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Axillary Micrometastases and Isolated Tumor Cells Are Not an Indication for Post-Mastectomy Radiotherapy in Stage 1 and 2 Breast Cancer

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Abstract

Background—Randomized trials demonstrate equivalent locoregional control with sentinel node biopsy (SLNB) or axillary dissection (ALND) for T1–2, micrometastatic breast cancer, but include few mastectomy patients. Consensus is lacking on indications for post-mastectomy radiotherapy (PMRT) in this population. Herein we evaluate locoregional recurrence (LRR) in an unselected, modern cohort of T1–2 breast cancer patients with micrometastases or isolated tumor cells (N0i+/N1mi) having mastectomy.

Methods—We identified patients with T1–2N0i+/N1mi breast cancer treated with mastectomy from 1/2006–12/2011. Recurrent, bilateral, and neoadjuvant cases were excluded. The primary outcome of interest was LRR.

Results—352 patients, 211 (60%) with ITCs and 141 (40%) with micrometastases, were identified. 162 (46%) had SLNB alone and 1 node was positive in 295 (84%) cases. 31 (9%) had PMRT. 95% had systemic therapy. At median 6 years follow-up, the overall crude LRR rate was 2.8% (n=9), with no axillary recurrences, and the crude LRR rate was 3.9% among those who had SNB alone. Those with LRR had median age 55yrs, median tumor size 1.7cm, and ductal histology; the majority were high-grade (89%), estrogen receptor positive (78%), with 1 positive node (89%). There was no association between LRR and receipt of PMRT (p=0.4), SNB vs ALND (p=0.2), or number of positive nodes (p=0.7) by the log-rank test.

Conclusions—LRR was infrequent among T1–2N0i+/N1mi patients treated with mastectomy without PMRT, with no axillary failures, suggesting that PMRT or nodal radiotherapy are not routinely indicated in this population.

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Keywords

micrometastases; mastectomy; sentinel lymph node biopsy; post-mastectomy radiotherapy; locoregional recurrence

INTRODUCTION

Management of the axilla in clinically node-negative patients has evolved over the last decade with the widespread adoption of sentinel lymph node biopsy (SLNB). The ability to perform a more detailed pathologic examination of a small number of sentinel nodes led to the emergence of the entities of isolated tumor cells (ITCs) (size ≤ 0.2 mm), and micrometastases, (size > 0.2 mm and ≤ 2 mm), found in 10%–15% of patients who undergo SLNB.[1–3]

The impact of micrometastases on the need for axillary dissection (ALND) and post-mastectomy radiotherapy is uncertain. Randomized trials demonstrated equivalent locoregional control when comparing SLNB alone to axillary dissection (ALND) in patients with micrometastases, but included small numbers of patients treated with mastectomy, and varying adjuvant treatments.[4–6] Current guidelines[7] recommend consideration of PMRT for patients with metastases in 1–3 axillary nodes based on trials demonstrating benefit in patients with nodal macrometastases. The impact of micrometastases or isolated tumor cells on locoregional recurrence, and hence whether they should be included in node counts when determining the need for PMRT, is not well studied. The risk of LRR in patients with micrometastases in combination with other features which have been associated with an increased risk of LRR[8–11] such as age < 40 years, high nuclear grade, medial/central tumor location, multifocality/multicentricity, triple-negative (TN) receptor status, and lymphovascular invasion (LVI) is particularly unclear. Given the lack of consensus on the utility of further axillary treatment with surgery or radiotherapy in patients with early-stage breast cancer and minimal nodal disease burden treated with mastectomy, we sought to evaluate patterns of treatment and rates of locoregional recurrence (LRR) in an unselected, contemporary cohort of patients with T1–T2 tumors undergoing mastectomy and found to have isolated tumor cells (ITCs) or micrometastases (T1–T2N0i+/N1mi), but no macrometastases in the axillary nodes.

METHODS

Following Institutional Review Board approval, all women diagnosed with T1–T2N0i+/N1mi breast cancer who had a mastectomy at Memorial Sloan Kettering Cancer Center between January 2006 and December 2011 were identified. Micrometastases were defined as the presence of metastatic lymph node deposits measuring between 0.2 mm and 2 mm in dimension, and ITCs were defined as deposits measuring ≤ 0.2 mm[12], seen in one or more lymph nodes on hematoxylin and eosin (H&E) or immunohistochemical evaluation. “High-risk” features were defined as age less than 40 years at diagnosis, multifocal or multicentric tumor, TN receptor status, presence of LVI, medial/central tumor location, and high nuclear grade. Patients with recurrent disease, bilateral tumors, and those who received neoadjuvant chemotherapy were excluded.

