The American Journal of Surgery (2017) 213, 810-813

The American Journal of Surgery®

Invited Commentary

Outcomes and feasibility of nipple-sparing mastectomy for node-positive breast cancer Patients

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KEYWORDS:
Nipple-sparing mastectomy;
Breast cancer;
Node-positive;
Lymph node;
Local recurrence;
Outcomes

Abstract

BACKGROUND: While nipple-sparing mastectomy (NSM) is gaining acceptance for risk reduction and for treatment of early stage breast cancer, node-positive disease remains a relative contraindication. Our aim was to evaluate the use and outcomes of NSM in node-positive breast cancer patients.

METHODS: We identified 240 cancers in 226 patients (14 bilateral) scheduled for NSM and operated on between 1/2009 and 6/2014. We compared outcomes for 58 node-positive vs 182 node-negative patients.

RESULTS: Intraoperative conversion to skin-sparing mastectomy was similar for node-positive and node-negative patients, 10% and 7%, as was 1-year success of NSM, 84% and 90%, respectively. Five-year locoregional disease-free estimates were 82% (95% CI 68%–99%) for node-positive and 99% (95% CI 96%–100%) for node-negative patients, $P = .004$; however, there were no nipple-areolar recurrences among node-positive patients.

CONCLUSIONS: With careful consideration of biologic and anatomic risk factors for recurrence, these data suggest that NSM is a reasonable option for selected node-positive breast cancer patients.

The indications for nipple-sparing mastectomy (NSM) in breast cancer patients continue to evolve.[1] Current National Comprehensive Cancer Network guidelines recommend removal of the nipple-areolar complex (NAC) for the majority of breast cancer patients treated with mastectomy.[2] While NSM has been considered for highly selected cancer patients, primarily those with tumors less than 2 cm in size and located greater than 2 cm from the nipple, more recently NSM is being performed more liberally.[1,3–5] Still, NSM generally is thought best-suited for early stage patients without nodal involvement based on limited data suggesting a higher rate of nipple involvement among lymph node-positive patients.[2,6,7] While prior reports have noted an increase in the performance of NSM over time, there remains a paucity of data on oncologic

SRJ has served as a consultant to LifeCell and Novadaq; no other relevant financial disclosures.

The authors declare no conflicts of interest.

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Manuscript received May 19, 2016; revised manuscript July 12, 2016

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http://dx.doi.org/10.1016/j.amjsurg.2016.07.031

outcomes among NSM in node-positive patients. To address the issues of feasibility and oncologic safety, we undertook this study to evaluate the use and early outcomes of NSM in node-positive breast cancer patients.

With institutional review board approval, we identified 226 patients with newly diagnosed breast cancer scheduled for 240 NSMs (14 bilateral cancers) from our prospective breast surgery registry and operated on at our institution between January 2009 and June 2014. Data on intraoperative conversion to skin-sparing mastectomy (SSM), reconstructive outcomes, and cancer recurrence were obtained from electronic medical record review. Success of NSM was defined as retention of the native nipple at 1 year. Recurrence and breast cancer-specific survival estimates were calculated using the Kaplan-Meier method, with 95% confidence intervals estimated based on the log of the survival function and compared between groups using the log-rank test. Patient and tumor variables were compared between node-positive and node-negative patients using Wilcoxon rank-sum tests for continuous and ordinal variables and chi-square tests for nominal variables. We considered P values of less than .05 as significant.

Of the 240 cancers, 182 were node-negative and 58 were node-positive. Of the 58 node-positive cases, 19 (33%) were cN1 confirmed by positive fine needle aspiration cytology and 39 (67%) were cN0 but node-positive on final pathology. Ten patients were node-positive at diagnosis and received neoadjuvant therapy (NT) followed by operation (of which 6 remained node-positive and 4 were rendered node-negative). Overall, 39 cN0 (4 NT, 35 primary surgery) and 15 cN1 (9 primary surgery, 6 NT) patients were node-positive on final pathology at operation with a median of 1 positive node. All final breast margins were negative. NSM was performed via an inframammary fold incision in 29% of the patients, a periareolar incision in 35%, a radial incision in 32% and a reduction pattern in the remainder. Direct to implant immediate breast reconstruction was performed in 11% of the patients while tissue expanders were placed in the remainder. After surgery, 47% of node-positive and 2% of node-negative patients received postmastectomy radiation ($P < .0001$). Patient and tumor variables are summarized in Table 1.

Six node-positive patients (10%) were converted to SSM either at initial operation (n = 5) due to atypia or neoplasm in the central nipple ducts on frozen section pathology, or at a second operation due to atypia on final pathology (n = 1). Among node-negative patients, 13 of 182 (7%) were converted to SSM: 9 at initial operation and 4 secondarily ($P = .44$ for node-positive vs node-negative patients). The overall success of NSM at 1 year was 84% for node-positive and 90% for node-negative patients, $P = .25$. Among node-positive patients, the NAC was removed due to atypia in 2, neoplasm in 4, and necrosis

Table 1 Comparison of patient and tumor variables between node-positive and node-negative breast cancer patients treated with nipple-sparing mastectomy

Variable	Node-positive (N = 58)	Node-negative (N = 182)	Total (N = 240)	*P* value
Age, median (IQR)	46 (41–52)	49 (45–56)	48.5 (43–54)	.02
Clinical T stage, n (%)				<.0001
T0	1 (1.7)	4 (2.2)	5 (2.1)	
Tis	2 (3.4)	66 (36.3)	68 (28.3)	
T1	28 (48.3)	81 (44.5)	109 (45.4)	
T2	20 (34.5)	27 (14.8)	47 (19.6)	
T3	7 (12.1)	4 (2.2)	11 (4.6)	
ER status, n (%)				.79
Positive	50 (86.2)	155 (87.6)	205 (87.2)	
Negative	8 (13.8)	22 (12.4)	30 (12.8)	
Missing	0	5	5	
Her2 status*, n (%)				.33
Positive	8 (14.3)	10 (9.2)	18 (10.9)	
Negative	48 (85.7)	99 (90.8)	147 (89.1)	
Missing	2	13	15	
Tumor histology, n (%)				<.0001
DCIS	0	60 (33.0)	60 (25.0)	
DCIS with microinvasion	0	3 (1.6)	3 (1.3)	
Invasive ductal	47 (81.0)	91 (50.0)	138 (57.5)	
Invasive lobular	5 (8.6)	13 (7.1)	18 (7.5)	
Mixed mammary	4 (6.9)	8 (4.4)	12 (5.0)	
Other	2 (3.4)	7 (3.8)	9 (3.8)	
Tumor LVI present*	21 (36.8)	5 (4.1)	26 (14.6)	<.0001
Number of positive nodes at final pathology, median (IQR)	1 (1–2)	–		–
Extranodal extension present	17 (29.3)	–		–

DCIS = ductal carcinoma in situ; ER = estrogen receptor; IQR = interquartile range; LVI = lymphovascular invasion.
*Invasive cancer cases.