Six-Year Follow-Up of Patients With Microinvasive, T1a, and T1b Breast Carcinoma

G. Bruce Mann, MB, BS, PhD, FRACS,* Elisa Rush Port, MD, Christine Rizza, BS, RPA-C, Lee K. Tan, MD,** Patrick I. Borgen, MD, and Kimberly J. Van Zee, MS, MD, FACS

Background: Management of patients with breast cancers ≤1 cm remains controversial. Reports of infrequent nodal metastases in tumors ≤5 mm has led to suggestions that axillary dissection should be selective, and that tumor characteristics should guide adjuvant therapy.

Methods: A retrospective review of 290 patients with breast cancer 1 cm in size or smaller from 1989 to 1991 was done. Distant disease-free survival (DDFS) was the primary outcome measure.

Results: There were 95 T1a (≤5 mm) and 196 T1b (6–10 mm) cancers. Nodal metastases were found in 8 T1a and 26 T1b tumors. Larger size, poorer differentiation, and lymphovascular invasion (LVI) were associated with more nodal metastases, but none of these trends reached statistical significance. The 6-year DDFS was 93% for node-negative and 87% for node-positive patients (P = .02). Overall, breast cancers with poorer differentiation and LVI trended toward a poorer outcome. For patients with node-negative tumors, LVI was associated with a poorer outcome (P = .03). The size of the primary tumor was not predictive of outcome. There were no nodal metastases or recurrences in the 18 patients with microinvasive breast cancer.

Conclusions: Lymph node status is the major determinant of outcome in breast cancers 1 cm in size or smaller. Accurate axillary assessment remains crucial in management of small breast cancer.

Key Words: Early breast cancer—Minimal breast cancer—Microinvasive breast cancer—Axillary lymph node metastases—Axillary dissection—Regional metastases—Prognosis disease-free survival—Sentinel node biopsy.

Optimal management of the patient with a small breast cancer remains controversial. Traditional treatment involves appropriate local therapy to the breast as well as axillary dissection to predict recurrence, to guide decisions about adjuvant therapy, and to improve locoregional control. The NIH consensus statement in 1991 concluded that “because nodal status is the most important available prognostic factor, a level I-II axillary dissection should be routine.”1 In an attempt to simplify breast cancer management and avoid the morbidity of axillary dissection, some have advocated selective axillary dissection or avoiding dissection altogether in women with small breast cancers.2–7 They argue that no trial has proven a survival advantage for axillary dissection, that pathological characteristics of the primary tumor can provide adequate information for treatment decision making and prognostication, and that the incidence of nodal metastases is so small that any benefit accrued to the patients with node-positive tumors is more than outweighed by the morbidity suffered by the whole group.2–5,7 Support for this view comes from several series of studies that show a very low incidence of nodal metastases in tumors 5 mm in diameter or smaller (T1a).4,8–10 It is important to note, however, that other series of studies have found a higher incidence of metastases in small tumors.11–15 The inability to reliably

---

Received February 23, 1999; accepted May 5, 1999.
From Breast Service, Department of Surgery (GBM, ERP, CR, PIB, KJVZ) and the Department of Pathology (LKT), Memorial Sloan-Kettering Cancer Center, New York, New York.
*Current address: Department of Surgery, University of Melbourne, Royal Melbourne Hospital, Parkville, 3050, Victoria, Australia.
**Current address: Department of Diagnostic Pathology and Laboratory Medicine, Beth Israel Medical Center, First Avenue at 16 Street, New York, New York.
Presented at the 51st Annual Cancer Symposium of the Society of Surgical Oncology, San Diego, California, March 1998.
Address correspondence to: Kimberly J. Van Zee, MD, Department of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., MRI-1026, New York, NY 10021; Fax: 212-794-5812.
define a subset of patients with negligible risk of axillary metastasis, as well as unwillingness to deny a potential survival advantage to some patients, leads others to caution against abandoning the procedure.\textsuperscript{16–18} Significantly, high rates of axillary relapse have been reported in patients treated with tumor excision alone.\textsuperscript{14,19} An association between the extent of axillary dissection and survival in patients with stage I breast cancer has also been found.\textsuperscript{20} This may reflect more accurate staging, but is possibly due to a therapeutic effect. The recent introduction of sentinel node mapping and biopsy\textsuperscript{21,22} has altered this debate somewhat, yet the controversy remains.

