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A comparison of sentinel node biopsy before and after neoadjuvant chemotherapy: timing is important

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Abstract

Background: Because neoadjuvant chemotherapy is being used more frequently, the optimal timing of sentinel node biopsy (SNB) remains controversial. We previously evaluated the predictive value of SNB before neoadjuvant chemotherapy in clinically node-negative breast cancer. Our identification rate of the sentinel node among 52 patients before chemotherapy with a mean tumor size of 4 cm was 100%. In this study, we compared the identification rates of SNB before and after neoadjuvant chemotherapy and evaluated the false-negative rate of SNB after chemotherapy.

Methods: A retrospective institutional database review identified 36 women who underwent SNB after neoadjuvant chemotherapy for breast cancer from 1999 to 2004. The initial clinical tumor size and lymph node status, SNB pathology, axillary lymph node dissection pathology, and residual pathologic tumor size were reviewed.

Results: Sixteen of 36 patients had a clinically negative axilla before neoadjuvant therapy. SNB after neoadjuvant therapy was successful in 29 patients (80.6%), although 7 patients did not map (19.4%). Six of the 7 patients who failed to map had a clinically positive axilla initially. Axillary disease was found in 6 of 7 of these patients at dissection (85.7%). Of the 29 patients who mapped successfully, 13 (45%) were SNB negative, and 16 (55%) were SNB positive. Of the 13 SNB-negative patients, 2 had a positive axillary lymph node dissection, yielding a false-negative rate of 11%. Thirteen patients who mapped had a clinically positive axilla before therapy (45%). Of the 11 patients with true-negative SNBs, 7 (64%) were clinically node negative at presentation. The initial tumor sizes on examination ranged from 2 to 9 cm (mean, 5.0 cm), and residual pathologic tumor sizes ranged from 0 to 6 cm (mean, 1.8 cm). Failure to map correlated with a clinically positive axilla at presentation (100% vs 45%) but did not correlate with initial tumor size.

Conclusions: Sentinel node identification rates are significantly better when mapping is performed before neoadjuvant chemotherapy (100% vs 80.6%), with failure to map correlated with clinically positive nodal disease at presentation and residual disease at axillary lymph node dissection. Among patients who map successfully after chemotherapy, the false-negative rate is high (11%). Given these findings, we currently recommend SNB before neoadjuvant chemotherapy for clinically node-negative patients, and raise concerns about the use of SNB after neoadjuvant therapy in patients with an initially clinically positive axilla.

Keywords: Breast cancer; Sentinel lymph node biopsy; Neoadjuvant chemotherapy

Neoadjuvant chemotherapy is being used with increasing frequency for the treatment of breast cancer, beyond its initial indications for locally advanced disease. Treatment with chemotherapy before surgery permits the observation of clinical and molecular responses to treatment, providing prognostic information [1] and a valuable tool in the development of new therapies. Neoadjuvant chemotherapy also is used increasingly to downstage tumors that, although not locally advanced, otherwise would require a mastectomy [2–7]. Thus, an increasing number of clinically node-negative patients are candidates for neoadjuvant therapy.

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Table 1
Sentinel lymph node mapping success: preneoadjuvant versus postneoadjuvant therapy

	Sentinel node mapping	
	Success	Failure
SNB preneoadjuvant cN0 (n = 52)	52 (100%)	0
SNB postneoadjuvant cN0 (n = 17)	16 (94%)	1 (6%)
SNB postneoadjuvant cN1 (n = 19)	13 (68%)	6 (32%)

The appropriate use and optimal timing of sentinel node biopsy (SNB) in the setting of neoadjuvant chemotherapy remains controversial. In clinically node-negative patients, an SNB before neoadjuvant chemotherapy allows accurate nodal staging, avoiding the possibility of lymphatic scarring or uneven tumor response in the axillary nodes. On the other hand, clinically node-positive patients may have a significant rate of axillary clearance after chemotherapy [8], and staging after chemotherapy may provide those patients who become clinically node negative (N0) with options for less-invasive axillary therapy.