Standard clinicopathologic data were collected, including age at diagnosis, clinical presentation of disease, tumor size, nuclear grade, subtype, and final tumor and node pathologic findings. Rates of administration of radiotherapy and systemic therapies, and regimens utilized, were assessed. The primary outcome of interest was LRR, defined as a biopsy-proven recurrence of disease in the ipsilateral chest wall, or in the ipsilateral regional lymph nodes including the axillary, internal mammary, or supraclavicular lymph nodes. Development of disease at any other site was considered a distant recurrence.

Continuous variables were compared using the Wilcoxon test, and categorical variables were compared using the Chi square or Fisher's exact tests. Crude overall rates of LRR were calculated. Kaplan-Meier methods and the log-rank test were used to analyze associations between clinicopathologic variables and LRR. All statistical analysis was performed using SAS 9.2 (SAS Institute, Cary, NC, USA) and R version 3.1.1 (https://www.r-project.org/). Any p value less than 0.05 was considered statistically significant.

RESULTS

From January 2006 to December 2011, 352 women with T1–T2N0i+/N1mi breast cancer underwent mastectomy. Of these patients, 211 (60%) had ITCs, and 141 (40%) had micrometastases. A single lymph node was positive in 295 (84%) patients, while 57 (16%) patients had 2 to 5 positive nodes but no macrometastases. SLNB alone was performed in 162 (46%) patients, and 190 (54%) had ALND. The proportion of patients undergoing SLNB alone increased from 46% in 2006 to 60% in 2011 (p=0.5). Overall, 321 (92%) patients were treated without PMRT during the 6-year study period, and the remainder of the analysis is confined to this group. Clinicopathologic characteristics of all patients, and a comparison of those treated without and with PMRT, are summarized in Table 1. Among 321 patients treated without PMRT, the majority of tumors were of ductal histology (79%), intermediate or high grade (83%), located in a lateral position in the breast (68%), and estrogen receptor positive (ER+) (82%). No high-risk features were seen in 35 (11%), and one, two, three, and four or more high-risk features were seen in 65 (20%), 87 (27%), 72 (22%), and 18 (6%) patients, respectively, while 44 (14%) patients were excluded from risk factor categorization due to unknown nuclear grade or receptor status. A single lymph node was positive in 272 (85%) patients. SLNB alone was performed in 151 (47%) patients, and 170 (53%) had ALND. Among patients with ITCs (n = 196), 118 (60%) had SLNB alone while 78 (40%) had ALND; among patients with micrometastases (n = 125), 33 (26%) had SLNB alone and 92 (74%) had ALND, respectively. A median of 4 (range 1–14) sentinel nodes were removed at SLNB, and a median of 20 (6–48) lymph nodes were removed at ALND. Systemic adjuvant therapy was received by 305 (95%) patients: 198 (62%) received both chemotherapy and endocrine therapy, 43 (13%) received chemotherapy alone, and 64 (20%) received endocrine therapy alone. Fourteen (4%) patients had no systemic therapy, and adjuvant treatment was unknown in 2 patients. Of the 241 patients who received chemotherapy, 170 (71%) had doxorubicin, cyclophosphamide and paclitaxel (ACT) and 61 (25%) had cyclophosphamide, methotrexate and 5-fluorouracil (CMF). Fifty-nine (92%) of 64 patients with human epidermal growth factor 2 overexpressing (HER2+) tumors received trastuzumab. Among 265 ER+ patients, 255 (96%) received endocrine therapy.

At median follow-up of 6.0 years (range 0–114) months, 9 (2.8%) patients treated without PMRT had LRR; 6 isolated LRRs and 3 simultaneous (diagnosed within one month) LRR and distant recurrences. Ten (3.1%) patients have experienced distant recurrence alone. Location of LRR was the chest wall in 8 cases (89%) and internal mammary node in 1 case (11%). There have been no axillary or supraclavicular recurrences to date. The median time to LRR was 19 months (range 8–45). Clinicopathologic characteristics of the 9 patients with LRR are summarized in Table 2. These patients had a median age 55 years, median tumor size 1.7 cm, and the majority had ER+ (78%) and high-grade (89%) tumors. A single lymph node contained metastases in 8 cases. Five LRRs occurred in patients with micrometastases and 4 in patients with ITCs. Although the number of events was too small to permit analysis of associations between LRR and high-risk features, LRR occurred in patients with 1 to 5 high-risk features. Eight of 9 patients with LRR received chemotherapy, and recommended endocrine therapy was declined by 1 of 7 (14%) ER+ patients with LRR.

Only 31 (9%) patients received PMRT during the study period; 13 (42%) had chest wall irradiation alone, and 18 (58%) received chest wall and regional nodal irradiation. All of these patients also received adjuvant systemic therapy. No LRR events occurred among those who received PMRT, and 1 patient (3.2%) experienced distant recurrence alone.

