Factors Associated with Local Breast Cancer Recurrence After Lumpectomy Alone

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**Background:** The purpose was to determine the rate of local breast relapse in patients with breast cancer uniformly treated with partial mastectomy but without postoperative radiotherapy and without systemic adjuvant therapy. We also systematically examined the factors associated with local recurrence to determine whether a low-risk subgroup existed.

**Methods:** A retrospective review of a prospectively followed (median, 8 years) cohort of 293 patients was performed. The end-point was ipsilateral local breast cancer recurrence. The patient's age, tumor size, nodal status, estrogen and progesterone receptor status, histology, and tumor and nuclear grade were studied, as were the presence and amount of carcinoma in situ and the presence of tumor emboli using univariate Kaplan-Meier and Cox step-wise multivariate analyses.

**Results:** The overall local relapse rate was 26% (77 recurrences). Univariate factors significantly associated with decreased local relapse included older age, negative nodes, small tumor size, positive estrogen receptor status, and absence of tumor emboli. Significant multivariate variables were age, nodal status, estrogen receptor status, absence of comedo carcinoma in situ, and tumor emboli. A low-risk subgroup of 66 patients was defined with a 6% 10-year local recurrence rate.

**Conclusion:** Important patient and tumor variables associated with local breast cancer relapse after breast-conserving surgery can define a low-risk subgroup.

**Key Words:** Breast cancer—Local recurrence—Lumpectomy.

Randomized clinical trials have shown that breast irradiation significantly reduces the rate of ipsilateral breast cancer recurrence after breast conservation surgery (1-4). The local breast cancer relapse rate after lumpectomy without radiation was 43% at 9 years in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-06 trial (1) and 26% at 4 years in a study (3) that was limited to patients without lymph node metastases. These studies did not or could not define a subgroup of patients at low risk for local recurrence in the nonirradiated patients. Single institution series report local breast recurrence rates of 6-29% (5-11) after lumpectomy without radiation. These differences are likely secondary to the patient selection process, different follow-up times, tumor factors, tumor margin assessment, and the fact that in some series recurrences in the ipsilateral breast distant from the index tumor were not considered to be local relapses.

Although some investigators have studied the factors that are apparently important for the development of local recurrence after lumpectomy with breast irradiation (12,13), there is little in the literature regarding a systematic review and multivariate analysis of the possible variables associated with breast recurrence in patients treated by lumpectomy without radiotherapy. This knowledge would be important because it is possible that a subset of patients who are at low risk for breast relapse could be defined and thus be spared the cost and morbidity of breast irradiation.
We have been following a cohort of patients with breast cancer who were uniformly treated between 1977 and 1986 with lumpectomy alone. These patients received no radiation and no adjuvant systemic therapy. Although the majority of patients had an axillary dissection with their primary surgery, many did not. The purpose of this study was to determine the prognostic factors involved with local breast cancer recurrence after breast conservation surgery alone in order to define a low-risk subgroup of patients that might not need postoperative radiotherapy.

PATIENTS AND METHODS

Between 1977 and 1986, 1,097 women with invasive breast cancer were treated at Women's College Hospital, University of Toronto. Breast-conserving surgery was performed in 476 patients. The patient population in the present study consists of 293 patients with primary invasive breast cancer who had a lumpectomy and tumor-free margins with or without an axillary dissection for invasive breast cancer and who did not receive any postoperative adjuvant radiation, hormonal treatment, or chemotherapy. Some patients were entered into randomized trials designed to determine the benefit of radiation and drew the no-radiation arm, but most were treated this way because of surgeon and patient preference. Most of these breast cancers were palpable. Axillary dissection was performed at the discretion of the treating surgeon and patient.

The patients were identified using a hospital-based research database (14). The charts of these patients were reviewed and demographic data noted. We had 90% clinical follow-up to 1991 and 79% to 1993. Interim analysis in 1991 has been reported in abstract form (15) and differed little from this final report. The median age of the patients at initial diagnosis was 63 years, and the median follow-up for disease-specific survival is 8 years. This study's endpoint was local breast recurrence, which was defined as any subsequent, pathologically confirmed breast cancer in the ipsilateral breast that was originally treated with a lumpectomy without radiotherapy for breast cancer. Local disease-free survival (DFS) is defined as the additive inverse of the recurrence rate and is expressed as a percentage, much the same way as overall survival is the additive inverse of the mortality rate. Axillary node recurrences were not considered local breast recurrences and will be the subject of a separate report. There were 83 deaths (28%) in the initial cohort of 293. Fifty-one of those deaths were disease specific (17%). Death from other causes was treated as censored. The treatments of the patients who developed local recurrence and the primary tumor characteristics have been published previously (16,17).

Pathology Review

The tumor size was assessed on gross examination of the lumpectomy specimen and was recorded on the original pathology report. All patients in this study had negative pathologic margins. Original hematoxylin and eosin (H & E) sections on all patients were reviewed without knowledge as to outcome and assessed for the following parameters:

Histologic type was documented.

Tumor and nuclear grade using Fisher's grading system (18) was established.

Presence or absence of carcinoma in situ (CIS) and/or comedo subtype at the periphery or within the tumor mass was documented (none, noncomedo CIS, comedo CIS).

Extent of CIS was subjectively evaluated and the percentage of CIS in the main tumor mass was given.

Presence of tumor emboli in endothelial-lined spaces (Fig. 1) was documented. This finding was considered positive when tumor cells were present in clearly defined spaces lined by flattened endothelial cells. The tumor cells were sometimes mixed with red blood cells. These spaces were usually grouped in a neurovascular bundle. There was no distinction as to whether the tumor emboli were within or outside the main tumor mass.

The axillary contents were examined and every identified lymph node submitted in toto. Each node, depending on its size, was serially sectioned at 2- to 3-mm intervals and examined microscopically. The presence or absence of metastatic tumor was assessed on light microscopy of the HE sections and recorded. No special stain (e.g., immunohistochemistry for keratin) was used as an adjunct to diagnosis.

Estrogen and Progesterone Receptor Assays

Fresh samples of tumor tissue were assayed for estrogen and progesterone receptors (ER, PgR) using standard methodology (19,20). Ten fmol/mg protein was used as the positive/negative cut-point for both estrogen and progesterone receptors.