We previously showed a 100% identification rate when SNB was performed before neoadjuvant chemotherapy in clinically node-negative patients [9]. We sought to evaluate our experience with SNB after neoadjuvant chemotherapy and to compare it with our findings when performed before chemotherapy.

Methods

An institutional review board–approved retrospective study identified 36 women treated with neoadjuvant chemotherapy who subsequently underwent an SNB and completion axillary dissection at the time of definitive surgery between 1999 and 2003. All patients were treated on 1 of 2 neoadjuvant protocols, and received either sequential single-agent doxycycline (4 cycles, q 2 weeks) and paclitaxel (weekly for 9 cycles), or 12 weeks of trastuzumab (weekly) and paclitaxel (q 3 weeks), followed by adjuvant doxycycline and cyclophosphamide (4 cycles). All patients received adjuvant radiation.

For SNBs performed before neoadjuvant chemotherapy, data were obtained in an institutional review board–approved retrospective review of patients receiving neoadjuvant chemotherapy during the same time period [9]. In this setting, patients with negative sentinel nodes did not undergo a completion axillary dissection unless they progressed during chemotherapy (1 patient). Patients with a positive sentinel node were dissected at the discretion of the treating physician.

Sentinel node mapping techniques were chosen according to surgeon preference. Histologic evaluation of the sentinel nodes differed by institution. All patients had hematoxylin and eosin evaluation of 3 levels of the sentinel node. At Massachusetts General Hospital, immunohistochemical staining was performed if the hematoxylin and eosin stains were negative. Three cytokeratin sections per block were evaluated at approximately 200-μm intervals. Immunohistochemistry was not performed at Brigham and Women's Hospital.

Results

Sentinel node after neoadjuvant chemotherapy

Thirty-six women with T2–4, N0-1 invasive breast cancer underwent an SNB at the time of definitive surgery after neoadjuvant chemotherapy (without any prior axillary surgery). Nineteen patients (53%) had clinically involved axillary nodes at presentation. Eight of these patients had nodal involvement confirmed by fine-needle aspiration cytology before neoadjuvant chemotherapy. Overall, 86% of patients responded to neoadjuvant chemotherapy: 33% had a clinical complete response, 53% had a clinical partial response. Eight percent of patients had stable disease (6% unknown). The pathologic complete response rate was 16.7% (including patients with residual ductal carcinoma in situ only).

SNB was successful in 29 patients (81%) (Table 1). Mapping failed to identify a sentinel node in 7 patients (19%). All of these 7 patients had mapping with both technetium and blue dye. Six of the 7 patients who failed to map had a clinically positive axilla initially, and 6 of the 7 patients had residual disease at axillary dissection (Table 2). Among the 29 patients who were mapped successfully, 16 (55%) were SNB positive, and 13 (45%) were SNB negative. Two patients with a negative SNB had residual axillary disease, for a false-negative rate of 11% (2 of 18). Immunohistochemistry was used in only 7 patients (24%); it was not used for the 2 patients with false-negative sentinel nodes.

Among 19 patients with a clinically positive axilla before therapy, 13 mapped successfully. Seven patients had a positive sentinel node, and all of these 7 patients had additional axillary disease at dissection. Six patients had a negative sentinel node. Five of these patients had no additional disease (true negatives); 1 patient had 5 positive axillary nodes, all containing macrometastatic tumor foci (false negative).

Table 2
SNB examination and axillary pathology after neoadjuvant chemotherapy by clinical lymph node status

	cN0 (n = 17)		cN1 (N = 19)	
	ALND−	ALND+	ALND−	ALND+
SNB negative	6	1	5	1
SNB positive	6	3	0	7
SNB failed	0	1	1	5

ALND = axillary lymph node dissection.