Although all LRR events occurred in the group treated without PMRT, Kaplan-Meier estimation showed no significant difference in LRR with or without PMRT (log-rank p = 0.4, Fig. 1). The crude rates of LRR among patients treated by SLNB alone vs ALND, regardless of radiotherapy, were 3.7%, vs 1.6% (log-rank p = 0.2, Fig. 2). In those treated without PMRT, the crude rates of LRR after SLNB alone vs. ALND were 4.0% and 1.8%, respectively (log-rank p = 0.2, Fig. 3a), and 2.9% vs. 2.0%, (p=0.7, Fig. 3b) among those with 1 vs > 1 positive lymph node. Of the 135 patients who underwent SLNB alone, had a single involved node, and did not receive PMRT, 4.4% had LRR.

DISCUSSION

In this unselected, contemporary population with T1–T2N0i+/N1mi breast cancer treated with mastectomy, the rate of LRR at 6 years was 2.8% without PMRT, with no axillary failures to date. The type of axillary surgery (p = 0.2) or number of positive nodes (p = 0.7) did not identify a group at high risk for LRR. While the number of LRR events was too small to permit predictive statistics, there was no observed association between LRR and patient or primary tumor features which have been described as increasing the risk of LRR in other populations.[8–11] This finding is consistent with our previous work examining predictors of LRR in patients with T1–2 node-negative breast cancer treated without PMRT, where only tumor size was found to be predictive of LRR.[13]

This study provides insight into a population that is underrepresented in most clinical trials of micrometastatic disease, which largely focus on patients undergoing lumpectomy and radiotherapy. The International Breast Cancer Study Group (IBCSG) 23-01 trial randomized 934 patients with T1–T2, micrometastatic disease to SLNB alone or ALND, and found 5-year axillary recurrence rates < 1%, but only 9% of patients had mastectomy.[4] The AATRM trial similarly randomized 233 patients with tumors < 3.5 cm in size and micrometastases to

SLNB alone or ALND, with axillary recurrence rates < 3% in both arms, but only 8% underwent mastectomy.[5]

Non-sentinel node metastases are reported in 10%–20% of patients with micrometastases in the sentinel nodes[2,4,14,15] and 20%-40%% of these are macrometastases.[16,17] In spite of this, axillary recurrence rates are low, even in the absence of the tangent field irradiation that is part of breast-conserving surgery.

The majority of patients in this study (84%) had a single positive lymph node, consistent with previously reports.[4] We found that neither the number of involved lymph nodes (p = 0.7), nor the type of axillary surgery in the absence of PMRT (p = 0.2) was associated with an increasing risk of LRR.

Importantly, there have been no axillary recurrences at median 6 years of follow-up in this study, even though 46% of patients had SLNB alone and no PMRT. This rate is lower than previously reported rates of 0.3%–5% in trials of patients with micrometastases, although the majority of these patients were treated with breast-conserving surgery and received a variety of radiotherapy treatments.[4–6,18] The IBCSG 23-01 trial showed axillary failure rates of less than 1% among patients with T1–T2, micrometastatic disease, regardless of randomization to either SLNB alone or ALND.[4] The MIRROR trial reported a 5% rate of axillary failures in patients with micrometastases treated without ALND, but this was reduced with the addition of adjuvant therapies.[6] A meta-analysis including 3468 patients in 27 studies with SLN micrometastases managed without further axillary surgery showed a cumulative axillary recurrence rate of 0.3%.[18] Smaller studies also including patients treated with both mastectomy and breast conservation with varying radiotherapy approaches have also reported axillary recurrence rates of less than 3% among patients with nodal micrometastases.[1,19–22] To our knowledge, our study is the first validation of these favorable results in a large contemporary cohort of patients with T1–T2N0i+/N1mi disease treated with mastectomy and without PMRT.

The use of PMRT in this population is controversial. Current guidelines[7] recommend strong consideration of PMRT to the chest wall and regional lymph nodes for patients who undergo mastectomy with 1 to 3 positive nodes, but whether micrometastases contribute to the positive node count is uncertain.[23] In our study, we found no difference in LRR with or without PMRT by Kaplan-Meier estimation (p = 0.4). More importantly, the vast majority of patients did not receive PMRT, and rates of LRR in this group were less than 5%, far lower than the rates of LRR in the no-radiotherapy arms of the clinical trials that suggested a benefit for PMRT in patients with 1–3 nodal metastases.[7,24] The 10-year results of the MA. 20 and EORTC trials showed decreased LRR and improved disease-free survival with comprehensive nodal irradiation in patients with T1–T3, node-positive or ‘high-risk’ node-negative disease. The majority of patients underwent breast conservation, and micrometastases were not analyzed separately; the improvement in locoregional control was attributed in part to a decrease in internal mammary recurrences.[10,11] In our study, we observed only one internal mammary recurrence, suggesting limited benefit to regional nodal irradiation for this purpose in patients with micrometastases. Although the number of events was too small to permit analysis of the impact of the defined “high-risk” features, we

observed a wide distribution of these risk factors among those with LRR, and only a single positive node in most cases.