We recently published a single institutional series of 247 patients with breast cancers \( \leq 1 \) cm in diameter who had axillary dissection, that showed an incidence of axillary metastases of 10\% and 15\% for T1a (no larger than 5 mm) and T1b (larger than 5 mm, but no larger than 10 mm) tumors, respectively, in women with adequately evaluated axillae (at least 10 lymph nodes examined).\textsuperscript{15} In our group of patients, we were unable to identify any subgroup of patients with a minimal incidence of metastases. Our conclusion was that it remains important to assess the axilla in all cases of invasive breast cancer.

The purpose of this article is to provide follow-up on a larger group of patients with T1a and T1b breast cancer, of which the previously reported group was a subset. We also specifically analyzed the subset of our patients who had microinvasive disease to compare their behavior with others with T1a tumors.

**MATERIALS AND METHODS**

The pathology reports of all patients who had definitive surgery for invasive breast cancer at Memorial Sloan-Kettering Cancer Center (MSKCC) between January 1, 1989, and December 31, 1991, were reviewed. Our breast specialist pathologists reviewed all pathology reports and slides from biopsies performed elsewhere and independently assessed the size of the tumor. All patients with invasive breast cancer 1 cm or smaller were included except those with previously diagnosed invasive breast cancer, or with a synchronous breast cancer larger than 1 cm in diameter. Where there was doubt about the size of the lesion, or where a pathology report found microinvasive disease, the slides were re-reviewed by a single breast pathologist (LKT) to confirm that invasive disease was present and to establish the precise size of the invasive carcinoma. Microinvasion was defined as an invasive component smaller than 1 mm in size (usually in the form of single cells) in association with a larger volume of ductal carcinoma in situ (DCIS).

Demographic and clinical data were obtained from the medical record, and follow-up details were confirmed with the patient, family, or local physician where hospital records were incomplete. We adopted strict criteria for assessing palpability. Unless unequivocal evidence was available, the tumor was classified as “unknown.” This is because some screen-detected tumors are palpable, as are some excised after needle localization, making it unsafe to assume that such tumors were impalpable.

Pathological data, which included tumor size and grade, receptor status, the presence of LVI, and the status of axillary lymph nodes, were obtained from MSKCC pathology reports. If either lymphatic or vascular invasion was noted in or around the primary tumor, LVI was classified as present. Lymph node status was determined by standard histological sectioning and hematoxylin and eosin staining. A single section of each node was examined, with no serial sectioning or immunohistochemistry performed on the axillary lymph nodes.

Statistical significance was determined by \( \chi^2 \) and Fisher’s exact test, and Kaplan-Meier survival curves were analyzed using the log-rank method. Distant relapse was considered the end point for survival analysis. Analyses of nodal status and DDFS were performed for all patients, and repeated to include only those patients who had at least 10 lymph nodes examined. Mathematical modeling suggests that this is the number of nodes that must be examined to be 90\% certain of not missing axillary metastases.\textsuperscript{23}

**RESULTS**

**Demographic Description**

We identified 290 female patients who had invasive breast cancer 1 cm in diameter or smaller. One patient had bilateral tumors smaller than 1 cm, resulting in a total of 291 tumors. The median age was 56 years (range, 25–87).

Breast conservation surgery was selected by 172 patients and mastectomy by 119 patients. The general policy for management of early stage invasive breast cancer at our institution has been to recommend axillary dissection, and 270 of these patients had some form of lymphadenectomy (defined as examination of at least 4 nodes). Two hundred forty-five patients had at least 10 nodes examined histologically. Of the 21 patients who did not have a lymphadenectomy, 5 had microinvasive disease, 10 had other tumors at least 1 mm but no larger than 5 mm (other T1a), and 6 had tumors larger than 5 mm but no larger than 10 mm (T1b).