapeutic concerns, at least level I and II lymph nodes have to be removed to provide adequate local control.^{6,7}

ALND controls local disease; however, the impact on survival remains a point of contention. The National Surgical Adjuvant Breast and Bowel Project (NSABP) B-04, in which clinically node-negative patients were randomized to undergo ALND, axillary radiation therapy, or no direct axillary treatment, showed no significant differences in survival among these 3 treatment arms after 25 years of follow-up.⁸ Although this study has failed to show a significant survival advantage, a meta-analysis of trials addressing treatment of the axilla has shown a 5.4% (95% confidence interval, 2.7%–8.%) absolute benefit in survival.⁹ The main point of discussion is that the NSABP B-04 did not include enough patients to exclude a small survival advantage. The existence of a survival benefit in patients with clinically negative lymph nodes treated with an ALND is still controversial.

Primary systemic therapy or neoadjuvant chemotherapy is increasingly being implemented in the treatment of breast cancer. Recent published studies have demonstrated a decreased axillary lymph node retrieval in patients after neoadjuvant therapy, resulting in a general acceptance of a low lymph node count after neoadjuvant chemotherapy. Basliam et al found a significant lower mean lymph node retrieval for patients treated with neoadjuvant chemotherapy, compared to patients in whom surgery was performed first, 14.3 ± 6.7 versus 16.9 ± 8.8 , respectively.¹⁰ Neuman et al reported a significant increase in the number of patients, in which less than ten lymph nodes were removed when surgery was performed after neoadjuvant chemotherapy, 13% versus 4%, respectively.¹¹ In our experience, we did not retrieve fewer lymph nodes while performing an ALND following neoadjuvant chemotherapy. Therefore, the aim of this retrospective study was to analyze these clinical observations.

Patients and Methods

Between 2001 and 2006, 191 patients with proven axillary lymph node metastasis were treated with neoadjuvant chemotherapy in The Netherlands Cancer Institute. All included patients had proven axillary lymph node metastases by fine-needle aspiration (FNA) cytology ($n = 171$) or a positive sentinel node biopsy prior to chemotherapy ($n = 20$). The majority of patients participated in 2 randomized

Table 1 Patient, tumor, and treatment characteristics

	Neoadjuvant chemotherapy		Primary surgery	
No. of patients	191		192	
Age, y (range)	47 (23–76)		56 (29–88)	
Clinical tumor category				
T0	1	5%	0	0%
T1	19	10%	114	60%
T2	96	50%	76	39%
T3	46	24%	0	0%
T4	28	15%	2	1%
Clinical node category				
N0	20	11%	192	100%
N1	144	75%		
N2	14	7%		
N3	13	7%		
Histology				
Lobular	20	11%	23	12%
Ductal	140	73%	160	83%
Others	31	16%	9	5%
Surgery tumor				
No surgery	1	1%		
WLE	88	46%	122	63%
Mastectomy	102	53%	70	37%
Neoadjuvant chemotherapy				
AC	146	76%	n/a	
CD	13	7%		
PTC	12	7%		
Other	20	10%		

WLE = wide local excision; AC = doxorubicin and cyclophosphamide; CD = docetaxel and capecitabine; PTC = paclitaxel, carboplatin, and trastuzumab.

trials comparing anthracycline- and/or taxane-based chemotherapy regimens (Table 1). These studies were approved by the institutional review board. Since 2005, patients with a Her2 amplification were treated with trastuzumab-based chemotherapy regimens.

A database of patients who underwent sentinel node biopsy at The Netherlands Cancer Institute between 1999 and 2005 was used to select a control group of patients not treated with neoadjuvant chemotherapy. From this database the first consecutive 192 patients with a positive sentinel node, followed by axillary lymph node dissection, were included.

In both groups level I, II dissection was performed combined with breast-conserving therapy or mastectomy. Level III sampling was done to stage for adjuvant radiotherapy indications.¹² All procedures were performed by experienced surgeons or under their supervision by a resident or fellow. Patients were treated with uniform protocols regarding pathological workup, and the surgical and pathological teams were the same in both groups. The total number of lymph nodes removed was calculated by the sum of the sentinel nodes, non-sentinel nodes, and additional nodes retrieved during ALND.

Histopathological analyses of the ALND specimen consisted of accurate visual and palpable inspection, in which the specimen was sliced per millimeter. Identification of

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