Our results support the concept that tumor biology is the primary driver of locoregional recurrence in patients with micrometastases, rather than their minimal nodal burden. Systemic therapies are recognized to improve locoregional control[25] and are a valuable element in contemporary treatment. The receipt of systemic therapy by 95% of patients in this study is likely a significant contributor to the low LRR rate. The majority of LRRs in similar populations occurred within the first 3 years after initial diagnosis[21,26,27], suggesting that our results with a median 6 years of follow-up are unlikely to change substantially, even in a largely ER+ population where late distant recurrences are common.

Our study is limited by its retrospective nature and the potential for selection bias, as well as relatively small subsets of patients with micrometastases and ITCs treated with SLNB or ALND. However, only 31 patients (9%) patients treated during the study period underwent PMRT, making it unlikely that the low rates of LRR are due to selection of a particularly favorable cohort. Also, while there were too few LRR events to analyze for association with high-risk disease features, these results provide insight into a well-defined, unselected contemporary cohort of patients in a population that is underrepresented in clinical trials.

CONCLUSION

In this modern cohort of patients with T1–T2N0i+/N1mi breast cancer treated with mastectomy without PMRT, of which 95% received adjuvant systemic therapy, we found a low crude LRR rate of 2.8% at median 6 years of follow-up. There have been no axillary failures, and no significant association seen between LRR and administration of PMRT, type of axillary surgery, or number of positive lymph nodes. Among patients with T1–T2N0i+/N1mi disease having mastectomy and SLNB, LRR risk is low without further axillary treatment, and tumor biology, rather than nodal disease, appears to a primary driver of LRR. In patients with early-stage disease with micrometastases or ITCs undergoing mastectomy, particularly those with a single involved lymph node, excellent locoregional control may be achieved without PMRT or nodal radiotherapy.

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References

1. Houvenaeghel G, Classe JM, Garbay JR, et al. Prognostic value of isolated tumor cells and micrometastases of lymph nodes in early-stage breast cancer: a French sentinel node multicenter cohort study. Breast. Oct; 2014 23(5):561–566. [PubMed: 24874284]
2. Cserni G, Bianchi S, Vezzosi V, et al. Variations in sentinel node isolated tumour cells/micrometastasis and non-sentinel node involvement rates according to different interpretations of the TNM definitions. Eur J Cancer. Oct; 2008 44(15):2185–2191. [PubMed: 18691877]
3. Yi M, Giordano SH, Meric-Bernstam F, et al. Trends in and outcomes from sentinel lymph node biopsy (SLNB) alone vs. SLNB with axillary lymph node dissection for node-positive breast cancer patients: experience from the SEER database. Ann Surg Oncol. Oct; 2010 17(Suppl 3):343–351.

4. Galimberti V, Cole BF, Zurrida S, et al. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. Lancet Oncol. Apr; 2013 14(4):297–305. [PubMed: 23491275]
5. Sola M, Alberro JA, Fraile M, et al. Complete axillary lymph node dissection versus clinical follow-up in breast cancer patients with sentinel node micrometastasis: final results from the multicenter clinical trial AATRM 048/13/2000. Ann Surg Oncol. Jan; 2013 20(1):120–127. [PubMed: 22956062]
6. de Boer M, van Deurzen CH, van Dijck JA, et al. Micrometastases or isolated tumor cells and the outcome of breast cancer. N Engl J Med. Aug 13; 2009 361(7):653–663. [PubMed: 19675329]
7. Recht A, Comen EA, Fine RE, et al. Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update. J Clin Oncol. Sep 19.2016
8. Sharma R, Bedrosian I, Lucci A, et al. Present-day locoregional control in patients with t1 or t2 breast cancer with 0 and 1 to 3 positive lymph nodes after mastectomy without radiotherapy. Ann Surg Oncol. Nov; 2010 17(11):2899–2908. [PubMed: 20443145]
9. Wallgren A, Bonetti M, Gelber RD, et al. Risk factors for locoregional recurrence among breast cancer patients: results from International Breast Cancer Study Group Trials I through VII. J Clin Oncol. Apr 01; 2003 21(7):1205–1213. [PubMed: 12663706]
10. Poortmans PM, Collette S, Kirkove C, et al. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. N Engl J Med. Jul 23; 2015 373(4):317–327. [PubMed: 26200978]
11. Whelan TJ, Olivotto IA, Parulekar WR, et al. Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med. Jul 23; 2015 373(4):307–316. [PubMed: 26200977]
12. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. Jun; 2010 17(6):1471–1474. [PubMed: 20180029]
13. Mamtani A, Patil S, Stempel M, Morrow M. Are There Patients with T1-T2, Node-Negative Breast Cancer Who Are “High-Risk” for Locoregional Recurrence? Cancer. 2017 (accepted February 2017, in press).
14. Tallet A, Lambaudie E, Cohen M, et al. Locoregional treatment of early breast cancer with isolated tumor cells or micrometastases on sentinel lymph node biopsy. World J Clin Oncol. Apr 10; 2016 7(2):243–252. [PubMed: 27081647]
15. Pilewskie ML, Morrow M. Management of the clinically node-negative axilla: what have we learned from the clinical trials? Oncology (Williston Park). May; 2014 28(5):371–378. [PubMed: 25004648]
16. Cserni G, Gregori D, Merletti F, et al. Meta-analysis of non-sentinel node metastases associated with micrometastatic sentinel nodes in breast cancer. Br J Surg. Oct; 2004 91(10):1245–1252. [PubMed: 15376203]
17. van Deurzen CH, de Boer M, Monninkhof EM, et al. Non-sentinel lymph node metastases associated with isolated breast cancer cells in the sentinel node. J Natl Cancer Inst. Nov 19; 2008 100(22):1574–1580. [PubMed: 19001602]
18. Francissen CM, Dings PJ, van Dalen T, Strobbe LJ, van Laarhoven HW, de Wilt JH. Axillary recurrence after a tumor-positive sentinel lymph node biopsy without axillary treatment: a review of the literature. Ann Surg Oncol. Dec; 2012 19(13):4140–4149. [PubMed: 22890590]
19. Karam I, Lesperance MF, Berrang T, Speers C, Tyldesley S, Truong PT. pN0(i+) breast cancer: treatment patterns, locoregional recurrence, and survival outcomes. Int J Radiat Oncol Biol Phys. Nov 15; 2013 87(4):731–737. [PubMed: 24035330]
20. Rayhanabad J, Yegiyants S, Putchakayala K, Haig P, Romero L, Difronzo LA. Axillary recurrence is low in patients with breast cancer who do not undergo completion axillary lymph node dissection for micrometastases in sentinel lymph nodes. Am Surg. Oct; 2010 76(10):1088–1091. [PubMed: 21105616]
21. Pernas S, Gil M, Benitez A, et al. Avoiding axillary treatment in sentinel lymph node micrometastases of breast cancer: a prospective analysis of axillary or distant recurrence. Ann Surg Oncol. Mar; 2010 17(3):772–777. [PubMed: 20183912]

22. Milgrom S, Cody H, Tan L, et al. Characteristics and outcomes of sentinel node-positive breast cancer patients after total mastectomy without axillary-specific treatment. Ann Surg Oncol. Nov; 2012 19(12):3762–3770. [PubMed: 22576064]

23. Gradishar WJ, Anderson BO, Balassanian R, et al. Invasive Breast Cancer Version 1.2016, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. Mar; 2016 14(3):324–354. [PubMed: 26957618]

24. McGale P, Taylor C, Correa C, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet. Jun 21; 2014 383(9935):2127–2135. [PubMed: 24656685]

25. Anderson SJ, Wapnir I, Dignam JJ, et al. Prognosis after ipsilateral breast tumor recurrence and locoregional recurrences in patients treated by breast-conserving therapy in five National Surgical Adjuvant Breast and Bowel Project protocols of node-negative breast cancer. J Clin Oncol. May 20; 2009 27(15):2466–2473. [PubMed: 19349544]

26. Houvenaeghel G, Nos C, Mignotte H, et al. Micrometastases in sentinel lymph node in a multicentric study: predictive factors of nonsentinel lymph node involvement–Groupe des Chirurgiens de la Federation des Centres de Lutte Contre le Cancer. J Clin Oncol. Apr 20; 2006 24(12):1814–1822. [PubMed: 16567771]

27. Louis-Sylvestre C, Clough K, Asselain B, et al. Axillary treatment in conservative management of operable breast cancer: dissection or radiotherapy? Results of a randomized study with 15 years of follow-up. J Clin Oncol. Jan 1; 2004 22(1):97–101. [PubMed: 14701770]

Synopsis

Among 352 T1–2N0i+/N1mi patients having mastectomy, 321 did not receive PMRT. In the no-RT group 2.8% had LRR at 6 years of follow-up, with no axillary failures. There was no association between LRR and receipt of PMRT, type of axillary surgery, or number of positive nodes.

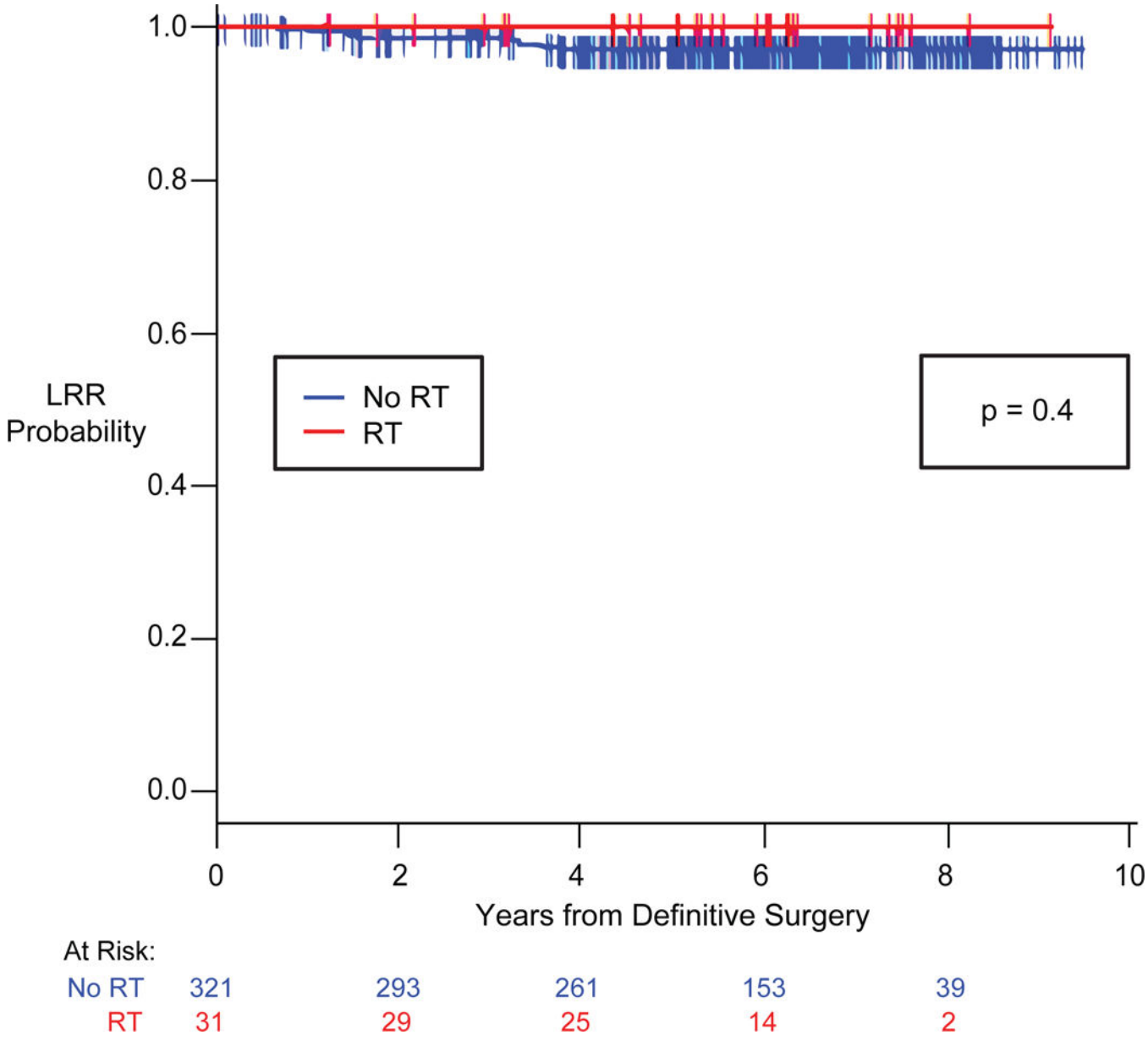

Fig. 1.

Kaplan-Meier estimates of locoregional recurrence by post-mastectomy radiation therapy status

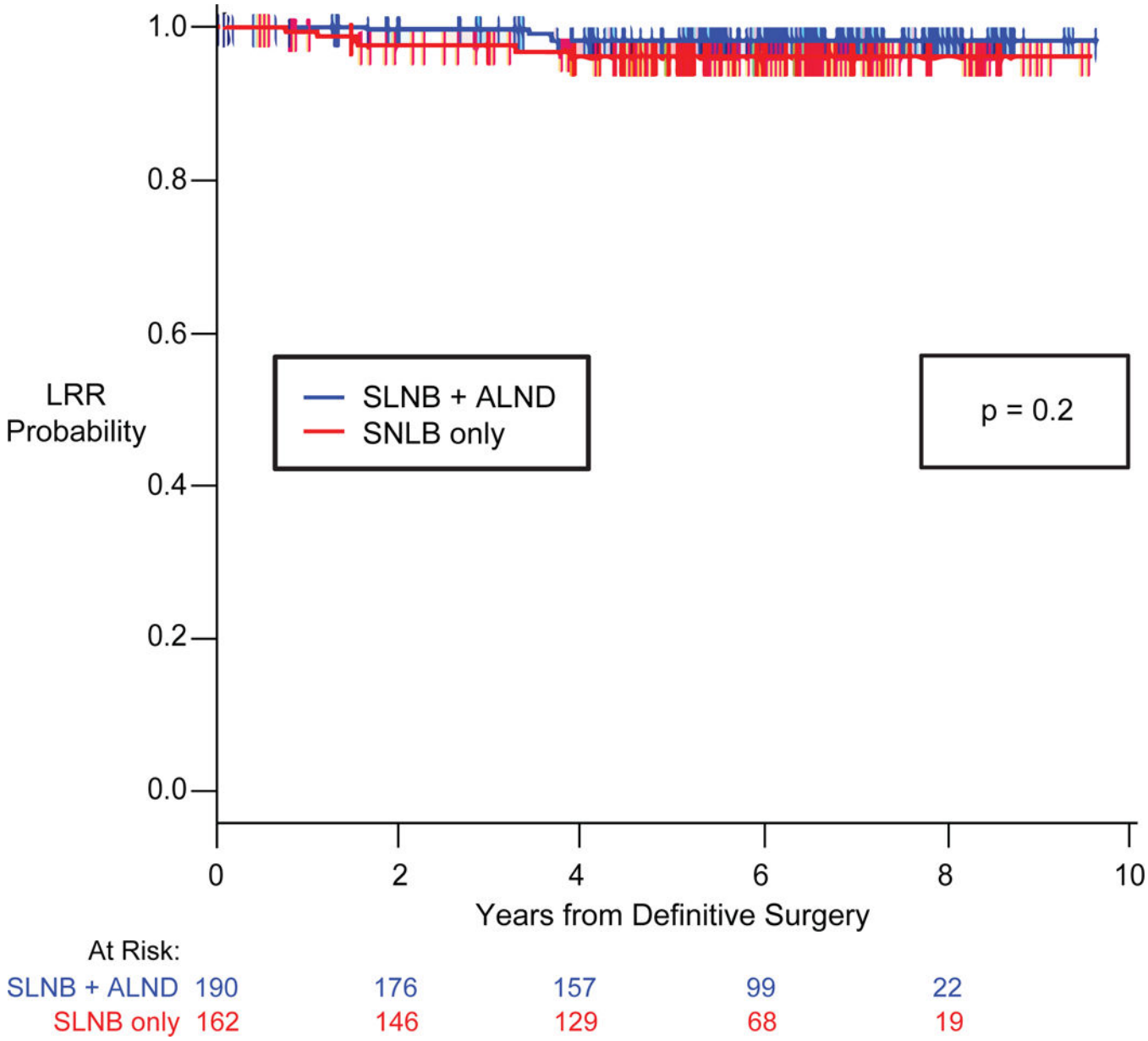

Fig. 2.

Kaplan-Meier estimates of locoregional recurrence by axillary surgery, among all patients (regardless of post-mastectomy radiation therapy status)

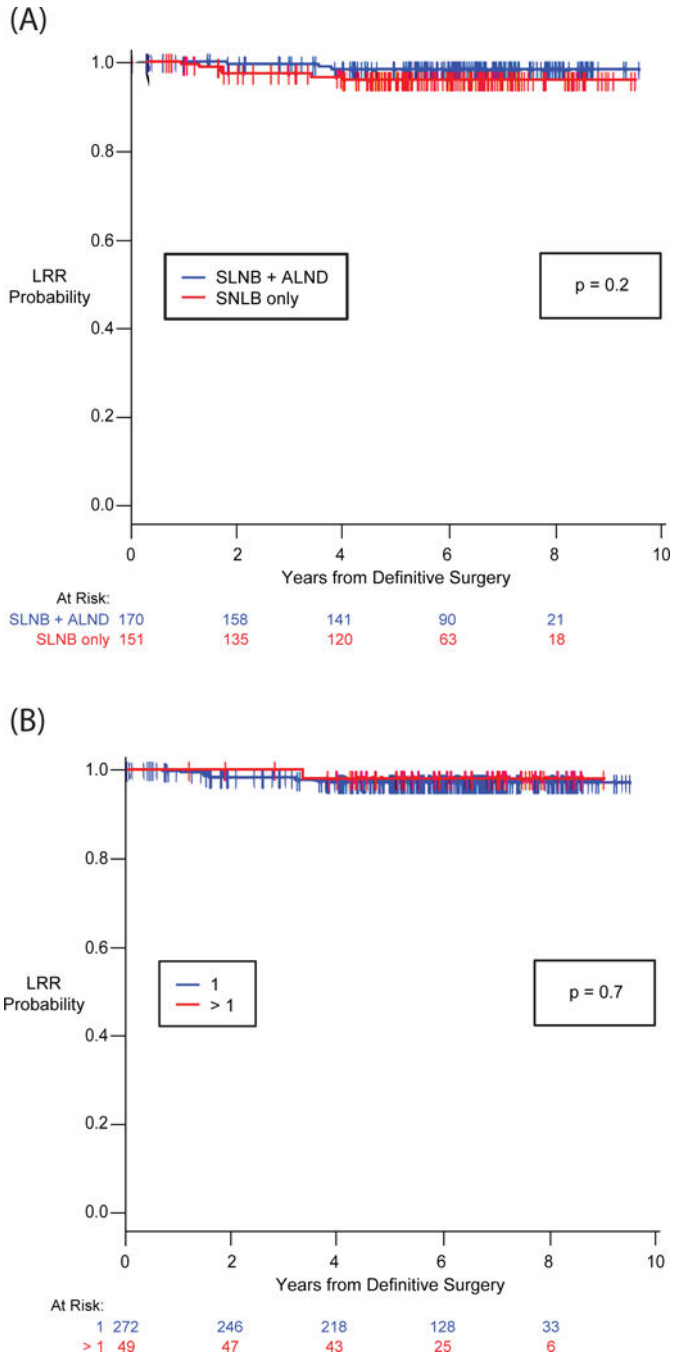

Fig. 3.

(a) Kaplan-Meier estimates of locoregional recurrence by axillary surgery, among patients treated without post-mastectomy radiation therapy (b) Kaplan-Meier estimates of locoregional recurrence by number of positive lymph nodes, among patients treated without post-mastectomy radiation therapy

TABLE 1

Patient population

	All Patients n = 352	No PMRT n = 321	PMRT n = 31	P *
	Median (Range)			
Age, years	50 (24–90)	50 (24–90)	49 (30–73)	0.3
Pathologic tumor size, cm	1.6 (< 0.1–5.0)	1.5 (< 0.1–4.8)	2.1 (0.4–5.0)	0.0003
	N (%)			
Histology				0.8
Ductal	278 (79%)	254 (79%)	24 (77%)	
Lobular or mixed	74 (21%)	67 (21%)	7 (23%)	
Associated DCIS				0.8
< 25%	216 (61%)	197 (61%)	19 (61%)	
> 25%	125 (36%)	115 (36%)	10 (32%)	
Unknown	11 (3%)	9 (3%)	2 (6%)	
Grade				0.5
Low	18 (5%)	16 (5%)	2 (6%)	
Intermediate	142 (40%)	133 (41%)	9 (29%)	
High	150 (43%)	135 (42%)	15 (48%)	
Unknown	42 (12%)	37 (12%)	5 (16%)	
Receptor status				0.7
ER+/HER2−	245 (70%)	222 (69%)	23 (74%)	
ER+/HER2+	45 (13%)	43 (13%)	2 (6%)	
ER–/HER2+	24 (7%)	21 (7%)	3 (10%)	
ER–/HER2−	31 (9%)	28 (9%)	3 (10%)	
Unknown **	7 (2%)	7 (2%)	0 (0%)	
Lymphovascular invasion	133 (38%)	112 (35%)	21 (68%)	0.0003
Multifocal/multicentric	185 (53%)	162 (50%)	23 (74%)	0.01
Tumor location				
Medial or central	119 (34%)	103 (32%)	16 (52%)	0.03
Lateral	233 (66%)	218 (68%)	15 (48%)	
# of risk factors				0.0003
0	35 (10%)	35 (11%)	0 (0%)	
1	67 (19%)	65 (20%)	2 (6%)	
2	93 (26%)	87 (27%)	6 (19%)	
3	83 (24%)	72 (22%)	11 (35%)	
4 or 5 or 6	25 (7%)	18 (6%)	7 (23%)	

	All Patients n = 352	No PMRT n = 321	PMRT n = 31	P *
Unknown ***	49 (14%)	44 (14%)	5 (16%)	
# of positive lymph nodes				0.1
1 node	295 (84%)	272 (85%)	23 (74%)	
> 1 node	57 (16%)	49 (15%)	8 (26%)	

* Unknown values excluded from statistical analyses

** Cases with insufficient sample to test ER and/or HER2

*** Those with unknown nuclear grade or receptor status were excluded from risk factor analysis

PMRT, post-mastectomy radiotherapy; DCIS, ductal carcinoma in situ; ER, estrogen receptor; HER2, human epidermal growth factor 2

TABLE 2

Clinicopathologic characteristics of patients who experienced locoregional recurrence

	Experienced LRR n = 9
	Median (Range)
Age at diagnosis, years	55 (24–81)
Tumor size, cm	1.7 (< 0.1–2.9)
Time to recurrence, months	19 (8–45)
	N (%)
Ductal histology	9 (100%)
High nuclear grade	8 (89%)
Receptor status	
ER+/HER2−	5 (56%)
ER+/HER2+	2 (22%)
ER–/HER2+	0 (0%)
ER–/HER2−	2 (22%)
Lymphovascular invasion	3 (33%)
Multifocal/multicentric	6 (67%)
Medial or central tumor location	3 (33%)
# of risk factors	
1	2 (22%)
2	3 (33%)
3	1 (11%)
4	2 (22%)
5	1 (11%)
6	0 (0%)
# of positive lymph nodes	
1 node	8 (89%)
> 1 node	1 (11%)

PMRT, post-mastectomy radiotherapy; ER, estrogen receptor; HER2, human epidermal growth factor 2